ANESTHESIA & ANALGESIA

Journal of the International Anesthesia Research Society, the Society of Cardiovascular Anesthesiologists, the Society for Pediatric Anesthesia, the Society for Ambulatory Anesthesia, the International Society for Anaesthetic Pharmacology, and the Society for Technology in Anesthesia

Abstracts of Posters
Presented at the
International Anesthesia Research Society
79th Clinical and Scientific Congress
Honolulu, Hawaii
March 11-15, 2005

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IARS SCA SPA SAMBA ISAP STA

Manuscripts and editorial correspondence should be addressed to Ronald D. Miller, MD, Editor-in-Chief, *ANESTHESIA & ANALGESIA*, The Hearst Building, 5 Third Street, Suite 1216, San Francisco, CA 94103; telephone: (415) 777-2750; FAX: (415) 777-2803. Editorial Office E-Mail Address: aaeditor@pacbell.net. For information concerning preparation of manuscripts, see "A Guide for Authors."

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SOCIETY OF CARDIOVASCULAR ANESTHESIOLOGISTS (SCA) is a nonprofit, educational foundation and is a recognized sub-specialty organization of the American Society of Anesthesiologists. Membership dues for 2005 are $175 which include a reduced-rate subscription to ***ANESTHESIA & ANALGESIA***. *Residents*: see *Joint Resident Membership* information below. All SCA membership payments and correspondence should be sent to: SCA, 2209 Dickens Road, P.O. Box 11086, Richmond, Virginia 23230-1086. Telephone (804) 282-0084; Fax (804) 282-0090; e-mail: sca@societyhq.com; Web site: www.scahq.org

SOCIETY FOR PEDIATRIC ANESTHESIA (SPA) is a nonprofit organization and is a recognized subspecialty organization of the American Society of Anesthesiologists. Membership dues for 2005 are $125 for active and affiliate membership, $50 for international membership. *Residents*: see *Joint Resident Membership* information below. All SPA membership payments and correspondence should be sent to: SPA, 2209 Dickens Road, P.O. Box 11086, Richmond, VA 23230-1086. Telephone (804) 282-9780; Fax (804) 282-0090; e-mail: spa@societyhq.com; Web site: www.pedsanesthesia.org

SOCIETY FOR AMBULATORY ANESTHESIA (SAMBA) is a nonprofit organization and is a recognized subspecialty organization of the American Society of Anesthesiologists. Membership dues for 2005 are $150 for active, affiliate and international membership, or $235 which includes a subscription to ***ANESTHESIA & ANALGESIA***. *Residents*: see *Joint Resident Membership* information below. All SAMBA membership payments and correspondence should be sent to: SAMBA, 520 N. Northwest Highway, Park Ridge, Illinois 60068-2573. Telephone (847) 825-5586; Fax (847) 825-5658; e-mail: samba@asahq.com; Web site: www.sambahq.org

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SOCIETY FOR TECHNOLOGY IN ANESTHESIA (STA) The Society for Technology in Anesthesia is an international organization of physicians, engineers, students, and others with an interest in anesthesia-related technologies. Membership is open to all who are interested. The Society's mission is to improve the quality of patient care by improving technology and its application. The Society promotes education and research, collaborates with local, national, and international organizations, sponsors meetings and exhibitions, awards grants, and recognizes achievement. Membership dues for 2005, Regular Membership is $100 annually; Student/Resident membership is free. Add *Anesthesia and Analgesia* for only $85. All STA correspondence should be sent to: STA, Attn: Beverlee Anderson, PMB 300, 223 N. Guadalupe, Santa Fe, NM 87501. Telephone (505) 983-4923; Fax (505) 983-5109; e-mail: STA@AnesTech.org; Web site: www.AnesTech.org

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Abstracts of Posters Presented at the International Anesthesia Research Society 79th Clinical and Scientific Congress Honolulu, Hawaii March 11-15, 2005

IARS 79th Clinical and Scientific Congress
Abstract Presenter Presentation Schedule

Ambulatory Anesthesia

(S-1) Kranke, P., Monday 9:15
(S-2) Macaluso, A., Monday 9:15
(S-3) Redmond, M.J., Monday 9:15
(S-4) Apfel, C., Monday 9:15
(S-5) Deal, E., Monday 9:15
(S-6) Gunter, J., Monday 9:15
(S-7) Wajda, M.C., Monday 9:15
(S-8) Kleiin, K.W., Sunday 7:00
(S-9) Brock, M., Sunday 7:00
(S-10) Gratz, I., Sunday 7:00
(S-11) O'Connor, C.J., Sunday 7:00
(S-12) Nielsen, K.C., Sunday 7:00
(S-13) Cutter, T., Sunday 7:00
(S-14) Sarmah, A., Sunday 7:00
(S-15) Cutter, T., Sunday 7:00
(S-16) Wender, R.H., Monday 7:00
(S-17) Cutter, T.W., Monday 7:00
(S-18) Kranke, P., Monday 7:00
(S-19) Stierer, T.L., Monday 7:00
(S-20) Wright, T.B., Monday 7:00
(S-21) Mueller, J.T., Monday 7:00
(S-22) Tazuke-Nishimura, M., Monday 7:00
(S-23) Stierer, T.L., Monday 7:00
(S-24) Oei-Lim, V.L., Monday 9:15
(S-25) Neligan, P.J., Monday 9:15
(S-26) Oei-Lim, V.L., Monday 9:15
(S-27) McKay, R.E., Monday 9:15
(S-28) Deal, E., Monday 9:15
(S-29) Abdel Bar, M.A., Monday 9:15
(S-30) Conahan, T.J., Monday 9:15

Cardiothoracic & Vascular - Basic Science

(S-31) Marinovic, J., Saturday 7:00
(S-32) Tse, J., Saturday 7:00
(S-33) Ljubkovic, M., Saturday 7:00
(S-34) Aizawa, K., Saturday 7:00
(S-35) del Rio, C., Saturday 7:00
(S-36) Romer, A.J., Saturday 7:00
(S-37) Kurokawa, H., Saturday 7:00
(S-38) Riess, M.L., Saturday 7:00
(S-39) Yoshino, J., Saturday 11:30
(S-40) Yoshino, J., Saturday 11:30
(S-41) Gupta, D.K., Saturday 11:30
(S-42) Kusza, K., Saturday 11:30
(S-43) Murray, P.A., Saturday 11:30
(S-44) Yoshino, J., Saturday 11:30
(S-45) Nakagawa, A., Saturday 11:30
(S-46) Gupta, D.K., Saturday 11:30
(S-47) An, J., Saturday 11:30
(S-48) Kehl, F., Saturday 11:30
(S-49) Theilmeier, G., Saturday 11:30
(S-50) de Klaver, M.J., Saturday 11:30
(S-51) Damron, D.S., Saturday 11:30
(S-52) Kehl, F., Saturday 11:30
(S-53) Yuasa, H., Saturday 11:30
(S-54) de Klaver, M.J., Saturday 11:30
(S-55) de Klaver, M.J., Monday 11:30
(S-56) Hayes, J.K., Monday 11:30
(S-57) Maybauer, D.M., Monday 11:30
(S-58) Hattori, J., Monday 11:30
(S-59) Jurk, K., Monday 11:30
(S-60) Hare, G.M., Monday 11:30
(S-61) Balyasnikova, I.V., Monday 11:30
(S-62) Ding, X., Monday 11:30
(S-63) Kurahashi, K., Saturday 7:00
(S-64) Weitkamp, B., Saturday 7:00
(S-65) Tse, J., Saturday 7:00
(S-66) Terajima, K., Saturday 7:00
(S-67) Damron, D.S., Saturday 7:00
(S-68) Danilov, S.M., Saturday 7:00
(S-69) Ding, X., Saturday 7:00
(S-70) Kitagawa, H., Saturday 7:00
(S-71) Deem, S., Sunday 7:00
(Research Awards Panel)

Cardiothoracic & Vascular - Clinical

(S-72) Mathews, D.M., Saturday 7:00
(S-73) Vigoda, M., Saturday 7:00
(S-74) Ee, P., Saturday 7:00
(S-75) Ikeshita, K., Saturday 7:00
(S-76) Iwasawa, K., Saturday 7:00
(S-77) Sugiyama, Y., Saturday 7:00
(S-78) Ritter, M.J., Saturday 7:00
(S-79) Campos, J.H., Saturday 9:15
(S-80) Kakazu, C.Z., Saturday 9:15
(S-81) Yajima, S., Saturday 9:15
(S-82) Awad, A.A., Saturday 9:15
(S-83) Dote, K., Saturday 9:15
(S-84) Ejova, I.V., Saturday 9:15
(S-85) Murray, P., Saturday 9:15
(S-86) Innami, Y., Saturday 9:15
(S-87) Leyvi, G., Saturday 9:15
(S-88) Lo, B., Saturday 9:15
(S-89) Nygren, A., Saturday 9:15
(S-90) Nakasuji, M., Saturday 9:15
(S-91) Bognar, A., Saturday9:15
(S-92) Yazicioglu, H., Saturday 9:15
(S-93) Ancona, M., Saturday 9:15
(S-94) Isetta, C.J., Saturday 9:15
(S-95) Su, H., Monday 11:30
(S-96) Yamaguchi, K., Monday 11:30
(S-97) Abosedira, M.A., Monday 11:30
(S-98) Park, K.W., Monday 11:30
(S-99) Schmidt, A., Monday 11:30

IARS 79th Clinical and Scientific Congress
Abstract Presenter Presentation Schedule

(S-100) Wakisaka, E., Monday 11:30
(S-101) Kakazu, C.Z., Monday 11:30
(S-102) Nakasuji, M., Monday 11:30

Critical Care and Trauma

(S-103) Kase, Y., Saturday 7:00
(S-104) Lee, H., Saturday 7:00
(S-105) Wischmeyer, P.E., Saturday 7:00
(S-106) Lehmann, C., Saturday 7:00
(S-107) Masud, F., Saturday 7:00
(S-108) Hiruta, A., Saturday 7:00
(S-109) Westphal, M., Saturday 7:00
(S-110) Enkhbaatar, P., Saturday 7:00
(S-111) Kurosaki, D., Saturday 11:30
(S-112) Jans, F., Saturday 11:30
(S-113) Singleton, K.D., Saturday 11:30
(S-114) Jans, F., Saturday 11:30
(S-115) Shirane, A., Saturday 11:30
(S-116) Brodde, M.F., Saturday 11:30
(S-117) Gammelin, H., Saturday 11:30
(S-118) Wagener, G., Saturday11:30
(S-119) Hilmi, I.A., Monday 11:30
(S-120) O'Connor, M.F., Monday 11:30
(S-121) Hare, G.M., Monday 11:30
(S-122) Tsueshita, T., Monday 11:30
(S-123) Driessen, B., Monday 11:30
(S-124) Kentner, R., Monday 11:30
(S-125) Kehrel, B.E., Monday 11:30
(S-126) Zafirova, Z., Monday 11:30
(S-127) Badenes, R., Monday 11:30
(S-128) Badenes, R., Monday 11:30
(S-129) Jules-Elysee, K., Monday 11:30
(S-130) Roy, T.K., Monday 11:30
(S-131) Her, C., Monday 11:30
(S-132) Johnson, K.L., Monday 9:15
(S-133) Kentner, R., Monday 9:15
(S-134) Kodali, N., Monday 9:15
(S-135) Makita, T., Monday 9:15
(S-136) Brown, M., Monday 9:15
(S-137) Planinsic, R.M., Monday 9:15
(S-138) Kusunoki, S., Saturday 9:15
(S-139) Chee, W., Saturday 9:15
(S-140) Hemmerling, T.M., Saturday 9:15
(S-141) Vu, M.P., Saturday 9:15
(S-142) Maybauer, M.O., Saturday 9:15

Economics, Education and Patient Safety

(S-143) Gilula, M.F., Saturday 7:00
(S-144) Barach, P., Saturday 7:00
(S-145) Fukui, Y., Saturday 7:00
(S-146) Albrecht, M.A., Saturday 7:00
(S-147) Parsa, P., Saturday 7:00
(S-148) Hanson, R.D., Saturday 7:00
(S-149) Sweitzer, B., Saturday 7:00
(S-150) Barach, P., Saturday 7:00
(S-151) Gottlieb, O., Saturday 9:15
(S-152) Savoldelli, G.L., Saturday 9:15
(S-153) Rebel, A., Saturday 9:150
(S-154) Blum, J., Saturday 9:15
(S-155) Chee, W., Saturday 9:15
(S-156) Chee, W., Saturday 9:15
(S-157) Azocar, R.J., Saturday 9:15
(S-158) Gottlieb, O., Saturday 9:15
(S-159) Szpisjak, D.F., Sunday 7:00
(S-160) Morris, G.F., Sunday 7:00
(S-161) Kaplan, R.F., Sunday 7:00
(S-162) Krieter, H., Sunday 7:00
(S-163) White, P.F., Sunday 7:00
(S-164) Morris, G.F., Sunday 7:00
(S-165) Overdyk, F.J., Sunday 7:00
(S-166) O'Connor, M.F., Sunday 7:00
(S-167) Tung, A., Monday 7:00
(S-168) Fiadjoe, J.E., Monday 7:00
(S-169) Sakai, T., Monday 7:00
(S-170) Pei, L., Monday 7:00
(S-171) Sanneman, T.C., Monday 7:00
(S-172) Brown, M., Monday 7:00
(S-173) Brown, M., Monday 7:00
(S-174) Brown, M., Monday 7:00
(S-175) Phillips, T., Sunday 7:00
(S-176) Rebel, A., Sunday 7:00
(S-177) Agah, M., Sunday 7:00
(S-178) Jankowski, C.J., Sunday 7:00
(S-179) Buvanendran, A., Sunday 7:00
(S-180) Henriksen, K.J., Sunday 7:00
(S-181) Roizen, M.F., Sunday 7:00
(S-182) Barach, P., Sunday 7:00

Equipment & Monitoring

(S-183) Hoffman, W.E., Saturday 11:30
(S-184) Ho, S.S., Saturday 11:30
(S-185) She, S., Saturday 11:30
(S-186) Kakinohana, M., Saturday 11:30
(S-187) Mizuno, R., Saturday 11:30
(S-188) Nepveu, M., Saturday 11:30
(S-189) Ghelber, O., Saturday 11:30
(S-190) Vigoda, M., Saturday 11:30
(S-191) Tokumine, J., Monday 7:00
(S-192) Paulsen, A.W., Monday 7:00
(S-193) Armbruster, S., Monday 7:00
(S-194) McNeer, R., Monday 7:00
(S-195) Javernick, E.N., Monday 7:00
(S-196) Vaillancourt, M., Monday 7:00
(S-197) Barach, P., Monday 7:00
(S-198) Ahluwalia, N., Monday 7:00

IARS 79th Clinical and Scientific Congress
Abstract Presenter Presentation Schedule

(S-199) Satoh, J., Sunday 7:00
(S-200) Satoh, J., Sunday 7:00
(S-201) Ishikawa, A., Sunday 7:00
(S-202) Singbartl, G., Sunday 7:00
(S-203) Singbartl, G., Sunday 7:00
(S-204) Schmidt, A., Sunday 7:00
(S-205) Strümper, D., Sunday 7:00
(S-206) Philip, B.M., Sunday 7:00
(S-207) Oshiro, M., Monday 9:15
(S-208) Lebon, J., Monday 9:15
(S-209) Sobue, K., Monday 9:15
(S-210) Akata, T., Monday 9:15
(S-211) Hagberg, C.A., Monday 9:15
(S-212) Hagberg, C.A., Monday 9:15
(S-213) Redford, D.T., Monday 9:15
(S-214) Redford, D.T., Monday 9:15
(S-215) Tanaka, T., Tuesday 7:00
(S-216) Szmuk, P., Tuesday 7:00
(S-217) Schmiesing, C., Tuesday 7:00
(S-218) Ogunnaike, B., Tuesday 7:00
(S-219) Mizushima, A., Tuesday 7:00
(S-220) Sakata, D., Tuesday 7:00
(S-221) Robicsek, S., Tuesday 7:00
(S-222) Howard, H.C., Tuesday 7:00
(S-223) White, P.F., Tuesday 9:15
(S-224) Olufolabi, A.J., Tuesday 9:15
(S-225) Sakata, D., Tuesday 9:15
(S-226) Sakata, D., Tuesday 9:15
(S-227) Soto, R.G., Tuesday 9:15
(S-228) Pei, L., Tuesday 9:15
(S-229) Jensen, E.W., Tuesday 9:15
(S-230) Kawasaki, J., Monday 7:00
(S-231) Hahn, C.P., Monday 7:00
(S-232) Ansermino, J.M., Monday 7:00
(S-233) Vigoda, M., Monday 7:00
(S-234) Hamada, Y., Monday 7:00
(S-235) Yamaguchi, K., Monday 7:00
(S-236) Akata, T., Monday 7:00
(S-237) Kainuma, M., Monday 7:00

Genetics/Genomics

(S-238) Nagele, P., Tuesday 7:00
(S-239) Candiotti, K., Tuesday 7:00
(S-240) Moller, D.H., Tuesday 7:00
(S-241) Bell, A.H., Tuesday 7:00
(S-242) Voskresenskiy, A.M., Tuesday 7:00
(S-243) Dana, J.F., Tuesday 7:00
(S-244) Rampil, I.J., Tuesday 7:00
(S-245) Weitkamp, B., Tuesday 7:00

Neuroanesthesia

(S-246) Roth, S., Tuesday 9:15
(S-247) Lee, C.Z., Tuesday 9:15
(S-248) Yaster, M., Tuesday 9:15
(S-249) Loepke, A.W., Tuesday 9:15
(S-250) Meng, L., Tuesday 9:15
(S-251) Adachi, T., Tuesday 9:15
(S-252) Vavilala, M.S., Tuesday 9:15
(S-253) Devadoss, U., Tuesday 9:15

Obstetric Anesthesia

(S-254) Hussain, K., Sunday 7:00
(S-255) Ghelber, O., Sunday 7:00
(S-256) Supandji, M., Sunday 7:00
(S-257) Mantha, V.R., Sunday 7:00
(S-258) Aronsohn, J., Sunday 7:00
(S-259) Arakawa, M., Sunday 7:00
(S-260) Oshima, M., Sunday 7:00
(S-261) Okutomi, T., Sunday 7:00
(S-262) Wong, C.A., Sunday 7:00
(Research Awards Panel)

Pain - Basic Science

(S-263) Howard, R.F., Saturday 9:15
(S-264) Sugawara, T., Saturday 9:15
(S-265) Kinjo, S., Saturday 9:15
(S-266) Iohom, G., Saturday 9:15
(S-267) Koszowski, A.G., Saturday 9:15
(S-268) Walker, S.M., Saturday 9:15
(S-269) Yokoyama, M., Saturday 9:15
(S-270) Walker, S.M., Saturday 9:15
(S-271) Fu, E.S., Monday 11:30
(S-272) Jones, D.J., Monday 11:30
(S-273) Xu, X., Monday 11:30
(S-274) Kohno, T., Monday 11:30
(S-275) Aramaki, Y., Monday 11:30
(S-276) Fuchigami, T., Monday 11:30
(S-277) Umeda, E., Monday 11:30
(S-278) Kraft, B., Monday 9:15
(S-279) Bhat, M.B., Monday 9:15
(S-280) Liu, E.H., Monday 9:15
(S-281) Lu, Y., Monday 9:15
(S-282) Flood, P., Monday 9:15
(S-283) Kress, H.G., Monday 9:15
(S-284) Song, H., Monday 9:15
(S-285) Pentyala, S.N., Monday 9:15
(S-286) Schumacher, M.A., Sunday 7:00

IARS 79th Clinical and Scientific Congress
Abstract Presenter Presentation Schedule

Pain - Clinical

(S-287) Rebel, A., Saturday 11:30
(S-288) Bader, S.O., Saturday 11:30
(S-289) Larijani, G.E., Saturday 11:30
(S-290) Kumagai, K., Saturday 11:30
(S-291) Kontrimaviciute, E., Saturday 11:30
(S-292) Goldberg, M.E., Saturday 11:30
(S-293) Larijani, G.E., Saturday 11:30
(S-294) Goldberg, M.E., Saturday 11:30
(S-295) Govindarajan, R., Saturday 9:15
(S-296) Fukushima, K., Saturday 9:15
(S-297) Abreu, E., Saturday 9:15
(S-298) Reuben, S.S., Saturday 9:15
(S-299) Kodaka, M., Saturday 9:15
(S-300) Agah, M., Saturday 9:15
(S-301) Steinlechner, B., Saturday 9:15
(S-302) Lee, J., Saturday 9:15
(S-303) Gottschalk, A., Tuesday 7:00
(S-304) Koitabashi, T., Tuesday 7:00
(S-305) Coleman, J.E., Tuesday 7:00
(S-306) Agarwal, A., Tuesday 7:00
(S-307) Subramaniam, K., Tuesday 7:00
(S-308) Seki, H., Tuesday 7:00
(S-309) Shah, S.M., Tuesday 7:00
(S-310) Nitta, R., Tuesday 7:00
(S-311) Kroll, H.R., Tuesday 9:15
(S-312) Momenzadeh, S.E., Tuesday 9:15
(S-313) Woo, C., Tuesday 9:15
(S-314) Stricker, P., Tuesday 9:15
(S-315) Lin, A., Tuesday 9:15
(S-316) Narouze, S.N., Tuesday 9:15
(S-317) Worrich, S.P., Tuesday 9:15
(S-318) Chang, w., Tuesday 9:15
(S-319) Flood, P., Sunday 7:00
(Research Awards Panel)

Pediatric Anesthesia

(S-320) Szmuk, P., Monday 9:15
(S-321) Seidman, P.A., Monday 9:15
(S-322) Arai, Y.P., Monday 9:15
(S-323) Ito, H., Monday 9:15
(S-324) Tobin, P., Monday 9:15
(S-325) Gopalakrishnan, S., Monday 9:15
(S-326) Lo, S.S., Monday 9:15
(S-327) Bryan, Y.F., Monday 9:15
(S-328) Bartolek, D., Tuesday 7:00
(S-329) Nordmann, G.R., Tuesday 7:00
(S-330) Hache, M., Tuesday 7:00
(S-331) El-Shammaa, N., Tuesday 7:00
(S-332) Verghese, S.T., Tuesday 7:00
(S-333) Mostello, L.A., Tuesday 7:00
(S-334) Lo, S.S., Tuesday 7:00
(S-335) Gooden, C.K., Tuesday 7:00

Pharmacology-Basic Science

(S-336) Gerhardt, M.A., Saturday 11:30
(S-337) Hoover, J.M., Saturday 11:30
(S-338) Hoover, J.M, Saturday 11:30
(S-339) Hoover, J.M, Saturday 11:30
(S-340) Monreal, G., Saturday 11:30
(S-341) Buvanendran, A., Saturday 11:30
(S-342) Ooshima, K., Saturday 11:30
(S-343) OTA, S., Saturday 11:30
(S-344) Lee, C., Sunday 7:00
(S-345) Albrecht, M.A., Sunday 7:00
(S-346) Jans, F., Sunday 7:00
(S-347) Hoover, J.M, Sunday 7:00
(S-348) Sato, A., Sunday 7:00
(S-349) Yamaguchi, M., Sunday 7:00
(S-350) Yamakage, M., Sunday 7:00
(S-351) Archer, D., Sunday 7:00
(S-352) Whittington, R.A., Tuesday 7:00
(S-353) Hemmings, H.C., Tuesday 7:00
(S-354) Kaminoh, Y., Tuesday 7:00
(S-355) Crosby, G., Tuesday 7:00
(S-356) Herroeder, S., Tuesday 7:00
(S-357) Hudetz, A.G., Tuesday 7:00
(S-358) Archer, D., Tuesday 7:00
(S-359) Alkire, M.T., Tuesday 7:00
(S-360) Shastri, U.D., Tuesday 9:15
(S-361) Dworschak, M., Tuesday 9:15
(S-362) Lessa, M.A., Tuesday 9:15
(S-363) Yamada, S., Tuesday 9:15
(S-364) Novalija, E., Tuesday 9:15
(S-365) Culley, D.J., Tuesday 9:15
(S-366) Wu, R.S., Tuesday 9:15
(S-367) Takita, K., Tuesday 9:15
(S-368) Njoku, D.B., Tuesday 9:15
(S-369) Parat, M., Tuesday 9:15
(S-370) Nishioka, K., Tuesday 9:15
(S-371) Hoover, J.M, Tuesday 9:15
(S-372) Lessa, M.A., Tuesday 9:15
(S-373) Xie, Z., Tuesday 9:15
(S-374) Helmy, H., Tuesday 9:15
(S-375) Buvanendran, A., Tuesday 9:15
(S-376) Withdrew
(S-377) Withdrew
(S-378) Masaki, Y., Monday 11:30
(S-379) Mikawa, K., Monday 11:30
(S-380) Maharaj, C.H., Monday 11:30
(S-381) Withdrew
(S-382) Lee, y., Monday 11:30
(S-383) Davis, M.J., Monday 11:30
(S-384) Hahnenkamp, K., Sunday 7:00
(Research Awards Panel)

IARS 79th Clinical and Scientific Congress
Abstract Presenter Presentation Schedule

Pharmacology-Clinical

(S-385) Klein, K., Saturday 9:15
(S-386) Withdrew
(S-387) Walker, J., Saturday 9:15
(S-388) She, S., Saturday 9:15
(S-389) Hwang, K., Saturday 9:15
(S-390) Glick, D.B., Saturday 9:15
(S-391) Desai, R.G., Saturday 9:15
(S-392) Candiotti, K., Saturday 9:15
(S-393) Buvanendran, A., Monday 9:15
(S-394) Satterfield, K., Monday 9:15
(S-395) Adsumelli, R.S., Monday 9:15
(S-396) Kaye, R., Monday 9:15
(S-397) Shibata, Y., Monday 9:15
(S-398) Ohara, S., Monday 9:15
(S-399) Klein, K., Monday 9:15
(S-400) Yamakage, M., Monday 9:15
(S-401) Nitsun, M., Tuesday 9:15
(S-402) Heath, M., Tuesday 9:15
(S-403) Wittwer, E., Tuesday 9:15
(S-404) Ogura, T., Tuesday 9:15
(S-405) Gupta, D.K., Tuesday 9:15
(S-406) Sato, E., Tuesday 9:15
(S-407) Firestone, L., Tuesday 9:15
(S-408) Stool, L., Tuesday 9:15
(S-409) Adams, P.M., Tuesday 9:15
(S-410) Bertram, S.T., Tuesday 9:15
(S-411) Alkire, M.T., Tuesday 9:15
(S-412) Kakinohana, M., Tuesday 9:15
(S-413) Yuan, C., Tuesday 9:15
(S-414) Le, N., Tuesday 9:15
(S-415) Sato, N., Tuesday 9:15
(S-416) Zhang, R., Tuesday 9:15
(S-417) Bhatt, S.B., Saturday 11:30
(S-418) Steinberg, D., Saturday 11:30
(S-419) Bhatt, S.B., Saturday 11:30
(S-420) Rengasamy, S.K., Saturday 11:30
(S-421) Steinberg, D., Saturday 11:30
(S-422) Steinberg, D., Saturday 11:30
(S-423) Steinberg, D., Saturday 11:30
(S-424) Steinberg, D., Saturday 11:30
(S-425) Svensen, C., Tuesday 9:15

Regional

(S-426) Diarra, D.P., Monday 11:30
(S-427) Sakamoto, S., Monday 11:30
(S-428) Tezuka, M., Monday 11:30
(S-429) Iyer, C., Monday 11:30
(S-430) Rhee, K., Monday 11:30
(S-431) Agah, M., Monday 11:30
(S-432) Amar, D., Monday 11:30
(S-433) Raphael, D.T., Monday 11:30
(S-434) Sandhu, N.S., Tuesday 9:15
(S-435) Dingemans, E., Tuesday 9:15
(S-436) Horikawa, Y., Tuesday 9:15
(S-437) Buvanendran, A., Tuesday 9:15
(S-438) Schafhalter-Zoppoth, I., Tuesday 9:15
(S-439) Williams, R., Tuesday 9:15
(S-440) Rebel, A., Tuesday 9:15
(S-441) Strodtbeck, W.M., Monday 7:00
(S-442) Lee, B.B., Monday 7:00
(S-443) Williams, R., Monday 7:00
(S-444) Jafari, S., Monday 7:00
(S-445) Auffant, R.A., Monday 7:00
(S-446) Miyashita, K., Monday 7:00
(S-447) Gopalakrishnan, S., Monday 7:00

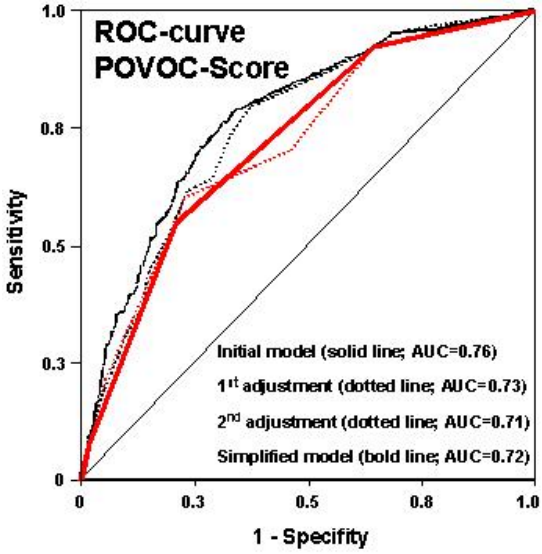
Ambulatory Anesthesia

S-1.

DEVELOPMENT AND VALIDATION OF A RISK SCORE TO PREDICT THE PROBABILITY OF POSTOPERATIVE VOMITING IN PEDIATRIC PATIENTS

AUTHORS: **P. Kranke**[1], G. Geldner[2], A. Morin[2], H. Treiber[3], H. Wulf[2], L. Eberhart[2];
AFFILIATION: [1]University of Würzburg, Würzburg, Germany, [2]University of Marburg, Marburg, Germany, [3]Ambulatory Surgical Center Söflingen, Ulm, Germany.

Introduction: Risk scores to predict the occurrence of postoperative vomiting (PV) or nausea and vomiting (PONV) that were developed for adult patients do not fit for children since several risk factors are difficult to assess or are usually not applicable in pediatric patients (e.g. smoking status). Thus, the aim of the present study was to develop and to validate a simple to predict postoperative vomiting in children (POVOC-score).
Methods: Development and validation of the new score was based on data of 1257 children (0-14 years) from four independent institutions undergoing various types of surgery under general anesthesia without antiemetic prophylaxis. Preoperatively, several potential risk factors were recorded. Postoperatively, the occurrence of PV was observed for up to 24 hours. The dataset was randomly split into an evaluation set (n=657) that was analyzed using a forward logistic regression technique and a validation set (n=600) that was used to confirm the accuracy of prediction by means of the area under a ROC-curve.
Results: Four independent risk factors for PV were identified in the final analysis: duration of surgery >/= 30 minutes, age >/= 3 years, strabismus surgery, and a positive history of PV in the children or PV/PONV in relatives (mother, father, or siblings). The incidence of PV was 9%, 10%, 30%, 55%, and 70% for 0, 1, 2, 3, and 4 risk factors observed. Using these incidences as cut-off values in the validation dataset, the AUC under the ROC-curve was 0.72 (95%-confidence interval: 0.68 - 0.77) [Figure 1].
Discussion: The present data suggest that PV can be predicted with an acceptable accuracy using a 4-item simplified risk score. Using "duration of surgery >/= 30 minutes", "age >/= 3 years", "strabismus surgery", and "positive history of PV/PONV in the children or in relatives" as risk factors, the predicted incidence of PV is 9%, 10%, 30%, 55%, and 70% if 1, 2, 3 or 4 of these risk factors are present. However, this model must be validated in other institutions before its widespread use can be recommended.



S-2.

IS TRANSDERMAL SCOPOLAMINE A SAFE AND EFFECTIVE ALTERNATIVE TO DROPERIDOL FOR ROUTINE ANTIEMETIC PROPHYLAXIS?

AUTHORS: D. Song, M. Hamza, **A. Macaluso**, R. Kapu, P. F. White;
AFFILIATION: University of Texas Southwestern Medical Center, Dallas, TX.

Introduction: Following the recent controversy surrounding the use of droperidol for antiemetic prophylaxis, there has been increasing interest in finding a less expensive alternative to the 5-HT_3 antagonists. This randomized, double-blinded sham and placebo-controlled study was designed to compare the antiemetic efficacy and adverse event profile of transdermal scopolamine to a standard 1.25 mg IV dose of droperidol.
Methods: After obtaining IRB approval and written informed consent, 66 patients undergoing major laparoscopic or cosmetic surgery procedures received either an “active” transdermal scopolamine patch (containing 1.5 mg) or a similar-appearing “sham” patch 60-90 min prior to induction of anesthesia. All patients received a standardized general anesthetic technique. After anesthetic induction, a second study medication in a 1 ml unlabeled syringe containing either saline (for active scopolamine patch group) or droperidol 1.25 mg (for the sham patch group), was administered intravenously. The occurrence of postoperative nausea, and vomiting/retching, visual disturbance, dry mouth, drowsiness and restlessness were evaluated for up to 72 hours, *p<0.05 vs Droperidol group.
Results: There were no differences in emetic outcomes between the two treatment groups (with “complete response” rates of 41% in both groups). However, the severity of dry mouth was significantly greater in the transdermal scopolamine vs droperidol group during the initial 48 h observation period.

	Transder-mal Scop	Droperi-dol
Age (yr)	43±14	45±11
Weight (kg)	95±41	91±36
Gender (male / female) (n)	3 / 29	7 / 27
Type of surgery (laparoscopy / plastics) (n)	15 / 17	18 / 16
Postoperative nausea 0-24 h (n,%)	15,47	17,50
At 24-48 h (n,%)	6,19	5,15
At 48-72 h (n,%)	2,6	3,9
Postoperative vomiting 0-24 h (n,%)	5,16	5,15
At 24-48 h (n,%)	1,3	2,6
At 48-72 h (n,%)	0	0
Rescue antiemetics 0-24 h (n,%)	11,34	7,21
At 24-48 h (n,%)	0	2,6
At 48-72 h (n,%)	0	0
Complete response rate (no emesis, no rescue) (n,%)	13,41	14,41
Postoperative visual disturbance 0-24 h (n,%)	6,19	5,15
At 24-48 h (n,%)	4,13	2,6
At 48-72 h (n,%)	2,6	2,6
Postoperative restlessness 0-24 h (n,%)	3,9	4,12
At 24 -48 n (n,%)	0	0
At 48-72 h (n,%)	0	0
Postoperative drowsiness 0-24 h (median and quartile)	4 (3-8)	3 (0-8)
Postoperative dry mouth 0-24 h (median and quartile)	7 (5-9)*	2 (0-5)
At 24-48 h (median and quartile)	4 (2-5)*	1 (0-4)
At 48-72 h (median and quartile)	1 (0-4)	0 (0-4)

Discussion: Transdermal scopolamine possessed similar antiemetic efficacy to low-dose droperidol when used for antiemetic prophylaxis of high-risk outpatients undergoing major laparoscopic or cosmetic surgery. Use of the scopolamine patch is a more a cost-effective alternative to the 5-HT3 antagonists for routine antiemetic prophylaxis

S-3.

PHENERGAN AND DECADRON; AN OLD, CHEAP BUT EFFECTIVE ANTI-EMETIC COMBINATION

AUTHORS: F. B. Florence, **M. J. Redmond**, P. S. Glass, E. J. Romano, W. Papaccio, J. L. Edom;
AFFILIATION: SUNY @ Stony Brook, Stony Brook, NY.

Introduction: Post operative nausea and vomiting is a concern for patients undergoing ambulatory surgery. Recently a study of over 5,000 patients concluded that different anti-emetic interventions are similarly effective and therefore the safest and least expensive should be used first. Droperidol has a black box warning in the United States and ondansetron is expensive. We wished to determine if low dose Phenergan (8mg) in combination with dexamethasone (D) would provide minimal sedation and be equally effective as the more expensive combination of ondansetron (O) and dexamethasone.
Methods: Ambulatory surgical patients undergoing general anesthesia were randomized in this double blind study to Group A, who received 8mg D plus 8mg P and, Group B who received 8mg D plus 4 mg O. In the PACU patients were evaluated every 30 minutes until discharge for the presence of PONV, level of sedation and pain. The patients also received a 24 and 48 hour post-operative call to record PONV, sedation and pain. Rescue anti-emetics, opiate use and time of discharge were recorded. The subjects were stratified by relative risk for PONV based on gender, history of PONV or motion sickness, smoking history and receiving opiates in the PACU. Power analysis indicated that 50 subjects per group were required to demonstrate a 20% difference or 110 per group for a 15% difference with 80% power. Data was analyzed using either simple t test or Chi squared as appropriate. $P<0.05$ was considered significant.
Results: To date 156 patients were evaluated with 81 patients in group A and 75 in group B. There were no significant differences between the groups with respect to age, gender, discharge time, pain or opiate use, risk of PONV and incidence of PONV. The observed sedation is also presented (See table).

	Group A	Group B
Risk Factors		
None	4	4
1	26	29
2	35	26
3	14	15
4	2	1
Age (years)	41 (s.d.+/- 12)	41 (s.d. +/-11)
M/F	15/66	14/61
Discharge (min.)	106 (s.d.+/-26.5)	98 (s.d.+/-38)
30 Min. PONV (%)	1.2	2.6
PACU PONV (%)	4.7	6.7
PACU-24 Hr PONV (%)	5.6	3.3
24-48 Hr. PONV (%)	5.4	1.9
Sedation (N/M/MD/S) (n)		
30 min (%)	74/9/14/3 (78)	76/12/11/1 (66)
60 min. (%)	82/4/12/2 (52)	84/14/12/0 (44)
90 min. (%)	61/6/28/6 (18)	82/18/0/0 (17)

(N= none, M= mild, MD=moderate, S=severe)
Discussion: P plus D reduces PONV similarly to the expensive combination of O plus D. Sedation and discharge times were similar between the groups. The combination of P plus D offers the added advantage of having O as the rescue medication without the risk of sedation delaying discharge. We conclude that P plus D is an inexpensive and effective prophylactic anti-emetic regime for patients presenting for ambulatory surgery.
Reference: NEJM, vol. 350 (24):2441-2451, June 10, 2004.

S-4.

ONDANSETRON COMPARABLY REDUCES THE RELATIVE RISK OF NAUSEA AND VOMITING

AUTHORS: **C. Apfel**[1], A. Paura[2], R. Jokela[3], D. I. Sessler[1], K. Korttila[3];
AFFILIATION: [1]University of Louisville, Louisville, KY, [2]Klinikum Lüeneburg, Lüneburg, Germany, [3]University of Helsinki, Helsinki, Finland.

Background: Nausea and vomiting are physiologically distinct symptoms, and results of Stadler et al. (1) suggest that type of surgery might be a risk factor for nausea but not for vomiting. Likewise, serotonin antagonists such as ondansetron are thought to have greater anti-vomiting than anti-nausea activity (2). We have recently conducted a double-blind randomized controlled trial of factorial design and found that there are no significant interactions between antiemetic strategies when looking at the overall endpoint of postoperative nausea and vomiting within 24 hours (3). This analysis sought to determine whether the relative reduction rate (rRR) of ondansetron for nausea is similar to its rRR for vomiting.
Methods: With approval of the ethics committees, informed consent was obtained from 5199 patients scheduled for elective surgery and at increased risk for PONV according to a validated simplified risk score (4). All patients received standardized general anesthesia and were randomized to 4 mg ondansetron or nothing (control) at the conclusion of surgery (5). Patients were also randomized to 4 mg dexamethasone vs. control, 1.25 mg droperidol vs. control, and propofol vs. volatile anesthetics with group comparability ensured by a factorial design. An absolute difference of 10% or a relative difference of 25% in the rRR between nausea and vomiting was defined to be clinically relevant.
Results: All relevant patients characteristics such as age, gender, non-smoking status, history of PONV, etc. were similar between the groups ($P>0.05$). The rRR for ondansetron was similar between nausea and vomiting (Table 1; $P>0.05$ at all time intervals). However, the incidence of nausea was considerably higher than that of vomiting ($P<0.001$), resulting in a larger absolute risk reduction for nausea than for vomiting. Consequently, fewer patients needed to be treated to prevent nausea than vomiting.
Discussion: Prophylaxis with ondansetron comparably reduced the relative risk of nausea and vomiting. But as baseline risk is greater for nausea than for vomiting, absolute risk reduction is higher for nausea than vomiting. This contrasts with the interpretation but not with the results of a previous meta-analysis (6).
References
1. Anesthesiology 98: 46-52, 2003.
2. Anesth Analg 97: 62-71, 2003
3. New Engl J Med 350: 2441-51, 2004.
4. Anesthesiology 91: 693-700, 1999.
5. Anesth Analg 86: 274-282, 1998.
6. Anesthesiology 87: 1277-1289, 1997.

Absolute risk difference, number needed to treat, relative risk, and relative risk reduction (rRR)

Postoperative Period	Symptom	Control Group (# with / without symptom)	Control Group Risk	Ondansetron group (# with / without symptom)	Ondansetron Group Risk	Absolute Risk Difference	Number Needed to Treat (NNT)	Relative Risk	rRR
Early (0-2 hr)	Vomiting	136 / 2472	0.055	85 / 2506	0.034	-0.02	47.4	0.63	0.37
	Nausea	479 / 2118	0.226	322 / 2261	0.142	-0.08	11.9	0.68	0.32
	Postoperative Nausea and Vomiting (PONV)	492 / 2105	0.234	334 / 2249	0.149	-0.09	11.7	0.68	0.32
Delayed (2-24 hr)	Vomiting	345 / 2263	0.152	238 / 2353	0.101	-0.05	19.5	0.69	0.31
	Nausea	769 / 1788	0.445	591 / 1981	0.298	-0.15	6.8	0.75	0.25
	Postoperative Nausea and Vomiting (PONV)	820 / 1764	0.465	617 / 1957	0.315	-0.15	6.7	0.76	0.24
Overall (0-24 hr)	Vomiting	441 / 2167	0.204	293 / 2298	0.128	-0.08	13.2	0.67	0.33
	Nausea	969 / 1616	0.600	715 / 1859	0.385	-0.22	4.7	0.74	0.26
	Postoperative Nausea and Vomiting (PONV)	996 / 1589	0.627	735 / 1841	0.399	-0.23	4.4	0.74	0.26

S-5.

POSTDISCHARGE NAUSEA AND VOMITING: ANOTHER "BIG, 'LITTLE PROBLEM' FOLLOWING AMBULATORY SURGERY" THAT REFUSES TO GO AWAY

AUTHORS: E. Deal, I. Gratz, K. Sailor, M. Goldberg;
AFFILIATION: Cooper Health System, Camden, NJ.

Introduction: For ambulatory surgical patients, nausea and vomiting have been reported to be more common in the post discharge period than in the recovery room. However, once a patient leaves the hospital setting we often lose the ability to adequately monitor and treat postoperative nausea and vomiting. Those patients without effective treatment options and are at risk for complications and delays in resuming normal daily activities. Limited information is available on post discharge nausea and vomiting (PDNV) and the patients' at home management of this symptom. The purpose of this study was to evaluate nausea and vomiting in outpatients 24 hours after discharge from the hospital.
Methods: The study protocol was approved by the local Institutional Review Board. No attempt was made to standardize the anesthetic technique or surgical procedure. Patients who had under gone ambulatory surgery were contacted by phone twenty-four hours following discharge. Informed verbal consent was obtained at that time. Patients were asked various questions regarding their postoperative course including specific questions about the incidence of nausea and/or emetic episodes and prescriptions provided including the use of over-the-counter medications (antacids, histamine H2 antagonists, antidiarrheals, and antiflatulents).
Results: One hundred and forty seven patients were contacted by phone twenty-four hours following discharge. Patients had a mean age of 39 years, were mostly of female gender (107 f, 40 m). Nausea and or vomiting was reported in 31% (N=45) of the patients. While the majority of patients (85%, N=125) were discharged with analgesic agents or a prescription for such, a majority of patients (N=140, 95%) were not discharged with antiemetics or given a prescription. Patients attempted to relieve their symptoms by self-medicating with non-prescription drugs and utilizing food/beverages.
Discussion: The ever-increasing number of outpatient surgeries creates a demand for the anesthesia care provider to provide essential features of rapid recovery while providing adequate analgesia and control of adverse side effects of nausea and vomiting. It is obvious from the relatively high percent (31%) of ambulatory patients that complained of nausea and vomiting that this goal remains elusive. This study further demonstrates that nausea and vomiting is under treated in postoperative patients and needs to be followed beyond the time of discharge. Transdermal delivery systems (transdermal scopolamine {TDS}) may have a place in this population in that they can be applied prior to surgery and have a relatively long duration of action. PDNV and patient management of these symptoms warrants further study.

S-6.

CIRCADIAN VARIATION IN THE INCIDENCE OF POST-OPERATIVE EMESIS

AUTHORS: J. Gunter, J. McAuliffe, E. Beckman;
AFFILIATION: Children's Hospital Medical Center, Cincinnati, OH.

Introduction: The mechanism of the anti-emetic action of dexamethasone is unknown. Nausea with chemotherapy varies inversely with urinary excretion of cortisol[1], suggesting that nausea may be related to adreno-cortical activity. If so, the incidence of PONV should vary with the circadian activity of the adren-cortical axis.
Methods: Our IRB waived Informed Consent for this purely observational study. Data sheets were distributed with all out-patient surgery patients. Data included age in months, history of PONV, high-emesis-risk surgery, anesthesia start and end times (to the next nearest hour), opioids, emesis prophylaxis, and emesis in PACU. Derived factors included age groupings and duration of surgery. Data were analyzed with multi-variable logistic regression, beginning with individual factors followed by pair-wise interactions. All models were hierarchically well-formed; that is, lower order factors contained in significant interactions were retained irregardless of their significance. Model fit was assessed by the area under the Receiver Operating Characteristic (ROC) curve. Power analysis mandated collection of 2000 data sets. Analysis was performed in SPSS v 11.5.
Results: 2050 data sheets were completed; 106 experienced emesis in PACU. Odds ratios for significant factors and interactions are shown in the Table. The incidence of emesis was less between the hours of 0900 and 1300; however, an interaction with female gender effectively eliminated this decrease in females. Reanalysis of the data separately for males (n=1212) and females (n=838) generated unique models for each gender; interactions accentuated the adverse effects of opioids in males over 2 years not receiving prophylaxis and in females having high-emesis-risk surgery. The ROC area for the gender specific models was superior to that for the combined model.
Discussion: The expected result (peak incidence of PONV in the early morning followed by a decrease later in the day) was seen only in males, and both males and females demonstrated an unexpected increase in the odds of emesis late in the day. The reason for the late day increase in emesis was not apparent, but was not related to the duration of surgery. In males, the incidence of PONV varies, at least in part, in concert with the activity of the adeno-cortical axis. Further work is indicated to explore the interplay between gender, hypothalamus, pituitary, adrenals and PONV.
Reference: 1. *Br J Cancer* 1992;65:779-780

	MODEL					
FACTOR/ INTERACTION	Combined (P=0.00003)		Male (P=0.00004)		Female (P=0.004)	
	OR	P	OR	P	OR	P
Female	0.68	.148				
High Risk	3.48	.112			0.71	.014
Opioid	2.59	.0008	1.19	.064	0.46	.10
Prophylaxis	0.49	.005	1.64	.0002		
Start 0900-1300	0.47	.007	0.46	.006		
Start After 1500					2.30	.049
Over 2 Years	3.10	.0003	0.72	.0009	3.72	.035
High Risk X Opioid	0.21	.058			13.67	.009
0900-1300 X Female	2.10	.080				
Opioid X Over 2 Years			6.94	.015		
Opioid X Prophy-laxis			0.17	.016		
ROC Area	.63			.67		

S-7.

A RANDOMIZED PROSPECTIVE COMPARISON OF THE USE OF LAVENDER OIL AROMATHERAPY IN DECREASING PAIN, NAUSEA, AND RECOVERY ROOM DISCHARGE TIME AS WELL AS INCREASED PATIENT SATISFACTION POSTOPERATIVELY

AUTHORS: **M. C. Wajda**, D. Serota, G. Cuff, P. Jayapratap, K. Jackus, J. T. Kim;
AFFILIATION: New York University Medical Center, New York, NY.

Introduction: Common anesthetic goals in the post-operative period include minimizing pain, nausea, and decreasing time to discharge. However, many of the current pain medications, specifically opioids and NSAIDS are associated with side effects including respiratory depression, nausea, pruritis and bleeding. The aim of this pilot study is to determine whether inhalation of lavender oil vapor can decrease the requirement for post-operative pain medication. The total time to discharge from the recovery room, pain scale and overall patient satisfaction was measured to determine if lavender oil makes a significant difference.
Methods: With IRB approval, 30 consented ASA I-II patients scheduled for breast biopsy were randomly assigned to receive either lavender aromatherapy or a standard face mask post-operatively. Intraoperatively, patients received Fentanyl (1.5 ug/kg), Versed (0.05 mg/kg), and small boluses of Propofol as needed for sedation. Additionally, the surgeon infiltrated the surgical site with 1% Lidocaine. Upon arrival to the PACU, two drops of lavender oil were applied to the face mask of the patients assigned to Group A , and a standard face mask with no oil was given to the patients assigned to Group B. The outcome measures were pain scores (VAS) from 0-10 at 5, 30, and 60 minute intervals, overall patient satisfaction and total time to discharge.
Results: Using the Mann-Whitney Rank Sum Test, there is not a statistically significant difference in the two groups pain scales (p=.104 for 5minutes, p=.504 for 30 minutes, p=.4164 for 60 minutes). Using the t-test to compare total recovery room time between the two groups shows no statistically significant difference between the two groups (p=.0541). There is a statistically significant difference between the two groups regarding patient overall satisfaction (p=.015). The results for overall satisfaction with lavender, on a scale from 0-10, revealed 12/15 with a 10 rating, 1/15 with a 9, 1/15 with an 8.5 and 1/15 with an 8. Those who did not receive lavender had 4/15 with a 10 rating, 1/15 with a 9.5, 5/15 with a 9, 4/15 with an 8 and 1/15 with a 7 rating.
Discussion: Lavender aromatherapy contributes to overall satisfaction for patients having breast biopsy surgery. There was no significant difference between the two groups in regard to pain and total recovery room time. The differences in the median values among the two groups is not great enough to exclude the possibility that the difference is due to random sampling variability. This may be a result of the small sample size.

S-8.

IS VALDECOXIB AN EFFECTIVE ALTERNATIVE TO CELECOXIB AND ROFECOXIB FOR PREVENTING PAIN AFTER OUTPATIENT ENT SURGERY?

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Introduction: Non-opioid analgesics are commonly administered as part of a multi-modal regimen for preventing pain after ambulatory surgery. The COX-2 specific inhibitors are allegedly associated with fewer side effects than traditional non-selective NSAIDs. This randomized, double-blinded, placebo-controlled study compared valdecoxib (Bextra™) to celecoxib (Celebrex®) and rofecoxib (Vioxx®) with respect to their preventative analgesic efficacy when administered prior to and after ambulatory ENT surgery.
Methods: 137 consenting outpatients undergoing ENT surgery were randomly assigned to receive a placebo (Control), celecoxib 400 mg, rofecoxib 50 mg, or valdecoxib 40 mg orally 30-45 min before the induction of anesthesia. A second dose of the same medication was given on the morning of the first postoperative day. Verbal rating pain scores (0=no pain and 10=worst pain), time from end of surgery to patient achieving discharge home criteria, and incidences of nausea and vomiting, were assessed at specific intervals during the postoperative period. In addition, oral analgesic requirements and patient satisfaction with their pain management (on a 100-point scale) were assessed at the time of discharge home. A follow-up evaluation was performed 24 h after surgery. Data were analyzed using ANOVA or Chi square test, with *p<0.05 vs Control group.
Results: Demographic data, intraoperative anesthetic dosages and duration of anesthesia and surgery did not differ among the four groups. Both the postoperative pain scores and the amount of analgesic medication, as well as nausea and vomiting, were significantly decreased in all three COX-2 inhibitor (vs placebo) groups. Times to discharge home were also shorter in the COX-2 inhibitor groups.

	Control (n=35)	Celecoxib (n=34)	Rofecoxib (n=34)	Valdecoxib (n=34)
Age (yr)	42±14	42±14	44±13	45±12
Weight (kg)	84±26	79±17	82±20	80±19
Anesthesia time (min)	106±45	101±56	97±47	99±36
Surgery time (min)	86±53	80±55	78±48	76±36
Remifentanil (mg)	1.0±0.6	0.9±0.5	0.9±0.5	1.0±0.5
Desflurane (%ET)	4.1±1.1	4±1.1	4.2±1	4.1±1
Fast-track score >12 (min)	43±18	31±13*	26±10*	26±9*
Aldrete score of 10 (min)	60±22	48±14*	47±17*	48±16*
Discharge home (miin)	166±57	138±39	142±54	143±53
Maximum pain score prior to discharge (0-10)	7 (5-8)	4 (2-6)*	4 (2-5)*	4.5 (3-5)*
PACU fentanyl (μg)	138±119	89±91*	80±73*	78±84*
Nausea / vomiting prior to discharge (n,%)	12,40	6,24*	6,26*	6,21*
Maximum pain score <24 h	4 (3-6)	3 (1-4)*	3 (0-4)*	3 (1-4)*
Oral analgesics required <24 h	3.5±2.5	2.4±2.1	2.3±2.2	2.3±2.5
Nausea <24 h (N,%)	9,27	4,12	3,9	5,15
Patient satisfaction with pain management at 24 h	85±16	94±8*	97±5*	96±9*

Discussion: Preoperative administration of valdecoxib 40 mg improved pain management after ambulatory surgery. The newest oral COX-2 inhibitor produced comparable postoperative analgesia to celecoxib 400 mg and rofecoxib 50 mg.

S-9.

"TIMING" OF LIDOCAINE FOR PREVENTION OF PAIN UPON INDUCTION WITH PROPOFOL OR ETOMIDATE: DOES IT REALLY MATTER?

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Introduction. Lidocaine (LIDO) is often used to reduce the pain of injection with induction doses of propofol (PROP) and etomidate. Several dosing, timing, and delivery techniques have been tried with mixed results (1,2). Accordingly, there has been ongoing disagreement among the staff at our institution as to the most effective method to alleviate this pain using LIDO. In this prospective, randomized, double-blind study, we compared the efficacy of LIDO "timing" on alleviation of pain upon induction using PROP or etomidate (ETOM). We hypothesize that patients who receive preemptive LIDO (pre-LIDO) (2%) will have less discomfort upon induction than those patients receiving LIDO at the "same time" as the induction drug.
Methods. After IRB approval, 80 ASA I-III adults, undergoing general surgery, were randomly assigned into 2 groups of 40 each. Group A (simultaneous LIDO) received 4 ml preemptive saline and 4 ml LIDO (80 mg) mixed with either 20 ml PROP (n=20) or ETOM (n=20). Group B (preemptive LIDO) received 4 ml pre-LIDO and 4 ml saline mixed with either 20 ml PROP (n=20) or ETOM (n=20). The 4 ml of preemptive drug dwelled for 3 min. The induction mixture (2 mg/kg PROP or 0.3 mg/kg ETOM) was then injected over 60 sec while the patient was assessed for pain using a 4-point scale (0=no pain, 1=mild, 2=moderate, and 3=severe). Numerical data and pain scores were compared using one-way ANOVA; categorical demographic data with χ^2. $P<0.05$ was considered significant.
Results. Both groups were comparable demographically. There were no differences between groups with respect to incidence of pain: none [A: 38 % vs B: 35 %], mild [A: 40% vs B: 35%], moderate [A: 15% vs B: 27%], and severe [A: 7% vs B: 3%]. The mean induction pain score, point estimate difference, and 95% CI for "simultaneous" vs. preemptive and PROP vs. ETOM comparisons are shown below.

	Simulta-neous	Preemp-tive	Differ-ence	Propofol	Etomi-date	Difference
Number	40	40	40	40	40	40
Mean Pain	0.93	0.97	-0.05	1.00	0.90	0.10
(95% CI)	(0.63-1.21)	(0.68-1.26)	(-0.45-.35)	(.72-1.3)	(.62-1.2)	(-0.30-.50)
P-value			*0.802*			*0.616*

Conclusion. We found that alleviation and intensity of post-injection pain were not significantly influenced by the "timing" of 80 mg LIDO administration or by the specific induction drug. Pre-LIDO and "simultaneous" LIDO with either PROP or ETOM prevented severe pain in 95% (76/80) of patients.
References.
1) Anesth Analg 2000;90:963-9;
2) Anasth Intensivther Notfallmed 1990;25:31-3.

S-10.

ADEQUACY OF PAIN CONTROL IN AMBULATORY DISCHARGED PATIENTS: FACT OR FALLACY?

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Introduction: Recent studies focusing on the inadequate treatment of pain in hospital settings has led the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) to introduce its new policy of 'pain as the fifth vital sign'. Pain management guidelines have subsequently been implemented including numerical pain score documentation and treatment algorithms as recommended by the National Comprehensive Cancer Network (NCCN). However, once a patient leaves the hospital setting we often lose the ability to adequately monitor and treat postoperative pain. The purpose of this study was to evaluate pain, nausea, vomiting and sedation in outpatients 24 hours after discharge from the hospital.
Methods: The study protocol was approved by the local Institutional Review Board. No attempt was made to standardize the anesthetic technique. Patients who had under gone ambulatory surgery were contacted by phone twenty-four hours following discharge. Informed verbal consent was obtained at that time. Patients were asked various questions regarding their postoperative course including specific questions about postoperative control of pain and prescriptions provided. Patients were asked to rate pain on a 0 to 10 scale. Moderate-to-severe postoperative pain (pain of > 5 on a 0-10 scale) during the 24 hours post hospital discharge was considered to be incomplete pain relief. The incidence of nausea and/or emetic episodes was recorded.
Results: One hundred and thirty six patients were contacted by phone twenty-four hours following discharge. Patients had a mean age of 39 years, were mostly of female gender (99 f, 37 m). Nausea and or vomiting was reported in 33% (N=45) of the patients. Slightly less than one-third (N=41) of the patients reported moderate-to-severe postoperative pain (pain of > 5 on a 0-10 scale) during the 24 hours post hospital discharge. While the majority of patients (85%, N=115) were discharged with analgesic agents or a prescription, a significant number (15%, N=22) were not given analgesic agents or were unable to have their prescriptions filled for various reasons.

Discussion: The ever-increasing number of outpatient surgeries creates a demand for the anesthesia care provider to provide essential features of rapid recovery while providing adequate analgesia. It is obvious from the relatively high percent (30%) of ambulatory patients that complained of moderate to severe pain that this goal remains elusive. This study further demonstrates that pain is under treated in postoperative patients and needs to be followed beyond the time of discharge. Despite the advances in the understanding of the pathophysiology of acute pain, and in the development of new analgesic medications, a portion of the population remains isolated from effective pain management in this ambulatory setting .

S-11.

LIDOCAINE FOR REDUCTION OF PROPOFOL-INDUCED PAIN: A SUCCESSFUL NEW ALTERNATIVE TO A COMMON APPROACH

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INTRODUCTION: Propofol-induced pain during IV injection, encountered in 68-100% of patients[1], produces significant patient discomfort and is an important clinical problem[2]. While many techniques have been advocated to reduce this pain, including pre-administration of lidocaine/opioids and rapid or slow injection, only lidocaine used with a tourniquet (i.e. a Bier block-type technique) has been shown effective[1]. We describe a new technique to reduce propofol-associated pain using a near-simultaneous injection of lidocaine and propofol.
MATERIALS AND METHODS: Following IRB approval, 222 male and female patients undergoing a variety of general surgical procedures were assessed. Each had 20# catheters placed in the wrist (WR), dorsum of the hand (DH), or forearm (FA). No premedication was administered. Two mg/kg of propofol was injected in a proximal IV port, preceded by co-administration of 50 mgs of lidocaine into the most distal port of the IV. Parameters assessed included patient age, sex, IV location, and pain scores. The latter were evaluated on a 0-4 score, and then dichotomized as pain or no pain, with pain assessed as: 0 - no vocal response, face impassive, extremity immobile; 1 - vocal response "cool", face impassive, extremity immobile; 2 - verbal response " stings, pinches, or tingles", face impassive, extremity immobile; 3 - verbal response "hurts or burns", with or without extremity removal. No controls were used; instead, cumulative patient responses were compared with meta-analysis estimated population values using a Chi-square test. Comparisons were also made between IV site, age, gender, and pain scores.
RESULTS: There were 130 female and 92 males (mean age 49). IV sites included 160 DH, 44 WR, and 18 FA. Compared to a meta-analysis reported incidence of 73.3%[1], our group had statistically fewer, only 13 out of 222, patients (5.9%) with propofol-induced pain (p-value < 0.0001). There were no differences in pain according to age, gender, or IV site.
DISCUSSION: Our results in a large group of patients suggest that lidocaine co-administration in distal IV ports can reduce the incidence of propofol-induced pain from 68-100%[1] to 5.9%. This 94.1% success rate compares favorably with an 89% rate when lidocaine is given as a Bier block of the forearm[1]. The possible mechanism of our approach may be similar to that of a Bier-block, i.e. instantaneous filling of the vein with lidocaine almost immediately prior to the propofol reaching the involved vein. Although it is suggested that a Bier block is easy, we believe our method is simpler, quicker, and more practical.
REFERENCES:
1) Anesth Analg 2000; 90: 963-9;
2) Anesth Analg 1999; 88: 1085-91

S-12.

THORACIC PARAVERTEBRAL BLOCKADE FOR AMBULATORY BREAST CANCER SURGERY

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Introduction: General anesthesia is currently the standard technique used for surgical treatment of breast cancer. Patients undergoing breast cancer surgery under this type of anesthesia have significant pain and postoperative nausea and vomiting (PONV) requiring considerable intravenous opioid use, and extended hospital stay. Regional anesthesia using paravertebral blockade (PVB) is an ideal alternative to general anesthesia for this type of surgery. Benefits include a reduction in PONV, prolonged postoperative analgesia and potential for ambulatory discharge and considerable healthcare cost savings. This technique has been successfully used in our institution to achieve effective surgical anesthesia and postoperative pain control for breast cancer surgery since 1994.
Methods: In this prospective case series, 3,450 patients classified as ASA physical status I-IV, with a mean age of 55 ± 13 years, underwent breast cancer surgery at the Duke Ambulatory Surgery Center (Duke ASC) between July 1998 and February 2004. Data for each patient was collected prospectively in the Duke ASC Database. This database compiles information on demographic as well as anesthesia and surgery procedures. In addition, trained nurses collect data in the postanesthesia care unit (PACU) and at 24 hr by telephone calls. Research assistants collect 7-day postoperative data by telephone calls. In the PACU and first postoperative day, patients were asked to record their worst pain at the surgical site using a verbal analog pain score (VAS) (0=no pain; 10=worst pain imaginable). Patients also rated their worst PONV using a similar score (0=no nausea; 10=worst nausea imaginable). Patients were asked to rate their overall satisfaction with the anesthesia as well as with the ASC experience on a five-point scale (1=very dissatisfied to 5=very satisfied) and "would you recommend the same type of anesthesia to a relative or friend?"
Results: Breast cancer procedures were performed under PVB in the majority of the breast cancer patients. Surgery was successfully completed in 90.2% of the cases by using PVB alone, and in 95.6% of the cases, surgery was completed by using PVB supplemented with local anesthetic infiltration. There was a 1% incidence of acute complications associated to PVB. All complications were managed with conventional measures and none required the postponement or cancellation of surgery. Postoperative pain as well as PONV scores were low in the PACU (mean pain VAS 0.7, mean PONV VAS 0.46) and at 24 hr (mean pain VAS 1.75, mean PONV VAS 0.74). Patient satisfaction with anesthesia and ASC experience was high.
Conclusions: PVB can be successfully used to perform major operations for breast cancer with minimal complications and a low rate of conversion to general anesthesia. PVB clearly improves the quality of recovery after breast cancer surgery in the ambulatory setting. In addition, great patient satisfaction is associated with this technique.

S-13.

THREE-IN-ONE BLOCK VERSUS LOCAL INFILTRATION/ INTRAARTICULAR INJECTIONS FOR OUTPATIENT KNEE ARTHROSCOPY: A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND STUDY OF PAIN RELIEF AND ANALGESIC USE

AUTHORS: **T. Cutter**, J. L. Apfelbaum, W. L. Binstock, B. Reider, S. Ho, M. Drum;
AFFILIATION: Pritzker School of Medicine, Chicago, IL.

Introduction: Anesthesia for knee arthroscopy can be general, a neuraxial regional technique, a peripheral regional block such as the three-in-one (TIO) block (with or without a sciatic block), or an injection of local anesthetic into the joint and surrounding tissues. We compared the efficacy of the latter two techniques for pain relief after arthroscopy.
Methods: After IRB approval and informed consent, patients (n = 120) were randomized in a 1:1 ratio to receive TIO block with 40cc 0.5% bupivacaine at 0.2mA and intraarticular injection per the surgeon with saline or vice versa, with the surgeon injecting a solution of lidocaine and bupivacaine. Differences in pain and analgesic use were assessed for 72 hours postoperatively. Pain was measured on a 6-point Likert scale with responses obtained at 0.5, 24, 48 and 72 hours after surgery. Use of analgesic medication was recorded in the PACU and on days 1, 2 and 3.
Results: The odds of any pain were 2.5 times greater in the TIO group (odds ratio = 2.53, 95% CI = (1.40, 4.57), p = 0.002). Compared to 30 minutes after surgery, patients in the TIO group were significantly more likely to report pain at 24 hours (OR = 1.65, 95% CI = (1.05, 2.59), p = 0.03) and 48 hours (OR = 2.16, 95% CI = (1.36, 3.42), p = 0.001) after surgery. The odds of more than minimal pain were 2.4 times greater in the TIO group (odds ratio = 2.43, 95% CI = (1.34, 4.40), p = 0.003). No statistically significant differences were found between treatment groups for moderate or severe pain. There were no differences between groups for analgesic use.
Discussion: Intraarticular injection of local anesthetic yielded no advantage to peripheral nerve block and provided superior postoperative analgesia at 24 and 48 hours. The absence of any difference in analgesic use between the groups indicates that this may be of little consequence, but with the potential for adverse effects such as local anesthetic toxicity, nerve damage or injury from a fall because of associated paralysis, the risk-benefit ratio for TIO block may be less favorable than we previously thought.

S-14.

LOW DOSE SADDLE BLOCK VS GENERAL ANAESTHETIC FOR AMBULATORY PROSTATE BRACHYTHERAPY

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Introduction: Transperineal radioactive prostate seed brachytherapy is performed as an outpatient procedure. To determine the optimal anaesthetic a randomized controlled trial was conducted to compare outcome in patients undergoing general anaesthetic versus low dose saddle block.
Methods: Consented patients (n=119) were randomized to receive either a general anaesthetic (GA) or low dose lidocaine saddle block (SB). The GA group received a standardized GA using a combination of iv fentanyl 0.5-1 μg/kg, propofol 1-4mg/kg and laryngeal mask airway. Maintenance was sustained using sevoflurane in a 30:70 ratio of oxygen:nitrous oxide. Any increase in heart rate or mean arterial pressure >20% of baseline was treated by increasing sevoflurane and, if necessary, followed with 25-50μg fentanyl. SB patients received 1-3mg midazolam and spinal injection of 1ml 2% preservative free lidocaine, 1ml 10% dextrose and 10μg fentanyl, total volume 2.2ml. The ideal composition of the injectate was determined in an earlier pilot study.[1] After 5 minutes of sitting, patients were placed in 15× reverse Trendelenberg lithotomy position. Sensory and motor block were assessed by pinprick and modified Bromage scale. Intraoperative pain/hypotension (30% decrease in MAP) were recorded. Postoperative VAS, time to ambulation, urination and discharge were recorded. Patients were contacted by telephone on POD3 to assess patient satisfaction, analgesic use and side effects including Transient Neurologic Symptoms (TNS).
Results: Each group consisted of 59 (one was cancelled due to active reflux). In the PACU, SB patients had consistently lower VAS scores than GA patients. Despite being slower to urinate, SB patients were faster to ambulate and discharge (see Table 1). Hypotension 24/118 was exclusive to the GA group and higher sedation scores in the PACU. There was no difference between groups in PONV or urinary catherization. One equivocal postdural puncture headache was reported and managed conservatively. Unlike other studies no incidence of TNS was reported.[2,3] Home Tylenol #3 use was significantly lower in SB patients. All patients were extremely satisfied with their anaesthetic experience.
Discussion: When compared to a general anaesthetic a low dose spinal lidocaine provides superior anaesthesia and analgesia with minimal side effects. Patients meet discharge criteria in less than 2 hours from injection.
References:
1. IARS 74th Clinical and Scientific Congress, March 2000
2. Anesthesiology 2003:98:485
3. Acta Anaesthesiol Scan 2001;45:240

Summary Findings - SB vs GA

	Injection to Ambulation	Injection to Urination	Injection to Discharge	POD3 T#3 Use
SB	105.53 ± 26.38	171.35 ± 40.53	108.67 ± 23.25	1.00± 0.00
GA	121.71 ± 43.73	150.96 ± 62.21	124 ± 37.28	1.24 ± 0.44

S-15.

THREE-IN-ONE BLOCK VERSUS LOCAL INFILTRATION/ INTRAARTICULAR INJECTIONS FOR OUTPATIENT KNEE ARTHROSCOPY: A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND STUDY OF THEIR IMPACT ON POSTOPERATIVE NAUSEA

AUTHORS: **T. Cutter**, J. L. Apfelbaum, W. B. Binstock, B. Reider, S. Ho, M. Drum;
AFFILIATION: Pritzker School of Medicine, Chicago, IL.

Introduction: Anesthesia for knee arthroscopy can be general, a neuraxial regional technique, a peripheral regional block such as the three-in-one (TIO) block (with or without a sciatic block), or an injection of local anesthetic into the joint and surrounding tissues. We compared the impacts of the latter two techniques on postoperative nausea.
Methods: After IRB approval and informed consent, patients (n = 120) were randomized in a 1:1 ratio to receive TIO block with 40cc 0.5% bupivacaine at 0.2mA and intraarticular injection with saline or vice versa, with the surgeon injecting a solution of lidocaine and bupivacaine. Nausea was measured using a 6-point Likert scale with response options 0-5. Measurements of nausea were obtained at 0.5, 24, 48 and 72 hours after surgery.
Results: Occurrence of postoperative nausea differed significantly, peaking at 24 hours at 22 and 39%, in the intraarticular and TIO groups respectively, from a low of 2 and 6% at 30 minutes after surgery. There was a trend toward more nausea in the TIO group (OR=1.84, 95% CI = (0.95, 3.56), p = 0.069).
Discussion: The increased odds ratio for the TIO block indicates that its use should be limited to patients at low risk for postoperative nausea.

S-16.

USE OF DESFLURANE VS SEVOFLURANE FOR MAINTENANCE OF ANESTHESIA - IMPACT ON FAST TRACK RECOVERY AFTER AMBULATORY SURGERY

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Introduction: Controversy remains regarding the relative benefits of desflurane vs sevoflurane when used for maintenance of anesthesia in the ambulatory setting. Although studies have demonstrated a faster emergence with desflurane (vs sevoflurane), the impact of this difference on the later recovery process has been questioned. Therefore, we performed a randomized, single-blinded study to compare the recovery profile of the two volatile anesthetics after ambulatory surgery.
Methods: 33 healthy outpatients undergoing superficial surgical procedures requiring general anesthesia were randomized to one of two volatile anesthetic groups. All patients were induced with propofol, 2-2.5 mg/kg IV, and after placement of a laryngeal mask airway, anesthesia was maintained with either sevoflurane 2% or desflurane 6% in an air/oxygen mixture. The inspired concentration of the volatile anesthetic was subsequently varied to maintain hemodynamic stability. Analgesia was provided with local anesthetic infiltration and ketorolac, 30 mg IV. Antiemetic prophylaxis consisted of a combination of ondansetron (4 mg), dexamethasone (4 mg) and metoclopramide (10 mg) at the end of surgery. Assessments included intraoperative complications (e.g., coughing, purposeful movements), early, intermediate and late recovery times, as well as the requirements for postoperative analgesic and antiemetic drugs. Preliminary data analysis was performed using Student t-test and chi-square test or Fisher's exact test, with *p<0.05 vs Sevoflurane.
Results: The two study groups had comparable demographic characteristics. Although emergence was more rapid after desflurane, all patients achieved fast-track recovery criteria (fast track score ≥12) on arrival in the day-surgery recovery area, and were discharged home in less than 90 min. Coughing was more frequent with desflurane (30%) than sevoflurane (12%).

	Sevoflurane	Desflurane
Age (yrs)	44±14	45±11
Weight (kg)	74±20	72±11
Surgery time (min)	25±17	27±13
Propofol (mg)	184±29	178±26
Local anesthetics (ml)	17±7	16±7
Ave. volatile conc. (% ET)	2.0±0.4	6.2±1.0
Eye opening (min)	8±2	6±2*
Following commands (min)	7±3	6±2*
Orientation (min)	9±3	7±2*
Fast-tracking score on arrival in PACU (0-14)	13 (12-14)	14 (13-14)
Sitting up (min)	35±19	27±13
Tolerating oral fluids (min)	43±22	32±13
Standing up (min)	65±30	64±17
Ambulating alone (min)	66±31	68±18
"Fit" for discharge (min)	60±17	58±15
Actual discharge (min)	87±61	84±10
Oral opioid analgesic required (%)	18	13
Coughing during and/or after surgery (%)	12	30
Movement during surgery (%)	47	43
Postoperative nausea and vomiting < 24 h (%)	18	13

Discussion: Use of desflurane (vs sevoflurane) for maintenance of anesthesia provided a faster emergence from anesthesia. However, desflurane was associated with more coughing during and immediately after surgery. We conclude that both volatile anesthetics can facilitate fast-track recovery after ambulatory anesthesia.

S-17.

THREE-IN-ONE BLOCK VERSUS LOCAL INFILTRATION/ INTRAARTICULAR INJECTIONS FOR OUTPATIENT KNEE ARTHROSCOPY: A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND STUDY OF LENGTH OF STAY AND PATIENT SATISFACTION

AUTHORS: **T. W. Cutter**, J. L. Apfelbaum, W. B. Binstock, B. Reider, S. Ho, M. Drum;
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Introduction: Anesthesia for knee arthroscopy can be general, a neuraxial regional technique, a peripheral regional block such as the three-in-one (TIO) block (with or without a sciatic block), or an injection of local anesthetic into the joint and surrounding tissues. We compared the latter two techniques for length of stay and patient satisfaction.
Methods: After IRB approval and informed consent, patients (n=120) were randomized in a 1:1 ratio to receive TIO block with 40cc 0.5% bupivacaine at 0.2mA and intraarticular injection with saline or vice versa, with the surgeon injecting a solution of lidocaine and bupivacaine. Length of stay in the PACU was analyzed on the log scale using the two-sample t-test. The chi-square test of association was used to evaluate the relationship between treatment group and satisfaction in the PACU and on the first postoperative day.
Results:
Length of stay in the PACU did not differ significantly between treatment groups. Mean length of stay in the PACU was 95.8 minutes in the intraarticular group and 100.9 minutes in the TIO group. Median length of stay was 95 minutes in both groups. Most patients (75%) reported very high PACU satisfaction (score = 5). PACU satisfaction did not differ significantly between treatment groups.
Discussion: Intraarticular injection of local anesthetic yielded no advantage to peripheral nerve block in PACU length of stay or patient satisfaction. They should be considered equivalent choices with respect to these variables.

S-18.

IDENTIFICATION OF INDEPENDENT RISK FACTORS FOR POSTOPERATIVE SHIVERING - RESULTS FROM A PROSPECTIVE SURVEY

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Introduction: Postanesthetic shivering (PAS) is uncomfortable for patients and potentially risky (1). However, treatment of established shivering is effective and inexpensive (2). The aim of this observational trial was to identify independent risk factors for PAS in order to more rationally administer preventive anti-shivering interventions.
Methods: Potential risk factors for PAS were recorded in 1,195 consecutive patients. Signs of shivering, peripheral and core temperature, and thermal comfort were recorded in the postanesthetic care unit. The data were split into an evaluation dataset (n=1000) and a validation (n=195) dataset. The initial set was used to identify independent risk factors for PAS and to formulate a risk score using backward logistic regression analyses. The proposed model was subsequently tested for its discrimination and calibration properties using ROC-curve analysis and linear correlation between the predicted and the actual incidences of PAS in the validation group.
Results: The incidence of PAS was 11.6%. There were four primary risk factors: young age, prolonged surgery, orthopedic surgery, and hypothermia - with age being the most important of the four. The risk score derived from this analysis had a reasonable discriminating power, with an area under the ROC-curve of 0.73 (95%-CI: 0.63 - 0.82; $P<0.0001$). Furthermore the equation of the calibration curve ($y=1.01x + 1.7$; $R2=0.94$; $P<0.05$) indicated an excellent and statistically significant agreement between predicted and actual PAS incidence.
Discussion: Postanesthetic shivering can be predicted with acceptable accuracy using the four risk factors identified in the present study. The presented model may serve as a clinical tool to help clinicians to rationally administer anti-shivering drugs (3).

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S-19.

DISCHARGE PRESCRIPTION ERRORS IN A SAME DAY SURGERY CENTER: A PRELIMINARY STUDY OF 75 PATIENTS

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Introduction: Medication errors caused by mistakes in prescription writing are a common and preventable cause of iatrogenic injury (1,2). Most studies investigating prescription errors have focused on inpatients and no information exists regarding same day surgery patients. We investigated prescription writing errors by health care providers for patients postoperatively in a same day surgery center.
Methods: With approval from the IRB, the investigators photocopied prescriptions and discharge forms of surgical patients at a day surgery facility. The prescriptions were written by the patient's primary surgical service. A preliminary analysis of the first 75 patients, with data collected over a 7 day period, was performed to assess prescribing errors. Errors were classified as dose errors, missing information, and patient identification errors. Determination of medication errors and safe prescription writing practices were based on guidelines from the Institute for Safe Medication Practices (ISMP) and the hospital formulary. Errors were classified as potential adverse drug events (ADEs) if the investigators determined that the error had the potential for patient injury. Medication errors and potential ADEs were reported as the percentage of prescriptions with errors. The clinical services observed were not informed of the study in order to obtain an accurate reflection of the current clinical practice and to avoid the potential Hawthorne effect. The Anesthesiology Service rewrote any prescriptions that contained any errors which would be considered potential ADEs.
Results: 75 patients (M:F 27:48) averaging (S.D.) age 38.5± 20.7 yrs, and weight 71.9± 25.2 kgs were studied. The age range of the patients was from 1.3 to 84 years. Analgesics were the most commonly prescribed medications with 67 patients receiving opioids (89%) and 17 patients receiving NSAIDs (23%). Thirty-eight patients (51%) were discharged with two or more prescriptions. There were 122 prescriptions analyzed and 57% of prescriptions had one or more errors. There were 2.5% of prescriptions (N=3) with the potential for significant medical injury and were considered potential ADEs. These events involved improper dosing of analgesic medications. Many prescribing errors involved information regarding dispensing of medications with the quantity to be dispensed not properly recorded in 51% of the prescriptions. There was no weight recorded on 91% of prescriptions for patients weighing < 40 kg (N=11). Only 45 prescriptions (37%) met the "safe practice" standards identified by the hospital formulary or the ISMP.
Discussion: Discharge prescription errors for day surgery patients are very common. Some of the errors were potentially harmful to the patient. Efforts to reduce these errors are an important research priority.
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2) JAMA 1995:274:29-34.

S-20.

INTEGRATED RECOVERY SPEEDS DISCHARGE AFTER OUTPATIENT SURGERY AT INPATIENT FACILITIES

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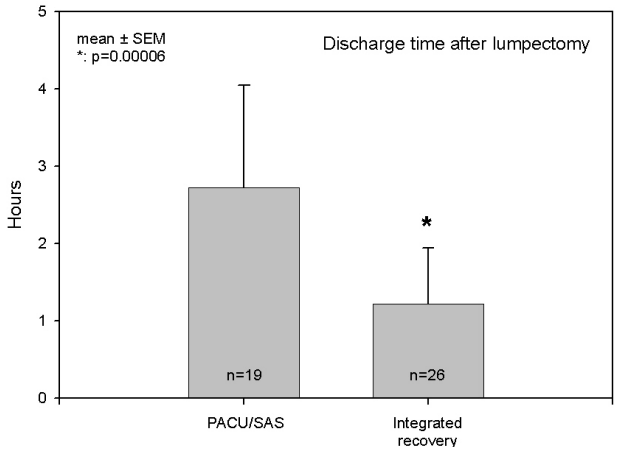
Introduction: Whereas ambulatory surgery centers are designed to minimize duration of patient stay, inpatient facilities increasingly mix outpatients and inpatients. Commonly, recovery takes place in a Post Anesthesia Care Unit (PACU) after which the patient is transferred to an Admission/Discharge Unit (ADS) for postoperative instructions and discharge. This procedure could potentially delay discharge. We recently instituted a system of Integrated Recovery (IR), where both functions are performed by a single nurse at a single location. We hypothesized that the IR system would accelerate discharge.
Methods: We retrospectively studied forty-five patients who underwent breast lumpectomies under general anesthesia. Patient and surgical parameters were similar. Nineteen patients were recovered using a PACU/ADS system; during the same time period, 26 patients were recovered and discharged using IR. Time from admission to the recovery unit until discharge was determined and compared using t-test.
Results: IR resulted in a 55% decrease in time from admission to the recovery unit to discharge. See Fig.1
Discussion: An IR system, implemented in an inpatient facility, has major advantages. Cross-training nurses in the recovery and discharge of patients will decrease significantly the time outpatients spend in the recovery unit as much of the discharge preparation can take place during recovery from anesthesia. Paperwork and reporting are minimized when patients are recovered and discharged from the same location. Transport between locations is eliminated, and nursing personnel cost is reduced. In addition, space can be used more effectively.



S-21.

THE EFFECT OF A SEPARATE OUTPATIENT PHASE 1 RECOVERY AREA ON SURGICAL OUTPATIENT RECOVERY DURATION

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Introduction: Several factors are known to affect total recovery time after outpatient surgery and anesthesia (1-3). This study was undertaken to determine if separation of outpatients and inpatients during phase 1 of recovery affects total duration of outpatient recovery from general anesthesia.
Methods: This retrospective study examines outpatients receiving general anesthesia in a closed staff academic hospital. Total recovery time began upon the patient's arrival in PACU and ended at patient discharge. Prior to June 2003 inpatients and outpatients at our institution underwent phase 1 recovery in the same post anesthesia care unit (PACU). After phase 1 recovery was completed, inpatients were transferred to an inpatient nursing unit and outpatients were transferred to the phase 2 outpatient recovery unit. This process was changed in June 2003. Phase 1 recovery of inpatients continued to occur in the same PACU. The location of phase 1 recovery for outpatients was changed to the area previously used exclusively for phase 2 recovery of outpatients; both phase 1 and phase 2 recovery of outpatients occurred in the same location. The average recovery time for a sample of outpatients undergoing surgery before the reconfiguration (group 1) was compared to a sample undergoing surgery after the change (group 2). Group 1 underwent surgery during September 2002 and group 2 during September 2003. Thirty group 1 patients were selected with a random number generator from a list of all outpatients receiving general anesthesia from September 1, 2002 to September 19, 2002. Of these 30 randomly selected patients, five were excluded due to unavailable data, three were excluded due to unplanned hospital admission, and one was excluded because he had undergone an interventional pain procedure. Group 2 consisted of all 144 outpatients that underwent surgery with general anesthesia from September 1, 2003 to September 16, 2003. The mean (SD) age of group 1 was 58 (19) and group 2 was 60 (19). No significant changes occurred in the scope of outpatient surgical practice or physician staffing model during the study period. Statistical significance was calculated with the two-sample *t* test.
Results: The mean total recovery time for group 1 was 146 (97) minutes. Total recovery time for group 2 was 100 (66) minutes. A mean decrease of 46 minutes (P=.007, 95% CI 13 to 78 minutes) occurred when the location of phase 1 outpatient recovery was changed from a mixed PACU to a separate outpatient recovery area.
Discussion: This preliminary data indicates that total recovery time is shorter for outpatients recovering in an exclusive outpatient recovery area compared to outpatients whose phase 1 recovery occurs in a mixed inpatient-outpatient PACU.
References:
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3. Anesthesiology 2002; 97: 66-74.

S-22.

DELAYED DISCHARGE IS ASSOCIATED WITH LOW ACCEPTABILITY OF AMBULATORY SURGERY IN ADULT OUTPATIENTS

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Introduction: A successful ambulatory surgical program depends on the appropriate and timely discharge patients after anesthesia. Although delay in discharge impairs its cost-effectiveness, it is not self-evident that the delay worsens patient acceptability of ambulatory surgery. The aims of this study were to document factors affecting delay in discharge and patient acceptability of ambulatory surgery.
Methods: Factors that affected delay in home-readiness and discharge were collected prospectively on consecutive adult patients who were scheduled to receive a same-day surgery under general anesthesia (15-84 yr; n=726, male 167, female 559). Home-readiness was defined as obtaining a score of modified postanestheisa scoring system system ≥9 (1). Home-readiness and discharge times were defined as the length of time from entry into postanesthsia care unit to home-readiness and that until the patient was actually discharged, respectively. Discharge-waiting time was defined as the length of time from home-readiness to discharge. Patients were followed up 24h after discharge using a standardized questionnaire to identify post-discharge symptoms, patient's self-rated score of resumption of normal activity (RNA; score 0-10) and preference of outpatient procedure (yes/no).
Results: Ninety-eight percent of study patients discharged home on the day of surgery (discharge time = 214±57, mean±SD, min). Patients with discharge time ≥270 (mean+1SD) min and <270 min were arbitrarily regarded as delayed (n=119) and non-delayed (n=592), respectively. There were no significant differences in age, body weight and ASA PS between delayed and non-delayed patients. Delayed patients had longer duration of surgery and home-readiness and discharge-waiting times. They reported post-discharge pain more frequently (53%) and a lower 24h postoperative RNA score (7.2±1.8) and preference ratio (76%) than non-delayed (34%, 8.0±1.9, 87%, respectively; $P<0.001$). There were no differences in frequency of post-discharge drowsiness (32 vs. 32%), dizziness (12 vs. 11%), general malaise (34 vs. 24%) and nausea and vomiting (NV; 8 vs. 6%) between delayed and non-delayed. The almost all reasons of prolonged home-readiness time (≥165, or mean+1SD, min) were adverse symptoms (53% for drowsiness/dizziness/general malaise, 16% for pain, 12% for NV). The reasons of prolonged discharge-waiting time (≥150, or mean+1SD, min) were persistent symptoms (40% for drowsiness/dizziness/general malaise, 9% for pain, 5% for NV) or social/system problems (19% for waiting for approval of surgeons/physicians, 13% for waiting for escort persons).
Discussion: Our study demonstrates that delayed discharge is associated with lower patient acceptability and RNA score and more frequent post-discharge pain. The delay in discharge is mostly due to side-effect symptoms or waiting for surgeons/physicians or escort persons. Adequate prevention and better management of postoperative symptoms, better education of surgeons, anesthesiologists, nursing

S-23.

RISK ASSESSMENT FOR SLEEP APNEA IN AN AMBULATORY SURGICAL POPULATION

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Introduction: Obstructive sleep apnea (OSA) is a chronic condition associated with recurrent collapse of the upper airway during sleep. Patients with OSA may be at higher risk for adverse perioperative outcomes, including death. In the patient diagnosed with OSA, planned management can include securing a known difficult airway and providing prolonged postoperative monitoring. However, a significant risk of perioperative morbidity and mortality may remain. Moreover, patients with undiagnosed OSA pose a dilemma for anesthesiologists. The primary objective of the current study was to examine the utility of a previously validated self-report instrument in defining the prevalence of OSA symptoms in an ambulatory surgical population.
Methods: Patients presenting for ambulatory surgery completed a self-administered questionnaire to assess demographics (age, gender, race, body mass index [BMI]) and sleep symptoms. History of angina, myocardial infarction, stroke, heart failure, and coronary artery revascularization was also acquired by self-report. Frequency of sleep-related symptoms (e.g., snoring, witnessed apneas) was recorded on a 6-point Likert Scale (never, rarely, sometimes, often, usually, and always). Daytime somnolence was assessed with the Epworth Sleepiness Scale (ESS). OSA risk status was based on two complementary methods. First, habitual snorers (usually or always) with daytime somnolence (ESS score $\geq$ 11) were considered at high risk for OSA. Second, the previously validated prediction model was used to determine the pre-test probability for OSA.
Results: The study sample consisted of 512 subjects (34.1%) with a median age of 47 years (25th percentile = 35 years; 75th percentile = 60 years). The average BMI was 27.2 kg/m^2 (SD:5.7). Using habitual snoring with daytime somnolence to determine OSA risk, 11.5% of men and 5.9 % of women were considered at high risk. Of the patients considered at high risk (19 men, 19 women), only 3 men had a diagnosis of OSA. Using the previously validated prediction model for determining the pre-test probability, 15.0% of men and 7.2% of women had more than a 70% pre-test probability of OSA. Of the patients considered at high risk based on the prediction model (26 men, 24 women), only 8 men and 2 women had a previous diagnosis of OSA.
Discussion: The results of this study demonstrate that: a) OSA is common in an ambulatory surgical population and b) a majority of patients with OSA that present for ambulatory surgery remain undiagnosed. Given that upper airway collapse in patients with OSA is often potentiated by sedatives and narcotics, an efficient means for risk stratifying patients for OSA is necessary to improve patient safety and to reduce potential perioperative complications. Ongoing prospective work at our center is examining whether the presence of diagnosed or undiagnosed OSA is a risk factor for adverse perioperative outcomes.

S-24.

DOES CEREBRAL MONITORING IMPROVE THE OPHTHALMIC SURGICAL OPERATING CONDITIONS DURING PROPOFOL INDUCED SEDATION?

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Introduction: During ophthalmic surgery too deep levels of sedation may cause sudden movement of the head, which can be detrimental to the eye. The bispectral index (BIS) and the Alaris Mid-Latency Auditory Evoked Potentials (AAI) have been reported to indicate the level of sedation and predict loss of consciousness (1). The current study was conducted to assess whether BIS or AAI-guided propofol sedation can optimize ophthalmic surgical conditions.
Methods: One hundred consenting adult patients, scheduled for elective eye surgery, were sedated with propofol delivered via a target controlled infusion system and randomly allocated to the following groups: BIS-G, AAI-G, BIS/AAI-G and non-G (n=25 per group). Each patient was always connected to both devices. The sedation provider was blinded to the non-allocated device. S-ketamine 5 mg was administered as an analgesic adjunct prior to peri-ocular local anesthetic infiltration. The initial target concentration of propofol was 0.5 µg.ml^{-1}in patients older than 70 yr and 1.0 µg.ml^{-1} in all other patients. The concentration was increased every 3 minutes in steps of 0.2 µg.ml^{-1} until the patient had reached a BIS value of 75 or an AAI of 40 (1), and maintained during surgery between 70-95 (BIS) or 35- 60 (AAI). The propofol concentration was decreased whenever the patient became either unresponsive or uncooperative. Level of consciousness (prompt response to gentle hand squeeze) was recorded every 3 minutes. The surgeon assessed treatment quality according to the following criteria for suboptimal operating conditions: movement during surgery, falling asleep, verbal encouragement to lie still, patient talking and cooperation. For every event, five or more occurrences were scored as 3, 3-5 events as 2, 1-2 events as 1 and no events as 0 (ideal operating conditions). Summed values were taken as the total score of events. Group comparisons were made by non-parametric Kruskal-Wallis tests for the total event score and surgical satisfaction, and by one-way analysis of variance for total propofol dose. P-value < 0.05 indicates significance.
Results: The table shows event and satisfaction data. Four patients required conversion to general anesthesia, due to excessive head movement.

	BIS-G	AAI-G	BIS/AAI-G	Non-EEG-G
Gender F/M	14/11	18/7	11/14	15/10
Age (yrs)	63±16 (27-87)	61±15 (31-83)	62±13 (33-82)	60±19 (18-81)
Weight (kg)	75±12 (50-104)	76±13 (60-115)	80±16 (55-120)	79±12 (51-100)
Duration of sedation (min)	70±26 (22-119)	73±33 (31-161)	67±23 (29-131)	72±41 (33-219)
Target Concentration propofol (µg.ml^{-1})	1.09±0.32 (0.6-1.6)	0.96±0.31 (0.4-1.6)	0.99±0.40 (0.3-1.9)	0.91±0.36 (0.5-1.7)
Total dose propofol mg.kg^{-1}.hr^{-1}	2.9±1.2 (1.1-5.3)	2.8±1.4 (1.1-7.5)	2.8±0.9 (0.9-4.05)	2.5±0.98 (0.75±4.9)
Total score of events	3.3±3.6 (0-12)	3.2±3.4 (0-10)	3.2±3.2 (0-10)	4.4±4.4 (0-16)
Surgical satisfaction (LAS, 10=highly satisfied)	7.9±2.1 (1-10)	8.4±1.2 (6-10)	8.0±1.6 (5-10)	7.4±2.3 (1-10)
Prop sedation converted into general anesthesia, (n= number of patient)	1	0	1	2

* = P< 0.05, Means ± SD (range)
Discussion:
The results show that neither BIS nor AAI monitoring improves ophthalmic surgical operating conditions, nor does it reduce the amount of propofol needed.
Reference:
Anesthesiology. 2002;96: 803-16.

S-25.

VOCAL CORD ABDUCTOR DYSFUNCTION IS A CAUSE OF AIRWAY OBSTRUCTION UNDER GENERAL ANESTHESIA

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Introduction: Stridor is frequently observed in spontaneously breathing patients under general anesthesia with LMA. It is usually ascribed to LMA malposition or inadequate depth of anesthesia. We are reporting a series of 5 patients with intraoperative stridor, in whom fiberoptic laryngoscopy revealed vocal cord abductor dysfunction resulting in paradoxical vocal cord motion (PVCM). This has not been previously reported in patients under general anesthesia. PVCM involves passive adduction of the true vocal cords during inspiration, leading to inspiratory stridor. The classic picture is adduction of the anterior two thirds of the vocal cords with a posterior diamond shaped chink through which gas flows in inspiration (1). During expiration, the glottis opens normally.
Background: Normal sleep induced airway obstruction caused by vocal cord abductor dysfunction has been reported in patients with Shy-Drager syndrome and Multiple System Atrophy (2). PVCM has been described extensively in the otolaryngology literature in patients initially treated for asthma. Several case reports describe PVCM in the recovery room (3).
Methods: Five male patients, age range 27 to 69, underwent urologic surgery under general anesthesia with isoflurane or sevoflurane, following propofol induction and LMA placement. Each patient developed inspiratory stridor soon after induction. When the signs persisted, following airway manipulation and deepening of anesthesia, correct LMA placement was confirmed fiberoptically.
Results: In each case, the classic picture of PVCM was seen. Increased depth of anesthesia produced further impairment of vocal cords abduction during inspiration. Assisted ventilation and CPAP and lightning of anesthesia improved the symptoms.
Two patients were switched to total intravenous anesthesia with propofol, which led to further deterioration necessitating endotracheal intubation. Following emergence from anesthesia and resumption of spontaneous ventilation the patients were extubated without any evidence of obstruction.
In the remaining cases, stridor disappeared with discontinuation of volatile anesthesia, and emergence. There was no evidence of stridor in the recovery room. Only one of the five patients had an antecedent history of obstructive sleep apnea.
Discussion: This case series (with video evidence), indicates that selective vocal cord abductor dysfunction is induced by general anesthesia. This leads to PVCM manifested by inspiratory stridor, in otherwise asymptomatic patients. This report underscores the fact that airway obstruction during general anesthesia can be caused by mechanisms others than supralaryngeal obstruction. Fiberoptic laryngoscopy via LMA can be important in establishing the reason for intraoperative airway obstruction.
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2. Iranzo A. Continuous positive air pressure eliminates nocturnal stridor in multiple system atrophy. Barcelona Multiple System Atrophy Study Group. Lancet 2000;356:1329-30.
3. Larsen B. Paradoxical vocal cord motion: an often misdiagnosed cause of postoperative stridor. J Clin Anesth 2004;16:230-4.

S-26.

ALARIS AUDITORY EVOKED POTENTIAL INDEX FREQUENTLY EXCEEDS ITS TARGET RANGE IN PROPOFOL INDUCED SEDATION FOR OPHTHALMIC SURGERY COMPARED WITH BIS

AUTHORS: **V. L. Oei-Lim**[1], M. G. Dijikgraaf[1], M. D. deSmet[1], C. J. Kalkman[2];
AFFILIATION: [1]Academic Medical Center, Amsterdam, Netherlands, [2]University Medical Center, Utrecht, Netherlands.

Introduction: The Bispectral Index (BIS) and the Alaris Mid-Latency Auditory Evoked Potentials (AAI) were reported to be reliable indicators for the level of sedation and loss of consciousness (1). This study was conducted to assess the performance of BIS and AAI during ophthalmic surgery with iv propofol targeted for moderate sedation and prevention of head movement. We studied the degree to which the index of each device could be maintained within the target range.
Methods: Fifty consenting patients scheduled for elective eye surgery, were sedated with propofol delivered via a Target Controlled Infusion system and randomly allocated to the following groups: BIS-G or AAI-G (n=25 per group; G=Guided). Each patient was connected to both devices (BIS^{XP} A2000 Aspect Medical System and A-line ARX index monitor, Danmeter, Denmark). The sedation provider was blinded to the non-allocated device. Propofol was infused to an initial target concentration of 0.5 $\mu g.ml^{-1}$ in patients older than 70 years and 1.0 $\mu g.ml^{-1}$ in all other adult patients. The propofol concentration was increased every 3 minutes in steps of 0.2 µg.ml-1 until the patient had reached a BIS value of 75 (target range 70-95). The target AAI was 40 during surgery, (target range 35-60). (1) The propofol target concentration was decreased whenever the patient fell asleep or became uncooperative. The level of consciousness (prompt response to gentle hand squeeze) was intermittently monitored and recorded every 3 minutes. In addition, 5 mg ketanest-S 25 was administered as an analgesic adjunct immediately prior to the peri-ocular anesthetic. Differences in the proportions of out-of-range BIS and AAI values during propofol sedation with only BIS-G or AAI-G monitoring respectively, were tested with Mann-Whitney U tests. A p-value below 0.05 indicates significance.
Results:

	BIS-G	AAI-G
Gender F / M	14 / 11	18 / 7
Age (yrs)^	63±16 (27-87)	61±15 (31-83)
Duration of sedation (min)^	70±26 (22-119)	73±33 (31-161)
Target Concentration propofol ($\mu g.ml^{-1}$)^	1.09±0.32 (0.6-1.6)	0.96±0.31 (0.4-1.6)
Proportion of out-of range values# during propofol sedation	0.07 (0.013-0.26)	0.58 (0.38-0.85)*
Prop sedation converted into general anesthesia, (n= number of patients)	1	0

^ Means ± SD (range)
# Median (interquartile ranges, 25th- 75th); BIS values in case of BIS guidance, AAI values in case of AAI guidance;
* P< 0.05
Discussion: The AAI showed large variability; it was out of range 58% of time versus 7% for BIS.
Reference:
Anesthesiology. 2002;96:803-16.

S-27.

UPPER AIRWAY IRRITABILITY DOES NOT DIFFER IN SMOKERS UNDERGOING ANESTHESIA WITH DESFLURANE VS. SEVOFLURANE

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INTRODUCTION:
Cigarette smoking increases the risk of intra-operative respiratory complications, including coughing, breath holding, laryngospasm, and desaturation.(1) A study comparing desflurane with sevoflurane administered via an LMA found no difference in incidence of coughing, breath holding or laryngospasm, despite the nominally lesser pungency of sevoflurane.(2) However, only a few patients in that study were smokers.
The present study sought to determine whether, relative to sevoflurane, desflurane significantly increased respiratory complications during anesthesia in patients who smoke.

METHODS:
After obtaining IRB approval, patients scheduled for surgery not requiring paralysis were recruited. All patients currently smoked five or more cigarettes per day for a period exceeding six months prior to enrollment.
Patients received midazolam (2 mg), propofol and fentanyl, followed by insertion of an LMA. Anesthesia was maintained with desflurane or sevoflurane (randomly assigned) in 50% nitrous oxide. All patients breathed spontaneously. An observer, blinded to the choice of anesthetic agent, noted the presence and severity of coughing, breath holding or laryngospasm, and recorded the lowest oxygen saturation reached during each 15-minute epoch of anesthesia. The time from discontinuation of inhaled anesthetic administration to response to commands was recorded.

RESULTS:
Twenty patients received desflurane and twenty received sevoflurane. Patient characteristics in both groups were similar except that those receiving desflurane had a more extensive smoking history.

One patient given desflurane and four patients given sevoflurane coughed during anesthesia. In all cases, coughing lasted less than 30 seconds and SpO_2 exceeded 94%. Coughing always occurred during the first 15 minutes of anesthesia (soon after LMA insertion) or during emergence, and the end-tidal anesthetic concentration was less than 0.75 MAC. One patient given desflurane and one patient given sevoflurane had breath holding lasting less than 60 seconds. The lowest oxygen saturation was similar across both anesthetics (96.4% versus 97.5% in the desflurane and sevoflurane groups respectively). As found in other studies, patients given desflurane awoke sooner than those given sevoflurane.

DISCUSSION:
Manifestations of airway irritation in smokers undergoing anesthesia with desflurane versus sevoflurane are similar, and are of little clinical significance. The present results suggest that coughing usually correlates with low (possibly inadequate) levels of anesthesia rather than irritant effects of the volatile agent.

	Desflurane	Sevoflurane	P < 0.05
Age (years)	43.3 ± 9.9	37.4 ± 11.6	n.s.
Smoking history (pack x years)	24.6 ± 32.0	9.2 ± 5.5	*** P = 0.022**
BMI (kg/ m^2)	25.7 ± 6.0	25.7 ± 4.4	n.s.
Baseline SpO_2	97.0 ± 1.6	98.2 ± 1.0	n.s.
Asthma / COPD (n)	3	2	
ASA	I: 2 / II: 13 / III: 5	I: 6 / II: 14 / III: / 0	
Orthopedic Surgery (n)	9	14	
Urologic / GYN (n)	7	3	
General Surgery (n)	4	3	
Average MAC fraction	0.60 ± 0.19	0.71 ± 0.16	n.s.
Fentanyl (micrograms)	140 ± 73	144 ± 101	n.s.
Propofol (mg)	211 ± 71	205 ± 57	n.s.
Regional Anesthetic (n)	10	11	
Anesthesia duration (minutes)	94.4 ± 53.0	122.3 ± 81.5	n.s.
First response to commands (seconds)	236 ± 123	331 ± 122	***P = 0.019**
Cough (n)	1	4	n.s.
Breath-holding (n)	1	1	n.s.
Laryngospasm (n)	0	0	n.s.
Lowest SpO_2	96.4 ± 4.5	97.5 ± 2.3	n.s.

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2)Anesth Analg 2003;96:701-5

S-28.

UTILITY OF KETAMINE AS AN ADJUNCT TO PROPOFOL FOR SEDATION OF ADULTS HAVING OUTPATIENT COLONOSCOPY

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Intro
Today's clinical environment dictates the need for safe, effective therapies while not compromising cost or delays. With the number of outpatient procedures growing at an ever-increasing rate effective patient care needs to be balanced with prudent financial responsibility. The necessity to treat more patients in a given period of time demands the choice of therapy must take into account not only clinical, but also administrative and financial issues. The purpose of our investigation was to evaluate whether the addition of ketamine to a propofol infusion effects medication usage and discharge time.

Methods
After IRB approval and informed consent 45 patients scheduled for outpatient colonoscopy were enrolled in the investigation. Patients were randomly (n=15 each group) assigned to receive propofol (10mg/ml), propofol/ketamine .25mg/ml (low dose), propofol/ketamine 0.5mg/ml (high dose). All patients received midazolam 1-2mg IV prior to start of procedure.

Results
There were no statistical significance among patient demographics, duration of endoscopy or attentiveness score. There was a statistical correlation (.043) between amount of propofol used in the propofol group (mean 23.93cc) and the propofol/ketamine high dose (mean 18.60cc). There was no difference among the groups regarding adverse effects, patient satisfaction or time to wakefulness.

Discussion
Today's health care environment necessitates the need for safe, effective care keeping in mind that health care resources are limited. With the cost of medication escalating, the anesthetic choices must be tailored to optimize all variables. In our investigation we have shown that the addition of a small dose of ketamine (0.5 mg/ml) you can significantly decrease the amount of propofol used without causing any adverse effects or prolonging the patient's hospital course.

S-29.

PROPOFOL CIRCULATORY EFFECTS - ARE THEY ENDOTHELIM MEDIATOR DEPENDENT?

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Introduction: Mediators of propofol- induced hypotension are quite controversial and based on experimental in-vitro tissue preparation.(1) This study examines the relationship between propofol anaesthesia and some endothelium dependent mediators in man.
Methods: This study was conducted on 20 ASA class I or II, adult patients undergoing elective abdominal surgery, premedicated with midazolam and monitored with 5-lead ECG, oxygen saturation and non-invasive blood pressure. After induction with fentanyl, propofol, vecuronium and tracheal intubation, anaesthesia was maintained with oxygen, propofol infusion (6-12 mg/kg/h) and incremental fentanyl and vecuronium. Recording of arterial blood pressure and heart rate was done every 5 minutes. At the end of surgery, propofol infusion was discontinued and residual curarization reversed. Venous blood was collected, from a dedicated intravenous catheter, before induction of anaesthesia; 15, 30 and 60 minutes post-anaesthesia; at the end of and fifteen minutes after stopping anesthesia. Each blood sample was analysed for endothelin (enzyme immunoassay), substance P (radioimmunoassay) and nitric oxide colorimetric assay (Bioxytech) (1).
Results: Systolic and diastolic blood pressure decreased significantly 15 min post-induction, returning to pre-induction values 30 minutes post-induction and remained stable thereafter. The heart rate was significantly reduced 15 minutes post-induction and recovered pre-induction values 15 minutes post-anaesthesia.

Table 1: Alterations in blood levels of NO, Endothelin and Substance P following propofol (mean ±SD): ** p <0.01 Compared to pre-induction values.

	Pre-Induction	15 min.	30 min.	60 min.	Anesthesia discontinued	15 mins after anesthesia dis-continued
NO (iM)	7.17 (3.3)	6.6 (3.9)	6.36(3.7)	6.2 (4.2)	7.14 (3.9)	8.4 (4.2)
Substance P pmol / ml	14.1 (5.8)	6.1* (3)	5.0* (4)	10.8 (12)	18.7 (13.4)	14.07(6.5)
Endothelin (fmol / ml)	1.07 (0.47)	0.78 (0.5)	1.31 (1.11)	1.17 (0.96)	1.03 (0.63)	0.87 (0.5)

Discussion: Changes in endothelin and blood pressure followed exactly the same pattern suggesting a cause-effect relationship. These changes probably reflect the body's response to surgery rather than propofol anaesthesia. NO level varied minimally indicating no direct relation to the hemodynamic changes during propofol-fentanyl anaesthesia. Substance P level changes are inversely to changes in blood pressure. This probably reflects the suppressive effect of fentanyl on substance P release. Conclusion: The measured mediators do not contribute to propofol-induced hypotension in-vivo in man.

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S-30.

MINIMIZING TEMPERATURE LOSS DURING AMBULATORY ANESTHESIA: HEATED MATTRESS VS. WARM AIR BLANKET

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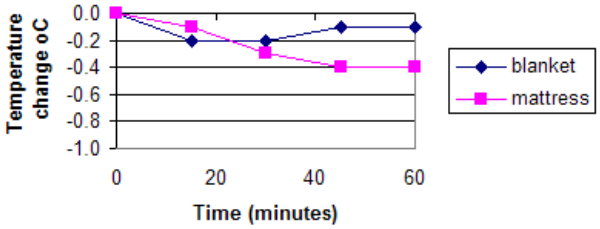
Introduction: The negative effects of heat loss during surgery have been reported extensively. They include delayed recovery, increased oxygen demand, myocardial ischemia, wound infection, coagulopathy and patient discomfort[1]. Convenient, efficient methods for decreasing heat loss under anesthesia have assumed increasing importance, particularly in ambulatory patients. This study compares the upper body warm air blanket with a torso-length mattress heated by an internal resistance heater in patients scheduled for surgery in the lithotomy position in an ambulatory surgery unit.
Methods: After receiving IRB approval, forty patients were enrolled, and randomly assigned to be warmed by either the heated mattress or the warm air blanket. The study was conducted employing these devices as they are commonly applied in our operating rooms, with the mattress activated prior to the patient entering the operating room and the blanket inflated after the operative drapes were in place. Both units were set to the maximum safe temperature (mattress 39°C, warm air blanket, 43°C). Patient temperature was recorded from the nasopharynx or esophagus using the temperature module in the Datascope Passport 2 monitor, after general anesthesia was induced and the airway secured, and at 15 minute intervals until the end of the anesthetic. Statistically significant differences in patient temperature were sought using Student's t-test, corrected for multiple tests. Population differences were tested using Student's t-test.
Results: There were no statistically significant differences between the two study groups in patient weight or length of surgery. Both the heated mattress and the warm air blanket maintained patient temperature within 0.5°C of the initial value over the course of the anesthetic.



Discussion: The heated mattress was as effective as the warm air blanket in reducing heat loss under anesthesia in the population studied. The heated mattress offers several advantages, including ready availability (the mattress is already on the operating table) and avoidance of the cost and other problems attendant to the purchase, stocking, and disposal of single-use warm air blankets.

Reference:

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Cardiothoracic & Vascular - Basic Science

S-31.

ISOFLURANE INDUCES SENSITIZATION OF THE RAT CARDIAC SARCOLEMMAL K_{ATP} CHANNEL BY PKC ε MEDIATED MECHANISM

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Background: Exposure to volatile anesthetics protects the myocardium from ischemia-reperfusion injury. This cardioprotection persisting even after anesthetic withdrawal has been termed anesthetic-induced preconditioning (APC). Activation of the sarcolemmal K_{ATP} channels ($sarcK_{ATP}$) is considered to be an important step in the preconditioning mechanism, although there is some controversy. Moreover, activation of PKC δ and ε is an essential component of the preconditioning cascade. Previous studies demonstrated that isoflurane can increase $sarcK_{ATP}$ channel activity by sensitizing the channel to its opener pinacidil. In addition, isoflurane was found to translocate both PKC δ and ε to sarcolemma and mitochondria, respectively. However, whether this affects the $sarcK_{ATP}$ channel has not been elucidated. Therefore, hypothesis of this study is that isoflurane-induced PKC δ translocation is responsible for the sensitization of the $sarcK_{ATP}$ channel by isoflurane.
Methods: Using a whole-cell patch clamp technique we monitored $sarcK_{ATP}$ channel current (I_{KATP}) from isolated rat ventricular myocytes. To study an effect of isoflurane on $sarcK_{ATP}$ channel we measured pinacidil (5 μM) -elicited current in five experimental groups: 1. control group without isoflurane pretreatment; 2. after *in vitro* exposure to isoflurane (0.5 mM) and 10 min period of anesthetic washout; 3. protocol (2) repeated in the presence of non-specific PKC inhibitor chelerythrine (5 mM); 4. protocol (2) repeated in the presence of PKC δ -specific peptide inhibitor; and 5. protocol (2) repeated in the presence of PKC ε-specific peptide inhibitor.
Results: Under control conditions (without isoflurane exposure) pinacidil-elicited current was 3.8 ± 1.1 pA/pF (n=11). Isoflurane pretreatment sensitized the $sarcK_{ATP}$ channel and increased pinacidil-activated I_{KATP} to 15.6 ± 3.3 (n=12). In the presence of chelerythrine or PKC δ peptide inhibitor, isoflurane pretreatment failed to induce sensitization of the $sarcK_{ATP}$ and pinacidil-activated current was 6.6 ± 1.4 (n=11) and 7.7 ± 7.6 (n=12) pA/pF, respectively. However, PKC ε inhibition did not abolish isoflurane effects on the $sarcK_{ATP}$ channel and pinacidil-activated current after isoflurane exposure was 13.2 ± 2.2 pA/pF (n=18).
Discussion: These results indicate two novel findings. First, that isoflurane-induced sensitization of the $sarcK_{ATP}$ channel persists even after anesthetic removal. This enhancement of the channel activity, which persists even after anesthetic withdrawal, may correspond to an early memory phase of APC. Second, we show that isoflurane effect on the $sarcK_{ATP}$ channel is mediated by PKC δ, an essential mediator of APC signaling mechanism. This complements previous studies that show translocation of PKC δ to sarcolemma in APC and demonstrates that this translocation modifies $sarcK_{ATP}$ channel function.

S-32.

NEGATIVE MYOCARDIAL EFFECTS OF CYCLIC GMP ARE ENHANCED IN OBESE RATS

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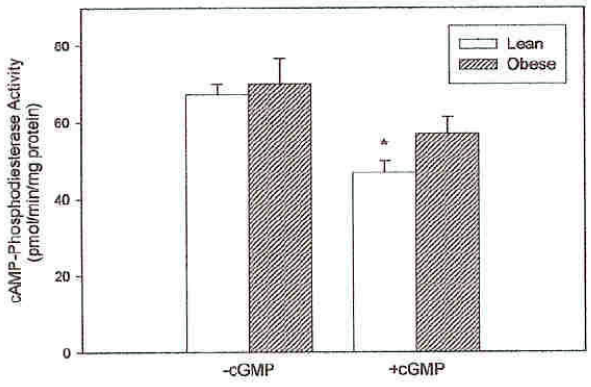
Introduction: Obesity plays a pivotal role in the pathophysiology of many metabolic and cardiovascular diseases. Lack of leptin, a regulator of food intake, or leptin resistance leads to obesity[1]. In leptin-deficient mice, functional decrements in isolated ventricular myocytes caused by cyclic GMP (cGMP) are greatly increased[2]. We tested the hypothesis that the negative myocardial responses to cGMP would be enhanced in leptin-resistant obese rats. We also studied the mechanism underlying the cGMP-induced changes in myocardial responses in the obese rats.
Methods: Experiments were performed in anesthetized open chest 16 male Zucker obese rats and 13 age-matched lean control rats after ICACUC approval. Arterial blood gases, heart rates and blood pressures were obtained after stabilization and 15 min after applying either vehicle (saline) or 8-Br-cGMP (1 mM) topically to the left ventricular surface. Coronary blood flow (^{141}Ce-labeled microspheres) and O_2 extraction(microspectrophotometry) measurements were used to determined myocardial O_2 consumption (VO_2). Protein phosphorylation by cGMP protein kinase (SDS-polyacrylamide gel eletrophoresis) and low Km cAMP phosphodiesterase (A-PDE) (total and cGMP-inhibited) activities were determined in myocardial extract of untreated rats. ANOVA was used for statistical analysis. A value of $p<0.05$ was accepted as significant. Data presented as the Mean±S.E.M.
Results: The body weights (g) of the Zucker obese rats were greater than controls (523±17 vs. 322±12) and their heart weights (g) were also greater (1.24±0.05 vs. 1.06±0.03). The obese rats had higher basal systolic BP (mmHg) than controls (129±7 vs. 95±8). 8-Br-cGMP reduced cardiac output (ml/min) in the obese rats (296±71 to 168±25) but not in controls (228±41 to 207±30). 8-Br-cGMP reduced myocardial VO_2 (ml O_2/min/100g) in the obese rats (54±9 to 35±6) but not in controls (53±13 to 45±7). There were no differences in the pattern of basal or cGMP-stimulated protein phosphorylations between the groups. There were no differences in total A-PDE activities between the groups. However, addition of cGMP significantly inhibited A-PDE activities in controls (-30±4%) but not in the obese rats (-15±12%).
Discussion: The data showed that the cGMP-induced negative metabolic and functional myocardial effects were enhanced in leptin-resistant obese rats. This could be caused by a decrease in myocardial cGMP-inhibited cAMP phosphodisterase activities in the obese rats.
References: 1. Curr Opin Nephrol Hypertens 13:215, 2004. 2. Am J Physiol 285: H2111, 2003.



S-33.

EFFECT OF ISOFLURANE ON MITOCHONDRIAL ATP-SENSITIVE POTASSIUM CHANNEL IN RAT CARDIOMYOCYTES

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Introduction: Brief periods of ischemia and reperfusion can protect myocardium against the damaging effects of subsequent prolonged ischemia. This phenomenon is known as ischemic preconditioning (IPC). Cardioprotection can also be achieved when short episodes of ischemia are replaced with administration of various pharmacological agents, including volatile anesthetic. Because the opening of mitochondrial ATP sensitive potassium channels (mitoK_{ATP}) is considered one of the crucial events in the mechanism of cardioprotection, the goal of our study was to investigate the influence of volatile anesthetic isoflurane on mitochondrial function in intact rat cardiomyocytes by recording flavoprotein fluorescence, an indirect measure of mitoK_{ATP} activity.
Methods: Wistar rat cardiomyocytes were isolated enzymatically and superfused with Tyrode solution. MitoK_{ATP} channel activity was monitored by measuring mitochondrial flavoprotein fluorescence (MFF) as an index of mitochondrial redox state. MFF was excited by the 488-nm line of an argon laser and the emission at 515/530 nm was recorded. The relative change in fluorescence was calculated as $\Delta F/F_0$ where F_0 is initial MFF level and ΔF is (F_t - F_0) at each sample time t. Data are presented as means ± SEM.
Results: Isoflurane dose-dependently increased MFF in rat cardiomyocytes. 1 MAC isoflurane increased MFF to $\Delta F/F_0$= 0.73 ± 0.21 (n=7) and 2 MAC to ΔF/F0= 1.4 ± 0.12 (n=8), reflecting an increased opening of the mitoK_{ATP} channel. When isoflurane was co-administered with selective mitoK_{ATP} channel blocker 5-hydroxydecanoate (5-HD, 500 µM), increase in MFF was significantly diminished ($\Delta F/F_0$= 0.25 ± 0.17). We then compared the isoflurane effect with the effect of mitoK_{ATP} channel opener diazoxide on the MFF of intact rat myocytes. A dose-response curve revealed that 20 µM diazoxide produces an increase of MFF ($\Delta F/F_0$= 0.69 ± 0.09) comparable to 1 MAC isoflurane that was reversed by the addition of 5-HD ($\Delta F/F_0$= 0.11 ± 0.1).
Discussion: The principal finding from this study is that isoflurane increases flavoprotein oxidation in the intact rat ventricular myocytes in a dose-dependant manner. Inhibition of this effect by 5-HD, a selective mitoK_{ATP} channel blocker, indicates that this response is mediated by the mitoK_{ATP} channel opening. This process is likely to contribute to volatile anesthetic-induced cardioprotection. The level of flavoprotein oxidation induced by 1 MAC isoflurane is comparable to that induced by 20 µM diazoxide, a concentration that was shown to produce cardiac preconditioning.

S-34.

EFFECTS OF ANESTHETIC-INDUCED PRECONDITIONING ON THE CARDIAC L-TYPE CALCIUM CHANNEL

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Introduction: Cardioprotection by volatile anesthetic-induced preconditioning (APC) confers anti-ischemic as well as anti-arrhythmic effects. However, the mechanism underlying the anti-arrhythmic effect is unknown. APC has been demonstrated to shorten the action potential duration in APC rat hearts, but its effects on the voltage-gated ion channel proteins are not known. Studies have also shown that APC attenuates calcium overload during reperfusion following ischemia. Consequently, the calcium channel protein may play a critical role as an effector of APC. In this study, we tested the hypothesis that APC by isoflurane confers functional changes in the cardiac L-type calcium channel, contributing to the mechanism of cardioprotection.
Methods: The whole-cell configuration of the patch clamp technique was used. The calcium current (ICa) was recorded from cardiac ventricular myocytes isolated from two groups of adult Wistar rats. In the APC group, rats were exposed to 1.4 % isoflurane (1.0 MAC) for 30 minutes with a 30-minute recovery period prior to cell isolation. In the non-APC group, rats were not exposed to isoflurane. ICa was elicited during 400 ms depolarizing test pulses. For analysis of the current inactivation kinetics, a double-exponential function was used. Standard voltage protocols were utilized for steady state activation and inactivation curves. Results are reported as means±SEM. Statistical analysis was performed using unpaired Student's t-test and $p<0.05$ was considered significant.
Results: APC induced weight-dependent changes in the ICa inactivation kinetics recorded at a membrane potential of +20 mV. In cardiac myocytes isolated from rats with an average body weight of 243±8g, ICa inactivation was delayed whereby the slow time constant (τslow) was significantly prolonged from 100.9±3.1 ms in the non-APC group to 159.6±6.1 ms in the APC group (n=7). However, in myocytes from rats with significantly less body weight (220±7g), tslow of ICa inactivation was significantly accelerated whereby tslow shortened from 105.1±4.0 ms in the non-APC group to 89.4±4.1 ms in the APC group (n=15). The non-APC tslow values between the two weight groups were not significantly different. In contrast, the fast time constant was not significantly different between the respective non-APC and APC groups. There were no significant differences in the steady-state activation and inactivation curves between the non-APC and APC groups. Conclusion: The novel finding from this study showed that APC induced changes in the inactivation kinetics of ICa. This can lead to changes in calcium entry, and consequently to the degree of calcium overload experienced by the myocardium during reperfusion. An acceleration or delay of ICa inactivation would lead to decreased or increased calcium entry, respectively. The weight-dependent changes observed in this study imply that body weight has a profound effect on APC-induced changes in ICa and thus, on the cell's ability to attenuate calcium overload.

S-35.

CORRELATION BETWEEN CELL-TO-CELL UNCOUPLING AND REMODELING IN AN OVINE MODEL OF ISCHEMIC HEART FAILURE

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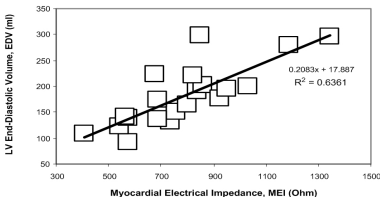
Introduction: Heart Failure (HF) is associated with sudden death due to ventricular fibrillation. Electronic cell-to-cell uncoupling has been suggested as a mechanism underlying these arrhythmias[1]. However, despite the altered expression of Connexin43 (a coupling protein) in HF[2], studies linking remodeling and uncoupling are lacking.
Myocardial electrical impedance (MEI) has been found to detect cell-to-cell electrical uncoupling, as induced by myocardial ischemia[1]. Hence, this experiment was designed to study the relationship between uncoupling and remodeling during HF.
Methods: Adult sheep were chronically instrumented with sonomicrometry crystals and bipolars pacing electrodes for left ventricular (LV) geometry determination and MEI measurements (respectively). The pacing wires were stitched into the myocardial wall of the LAD and LCX distributions.
The animals were allowed to recover and ischemic HF (ejection fraction, EF<35% and end-systolic volume, ESV>80ml) was created by serial LCX microembolizations[3].
We report on the LV volume (end-systolic and end-diastolic, EDV), pressure (end-diastolic, EDP) and MEI of five sheep (N=5), at four different time points: baseline, and weeks 1, 3, and 5 after HF establishment. Differences were analyzed using one-way ANOVA and Tukey post hoc tests (α=0.05).
Results: Data are presented in Table I (mean±SEM).

Table I. LV Parameters

Time	MEI LCX (Ohm)	MEI LAD (Ohm)	HR (bpm)	EDP (mmHg)	ESV (ml)	EDP (ml)	EF (%)
Baseline	568.5±14.3	556.1±44.8	106.4±4.4	15.0±2.4	60.0±6.3	119.9±8.8	50.2±3.1
Week 1	614.2±36.1	746.3±60.8 *	114.0±7.2	21.4±2.4 *	105.6±16.2 *	169.3±15.6 *	31.9±3.5 *
Week 3	675.0±32.3 *	881.8±89.7 *	114.0±11.0	27.2±2.0 *	140.0±18.0 *	207.9±21.2 *	30.6±2.6 *
Week 5	684.7±42.5 *	976.2±100.4 *	106.4±8.3	25.8±1.8 *	167.6±29.8 *	232.9±27.2 *	26.4±3.8 *

*: P<0.05 vs. Baseline

Myocardial LV dilatation was accompanied by electrical uncoupling, as indicated by MEI. Furthermore, a linear relationship (P<0.001) was observed between LV volume (EDV and ESV) and the MEI of remote myocardium (R=0.798 and R=0.753, respectively) (see figure). However, no linear relationship was observed with the MEI of infracted myocardium (EDV: R=0.231, ESV: R=0.157)



.**Discussion:** The myocardial electrical impedance, a property sensitive to cell-to-cell uncoupling, has been shown to increase progressively in the failing heart. Thus, suggesting uncoupling as a potential mechanism linking remodeling and the arrhythmic substrate in HF.

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S-36.

PRELIMINARY CARDIOVASCULAR EVALUATION OF MICE WITH DISRUPTION OF THE BETA2 ADRENERGIC RECEPTOR PDZ MOTIF

AUTHORS: **A. J. Romer**, M. Walsh, M. Feliu-Mojer, R. Agrawal, J. Wong, A. J. Patterson;
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Introduction
beta1 and beta2 adrenergic receptors (ARs) are seven transmembrane helix, G-protein coupled receptors that mediate the primary physiologic responses to catecholamines in the mammalian heart. Prolonged activation of beta1ARs causes myocyte toxicity while continuous beta2AR stimulation may protect the heart. Mice with five to fifteen-fold overexpression of beta1ARs develop significant ventricular remodeling (including fibrosis) and heart failure (1). In contrast, mice in which beta2ARs are overexpressed sixty-fold exhibit enhanced cardiac function without increased mortality (2).
beta1ARs couple to stimulatory G proteins (Gs) and are primarily responsible for regulation of heart rate in vivo. beta2ARs couple initially to Gs, then to inhibitory G proteins (Gi) if activation persists. Biochemical studies suggest that functional differences between beta1ARs and beta2ARs in cardiac myocytes may be mediated by their carboxy terminus PDZ domains. In vitro data indicate that disruption of the beta2AR PDZ motif impairs coupling of beta2ARs to Gi and causes beta2ARs to function like beta1ARs (3).
We hypothesized that disruption of the beta2 PDZ motif in mice (beta2PDZ) (4) would lead to elevated heart rates and cardiac remodeling in adult animals.

Methods
We performed functional, structural, and biochemical studies using beta2PDZ mice. We performed measurements of heart rate, ECG-gated MRIs, graded exercise treadmill studies, ventricular pressure measurements, systemic blood pressure assessments, organ weight to body weight ratio analyses, electron microscopy, and in situ TUNEL staining to assess myocyte apoptosis.

Results
Preliminary results reveal higher heart rates (see Figure 1), impaired cardiovascular function, and cardiac remodeling in beta2PDZ mice. Electrocardiography and infrared tail sensor measurements demonstrate that beta2PDZ mice have higher heart rates than wild type animals (p=0.003 and p=0.02, unpaired t-tests). Treadmill studies indicate diminished exercise capacity in beta2PDZ mice. Heart weight to body weight ratio analyses reveal larger hearts in beta2PDZ mice compared to control animals.

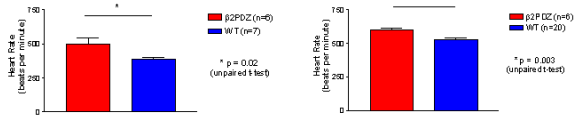

Figure 1. **Heart Rate Measured by Electrocardiography and by Infrared Tail Sensor.** Electrocardiography measurements of heart rate were performed using spontaneously breathing mice anesthetized using isoflurane. Infrared tail sensor measurements of heart rate were performed using resting awake mice after two weeks of device-tolerance training.

Discussion
Preliminary studies indicate that disruption of the beta2AR PDZ motif may cause beta2ARs to behave like beta1ARs in vivo, as it does in vitro. Initial studies suggest that beta2PDZ mice have elevated heart rates, reduced exercise capacity, and cardiac enlargement compared to control animals.

References
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(4) Animals generated by Dr. Robert Lefkowitz, Duke University.

S-37.

PROPOFOL POTENTIATES CHOLERA TOXIN-INDUCED CYCLIC ADENOSINE MONOPHOSPHATE ACCUMULATION IN RAT CARDIOMYOCYTES

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Background:
G-protein-coupled receptors (GPCRs) modulate a wide variety of biological processes, while beta-adrenergic receptors (ßARs) belong to GPCRs and modulate cardiac functions via a cascade of molecular second messengers. We previously demonstrated that the intravenous anesthetic agents propofol[1]) and ketamine[2]) have an effect on the ßAR signaling pathway, and noted that the site of action for propofol seemed to be between ßAR and adenylyl cyclase[1]) Cholera toxin (CTX) exerts an influence on G-protein by ADP-ribosylation of the stimulatory G protein alpha isoform. In the present study, we investigated the effective site of action for propofol in greater detail as well as its effect on CTX-stimulated cyclic adenosine monophosphate (cAMP).
Methods:
Freshly isolated ventricular myocytes were obtained from adult rat hearts and cAMP production was assessed in suspensions of myocytes using an enzyme immunoassay kit. In Protocol[1], suspensions of rat ventricular myocytes were incubated with CTX (1 µg/mL) for 30 minutes, 1 hour, and 3 hours at 37°C, and the effects on cAMP concentrations were assessed. In Protocol 2, following preincubation with propofol (10^{-4}~10^{-7}M) for 10 minutes, CTX (1 µg/mL) was added for 1 hour and the effects on cAMP concentrations were assessed. Data are shown as the mean ± standard error of the mean. Statistical comparisons were made by one-way analysis of variance with a post hoc test. P values greater than 0.05 were considered statistically significant.
Results:
In Protocol 1, CTX (1 µg/mL) increased cAMP production in a time-dependent manner (145±9% after 30 minutes, 169±16% after 1 hour, and 292±54% after 3 hours) as compared to the control. In Protocol 2, propofol (10^{-4}~10^{-7}M) potentiated CTX (1 µg/mL)-stimulated increases in cAMP production by 119±10%, 218±79%, 283±29%, and 304±54%, respectively, of the CTX-stimulated state.
Discussion:
CTX increases cAMP by ADP-ribosylation of the stimulatory G protein alpha isoform and propofol was shown to potentiate this CTX-stimulated increase in cAMP production. Our results suggest that G protein contributes to the effective site of action for propofol.
References:
1) Anesthesiology 2002, ASA 2004
2) ASA 2001

S-38.

SEVOFLURANE INDUCES MITOCHONDRIAL MATRIX SWELLING VIA K_{ATP} CHANNEL OPENING IN GUINEA PIG CARDIAC MITOCHONDRIA

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Introduction: Mitochondrial (m)K_{ATP} channel opening may be a trigger and/or effector of cardioprotection induced by volatile anesthetics. However, the effect of mK_{ATP} channel opening on mitochondrial function is still unclear [1,2]. Maintenance of mitochondrial matrix volume (MMV) has been implicated as a possible mechanism of protection [2]. Since anesthetics, like mK_{ATP} channel openers, are cardioprotective [1,2,3], we investigated if sevoflurane, like diazoxide, alters MMV by mK_{ATP} channel opening under "state 4" conditions.
Methods: Mitochondria from fresh guinea pig hearts were isolated by differential centrifugation and diluted (100 µg protein/ml) in hypotonic buffer (65 mOsm, pH 7.2) at 25°C containing 10 mM succinate (plus 10 µM rotenone) to feed electrons into complex II, and 250 µM ATP and 100 µM oligomycin to inhibit ATP synthase (state 4). Changes in MMV were measured by light scattering at 520 nm [2] in the absence or presence of different sevoflurane concentrations. All data are mean ±SEM; statistics: ANOVA and Bonferroni, $P<0.05$.
Results: Compared to non-treated control experiments (n=28), 30 and 100 µM sevoflurane increased the rate of MMV swelling by 27±9% (n=11) and 42±18% (n=11), respectively. The latter value was not significantly different from the 46±14% increase observed with 30 µM diazoxide (n=8), a mK_{ATP} channel opener. These effects of sevoflurane and diazoxide were abolished by 300 µM 5-hydroxydecanoate, a mK_{ATP} channel inhibitor. Higher sevoflurane concentrations (300 µM, n=10, and 1 mM, n=11) and 5-hydroxydecanoate alone (n=9) had no significant effect on MMV.
Discussion: Cardiac ischemia is thought to decrease MMV resulting in mitochondrial dysfunction [2]. Here, we show that low, clinically relevant concentrations of sevoflurane lead to an increased MMV during state 4 respiration. The finding that 5-hydroxydecanoate blocks sevoflurane effects on MMV strongly suggests that these MMV changes are mediated by mK_{ATP} channel opening. Better preservation of structural and functional mitochondrial integrity may explain the cardioprotective effects of sevoflurane against ischemia/reperfusion injury. The lack of change in MMV at higher sevoflurane concentrations is probably caused by marked inhibition of mitochondrial respiration [3].
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S-39.

COMPARISON OF THE DIRECT ACTION OF SEVOFLURANE ON CONTRACTILE RESPONSE TO NOREPINEPHRINE IN MESENTERIC RESISTANCE ARTERIES BETWEEN HYPERTENSIVE AND NORMOTENSIVE RATS

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Introduction: Patients with untreated hypertension are more susceptible to the circulatory depressant effects of volatile anesthetics than normotensive healthy patients. Vascular responsiveness to volatile anesthetics may alter in the presence of untreated hypertension, possibly contributing to such susceptibility. This study was designed to compare the direct action of sevoflurane on systemic resistance arteries between spontaneously hypertensive rats (SHR) and age-matched normotensive rats.
Methods: Isometric force was recorded in endothelium-intact or endothelium-denuded small mesenteric arteries isolated from SHR (24-27 weeks) and age-matched normotensive Wister rats. All experiments were performed in HEPES-buffered (pH 7.35, 35°C) physiological salt solution. The concentrations of sevoflurane in the bath solutions were determined by gas chromatography. After the equilibration period, a cumulative concentration-response curve to norepinephrine (0.1 μM-30 μM) was generated. After a 15 min recovery period, the arteries were precontracted with 10 μM norepinephrine and subjected to increasing concentrations (0.01 nM-10 μM) of acethylcholine. After a recovery period of 15 min, the effects of sevoflurane on contractile response to norepinephrine were finally examined. Specifically, norepinephrine was applied for 3 min at 7-min intervals so as to obtain reproducible responses, and sevoflurane was applied for 5 min before and during applications of norepinephrine until the steady-state effects were observed. Data are mean ± SD.
Results: 1) Systemic arterial pressure was significantly higher ($P < 0.01$, n=11) in SHRs (231±20 mmHg) than control rats (137±15 mmHg). 2) The concentration-response curve to norepinephrine in the endothelium-intact arteries was shifted to the left in SHRs (EC_{50} = 1.0±0.5 μM) compared with normotensive rats (EC_{50} = 1.9±0.7 μM)($P<0.05$, n = 5). Endothelial denudation shifted the concentration-response curve to norepinephrine to the left in normotensive rats (endothelium-denuded, EC_{50} = 0.7±0.2 μM), but little influenced in SHRs (endothelium-denuded, EC_{50} = 0.8±0.2 μM). 3) The concentration-response curve to acethylcholine was shifted to the right in SHRs (IC_{50} = 15±9 nM) compared with normotensive rats (IC_{50} = 1.9±1.2 nM, $P<0.05$, n = 6). 4) Contractile response to norepinephrine (10 μM) was significantly enhanced ($P<0.05$, n=4-12) during exposure to sevoflurane (2-7.5%, 0.3-1.05 mM) in the endothelium-intact arteries from normotensive rats, but not in those from SHRs. By contrast, contractile response to norepinephrine (0.5 μM, EC_{50}) was similarly inhibited during exposure to sevoflurane (3-5%) both in the endothelium-denuded arteries from SHRs and those from normotensive rats.
Conclusion: In mesenteric arteries, endothelial function is presumably impaired in the presence of untreated hypertension, leading to enhanced response to norepinephrine and attenuated response to acethylcholine. In addition, the endothelium-dependent enhancing action of sevoflurane on norepinephrine response appears to be inhibited in the presence of untreated hypertension, possibly underlying the increased susceptibility of hypertensive subjects to hypotensive effects of sevoflurane.

S-40.

ALTERATIONS IN VASCULAR RESPONSIVENESS TO VOLATILE ANESTHETICS IN MESENTERIC RESISTANCE ARTERIES FROM THE STREPTOZOTOCIN-INDUCED DIABETIC RATS

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Introduction: Diabetic patients are generally believed to be at increased risk for cardiovascular instability during general anesthesia (1). Recent studies have shown that in systemic resistance arteries, volatile anesthetic actions on vascular reactivity are greatly influenced by endothelium (2, 3). Since diabetes mellitus is associated with alterations in endothelial function, volatile anesthetics may influence vascular reactivity differently in diabetics. This study was designed to investigate possible changes in vascular responsiveness to volatile anesthetics in diabetics.
Method: Isometric force was recorded in endothelium-intact small mesenteric arteries from the streptozotocin-induced diabetic (FBS = 450±139 mg/dl, BW = 324±52 g, n =16) and age-matched (24-27 weeks) non-diabetic (FBS = 112±12 mg/dl, BW = 526±62 g, n =16) rats. All experiments were performed in HEPES-buffered (pH 7.35, 35°C) physiological salt solution. After the equilibration period, the cumulative responses of arteries to norepinephrine were determined (0.1 μM-30 μM), the concentration being increased at 1-min intervals. After a 15 min washout period, the arteries were precontracted with 10 μM norepinephrine and subjected to increasing concentrations (0.01 nM-10 μM) of acethylcholine at 1-min intervals. After a recovery period of 15 min, the effects of isoflurane or sevoflurane on contractile response to norepinephrine were finally examined. Specifically, norepinephrine was applied for 3 min at 7-min intervals so as to obtain reproducible responses, and either anesthetic was applied for 5 min before and during applications of norepinephrine until the steady-state effects were observed. Data are mean±SD. ANOVA, Scheffe F test, and contrast were used to determine significance ($P<0.05$), as appropriate.
Results: 1) The concentration-response curve to norepinephrine was shifted to the left in diabetic rats (EC_{50} = 0.9±0.1 μM) compared with non-diabetic (EC_{50} = 1.5±0.6 μM) rats ($P<0.05$, n = 12). 2) The concentration-response curve to acethylcholine was shifted to the right in diabetic rats (IC_{50} = 0.81±0.04 μM) compared with non-diabetic (IC_{50} = 2.3±0.8 nM) rats ($P<0.05$, n = 12). 3) Isoflurane (2-5%, 0.4-1.1 mM) and sevoflurane (2-5%, 0.3-0.7 mM) enhanced both submaximal and maximal responses to norepinephrine (2 μM and 10 μM) in non-diabetic rats, but not in diabetic rats (n = 6-12, $P<0.05$).
Discussion: In mesenteric resistance arteries from diabetic subjects, endothelial function appears to be impaired, leading to enhanced contractile response to norepinephrine, attenuated vasodilator response to acethylcholine, and altered vascular response to volatile anesthetics. The enhancing action of isoflurane or sevoflurane on contractile response to norepinephrine, which has been shown to be mediated by endothelium in rat small mesenteric arteries (2, 3), might be inhibited in diabetics, possibly contributing to the cardiovascular instability often observed in diabetics during anesthesia with isoflurane (1) or sevoflurane.
References: 1. Anesthesiology 1989; 70:591-7 2. Anesthesiology 2000; 92:1426-40 3. Anesthesiology 2001; 95:990-8

S-41.

THE EFFECTS OF SODIUM NITROPRUSSIDE ON VASCULAR SMOOTH MUSCLE CONTROL OF THE MICROVASCULATURE OF PORCINE MYOCUTANEOUS ROTATIONAL AND FREE FLAPS

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Introduction: Microvascular resistance to blood flow in a myocutaneous flap is dependent on endothelial, neuronal, and vascular smooth muscle control. Ischemia/reperfusion injury results in a loss of endothelial vasodilating forces and contributes to the "no-reflow" observed after free-flap reperfusion. The loss of sympathetic tone may result in maximal vasodilation of the microvasculature, thereby preventing any pharmacologic increases in blood flow by vasodilators. Furthermore, it is unclear if the vascular smooth muscle is able to vasodilate due to ischemia/reperfusion injury.(1) We hypothesized that systemically administered sodium nitroprusside (SNP) would be unable to vasodilate the microvasculature of a myocutaneous free flap due to vasoparalysis of the vascular smooth muscle.
Methods: After IACUC approval, seven vertical rectus abdominus myocutaneous (VRAM) rotational flaps and seven VRAM free flaps were dissected in pigs. Laser Doppler flow probes (Perimed, Inc.) were affixed to the skin in the center of the myocutaneous flap to measure microvascular perfusion. After baseline hemodynamic measurements, SNP (8 mcg/kg/min) was administered systemically and the hemodynamic parameters were recorded after an appropriate steady-state period had been achieved. The data were tested for normality using the Kolmogorov-Smirnov test and the non-normally distributed data (microvascular resistance) were reported as median (range) whereas the normally distributed data (systemic mean arterial pressure) were reported as mean (standard deviation). The percent change in hemodynamic parameters from baseline values was compared between flap types utilizing the unpaired t-test (normally distributed data) or the Wilcoxin Signed Rank Test (non-normally distributed data) with $P < 0.05$ considered significant.
Results: In rotational flaps, sodium nitroprusside decreased the systemic mean arterial pressure 32.6% (SD 9.7%) and the microvascular resistance 39.6% (range 41.32%) from baseline values. In free flaps the microvascular resistance decreased 41.5% (range 70.6%, P = 0.612 Rotational vs. Free) and the systemic mean arterial pressure decreased 38.5% (SD 7.5%, P = 0.473).
Discussion: Sodium nitroprusside decreased the microvascular resistance of both rotational and free myocutaneous flaps to a similar extent. It appears that sympathectomy of the free flap does not result in maximal vasodilation of its microvasculature. Furthermore, the vascular smooth muscle of free flaps is responsive to direct, endothelium independent vasodilation by the nitric oxide pathway, in contrast to the myocardium which does not vasodilate in response to sodium nitroprusside after ischemia-reperfusion injury.(1) This porcine model will allow further investigation into the biology of the endothelial and vascular smooth muscle mediated vascular responses of myocutaneous rotational and free flaps.
References: (1) J Physiol Pharmacol 1999; 50(4): 606-15.

S-42.

PROTECTIVE EFFECTS OF HALOTHANE PRETREATMENT ON LEUKOCYTES ACTIVATION AND FUNCTIONAL CAPILLARY DENSITY IN PERIPHERAL MICROCIRCULATION AFTER EXPERIMENTAL CARDIAC ARREST IN THE RAT MODEL

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Introduction: Complex reconstructive microsurgical procedures are time consuming and expose patients to deleterious effects of prolonged anesthesia. The question arises whether any anesthetics may influence free tissue survival (1). The aim of this study was investigate the protective effects of halothane and isoflurane on leukocytes behavior in peripheral microcirculation after experimental cardiac arrest using muscle flap for intrvital microscopic study.
Methods: Twelve male Sprague-Dawley rats were studied in two experimental groups. Group I cardiac arrest under halothane anesthesia (n=6). Following induction of anesthesia with pentobarbital (40 mg kg^{-1} ip.) the lungs were ventilated with 1MAC of halothane and oxygen (FiO_2 = 0.35). Next, modified cardiac arrest was performed for 5 minutes and animals were resuscitated. Group II cardiac arrest under isoflurane anesthesia (n=6). The same experiment was performed under 1MAC of isoflurane anesthesia. Vital parameters such as ECG, MAP, CVP, PaO_2, $PaCO_2$, pH and oesophageal temperature were measured. In both groups the cremaster muscle was isolated as a flap for intravital microscopy. The following peripheral microcirculatory parameters were measured for 4 h after resuscitation: leukocytes activation (roller, adherent, and transmigrating WBC) endothelial edema index and functional capillary density.
Results: Immediately after resuscitation the number of rolling lekocytes decreased in halothane group (11,4%) and isoflurane group (38,6%) when compared with baseline values ($p< 0.05$). At 4 h after resuscitation numbers of leukocytes rollers in halothane group was higher (17,8%) compared to isoflurane group ($p< 0.01$). Number of transmigrating leukocytes significantly increased in the isoflurane group (19,7%) compared to the halothane group ($p<0.01$). Following resuscitation (19,3%) increasing in capillary perfusion was found in the halothane group ($p< 0.01$). Endothelial edema index increased in the isoflurane group (19,8%) when compared to the halothane group ($p<0.01$)
Discussion: In this study 1MAC halothane anesthesia attenuated the harmful effect of cardiac arrest on peripheral microcirculation by significantly decreased numbers of transmigrating leukocytes, constant endothelial edema index in postcapillary venules and by increased of functional capillary density. This beneficial effect of halothane anesthesia on peripheral microcirculation introduced 30 minutes before cardiac arrest can be recognize as a pretreatment effect on cremaster muscle flap microcirculatory hemodynamics and should be consider when appropriate anesthesia for free muscle flap is provided (2).
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S-43.

ACETYLCHOLINE INDUCES CANINE PULMONARY VENOUS SMOOTH MUSCLE CONTRACTION THAT IS ASSOCIATED WITH ACTIVATION AND TRANSLOCATION OF THE ALPHA ISOFORM OF PROTEIN KINASE C

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Introduction: Protein kinase C is an enzyme involved in the regulation of various cellular processes such as growth, metabolism and smooth muscle contraction. We investigated whether acetylcholine (ACh)-induced contraction in pulmonary venous smooth muscle (PVSM) is associated with the activation of specific PKC isoforms.
Methods: All procedures were approved by the Institutional Animal Care and Use Committee. Isolated canine PV rings without endothelium (E-) were suspended in modified Krebs-Ringer buffer for measurement of isometric tension. The effect of PKC inhibition (bisindolylmaleimide I (BIS1); 10^{-6} M) on the ACh dose-response (10^{-8}~10^{-3} M) relationship was assessed. Western immunoblotting was performed in PV cells, and the expression of PKC isoforms was measured. The immunofluoresence technique and confocal microscopy were used to localize the cellular distribution of PKC isoforms before and after the addition of ACh (10^{-6} M). Statistical analysis utilized paired Student's *t* test, with $P<0.05$ considered statistically significant. Values are means ± SEM.
Results: ACh induced dose-dependent contraction ($LogEC_{50}$= -5.89±0.05) in E- PV, with the maximum response (R_{max}) equal to 190±7% of the response to 60 mM KCl. Pretreatment with BIS1 attenuated ACh contraction (R_{max}=111±12%; $LogEC_{50}$= -5.52±0.06). The expression of conventional PKC isoforms (alpha, beta, gamma), novel PKC isoforms (delta, epsilon, theta), and atypical PKC isoforms (zeta, iota, mu) was measured in PV cells by Western blot analysis. Under baseline conditions, PKC alpha, zeta, iota, and mu were expressed, whereas PKC beta, gamma, delta, epsilon and theta were not expressed. Immunofluoresence staining for PKC isoforms showed that in untreated cells, PKC alpha and PKC mu were detected only in the cytoplasm. PKC zeta and PKC iota also exhibited a cytoplasmic immunofluoresence pattern, which was especially abundant in the perinuclear zone. Activation with ACh induced translocation of PKC alpha from cytoplasm to membrane, whereas ACh had no effect on the other PKC isoforms.
Disscussion: ACh contraction is attenuated by PKC inhibition in pulmonary venous smooth muscle. ACh increases the activation and induces translocation of PKC alpha from cytoplasm to membrane in pulmonary venous smooth muscle. These results suggest that PKC-dependent ACh contraction in PVSM may involve activation and translocation of PKC alpha.

S-44.

AGE-RELATED CHANGES IN VOLATILE ANESTHETIC ACTIONS ON CONTRACTILE RESPONSE TO NOREPINEPHRINE IN RAT MESENTERIC RESISTANCE ARTERIES

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Introduction: Systemic arterial pressure tends to fall more considerably during administration of volatile anesthetics in geriatric patients compared with younger patients. Vascular responsiveness to volatile anesthetics may alter with the advance of age. This study was designed to investigate possible age-related changes in volatile anesthetic actions on systemic resistance arteries.
Methods: Isometric force was recorded in endothelium-intact or endothelium-denuded small mesenteric arteries isolated from young (7~8 weeks), middle-aged (24~27 weeks), and geriatric (81~84 weeks) rats. All experiments were performed in HEPES-buffered (pH 7.35, 35°C) physiological salt solution. After the equilibration period, a cumulative concentration-response curve to norepinephrine (0.1 μM~30 μM) was generated. After a 15 min recovery period, the arteries were precontracted with 10 μM norepinephrine and subjected to increasing concentrations (0.01 nM~10 μM) of acethylcholine. In the final series of experiments, norepinephrine was applied for 3 min at 7-min intervals so as to obtain reproducible responses, and either isoflurane (2~5%, 0.42~1.05 mM) or sevoflurane (2~5%, 0.26~0.67 mM) was applied for 5 min before and during subsequent applications of norepinephrine until the steady-state effects were observed. Data are mean ± SD. ANOVA, Scheffe F test, and contrast were used to determine significance ($P<0.05$), as appropriate.
Results: 1) The concentration-response curve to norepinephrine in the endothelium-intact arteries was significantly shifted to the left in geriatric rats (EC_{50} = 0.8±0.2 μM) as compared to young (EC_{50} = 2.1±0.3 μM) or middle-aged (EC_{50} = 1.9±0.7 μM) rats ($P<0.05$). Endothelial denudation significantly shifted the concentration-response curve to norepinephrine to the left in middle-aged rats (endothelium-denuded, EC_{50} = 0.7±0.2 μM), but less influenced in geriatric rats. 2) The concentration-response curve to acethylcholine in the endothelium-intact arteries was significantly shifted to the right in geriatric rats (IC_{50} = 16±10 nM) as compared to young (IC_{50} = 0.4±0.2 nM) or middle-aged (IC_{50} = 1.5±0.9 nM) rats ($P<0.05$). 3) In the arteries from young and middle-aged rats, contractile response to norepinephrine was notably enhanced during exposure to either anesthetic (2~5%) in the presence of endothelium, but inhibited in its absence ($P<0.05$). However, in the arteries from geriatric rats, contractile response to norepinephrine was not influenced during exposure to either anesthetic (2~5%) in the presence of endothelium, but inhibited in its absence.
Conclusion: In mesenteric resistance arteries, endothelial function appears to be impaired in the advanced age, leading to enhanced contractile response to norepinephrine, attenuated vasodilator response to acethylcholine, and altered vascular response to volatile anesthetics. The endothelium-dependent enhancing action of isoflurane or sevoflurane on norepinephrine response (1, 2) is inhibited in the advanced age, possibly contributing to the incidence and severity of systemic hypotension observed in geriatric subjects during administration of either anesthetic.
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2. Anesthesiology 2001; 95:990-8

S-45.

DIRECT ACTION OF ETOMIDATE ON CONTRACTILE RESPONSE TO NOREPINEPHRINE IN RAT SMALL MESENTERIC ARTERIES

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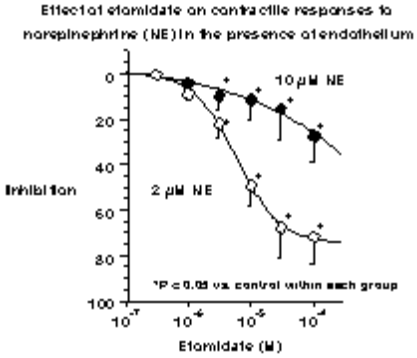
Introduction: Etomidate has been used not only for induction of anesthesia but also for pharmacologic cerebral protection. When administered in standard induction doses, it minimally influences hemodynamics or causes only modest decreases in systemic arterial pressure. However, when administered in higher doses for electroencephalographic burst suppression, it produces immediate decreases in systemic arterial pressure that can sustain without vasopressor support. Less information is available regarding the direct action of etomidate on systemic resistance arteries, which are different from conduit arteries in many of their physiological and pharmacological properties.
Methods: With institutional approval, endothelium-intact or endothelium-denuded strips were prepared from rat (7-8 W, male) small mesenteric arteries. Using the isometric-force recording method, the effects of etomidate on contractile response to norepinephrine, a neurotransmitter that plays a central role in the sympathetic maintenance of systemic vascular resistance, were examined in HEPES-buffered (pH 7.35, 35°C) physiological salt solution. Specifically, norepinephrine (2 μM and 10 μM in the endothelium-intact strips; 0.5 μM and 10 μM in the endothelium-denuded strips) was applied for 3 min at 7-min intervals so as to obtain reproducible responses, and etomidate was applied for 5 min before and during subsequent applications of norepinephrine until the steady-state effects were observed. Since the plasma concentrations of etomidate (~75% protein bound) necessary for induction of anesthesia and cerebral protection are 1-4 μM (i.e., 0.25-1 μM as free etomidate) and 8-28 μM (i.e., 2-7 μM as free etomidate), respectively, the concentrations of etomidate tested in this study were 1-100 μM. ANOVA, Scheffe F test, and contrast were used to determine significance ($P<0.05$), as appropriate.
Results: Etomidate (≥3 μM) significantly inhibited both submaximal and maximal contractile responses to norepinephrine (2 μM, EC~50; 10 μM, maximum) in the endothelium-intact strips in a concentration-dependent manner. Etomidate (≥10 μM) also inhibited both submaximal and maximal contractile responses to norepinephrine (0.5 μM, EC~50; 10 μM, maximum) in the endothelium-denuded strips.
Conclusion: Systemic arterial hypotension caused by etomidate used as a neuroprotectant is presumably due, at least in part, to its direct (i.e., non-neural) inhibitory action on contractile response to norepinephrine. In addition, the attenuated contractile response to norepinephrine by etomidate is due, at least in part, to its direct (i.e., endothelium-independent) inhibitory action on vascular smooth muscle.



S-46.

THE EFFECTS OF ACUTE REMOTE ISCHEMIC PRECONDITIONING ON MICROVASCULAR PERFUSION IN PORCINE MYOCUTANEOUS FREE FLAPS

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Introduction: Acute remote ischemic preconditioning has been shown to decrease necrosis and flap failure of myocutaneous flaps. It is unknown whether remote preconditioning produces this protective effect by modulating microvascular perfusion versus inhibiting reperfusion injury. Because remote preconditioning protects the coronary artery smooth muscle from ischemia/reperfusion injury, we sought to determine if the hemodynamic response to nitroprusside, a direct, endothelium independent vasodilator, and phenylephrine, a direct, endothelium independent vasoconstrictor was different in remote preconditioned myocutaneous free flaps compared to control myocutaneous free flaps.(1) We hypothesized that remote preconditioning would protect the vascular smooth muscle from ischemia/reperfusion injury and result in a more robust vasoactive response.
Methods: After IACUC approval, sequential, bilateral vertical rectus abdominus myocutaneous (VRAM) free flaps were dissected in four pigs. The initial flap had an ischemia time of one hour producing a remote preconditioning stimulus for the contralateral free flap, whose microvascular reanastomosis was also completed in one hour. Laser Doppler flow probes (Perimed, Inc.) were affixed to the skin in the center of the myocutaneous flap to measure microvascular perfusion. After baseline hemodynamic measurements, phenylephrine (80 mcg/min) or nitroprusside (8 mcg/kg/min) was administered systemically and the hemodynamic parameters were recorded after an appropriate steady-state period had been achieved before moving to the second drug. The data were tested for normality using the Kolmogorov-Smirnov test and the non-normally distributed data were reported as median (range) whereas the normally distributed data were reported as mean (standard deviation). The percent change in microvascular resistance from baseline values was compared between flap types utilizing the Paired Sign Test with $P < 0.05$ considered significant.
Results: Administration of phenylephrine increased the systemic mean arterial pressure 94.8% (SD 37.3%) from baseline values. Microvascular resistance increased in both the control free flap (77.7%, range 66.6%) and the preconditioned free flaps (96.0%, range 124.3%, $P = 0.1250$ Control vs. Preconditioned). With nitroprusside, the mean arterial pressure decreased 38.5% (SD 8.1%) and the microvascular resistance of both types of flaps decreased a similar amount (Control = 41.5%, range 99.0% and Preconditioned = 44.0%, range 70.6%, $P = 0.625$).
Discussion: These data demonstrate that acute remote ischemic preconditioning does not result in a more robust vasoactive response to direct vascular smooth muscle vasoactive drugs. The vascular smooth muscle of free flaps does not appear to be protected by remote preconditioning in contrast to the ischemic myocardium which demonstrates a more robust vasodilatory response to nitroprusside after remote preconditioning.(1) However, it is possible that the vascular smooth musculature of free flaps are different from that of the myocardium in that ischemia/reperfusion injury may not inhibit vascular responsiveness to vasoactive agents.
References:
(1) J Physiol Pharmacol 1999; 50(4): 606-15.

S-47.

IMPROVED MITOCHONDRIAL BIOENERGETICS AND MYOCARDIAL FUNCTION BY ISCHEMIC AND ANESTHETIC PRECONDITIONING BEFORE HYPOTHERMIC ISCHEMIA IN ISOLATED GUINEA PIG HEART; DIFFERENT ROLES OF MITOCHONDRIAL K_{ATP} CHANNEL

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Background: Ischemic preconditioning (IPC) and anesthetic-induced preconditioning (APC) cause distinctive changes in mitochondrial bioenergetics during warm ischemia and lead to improved function and tissue viability on reperfusion.[1] We reported previously that IPC before 17ºC (moderate) hypothermic ischemia (HI) adds to the cardioprotective effects of hypothermia and may involve activation of the K_{ATP} channel.[2] Here we investigated if IPC or APC before 27ºC (mild) HI affords additive cardioprotection and improved mitochondrial bioenergetics in the intact hearts. The potential role of mitochondrial (m) K_{ATP} channel opening was also examined. **Methods:** Mitochondrial NADH and FAD fluorescence were assessed by online-measures in the isolated guinea pig hearts using a fiberoptic probe placed at the left ventricular wall.[1] Hearts were assigned into six groups (n=8 each): Hypothermia with or without ischemia (groups 1,2), IPC or APC with or without 5-HD plus HI (groups 3,4,5,6). IPC was achieved by two 5-min periods of ischemia and APC was initiated by giving 2.5% sevoflurane for 15 min followed by a 15 min washout before 2-h, 27ºC HI and 2-h normothermic reperfusion. 5-HD (200 200 μm / l) was perfused from 5 min before to 5 min after IPC, i.e. 10 min before the onset of global hypothermic ischemia. **Results:** IPC and APC before mild HI improved recovery of cardiac function compared to HI alone. 27½C HI caused an increase in NADH and a decrease in FAD. Rewarming and reperfusion to 37½C after 2-h HI led to a rapid and significant decrease in NADH and an increase in FAD. IPC and APC before HI attenuated this alteration in NADH and FAD. 5-HD inhibited the additive protection by IPC and APC. 5-HD also blocked IPC-induced attenuation in NADH and FAD, but not APC-induced attenuation. **Conclusions:** IPC or APC before mild HI exerted additive cardiac protection and preservation of mitochondrial bioenergetics. mK_{ATP} channel opening was involved in improving cardiac protection by IPC and APC before mild HI. The preservation of mitochondrial bioenergetics in IPC, but not in APC, was related to the mK_{ATP} channel opening. It is suggested that mK_{ATP} channel plays differential roles in the mitochondrial bioenergetics during the IPC and APC before mild HI.

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S-48.

DESFLURANE-INDUCED CARDIOPROTECTION AGAINST MYOCARDIAL INFARCTION IS PHASE-SPECIFIC AND MEDIATED BY NITRIC OXIDE DURING REPERFUSION

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Introduction: Desflurane (DES)-induced preconditioning is mediated by NO[1]. DES administration after ischemia (postconditioning) has also been shown to confer cardioprotection during early reperfusion[2]. Conclusive systematic studies comparing the beneficial effects of volatile anesthetics[3] administered during the three distinct periods within the ischemia/reperfusion paradigm in one animal model are lacking. We tested the hypothesis that DES-induced cardioprotection depends on the timing of application and that DES-induced postconditioning is mediated by NO.

Methods: All procedures conformed to the guidelines of the APS, NIH and the institutional Animal Care and Use Committee. Barbiturate-anesthetized male NZW rabbits (n=54) were instrumented for measurement of systemic hemodynamics (LVSP, MAP, CO) and subjected to a 30-min coronary artery occlusion (CAO) followed by 180-min of reperfusion. Infarct size (IS) was assessed with TTC staining and area at risk (AAR) with patent blue, respectively. DES was administered at 1.0 MAC. Groups were: 1) Con, control animals; 2) Pre, DES for 30 min, until CAO; 3) Isch, DES during 30-min CAO; 4) Rep, DES for 30 min after CAO; 5) Pre+Rep, DES for 30 min before and after CAO, but not during CAO; 6) Pre+Isch+Rep, DES continuously for 90 min starting 30 min prior to CAO; 7) LNA, the NO synthase (NOS) inhibitor N-omega-nitro-L-arginine (L-NA) was administered before Rep; 8) LNA+Rep, Rep in the presence of L-NA. Statistics: repeated measures ANOVA followed by posthoc Duncan test. Data are mean±SEM.

Results: Systemic hemodynamics during baseline and AAR were not significantly different among groups. Infarct size was 67±5% (IS/AAR) in control experiments (N=7). DES significantly (*p<0.05) reduced IS in Pre (43±4*%, N=7) and Rep (49±5*%, N=7), but not in Isch (64±6%, N=8). Pre+Isch+Rep and Pre+Rep produced similar reduction in infarct size to 47±5*% (N=7) and 45±3*% (N=6), respectively. L-NA alone had no effect on IS (LNA, 64±4%, N=5) but totally blocked postconditioning (Rep+LNA, 68±4%, N=7).

Discussion: Desflurane induces pre- and postconditioning, but confers no cardioprotection during ischemia in this model. The combination of Pre and Rep or continuous application does not provide further cardioprotection. The results demonstrate, that DES-induced cardioprotection is phase-specific. Inhibition of NOS during reperfusion blocks DES-induced postconditioning. The results suggest, that DES-induced postconditioning is mediated by NO.

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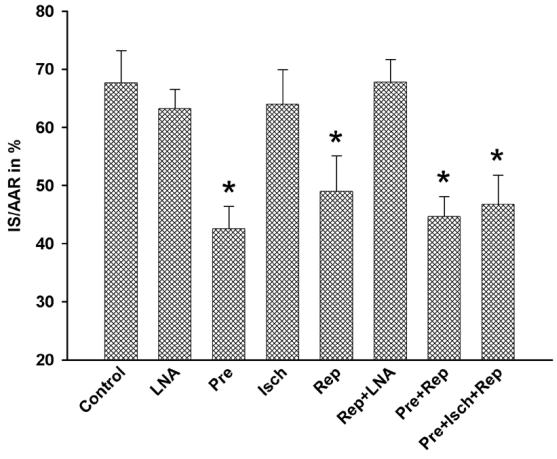

S-49.

ENGAGEMENT OF THE EDG-3 RECEPTOR FOR SPHINGOPHOSPHOLIPIDS CONTAINED IN HIGH DENSITY LIPOPROTEIN (HDL) REDUCES MYOCARDIAL DAMAGE AFTER ISCHEMIA IN MICE

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Introduction: Reperfusion injury after transient myocardial ischemia (MI) is characterized by inflammation due to leukocyte recruitment. HDL has been shown to exert anti-inflammatory effects. Sphingophospholipids, sphingophosphorylcholine (SPC) and sphingosine-1-phosphate (S1-P), are components of HDL that exert vasoprotective effects. SPC and S1-P are ligands for the EDG-receptor family. We examined their potential to modulate myocardial wound healing after myocardial ischemia with reperfusion (MI/R) in a mouse model and sought to dissect the involved signaling pathway. HDL through SPC and S1-P reduces reperfusion injury after myocardial ischemia via the EDG-3 receptor. The effect is abolished in EDG-3-deficient mice (EDG-$3^{-/-}$) and by inhibition of the NOS pathway.
Methods: MI was performed in age and gender matched mice by surgical occlusion of the left anterior descending coronary artery. After 30 minutes, reperfusion was initiated. Infarct size and area-at-risk (AAR) were morphometrically measured after 24h using the TTC-method. Neutrophil infiltration 24h after MI/R was quantitated immunohistochemically. Human HDL (2mg/kg bw), SPC (360µg/kg bw) or S1-P (36µg/kg bw) were injected IV in WT, EDG-$3^{-/-}$ or NOS-inhibited WT-mice prior to MI/R. The NOS-inhibitor L-NAME was administered via the drinking water for 3 weeks prior to MI/R. Neutrophil recruitment to the infarct was quantitated morphometrically on immunohistochemical stainings. Number of apoptotic cells in the infarction was quantitated using a TUNEL-staining. The effect of SPC on leukocyte adhesion to TNFalpha activated endothelial cells (EC) in vitro was examined in a parallel plate flow chamber.
Results: Infarct/AAR was significantly reduced by HDL (20%, n=8, p<0.05), SPC (39%, n= 10, p<0.01) and S1-P (40%, n=5, p<0.01) compared to the respective vehicles. SPC reduced the content of neutrophils in the infarct by 48% (n=6, p<0.05) In vitro, S1-P and SPC reduced adhesion of neutrophils and peritoneal macrophages to TNFalpha activated endothelial cells without affecting rolling. The anti-adhesive effect was abolished by L-NAME treatment. (n=4-8, p<0.05) In the infarct area of SPC-treated mice, 643±66 cells/mm2 were apoptotic compared to 920±225 in controls (n=4, p<0.05). In EDG-$3^{-/-}$, treatment with HDL, SPC and S1-P did not significantly reduce infarct size (n=5 each, p=NS). NOS-inhibition also abolished myocardial protection by S1-P.
Conclusion: HDL protects from reperfusion injury after myocardial ischemia. This effect is mimicked by its components SPC and S1-P. The protective effect is mediated through the EDG-3 receptor for sphingophospholipids. EDG-3-engagement reduces leukocyte recruitment to the post-ischemic myocardium and reduces cardiomyocyte apoptosis. This effect depends on activation of NOS. HDL and its sphingophospholipids may represent attractive molecules to reduce reperfusion injury after transient myocardial ischemia.

S-50.

THE ABILITY OF ISOFLURANE TO ACTIVATE MITOK_{ATP} CHANNELS DEPENDS ON THE DURATION OF EXPOSURE TO ISOFLURANE

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Introduction: Mitochondrial adenosine triphosphate-sensitive potassium channels (mitoK_{ATP}) have been implicated to mediate the protective effects triggered by anesthetic preconditioning (APC). Isoflurane enhances the mitoK_{ATP} channel activation induced by diazoxide (DZX) suggesting that volatile anesthetics only primes but not activates mitoK_{ATP} channels.[1] However, other studies demonstrated that ISO facilitates mitoK_{ATP} channel activation in absence of DZX. To date, the response of the mitoK_{ATP} channels to isoflurane (ISO) and /or DZX in endothelial cells remain unexplored. We hypothesized that ISO has the ability to prime and activate mitoK_{ATP} channels in endothelial cells.
Methods: The mitoK_{ATP} channels response to ISO, DZX, and/or PMA in endothelial cells can be investigated by monitoring the flavoprotein fluorescence (FPF). The FPF-response is expressed as percentage of dinitrophenol (DNP, 100 µM)-induced FPF. A dose-response FPF experiments with DZX were performed in absence of ISO, establishing a baseline response to DZX. This was compared to the FPF response to ISO only or ISO plus DZX.
Results: DZX (10µM) produced no significant increase of FPF in either cell line (both < 5%) compared to baseline (= 0). A tenfold increase in DZX concentration resulted in a tenfold increase of FPF-levels (Figure 1). In the presence of ISO, the FPF induced by each concentration of DZX was significantly enhanced compared to DZX only. Isoflurane in absence of DZX (0.75%) induced an increase in FPF compared to baseline (=0) by 19% and 2.5% FPF in HMEC and BPAEC respectively (Figure 1).
Discussion & Conclusion: Our results showing that each concentration of ISO significantly increased DZX-induced FPF, further supporting evidence that ISO primes mitoK_{ATP} channels.[1-3] Our data also demonstrates that ISO induced FPF in absence of DZX. The discrepancy between our study and reports from Zaugg et al. may be explained by recent data demonstrating that an FPF-response to ISO was not detectible up to 15 minutes of ISO exposure.[2] Thus, in absence of DZX, the duration of ISO exposure, may be a critical factor influencing the response of endothelial mitoK_{ATP} channels.

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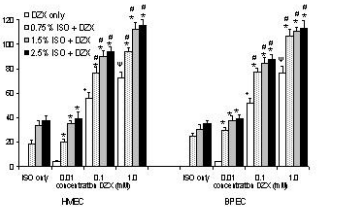

Figure 1A . Flavoprotein fluorescence induced by isoflurane (ISO), diazoxide (DZX) or ISO plus DZX in human microvascular endothelial cells (HMEC) and bovine pulmonary endothelial cells (BPEC). + Denotes that 0.1 mM induced a significantly ($p<0.05$, n= 5) higher FPF-response compared to 0.01 mM DZX. ¥ Denotes that 1.0 mM induced a significantly higher FPF response compared to 0.1 mM DZX. * Denotes that at each concentration of DZX (0.01 – 1mM), ISO significantly increased the DZX-induced FPF compared to DZX only. # Denotes that for each concentration of ISO, FPF induced by DZX plus ISO was significantly higher compared to ISO only. Data are mean ± SD

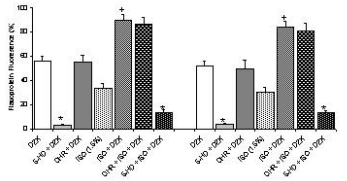

Figure 1B. Effect of Diazoxide (DZX, 100 µM) and isoflurane (ISO, 1.5%) on Flavoprotein fluorescence in the presence and absence of chelerythrine (CHR, 10 µM) and 5-hydroxydecanoate (5-HD, 100 µM) in human microvascular endothelial cells (HMEC) and bovine pulmonary endothelial cells (BPEC). + Denotes that FPF induced by DZX in presence of ISO is significantly ($p<0.05$, n=5) higher compared to FPF induced by DZX only. * Denotes that 5-HD significantly reduced FPF induced by DZX only and DZX in presence of ISO. Data are mean ± SD.

S-51.

EXPERIMENTAL PARAMETERS ARE IMPORTANT DETERMINANTS OF PROPOFOL-INDUCED NEGATIVE INOTROPY IN RAT CARDIOMYOCYTES

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Introduction: Temperature and stimulation frequency are known to modulate cellular mechanisms that regulate intracellular free Ca^{2+} concentration ($[Ca^{2+}]_i$) and myofilament Ca^{2+} sensitivity in cardiac muscle.[1,2] Our objective was to investigate the influences of temperature and electrical field stimulation frequency on propofol-induced alterations in $[Ca^{2+}]_i$ and contraction in individual, electrically stimulated cardiomyocytes. We also assessed the effects of temperature on propofol-induced cardiac depression in Langendorff perfused hearts.
Methods: Freshly isolated myocytes were obtained from adult rat hearts, loaded with fura-2, and placed on the stage of an inverted fluorescence microscope in a temperature-regulated bath. $[Ca^{2+}]_i$ and myocyte shortening (video edge detection) were simultaneously measured in individual cells at 28°C or 37°C at various stimulation frequencies (0.3, 0.5, 1, 2 and 3 Hz). Langendorff perfused hearts paced at 330 beats per minute were utilized to assess the effects of propofol on overall cardiac function. Statistical analysis was performed using analysis of variance and Bonferroni post hoc test with a significance level set at $p < 0.05$. Values are means ± SD.
Results: At 28°C (hypothermic), and to a lesser extent at 37°C (normothermic), increasing stimulation frequency increased peak shortening and $[Ca^{2+}]_i$. Time to peak (Tp) shortening and rate of relengthening was accelerated at 37°C compared to 28°C at low stimulation frequencies (0.3 Hz), whereas the same parameters for $[Ca^{2+}]_i$ were not altered by temperature. At 0.3 Hz and 28°C at low stimulation frequencies (0.3 Hz), whereas the same parameters for $[Ca^{2+}]_i$ were not altered by temperature. At 0.3 Hz and 28°C, propofol (30-1000 μM) caused a dose-dependent decrease in peak shortening and peak $[Ca^{2+}]_i$. These changes were attenuated at 37°C compared to 28°C. At a frequency of 2 Hz, there was a rightward shift in the dose-response relationship for propofol on $[Ca^{2+}]_i$ and shortening at both 37°C and 28°C compared to that observed at 0.3 Hz. In Langendorff perfused hearts, propofol (100 μM) decreased pulse pressure by 51 ± 5% (37°C, 330 beats per min) and by 85 ± 4% (28°C, 330 beats per min).
Discussion: These results demonstrate that temperature and stimulation frequency alter the inhibitory effect of propofol on cardiomyocyte $[Ca^{2+}]_i$ and contraction. Under hypothermic conditions in cardiomyocytes, the effect of propofol is more pronounced compared to normothermic conditions. In contrast, increasing stimulation frequency potentiates the inhibitory effect of propofol on cardiomyocyte $[Ca^{2+}]_i$ and contraction. Similarly, propofol caused cardiac depression to a greater extent under hypothermic conditions in isolated perfused hearts.
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S-52.

A SHORT STIMULUS OF 30-MIN DESFLURANE INDUCES BOTH EARLY AND DELAYED PRECONDITIONING AGAINST MYOCARDIAL INFARCTION

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Introduction: In ischemic preconditioning (IPC) one short ischemic stimulus induces two time windows of cardioprotection, i.e. early and late preconditioning[1,2]. These time windows are separated by an intervening time interval without cardioprotection[1]. It is unknown whether volatile anesthetic-induced preconditioning (APC) induces this characteristic time pattern. In experimental studies either early[3] or late preconditioning[4] have been demonstrated. Therefore we tested the hypothesis that a 30-min administration of desflurane induces both early and late preconditioning separated by a time interval of no cardioprotection in an *in vivo* rabbit model of myocardial infarction.
Methods: All experimental procedures conformed to the guidelines of the APS and NIH and were approved by the institutional Animal Care and Use Committee. Barbiturate-anesthetized male NZW rabbits (N=41) were instrumented for measurement of systemic hemodynamics (AP, CO). All rabbits were subjected to 30-min coronary artery occlusion (CAO) followed by 180 min of reperfusion. Myocardial infarct size (IS) was assessed with TTC and area at risk (AAR) with patent blue, respectively. Rabbits were randomized to 6 groups, that received 0.0 or 1.0 MAC desflurane (Des) for 30 min either 30 min (Des+30min), 12 hrs (Des+12hrs), 24 hrs (Des+24hrs), 48 hrs (Des+48hrs) or 96 hrs (Des+96hrs) prior to CAO. Statistics: repeated measures ANOVA, posthoc Duncan test. Data are mean±SEM.
Results: Systemic hemodynamics during baseline and AAR were not significantly different among groups. Infarct size was 63±5% (IS/AAR) in controls (N=7). Des significantly (*p<0.05) reduced IS in Des+30min (35±2*%, N=7), Des+24hrs (31±3*%, N=7) and Des+48hrs (30±5*%, N=6), but not in Des+12hrs (71±3%, N=7) and Des+96hrs (66±2%, N=7).
Discussion: A short 30-min administration of Des induces early preconditioning at 30 min that is absent at 12hrs. The same short administration of Des induces late preconditioning at 24 and 48 hrs that disappears after 96 hrs. These results demonstrate that APC follows the same characteristic time pattern as that of IPC and that APC mimics IPC with regard to temporal relationships.
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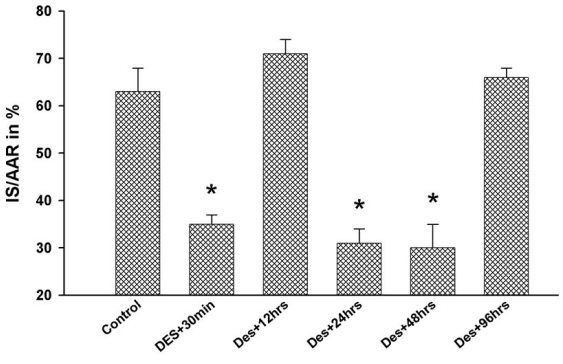

S-53.

EFFECT OF HYDROXYETHYL STARCH 70KDA ON WHOLE BLOOD AGGREGATION

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Introduction: It has been assumed that hydroxyethyl starch (HES) inhibits platelet aggregation based on studies performed using platelet rich plasma (PRP). Whole blood aggregation is a new method to evaluate platelet function. This method uses whole blood, which is closer to the environment in the living body than PRP. In addition, HES dilutes the circulating blood, when it is administered to avoid blood transfusion. We examined platelet function in samples of whole blood diluted with HES.
Materials and Methods: Whole blood was collected from healthy volunteers into plastic syringes containing sodium citrate at a final concentration of 0.38% using a 21-G needle without a tourniquet. Each whole blood sample was diluted (0, 20, 40, 60, 80 %) with 6% wt/vol 70 kDa HES or physiological saline. Platelet aggregation was induced using ADP (0.5, 1.0, 2.0, 4.0 μM) was measured by the screen filtration pressure method (whole blood aggregometer /Mebanix Tokyo, Japan). The pressure rate was standardized using a grading curve produced by plotting data with four concentrations of ADP on the horizontal axis and the pressure rate (%) on the longitudinal axis. The concentration of ADP inducing a 50% pressure rate was calculated and taken as the platelet aggregatory threshold index (PATI). The data obtained from triplicate measurements in three independent experiments were averaged and expressed as mean ± SD. Statistical significance was evaluated using paired t-test; $p<0.05$ was considered statistically significant.
Results: PATI values were increased by HES in a dilution-dependent manner. PATI values of samples obtained from blood diluted with HES (60% and 80%) were significantly higher than that of undiluted control (6.8 ±. 0.8, 7.5 ± 1.2 vs 2.3 ± 0.3 μM). Also, PATI values were increased by physiological saline in a dilution-dependent manner. PATI values of samples obtained from blood diluted with physiological saline (60% and 80%) were significantly higher than that of undiluted control (5.2 ± 1.0, 6.3 ± 0.8 vs 2.3 ± 0.4 μM). PATI values with both 80 % and 60 % HES were significantly higher than those with physiological saline.
Conclusion: Hemodilution wtih more than 60% HES or physiological saline induced a decrease in whole blood aggregation. Furthermore, HES inhibited whole blood aggregation more than physiological saline. When circulating blood is supplemented with HES at more than 60%, a bleeding tendency may result from inhibition of platelet function.

S-54.

INTERACTION BETWEEN PROTEIN KINASE C AND MITOCHONDRIAL ADENOSINE TRIPHOSPHATE-SENSITIVE POTASSIUM CHANNELS IN ANESTHETIC PRECONDITIONING OF THE VASCULATURE

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Introduction: The mechanisms linking anesthetic preconditioning (APC) to the immediate and delayed protective end-effectors are not completely understood, however, a role for protein kinase C (PKC) and mitochondrial adenosine triphosphate sensitive potassium ($mitoK_{ATP}$) channels as significant mediators of APC has been well established[1-2] . The objective of this study is to investigate the interaction between PKC and $mitoK_{ATP}$ channels in endothelial cells pretreated with isoflurane (ISO) in absence or presence of $mitoK_{ATP}$ agonist, diazoxide (DZX) or the PKC agonist phorhol 12-myristate 13-acetate (PMA).
Methods: The bovine pulmonary aortic endothelial cells (BPAEC) were pretreated with ISO, DZX or PMA in an immediate and delayed preconditioning protocol, in absence or presence of PKC or $mitoK_{ATP}$ channels antagonists. Cell viability was determined after pretreated and non-pretreated cells were exposed to a combination of cytokines: tumor necrosis factor-α (1nM), interferon-γ (5 nM) and interleukin-1β (5 nM).
Results: DZX and PMA facilitate immediate and delayed protection against cytokine-induced cell injury, with the same extent compared to isoflurane, increasing the cell viability with approximately 60%. Protection by ISO is significantly ($p < 0.05$) decreased by PKC and $mitoK_{ATP}$ antagonists. Protection induced by PKC activation is not affected by 5-HD and protection facilitated by $mitoK_{ATP}$ channel opening is not altered by PKC antagonists.
Conclusion: When pretreated with ISO, PKC and $mitoK_{ATP}$ channels appear to be co-dependent mediators of APC. The protective effects facilitated by DZX are not altered by PKC antagonists, and the protective effects induced by PMA are not altered by $mitoK_{ATP}$ antagonists. These results suggests that PKC and $mitoK_{ATP}$ channels are both mechanistically involved when cells are pretreated with ISO, but that PKC and $mitoK_{ATP}$ channel agonists may facilitate protection against inflammatory injury through mechanisms independent from the other mediator.

References

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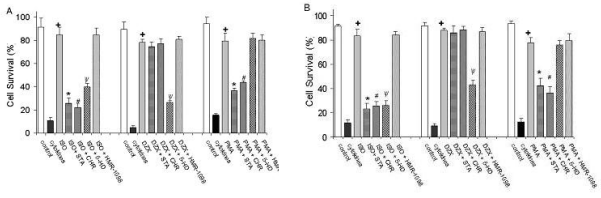

S-55.

ISOFLURANE ACTIVATES ENDOTHELIUM MITOK$_{ATP}$ CHANNELS INDEPENDENT OF PROTEIN KINASE C ACTIVATION

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Introduction: Our previous study showed that PMA and DZX mimic the immediate and delayed protective effects of ISO against injury caused by inflammatory cytokines. Protection induced by ISO is inhibited by PKC and K_{ATP} antagonists, which suggests that both PKC and mitoK$_{ATP}$ channels are essential mediators of APC. MitoK$_{ATP}$ have been shown to act as a trigger (upstream from PKC) and end-effector (downstream of PKC) anesthetic preconditioning (APC).[1] However, other studies demonstrated that PKC acts as transferring factor, acting upstream of mitoK$_{ATP}$.[2] The objective of this study is to investigate whether ISO activation of mitoK$_{ATP}$ is dependent or independent of PKC activation.
Methods: Autofluoresence of mitochondrial flavoproteins was used to evaluate response to ISO (0.75-2.5%) and/or PMA (1 μM) in absence or presence of chelerytrine (CHR = PKC antagonist, 10 μM) of mitoK$_{ATP}$ channels in bovine pulmonary aortic and human microvascular endotheliac cells.
Results: ISO increased the baseline FPF-response with approximately 20-35% in both cell types (Figure 1A). This increase in FPF was which was inhibited by 5-HD. However, the FPF-response induced by ISO was not altered by CHR. PMA also induced an increase of FPF-levels (by 22±4%) compared to baseline (0) in both cell types, which was reduced to approximately 5% by 5-HD and by CHR (Figure 1B). In presence of ISO, the PMA-induced increase in FPF levels was enhanced (to 60 ±5 %) compared to the FPF-response induced by PMA alone.
Conclusion: This study demonstrates that activation of PKC by the agonist PMA leads to activation of mitoK$_{ATP}$ channels in bovine pulmonary aortic and human microvascular endothelial cells. Furthermore, ISO facilitates mitoK$_{ATP}$ channel activation independent of PKC activation but also enhances mitoK$_{ATP}$ channel activation induced by PMA. These results are constent with other studies, reporting that PKC-activation mediates mitoK$_{ATP}$ channel activation. However, our study is the first to demonstrate that ISO augments the effects of PKC on mitoK$_{ATP}$ channels.

References

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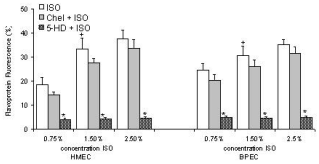

Figure 1A. Effect of isoflurane (ISO) on Flavoprotein fluorescence in absence or presence of chelerythrine (CHR) or 5-hydroxydecanoate (5-HD) in human microvascular endothelial cells (HMEC) and bovine pulmonary endothelial cells (BPEC). + Denotes that 1.5% ISO induced significantly ($p<0.05$, $n=5$) higher FPF levels compared to 0.75% ISO. * Denotes that 5-HD significantly reduced the ISO-induced FPF. Data are mean ± SD.

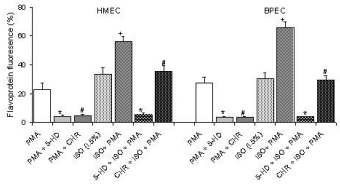

Figure 1B. Effect of phorbol 12-myristate 13-acetate (PMA 1mM) and isoflurane (ISO, 1.5%) on Flavoprotein fluorescence in the presence and absence of chelerythrine (CHR, 10 μM) and 5-hydroxydecanoate (5-HD, 100 μM) in human microvascular endothelial cells (HMEC) and bovine pulmonary endothelial cells (BPEC). + Denotes that FPF induced by PMA in presence of ISO is significantly ($p<0.05$, $n=5$) higher compared to FPF induced by PMA only. * Denotes that 5-HD significantly reduced FPF induced by PMA only and PMA in presence of ISO. #Denotes that CHR significantly reduced the FPF induced by PMA in absence and presence of ISO. Data are mean ± SD.

S-56.

ISOFLURANE INCREASES THE VISCOSITY OF HUMAN NEUTROPHILS AS DETERMINED BY MICROPIPETTE ASPIRATION

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Introduction: During inflammation, neutrophils undergo large physical deformations in order for them to leave the microcirculation and destroy the invading pathogen. Volatile anesthetics are reported to slow their movement across an endothelial monolayer toward a chemoattractant [1,2]. However, no study has investigated whether the decreased chemotacic response is due to increased viscosity of neutrophils secondary to anesthetic exposure. The aim of this study was to determine the effect of isoflurane (ISO) on the viscoelastic properties of human neutrophils using the technique of micropipette aspiration.
Methods: After IRB approval, 2020μl of human blood was placed into stoppered test-tubes containing Hanks buffered salt solution (HBSS) previously equilibrated or not equilibrated with ISO at 1.2% or 2.4% for 30- or 60-min. After 30-or 60-min, neutrophils were aspirated into a siliconized glass pipette (4.0 μm, I.D.) connected to a negative pressure source (3 cm H_2O). After a brief holding period of ~5 sec, the neutrophils were expelled from the pipette and allowed to return to their spherical shape. A video camera attached to an inverted microscope recorded the entire aspiration and recovery period. Measurements of cellular dimensions, time of deformation and recovery to spherical shape were obtained from videotaped neutrophils and entered into constitutive equations. These equations allowed us to calculate the viscoelastic coefficients necessary for assessing the effects of ISO on neutrophil mechanical properties.
Results: *Cell Entry Analysis* (length of time required for cells to aspirate): Control cells had the fastest entry time (2.3±0.79sec) followed by ISO-2.4% for 30 min (2.5±0.77sec). Cells treated with 1.2% ISO or 2.4% ISO for 60-min had significantly ($P<0.05$) longer aspiration times when compared to control cells. *Cytoplasmic Viscosity Analysis* (describes the viscoelastic properties of neutrophils): Cells treated with 2.4% ISO for 30-min had the lowest mean cytoplasmic viscosity (211.6±58.2 Pa-sec) followed by control cells (224.7±86.3 Pa-sec). Increasing the length of ISO exposure from 30- to 60-min at 1.2% (363.3±125.3 Pa-sec) and 2.4% (299.8±94.7 Pa-sec) significantly increased cell viscosity above control values. *Cell Recovery Analysis* (length of time required for cells to reach 90±5% recovery from deformation): Control cells recovered their spherical shape fastest (83.7±20.7 sec) whereas 1.2% ISO (30-or 60-min) only delayed recovery slightly (86.6±25.6 and 98.2±31.1 sec, respectively). Cells treated with 2.4% ISO (30- or 60-min) had significantly longer recovery times ($P<0.05$) compared to control cells (102.4±26.9 and 102.0±23.8 sec, respectively).
Discussion: Increasing the exposure of neutrophils to ISO tended to increase their viscosity as determined by cell entry, cytoplasmic viscosity and cell recovery analysis. Increasing the viscosity of neutrophils may compromise their ability to leave the microcirculation and transmigrate toward the site of infection.

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S-57.

THE NOVEL PEROXYNITRITE CATALYST WW-85 ATTENUATES INTERLEUKIN-2 INDUCED PULMONARY MICROVASCULAR PERMEABILITY DISTURBANCES IN SHEEP

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Introduction: Interleukin 2 (IL-2) is commonly used for immunotherapy in cancer patients (1). The problem, however, is that exogenous IL-2 may contribute to an increase in pulmonary microvascular permeability (2). Since the systemic side effects of IL-2 are linked to nitric oxide and its reactive metabolite peroxynitrite, we hypothesized that the peroxynitrite catalyst WW-85 attenuates IL-2-related changes in pulmonary microvascular permeability.
Methods: Adult sheep (30-40 kg) were operatively instrumented for chronic study. One week after surgery, sheep were randomly allocated to I) an untreated sham group, II) an IL-2-control group (0.1 mg/kg administered at baseline (BL) and every 8 h during the 48-h study period), or III) an intervention group that received IL-2 and WW-85 (IL-2 given as above; WW-85: bolus: 0.1 mg/kg; continuously: 0.5 mg/kg/h; n=6 each).
Pulmonary vascular permeability index (PI) was calculated using standard equation. QL and plasma nitrate/nitrite (NOx) levels (chemiluminescence) were measured intermittently. In addition, lung tissue 3-nitrotyrosine (3-NT) content (ELISA) was measured at the end of the 48-h study period. Data are expressed as mean ± S.E.M.; Significance $p<0.05$.
Results: QL (BL, 4.9±1.1, 24h, 6.4±1.6 mL/h), and PI (BL, 3.3±0.9, 24h, 3.9±0.8) remained stable in sham animals, while increased significantly in the IL-2-group (QL: BL, 6.6±0.5, 24h, 16±2.1 mL/h; PI: BL, 4.7±0.3, 24h, 10.7±1.5). This increase was significantly reduced in the intervention group and was comparable to BL values (QL: BL, 6.2±1.3, 24h, 8.1±1.5 mL/h; PI: BL, 4.1±0.8, 24h, 5.4±0.8). NOx plasma levels increased significantly after 24h in the IL-2 group (5.4 ± 0.5 μM) as compared to the sham group (4.4±0.6 μM), which was significantly prevented in the IL-2+WW-85 group (4.4±0.3 μM; $p<0.05$). IL-2 led to a significant increase in lung 3-NT content compared to the sham group (40±20 vs. 154±50 nM) that was prevented in the intervention group (88±35 nM).
Discussion: These results suggested that the peroxynitrite catalyst WW-85 is useful to attenuate the IL-2-associated deterioration in pulmonary microvascular permeability, triggered by nitric oxide.
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S-58.

EFFECTS OF HERBAL MEDICINES ON LYMPHATIC VESSEL ACTIVITY IN RATS

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Introduction: Herbal medicines are widely used for a variety of diseases (e.g., common cold and chronic pain). The plants contain biologically active components, that have anti-inflammatory, anti-hypersensitive, anti-edematous and the other effects. Lymphatic vessels have spontaneous activity and play an important role in the regulation of body fluid circulation and metabolism. However, the effects of the herbal medicines on the lymphatic vasomotion have not been elucidated. The purpose of the present study is to investigate the effects of the herbal medicines on spontaneous lymphatic vasomotion.
Methods: Thoracic duct (600 um maximum diameter) was isolated from male Wistar rats anesthetized with pentobarbital sodium (50 mg/kg intraperitoneally). The vessels were cannulated with two glass micropipettes, initially filled and superfused with Krebs solution bubbled with a gas mixture of 5 % CO2 and 95 % N2 at 37 degree. The constant intraluminal pressure was maintained at 5 cmH2O. The vessels chamber was placed on the stage of an inverted microscope and the changes in lymphatic vessel internal diameter were measured with video dimension analyzer. While the pressurized showed rhythmic spontaneous constriction and dilation (i.e. vasomotion), the amplitude of the vasomotion was calculated as subtraction of minimum diameter from maximum diameter. After the equilibration period, Bupleuri Radix (mainly including saikosaponins,-spinasterol, stigmasterol, palmitic acid, and the other), Ginseng Radix (mainly including ginsenoside Ro, Ra-Rn, panaxynol, -elemene, and the other) and Zingiberis Rhizoma (mainly including zingiberol, zingiberene, curcumene, gingerol and the other) in clinical relevant doses were administered respectively to superfused Krebs solution. The same protocol were done in the condition of Krebs solution with an NO synthase inhibitor N-nitro-L-arginine methylester (L-NAME; 10-4M). The responses to these herbal medicines were measured and presented as percentage of control.
Results: The vessels showed spontaneous vasomotion in normal Krebs solution (amplitude 260 um, frequency 12 min-1). In Krebs solution with L-NAME, the vessels also showed spontaneous vasomotion (amplitude 150 um, frequency 18 min-1). Bupleuri Radix and Ginseng Radix decreased the frequency and increase the amplitude concentration-dependently with and without L-NAME. Zingiberis Rhizoma did not have the effects of the lymphatic vasomotion either with or without L-NAME. The spontaneous vasomotion was abolished at higher concentration of Bupleuri Radix and Ginseng Radix with and without L-NAME.
Conclusion: These results indicated that the herbal medicines (Bupleuri Radix and Ginseng Radix) affected the spontaneous lymphatic vasomotion and the lymph flow. Because the herbal medicines (Bupleuri Radix and Ginseng Radix) also affected lymphatic vasomotion with NO synthase inhibitor L-NAME, these medicines (Bupleuri Radix and Ginseng Radix) seem to affect the endothelial cells, that control lymphatic vessel activity.

S-59.

CROSSTALK BETWEEN HAEMOSTASIS AND INFLAMMATION: PLATELETS MODULATE THE ADHESION AND TRANSMIGRATION PROCESS OF MONOCYTES

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Introduction: The emigration of leukocytes from the circulation is essential for inflammatory and infectious reactions leading to SIRS, sepsis and organ dysfunction. The adhesion process to the endothelium as well as the transmigration of leukocytes are tightly regulated. In the circulation of patients with inflammatory vascular diseases associates of monocytes with platelets are found to be increased. The detailed mechanism involved in the extravasation process of monocytes with platelets is not yet understood. In this study we examined the influence of platelets on monocytic adhesion to a microvascular endothelial (HMEC-1) monolayer, monocytic transmigration and participating adhesive mechanisms, in vitro.
Methods: Monocytes, isolated from human buffy coats, were cultured for 1 day and incubated as single cells or in association with gelfiltered platelets with a monolayer of HMEC-1 for 30 min (adhesion assay) or for 8 h (transmigration assay). The adhesion assay was performed in fibronectin-coated 96-well cell culture plates with confluently grown HMEC-1. Adherent monocytes were quantified by myeloperoxidase-staining. A standard two chamber transwell-system with confluently grown HMEC-1 on fibronectin-coated transwell filters was used for transmigration studies. Migrated monocytes were identified by staining with anti-CD14-PE, platelets by staining with anti-CD42a-FITC and counted by flow cytometry.
Results: The number of adhered monocytes immobilised with platelets was up to 1.75-fold increased compared to single monocytes. Both, the firm interaction between single as well as platelet-bound monocytes and HMEC-1 could be inhibited significantly by functional blocking antibodies against ICAM-1, VCAM-1, E-selectin and CD11a, respectively. In contrast, the peptide RGDS or functional blocking antibodies against β3-integrins, P-selectin and P-selectin ligand-1 blocked only the adhesion of platelet-monocyte associates but not of single monocytes. Further, platelets associated with monocytes migrated directly through the HMEC-1 monolayer. In contrast to adhesion the migration rate of associates was diminished up to 60% compared to single monocytes. The monoclonal antibody against the cell binding domain of thrombospondin-1 (TSP-1), clone C6.7, inhibited up to 60% the transmigration of monocytes and associates, whereas monoclonal antibodies against CD47, a counter ligand of TSP-1 and signal-regulatory protein-alpha, blocked trafficking almost completely. Preincubation of the HMEC-1 monolayer with anti-CD47 clone B6H12 or anti-TSP-1 clone C6.7 reduced monocyte as well as associate migration significantly.
Discussion: By forming heterotypic associates platelets modulate directly the adhesion and transmigration process of monocytes. Therefore, platelets may be important actors in regulating the extravasation process of monocytes during inflammation. The adhesion of platelet-monocyte associates to microvascular endothelium may be mediated primarily through the interplay of P/E-selectin-PSGL-1 and Icam-1-β3-integrins. In contrast, transendothelial migration of associates seems to be regulated predominantly by CD47 through a TSP-1 dependent mechanism.

S-60.

BETA 2 ADRENERGIC BLOCKADE INHIBITS CEREBRAL HYPEREMIA AND REDUCES CEREBRAL CORTICAL OXYGEN TENSION FOLLOWING HEMODILUTION IN RATS.

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Introduction: Patients exposed to hemodilutional anemia demonstrate evidence of neurological injury, possibly due to anemia induced cerebral hypoxia[1,2]. Physiological adaptations to acute hemodilution include a characteristic increase in cerebral blood flow (CBF) to optimize cerebral oxygen delivery. Experimental studies suggest that increased CBF may be regulated by nitric oxide[3] released from perivascular neurons under the influence of β2 adrenergic stimulation[4]. The current study assessed whether systemic β2 adrenergic blockade impaired cerebral hyperemia and tissue oxygen tension ($P_{Br}O_2$) following hemodilution.
Methods: Isofluorane anesthetized and ventilated rats (50% oxygen) underwent tail artery and vein cannulation to monitor mean arterial blood pressure (MAP) and perform hemodilution. A combined oxygen sensitive microelectrode (ruthenium decay) and laser Doppler flow probe (OxyLite and OxyFlo, Oxford Optronix) was placed in the hippocampus to measure cerebral tissue $P_{Br}O_2$ and regional CBF. After establishing baseline measurements, rats received a specific β2 adrenergic blocker (ICI-118,551, Biomol Int. 10 $mg \cdot kg^{-1}$ iv), or vehicle, and a second baseline was established (n=6 rats/group). Hemodilution was then performed by simultaneously exchanging 50% of the estimated blood volume (30 $ml \cdot kg^{-1}$) with pentastarch over 10 minutes. Measurements were then continued for 60 minutes. Total hemoglobin concentrations (co-oximetry) and arterial blood gases (ABGs) were measured before and after hemodilution (Radiometer). $P_{Br}O_2$ and CBF measurements were normalized to the initial baseline measurements and relative changes assessed after hemodilution. Data was analyzed by ANOVA, students t-test and paired t-test (mean ± SD). Significance was assessed at $p<0.05$.
Results: No differences were measured between groups at baseline, before or after initiation of β2 blockade. Following hemodilution, there were no differences in heart rate (HR) (380 ± 31 vs 358 ± 29 $beat \cdot minute^{-1}$) or MAP (108 ± 11 vs 96 ± 7 mmHg) between β2 blocker and control groups. In the control group, CBF increased by 81 ± 14% following hemodilution ($p<0.001$) while the $P_{Br}O_2$ remained comparable to baseline (17.5 ± 7.3 mmHg). In the β2 blockade group, CBF only increased by half of the control value (43 ± 13%) and the $P_{Br}O_2$ decreased significantly relative to baseline (7.0 ± 2.2 mmHg)($p<0.05$). In both cases, the $P_{Br}O_2$ and CBF in the β2 blockade group decreased relative to their control values ($p<0.05$). Co-oximetry and ABG's data did not differ between groups.
Discussion: Following hemodilution, maximally increased CBF maintained cerebral cortical tissue oxygen tension in the control group. However, β2 blockade inhibited the post-hemodilutional increase in CBF and reduced cerebral cortical tissue oxygen tension. These data support the hypothesis that cerebral hyperemia is mediated by β2 adrenergic cerebral vasodilation and maintains cerebral tissue oxygen tension during hemodilution. (CAS, PSI support).
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S-61.

PROPOFOL ATTENUATES ENDOTOXIN-INDUCED LUNG INJURY IN RATS

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Introduction. Previously, we observed that propofol attenuates ischemia-reperfusion and oxidative lung injury in the isolated perfused rat lung. We also demonstrated that the uptake of anti-angiotensin-converting enzyme (ACE) monoclonal antibodies (mAb) by the lung reflects the amount of ACE in the lung vasculature, and that shedding of ACE from the lung endothelium is an early marker of acute lung injury. The aim of this study was to evaluate the effect of propofol on LPS endotoxin-induced acute lung injury in the rat (a model of septic shock) using the uptake of anti-ACE mAbs as markers of lung endothelial integrity.
Methods. Forty Sprague-Dawley rats received one of 4 treatments: vehicle control, propofol (10 mg/kg bolus), LPS alone (2 mg/kg), or propofol administered 1h before injection of LPS. 16h after LPS injection, rats were injected with I^{125}-labeled anti-ACE mAb. The accumulation of radiolabeled mAb in the lung was evaluated 1 h later. ACE activity in rat plasma and lung homogenates was determined by enzymatic assay. Lung/body weight ratio (LW/BW) was also estimated in each group as an index of lung edema. Direct effects of propofol on ACE expression in rat lung microvascular endothelial cells (RLMVEC) treated with LPS was also investigated.
Results. LPS produced endothelial cell injury and lung edema as indicated by: 1) an increase in plasma ACE activity, 2) a decrease in lung ACE activity, 3) decrease in ACE mAb uptake by the lung, 4) an increase in lung weight/body weight ratio. In control rats, anti-ACE mAbs 9B9, 1A2, 4H3, and 2E1 accumulated specifically in the lung after systemic injection. LPS injection induced a decrease in mAb uptake by the lung; mAb 1A2 showed the largest difference in lung uptake between control and LPS-treated rats. Pretreatment of rats with propofol prior to LPS injection significantly inhibited the increase in LW/BW ratio, increase in ACE activity in the blood, decrease of ACE activity in the lung, and decrease in anti-ACE mAb uptake in the lung. *In vitro* experiments indicate that propofol directly protects the endothelium from endotoxin and decreases ACE release from the cell surface induced by LPS. Propofol at 1 and 5 ug/ml diminished LPS-induced ACE release by 20 and 53% respectively.
Discussion. 1) Lung accumulation of anti-ACE mAbs was significantly reduced 16 hr after LPS treatment of rats, while another marker of endothelial dysfunction and acute lung injury (edema formation) was considerably less indicative, suggesting that anti-ACE mAb (1A2) lung uptake may be a sensitive probe for monitoring endothelial dysfunction and acute lung injury during sepsis.2) Propofol pretreatment prevented LPS-induced lung injury and endothelial dysfunciton in rats and ACE shedding from cultured RLMVEC.

S-62.

ROLE OF ENDOTHELIUM IN THE RESPONSE OF DIABETIC RAT PULMONARY ARTERY TO PHENYLEPHRINE

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Introduction: Little information is available concerning pulmonary vascular regulation following the development of diabetes. We investigated the response of diabetic rat pulmonary artery to the alpha adrenoreceptor agonist, phenylephrine, and the role of the endothelium in this response.
Methods: All procedures were approved by the Institutional Animal Care and Use Committee. Isolated rat pulmonary arterial rings with endothelium (E+) were obtained from normal rats and from diabetic rats 8 weeks following the intraperitoneal injection of streptozotocin (60 mg/kg). Plasma glucose levels were 468±12 mg/dl in the 8 w diabetics (normal; 101±2 mg/dl). The rings were suspended in modified Krebs-Ringer buffer for measurement of isometric tension. Cumulative phenylephrine dose-response (10^{-8}~10^{-4}M) relationships were measured in both normal and diabetic rats. The effects of inhibition of nitric oxide synthase (L-NAME: 10^{-4} M) and cyclooxygenase (indomethacin: 10^{-5} M) on the phenylephrine dose-response relationship were assessed in both control and diabetic E+ pulmonary arterial rings. Statistical analysis was performed using paired Student's *t* test. Changes reported below were significant at $P<0.05$. Values are means ± SEM.
Results: Phenylephrine caused dose-dependent pulmonary artery contraction in both normal and diabetic rats. The contractile response to phenylephrine was attenuated in 8w diabetic rats, causing a rightward shift ($LogEC_{50\ (normal)}$ = -6.68± 0.08 vs $LogEC_{50\ (diabetic)}$ = -6.15±0.05) in the phenylephrine concentration-response curve, and a decrease in the maximal contractile response (R_{max}=57±3%) compared with normal rats (R_{max}=85±3%). In normal rats, L-NAME caused a leftward shift ($LogEC_{50\ (L\text{-}NAME)}$ =-8.12±0.23) in the phenylephrine concentration-response curve, and increased R_{max} (131±2%). In diabetic rats, L-NAME significantly increased R_{max} (153±5%) and decreased the EC_{50} (-6.87±0.04). Indomethacin increased R_{max} (96±4%), but had no effect on the EC_{50} values in normal rats. In diabetic rats, indomethacin also increased R_{max} (84±5%) without a change in the EC_{50}.
Conclusion: Phenylephrine-induced contraction is attenuated in pulmonary artery of diabetic rats compared with normal rats. Inhibition of nitric oxide synthase significantly potentiates phenylephrine contraction in pulmonary artery from normal rats, and reverses the attenuated contractile response to phenylephrine in pulmonary artery from diabetic rats. Inhibition of cyclooxygenase potentiates phenylephrine contraction in pulmonary artery from diabetic rats to a greater extent than normal rats. These results suggest that endothelium-derived relaxing factors modulate the contractile response to phenylephrine in diabetic pulmonary artery to a greater extent than normal pulmonary artery, thereby attenuating the contractile response to this alpha adrenoreceptor agonist.

S-63.

SMALL TIDAL VOLUME VENTILATION PROTECTS LUNGS FROM LIVER ISCHEMIA/REPERFUSION INJURY IN RATS

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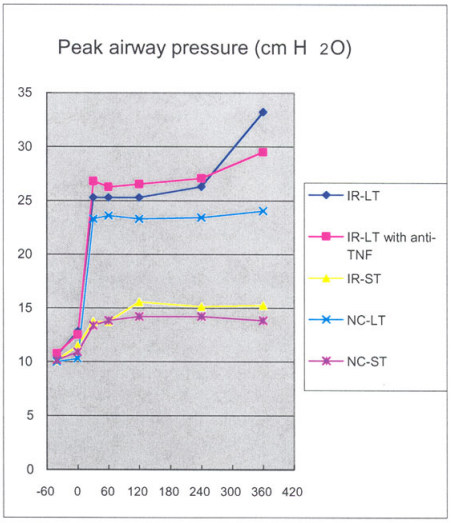
Introduction: Patients who underwent major surgery sometimes suffer acute lung injury (ALI) especially after ischemia/reperfusion of organs. Small tidal volume (V_T) ventilation had been shown to improve outcome of ALI patients. The goal of this study is to determine the utility of small V_T ventilation in preventing lung injury occuring from systemic inflammation following liver ischemia/reperfusion.
Methods: Anesthetized rats were mechanically ventilated through a tracheotomy with 6 ml/kg of V_T and ZEEP. Laparotomy was performed and total hepatic ischemia was produced by cross clamping of the hepatic artery and portal vein twice for 15 minutes with an interval of 5 minutes. After these procedures, rats were randomly assigned mechanical ventilation, either V_T 24 ml/kg, ZEEP (IR-LT) or V_T 6 ml/kg, PEEP 3 cm H_2O (IR-ST). Control animals that received laparotomy but not hepatic ischemia were also tested (NC-LT and NC-ST). Another set of rats received anti-tumor necrosis factor (TNF)-α antiserum just before hepatic ischemia; and was ventilated with large V_T after reperfusion. Arterial blood pressure and airway pressure were continuously monitored. F_IO_2 was set at 1.0 and ventilation frequency was adjusted to maintain $PaCO_2$ within 35-45 torr. Six hours after the assignment, rats were deeply anesthetized and lungs were harvested for broncho-alveolar lavage (BAL), wet to dry weight ratio (W/D), and histopathological examinations.
Results: There were decreases in blood pressure and base excess after reperfuion, more prominent in the IR-LT group. Peak airway pressure increased during large V_T ventilation after reperfusion (Fig. 1). The concentration of TNF-α in the circulation elevated transiently after the reperfusion regardless of the ventilation settings. Lung W/D and the concentration of TNF- α in BAL fluid were higher in the IR-LT group compared to that in the IR-ST group. Administration of anti-TNF-α antiserum prevented the increase in the concentration of TNF-α in the circulation and in BAL fluid, and prevented airway pressure elevation even with large V_T ventilation.
Discussion: The cross clamping of hepatic artery and portal vein caused systemic inflammation. A concomitant inflammation and injury of lungs occurred with large V_T ventilation. Either the control of inflammation by TNF-α neutralization or lung protective ventilation with small V_T prevented the lung injury. This study evidenced the complementary effect of systemic inflammation and large V_T ventilation on ventilator induced lung injury.



S-64.

INHIBITION OF ICAM-1 AMELIORATES NEUROLOGICAL AND HEPATIC DYSFUNCTION AFTER CARDIOPULMONARY RESUSCITATION IN MICE

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Introduction: Cardiac arrest and cardiopulmonary resuscitation (CPR) result in multi-organ damage due to global hypoxia, accompanied by massive recruitment of neutrophils in mice. Patients display all signs of a Systemic Inflammatory Response Syndrome (SIRS). Thus, inhibition of recruitment of neutrophils may serve as a potential tool to preserve organ function.
Methods: With approval of the Institutional Review Board, male swiss mice were subjected to cardiac arrest and resuscitation or sham surgery. Recruitment of neutrophils was quantified by imunnohistochemistry. To test neurological function, mice had to balance on bars of different width following CPR. Liver and kidney function were analysed by determing plasma ALT activity or creatinine levels. A group of mice received immunoneutralizing therapy with 100 µg anti-ICAM ip. Data were analysed with InStat ™ Software from Graphpad, using Kruskal-Wallis testing with consecutive Mann-Whithney U testing to identify differences between indivdual groups. Comparison of performance between groups in sensomotoric tests was done using the fischer's test. A p-value < 0.05 was considered significant.
Results: Functionall blockade of ICAM-1 with monoclonal antibodies immediately after ROSC leads to significantly reduced neutrophil recruitment to the kidney (11±2 vs. 39±22 [PMN/mm^2], aICAM vs. IgG, n=5/9, p<0.05) and the liver (32±8 vs. 87±23 [PMN/mm^2], aICAM vs. IgG, n=7/7, p<0.05), as determined 48 hours after ROSC. ALT-levels were also significantly decreased (22±2 vs. 53±11 [U/l], aICAM vs. IgG, n=5/7, p<0.05), while plasma creatinine did not change (0.19±0.07 vs. 0.16±0,02 [mg/dl], aICAM vs. IgG , n=6/11, p=NS. Neurological function was significantly improved two days after ROSC with ICAM-inhibition compared to control IgG-treatment. Nearly 80 % of mice treated with blocking ICAM antibodies were able to pass the balance test on a 1 cm beam after 1 d, indicating a recovery of neurological performance due to ICAM-blocking.
Discussion: Immunoneutralization of ICAM in CPR-mice after cardiac arrest of 5 min attenuates neutrophil-influx in the liver along with ALT-activity, while creatinine levels and neutrophil-influx in the kidney remained unchanged, indicating a functional recovery of the liver. Neurological outcome was significantly improved by ICAM-1 inhibition in vivo. Anti-inflammatory treatment may be useful to treat post-CPR-SIRS.

S-65.

NEGATIVE INOTROPIC EFFECTS OF C-TYPE NATRIURETIC PEPTIDE AND NITRIC OXIDE ARE ATTENATED IN PRESSURE-OVERLOAD-INDUCED VENTRICULAR HYPERTROPHY IN MICE

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Introduction: It has been shown that cardiac hypertrophy increased basal nitric oxide (NO) production[1] and atrial natriuretic peptide expression[2] in rats. However, the effects of NO[3] and natriuretic peptide[4] were attenuated in hypertrophic myocytes. We hypothesized that these changes were caused by alterations in cyclic GMP (cGMP) signal transduction pathway in cardiac hypertrophy. We tested this hypothesis in ventricular myocytes isolated from pressure-overload induced hypertrophic hearts in mice.
Methods: Ventricular hypertrophy was induced using aortic banding in mice over a 4-week period. Ventricular myocytes were isolated using collagenase from hypertrophic and age-matched mice Myocyte contraction was measured via a video edge detector (N=9). Myocytes were treated with S-nitroso-N-acetyl-penicillamine (SNAP, nitric oxide donor, $10^{-6}$and 10^{-5} M), C-type natriuretic peptide (CNP) (10^{-8} and 10^{-7} M), or Rp-8-[(4-Chlorophenyl)thio]-cGMPS Triethylamine (Rp, inhibitor of cGMP-dependent protein kinase, 5×10^{-6} M) followed by CNP (10^{-7} M) or SNAP (10^{-5}M). Guanylyl cyclase activities and cGMP-dependent protein phosphorylation were assessed in myocyte extracts (N=5). Protein electrophoresis was performed using SDS-polyacrylamide gel. ANOVA was used. A value of $p < 0.05$ was accepted as significant. Data were presented as Mean±S.E.M.
Results: The heart weight (wt) and heart wt-to-body wt ratio were increased in hypertrophic mice (237 ± 9 vs. control, 174 ± 11 mg; 10.6 ± 0.3 vs. control, 7.3 ± 0.2 mg/g). Basal percentage shortening (PCS) was similar in both groups (Fig). CNP or SNAP dose-dependently reduced PCS in both groups, but their effects were blunted in hypertrophic myocytes (15-18% vs control 32-37%). Maximal rate of shortening was depressed at basal level (control 59.5±2.2 vs. hypertrophic 49.4±2.9 μm/s) and both reagents had attenuated effects in hypertrophy (16-17% vs. control 25-35%). Addition of Rp blocked CNP or SNAP's effect in control myocytes (A) but not in hypertrophic myocytes (B) (Fig). Particulate and soluble guanylyl cyclase activities were not significantly changed in hypertrophy. The degree of cGMP stimulated protein phosphorylation was less in the hypertrophic myocytes compared with controls.
Discussion: The data suggest that in hypertrophic mice, diminished effects of NO or CNP on myocyte contraction are not due to changes in guanylyl cyclase but due to decreased cyclic GMP-dependant protein kinase activities.
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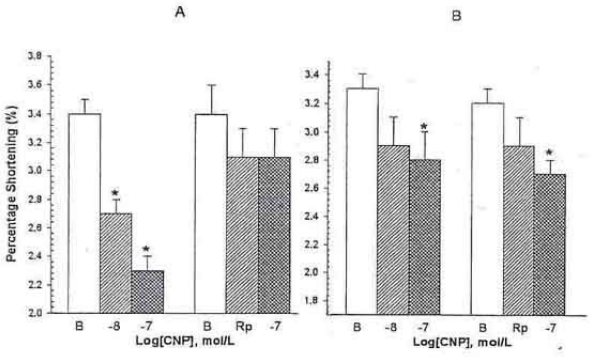

S-66.

NORMOVOLEMIC RESUSCITATION WITH HEMOGLOBIN VESICLE SOLUTION IN ANESTHETIZED RABBIT ACUTE HEMORRHAGIC SHOCK

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Introduction: Extracellular fluid replacement, plasma substitute and albumin, and transfusion of red blood cell or erythrocyte substitute are administered for supplementation of blood volume and recovery of O2 supply at resuscitation from hemorrhagic shock. Blood type and cross matching, and side effects of transfusion, such as Graft versus host disease, could be avoided if artificial oxygen carrier will be used. Hemoglobin-vesicle (HbV) has been developed as oxygen carrier with a liposome encapsulated hemoglobin. HbV solution has less effect of vasoconstriction than the conjugated or polymerized hemoglobins (1). HbV also has no colloid osmotic pressure, and the efficacy of blood volume depend on its solvent. Aim of the study was to evaluate the effects of hemodynamics, tissue oxygenation, blood osmotic pressure and blood volume after isovolemic resuscitation using HbV suspended in 5 g/dL recombinant human serum albumin (rHSA) in acute hemorrhagic shock model.
Methods: Twenty-one anesthetized, mechanically ventilated male rabbits (average weight 2.34 kg) were suffered to hemorrhagic shock by blood withdrawal to mean arterial pressure (MAP) of 30 to 35 mmHg in 15 min and maintained 30 min. Animals were resuscitated by isovolemic HbV/rHSA, rHSA or Ringer's lactated solution (RL), and then observed until 2 hours. Central hemodynamics, blood and tissues (brain, renal, hepatic, and muscle) PO2, blood osmotic pressure, and total blood volume were measured.
Results: Resuscitation using HbV/rHSA and rHSA improved central hemodynamics, base excess, serum lactate level, cardiac index, blood volume and osmotic pressure at two hours after resuscitation, while no such beneficial effect was observed when animals were resuscitated with RL. Serum lactate level and brain PO2 were improved immediate after resuscitation in HbV/rHSA group. O2 consumption in HbV/rHSA group was higher than the other groups.
Discussion: HbV had less effect of vasoconstriction and hypertension, and did not impaired the cordiac output. The total blood volume in vessel was not according to administration of HbV, and the solvent such as albumin maintained the blood volume within 2 hours after resuscitation. Increased O2 delivery lead to recovery of lactate level, base excess and tissue oxygenation immediately. Immediately improvement of tissue oxygemation after resuscitation may reduce the complication such as organ dysfunction or sepsis. Coagulopathy might be occurred in hemorrhagic shock, however the animals had no sign of bleeding in this study. The combination of HbV with rHSA provides immediately improvements in cardiac output, brain and renal PO2, serum lactate level, and base excess, suggesting a potential benefit for the initial management of controlled massive bleeding.
Acknowlegdement: This research was supported by a Health Science Research Grant (Reseach on Pharmaceutical and Medical Safety, Artificial Blood Project), Ministry of Health, Labour and Welfare, Japan.
Reference:
(1) Am J Physiol Heart Circ Physiol 279: H908-H915, 2000.

S-67.

DROPERIDOL DECREASES INTRACELLULAR PH AND STIMULATES NITRIC OXIDE PRODUCTION IN RAT CARDIOMYOCYTES

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Introduction: We previously demonstrated that droperidol attenuates cardiomyocyte contractility via a decrease in intracellular free Ca^{2+} concentration ($[Ca^{2+}]_i$) and myofilament Ca^{2+} sensitivity[1], however the cellular mechanisms responsible for these effects are not known. Our objective was to investigate the effect of droperidol on cellular mechanisms that regulate $[Ca^{2+}]_i$ and myofilament Ca^{2+} sensitivity in freshly isolated rat ventricular myocytes.
Methods: Freshly isolated myocytes were obtained from adult rat hearts. Measurement of intracellular pH (pH_i) with BCECF or $[Ca^{2+}]_i$ with fura-2 and cell length (video edge detection) was performed simultaneously in individual myocytes on the stage of an inverted fluorescence microscope in a temperature-regulated bath. Nitric oxide (NO) production was measured in suspensions of cardiomyocytes using an ELISA kit which measures total nitrate/nitrite production. Action potentials from individual cardiomyocytes were recorded using the whole cell patch clamp technique. Statistical analysis was performed using analysis of variance and Bonferroni post hoc test with a significance level set at $p < 0.05$. Values are means ± SD.
Results: Baseline pH_i was 7.2 ± 0.04. Droperidol (0.1 and 1 μM) caused a concentration- and time-dependent decrease in pH_i of 0.07 ± 0.02 and 0.13 ± 0.04, respectively. The decrease in pH_i was accompanied by an increase in resting cell length from 136 ± 3 μm to 140 ± 2 μm. Caffeine-induced release of Ca^{2+} from the sarcoplasmic reticulum (SR) was reduced by 22 ± 5% in the presence of droperidol (1 μM), however the fractional release of Ca^{2+} from the SR was no different than that observed in the absence of droperidol. Droperidol (1 μM) attenuated the KCl-induced (30 mM) increase in $[Ca^{2+}]_i$ by 27 ± 5%. Droperidol (1 μM) stimulated a 167 ± 18% increase in NO which was completely blocked by the nitric oxide synthase inhibitor, L-NAME (10 μM). Droperidol (1 μM) had no effect on action potential duration (APD_{90}; 57 ± 4 msec control vs. 59 ± 5 msec droperidol).
Discussion: These results demonstrate that the cellular mechanism likely responsible for the droperidol-induced decrease in $[Ca^{2+}]_i$ is a direct inhibitory effect of droperidol on the L-type Ca^{2+} channel. The decrease in SR Ca^{2+} release is secondary to the inhibitory effects of droperidol on the L-type Ca^{2+} channel. These results also demonstrate that the droperidol-induced decrease in myofilament Ca^{2+} sensitivity is likely mediated by a combination of elevated NO levels and cellular acidosis.
References:
1. Anesthesiology 99:A685, 2003.

S-68.

PROTECTIVE EFFECT OF KETAMINE ON ENDOTOXIN-INDUCED RAT LUNG INJURY ASSESSED BY LUNG UPTAKE OF ANTI-ACE ANTIBODY

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Introduction. The effect of anesthetics on basal and pathologically compromised lung microvascular endothelium has not been extensively examined, although various anesthetic agents and treatment regimens are currently used on critically ill septic patients with acute lung injury. Monoclonal antibodies (mAb) 9B9 to angiotensin-converting enzyme (ACE) preferentially accumulate in the lung. The decrease in the mAb 9B9 lung uptake represents a sensitive and earlier marker of lung endothelial cell injury. In the present study, we examined whether ketamine attenuates acute lung injury induced by intravenous injection of endotoxin (LPS-lipopolysaccaride), a reproducible model of septic shock.
Methods. Thirty six Sprague-Dawley rats received one of 3 treatments-control, LPS (1 or 4 mg/kg), in the presence or absence of ketamine (100 mg/kg) administered 1h before injection of LPS. 16h after LPS injection, rats were injected with I125-labeled mAb 9B9 and I131-labeled albumin. After 1 hr radioactivity in different organs (a reflection of mAb 9B9 distribution or lung permeability, respectively) was evaluated. ACE activity in rat plasma and lung homogenates was determined by enzymatic assay.
Results. LPS produced endothelial cell injury and lung edema as indicated by: 1) an increase in plasma ACE activity, 2) a decrease in lung ACE activity and mAb 9B9 binding, and 3) an increase in lung weight/body weight ratio. In non-LPS treated rats, anti-ACE mAb 9B9 accumulated specifically in the lung after systemic injection. LPS injection induced a dose-dependent decrease in the uptake of 125I-9B9 by the lung - from 13.5 % to 5.9 % of the injected dose per gram of tissue following treatment with 4 mg/kg LPS, while accumulation of a non-specific 125I-labeled IgG or 131I-albumin increased in the lung indicating an increase microvascular permeability and edema formation. Anti-ACE antibody distribution in other organs and its blood levels were similar to non-LPS treated control animals. Pretreatment of rats with 100 mg/kg ketamine prior to LPS injection significantly inhibited the increase in LW/BW ratio, increase in ACE activity in the blood, and decrease in 9B9 uptake in the lung.
Discussion. 1) Lung accumulation of anti-ACE mAb 9B9 was significantly reduced 16 hr after LPS treatment of rats, while other markers endothelial dysfunction and acute lung injury (edema formation, pulmonary uptake of serum albumin) were considerably less indicative, suggesting mAb 9B9 may be a sensitive probe for monitoring endothelial dysfunction and acute lung injury during sepsis. 2) Ketamine pretreatment had a protective effect on LPS-induced lung injury in rats. 3) Measurement of plasma and lung ACE activity or anti-ACE mAb binding in patients with septic shock may be useful for estimating the degree of lung injury. For example, gamma scintography of radiolabeled anti-ACE mAb in septic patients could be used clinically for early detection of potentially fatal pulmonary microvascular injury.

S-69.

EFFECT OF INTRAVENOUS ANESTHETICS ON CANINE ACETYLCHOLINE-MEDIATED CONTRACTION IN PULMONARY VENOUS SMOOTH MUSCLE

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Introduction: Pulmonary veins (PV) are a primary site for entry of vagal nerves into the left atrium. Pulmonary venous constriction is involved in pulmonary edema formation in congestive heart failure, as well as in high altitude pulmonary edema. In the present study, we investigated the extent and mechanism of action by which the intravenous anesthetics, ketamine, thiopental and etomidate, alter the PV smooth muscle response to the parasympathetic neurotransmitter, acetylcholine (ACh).
Methods: All procedures were approved by the Institutional Animal Care and Use Committee. Isolated pulmonary venous rings without endothelium (E-) were suspended in modified Krebs-Ringer buffer for measurement of isometric tension. Cumulative ACh concentration-response (10^{-8}~10^{-3} M) relationships were measured. The effects of ketamine (10^{-5}~10^{-3} M), thiopental (10^{-6}~10^{-4}M) and etomidate (10^{-6}~10^{-4}M) on the ACh dose-response relationship were studied. The effects of inhibiting protein kinase C (BIS1; 3×10^{-6} M) on ketamine (10^{-4} M) or etomidate (10^{-5} M) -induced changes in ACh contraction were also assessed. Statistical analysis was performed using analysis of variance and LSD, with $P<0.05$ considered significant. Values are mean ± SEM.
Results: ACh caused dose-dependent contraction in E- PV rings. The maximum contractile response (R_{max}) to ACh was 163 ± 7% ($logEC_{50}$ = -5.63 ± 0.11) of that obtained with 60 mM KCl. Thiopental (10^{-6}-10^{-4}M) had no effect on the ACh concentration-response relationship. Ketamine attenuated ACh contraction in a dose-dependent manner. For example, ketamine (10^{-4} M) caused a rightward shift in the ACh concentration-response relationship and decreased R_{max} from 160 ± 8% to 119± 2%. Etomidate (10^{-6} M and 10^{-5} M) potentiated ACh contraction, whereas etomidate (10^{-4} M) attenuated ACh contraction. BIS1 alone attenuated ACh contraction. The etomidate-induced attenuation in ACh contraction was abolished following BIS1 (47 ± 8% vs 43 ± 4%), whereas the ketamine-induced attenuation in ACh contraction was still observed following BIS1 (-5.46 ± 0.06 vs -5.21 ± 0.09).
Discussion: ACh caused contraction in pulmonary venous smooth muscle. Thiopental had no effect on ACh contraction. Clinical concentrations of ketamine attenuated ACh contraction, and this effect was independent of the protein kinase C pathway. Clinical concentrations of etomidate potentiated ACh contraction by activating the protein kinase C pathway, whereas a supraclinical concentration of etomidate attenuated ACh contraction in pulmonary venous smooth muscle.

S-70.

ISCHEMIA-INDUCED INTERSTITIAL MYOGLOBIN RELEASE IS GREATLY ACCELERATED BY REPERFUSION IN RABBITS

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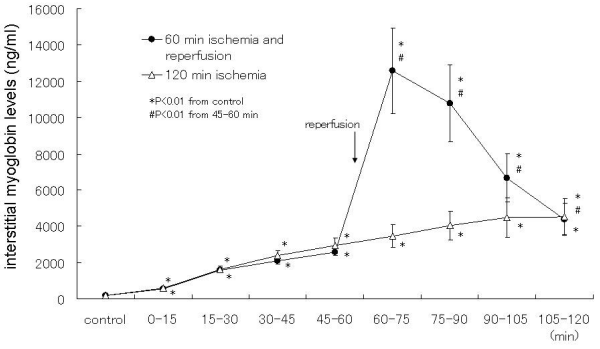
Introduction: Myoglobin is one of earliest biochemical markers in myocardial cell injury. In situ studies on myoglobin efflux in the cardiac ischemic region have been limited because of inherent sample collection problems in the ischemic region. Recently, cardiac dialysis technique has offered a powerful method for monitoring myocardial interstitial levels of low molecular compounds in the cardiac ischemic region. In the present study, we extended the molecular target to high molecular peptides and proteins by microdialysis probes with a high molecular mass cut-off and tried to monitor myocardial interstitial myoglobin levels.
Methods: We implanted a dialysis probe in the left ventricular free wall in anesthetized rabbits. The main coronary artery was occluded for 60 or 120 min. We examined the effects of myocardial ischemia and reperfusion on myocardial interstitial myoglobin levels (n=6-6).
Results: The interstitial myoglobin increased within 15 min-ischemia and furthermore progressively increased during 120 min-ischemia. After 60 min ischemia, reperfusion markedly accelerated interstitial myoglobin release from myocardial ischemic region. The interstitial myoglobin level at 0-15 min of reperfusion was 5-fold higher than that of 45-60 min of coronary occlusion. Reperfusion induced-increase in interstitial myoglobin accompanied with marked increases in blood myoglobin levels
Conclusion: Although sixty-minutes coronary occlusion induced interstitial myoglobin release, reperfusion markedly accelerated interstitial myoglobin release from myocardial ischemic region. This study suggests that massive disruption of myocardial membrane is mainly caused by reperfusion rather than myocardial ischemia.



S-71.

EFFECTS OF HEMODILUTION ON MICROVASCULAR HEMODYNAMICS IN ISOLATED RAT LUNGS

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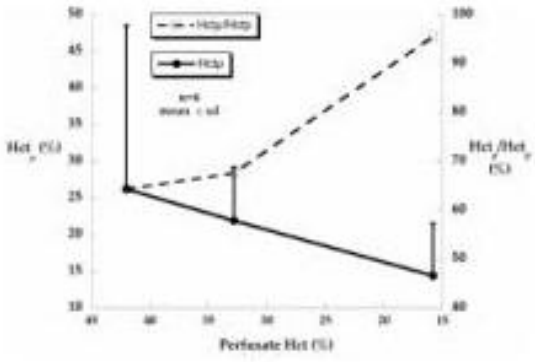
Introduction: Anemia has salutary effects on pulmonary gas exchange, which may be due to effects at the microcirculatory level, including capillary recruitment and reduced heterogeneity of capillary transit times and microvascular Hct (Hctμ). However, the effects of anemia on pulmonary microcirculatory hemodynamics are unknown. We investigated the effects of hemodilution on pulmonary microvascular hemodynamics in isolated, perfused rat lungs using intravital microscopy. Methods: A single lung was perfused with blood mixed with buffer, and the microcirculation was imaged with a Zeiss AXIOTECH vario 100 HD microscope with a 10X lens linked to a video camera with zoom. The lung was visualized either under reflected light (dark field) to visualize structural components of the lung or with a rhodamine filter with excitation and emission wavelengths of 546 and 590 nm, respectively, to visualize fluorescent-labeled cells. RBCs were labeled with fluorescent dye and added to the perfusate to achieve a labeled fraction of 1-2%. Microvascular hemodynamics, including Hctμ, red blood cell (RBC) flux, % perfused capillaries, capillary transit time, and the coefficient of variation of transit time (CVTT) were measured and calculated from video images at three Hcts: High (~45%); Middle (~30%), and Low (~15%), and at a range of perfusate flows from 3-16 mls/min. Results: Six total experiments were performed, although only two included data at High Hct. Hemodilution resulted in a fall in Hctμ at all flows, although the ratio of Hctμ to perfusate Hct (Hctμ/Hctp) increased as illustrated in Figure 1. Although capillary transit time did not change significantly with hemodilution, the heterogeneity of transit times (CVTT) decreased. The % of perfused capillaries fell with hemodilution. Discussion: Hctμ falls with hemodilution, but falls less than expected compared to central Hct. Hemodilution results in a reduction in the heterogeneity of capillary transit times. The resulting more uniform capillary Hct may be responsible for observations of improved pulmonary gas exchange with anemia. The mechanisms for the above observations may be in part due to changes in viscosity with hemodilution, but may also be related to the interactions of RBCs with various mediators including nitric oxide and purines.

Supported by the IARS Frontiers in Anesthesia Research Award.



Cardiothoracic & Vascular - Clinical

S-72.

ASSESSMENT OF A PREOPERATIVE BETA-BLOCKER SCREENING SCORE

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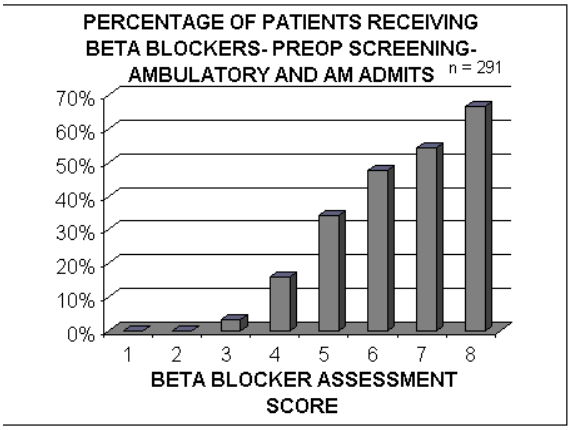
Introduction: Perioperative beta-blocker (BB) protocols are being developed at a number of institutions. BB therapy is indicated for patients with coronary artery disease (CAD) undergoing major surgery. Recommendations for patients with only risk factors for CAD or those with CAD undergoing less invasive procedures are less clear. As part of the development of a perioperative BB protocol, we sought to test the utility of a BB screening score that combines elements of patient medical risk and the surgical invasiveness of the procedure. We also assessed the effect of establishing a threshold screening score at which referral for BB will be implemented.
Methods: The preoperative charts of 291 outpatients (both ambulatory and AM admission patients) and 100 inpatients were screened for current BB utilization. A BB Assessment Score (BBAS) for each patient calculated by adding a medical risk score to a surgical risk score. The medical risk score was determined by adding number of the following entities: previous myocardial infarction, angina, congestive heart failure, cerebral vascular accident, diabetes, hypertension, smoking, age > 70, and vascular surgery. The surgical risk score was adapted from the Johns Hopkins Classification of Surgical Risk (1 = minimally invasive, 2 = minimally to moderately invasive, 3 = moderately to significantly invasive, 4 = highly invasive, 5 = critical risk to patient). The proportion of patients on BB therapy at each BBAS was determined. The possible threshold levels of BBAS for institution of BB therapy were investigated by determining the number of interventions required at each score.
Results: In both the ambulatory (figure) and the inpatients (data not shown) the BBAS correlated with the percentage of patients receiving BB therapy at time of screening. In both groups it was determined that establishing a threshold BBAS of six would require intervention in 7% of preoperative patients.
Discussion: A score that combines medical with surgical risk correlated with current BB use in preoperative patients at time of screening. We intend to require referral for the institution of BB therapy in all patients with a BBAS of six or greater. We expect this process to affect 7% of our surgical population. We will amend this practice if future evidence-based information finds that the risk-benefit ratio of BB therapy is significantly different from our threshold.



S-73.

SURGEONS β-BLOCKADE: ANESTHESIA INFORMATION SYSTEM DEMONSTRATES NEED FOR IMPROVEMENT

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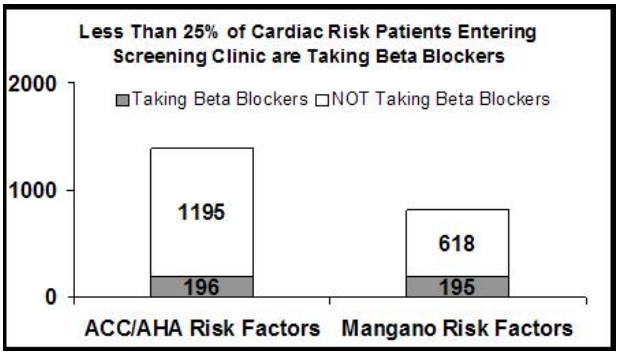
Introduction: Clinicians often fail to incorporate evidence-based medicine recommendations into their daily practice. Recommendations for use of perioperative β-blockers are clear, accepted, and not perfectly followed. A study of anesthesiologists indicated a greater than 95% awareness of these guidelines, although only 57% of these physicians prescribed β-blockers frequently or usually[1]. We evaluated a baseline level of how well our surgeons were following perioperative β-blocker guidelines based on two criteria.[2,3]
Methods: Data were collected using eVal, the PICIS (Wakefield, MA) electronic preoperative screening application. Custom data queries were run using Structured Query Language (SQL) on medical information collected from all patients presenting to a large academic tertiary care hospital's preoperative screening clinic from Nov. 03 - Feb. 04. An older (simplified) set of criteria[3] (current CAD or at least 2 risk factors of: age>65, hypertension, diabetes, current smoker, cholesterol > 240), as well as the more recently described ACC/AHA set of criteria[2] were used to determine who should be taking β-blockers perioperatively.
Results: A total of 3,902 patients were seen in the preoperative screening clinic during this study out of which 1,391 (35%) met the ACC/AHA criteria for cardiac risk factors and 813 (20%) met the older set of criteria. Of those who could be receiving perioperative β-blockers, only 14% (196/1391) and 24% (195/813) were actually receiving them when arriving to the preoperative screening clinic based on the ACC/AHA and older guidelines, respectively.
Discussion: Only a small proportion of at-risk patients are taking β-blockers preoperatively at this institution. We believe this is generalizable to other medical centers. Use of an automated anesthesia preoperative application allows for identification of individuals who would benefit from additional therapy, and, with further programming, could markedly impact the ability of physicians to adhere to established practice guidelines. Our long term goal is to use an anesthesia information system to automatically identify real-time errors of omission and to assist clinicians in providing recommended therapy. Compliance with recommended criteria for perioperative blockade administration, despite wide dissemination of the 2002 ACC/AHA guidelines, is poor. Only 24% of patients at risk for cardiac events were receiving β-blockers when seen in the screening clinic.

References:
1.Anesth Analg 2003;96:1558-1565.
2.Anesth Analg 2002;94:1052-64.
3.N Engl J Med 1996;335:1713-21.



S-74.

PERI-ANESTHETIC MYOCARDIAL INFARCTION (MI), CARDIAC EVALUATION, AND ELECTIVE LUMBAR SPINE SURGERY UNDER PERIOPERATIVE BETA-BLOCKADE ON THE 4TH DAY POST-MI: A CASE REPORT AND DISCUSSION.

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Introduction: While perioperative myocardial infarction (MI) and recommendations for post-MI intervals before elective surgery are well described, peri-anesthetic MI, and elective surgery within a week of MI is not.1 We present the clinical course of a 57-year-old woman developing MI after anesthetic induction/no surgery, cardiac evaluation confirming acute infarction, and successful lumbar spine surgery under perioperative beta-blockade 4 days later.
Case Report: A 57-year-old woman presented for microdiscectomy, with a medical history significant for 1-PPD smoking, hypertension, hyperlipidemia, and gastroesophageal reflux disease (GERD). Upon rapid sequence induction of general anesthesia, development of hypertension, ventricular arrhythmia, and marked ST-segment elevation, precluded surgery before evaluation for MI. While asymptomatic and with the ECG unchanged immediately post-operatively, within 24 hours, significantly elevated Troponin I level and ECG T-wave inversion in leads II, III, AVF and V3-6, confirmed MI. Cardiac evaluation included left heart catheterization (indicating no significant coronary disease and preserved ejection fraction). Subsequent adenosine thallium stress test confirmed a fixed antero-apical defect. Cardiac monitoring excluded new arrhythmia. Cardiology consultants recommended proceeding with surgery without further evaluation at surgeon's discretion. It was suggested that the ischemia may have been due to vasospasm, with symptoms of GERD as clinical signs. She was provided information and discussion regarding preference to delay surgery after MI, but strongly desired to proceed due to ongoing lumbar pain.
This patient underwent repeat anesthetic on the 4th day post MI, after inducing low-dose aspirin therapy and introducing maximal perioperative beta-blockade (PBB) immediately prior to induction (metoprolol and esmolol intravenous injection). Sluggish cardiac output was evident at induction. Continuously transduced arterial pressure was supported with phenylephrine infusion under isoflurane and 50% nitrous oxide anesthesia. She was discharged the next day home after uneventful recovery.
Discussion: The rapid evaluation of this patient and effective preparation disclosed multiple findings post-NSTEMI conducive to proceeding, yielded significant financial and personal benefit to the patient. Post-induction hemodynamics may have been significantly below those previously documented. The significant PBB administered and the individual natural progression of post MI healing may make it preferable to have specific hemodynamic data immediately prior to surgery. As the introduction of general anesthesia may further compromise hemodynamics effected by MI progression and increased PBB, invasive intraoperative monitoring may well be beneficial to individual outcome and understanding of this entity. Specific study of patients undergoing surgery shortly after MI is necessary to define risk groups and respective safety. This single positive outcome, in a patient undergoing bloodless surgery after limited compromise by NSTEMI raises multiple questions about current guidelines regarding PBB, post-MI intervals prior to elective surgery, when to evaluate cardiac function and necessary monitors for early surgery post infarction.2
References:
1) British Journal of Anaesthesia 93:9-20, 2004
2) Anesthesiology 101:801-806, 2004

S-75.

THE EFFECTS OF LANDIOLOL, A SHORT-ACTING, SELECTIVE BETA-1 BLOCKER, ON CARDIAC FUNCTION IN PATIENTS UNDERGOING OFF-PUMP CORONARY ARTERY BYPASS SURGERY

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Introduction: Tachycardia is known to be associated with myocardial ischemia. During off-pump coronary artery bypass surgery (OPCAB), it is important to treat tachycardia, but sometimes difficult to maintain cardiac function and blood pressure. Landiolol, a short-acting, selective beta-1 blocker, is reported to be effective in decreasing heart rate with less negative inotropic action than esmolol (1). We examined the effects of landiolol on cardiac function in patients undergoing OPCAB.
Method: The study subjects were 12 patients undergoing OPCAB, from whom informed consent had been obtained. Anesthesia was induced with midazolam (0.05-0.1 mg/kg) and fentanyl (2-4 μg/kg), and maintained with isoflurane (0.5-1.5 %). The study was performed during the harvest of the left internal thoracic artery graft. After hemodynamic stabilization, if the patient's heart rate was over 80 bpm for more than 10 minutes, landiolol was administered (0.06 mg/kg/min) until the heart rate was reduced by 15-20 %. Hemodynamic data were collected before the administration of landiolol and at 0, 5, 10 and 15 minutes after the withdrawal of landiolol. The parameters used in this study were heart rate (HR), blood pressure (BP), pulmonary artery pressure (PAP), pulmonary artery occlusion pressure (PAOP), cardiac index (CI), stroke volume index (SVI), ejection fraction (EF), peak E and A velocity and deceleration time of the peak E wave (DT). PAP, PAOP and CI were measured with a pulmonary artery catheter, and EF, peak E and A velocity and DT were measured with transesophageal echocardiography (TEE). The data were expressed by mean±SD, and were analyzed by ANOVA and Fisher's PLSD test. $P<0.05$ was considered statistically significant.

Results: Landiolol was administered for 5±2 minutes (0.3±0.1 mg/kg), and no bradycardia or hypotension requiring treatment was observed. The data are shown in the table.

	control	after administration of landiolol			
		0 min	5 min	10 min	15 min
HR (bpm)	84 ± 5	69 ± 5*	71 ± 4*	69 ± 5*	70 ± 5*
mean BP (mmHg)	89 ± 10	86 ± 13	86 ± 11	88 ± 11	87 ± 11
PAOP (mmHg)	11 ± 3	10 ± 3	11 ± 3	11 ± 2	10 ± 1
CI (l/min/m2)	2.9 ± 0.4	2.6 ± 0.5*	2.5 ± 0.6*	2.7 ± 0.5	2.7 ± 0.5
SVI (ml/m2)	35 ± 4	38 ± 7	36 ± 9	39 ± 8	39 ± 8
EF (%)	58 ± 10	59 ± 9	59 ± 10	61 ± 8	60 ± 9
E/A	1.1 ± 0.3	1.2 ± 0.2	1.2 ± 0.3	1.2 ± 0.2	1.2 ± 0.3
DT (msec)	166 ± 25	182 ± 35	175 ± 26	172 ± 19	174 ± 25

*$P<0.05$ vs. control

Discussion: Following the administration of landiolol, the mean heart rate reduction was 18%. The mean blood pressure remained unchanged throughout the study. The SVI did not change, and it was considered that the CI decreased with the reduction in heart rate. The echocardiographic data showed that systolic and diastolic cardiac function was maintained. Landiolol was able to reduce heart rate with little negative inotropic action, and is safe and effective in decreasing heart rate in patients undergoing OPCAB.
Reference:
(1) Can J Anaesth 2001;48:985-9

S-76.

EFFECTS OF LANDIOLOL HYDROCHLORIDE, ULTRA-SHORT-ACTING, HIGHLY CARDIOSELECTIVE BETA-BLOCKER, ON HEMODYNAMICS IN PATIENTS WHO UNDERWENT CORONARY ARTERY BYPASS GRAFTING

AUTHORS: **K. Iwasawa**, H. Nakagawa, M. Katou, S. Ide, M. Nishizawa;
AFFILIATION: Nagano Red-Cross Hospital, Nagano, Japan.

Introduction: Landiolol hydrochloride is highly cardioselective beta-blocker which has rapid onset and short duration of activity (1). The purpose of this study was to evaluate landiolol hydrochloride on cardiohemodynamics in patients who underwent coronary artery bypass grafting (CABG).
Methods: In 12 patients, heart rate (HR), mean arterial pressure (MAP), mean pulmonary arterial pressure (MPAP), central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), and cardiac output were measured. Anesthesia was induced with midazolam, fentanyl and vecuronium, and maintained with sevoflurane and fentanyl. During preparation of the internal thoratic artery, landiolol hydrochloride was administered at the rate of 0.125mg/kg/min for 1min followed by 0.04mg/kg/min for 30min. Hemodynamic measurements were obtained before and at every 5 min after administration of landiolol hydrochloride. Cardiac index (CI), stroke volume index (SVI), systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR) were calculated from the results. ANOVA followed by Dunnett's procedure was used for statistical analysis. *P<0.05 was considered statistically significant for control.
Results: HR significantly decreased from 72.8±19.4 to 58±10.8* beats/min in 5 min. MAP and CI significantly decreased from 88.4±12.8 to 69.5±4.5* mmHg and from 3.0±0.9 to 2.0±0.8* l/min/m^2 respectively, however, SVI was not changed. No significant changes in MPAP, CVP, PCWP SVR and PVR occurred.
Discussion: These results suggest that landiolol hydrochloride possesses rapid onset of negative chronotropic action without reduction of SVI. Landiolol hydrochloride doesn't affect both SVR and PVR because of high cardioselectivity. The observed decrease in MAP and CI remain within safety margins for the patients. Landiolol hydrochloride can be useful for CABG surgery to control HR.
References:
(1) Chem Pharm Bull 40,1462-9,1992

S-77.

THE EFFECT OF LANDIOLOL ON HEMODYNAMIC RESPONSES FOLLOWING ENDOTRACHEAL EXTUBATION

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[Background]
Tracheal extubation often causes tachycardia and hypertension. These hemodynamic changes increase oxygen demand and may cause the severe complications in patients with coronary arterial disease. Many drugs have been used to attenuate these hemodynamic changes.(1, 2) However, most of drugs need to administer before extubation because of their relatively slower onset. In this study, we examined the effect of landiolol, an ultrashort-acting cardioselective beta1-adrenoceptor blocker, on hemodynamic changes following endotracheal extubation.
[Methods]
After obtaining institutional approval and informed consent from all patients, we studied 30 patients undergoing minor orthopedic surgery under general anesthesia. The patients were randomly allocated into three groups: saline group (control) (n=10), Lan 0.1 group (n=10) landiolol 0.1 mg/kg, and Lan 0.2 group (n=10) landiolol 0.2 mg/kg. Anesthesia was induced with propofol (0.2 mg/kg) and vecuronium (0.1 mg/kg), and maintained with 2% sevoflurane plus 50% nitrous oxide. At the completion of surgery, sevoflurane and nitrous oxide were discontinued. We also began to measure heart rate (HR) and blood pressure (BP) every minute. We waited until the patients could breathe spontaneously and open eyes. After that, we administrated each drug intravenously and simultaneously extubated with tracheal suction. Oropharyngeal secretions were aspirated just before extubation. Immediately after extubation, 100% oxygen was given via a face mask. Five minites after extubation, we reversed muscle relaxant. All data were expressed as means ± SD. Differences between groups and from the baseline value were analyzed using unpaired t-test and repeated measures ANOVA, respectively. P < 0.05 was taken as significant.
[Results]
HR and mean BP (MBP) significantly increased in response to extubation, and no differences were found among the three groups. In the control group, the increase in HR sustained for 5 minutes after extubation. In contrast, the HR decreased to the baseline level 2 minutes after extubation in the Lan 0.1 and Lan 0.2 groups. There was no significant difference in deceases in the HR between the Lan 0.1 and Lan 0.2 groups. There were no differences in changes in MBP among the three groups.
[Conclusion]
Landilol rapidly restores the increases in HR following endotracheal extubation. Our present results indicate that landiolol 0.1 mg/kg was appropriate for treatment of tachycardia following endotracheal extubation.
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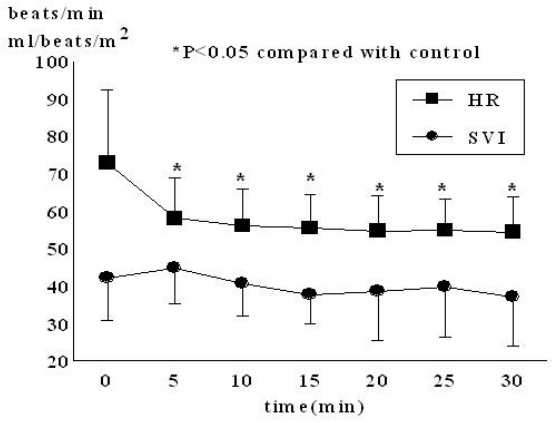

S-78.

LONG-TERM SURVIVAL FOLLOWING CARDIAC ARREST DURING CORONARY ANGIOGRAPHY

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Introduction: Patients undergoing coronary angiography constitute a high-risk population for experiencing cardiac arrest (CA). It is unknown whether CA occurring during coronary angiography is associated with a higher mortality after controlling for co-morbidities. We sought to determine the incidence of CA during coronary angiography and compare long-term survival of this group with that of a control population who did not experience CA during angiography.
Methods: We reviewed medical records of all patients who experienced CA during anesthesia-attended coronary angiography between January 1, 1990 and December 31, 2000, and survived hospitalization (n = 64). We compared long-term survival to that of a case-control population selected from the Mayo Clinic Coronary Angiography Registry who did not experience CA during angiography and survived hospitalization. Controls were matched in a 2:1 fashion (n = 128) for age (+/- 5 years), gender, date of procedure (+/- 1 year) and emergency status. Long-term survival was calculated from the date of catheterization to the last follow-up date or last date known to be alive. Survival was compared between groups and with the general Minnesota population, matched for age and sex, using a log-rank test. Percent survival was estimated at multiple time points using the Kaplan-Meier method. A Cox proportional hazards model was developed to estimate the relative risk (RR) of mortality in the study group versus the control group. An adjusted RR was estimated after including potential confounders such as co-morbidities (hypertension, congestive heart failure, prior myocardial infarction, prior coronary intervention) and procedure-related factors (diagnostic angiography, angioplasty +/- stent placement). All analyses were performed using SAS Software Release 8.2 (SAS institute Inc., Cary, NC).
Results: Median follow-up was 5.5 and 6.8 years for the study and control populations, respectively. Median survival was 8.7 years for the study group versus 11.9 years for the control group. Study patients had a 50% higher risk of a lower 10-year survival (RR 1.5, 95%CI 0.92-2.42, p = 0.1). More patients in the study group had a prior PTCA (33 vs 13%, p < 0.01). Furthermore, 70.4% of study patients had coronary intervention (PTCA +/- stent) compared with 44% of controls. The survival of the general Minnesota population was better than either angiography group (p < 0.01).
Discussion: Cardiac arrest during coronary angiography was more likely in patients with a history of previous PTCA and in those who required any coronary intervention. 10-year survival for the study patients was lower than that of control patients (40% vs. 56%). However, this was not statistically significant. Thus, experiencing CA during coronary angiography does not imply a higher long-term mortality. Not surprisingly, any need for coronary angiography appears to be associated with a higher mortality than the general population.

S-79.

DEFINING THE BEST ENDOTRACHEAL TUBE FOR LUNG ISOLATION AMONG NON-THORACIC ANESTHESIOLOGISTS: EVALUATION OF DOUBLE-LUMEN ENDOTRACHEAL TUBE, TORQUE CONTROL BLOCKER UNIVENT AND WIRE- GUIDED ENDOBRONCHIAL BLOCKER

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Introduction: One-lung ventilation (OLV) can be accomplished in two ways: 1) a double-lumen endotracheal tube (DLT) or 2) a bronchial blocker.[1] Previous studies of OLV reported that DLT's and bronchial blockers are comparable.[2] The results of these studies may not be generalized, because they have been performed by cardiothoracic anesthesiologists (CTA). With increasing demand for OLV, it is important to define a suitable device for use by non-thoracic anesthesiologists (NTA). The aim of this study was to define the best device for OLV (DLT or bronchial blocker) among NTA considering: 1) time for placement, 2) malposition, and 3) frequency of fiberoptic bronchoscopy (FOB).
Methods: After IRB approval, 66 patients requiring OLV were studied in a prospective and randomized fashion: Group A left-sided DLT n=22, Group B Univent® n=22 and Group C Arndt® blocker n=22 patients. NTA who performed <2 OLV per month were paired with a CTA and included in the study (Faculty n=17, CA3 n=11).
The following variables were recorded: 1)time to achieve optimal position, 2) number of malpositions and 3) number of FOB.
After the NTA indicated the device was optimally positioned, the CTA confirmed tube placement. If the tube was malpositioned it was considered a failed study.
Statistical analysis: Values are expressed as median ±SE. The log-rank test was used to compare time for successful tube positioning of the three devices. The failed attempts were included in the analysis but times were censored for the failed attempts. Kruskal-Wallis test was used to determine the number of FOB. Comparison between successful and failed placement of tubes were performed using the Wilcox rank-sum test. *P* values <0.05 indicated a statistical difference.
Results: Figure 1 shows positioning times. The percentage of failed studies was 38% and was equivalent among the three devices. Failure was equivalent between faculty (39%) and residents (36%). The number of FOB (2-5) did not differ among the three devices.
Discussion: This study demonstrates a high incidence of unrecognized malpositions among NTA placing a DLT, Univent® or Arndt®. Among NTA no device had an advantage over the other devices. Therefore, the limiting factor was not the device itself. A review of failed studies indicates that a combination of unfamiliarity with bronchial anatomy and FOB were responsible for the malpositions among NTA.
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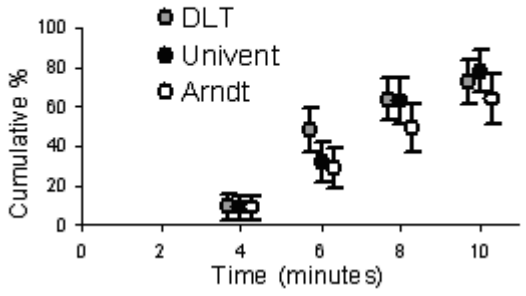
Figure 1: Cumulative Percentage (±SE) of Tubes Successfully Positioned



S-80.

THORACIC AORTIC ANEURYSM REPAIR IN THE AWAKE ELDERLY PATIENT: A PROSPECTIVE STUDY ON AN ALTERNATIVE ANESTHETIC TECHNIQUE

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Introduction: As technological advancements create a trend toward less invasive surgery, the anesthetic requirements to meet the goals of surgery are also modified. Endovascular aortic aneurysm repair (EVAAR) using a stent graft is a new less invasive alternative to traditional open repair. In 1999, Henretta et al. suggested a MAC/local anesthesic technique(1) and subsequently the first case report using this technique in the anesthesia literature was in 2003 by Lippmann et al.(2). We performed the first prospective study on elderly patients undergoing thoracic EVAAR using MAC anesthesia (local combined with analgesics and sedative drugs).
Methods: After IRB approval and informed consent, a prospective study from June 1998 to Jan 2004 (67 months) was performed on 100 elderly patients to determine if MAC anesthesia benefits elderly patients undergoing thoracic EVAAR. Data recorded included drugs (fentanyl, midazolam, and lidocaine 0.5%), blood loss, blood and fluid replacement. Standard monitors, two large bore IV lines, and an arterial line were utilized. Postoperatively, patients were admitted to the SICU or PACU.
Results: 100 patients, 62 males and 38 females, were studied. Mean age was 73 (range 30-92). ASA classification were III & IV = 76 and IVE = 24. Other data are shown in table below.

	Age (yrs)		Height (cm)		Weight (kg)		Midazolam (mg)		Fentanyl (mcg)		0.5%lidocaine (mL)	
	M	F	M	F	M	F	M	F	M	F	M	F
Mean	70.6	67.8	171.7	158.0	82.2	68.9	1.1	1.1	325	463	60.7	46.4
High	85.0	92.0	187.0	182.0	143.0	167.0	5.0	15.0	750	1500	200	100.0
Low	38.0	30.0	150.0	113.0	47.0	38.4	0	0	50	50	0.0	10.0
+/- SD	10.3	14.0	9.5	13.4	16.8	22.7	1.4	2.7	160	319	38.8	22.9

	Blood Loss (mL)		AutoVac (mL)		Blood replacement (Units)		Hespan (mL)		Plasmalyte (mL)	
	M	F	M	F	M	F	M	F	M	F
Mean	869	653	624	430	0.7	1.6	264	214	1868	1741
High	7500	2400	4400	1900	14.0	20.0	2000	1000	4600	3500
Low	100	100	0	0	0	0	0	0	130	400
+/- SD	500	400	200	275	2.0	3.6	387	311	947	794

Discussion: Since thoracic EVAAR is a less invasive surgical approach, local anesthesia with MAC is feasible and offers great advantages over general anesthesia. Maintenance of consciousness is attributed to our avoidance of general anesthesia and minimal midazolam, yet sedating our patients primarily with fentanyl. This allows the patient to eat and ambulate earlier, which in turn, reduces post procedure discharge to 1.5-2.5d; significantly cutting hospital cost. Avoidance of inhalational agents and airway instrumentation provides smoother intraoperative hemodyanmics, resulting in less cardiopulmonary complications that often occur in these elderly patients in whom multidisease entities already exist. Stable hemodynamics is also achieved by 0.5% lidocaine injected by the surgeon during the femoral cut down, not to mention, less blood loss and blood replacement, swings in blood pressure are minimized.
Reference:
1. Feasibility of endovascular repair of abdominal aortic aneurysms with local anesthesia with intravenous sedation. J Vasc Surg 1999;29:793-8
2. An alternative anesthestic technique in a Morbidly obese patient undergoing Endovascular Repair of an Abdominal Aortic Aneurysm. Anesth Analg 2003;97:981-983

S-81.

COMBINED SPINAL AND EPIDURAL ANESTHESIA INCREASES THE INCIDENCE OF MESENTERIC TRACTION SYNDROME

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INTRODUCTION: Traction on the mesenteric root during major abdominal surgery provokes sudden hypotension, tachycardia and flush, known as mesenteric traction syndrome (MTS)[1)]. Comparing with general anesthesia (GA), we had frequently experienced those severe symptoms under GA with combined spinal-epidural technique (CSE) even after appropriate fluid loading stabilized patient's hemodynamic state. We hypothesized that increased intestinal motility by CSE could affect an incidence of MTS. The purpose of this study is to compare the incidence of MTS associated with two anesthetic techniques - GA and GA with CSE.
METHODS: After written informed consent was obtained, 59 patients scheduled for major abdominal surgery were enrolled in this IRB approval study. They were randomly assigned to two groups; GA with CSE (GC) and GA (G) group. In the operating room, thoracic epidural catheter was inserted to all patients. Epidural mepivacaine (120-200 mg) and spinal bupivacaine (L3/4, 20 mg) were administered to group GC patients, and no epidural anesthetics were administered to group G patients during interventions. Patients were intubated with intravenous administration of propofol and vecuronium. Anesthesia was maintained with sevoflurane (1.5-2.0 % at end-tidal concentration), as BIS (A-2000; Aspect Medical Systems Inc. Newton, MA, USA) index would be kept less than 60. Intravenous fentanyl (6 - 10microgram.kg(-1)) was administered to group G patients. In addition to the standard monitoring, radial artery was cannulated for measuring arterial blood pressure and blood gas analysis. In both groups, phenylephrine was continuously administered at 0.5-1.0 mg.h(-1) for maintaining systolic blood pressure as high as preoperative level (regarded as the baseline value) before laparotomy. End-tidal sevoflurane and the administering speed of phenylephrine were unchanged within thirty minutes after laparotomy. Clinical signs of MTS including hypotension (20% decrease in systolic blood pressure from baseline), tachycardia (20% increase) and flush, observed by a blinded observer within thirty minutes after laparotomy, were defined as the primary end point in this study. Patients, who represented hemodynamic instability (2 patients) and showed over 60 of BIS index during observation (1 patient), were excluded. Type of anesthesia and the incidence of MTS were compared through chi-square test, where $P<0.05$ was considered significantly different.
RESULTS: There was no significant difference between GC and G groups for the following variables: sex; type of surgery; mean body mass index; mean age; mean end-tidal concentration of sevoflurane. The incidence of MTS was 84.6% in group GC vs. 33.3% in group G ($P < 0.001$).
DISCUSSION: CSE increased an incidence of clinical symptoms of MTS. We are considering that strongly blocked splanchnic nerves and increased intestinal motility by CSE could be related to a quantity of a release of prostacyclin. This result would suggest a necessity of prophylaxis against MTS for patients under CSE.
References:
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S-82.

DIFFERING EFFECTS OF SPONTANEOUS AND POSITIVE PRESSURE VENTILATION ON HEART RATE VARIABILITY

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Introduction: It previously has been shown that measurements of heart rate variability (HRV) may be significantly influenced by the rate of respiration (1). Not uncommonly in the perioperative setting, we also encounter changes in the type of ventilation and in the pressures generated during ventilation. The present study was undertaken to compare the effects of spontaneous ventilation (SV), inspiratory positive airway pressure (IPAP), and positive expiratory pressure (PEP) on HRV in healthy volunteers.
Methods: With IRB approval, 8 volunteers underwent EKG monitoring while lying semirecumbent on a stretcher in an isolated study room. After training with the different breathing devices, each subject underwent assessment during 3 phases: SV at the subject's resting rate and tidal volume; IPAP via a facemask that transmitted 20 cm H_2O pressure from a Sullivan VPAP II machine; PEP via a partially occluded expiratory limb that generated 20 cm H_2O of pressure. The rate and depth of respiration were quantified with a force transduction belt around the chest; the pressures during IPAP and PEP were recorded with an interfaced transducer. Signals from each of these devices as well as the EKG were interfaced with a data acquisition system (ADInstruments) at a sampling rate of 400 Hz. The successive R-R intervals were determined, and the R-R tachogram was generated. Time-domain analysis of HRV included standard deviation among the R-R intervals of the different beats (SDNN in msec), root mean square of successive differences in the R-R intervals (RMSSD), and pNN50. Spectral-domain analysis determined oscillatory power at the high "respiratory" frequency of the R-R tachogram ($msec^2$/Hz). Differences among methods of ventilation were assessed by ANOVA and paired t-test.
Results: For each index of HRV, there was a significant difference among the different methods of ventilation ($p<.03$ by ANOVA). As shown in the Table, for each variable the methods for delivering positive pressure (IPAP and PEP) generated significantly greater HRV than did SV.
Discussion: The findings confirm that the pattern and method of ventilation have a significant impact on HRV. Hence, a failure to appreciate the impact of ventilation may lead to inaccurate assessments of sympathovagal balance. This is especially important in the perioperative setting, where we often encounter different rates, patterns, and depths of respiration.
References:
1. Anesthesiology 1999;91A:608

	SV	IPAP	IPAP vs. SV	PEP	PEP vs. SV
HR	72.7±3.0	73.5±2.5	P > 0.1	75.7±2.4	P = 0.05
SDNN	44.6±3.8	79.03±7.9	0.004	83.9±5.8	0.0003
RMSSD	31.4±5.0	60.4±6.3	0.0003	53.6±4.3	0.003
pNN50	5.13±2.1	37.5±4.4	0.0002	31.5±3.3	0.0001
Total power	1586.2±315.6	6819.4±1272.8	0.003	7077.9±1016.5	0.0005
High Frequency Power	611.5±179.7	2712.5±576.2	0.013	2475.±788.5	0.05

S-83.

TWO CASES OF PULMONARY THROMBOEMBOLISM SUCCESSFULLY TREATED WITH PERCUTANEOUS THROMBECTOMY UNDER PERCUTANEOUS CARDIOPULMONARY SUPPORT

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INTRODUCTION: Massive pulmonary thromboembolism is usually fatal if not treated aggressively, but management is not standardized(1). We experienced two cases of massive pulmonary thromboembolism.
CASE 1: A 57-year old male patient underwent oral and maxillofacial surgery. After nine days, he developed into shock and cyanosis. As administration of catecholamines and mechanical ventilation failed to improve the shock, percutaneous cardiopulmonary support (PCPS), a kind of extracorporeal membrane oxygenation widely available in Japan(2), was introduced. Since massive pulmonary thromboembolism was suspected as results of electrocardiogram and echocardiogram, percutaneous transluminal aspiration of thrombus using percutaneous transluminal coronary angioplasty (PTCA) catheter was performed. The pulmonary artery was recanalized and his hemodynamic parameters became stable. The treatment with PCPS was continued for 32 hours. He discharged with no comprications after 155 hospital days.
CASE 2: A 74-year old female patient developed into shock and cyanosis in her house. She was still shock, when she was transferred to the emergency unit of our university hospital. Since administration of catcholamines and mechanical ventilation failed to improve the shock, PCPS was introduced. Massive pulmonary thromboembolism was diagnosed as results of electrocardiogram and echocardiogram. Percutaneous transluminal aspiration of thrombus using a PTCA catheter was attempted as in case1. The pulmonary artery was recanalized and her hemodynamic parameters became stable. The treatment with PCPS was continued for 78 hours. She discharged with no complications after 68 hospital days.
CONCLUSION: We experienced two cases of massive pulmonary thromboembolism, which were successfully treated with percutaneous transluminal aspiration of pulmonary thrombus under percutaneus cardiopulmonary support. These experiences suggest that this combined therapeutic strategy may improve the result of treatment for massive pulmonary thromboembolism.
REFERENCES
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S-84.

INFLUENCE OF DORMICUM, PROPOFOL AND FENTANYL ON THE CONDUCTION SYSTEM OF THE HEART DURING ELECTROPHYSIOLOGICAL EXAMINATION AND RADIO-FREQUENCY ABLATION

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INTRODUCTION: Dormicum, propofol, and fentanyl are commonly used during electrophysiological examination and radio-frequency ablation, however their dose dependent effect on the conduction system of the heart remains disputable. The aim of this study is to investigate the influence of dormicum, propofol and fentanyl on sino-atrial and atrio-ventricular conduction as well as to reveal dose dependent differences.
METHODS: Electrophysiological examination was performed in 35 patients with different tachyarrhythmias (WPW syndrome - 6, supraventricular tachycardia - 5, atrioventricular nodal tachycardia - 5, ectopic atrial fibrillation - 7, ventricular tachycardia - 7, sinus tachycardia - 5). The following types of anaesthesia were used: group 1: intravenous infusion of dormikum in the dosage of 0.3 mg/kg/h and fentanyl in the dosage of 0.5-1 μg/kg/h (n=15); group 2: intravenous infusion of dormikum in the dosage of 0.5-1 mg/kg/h (n=10); group 3: intravenous infusion of propofol in the dosage of 2-12 mg/kg/h (n=10).
RESULTS: There were no conduction disturbances in patients of groups 1 and 2, with the drug dosages used. However, patients with atrial fibrillation/flutter demonstrated elongation of atrial refractory period ($p<0.01$). Patients converted to permanent atrial fibrillation were unresponsive to treatment. In patients of group 3, no rhythm disturbances were noticed if the dose of propofol did not exceed 6 mg/kg/h. However, when the dosage reached 8-12 mg/kg/h, there was sino-atrial node depression, as well as changes in sino-atrial and atrio-ventricular conduction ($p<0.01$).
DISCUSSION: According to our data, dormicum, propofol and fentanyl do not significantly influence the cardiac conduction system. However conversion to a resistant form of atrial fibrillation/flutter could happen. The possibility of depression of the sino-atrial and atrio-ventricular conduction should be taken into consideration when the dosage of propofol and fentanyl exceeds 8 mg/kg/h and 1 μg/kg/h, respectively. Therefore, such high doses are not recommended for patients with sinus node dysfunction and different types of atrio-venricular blockade.
REFERENCES:
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S-85.

SHUTTLE WALK EXERCISE TESTING PREDICTS OESOPHAGECTOMY OUTCOME

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Surgical resection of oesophageal malignancy is associated with considerable risk of perioperative morbidity and mortality. Formal cardiopulmonary exercise testing (CPX) can identify high risk patient groups prior to major abdominal surgery (1) and oesophagectomy (2).
Shuttle walk exercise testing is a relatively simple procedure. Patients walk around traffic cones 10m. apart at increasing speed until unable to maintain pace set by an audible ‘beep’. Distance achieved correlates well with measures of V02 max obtained in formal metabolic assessment , having been validated in groups of patients with impaired cardiac and pulmonary function (3).
Preoperative shuttle tests were performed by 35 patients undergoing Ivor Lewis) or transhiatal oesophagectomy from April 2002. Current 30 day mortality for this procedure in our hospital is 9%. A clear relationship between perioperative mortality and exercise capacity is evident. Five postoperative deaths occurred in the tested group. These patients were among a group of 9 who had shuttle walks below 350m.
No postoperative deaths were recorded in patients with a shuttle walk greater than 350m.
The apparent threshold distance of 350m approximates to an anaerobic threshold of 11ml/min/kg on CPX proposed by Older et al. to identify high operative risk.
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S-86.

LIFE THREATENING HEMOTHORAX RESULTING FROM RIGHT BRACHIOCEPHALIC VEIN PERFORATION DURING INTERNAL JUGULAR VEIN CATHETERIZATION

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Introduction: Central venous catheters may be associated with serious complications. We present a case of hemothorax resulting from right brachiocephalic vein perforation during internal jugular vein catheterization.
Case: A 78-yr-old man was presented for Y-graft replacement of abdominal aortic aneurysm. Following induction, the right internal jugular vein was successfully punctured with a 22-gauge "finder" needle. The blood flowing from the needle was dark in color and nonpulsatile. An angle-tip guidewire was threaded through a needle, and a 12-gauge double-lumen catheter (ArgyleTM, Nihon Sherwood, Japan) was inserted over the wire. Even though the catheter was inserted smoothly, blood could not be aspirate from both proximal and distal ports, so the catheter was removed. At the left internal jugular vein and with the same technique, a double-lumen catheter was placed. The aspirated blood was dark in color and nonpulsatile.
Two hours after beginning of the surgery, the blood loss increased. Despite adequate administration of volume, the patient exhibited worsening clinical signs of hypovolemia. Physical examination revealed decreased breath sounds over the right hemithorax to auscultation. Emergency chest radiograph showed a significant hemothorax. Immediately, a 28-French chest tube was inserted into the right chest, and 1000ml of blood were drained. A right thoracostomy was performed to identify the source of the bleeding. A continuous bleeding was found from a catheter-sized hole in right brachiocephalic vein. Following the surgeon repaired the vein, the patient recovered hemodynamically stable. The patient was transferred to a high care unit and the trachea was extubated 2 days later. Two weeks later, the patient made a full recovery.
Discussion: We present a case of right brachiocephalic vein injury secondary to internal jugular vein cannulation. A literature review identified no cases of guidewire induced brachiocephalic vein perforation, thus this is the first reported case of a life-threatening hemothorax caused by a brachiocephalic vein perforation. We consider that the guidewire punctured the vein extraluminally, because of the three reasons. First, the angle-tip guidewire is not curved like J-tip. Second, the dilator is too short to puncture the brachiocephalic vein and advanced more than to just dilate the skin and subcutaneous tissue. Third, the catheter was inserted smoothly over the guidewire. In only one reported case, the guidewire probably punctured the vein extraluminally, although the tip of the guidewire is not indicated. Despite proper technique, we conclude the angle-tip guidewire might perforate venous wall, therefore recommend using J-tip guidewire.
Reference:
Anesth Analg 2002; 95: 564

S-87.

COMPARISON OF REGIONAL CEREBRAL OXYMETRY AND JUGULAR VENOUS OXYGEN SATURATION IN PREDICTING GROSS OUTCOME IN SURGERY WITH DEEP HYPOTERMIC CIRCULATORY ARREST

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Introduction: Deep hypothermic circulatory arrest (DHCA) permits the correction of fatal aortic pathologies, but carries the risk of neurological complications. The purpose of this study was to compare two monitoring modalities utilized during such surgical corrections: jugular venous bulb saturation (SjvO2) and regional cerebral oxymetry by Near-Infrared Spectroscopy (NIRS). Previous studies have demonstrated that SjvO2 > 95% prior to institution of DHCA, permits a safe arrest period of 50 minutes (1). We examined the correlation between these measures during of ascending/arch aortic aneurysm repair. Likewise, the ability of either method to detect deleterious outcomes was reviewed.
Methods: We examined NIRS (INVOS 4100), SjvO2 (intermittent sampling) and temperature variables at stages of the procedure (baseline, cooling on cardiopulmonary bypass (CPB), arrest, rewarming on CPB and closure) in 19 patients who underwent DHCA. Mean data from NIRS left and NIRS right were compared to SjvO2. SjvO2 samples were not obtained during the period of arrest as a consequence of retrograde cerebral perfusion.
Results: Overall cerebral venous oxygen saturation obtained from NIRS was lower compared to SjvO2 at most time points ($p < 0.05$), especially during periods of low temperature. However, correlation was much tighter at normothermia. Moreover, NIRS and SjvO2 trends were similar. NIRS showed low saturation (< 50 %) in 9 patients. Four of these patients had undesirable outcomes (stroke (2 patients), death secondary to ischemic bowel (1 patient), and death secondary to biventricular failure following the procedure (1 patient). One of the two stroke patients had significant discrepancies between the left and the right NIRS measurements and had a massive stroke of the corresponding side of the brain. SjvO2 showed low saturation (< 50 %) in 6 patients. Amongst these six were the four previously mentioned patients with an undesirable outcome. Thus, both tests had sensitivity 100 %; specificity 67 % for NIRS and 87 % for SjvO2; predictive value 44 % for NIRS and 67 % for SjvO2.
Discussion: We concluded that NIRS does not closely correlate with SjvO2 during the cooling period; however, both measures trend in a similar fashion. Compared with SjvO2 NIRS has lower specificity and predictive value.
References:
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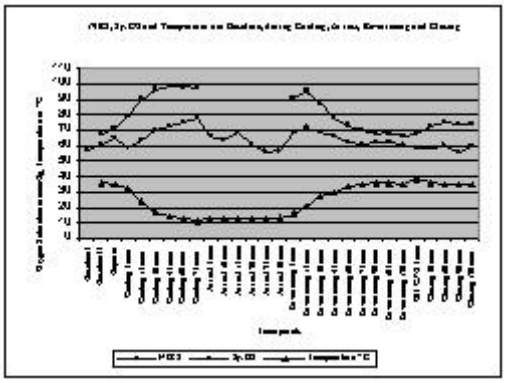

S-88.

POSTOPERATIVE D-DIMER LEVELS ARE ASSOCIATED WITH EARLY COGNITIVE OUTCOME AFTER OFF-PUMP CORONARY ARTERY BYPASS SURGERY

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Background: Several studies showed that cognitive decline also occurs after off-pump coronary artery bypass grafting (OPCAB), suggesting that other factors than the use of cardiopulmonary bypass (CPB) contribute to cognitive decline.[1, 2] We hypothesized that a hypercoagulable state after OPCAB may be responsible for cognitive decline.[3, 4]
Methods: In a sample of 60 consecutive patients undergoing OPCAB, we studied the association between postoperative D-dimer levels and cognitive outcome at the 4th day after surgery, as assessed by neuropsychological testing.
Results: D-dimer levels at two hours after the operation were strongly associated with cognitive decline on postoperative day 4 in the off-pump group, (p=0.004). When patients were divided in quartiles based on D-dimer levels 2 hours after the operation, a dose-response curve could be shown between postoperative D-dimer levels and early neurocognitive decline (see table).
In a multivariate logistic regression model postoperative D-dimer levels were a strong predictor for early cognitive decline in the off-pump group (p=0.006).
Discussion: Early postoperative D-dimer levels are associated with early cognitive outcome after off-pump coronary bypass surgery. Activation of hemostasis may therefore contribute to cognitive decline in off-pump surgery.

Quartiles of post-operative D-dimer levels (at 2 hours) in off-pump CABG and cognitive decline

	D-dimer levels	2 hours postoperatively	Cognitive decline	on postoperative day 4
	Median (μg/ml)	Range	no. of patients	(%)
Group 1	0.29	(0.23-0.39)	3/15	(20)
Group 2	0.58	(0.42-0.68)	5/15	(33)
Group 3	0.84	(0.73-1.06)	8/15	(53)
Group 4	1.58	(1.17-3.00)	10/15	(67)
Total	0.70	(0.23-3.00)	26/60	(43)

References:
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S-89.

AUTOREGULATION OF HUMAN JEJUNAL MUCOSAL PERFUSION DURING CARDIOPULMONARY BYPASS

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Introduction: There is a high incidence of systemic inflammatory response (SIRS) in cardiac surgery with cardiopulmonary bypass (CPB). One causal factor for the development of SIRS is the occurrence of splanchnic ischemia during CPB, which may lead to disruptured intestinal mucosal barrier function and subsequent translocation of endotoxin and microorganisms. Animal studies have suggested that intestinal autoregulation of blood flow is severely impared during CPB (1). In this study we evaluated the intestinal mucosal autoregulation of perfusion during CPB in man.
Methods: Ten patients undergoing elective cardiac surgery were included after informed consent and approval of institutional ethics committee. The patients were anesthetized with a combination of fentanyl, propofol and pancuronium. A custom-made two-probe laser Doppler catheter(Perimed, Sweden), was placed during fluoroscopic guidance through the nasogastric route endoluminally in the proximal jejunum, 20- 40 cm distal to the ligament of Treitz. During nonpulsatile CPB at standard pump flow of 2.4 l/min/m^2, anestesia was maintained with propofol. The pump flow was altered randomly and repeatedly to either 1.8 l/min/m^2 or 3.0 l/min/m^2. Mean arterial pressure (MAP) and jejunal mucosal perfusion (JMP) were recorded for three minutes periods at each pump flow rate.(1.8, 2.4, 3.0 l/min/m^2). Thereafter, at the standard pump flow rate, vasodilation was induced by a bolus of prostacyclin (Flolan®, 10 μg) (n=6), and the maximal change in MAP and JMP were recorded. ANOVA was used to evaluate the effects of varying pump flow rates on MAP and JMP. Wilcoxon signed rank test was used to compare pre and post prostacyclin values of JMP and MAP. Values are expressed as mean ±standard deviation.
Results: A typical pattern of flow motion was recorded in nine of ten patients during CPB. Variations in pump flow rates caused no significant changes in JMP (see table). Injection of prostacyclin completely abolished the flow motion waves and JMP increased from 192±53 to 277±70 (p<0.05) perfusion units despite a reduction in MAP from 59±12 to 45±10mmHg (p<0.05).

Pump flow index l/min/m^2)	1.8	2.4	3.0	ANOVA
MAP (mmHg)	50±15	63±17	74±16	p<0,0001
JMP (PerfusionUnits)	204±55	214±53	197±50	ns

Discussion: Autoregulation of intestinal mucosal perfusion is well maintained in humans during cardiopulmonary bypass within the range of pump flow rates studied. Myogenic mechanisms at the arteriolar level are probably responsible for this pressure-independent mucosal perfusion during CPB. Prostacyclin induced a profound inhibition of the arteriolar myogenic tone.
References:
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S-90.

RISK FACTORS FOR PROLONGED MECHANICAL VENTILATION AFTER CARDIAC SURGERY IN DIALYSIS - DEPENDENT PATIENTS

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INTRODUCTION: Cardiac disease is well known to be a leading cause of death in dialysis-dependent patients. Surgical procedure is one of the best strategy, but mortality in the early postoperative period has been still higher than the patients with normal renal function. Therefore, careful postoperative management to avoid complications is essential, such as prolonged mechanical ventilation (PMV) which is closely associated with mortality after cardiac surgery (1) and we investigated pre and intraoperative risk factors to predict PMV.
METHODS: We investigated forty dialysis-dependent patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) from 1997 to 2004. All these patients had conventional hemodialysis before surgery, hemofiltration during cardiopulmonary bypass, and continuous veno-venous hemodialysis (CVVHD) postoperatively. They were divided into two groups. Group E consisted of patients who were extubated within 24 hours after admission to the ICU. Group L consisted of patients requiring more than 24 hours for mechanical ventilation. We compared perioperative variables in the two groups and demonstrated risk factors for PMV by multiple logistic regression analysis.
RESULTS: Seventeen patients underwent isolated coronary artery bypass grafting (CABG) and twenty three underwent combined CABG or valve surgery. Groups E and L consisted of sixteen and twenty four patients respectively. There were significant differences in left ventricular ejection fraction and duration of dialysis as preoperative factors and duration of surgery as an intraoperative factor between the two groups. Multiple logistic regression analysis showed that duration of dialysis (more than 10 years) and surgery (more than 8 hours) were independent risk factors for PMV (more than 24 hours). There was significant difference in duration of ICU stay (3±1 days in Group E vs 7±5 days in Group L), but early mortality rate (within 30 days after surgery) in each group were similar (0% vs 4%).
DISCUSSION: Duration of dialysis and surgery proved to be predictors for PMV. This may be associated with coronary artery and cardiac valve calcification which is known to be advanced when duration of dialysis is more than 10 years (2). Coronary artery calcification deteriorates preoperative cardiac function and makes myocardial protection difficult during CPB. Cardiac valve calcification also complicates surgical procedure. Though sixty percent of all our patients needed more than 24 hours for mechanical ventilation, our early mortality rate was lower than that previously reported (3).
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3. Ann Thorac Surg 2000; 69: 96-101

S-91.

SAFETY CULTURE IN THE OPERATING ROOM: PERCEPTIONS OF PEDIATRIC CARDIAC SURGERY TEAMS

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INTRODUCTION
An organization's patient safety culture is the product of individual and group values, perceptions, competencies, and patterns of behavior. In this study, we analyzed the prevailing culture of pediatric cardiac surgery (PCS) teams. PCS demands a sophisticated organizational structure, coordinated team effort, and a high level of cognitive and technical performance to achieve safe outcomes.
METHODS
After IRB approval, an anonymous survey was sent to PCS teams at two academic health centers. Respondents evaluated on a four point scale (1-4) their perceptions about: a) patient adverse events (FP); b) Operating room (OR) management, and overall patient safety (PSOR); c) workload, staffing, and supervision in the OR (WSSOR); d) communication in the OR (COR); and, e) the effectiveness of the hospital safety and reporting systems (PSH).
Mean responses between study sites were analyzed using the Student t-test. Mean differences in response by the professional groups--anesthesia (11); surgery (4), perfusion (8), nursing (9)-- were analyzed in a one-way Analysis of Variance (AOV) followed by pair-wise t-tests between groups. Responses to questions showing significant differences were recoded in two categories (yes vs. no; or agree vs. disagree), and analyzed by Chi-Square.
RESULTS
The overall response rate was 55% (32/59). There were no significant differences in responses among the questions in the domains represented by FP, PSOR, and WSSOR. One site reported more effective reporting mechanisms and encouragement by colleagues to report safety concerns than did the other site. There were eleven significant differences concerning communications in the OR. One site was significantly different ($p<0.05$) than the other site in three categories: a) senior staff encourage questions from juniors; b) the different groups had open communications and understood the other's responsibilities; and c) disagreements could be openly discussed.
When comparing responses among the different professional groups, significant differences in all domains were found. In general, when a difference was found, the Surgeons and Anesthetists were in agreement but differed from both Perfusionists and Nurses. These differences reflected differing opinions about the impact of skills and knowledge on preventing adverse events, the reporting of errors and safety violations, and methods and channels of communication among OR staff. Anesthetists and Nurses indicated that OR staffing levels were sufficient, while Surgeons and Perfusionists significantly disagreed. Further differences were noted in open ended responses.
DISCUSSION
We found that there are different perceptions about staffing, communications and patient safety concerns among PCS professionals in, and between study sites. Future directions include full qualitative analysis and surveying PCS programs across the country using these results to direct system interventions.
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S-92.

COMPARISON OF LACTATE LEVELS IN CABG OPERATIONS DONE EITHER WITH INTERMITTENT AORTIC CROSS-CLAMPING WITH FIBRILLATION OR BLOOD CARDIOPLEGIC ARREST

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Introduction: Myocardial protection during coronary artery bypass grafting (CABG) operations is controversial especially when different approaches are used[1, 2]. In this retrospective study we compared the serial lactate levels of patients during CABG operations done either with intermittent aortic cross-clamping (IAC) with fibrillation or with cardioplegic cardiac arrest (CCA) method.
Methods: Patients who had two or three vessel disease with normal ventricular function determined by normal ejection fraction with no co-morbid disease other than regulated hypertension and/or type-2 DM were included in the study. Each group consisted of 15 of these patients who had CABG operations done all by the same surgeon with IAC technique (IAC Group) or by the same or 2 different surgeons with CCA method (CCA group). Partial CPB time, total myocardial ischemia times were recorded. Arterial blood samples obtained before the operation, prebypass period, during CPB, early following CPB and 1hour later in the ICU were examined especially with respect to lactate levels and statistically analyzed. Postoperative 24 hour myocardial ischemic changes were also assessed with ECG and CK-MB analysis.
Results: Demographic variables in both groups were statistically similar. Partial CPB period and total myocardial ischemia time were 74.64±6.3 min and 31.71±5.48 min (mean ±SEM) respectively in IAC group and 67.86±7.25min and 43.26±5.05min in CCA group. Lactate levels were highly elevated in both groups during CPB. Although lactate elevation during CPB were determined to be lower; 4.18±1.12 mmol / L (mean ±SD) in CCA group compared to IAC group; 4.72±1.12 mmol / L, this was statistically insignificant. There was no ischemic ECG or CK-MB changes recorded postoperatively in any of the groups.
Discussion: One of the parameters evaluated for myocardial protection is lactate; an anaerobic metabolism product. Despite total myocardial ischemia time was shorter in IAC group, lactate levels were found to be statistically indifferent between the groups. Not being able to measure the coronary sinus lactate levels is one of the faults of this study. Further prospective clinical studies involving biochemical and ultrastructural changes on myocardial tissue have already been started by our team to find out the more beneficial cardio protective effect of one of these procedures in CABG patients.
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S-93.

PERIPARTUM MANAGEMENT OF SEVERE AORTIC STENOSIS; A REGIONAL APPROACH

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INTRODUCTION: A 20year old primigravida at 38+1 week's gestation with medical history significant for congenital aortic stenosis, and septoplasty at 6 days of life presented for induction of labor. Prenatal care occurred at an outlying institution and was complicated by two syncopal episodes. Two days prior to admission, TTE revealed aortic valve area: 0.8 cm^2, peak systolic gradient > 100 mm Hg, mean systolic gradient: 60-70 mm Hg, and ejection fraction > 65 %. During pre-anesthetic assessment, the patient denied angina, dyspnea, or palpitations. Vital signs included HR 85 bpm, NIBP 125/70 mm Hg, and SPO2 of 99 % on room air. Physical exam revealed a III/VI holosystolic murmur radiating from the left sternal border into the right neck. Laboratory values were within normal limits, and ECG showed normal sinus rhythm. A multidisciplinary team was organized, and following discussions with the patient and spouse, an elective cesarean section under regional anesthesia was planned.
METHODS: On the date of elective cesarean section, the patient was transported to the cardiac operating suite. Standard ASA monitors, two large bore intravenous catheters and invasive arterial monitoring were placed. While in the sitting position, one liter of Ringer's Lactate was completed and an L2-L3 epidural catheter was placed without complication. The patient was positioned supine with left uterine displacement, and adhesive defibrillation pads were attached. A sterile preparation was completed, and while surgeons were at the bedside, a test dose of 60 mg lidocaine without epinephrine showed no evidence of intrathecal or intravascular injection. Over a 25-minute period, the patient received a total of 21 cc of 2% isobaric lidocaine in 3 cc increments, and 50 micrograms of epidural fentanyl. A T5 level of anesthesia was obtained and surgery was initiated. Seven minutes following incision a 2.67 kg male infant was delivered with apgars of 8 and 9. During the course of the epidural procedure, and cesarean section, the patient required a total of 150 micrograms of phenylephrine and 3200 cc Ringer's Lactate to maintain SBP >100 mm Hg and heart rate less than 90 bpm.
RESULTS: Upon completion of surgery the patient was transferred to the ICU and underwent continuous monitoring for 18 hours. Following an uncomplicated post-partum course, the patient and newborn son were discharged home POD #3.
DISCUSSION: Severe aortic stenosis in the parturient presents a significant challenge and has resulted in both maternal and fetal morbidity and mortality. There is no consensus on either obstetric or anesthesia management for this classification of patient. We present a case where proper patient selection, careful preoperative planning and use of a multidisciplinary approach resulted in the successful peripartum management of a parturient with severe aortic stenosis using regional anesthesia for a planned cesarean section.

S-94.

PLASMA LEVELS OF TRANEXAMIC ACID AFTER TWO ADMINISTRATION WAYS: TWO BOLUS OR CONTINUOUS INJECTION AFTER ONE BOLUS, DURING CARDIAC SURGERY WITH CARDIOPULMONARY BYPASS

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Introduction: The use of tranexamic acid (TA), an antifibrinolytic agent, during cardiac surgery with cardiopulmonary bypass (CPB) reduces the blood loss and the blood requirements after operation. The therapy should begin before skin incision or before CPB. The dosages employed differ from 10 to150 mg kg^{-1} for the first intravenous (IV) injection, eventually followed by a constant infusion (CI) of 1 mg kg^{-1} during 10 hour or by a second IV injection after CPB (1). The plasma levels of TA were determinated in patients receiving 1 bolus of TA followed by a constant infusion or 2 bolus of TA.
Methods: After institutional review board approval and written informed consent, two groups of 10 patients schedulled for cardiac surgery with CPB were randomly constituted. One (IV) received twice15 mg kg^{-1} of TA as a IV bolus: before skin incision and after protamine injection. The other group (CI) received 10 mg kg^{-1} of TA before skin incision followed by a TA constant infusion of 1 mg kg^{-1} up to the 6th postoperative hour. Blood samples were taken 2 minutes after the first injection (T1) after the start (T2) and at the end of CPB (T3) at the arrrival in the intensive care unit (T4) and at the 6th post operative hour (T5). The TA concentrations were measured by Hight Performance Liquid Chromatography. The results vere express as mean ± standart deviation.
Results: The two groups (IV/CI) were similar in term of age (62 ± 14/ 64 ± 11 years), body surface area (1,81 ± 0,11/1,89 ± 0,11 m^2) CPB time (129 ± 39/119 ± 37 min). In the CI group, after the peak, it was observed a gentle decrease of TA plasma concentrations, with a steady state from T4. A second peak was observed in the IV group at T4, 65 ± 18 min after the second TA injection. The infusion time, in the CI group, was 628 ± 44 min.

TA plasma concentration (µg/ mL) and time interval from T1 to T2 (min)						
IV	T1	T2	T3	T4	T5	T1-T2 time interval
IV	155 (16)	81 (28)	51 (13)	114 (15)	23 (8)	99 (31)
CI	144 (25)	91 (12)	76 (9)	69 (10)	54 (8)	110 (24)

Discussion: All the TA concentrations are above 13 µg ml^{-1}, a level considered effective for inhibing fibrinolysis (2). This study confirms clinical results (3). Two injections of TA are so effective than an injection followed by a constant infusion.
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(3) Anesth Analg 2004; 98: S-32

S-95.

A LARGE SERPENTINE EMBOLUS WAS DETECTED BY TRANSESOPHAGEAL ECHOGRAPHY FOLLOWING CARDIOPULMONARY RESUSCITATION INDUCED BY CEMENTED ARTHOPLASTY

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Introduction: Cemented arthroplasty has become the most common and effective orthostatic surgical procedures. However, "cement implantation syndrome" characterized by systemic hypotension, pulmonary hypertension, and even sudden death is a well-known complication. Although transesophageal echocardiography(TEE) has demonstrated these changes are associated with echogenic material in the right atrium or ventricle(1), it is not regularly available because of its high cost and required expertise(2). Here we described a patient undergoing treatment of a femoral fracture in whom a large serpentine embolus was detected by TEE following resuscitation. This finding might help anesthesiologists to make more correct diagnoses and better treatment of patients and also could clarify clinicians' attributing perioperative vital signs fluctuations as the effect of anesthesia(3).
Case report: This 71-year-old housewife with medical history of hypertension was admitted because of sustaining right femoral neck fracture in a fall. Bipolar hemiarthroplasty was performed with general anesthesia. The right femur was exposed and the femur was reamed with flexible reamers so that it could accept a long-stem bipolar prosthesis. Immediately after the placement of a cement-restrictor, patient's heart rate and blood pressure dropped and the end-tidal carbon dioxide decreased. The wound was temporally protected with sterile adhesive sheets and cardiopulmonary resuscitation was initiated after patient was turned to supine position. After fifteen minutes external cardiac massage and medical treatment with vasopressors, patient regained acceptable vital signs. Transesophageal echocardiography was performed about one hour after cardiopulmonary resuscitation and a large serpentine embolus was detected at right atrium. The patient died approximately one hour postoperarively after transferred to the cardiac care unit. No postmorterm examination was performed.
Discussion: The studies of using transesophageal echocardiography immediately after the attack of cement implantation syndrome were few. Our case report described the possible evidences of cement implantation syndrome by which could help the anesthesiologist to do further management and cast the doubts of surgeons about the potential cardiopulmonary reducing effect of general anesthesia. Therefore, we suggest that patients who have unstable hemodynamic signs during cemented arthroplasty should receive transesophageal echocardiography
examination.
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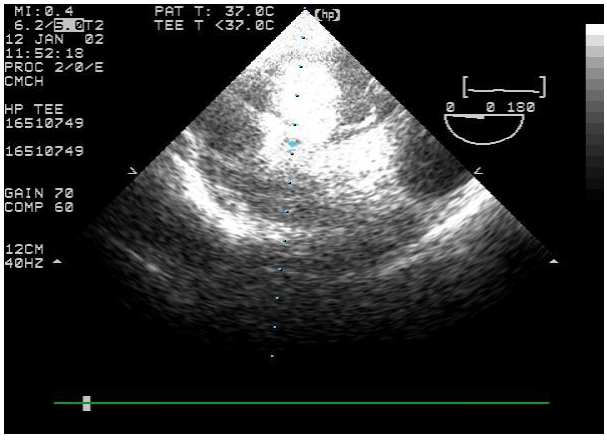
3. CAN J ANAESTH 1997/44:12/pp 107-111
Fig. Transesophageal echocardiography following resuscitation demonstrated a large serpentine embolus at right atrium



S-96.

IS CENTRAL VENOUS PRESSURE GOOD ENOUGH TO ESTIMATE EITHER LEFT ATRIAL PRESSURE OR PULMONARY ARTERY OCCLUSION PRESSURE DURING OFF-PUMP CORONARY ARTERY BYPASS SURGERY?

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Background: Hemodynamic derangement often occurs during cardiac displacement in off-pump coronary artery bypass grafting (OPCAB). One of the causes of hemodynamic derangement is the decreased preload. Accurate assessment of left ventricular end-diastolic volume (LVEDP) by transesophageal echocardiography may not be possible because of poor view during cardiac displacement. Thus, volume replacement during cardiac displacement is most often guided by cardiac filling pressures such as central venous pressure (CVP), and pulmonary artery occlusion pressure (PAOP). However, these pressures may not accurately reflect LVEDP because of cardiac displacement causing positional changes of the tip of the catheters. Therefore we tried to determine the relationship among CVP, PAOP, and left atrial pressure (LAP).
Methods: After institutional IRB approval and the informed consent, six patients undergoing elective OPCAB were enrolled. Anesthesia was induced with fentanyl and midazolam and was maintained with sevoflurane in oxygen and air. After induction of anesthesia, a pulmonary artery catheter (PAC) was inserted via the right jugular vein. The LAP catheter was inserted from the pulmonary vein into the left atrium. Blood pressure, heart rate, CVP, PAOP, and cardiac output were measured during the procedure. Measurements were made before coronary anastomosis (the heart in the normal position, baseline), during the left anterior descending artery anastomosis (LAD position), the right coronary artery anastomosis (RCA position), and left circumflex artery anastomosis (LCx position), and after all the anastomoses were completed. The data were analyzed using ANOVA and regression analysis.
Results: The data are summarized in table 1. There was a good correlation between PAOP and LAP at baseline. In the LAD position, the correlation between LAP and CVP was relatively poor. In the RCA position, all three pressures were well correlated. In the LCx position, the correlation between PAOP and CVP was very poor.
Conclusion: Excellent correlation between LAP and PAOP suggested LAP can be substituted by PAOP for guiding fluid therapy during OPCAB. However, poorer correlation between LAP and CVP suggested that CVP may mislead fluid therapy during the LAD position. In the LCx position, CVP did not reflect PAOP. When the patient undergoing OPCAB is managed without PAC, CVP during cardiac displacement should be interpreted with great caution. Furthermore, changes in ventricular compliance may complicate the interpretation of cardiac filling pressures to assess preload.

Regression analysis of LAP, PAOP and CVP (=R)

	baseline	LAD position	RCA position	LCx position
LAP vs. PAOP	0.97	0.91	0.90	0.98
LAP vs. CVP	0.75	0.55	0.79	0.89
PAOP vs. CVP	0.83	0.73	0.84	0.33

S-97.

THE INFLUENCE OF DEXMEDETOMIDINE ON SODIUM NITROPRUSSIDE INDUCED HYPOTENSION DURING ISOFLURANE ANAESTHESIA

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Introduction: Induced hypotension using sodium nitroprusside (SNP) is associated with reflex tachycardia, tachyphylaxis & the risk of cyanide toxicity [1,2]. Dexmedetomidine, a selective α_2-adrenoceptor agonist, produces a dose-dependent decrease in blood pressure and heart rate, sedation & analgesia suggesting that it would be a useful adjuvant to SNP deliberate hypotension [3]. This randomised, double blind & placebo controlled study was designed to investigate the influence of dexmedetomidine on SNP requirement for deliberate hypotension.
Methods: Thirty patients scheduled for elective body surface surgery were included in the study. After the institution of routine monitoring, one radial artery was cannulated (20 G) for direct blood pressure measurement. Patients were allocated randomly to receive, either placebo (20 ml saline) or dexmedetomidine (1 $\mu g.kg^{-1}$ in 20 ml saline) by intravenous infusion over 20 minutes, prior to induction. Anaesthesia was induced using morphine (0.1 $mg.kg^{-1}$) propofol (1-2 $mg.kg^{-1}$) and cis-atracurium (0.15 $mg.kg^{-1}$). Anaesthesia was maintained with 0.8% end-tidal isoflurane concentration in 50% N_2O in O_2 and incremental cis-atracurium. Once surgery started, SNP infusion was started at ($1\mu g.kg^{-1}min^{-1}$) and the rate adjusted to maintain mean arterial pressure (MAP) between 60-65 mmHg. The hear rate (HR) was recorded before, during steady-state SNP infusion & every 5 minutes after stopping SNP.
Results: The patients' demographic data, duration of surgery & duration of hypotension did not show statistically significant differences. The results are summarized in table 1. No adverse effects were noted during surgery or the post-operative period.

Table 1. The patients' demographic data, duration of surgery, duration of induced hypotension, SNP requirement and hemodynamic variables. Data are presented as mean values (SD) unless otherwise indicated.

	Control (N=15)	Dex. (N=15)	p -value
SNP omitted (%)	**1 (6.7 %)**	**5 * (33.3 %)**	**< 0.05**
SNP consumption	**5.8 (2.3)**	**1.78 * (0.8)**	**< 0.05**
SNP rate ($\mu g.kg^{-1}min^{-1}$)	**1.15 (0.5)**	**0.41 * (0.19)**	**< 0.05**
HR pre-SNP (B/min)	**67.3 (9.3)**	**72.2 (8.3)**	**> 0.05**
HR s.state -SNP (B/min)	**70.2 (7.8)**	**72.1 (14)**	**> 0.05**
HR post-SNP (B/min)	**65 (5.9)**	**67.8 (11.9)**	**> 0.05**
MAP pre-SNP	**77 (8.2)**	**74.7 (3.2)**	**> 0.05**
MAP steady state	**62.3 (1.3)**	**63 (1.1)**	**> 0.05**
MAP 5min post-SNP	**76.8 (9.9)**	**77.2 (7.5)**	**> 0.05**

Discussion: the results of this study reveal that dexmedetomidine may obviate the need for SNP, reduce the SNP dose requirement by 64.3 % without delaying the rate of recovery of MAP upon SNP withdrawal.
Conclusion: Single intravenous dose (1 µg/kg) is a safe adjuvant to SNP for induced hypotension under isoflurane anaesthesia. Direct comparisons of dexmedetomidine -SNP combination versus other combinations are needed.
Dexmedetomidine as a sole agent for deliberate hypotension should be studied.
References:
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[3] Taittonen MT et al. British Journal of Anaesthesia 1997; 78: 400-6

S-98.

UTILITY OF DIPYRIDAMOLE-THALLIUM STRESS TESTING PRIOR TO MAJOR VASCULAR SURGERY

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Introduction:
The American College of Cardiology (ACC) guidelines on preoperative cardiac evaluation[1] recommend preoperative stress testing prior to a peripheral vascular surgery (PVS), if the patient has an intermediate clinical predictor (ICP) or poor functional status. ICP's include history of congestive heart failure (CHF), history of myocardial infarction (MI), stable angina, chronic renal failure (CRF), and diabetes mellitus (DM). We examined whether the ACC guidelines were followed in obtaining preoperative stress testing and whether the tests predicted outcome in PVS.
Methods: Data on patients undergoing PVS from 11/03 to 3/04 were retrospectively analyzed for demographic variables, ICP's, medication usage, stress testing, and postoperative cardiac outcome (MI, CHF, death). Continuous variables were compared by t-tests and proportions by Monte Carlo randomization test, with $P < 0.05$ considered significant.
Results: 179 consecutive patients were enrolled. Preoperative comorbidities were not significantly different between those who were tested and those who were not.

	No test (N=91)	Test (N=88)	P value
Age	70.5 ± 11.3	69.8 ± 12.8	0.70
Gender (M:F)	52:39	60:28	0.19
Hx of CHF	13/91	14/88	0.85
Hx of MI	45/91	45/88	0.91
Hx of CRF	8/91	13/88	0.27
Hx of DM	48/91	53/88	0.35
Hx of IDDM	37/91	49/88	0.06
Poor function	71/91	67/88	0.84
Preoperative meds:			
ß-blocker	58/91	63/88	0.28
statin	51/91	51/88	0.89
aspirin	52/91	36/88*	0.03

Intraoperative use of ß-blockade was prevalent, regardless of the stress test result: 77/91 in those who were note tested, 47/62 in those with a negative test, and 18/26 in those with a positive test. Cardiac outcome was not significantly different between those tested and not tested or between those with a negative or a positive result on the stress test.

	No test (N=91)	(-) test (N=62)	(+) test (N=26)	P value
MI	4/91	3/62	2/26	0.81
CHF	6/91	2/62	1/26	0.69
Death	3/91	1/62	1/26	0.87
MI/CHF/death	7/91	7/62	3/26	0.73

Discussion: There was a large underutilization of the stress test with the majority of those who were not tested meeting the ACC criteria for a test. However, whether the patient had a stress test or whether the test was positive did not influence the cardiac outcome after PVS, possibly because of prevalent use of ß-blockade. The current ACC criteria for recommending preoperative stress testing may not be discriminating enough to identify high-risk patients at risk for adverse perioperative cardiac events.
References:
1. J Am Coll Cardiol 2002; 39:542-53

S-99.

INFLAMMATORY RESPONSE AND POST REPERFUSION SYNDROME IN ORTHOTOPIC LIVER TRANSPLANTATION

AUTHORS: A. Schmidt[1], H. Tomasdottir[2], A. Bengtsson[2];
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Introduction: In orthotopic liver transplantation (OLT) hemodynamic instability occurs frequently after graft reperfusion. This "postreperfusion syndrome" (PRS) is defined as a 30% decrease in mean arterial pressure from baseline for at least 1 minute within 5 minutes at reperfusion (1). The underlying mechanisms and mediators are still poorly understood. This study correlates cardiocirculatory changes after reperfusion with the release of inflammatory mediators with respect to the development of a PRS.
Methods: In 18 consecutive patients undergoing OLT hemodynamic profiles (obtained from standard monitoring during OLT including a pulmonary artery catheter) and plasma levels of inflammatory mediators (PMN elastase, TNF-α, IL-6 and PGE_2) were obtained preoperatively, 5 minutes before, and at 3, 10, 30 and 120 minutes after organ reperfusion. Comparisons were made between patients with (n=11) and without (n=7) PRS. P-values <0.05 were regarded significant.
Results: Increases in left (pulmonary capillary wedge pressure) and right (central venous pressure) cardiac filling pressures as well as the decrease in systemic vascular resistance did not differ between groups. Cardiac index, stroke volume index, and left ventricular work index were significantly lower in patients developing a PRS preoperatively and, including right ventricular work index, at all times post reperfusion ($p<0.05$). Plasma concentrations of PMN elastase, TNF-α, and IL-6 were elevated in the PRS group being significant from 10 minutes post reperfusion for PMN elastase and IL-6, and at 120 minutes post reperfusion for TNF-α. ($p<0.05$, respectively). PGE_2 levels did not differ between groups (table 1).
Discussion: The development of a PRS is mainly characterized by depressed myocardial function and accompanied by a pronounced though delayed increase in TNF-α, IL-6, and PMN elastase. Since cardiocirculatory deterioration precedes TNF-α, IL-6, and PMN elastase elevation for more than 10 minutes, these mediators are unlikely to trigger the development of a PRS. However, the increase in the target group suggests a role for these mediators in PRS, contributing to systemic vasodilation as well as to decreased myocardial performance in PRS (2,3).
References:
1. Transplant Proc 1987; 4:54-55.
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3. Am J Gastroenterol 1999; 94:169-177.

Mean values ± SEM are given, * indicates $p<0.05$ vs. non-PRS.

		Pre-op	3 min post reperfusion	10 min post reperfusion	30 min post reperfusion	120 min post reperfusion
Elastase	PRS	83±24	175±26	235±26*	238±38*	281±39*
[ng/ml]	non-PRS	73±45	130±22	182±34	173±24	126±28
TNF-α	PRS	7.3±1.8	11.4±4.0	14.2±5.5	19.5±6.4	73.3±21.7*
[pg/ml]	non-PRS	5.1±1.8	3.0±0.6	4.1±0.8	8.4±1.8	13.6±2.0
IL-6	PRS	102±57	114±28	168±45*	200±43*	336±58*
[pg/ml]	non-PRS	50±22	51±14	50±13	67±15	111±43
PGE2	PRS	120±13	129±17	124±17	133±23	116±2
[pg/ml]	non-PRS	170±27	117±14	110±11	117±12	83±8

S-100.

INCIDENCE OF THE ARTERIOVENOUS FISTULA FAILURE FOR HEMODIALYSIS AFTER GENERAL ANESTHESIA

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Introduction: In Japan, almost all of the patients with chronic renal failure on hemodialysis have been constructed arteriovenous fistula for blood access by surgical operation. In these patients, the blood pressure decreases remarkably in general anesthesia compared to the patients without this disease due to hypovolemia by preoperative hemodialysis, decrease of reserved capacity in circulatory system, and systemic arterial sclerosis. This severe hypotension during general anesthesia decrease the blood flow in the AV fistula, and can cause the thrombosis of AV fistula (AV fistula failure: AVF) was not reported on the incidence of blood access trouble such as occlusion or dysfunction necessary for repair by surgical operation. The aim of this study is to evaluate the incident of circulatory disorder such as hypotension / hypertension, and the incidence of AVF for reconstruction operation after recovery from general anesthesia.
Methods and Materials: We examined the patients with chronic renal failure on hemodialysis who underwent elective surgery under general anesthesia for the last one year. The anesthesia record and medical record were examined retrospectively up to the discharge in order to evaluate the abnormal hypertension / hypotension during general anesthesia, the drug use to the abnormal cardiovascular responses, and the status of AV fistula after general anesthesia.
Results: There were 312 patients on hemodialysis who under went elective surgery under general anesthesia for the last one year in our hospital, and we could follow up 90 patients. During perioperative period, 44 patients (48.8%) could be injected with phenylephrine and ephedrine, and it was necessary for 21 patients (23.3%) with dopamine and norepinephrine infusions. Moreover, 11% patients (10/90 patients) caused AVF after surgery, and underwent the reconstruction operation. The earliest one was done postoperative 4th day, and the latest postoperative day 53. In those 10 cases, at least 4 patients have experienced AVF before surgery under general anesthesia.Discussion: In our study, the patients on hemodialysis easily cause hypotension, but could be treated with vasoactive drugs. We found that there is common past history which repetition of AVF among the patients undergone the postoperative reconstruction operation. Although it is believed that perioperative hypotension was a major factor that causes AVF, we could not find any remarkable difference of continual hypotension period between the patients with postoperative AVF and those without it. As to the intraoperative position, it has been said AV fistula is likely to occlude when patients set the side of AV fistula lower in lateral position. However, our study did not suggest any tendency in the position during surgery. Therefore, we concluded that the major factor that induced postoperative AVF was not intraoperative hypotension or patient's position, but the problems related to patients themselves.

S-101.

A NOVEL ANESTHETIC TECHNIQUE FOR CAROTID ARTERY STENT PROCEDURE WITH THE USE OF BILATERAL BISPECTRAL INDEX IN THE AWAKE PATIENT

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Introduction: Carotid stenting systems (CSS) are new less invasive surgical approaches to traditional carotid endarterectomy (CEA). Presently, there are no published studies in the anesthesia literature regarding anesthetic management of patients undergoing CSS, because FDA approval is ongoing (1). While the learning curve is steep, we report our preliminary findings on a novel anesthetic technique for carotid artery stenosis repair by CSS.
Methods: After IRB approval and informed consent, an ongoing prospective study determining whether local anesthesia combined with MAC (sedation and analgesics) is feasible for CSS. Standard monitors, two large bore IV lines, and an arterial line were utilized. Patients were awake and conversant during the entire procedure. Bilateral bispectral index monitors measured BIS scores over the right and left cerebral hemispheres. Neurologic status was monitored with a "squeaky toy" placed in the patient's contralateral hand. The head was secured with bolsters fastened to the table with tape. Lidocaine 0.5% was injected by the surgeon for percutaneous femoral artery canulation.
Results: 13 consecutive patients, 8 male and 5 female, were studied. Mean age was 67yrs (range 57-78). ASA classification were III's=3 and IV's=10. Mean doses of fentanyl and 0.5% lidocaine were 130mcg and 10mL, respectively. Ipsilateral and contralateral BIS scores at baseline, occlusion and post-procedure are shown in the graph below.
Discussion: Preliminary results suggest MAC anesthesia is feasible for CSS surgery. An awake conversant patient allows early detection of neurologic insult and necessitates vigilance by the anesthesiologist. Constant monitoring of both hemodynamic and neurologic status can influence outcome if stroke, vagal reflexes, cardiac arrhythmias and myocardial ischemia are recognized and managed early. Midazolam is avoided in these elderly patients to preserve cognitive senses and foster cooperation, so that during critical stent deployment the patient does not move when precision is so essential. Although the BIS index is not intended to detect cerebral ischemia, it may be the first indication of a serious cerebral event (2). All our patients demonstrated BIS recovery. However, failed BIS recovery warrants further investigation (i.e. CT scan, angiogram, MRI, and/or serial neurologic exams).

Reference:

1. Carotid Revascularization Using Endarterectomy or Stenting Systems (CARESS): Phase I Clinical Trail. J Endovasc Ther 2003;10:1021-30.
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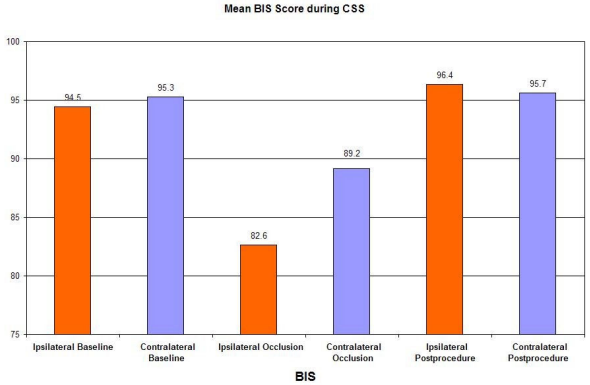

S-102.

POSTOPERATIVE STRATEGY FOR DIALYSIS-DEPENDENT PATIENTS UNDERGOING CARDIAC SURGEY

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INTRODUCTION: Perioperative management of dialysis-dependent patients has been improved. However, the mode of renal replacement therapy after cardiac surgery in such patients and the timing of its commencement remains to be resolved, especially in hemodynamically unstable patients. The present study was designed to examine the usefulness and safety of continuous veno-venous hemodialysis (CVVHD) immediately after cardiac surgery.
METHODS: We studied forty dialysis-dependent patients undergoing cardiac surgery with cardiopulmonary bypass from 1997 to 2004. CVVHD was commenced postoperatively after confirmation of hemostasis, irrespective of circulatory status. The rate of plasma removal was 100 ml/hr (blood flow rate; 100 ml/min, dialyzate flow rate; 900 ml/hr, diafiltrate flow rate; 1000 ml/hr). Activated clotting time was maintained between 140 and 160 seconds by titrating anticoagulants. We investigated the following variables to demonstrate the usefulness and safety of CVVHD; 1) time course of blood volume from drainage tube postoperatively before and after CVVHD, 2) circulatory, respiratory and biochemical status before and after CVVHD in patients requiring continuous intravenous adrenaline or intra-aortic balloon pump (IABP) (defined as unstable hemodynamic group), 3) early mortality rate (within 30 days after surgery).
RESULTS: Seventeen patients underwent isolated coronary artery bypass grafting (CABG) and twenty three underwent combined CABG or valve surgery. CVVHD was started at 4.4±3.8 hours after admission to the ICU and the duration of CVVHD was 48±59 hours. The blood volume from the drainage tube was significantly reduced after the start of CVVHD. After going with CVVHD for 12 hours, circulatory status was improved, PaO2/FIO2 was also increased from 262±147 mmHg to 320±104 mmHg, and serum creatinine was reduced from 5.2±2.4 mmol/L to 4.9±2.1 mmol/L significantly in unstable hemodynamic group (n=14). Early mortality rate was 0 % in CABG and 4% in valve surgery.
DISCUSSION: Continuous renal replacement therapy (CRRT) even for acute renal failure has been controversial (1). We consider that CRRT has possibility of life-saving potential for dialysis-dependent patients judging from lower early mortality rate than that previously reported (2).
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Critical Care and Trauma

S-103.

REMOVING ENDOGENOUS CANNABINOIDS USING DIRECT HEMOPERFUSION THERAPY WITH POLYMYXIN-B IMMOBILIZED FIBER IN SEPTIC PATIENTS

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[Introduction] Polymyxin-B absorbs endogenous cannabinoids, which are factors causing septic shock, and direct hemoperfusion therapy with polymyxin-B immobilized fiber (PMX-DHP) decreases the serum levels of endogenous cannabinoids.(1)However, it is still unclear whether removing endogenous cannabinoids leads to elevated blood pressure in septic patients.
[Methods] We report the time-course of endogenous cannabinoids (ANA and 2-AG) in septic patients. These were measured simultaneously using gas chromatography-mass spectrometry-selected ion monitoring.(2) We also measured interleukin-6 (IL-6) as a marker of inflammatory status, and 8-epiprostaglandin F2 alpha(8-epi) as the index of oxidative stress. To examine the mechanism of blood pressure elevation caused by PMX-DHP, we divided patients into two groups. The one was blood pressure elevation group, and the other was blood pressure constant group.
[Results] 2-AG decreased significantly in blood pressure elevation group. (figure1) Blood pressure elevation group demonstrated low serum levels of IL-6 and 8-epi, nevertheless the serum levels of 2-AG were high.
[Conclusions] We verified that removing endogenous cannabinoids accompanied by PMX-DHP was one of the mechanisms of the blood pressure elevation in septic patients. In particular, patients who have not received large insults showed remarkable blood pressure elevation. In the future, it is necessary to examine appropriate PMX-DHP conditions, which orient the adsorption of endogenous cannabinoids.
[References]
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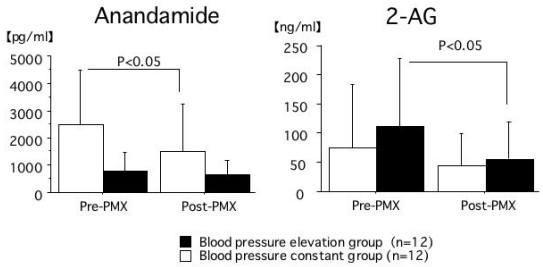

Figure 1

S-104.

LOCAL ANESTHETICS REDUCE MORTALITY AND PROTECT AGAINST RENAL AND HEPATIC DYSFUNCTION IN MURINE SEPTIC PERITONITIS

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Introduction: Mortality from sepsis frequently results from multiple organ injury and dysfunction. Cecal ligation and puncture (CLP) is an established murine model of sepsis characterized by an initial hyperinflammatory response. Local anesthetics have been shown to attenuate inflammatory responses both *in vivo* and *in vitro*. In the present study, the ability of local anesthetic infusions to protect against sepsis-induced mortality, as well as renal and hepatic dysfunction following CLP was investigated.
Methods: Male C57BL/6 mice (~25g) were anesthetized with pentobarbital (50 mg/kg i.p.) and implanted with sub-cutaneous mini-osmotic pumps that delivered 10% lidocaine, 1% bupivacaine or saline at a rate of 1µl/hr and subjected to CLP with a 20G needle. Renal function and hepatic function were assessed by measuring plasma creatinine (Cr) and AST/ALT, respectively. Seven day mortality was also assessed. To determine if local anesthetics protect by reducing inflammation, 24 hours following CLP we measured plasma KC & TNF-α levels, intercellular adhesion molecule-1 (ICAM-1) protein expression, myeloperoxidase (MPO) activity, and pro-inflammatory mRNA levels. Renal apoptosis was also assessed. The data was analyzed with one-way analysis of variance plus Tukey's post hoc multiple comparison test. Survival was compared with Log-rank test. Data is expressed as a mean $\pm$ S.E.
Results: Mice receiving local anesthetic infusion showed improved 7 day survival compared to saline-treated mice. Mice treated with 10% lidocaine or 1% bupivacaine infusion had significantly lower plasma Cr at 24 hours (0.5 ± 0.1 mg/dL, N=10 and 0.5 ± 0.1 mg/dL, N=5; $p<0.001$ respectively) compared to mice treated with saline-vehicle alone (1.2 ± 0.1 mg/dL, N=13; $p<0.05$). Similarly, mice receiving 10% lidocaine or 1% bupivacaine infusion had significantly lower AST (134±13 U/mL, N=7 and 169±28 U/mL, N=4 respectively; $p<0.001$) and ALT (78 ± 7 U/mL, N=7 and 95 ± 23 U/mL, N=4 respectively; $p<0.001$) compared to mice treated with saline-vehicle alone (AST= 349 ± 15 U/mL, N=15 and ALT= 142 ± 10 U/mL, N=12). At 24 hours, both TNF-α and KC plasma levels in mice undergoing CLP with saline-vehicle was significantly elevated compared to levels seen with local anesthetic infusion. In renal cortex, we observed attenuation in MPO activity (ΔOD/min./mg protein) following CLP with 10% lidocaine or 1% bupivacaine infusion (0.5 ± 0.1, N=3 and 0.3 ± 0.2, N=5; respectively) versus mice undergoing CLP with saline-vehicle (2.1 ± 0.2, N=9; $p<0.05$). Significant reductions in ICAM-1 protein expression, pro-inflammatory mRNA levels, and apoptosis were also observed 24 hours following CLP in the local anesthetic-treated renal cortices.
Conclusions: Local anesthetic infusions confer a protective effect in mice from septic peritonitis by attenuating the hyperacute inflammatory response. This suppression resulted in improved mortality and less progression to acute kidney and liver dysfunction. Given the protective benefit on survival and organ dysfunction observed with chronic local anesthetic infusion, our findings may have important therapeutic implications for patients in early sepsis.

S-105.

GLUTAMINE PREVENTS ACUTE RESPIRATORY DISTRESS SYNDROME FOLLOWING SEPSIS THE RAT: ROLE OF HEAT SHOCK PROTEIN-70

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Background: Heat Shock Protein 70 (HSP-70) is vital to cellular and tissue protection following stress or injury. Specifically, adenoviral transfection of HSP-70 into pulmonary epithelium has been shown to prevent lung injury and improve survival following sepsis (1). However, application of this powerful tool in human disease has been limited, as known enhancers of HSP-70 are toxic and not clinically relevant. Glutamine (GLN) can enhance HSP-70 expression in non-clinically relevant animal injury models. The aim of this study was to assess the ability of GLN to enhance pulmonary HSP-70 expression and prevent occurrence of the acute respiratory distress syndrome (ARDS) following sepsis in the rat.
Methods: We utilized a rat model of cecal-ligation and puncture (CLP) to induce sepsis. GLN (CLP/GLN) or saline vehicle (CLP) was administered 1-hour following initiation of sepsis. We analyzed HSP-70 via western blot and ELISA. Tissue metabolism was assayed by magnetic resonance spectroscopy. Occurrence of ARDS was determined via histopathologic examination. An inhibitor of HSP-70 expression, quercetin, was utilized to assess role of HSP-70 expression in prevention of sepsis-related mortality.
Results: GLN, given as post-treatment, increased pulmonary HSP-70, prevented the occurrence of ARDS, and improved survival following sepsis (Table) Further, GLN improved indices of lung metabolic function. Administration of the HSP-70 inhibitor quercetin (Q) blocked GLN-mediated enhancement of HSP-70 expression and abrogated GLN's survival benefit.
Discussion: GLN has been safely administered to critically ill patients and shown to improve outcome without clear understanding of the protective mechanism (2,3). This data indicates enhanced HSP-70 expression may be a vital mechanism by which GLN improves outcome in critical illness. Our results further indicate GLN may prevent the occurrence of ARDS and mortality following sepsis via enhanced HSP-70 expression. GLN may be a clinically relevant pharmacologic enhancer of HSP-70 and be beneficial in the treatment/prevention of ARDS.

References:

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Table
7 day mortality following CLP-induced sepsis

CLP	CLP/GLN	CLP/Q	CLP/GLN/Q
14/17 (78%)	6/18 (33%)	12/15 (80%)	11/15 (73%)

Shown are no. deaths/total no.of animals undergoing treatment.

S-106.

METRONIDAZOLE IMPROVES INTESTINAL MICROCIRCULATION IN SEPTIC RATS

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Introduction. Antibiotic treatment represents a key component of therapy for severe sepsis. In addition to their antimicrobial activity several antibiotics have been shown to exert effects on the intestinal microcirculation. Impairment of intestinal microcirculation has been recognized as an important factor in the pathogenesis of the septic syndrome (intestine = "motor" of multiple organ failure). The aim of this study was to evaluate the effects of metronidazole (MET) on the intestinal microcirculation in septic rats using intravital microscopy (IVM).
Methods. In a first series of experiments we induced sepsis by using CASP (Colon Ascendens Stent Peritonitis) model in the rat (16h prior microscopy). To differentiate antimicrobial from microcirculatory effects we performed the second series of experiments using a model of endotoxemia (lipopolysaccharide i.v. injection, LPS 15mg/kg). We evaluated functional capillary density (FCD) and leukocyte-endothelial interaction of the blood vessels in the wall of the terminal ileum by IVM. MET was given i.v. (100 mg/kg) 2 hours before microscopic examination.
Results. In the CASP model, treatment with MET increased significantly FCD in the muscular and mucosal layer (Musc. long.: control 174 ±11, CASP 130 ±14, CASP+MET 154 ±4; Musc. circ.: control 207 ±14, CASP 136 ±8, CASP+MET 173 ±27; Mucosa: control 504 ±34, CASP 395 ±35, CASP+MET 513 ±58; cm/cm2; mean ±SD; p>.05). The number of temporarily (roller) and firmly (sticker) adherent leukocytes was reduced in the CASP+MET group, as compared to the untreated CASP group (roller V3-venules: control 5.4 ±2.5, CASP 11.8 ±6, CASP+MET 7.3 ±2.5; n/min; mean ±SD; p<.05). In the LPS animals, MET treatment resulted in equally increased FCD (Musc. circ.: control 162 ±33, LPS 122 ±22, LPS+MET 147 ±16; Musc. long.: control 154 ±17, LPS 107 ±5, LPS+MET 1134 ±9; Mucosa: control 476 ±45, LPS 333 ±35, CASP+MET 385 ±23; cm/cm2; mean ±SD; p>.05).
Discussion. Metronidazole, which is often used in therapy of sepsis, may have effects on the septic rat intestinal microcirculation by increasing functional capillary density and diminishing leucocytes - endothelial interaction. Apart from the sensitivity of the causing microorganisms, when choosing antimicrobial agents in septic conditions, possible effects of antibiotics on the microcirculation should also be taken into account.

S-107.

EVIDENCED-BASED REDUCTION OF VENTILATOR ASSOCIATED PNEUMONIA IN THE POST-CARDIAC SURGICAL PATIENT

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Introduction: Ventilator-associated pneumonia (VAP) is the most common intensive care unit (ICU) nosocomial infection occurring in 4% - 48% of patients depending on the definition. Morbidity, mortality, and health care costs are all elevated in patients acquiring VAP, making its prevention paramount to successful ICU practices.[1-5] The purpose of this study was to determine if a multidisciplinary approach to managing ventilated patients would reduce the incidence of VAP in the postoperative cardiac patient.
Methods: A multidisciplinary team designed a Best Practices Model and Ventilator Bundle in the 40-bed cardiovascular ICU (CVICU). Education for all members of the CVICU care team was done during January 2004 highlighting the importance of reducing VAP; fact sheets and posters reinforcing these new policies were posted throughout the CVICU. The incidence and health care costs associated with VAP were subsequently compared between two patient populations: (1) those admitted between July 2003 and January 2004 not receiving consistent treatment; and (2) those admitted between February and July 2004 who were managed consistently. VAP was defined according to the NNIS system.
Results: Rates of VAP per 1000 ventilator days were calculated. There were 51 episodes of VAP in the CVICU during the thirteen-month study period (9.64/1000 ventilator days). VAP total rates dropped from 10.3/1000 ventilator days in the 7 months prior to consistent interventions to 8.7/1000 ventilator days in the 6 months following ($p = 0.6$). Decreased rates were also observed between the pre-protocol group (July 2003 to January 2004) and those patients who most recently exited the study (July 2004), 10.3/1000 ventilator days to 2.6/1000 ventilator days ($p = 0.09$) (Table 1). Additionally, health care costs also significantly decreased between the 2 study groups from $1,280,000 in group 1 to $760,000 in group 2 ($p < 0.01$).
Discussion: Utilizing a multidisciplinary team, educating all patient-care providers, as well as implementing and enforcing a consistent ventilator Best Practices Model and Ventilator Bundle decreased infection rates and subsequent CVICU costs. Further investigations are needed to determine optimal management strategies once a patient has been diagnosed.
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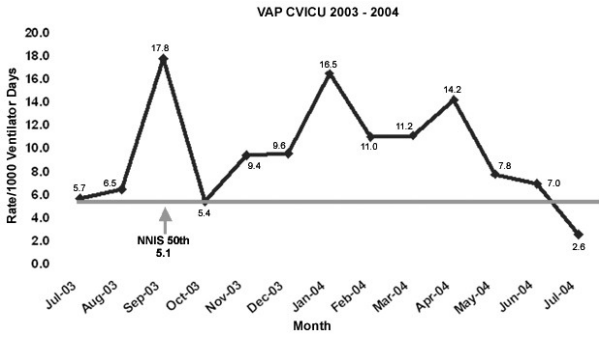

S-108.

VASOPRESSIN MAY BE USEFUL IN THE TREATMENT OF SYSTEMIC ANAPHYLAXIS: AN IN VIVO STUDY IN RABBITS

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Recent papers demonstrate that the administration of vasopressin (VP) is useful when treating hemorrhagic shock(1) and endotoxic shock(2). The effect of VP on systemic anaphylaxis has not, to our knowledge, been investigated. In rabbits, the administration of VP can cause increase of blood pressure(3)(4). Thus we evaluated the effect of VP on the circulatory depression provoked by systemic anaphylaxis and survival rates in rabbits with systemic anaphylaxis *in vivo*. Forty rabbits were sensitized to horse serum. After 14 days, the rabbits were randomly allocated to three groups: At 1 min after the administration of antigen, rabbits in group I (n=14), served as control, received a infusion of 0.9% NaCl solution at 0.4 ml•kg^{-1} for 30sec. Rabbits in group II (n=13) received infusion of VP at 0.8 U•kg^{-1} for 30sec. Rabbits in group III (n=13) received a infusion of VP at 0.08 U•kg^{-1} for 30sec. Hemodynamic parameters were monitored continuously for 45 min. Systemic anaphylaxis developed after the antigen challenge in all rabbits. Mean arterial pressure (MAP) was significantly higher in group III than in group I during 2 min to 5 min. The values were significantly higher in group II than in group I during 3 min to 5 min. Heart rate (HR) was significantly lower in group II at 2 and 3 min than in group I. The value was significantly lower in group II at 2 min than in group III. Central venous pressure (CVP), pulmonary resistance (R_L) and dynamic pulmonary compliance (C_{dyn}) were almost similar in all groups. Survival rates differed significantly between group III and group I, II. In group III, 9 of 13 rabbits were still alive 45 min after antigen challenge. In group I and II, 4 of 14 rabbits and 3 of 13 rabbits were alive 45 min after antigen challenge, respectively. All deaths were observed over 2 min after antigen challenge. In conclusion, the administration of 0.08U•kg^{-1} VP improved severe hypotension provoked by systemic anaphylaxis and survival rates, suggesting that this agent may be useful in treatment of systemic anaphylaxis.

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S-109.

NEURONAL NITRIC OXIDE SYNTHASE INHIBITION PRESERVES HYPOXIC PULMONARY VASOCONSTRICTION IN OVINE LUNG INJURY

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Introduction: Nitric oxide (NO) plays a pivotal role in the pathogenesis of pulmonary disorders of fire victims (1). We hypothesized that NO, derived from the neuronal nitric oxide synthase (nNOS), blunts hypoxic pulmonary vasoconstriction (HPV), thereby impairing gas exchange. This study was designed as a prospective, controlled and randomized laboratory experiment to examine the effects of 7-nitroindazole (7-NI), a specific nNOS inhibitor, on HPV and pulmonary function in an established ovine model of combined burn and smoke inhalation injury (2).
Methods: Following a baseline measurement, sheep were randomly assigned to I. healthy controls (sham), II. injured controls (40%, 3rd degree flame burn; 48 breaths of cotton smoke), or III. an injured intervention group treated with 7-NI (1 mg/kg) from 1h post injury until the end of the 48-h study period (n=7 each). Using an ultrasonic transit-time flow probe, positioned around the left pulmonary artery, HPV was assessed as decrease in left pulmonary blood flow (corrected for changes in cardiac index) in response to left lung hypoxic challenges performed at baseline, 24h and 48h post injury. Statistical analysis was performed using two-way ANOVA with Student-Newman-Keuls post hoc comparisons. Data are expressed as mean±SEM or %. A p-value <0.05 was considered as significant.
Results: All physiologic variables remained unchanged in sham animals. In injured controls, the hypoxic challenge at baseline led to a 56% decrease in left pulmonary blood flow. After 24h and 48h, HPV was markedly impaired (17% and 6%; p<0.001 vs. baseline) and associated with progressive pulmonary shunting and reciprocal decreases in PaO_2/FiO_2 (24h, sham: 498±19; injured controls: 208±45; p<0.05 between groups). While inducible nitric oxide synthase (iNOS) mRNA remained unchanged in injured control animals, nitrate/nitrite (NOx) plasma levels (chemiluminescence) increased and contributed to significant 3-nitrotyrosine formation (ELISA, immunohistochemistry), the stable biomarker of peroxynitrite. In vitro experiments confirmed that the administered 7-NI dose selectively inhibited nNOS and not iNOS. However, 7-NI significantly reduced iNOS mRNA, decreased NOx plasma levels, reduced lung tissue 3-nitrotyrosine concentrations, attenuated the loss of HPV (24h: 44%, 48h: 38%), and improved gas exchange (PaO_2/FiO_2 at 24h:434±47; p<0.05 vs. injured controls).
Discussion: The present study confirms that nNOS-derived NO plays an important role in the pathogenesis of acute lung injury secondary to combined burn and smoke inhalation injury and suggests that nNOS inhibition may be a goal-directed approach to attenuate the severity of injury. The notion that nNOS may potentially regulate iNOS needs to be confirmed in future studies.
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S-110.

EFFECTS OF AEROSOLIZED ANTICOAGULANTS ON PULMONARY FUNCTION IN SHEEP WITH BURN AND SMOKE INHALATION

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Introduction: Airway obstructive cast causes pulmonary gas exchange deterioration leading to the systemic hypoxemia. The cast consists, in part, from fibrin. Previously, we have shown that the lysis of fibrin by tissue plasminogen activator reduced the severity of acute lung injury in sheep with combined burn and smoke inhalation. In the present study we hypothesized that the prevention of the fibrin clot in airway casts by aerosolized anticoagulants improves pulmonary function. To test our hypothesis we developed an ovine model of acute lung injury and tested effects of different anticoagulants. Method: Female sheep were surgically prepared for chronic study. After recovery, a tracheostomy was performed under ketamine/halothane anesthesia, and given a burn (40% of total body surface, 3rd degree) and inhalation injury (cotton smoke). Sheep were given 4 ml/kg/24h of Ringer's lactate and mandatory ventilation. Sheep were divided into 5 groups: 1) non-injured, non-treated (sham, n=6); injured, nebulized with 2) saline (saline, n=6), 3) heparin (Hep, n=5), 4) antithrombin (AT, n=5), and heparin+antithrombin (Hep+AT, n=5). Saline, heparin (10,000u), and antithrombin (290u) were nebulized every 4h after the injury. To maximum mimic clinical situation, nebulization of the anticougulants was started 2 hrs after the insult. Statistical analysis was performed by ANOVA (Scheffe) test. Experiment lasted 48h. Results: The cardiopulmonary parameters were stable in sham animals. The saline group showed marked signs of acute lung injury evidenced by deteriorated gas exchange [PaO2/FiO2, pulmonary shunt (Qs/Qt)], increased lung lymph flow and increased lung water content associated with increased airway obstruction score and airway pressures. Posttreatment (nebulization) with heparin or antithrombin had no noticeable effects on these changes. However, combined heparin and antithrombin nebulization reversed those alterations. The pulmonary dysfunction seen in saline nebulized sheep was associated with significant decreased level of plasma antithrombin. Discussion: Taken together, the results suggest 1) prevention of fibrin clot in obstructing cast results in better airway clearance, thereby improved pulmonary function in sheep with combined burn and smoke inhalation injury. 2) Since effects of antithrombin and heparin are dependent on each other, combined therapy could be beneficial especially in such conditions when anthithrombin is depleted. .

	Sham	Saline	Heparin	AT	Heparin+AT
PaO2/FiO2					
0h	510±9	517±14	533±8	512±12	520±7
48h	560±60	149±31*	151±22	145±27	304±53†
Qs/Qt					
0h	0.18±0.01	0.13±0.03	0.15±0.01	0.15±0.02	0.19±0.02
48h	0.12±0.01	0.38±0.06*	0.34±0.01	0.44±0.05	0.22±0.03†

*p< 0.05 vs. sham, †<0.05 vs. saline

S-111.

IDENTIFICATION OF A CELL LINE HIGHLY SENSITIVE TO INDUCTION OF APOPTOSIS BY TNF-α

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Introduction: A cytokine, tumor necrosis factor-α (TNF-α), plays an important role in biological responses which require critical care, such as autoimmune and infectious diseases, septicemia, toxic shock syndrome, hemorrhage, ischemia/reperfusion injury, and so on [1]. Furthermore, TNF-α induces apoptosis in many normal and transformed cell lines. Several biological or immunological assays for the detection and quantification of this cytokine activity have been developed [2]. In bioassays to detect the cytotoxic effects of TNF-α, the L929 mouse fibroblast cell line has frequently been used. But previous assay methods using L929 cells require longer incubation periods and higher concentrations of TNF-α. So in order to enhance the susceptibility of L929 cells to TNF-α additional procedures to compensate for the low sensitivity of L929 cells have been introduced.
Material and Methods: *Cells.* The S+L-CCC feline kidney cell line 8C and the L929 murine tumorigenic fibroblast cell line were cultured at 37°C in Eagle's minimum essential medium (E-MEM) containing 10 % fetal calf serum (FCS) [3].
Methods. To estimate the susceptibility to TNF-α, cell viability of 8C and the L929 was assessed by trypan blue staining. MTS assay was used for examination of cytotoxic effect of TNF-α, FasL or TRAIL on 8C cells. In the presence of viable cells, tetrazolium salt, [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2-H-tetrazolium, inner salt; MTS], is converted to colored formazan. Absorbance was recorded using a microplate reader. In addition, to characterize the mode of cell death induced by TNF-α, 8C cells treated with rhTNF-α were stained with a DNA-binding dye, Hoechst 33,342 (Sigma) and AnnexinV/propidium-iodide [4].
Results: We found that the S+L-CCC feline kidney cell line, 8C, was about 100 times as susceptible to a cytotoxic effect of TNF-α as the L929 cell line, and that the mode of cell death of 8C cells induced by TNF-α was apoptosis.
Discussion: These findings enabled us to develop a new convenient bioassay for TNF-α, which is based on the function of viable cells that convert tetrazolium salt to colored formazan: the degree of 540 nm absorbance is proportional to the number of viable cells. This cytotoxity assay may offer advantages over bioassay systems available now, as it is sensitive and rapid.
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S-112.

BOTH NA+/H+-EXCHANGE ACTIVITY AND NAPI-COTRANSPORTER TYPE I CAUSE NA+-DEPENDENT ALKALINIZATIONS IN PRIMARY CULTURED RABBIT MTAL CELLS

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Introduction: Ischemic Acute Renal Failure (ARF) complicates up to 30% of post-operative admissions to Intensive Care Units. A better understanding of the pathophysiology of ischemic ARF at the cellular level may lead to new treatment strategies. Since changes in intracellular pH (pH_i) play a crucial role in ischemia-reperfusion injury (IRI) in hepatocytes, neuronal and myocardial cells, the goal of our research is to study pH_i during IRI in a new model of kidney cells (primary cell cultures of the medullary thick ascending limb of Henle (MTAL) from rabbit kidney)[1]. In this part, the pH-regulatory mechanisms expressed in these cultured cells were investigated in physiological conditions.
Methods: The pH_i in these primary cell cultures was measured fluorimetrically by using the pH-sensitive probe BCECF. The absence of HCO_3^--reabsorption in the rabbit MTAL segment allowed us to work with HCO_3^--free solutions. Indirect immunofluorescence for sodium-phosphate cotransporters (NaP_i) type I and II were performed with antibodies from the laboratory of H. Mürer (University of Zürich, Switzerland).
Results: Resting pH_i in cultured MTAL cells, when perfused on both sides with HEPES-buffered solutions at 37° C, was 7.22 ± 0.07 (n=5). Using Bafilomycin A_1, no evidence for a functional H^+-ATPase was found in these cells. Experiments on Na^+-dependent alkalinizations of acidified cells, revealed the presence of Na^+/H^+-exchange activity, both in the basolateral and in the apical cell membrane. Both exchangers could be completely blocked with ethyl-isopropyl-amiloride (EIPA, 10 μM). However, at the apical cell membrane, also EIPA-resistant Na^+-dependent alkalinizations were observed: in the presence of P_i in the apical superfusion solution, addition of Na^+ in the presence of EIPA (10 μM) alkalinized the cells at 0.07 ± 0.01 pH units/min (n=5). Also, the addition of 2 mM P_i to the apical superfusion solution alkalinized the cells at 0.09 ± 0.03 pH units/min (n=10), but only in the presence of Na^+. These results are consistent with the presence of a NaP_i-cotransporter in the apical cell membrane. With indirect immunofluorescence, the NaP_i-cotransporter expressed in these cultured cells could be identified as NaP_i type I.
Discussion: Taking into account data from the literature, the basolateral Na^+/H^+-exchanger probably is the NHE-1 isoform and the apical Na^+/H^+-exchanger could be, either NHE-1, NHE-2 or both. The finding of a NaP_i-cotransporter in these cultured cells was unexpected since no phosphate reabsorption takes place in the rabbit MTAL segment. Furthermore, the physiological role of NaP_i type I still is unclear. In proximal tubular cells and hepatocytes, NaP_i type I was shown to be upregulated by high glucose concentrations. Since a high-glucose medium was used for these primary cell cultures, the composition of the medium may have influenced the phenotype of these cultured MTAL cells.
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S-113.

ORAL GLUTAMINE ENHANCES HEAT SHOCK FACTOR-1 ACTIVATION, HEAT SHOCK PROTEIN 70 EXPRESSION, AND IMPROVES SURVIVAL FOLLOWING HEATSTROKE IN RATS

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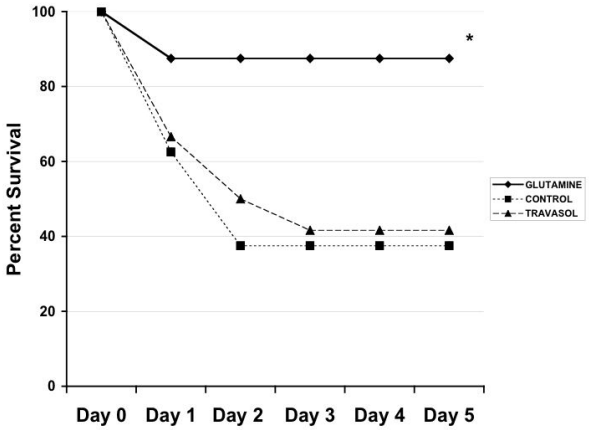
Background: No pharmacological agent has shown benefit in the treatment of heatstroke. Previous research has indicated that enhanced heat shock protein 70 (HSP-70) expression can improve survival following experimental heat stroke. However, no clinically relevant enhancer of HSP-70 has been utilized in human trials. We have previously shown that intravenously administered glutamine (GLN) can enhance tissue HSP-70 expression in rodent models of sepsis. This study attempted to test the hypothesis that orally administered GLN could enhance tissue HSP-70 expression and improve survival following heatstroke.
Methods: GLN (0.65 g/kg) (n=8), an iso-nitrogenous control solution (Travasol) (n=12), or saline placebo (n=8) was administered to Sprague-Dawley Rats (250-300 g) via gavage twice a day for 5 days prior to experimental heatstroke. Heatstroke was performed in anesthetized rats (ketamine/xylazine) by heating animals to 42 deg. C (rectal temperature) for 30 minutes. Survival was analyzed for 5 days post-heatstroke. In a separate set of animals, HSP-70 and Heat Shock Factor-1 activation (HSF-1) was analyzed at 1-hour and 24-hours post-heatstroke in colon, heart, and lung tissue via western blot (n= 10/ group).
Results: Marked mortality was observed in the iso-nitrogenous control animals and saline placebo treated animals, whereas oral GLN therapy significantly improved survival (*-$p < 0.05$) (See Figure). GLN administration enhanced HSP-70 1-hour post-HS in heart, lung, and colon. ($p < 0.01$ versus unheated animals and heated placebo animals). Colon, but not heart and lung, demonstrated enhanced HSP70 expression 24 hours post-HS. ($p<0.01$ versus heated placebo animals). Oral GLN administration led to significantly enhanced HSF-1 (the transcription factor for HSP-70) activation in colon prior to heat stress ($p < 0.05$ versus saline) and at 1 hr post-heat stress ($p < 0.01$ versus saline). No change in HSF-1 activation was seen following heatstroke in heart and lung.
Conclusions: These observations demonstrate for the first time that oral, *in vivo*, administration of GLN can improve survival following lethal heatstroke injury. These results also indicate for the first time that oral GLN can enhance tissue HSP-70 expression and HSF-1 activation immediately post-heatstroke injury. More rapid expression of HSP-70 and that this may be one mechanism of enhanced heatstroke survival via GLN. These data indicate that oral GLN may useful in prevention of mortality from heatstroke in at risk populations.



S-114.

EVIDENCE FOR INCREASED ACTIVITY OF THE NAPI-COTRANSPORTER TYPE I DURING ATP-DEPLETION IN PRIMARY CULTURED RABBIT MTAL CELLS

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Introduction: The cellular pathophysiology of Acute Tubular Necrosis remains incompletely understood. As in myocardial cells, changes in pH_i and $[Ca^{2+}]_i$ play an important role. However, their relative importance in the contribution to (or protection from) cell necrosis remains ill defined. Because the MTAL segment is very vulnerable to ischemic damage, we planned to investigate the simultaneous changes in $[Ca^{2+}]_i$, pH_i and $[ATP]_i$ in primary cell cultures of MTAL segments.
Methods: A new method was developed for obtaining functionally intact primary cell cultures of MTAL segments[1]. $[Ca^{2+}]_i$ and pH_i were, respectively, measured with the fluorescent probes Fura-2 and BCECF in a digital fluorescence microscopy set-up. $[ATP]_i$ was measured with the luciferin-luciferase assay. Metabolic inhibition was achieved with NaCN (2.5 mM) and 2-deoxyglucose (20 mM) (chemical ischemia). Reperfusion consisted of removal of the inhibitors together with the addition of glucose (20 mM) to the solutions. Data are expressed as means ± SEM. Statistical significance was evualuated with the Wilcoxon test.
Results: 60 minutes of chemical ischemia caused a profound but reversible decrease in $[ATP]_i$. The Fura-2 ratio, which reflects $[Ca^{2+}]_i$, started to rise gradually after $[ATP]_i$ had decreased to less than 5% of its control value. The Fura-2 ratio normalized very rapidly upon reperfusion (n=5). Intracellular pH decreased initially, followed by a transient alkalinization**.** When $[ATP]_i$ reached its lowest value (< 1% of control), the cells slowly acidified to reach a stable pH_i of 6.92±0.08 (n=4) after 50 minutes of chemical ischemia. During reperfusion, pH_i slowly recovered to its pre-ischemic value after 20 minutes. In the presence of ethyl-isopropyl-amiloride (10 µM) (a selective inhibitor of Na^+/H^+-exchangers), the pattern of changes in pH_i was unchanged and acidification was not increased (P=0.73). However, when P_i or Na^+ were omitted from the apical solutions during chemical ischemia, the transient alkalinization was no longer observed and the cytosol slowly acidified. Since previously it was demonstrated that only NaP_i-cotransporter type I is expressed in the apical cell membrane of these primary cell cultures, the transient alkalinization resulted from an increased NaP_i-cotransporter type I activity. Although the physiological role of NaP_i type I is unknown, it may be related with supply of P_i for glycolysis and cellular energy metabolism[2].
Discussion: Changes in $[Ca^{2+}]_i$ and $[ATP]_i$ in primary cell cultures from rabbit MTAL challenged with chemical ischemia were similar to observations from other cell types. To our knowledge, this is the first description of a transient alkalinization during chemical ischemia that is the result of increased activity of the NaP_i-cotransporter type I. Whether this is an epiphenomenon or may be cytoprotective, remains to be elucidated.
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S-115.

ALTERATION OF THE PATTERN OF GASTROINTESTINAL TRANSIT AFTER LIPOPOLYSACCHARIDE INJECTION IN MICE

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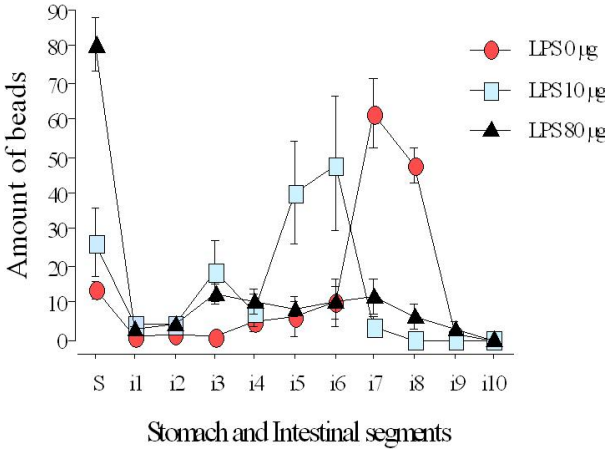
Introduction: Lipopolysaccharide (LPS) inhibits gastric emptying (1-3) but its effect on intestinal transit is controversial: LPS has been reported to either delay or accelerate gastrointestinal transit (1-4). The primary aim of the present study was therefore to study the effect of LPS on gastrointestinal transit of liquids in mice by observing the distribution of marker in the gastrointestinal tract using a newly developed flow cytometric method (5).
Methods: Ninety minutes after intraperitoneal injection of LPS, saline containing fluorescent markers was infused into the stomach. Thirty minutes later, the stomach and the intestinal tract were collected and the latter was divided into ten equal segments. Gastric emptying and gastrointestinal transit were calculated by measuring the quantity of the fluorescent microbeads in the divided gastrointestinal tract using flow cytometer.
Results: LPS dose-dependently inhibited the gastric emptying [90.8 ± 1.7% (mean ± SEM), 80.2 ± 3.7%, and 45.8 ± 4.3% with 0 μg, 10 μg, and 80 μg of LPS, respectively, $p < 0.0001$ by one-way ANOVA]. When the geometric center (GC) (the center of gravity) was used to assess gastrointestinal transit, both 10 μg and 80 μg of LPS delayed the transit (GC: 7.0 ± 0.1, 4.8 ± 0.3, and 4.8 ± 0.4 with 0 μg, 10 μg, and 80 μg of LPS, respectively, $p < 0.005$ by one-way ANOVA). With increasing doses of LPS, the marker distributed broader and the distinct peak in the distribution of beads disappeared (Figure).



The distribution of marker in the gastrointestinal tract. The amount of beads in each segment was shown. S = stomach, i1-i10: the intestinal tract was divided into ten equal segments. i1 indicates the most proximal portion and i10 the most distal portion.

Discussion: LPS had a marked effect on the gastrointestinal transit. It seems likely that the coordinated intestinal contraction to deliver the bulk of liquids toward the cecum is disrupted by LPS.

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S-116.

PROTHROMBOTIC TENDENCY UPON INFLAMMATORY CONDITIONS --- ALPHA DEFENSINS (HNP-1/2/3) ARE STRONG PLATELET AGONISTS

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Objectives: New concepts are emerging on the relationship between coagulation, inflammatory, and sepsis pathways. Neutrophils are central cells in acute inflammation. Neutrophil defensins, cationic, small cysteine- and arginine-rich peptides that comprise about 40% of the total protein content of azurophilic granules, are important constituents of the innate immune system and attack bacteria, fungi, viruses and parasites. They are released upon neutrophil activation by exocytosis. Platelets and neutrophils interact in host defense and haemostasis. Therefore the effect of alpha defensins in concentrations, that have been found in the plasma of sepstic patients, on different platelet functions was examined.
Methods: Activation of platelets by HNP-1 , HNP-2 or HNP-3 was assessed by flowcytometry. We analysed among other things, CD62 expression as a marker of alpha-granule secretion, CD63 expression as a marker of dense body secretion, and binding of fibrinogen, thrombospondin-1 and several coagulation factors to the platelet surface as well as platelet dependent thrombin formation. In addition platelet surface expression of CD40L, a protein belonging to the TNF family, that stimulates dendritic cells, B cells and endothelium cells, was measured and soluble CD40L was quantified by ELISA.
Results: The used alpha defensins induced strong platelet activation in a dose and time dependent manner. 10μM of HNP-1 or HNP-2 or HNP-3 induced platelet stimulation comparable to 1U/ml of the strong agonist thrombin. Platelets bound fibrinogen and thrombospondin-1, secreted the contents of their granules, bound coagulation factors leading to the formation of thrombin and built microparticles. HNP-1 , HNP-2 and HNP-3 induced CD40L expression on the platelet surface and soluble CD40L was found in the platelet supernatant when platelets were activated.

Conclusions: The alpha defensins HNP-1 to HNP-3 are very strong platelet agonists. Platelet activation by neutrophil secreted defensins might contribute to prothrombotic tendency upon inflammatory conditions, like reperfusion injury, sepsis, ARDS and many others.

S-117.

DEFICIENCY FOR THE LECTIN-LIKE DOMAIN OF THROMBOMODULIN IMPROVES RESISTANCE TO HYPOXIA IN A MOUSE MODEL FOR CARDIAC ARREST (CA) AND CARDIOPULMONARY RESUSCITATION (CPR)

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Introduction: Annually up to 750.000 Americans require CPR. About 30% reach the hospital, while only 14% are ultimately discharged. Post-CPR, patients suffer a syndrome similar to SIRS(2). Treatment options after hypoxic insults are scarcely available. We recently described the lectin-like domain of thrombomodulin as an anti-inflammatory molecule (3) and used a mouse CPR-model on mice deficient for this protein (TMLeD) or wild type (WT) to identify molecular targets useful to treat post-resuscitation syndrome.
Methods: 83 WT and 42 TMLeD-mice were used with approval of the Institutional Review Board. Arterial and venous femoral access was established for pressure recordings, blood draws, and drug administration in TMLeD or WT mice. Cardiac arrest (CA) was electrically induced (50 Hz, 10 V) and maintained for 5 or 6 minutes. Mechanical chest compression commenced and epinephrine was administered. If necessary, ventricular fibrillation was terminated by defibrillation (1 J). Return of spontaneous circulation (ROSC) was documented based on blood pressure. After weaning and extubation, mice were followed for 24h. Blood gas analyses were performed. The number of mice reaching ROSC and surviving 24 hours was recorded. The likelihood for ROSC and survival between genotypes was compared using fisher's exact test. Statistical significance was assumed with $p<0.05$.
Results: CA resulted in loss of perfusion pressure (MAP 65±13 vs 9±1mmHg, baseline (bsl) vs CA, n=6, p<0,05). Blood gas analyses drawn after 5' of cardiac arrest indicated hypoxia (pO_2=29±12, n=4), hypercarbia (pCO_2=101±22, n=4), acidosis (pH=6,83±0,08, n=4) and elevated lactate levels of up to 10 mmol/l. Mice with ROSC were still acidotic (pH 7,12±0,27, n=3) but not hypoxic (pO_2 338±93mmHg, n=3) or hypotensive (MAP: 58±10 mmHg, n=11). WT mice had a rate of ROSC of 73% after 5'CA and 65% after 6'CA. TMLeD-mice on the contrary reached ROSC in 78% after 5'CA(n= 60; p=NS vs WT) and 88% after 6'CA (n=36, p<0.05). While 63% of WT mice survived to 24h after 5'CA, 82% TMLeD-mice did (p<0.01). 9.8% WT mice survived 6'CA for a day compared to 88% TMLeD (p<0.001).
Discussion: We hypothesized that mice lacking TMLeD would be more susceptible to SIRS after CPR because their phenotype is largely hyper-inflammatory. To our surprise was the early outcome, that is mainly related to hypoxia susceptibility, because the inflammatory response has not mounted yet, significantly improved. This suggests involvement of TmLeD in hypoxia sensing or signalling that was previously unknown. Studies to identify the underlying molecular mechanism are underway.
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S-118.

NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (NGAL) IS ELEVATED EARLY AFTER CARDIOPULMONARY BYPASS

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Introduction: Both acute renal failure and renal dysfunction are associated with increased morbidity, increased length of stay and mortality after cardiac surgery. Cardiopulmonary bypass (CPB) and perioperative hypotension may induce renal hypoperfusion and ischemic injury. Early detection of acute renal injury could allow early renal protective strategies.
Neutrophil gelatinase-associated lipocalin (NGAL) mRNA is up-regulated early after ischemic injury to the rat kidney and can be identified in tiny quantities of urine. We hypothesized that NGAL expression is increased after cardiac surgery with CPB.
Methods: After IRB approval, 13 cardiac surgical patients were prospectively studied. Urine was collected pre & post CPB. Urinary NGAL was measured on 10 mcl urine samples with quantitative immune-blotting.
Discussion: There was no detectable urinary NGAL in any patients prior to CPB. NGAL was significantly elevated by 1 hour after CPB and peaked at 3 hours. (Fig.1)
Conclusions: Urinary NGAL is consistently elevated for 1 to 6 hours after CPB. It remains to be seen whether NGAL is a marker of clinical and subclinical acute renal injury and how it relates to outcome. Because urine NGAL can be consistently measured on tiny quantities of urine it could become a practical tool in the early detection of renal injury.
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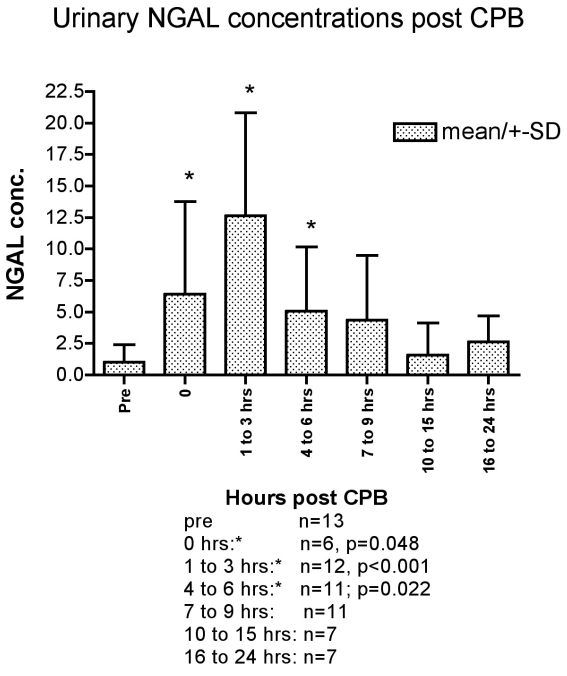

S-119.

THE EFFECT OF THE INTRA-OPERATIVE BLOOD AND BLOOD PRODUCTS TRANSFUSION ON THE OUTCOME OF PATIENTS UNDERGOING ORTHOTOPIC LIVER TRANSPLANTATION (OLT)

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INTRODUCTION: Massive blood transfusion during OLT is correlated with lower patient survival (1). Peri-operative blood transfusions may improve liver and kidney graft survival (2) due to the immunosuppressant effects of blood transfusions. However, morbidity and mortality are high in patients who received massive blood transfusion (MBT) (3) during OLT.
The aims of the study are: evaluating the effect of intra-operative MBT on patient and liver graft outcome and correlating the pre-operative risk factors for intra-operative bleeding.
METHODS: The medical records of 155 patients who underwent 1st time OLT from Jan 02 through Dec 02 were reviewed.The following data were collected and analyzed; the pre-operative data: INR, platelet count, hematocrit, severity of portal hypertension (defined by H/O TIPS, GI bleeding and ascitis), H/O abdominal surgeries, age and weight. Intra-operative data: number of units of RBC, FFP, Platelets and Cryoprecipitate transfused. Post-operative data: frequency of rejection and infection, duration of ICU and hospital stay and one-year patient survival. Excessive blood transfusion was defined as ≥ 10 RBC units transfused. Patients were divided into 2 groups. Group 1 (n = 102), is patients who recieved ≤ 9 (5 ± 3) units of RBC. Group 2 (n = 53) is patients who recieved ≥ 10 (19 ± 12) units of RBC. The Mann Whitney test, t-test, Chi-sequare test and Fisher-exact test were used to analyze the data. Data are presented as mean ± SD or Range and Median.

RESUTS: .

	Group-1 (n=102)	Group-2 (n=53)
Pre-operative Hct	32.1 ± 5.6%	29.0 ± 5.6*
INR(range & median)	0.9-3.0 (1.3)	1.5-2.5 (1.4) *
Incidence of Prolonged Ventilation (> 1 day)	59%	85% *
Hemodialysis (ARF)	8 %	26 %*
ICU days	10 ± 19	21 ± 30 *
Hospital days	19 ± 20	30 ± 29 *
Rejection Episodes / patient	16 (15 %)	11 (21 %)
Infection Episodes / patient	22 (21 %)	48 (94 %)*
Incidence of fibrinolysis	36.3 %	56.6%*

*P < 0.05 is statistically significant

There is no statistically significant difference between the 2 groups as far as age, weight, pre-operative platelet count and severity of portal hypertension. There is no statistically significant difference in frequency of rejection and one-year patient survival. There is no significant difference in the severity of reperfusion syndrome in the two groups.
CONCLUSION: Patients who received in excess of 10 unit RBC suffered higher incidence of infection, had longer ICU and hospital stay and more frequently to develop acute renal failure that required hemodialysis. Pre-operative clinical criteria and lab tests that correlate well with the risk of intra-operative bleeding is pre-operative Hct and INR.
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S-120.

ARGATROBAN ANTICOAGULATION IN PATIENTS WITH VENTRICULAR ASSIST DEVICES

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Introduction
An increasing number of patients with heart disease are becoming Heparin-Induced Platelet Antibody (HIPA) positive. This makes therapeutic anticoagulation with intravenous medications problematic in these patients. As a group, their hospital course is more likely to be complicated by acute renal failure which makes lepirudin and its derivatives less attractive as an alternative to heparin in these patients. Consequently, we have used argatroban, a short-acting direct thrombin inhibitor (DTI), as our alternative anticoagulant in HIPA positive patients over the past few years. We performed this retrospective chart review to characterize our experience.
Methods
The charts of all HIPA (+) patients who had undergone ventricular assist device (VAD) implantation over the past 4 years were reviewed and summarized.

Results

Number of patients	8
Age Mean (Range)	56.6 (38-79) Y
Gender	8M / 0F
Weight Mean (Range)	102.12 (60-161)kg
Comorbidities	6/8 HTN, 4/8 DM, 4/8 ICM, 4/8 CAD, 4/8 CRI, 5/8 CHF, 2/8 shock liver
Post VAD complications	2/8 Sternal bleeding, 5/8 respiratory failure, 5/8 renal failure needing dialysis, 3/8 anoxic brain injury
Thrombotic complications	2/8 BIVAD clots
Hemorrhagic complications	2/8 sternal bleeding requiring mediastinal re-exploration
Duration of argatroban therapy	0-3 Days 5 3-30 Days 3
Dose of argatroban Mean (Range)	0.815 (0.15-5)mcg / kg / min
Range of PTT Mean (Range)	87.28 (42.5-200)secs
Transfusion requirements Mean (Range)	PRBCs 11 (3-39) FFP 7 (1-31) Platelets 5.5 * (0-13)
Bleeding complications GIB, Hemorrhagic stroke	0/8

*In our institution platelets are in packs of 6

Discussion
Argatroban can be used as an alternative to heparin in HIPA (+) patients. Although our series is small, we had no hemorrhagic strokes or gastrointestinal bleeding in our patients. The dose required is usually 25% of that used for percutaneous coronary procedures. Argatroban like all DTIs inhibits thrombin generation and therefore elevates prothrombin time, making titration of warfarin in these patients difficult, as most had INRs in the 'therapeutic' range before commencement of concomitant warfarin therapy.
We conducted a retrospective review of our experience anticoagulating HIPA (+) patients with ventricular assist devices using argatroban. We had no major hemorrhagic complications like stroke or gastrointestinal bleeding, however, we did see 2 patients with evidence of clot in their VADs requiring replacement of the cannulae. The dose of argatroban required is approximately one quarter of the dose used for coronary procedures (1-2 mcg/kg/min being the dose). Argatroban is a safe and effective intravenous anticoagulant alternative to heparin in HIPA (+) patients.

S-121.

AUGMENTED RAT CEREBRAL TISSUE OXYGEN TENSION FOLLOWING FLUID RESUSCITATION WITH HEMOGLOBIN RAFFIMER AND FRESH, BUT NOT STORED, BLOOD

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Introduction: Increased morbidity and mortality associated with acute blood loss is compounded by risks attributed to the transfusion of stored allogeneic blood[1-3]. Reduced ability of stored blood to transport oxygen to tissue[4] supports the ongoing development of transfusion alternatives, including red blood cell substitutes. This study assesses the impact of hemorrhage and fluid resuscitation with a hemoglobin based oxygen carrier (HBOC) (Hemoglobin raffimer, Hemolink™), fresh or stored blood on cerebral tissue oxygen tension and cerebral blood flow in anesthetized rats.
Methods: Isoflurane anesthetized and ventilated rats (50% oxygen) underwent tail artery and vein cannulation to monitor mean arterial blood pressure (MAP) and perform hemorrhage resuscitation. A combined oxygen sensing microelectrode (ruthenium decay) and laser Doppler flow probe (OxyLite and OxyFlo, Oxford Optronix) was placed in the hippocampus to measure cerebral tissue oxygen tension ($P_{Br}O_2$) and regional cerebral blood flow (CBF). After establishing baseline measurements, 30% of the estimated blood volume (20 $ml \cdot kg^{-1}$) was hemorrhaged over 10 minutes. Thirty minutes later, resuscitation with an equivalent volume of hemoglobin raffimer, fresh or stored autologous blood (7 days, 4°C, CPDA-1) was performed and animals monitored for an additional 40 minutes (n=6 rats/group). Total hemoglobin concentrations (co-oximetry) and arterial blood gases (ABG) were measured (Radiometer). Data analyzed by two way ANOVA and post hoc Tukey tests were expressed as mean ± SD. Significance was assigned at $p<0.05$.
Results: No differences in any parameter were observed between groups at baseline or following hemorrhage. After resuscitation, MAP increased in the hemoglobin raffimer group (135 ± 18 mmHg, $p<0.05$) relative to rats receiving fresh or stored autologous blood (107 ± 15 and 93 ± 18 mmHg, respectively). Post-resuscitation $P_{Br}O_2$ values were higher in the fresh blood and hemoglobin raffimer group (39.3 ± 10.7 and 35.4 ± 10.7 mmHg, respectively, $p<0.05$), relative to the stored blood group (21.5 ± 4.4 mmHg). Normalized CBF increased after fresh blood resuscitation (2.0 ± 0.6, $p<0.05$) but not after old blood or hemoglobin raffimer resuscitation (1.2 ± 0.1 and 1.1 ± 0.1, respectively). All post-resuscitation co-oximetry and ABG values were similar, except for an increased methemoglobin content in the hemoglobin raffimer group (2.4 ± 0.9%, $p<0.05$) due to methemoglobin in the HBOC (5.8 ± 1.5%).
Discussion: Hippocampal $P_{Br}O_2$ was comparably increased by resuscitation with fresh autologous blood and hemoglobin raffimer. Increased $P_{Br}O_2$ with hemoglobin raffimer was associated with elevated MAP and no increase in CBF. Post resuscitation cerebral hyperemia occurred with fresh, but not stored, blood. These data demonstrate limitations in cerebral oxygen delivery with transfusion of stored blood, relative to fresh blood and hemoglobin raffimer (AIRE, Hemosol Corp, CAS support).
References:
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S-122.

EFFECTS OF HEMOGLOBIN-VESICLE SOLUTION ON COAGULATION WITH SONOCLOT ANALYSIS

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Introduction: Hemoglobin-vesicle (HbV), which is encapsulated Hemoglobin solution within phospholipids bilayer membrane, has been developed as an oxygen carrier. Crossmatching for transfusion is not needed and many side effects of transfusion based on immunostimulation and suppression may be avoided. HbV is expected as a supplement of the oxygen carrier in acute hemorrhagic patients. However, extensive administration of HbV may cause coagulopathy, and validity of fluid resuscitation using HbV for uncontrolled bleeding in traumatic patients is not established in prehospital setting. The SONOCLOT™ (SCT; Sonoclot II Coagulation and Platelet Function Analyzer, Sienco Co., Morrison, CO) analysis provides information of pletelet function, cellular and plasmatic coagulation for clot formation, maturation, and lysis using whole blood. Aim of the study was to evaluate the anticoagulant effect of HbV and the limit of fluid resuscitation using only HbV solution by routine laboratory variables and SCT.
Methods: After institutional ethical approval, seven male healthy volunteers without any recent drug intake donated 9 mL of blood for routine analysis, and an additional 2.4 mL for SCT, at nine different times. In order to minimize intrapersonal variability, the nine times of SCT for each person was performed continuously. Blood samples from volunteers were diluted to 0%, 20%, 40%, 60% and 80% of HbV (Hb concentration was 10 g/dL and suspended in saline) or lactated Ringer's solution (RL). Immediately after dilution, the specimens were measured with SCT. The following laboratory tests were performed: hematocrit, fibrinogen, red cell and platelt count, prothrombin time, and activated partial thromboplastin time. Activated clotting time (ACT), clot rate (CR), time to peak and maximal clot signal were measured with SCT.
Results: Routine laboratory variables were affected equally by the tested solution. ACT in HbV group was more prolonged than ACT in RL group, when the sample was diluted more than 40%. ACT at 40% dilution using HbV was equivalent to ACT at 60% dilution using RL. CR was reduced equally, when the sample was diluted within 40%.
Discussion: In this setting, RL affected SCT variables compared with the other reports (1-2). The affected SCT variables were kept pace with the routine laboratory values. The ACT was within 1.5 times of the baseline value and all CR values were within normal limit, if the blood was diluted within 40% dilution using HbV solution. HbV is estimated to use safely until 40 % of blood volume without supplementation of clotting factors.
References:
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S-123.

PHARMACOKINETICS OF HEMOGLOBIN-BASED OXYGEN CARRIER HEMOGLOBIN GLUTAMER-200 (BOVINE) IN THE HORSE

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Introduction: Hemoglobin-glutamer-200 (HBOC-200; Oxyglobin®; Biopure, Cambridge, MA) is a hemoglobin-based oxygen carrier (HBOC) comprised of glutaraldehyde-polymerized bovine hemoglobin (bHb) and is FDA-approved for use in dogs. It shares most properties with Hemoglobin glutamer-250 (Hemopure®; Biopure) that is currently in clinical trials and was recently approved for use in humans in South Africa. The purpose of this study was to determine the pharmacokinetics of this first generation HBOC following intravenous infusion of 32.5 g of HBOC-200 in horses.
Methods: Seven horses (531.3 ± 58.4 (SD) kg) were administered 250 mL of HBOC-200 solution containing 13 g/dL of bHb over 5 min. Subsequently blood samples were collected at 1, 5, 15, 30, 45 min and at 1, 1.5, 2, 4, 6, 8, 10, 12, 16, 20, 24, 36, 48, and 72 h. Quantification of HBOC-200 in plasma and urine was performed using a recently developed LC-MS/MS method.[1] The decline of the HBOC-200 plasma concentration versus time curve was described by a non-interchanging 2-compartmental (C_1, C_2) model.
Results: Elimination of HBOC-200 from plasma was bi-exponential and based on size distribution of its bHb polymers. The median elimination half-lives ($t_{1/2}$) from C_1 and C_2 were 1.3 and 12.0 h, respectively. Of the HBOC-200 infused, 47 % was eliminated in C_1, representing the smaller molecular weight (MW) and 53 % in C_2, representing the larger MW polymers. The area below the plasma concentration-time curve (AUC) was 5143.1 $\mu g \bullet h \bullet mL^{-1}$. Volumes of C_1 (V_1) and C_2 (V_2) were 86.9 and 63.9 mL/kg and clearances (CL) were 42.1 and 3.8 $mL \bullet kg^{-1} \bullet h^{-1}$, respectively. HBOC-200 was not detected in urine.
Discussion: Unlike previous studies assuming mono-compartmental elimination of HBOC-250 in humans[2,3], this investigation revealed a bi-exponential elimination process following HBOC-200 infusion. Our pharmacokinetic model identified the percentage of HBOC-200 eliminated from C_1 and C_2. Of the HBOC-200 infused, 47 % was eliminated from plasma in a $t_{1/2}$ of less than 2 h. The median V_1 was 91.1 mL/kg, which was larger than the expected plasma volume and represented the initial volume of distribution. This observation was due to the rapid diffusion of the smaller bHb aggregates out of the circulation into the extravascular compartments. The median V_2 of 63.9 mL/kg is compatible with published plasma volumes of resting horses (63.3 mL/kg). This volume represented the larger Hb aggregates still contained with the plasma volume. In conclusion, elimination of first generation HBOCs was shown to be more complex than previously assumed due to the heterogeneous nature of these solutions. Future studies evaluating the pharmacokinetic profile of individual HBOC solutions in hypovolemic subjects using animal models of hemorrhagic shock will yield further clinically relevant information.
References:
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S-124.

PERITONEAL DIALYSIS WITH HYDROXYETHYL STARCH IN RATS: THE COLLOIDOSMOTIC PRINCIPLE

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Introduction: Peritoneal dialysis (PD) is a standard procedure for treatment of chronic renal failure or, especially in pediatric ICUs for treatment of acute renal failure. Peritoneal dialysis fluids (PDFs) use glucose at various concentrations to produce an osmotic gradient to drag water and compounds across the peritoneal membrane. Glucose degradation products (1) or hyperglycemia-induced fibrosis of the peritoneal membrane (2) may limit the use of PD (3). We hypothesized that replacing the osmotic agent (glucose) with a colloidosmotic compound, hydroxyethyl starch 450/0.5 (HES) at various concentrations, provides effective PD.
Methods: Rats were nephrectomized and PD was started 3 days thereafter and continued for 1 to 5 days. Rats were randomized to 3 groups (group 1 HES 1.5%, group 2 HES 3%, group 3 HES 6%). End points were 1) water efflux (changes of body weight, fluid shift, hemoglobin concentration in blood), 2) membrane transfer assessed by peritoneal equilibrium test (PET), creatinine clearance (Kt/V), and changes of creatinine, BUN, and electrolytes before/after PD, 3) concentration of HES in serum and in organs. Blood and PDF samples were analyzed for potassium, sodium, chloride, phosphate, glucose, protein. At the last day of PD organs were harvested and HES concentration in serum, liver, spleen, and lung was measured. Kruskal-Wallis one-way ANOVA on ranks with Tukey-Kramer multiple-comparison or Wilcoxon signed-rank test were used, where appropriate.
Results: Body weight decreased in group 3 (mean ± SD, group 1 +2.2% ± 2.5, group 2 +0.29% ± 1.9, group3 -2.7% ± 1.0 vs. baseline, $p<0.01$), hemoglobin was decreased in group 1 (-3.3% ± 2.2, and increased in groups 2 and 3, +5.2% ± 4.2 and +5.1% ± 6.1 resp., $p<0.05$ vs. baseline). PET was not different between groups (0.85-0.96), Kt/V was 0.58 ± 0.04 in group 1, 0.51 ± 0.06 in group 2, and 0.57 ± 0.04 in group 3. Electrolytes, protein, creatinine and BUN concentration were reduced by PD without differences between groups. HES concentration (mg/ml) in serum were (median, interquartile range): 5.4, 4.0-5.9 (group 1); 9.8, 8.5-11.5 (group 2); 13.5, 11.2-14.6 (group 3). Increases of HES in organs were dependant on HES concentration of PDF and duration of PD.
Discussion: Fluid shift across the peritoneal membrane was dependant on HES concentration. Elimination of creatinine or BUN was not influenced by HES concentration. Thus, osmotic PDFs might be replaced by a colloidosmotic PDF. HES as PDF leads to accumulation of HES in blood and organs, limiting its potential use. The search for a colloidosmotic compound without tissue storage is warranted.
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S-125.

NEW FUNCTION FOR PROTEASE INHIBITORS ---- ALPHA1 ANTITRYPSIN AND ANTITHROMBIN III INHIBIT THE ACTIVATION OF HAEMOSTASIS BY ALPHA DEFENSINS FROM NEUTROPHILS

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Objectives: Prominent features of the septic response include uncontrolled inflammation and coagulation. Defensins are important constituents of the innate immune system, which recognises and inactivates microbial pathogens once they attempt to infect and colonise host tissue. They are released by neutrophils upon activation. But neutrophil activation in human sepsis correlates with the severity of organ dysfunction. Defensin levels in plasma from patients with sepsis at onset of disease has been reported to be elevated (900ng/ml to 17.000ng/ml in septic patients versus up to 53 ng/ml in healthy volunteers). We have shown (see other abstract), that the alpha defensins HNP-1, HNP-2 and HNP-3, in concentrations that are secreted in the neighbourhood of activated neutrophils, are very strong platelet agonists and induce full platelet activation leading to thrombin formation and CD40L expression and in that way amplify haemostasis and inflammation. HNP1 to 3 strongly bind to alpha1 antitrypsin and to antithrombin III. Therefore we tested whether these protease inhibitors might have an additional function and be able to inhibit the activation of haemostasis by alpha defensins.
Methods: Activation of platelets by HNP-1 to 3 was assessed by flow-cytometry. We analysed among other things, CD62 expression as a marker of alpha-granule secretion, CD63 expression as a marker of dense body secretion, and binding of fibrinogen, thrombospondin-1 and several coagulation factors to the platelet surface as well as platelet dependent thrombin formation. In addition platelet surface expression of CD40L, a protein belonging to the TNF family, that stimulates dendritic cells, B cells and endothelium cells, was measured and soluble CD40L was quantified by ELISA. Inhibition of all these effects of the alpha defensins on platelets was studied using alpha1 antitrypsin, antithrombin III at concentrations up to 20µM or up to 5U/ml hirudin.
Results: While addition of hirudin had no effect on HNP-1 , HNP-2 or HNP-3 induced platelet activation, alpha1 antitrypsin and antithrombin inhibited in a dose dependent manner. 1 to 2,5 µM alpha1 antitrypsin or 2,5 to 5 µM antithrombin inhibited in all tests platelet activation by the used alpha defensins completely.
Conclusions: HNP-1, HNP-2 HNP-3 activate platelets directly and primarily not indirectly via thrombin formation. Antithrombin III is a potent inhibitor of alpha defensin induced platelet activation. This inhibition is not dependent on heparin. The observed effect of antithrombin III might contribute to it's antithrombotic and antiinflammatory potential seen in animal studies. In addition to it's function as protease inhibitor also alpha1 antitrypsin is a potent inhibitor of the activation of haemostasis by alpha defensins. Animal studies are necessary to test it's potential therapeutic effect in diseases, characterized by activated inflammation and activated haemostasis, like ischaemia-reperfusion injury, sepsis and ARDS.

S-126.

CORRELATION OF PERIPHERAL VENOUS PRESSURE WITH CENTRAL VENOUS PRESSURE IN CRITICALLY ILL PATIENTS

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Introduction: Central venous pressure (CVP) is routinely monitored to measure the filling pressures of the right heart and to infer the circulating volume in both perioperative and critically ill patients. CVP monitoring is supplanting pulmonary artery catheterization in a variety of clinical applications as a consequence of growing evidence suggesting no additional benefit for such patients from pulmonary artery catheters. Both the cannulation of central veins and the presence of catheters within them are associated with complications. Studies in patients undergoing surgery have suggested that peripheral venous pressure (PVP) correlates well with CVP (1, 2). We designed a prospective study to assess the correlation of PVP with CVP in a broad population of critically ill adult patients.
Methods: After obtaining IRB approval and written informed consent, critically ill adult patients with both indwelling central and peripheral venous catheters were enrolled in this study. Absence of a sinusoid wave form and good flow through the peripheral catheter were the exclusion criteria. Patients were positioned supine and their pressure transducers were zeroed at the level of the right atrium. CVP and PVP were then simultaneously measured at the end of expiration using monitors (Spacelab Medical, Issaquah, WA) and critical care transducers (Abbott, Abbott Park, IL). CVP and PVP were analyzed by linear regression and Bland-Altman analysis.
Results: Excellent agreement was noted between CVP and PVP measurements. The correlation coefficient was 0.94 (CI 95%, 0.86 to 0.97) and bias - 0.160 (CI 95%, -0.82 to 0.50) (Fig.1).
Discussion: The results of this interim analysis strongly suggest that venous pressure measurements from peripheral veins with discernable waveform tracing are an acceptable alternative to CVP measurement. PVP may replace CVP measurement in a variety of settings, sparing patients the risk and cost of central venous cannulation.

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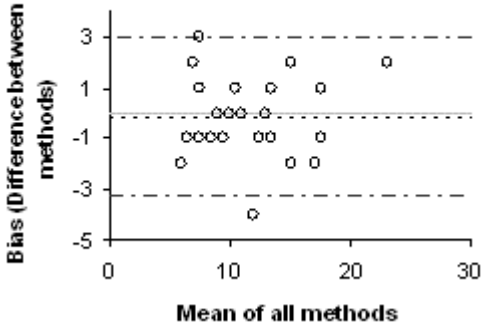
Fig.1 Bias plot



S-127.

CORRELATION BETWEEN BISPECTRAL INDEX AND RICHMOND AGITATION-SEDATION SCALE IN CRITICAL CARE PATIENTS

AUTHORS: **R. Badenes**, A. Maruenda, F. Martí, M. García-Pérez, J. García de la Asunción, J. Belda;
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Introduction: Maintaining an optimal level of comfort and safety for critically ill patients is an universal goal for critical practitioners. The assessment of sedation level remains a challenge for the intensivist in order to avoid over - or under- sedation phenomena. The indroduction of the bispectral index (an EEG parameter) could bring potential adventages in monitoring sedation. According to the repports, the Richmond Agitation-Sedation Scale (RASS) has been shown to be highly reliable among multiple types of healt care professionals. The RASS has an expanded set of scores at pivotal levels of sedation that are determinated by patients´ response to verbal vs physical stimulation, which will help the clinician in titrating medication.
Methods: This is a prospective, nonramdomized, observational study in a surgical and trauma tertiary intensive care of an universitary hospital. Twenty-six consecutive patients (age range 17-75 yrs, mean age 47 yrs) were included. They were sedated (with propofol by continuos infusion at an initial dose of 2 mg/kg/h, which could be modulated with steps of 0´5 mg/kg/h), in order to mantein an adecuated RASS score. BIS value was continuosly recorded, and manually calculated on a mean average of a minute during the measuring of RASS score, and every 10 minutes for 6 hours on par with RASS score. ECG, SpO_2, invasive arterial pressure, ventilatory module, $_{ET}CO_2$, FiO_2, temperature were also recorded. For the statistic analysis, Friedman test and Spearman coefficient were utilized.
Results: Nine hundred and thirty-six observations were carried out. The variation range of RASS score was between 0 and -5. BIS range varied from 27 to 96. Statistics analysis of the data obtained pointed out a significative correlation between RASS score and BIS ($p < 0,01$).
Discussion: Acording to the reports, Bispectral index correlates with levels of sedation on the sedation scales. In our personal experience, this study demonstrates the utility of BIS and RASS score to track levels of sedation in ICU patients.
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S-128.

FREQUENCY OF SPINAL REFLEX MOVEMENTS IN BRAIN-DEAD PATIENTS

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Introduction: Brain death (BD) is a catastrophic physiologic event associated with significant disturbances in the function of other organs. Spontaneous and reflex movements may occur in brain-dead patients. These movements originate from spinal cord neurons and do not preclude a brain-death diagnosis. They are considered spinal reflexes. These movements may occur spontaneously, during an apnea test, or after a painful stimulus applied out regions of cranial nerve distribution. Those health care workers involved in brain death diagnosis, organ procurement, and transplantation should be aware of the possible occurrence of spinal reflexes that may create difficulties to convince a family or even a physician unfamiliar with brain death that the patient is indeed dead despite of these movements.
Methods: This is a prospective, nonramdomized, observational study in a surgical and trauma tertiary intensive care in a universitary hospital. 42 consecutive patients (age range 17-75 yrs, mean age 47 yrs) diagnosticated of brain death during 2002 and 2003, but without brain death at the time of admision were studied. This study was observational and in no way interfered with our routine management of brain dead patients. Clinical brain death was diagnosticated according to the Spanish law.
Results: In 12 of the 42 brain-death patients (28´53%), spinal reflex movements were observed during the study period. The average age of the patients with and without spinal reflex movements was 20.7 ± 16.7 (range, 17 to 51) and 48.6± 28.3 (range, 34 to 75) years, respectively. The mean age of the patients with spinal reflexes was lower than the patients without spinal reflexes and this difference was statistically significant ($p<0,01$). Lazarus sign was no observed in any patient.
Discussion: Although these reported movements are of a highly complicated nature, they are known to be purely spinal in origin. The occurrence of spinal reflexes in brain-dead patients may certainly delay decision making, such as starting a transplantation procedure, because of difficulties in convincing the family or even a physician taking part in the diagnosis of brain death. An awareness of spinal reflexes may prevent delays in and misinterpretations of the brain-death diagnosis. In our study, the frequency of spinal reflexes was 28´53%. Although this frequency is a little lower than some results published previously (30-70%), our results also showed that this phenomenon does not seem to be rare.
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S-129.

CENTRAL VENOUS PRESSURE VERSUS PULMONARY ARTERY CATHETER MONITORING DURING BILATERAL TOTAL KNEE REPLACEMENT

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Introduction: Simultaneous bilateral total knee replacement (SBTKR) has been associated with a higher incidence of fat embolism syndrome (FES) compared to single total knee replacement (TKR). Since an increase in pulmonary arterial pressure (PAP) is a sign of FES, patients undergoing SBTKR are often monitored with a pulmonary artery catheter (PAC) to abort the second surgery and aid in management postoperatively[1]. Studies have questioned the utility of PAC monitoring[2]. This study compares PAC versus central venous catheter (CVP) monitoring in SBTKR patients.
Methods: Charts of 249 patients undergoing SBTKR over a one-year period were analyzed for co-morbidities, length of hospital stay and outcome. A PAC or a CVP was placed at the anesthesiologist's discretion. All patients except one received an epidural or combined spinal-epidural anesthesia.
Results: 117 patients were monitored with CVP and 132 with PAC. Both groups had similar demographic characteristics. The incidence of coronary artery disease (CAD) and hypertension (HTN) were significantly higher in the PAC group (**Table I**). There was no significant difference between groups in outcome, including FES and length of stay (**Table I**). One death occurred in the PAC group. This patient's clinical course was consistent with FES: mental confusion, diffuse alveolar infiltrates and hypoxemia requiring intubation within the first 24 hours of surgery. Intraoperatively no change in baseline PAP was noted. In three patients surgery was stopped after one TKR due to: 1) elevated PAP (70/30) prior to incision, 2) hypoxemia after the first TKR with low end tidal CO_2, and increased PAP, 3) surgical reasons.
Discussion: Monitoring with a CVP catheter is sufficient in patients undergoing SBTKR. PAC use did not alter outcome or help predict development of FES. Two patients from the PAC group did not undergo SBTKR; one may have had emboli released after first TKR giving rise to an alteration in PAP, but other clinical signs would have raised that possibility. In view of the higher cost of PAC, and potential morbidity, PAC should not be used routinely for patients undergoing BTKR.

References:
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Table: Co-morbidities and outcomes

Demographics	CVP	PAC	p-value
Age (yr.)	64 ± 9 (24 - 80)*	67 ± 8 (46 - 89)	
Significant History	n (%)	n (%)	
†HTN	48 (41.0)	72 (54.5)	0.03
†CAD	5 (4.3)	16 (12.1)	0.03
Pulmonary Disease	6 (5.1)	16 (12.1)	0.07
Outcome Measures			
Signs of †FES	5 (4.3)	8 (6.1)	0.58
Death	0	1 (0.76)	0.90
†MI	1 (0.85)	3 (2.3)	0.62
ξFluid Boluses	15 (12.8)	20 (15.2)	0.06
Respiratory Failure	2 (1.7)	1 (0.76)	0.60

*Average ± SD (range)
†HTN = hypertension, CAD = coronary artery disease, MI = myocardial infarction, FES = fat emboli syndrome.
ξ Guided by CVP or PAC.

S-130.

COMPARISON OF A CLOSED-LOOP INSULIN INFUSION ALGORITHM WITH A CONVENTIONAL INSULIN INFUSION ALGORITHM FOR GLUCOSE CONTROL IN CRITICALLY ILL PATIENTS

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Introduction: Hyperglycemia occurs frequently among critically ill patients, even those without a previous diagnosis of diabetes. Tight short-term glycemic control with insulin in critically ill patients has been demonstrated to decrease mortality[1]. The development and automation of an effective closed-loop algorithm to adjust insulin infusion rates based on hourly blood glucose measurements could potentially decrease nursing workload, increase patient safety, and improve outcome.
Hypothesis: A closed-loop controller will improve glycemic control compared to a conventional (hourly insulin infusion) algorithm by shortening time to target glucose level, increasing time spent within a target glucose range, and decreasing number of hypoglycemic episodes.
Methods: A mathematical model of glucose and insulin metabolism was developed and validated[2,3]. An external (decoupled PID) controller was developed for normal, Type 1 and Type 2 diabetic patients using frequency response analysis. In each case, the simulated performance of this closed-loop controller was compared to that of a standard conventional algorithm used at our institution, generating estimates for time to target glucose level (110 mg/dL), percent time within range (80 to 110 mg/dL), and number of hypoglycemic episodes (glucose < 60 mg/dL) in 24 hours. All simulations were conducted with an initial glucose level of 180 mg/dL.
Results: In the case of the normal patient, conventional insulin dosing resulted in a slightly shorter time to target than the external controller (Table 1) but caused an episode of hypoglycemia requiring exogenous glucose. The external controller took slightly longer to reach the target range but was more stable, spending more time within range without hypoglycemia. Use of the conventional algorithm in the Type 1 diabetic caused marked instability with recurring episodes of hypoglycemia and hyperglycemia vs none with the external controller. Performance of the conventional algorithm and external controller in the Type 2 diabetic was similar except for a markedly shorter time to target with the external controller.
Discussion: An optimized external controller can outperform a conventional insulin dosing algorithm in terms of time spent within a target glucose range and number of hypoglycemic episodes. Further simulations using multivariable control techniques to generate coordinated glucose and insulin infusion rates may optimize glycemic control even further.

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[1]NEJM 2001; 345:1359.
[2]Khoo MCK: Physiological Control Systems, p55, 124; 1999 IEEE Press (NJ).
[3]Comput Methods Programs Biomed 1986; 23:113.

	Glycemic Control Algorithm Performance					
Insulin Infusion Algorithm	Conventional Algorithm	Conventional Algorithm	Conventional Algorithm	External Controller	External Controller	External Controller
	Time to target	Percent time in range	Number of hypoglycemic episodes	Time to target	Percent time in range	Number of hypoglycemic episodes
Normal	41.4 min	74%	1	47.5 min	81%	0
Type 1 Diabetic	52.2 min	29%	4	76.0 min	93%	0
Type 2 Diabetic	149.9 min	81%	0	88.7 min	80%	0

S-131.

PULMONARY ARTERY SYSTOLIC STORAGE IN MORBID OBESITY

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Introduction: The possibility that increased pulmonary blood volume (PBV) due to the increased total body blood volume in morbidly obese patients can elevate pulmonary artery (PA) systolic storage (SS) was examined. SS is fraction of stroke volume stored in PA during systole. The elevated SS can augment the diastolic pulmonary capillary blood flow (PCBF), which can then increase the capillary blood volume participating gas diffusion. The increased PBV contributes to the pulmonary overperfusion with recruitment of capillaries, and then to the distension of PA. Since the distension of PA accounts for SS, the increased PBV in obesity should elevate SS. We examined this possibility by measuring SS at two different PBV in obese patients. Changes in PBV should correlate with changes in SS. If so, the elevated SS in morbid obesity may counteract the adverse effects of increased PBV on the distribution of ventilation-to-perfusion.
Method: We used N_2O-airway-pneumotachographic method, to measure the instantaneous PCBF from which SS was measured. During end-expiratory pause or short apneic period, the pulmonary capillary pulsation produces a pulsatile gas flow. With inhalation of N_2O, the uptake of N_2O by the pulmonary capillary blood attenuates the pulsatile gas flow. Subtraction of gas flow tracing during apnea after inhalation of N_2O from that after air or oxygen produces a pulsatile waveform of PCBF pulse. Since SS is the same as the flow volume of PCBF during diastole, SS was determined from the flow volume during diastole divided by the flow volume during a whole cardiac cycle. A phonocardiogram was used to define end-systole and -diastole. Included were 20 morbidly obese patients undergoing laparoscopic or open gastric bypass surgery under general anesthesia. The baseline measurement was done right after induction before hydration was begun. When the peritoneum was open or pneumoperitoneum was established, N_2O was discontinued. The measurement was repeated when the peritoneum was closed and N_2O was restarted. By this time, patients were adequately hydrated as assessed by pulmonary capillary wedge pressure and urine output. For the gas flow measurements, the side arm spirometry tubing was redirected from the spirometer monitor to pneumotachograph without disconnecting any part of airway or breathing circuit. Changes in right ventricular end-diastolic volume index (RV EDVI) was used to assess changes in PBV.
Results: There was a good correlation between changes in SS and changes in RV EDVI ($R^2 = 0.515$, $p<0.0001$). Mean body mass index was 55 ± 8.
Conclusion: Our data indicate that the high PBV in morbidly obese patients is associated with the elevated SS. Since an increase in SS is associated with improved overall ratio of ventilation- to-perfusion, the elevated SS in obesity should counteract adverse effects of the high PBV on distribution of ventilation-to-perfusion.

S-132.

THE AGE WAVE AND THE ICU: PREDICTING OUTCOMES IN OCTOGENARIANS

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Introduction: In an aging US population, concerns regarding access and utilization of health care resources are growing. Paralleling the rapid rise in the elderly population[1] are increasing hospital and ICU costs[2]. Both patients and health care providers may harbor preconceived opinions about the utility of health care resources and interventions depending on the likelihood of possible outcomes and returning to baseline functional status. This study was designed to assess the reliability of predicting outcomes in the superelderly ICU patient population[3].
Methods: After IRB consent, all octogenarians admitted to all ICU's at a major academic center between July 1, 2003 and June 30, 2004 were enrolled prospectively. Demographic and medical information was obtained via chart review, laboratory analysis, and interview. Variables considered include gender, age, baseline support level, location prior to admission, heart rate at ICU admission, type of ICU, number of ICU interventions, and organ system failures. The data were used in a logistic regression formula to make predictions regarding potential outcomes.
Results: Preliminary evaluation of 269 patients consecutively admitted to the ICU setting over the first 6 months was made. Of the 269 patients, 154 were female (57.25%), average age was 84.9, and average heart rate at ICU admission was 83.3. One hundred sixty seven of these patients performed independent ADL's (62.1%). Two hundred seven patients (77%) were admitted to medical ICU's, while 62 patients (23%) were admitted to surgical ICU's. Two hundred ten patients (78.1%) required no invasive interventions, such as PAC, mechanical ventilation, or vasopressor use. Only 30.11% of patients had organ system failure. One hundred thirty five patients (50.2%) were discharged home, 103 patients (38.3%) were discharged to a skilled nursing facility (SNF), and 31 patients (11.5%) died. The logistic regression analysis accurately predicted the actual outcome in 146 patients (54.3%). However, further analysis revealed variability in accuracy of the model based on outcome. Of the 135 patients discharged home, the model accurately predicted outcome in 126 patients (93.3%). In contrast, the model accurately predicted outcome in only 13 of the 103 patients (12.6%) discharged to a SNF and 8 of the 31 patients (25.8%) who died.
Discussion: Preliminary analysis of this data indicates that this logistic regression model can predict the likelihood of an octogenarian's discharge home following ICU admission at a major academic center. The power of this study will be increased when evaluation of all 698 study patients is completed. If this model can be verified, we may be better equipped to advise patients, families, and providers regarding potential outcomes and decision making with respect to invasive procedures and interventions, thereby improving resource utilization.
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3. Critical Care Medicine 2001;29(10):1853-1859

S-133.

PERITONEAL DIALYSIS BY COLLOIDOSMOSIS IN A RAT MODEL: HIGH MOLECULAR VS. MIDDLE MOLECULAR WEIGHT HYDROXYETHYL STARCH

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Background: Standard peritoneal dialysis fluids (PDFs) use glucose as an osmotic gradient to drag water and compounds across the peritoneal membrane. Glucose degradation products or hyperglycemia-induced fibrosis of the peritoneal membrane may limit the use of peritoneal dialysis (PD). In a previous study we have shown that the osmotic agent (glucose) can be replaced by hydroxyethyl starch (HES), a colloidosmotic compound. In this study we tested the effects of differences in the molecular weight of colloidosmotic PDFs for its use for peritoneal dialysis (PD). We hypothesized that the passage of HES through the peritoneal membrane and its storage in organs is influenced by the molecular weight without effects on PD.
Methods: Male Wistar rats were nephrectomized and PD was started 3 days thereafter for 1 - 5 days. Rats were randomized to 2 groups (group 1: 6% HES 450 kD/0.5, group 2: 6% HES 200 kD/0.5). End points were 1) concentration of HES in serum and in organs, 2) water efflux (changes of body weight, fluid shift, hemoglobin concentration in blood), 3) membrane transfer assessed by peritoneal equilibrium test (PET), creatinine clearance (Kt/V), and changes of creatinine, BUN, and electrolytes before/after PD. At the last day of PD organs were harvested and HES concentration in serum, liver, spleen, and lung was measured. One-way ANOVA or Wilcoxon signed-rank test were used, where appropriate.
Results: HES concentration in serum increased over the time without differences between groups (table). HES liver concentration was higher in group 2. HES concentration in organs correlated with duration of PD. PD reduced body weight (-2.6%±1.5 vs. -1.9±1.2%, group 1 vs. 2), creatinine (-34.4±5.4% vs. -32.4±4.4%) and BUN (-39.9±2.0% vs. -40.9±4.5%) in serum equally in both groups (all $p < 0.01$ vs. baseline). PET (0.86±0.15 vs. 0.77±0.09, p=0.24) and Kt/V were not different between groups (0.57±0.04 vs. 0.58±0.03).
Discussion: Both tested PDFs provided sufficient fluid shift across the peritoneal membrane and reduced creatinine and BUN concentration. Transfer of HES through the peritoneal membrane was not influenced by the molecular weight. Differences in organ accumulation are more likely due to the pharmacodynamic properties of different HES solutions.

	HES in serum and organs				
mean ± SD	Day 1	Day 2	Day 3	Day 4	Day 5
Serum (mg/mL)					
Group 1	6.0±1.3	13.5±2.9	14.9±2.8	12.9±2.2	14.4±3.4
Group 2	7.1±2.3	11.1±2.2	12.3±1.8	13.5±2.9	13.1±2.1
Liver (mg/g)	p<0.001	p=0.03	p<0.001	p=0.008	p=0.02
Group 1	0.9±0.2	2.7±0.7	4.2±0.7	7.1±1.0	8.2±1.5
Group 2	1.5±0.3	3.6±0.9	6.5±0.9	9.0±1.6	10.4±2.2
Spleen (mg/g)					
Group 1	1.6±0.4	6.8±2.1	8.8±2.4	15.5±2.3	18.6±3.2
Group 2	1.7±0.4	6.4±1.3	10.6±1.3	14.6±2.2	16.9±4.9
Lung (mg/g)	p=0.001		p=0.006		
Group 1	1.3±0.2	4.6±1.0	4.0±0.8	6.3±2.0	7.7±3.9
Group 2	1.9±0.5	3.9±0.8	4.9±0.6	6.9±1.9	6.9±2.5

S-134.

ROLE OF THIOPENTONE INFUSION FOR MANAGEMENT OF INTRACTABLE STATUS EPILEPTICUS(ISE) IN PEDIATRIC PATIENTS

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Introduction: ISE not responding to conventional pharmacotherapy is a medical emergency. Rapid termination of seizures, prompt control of airway, ensure oxygenation, prevent aspiration, and minimize permanent neurological damage are the main goals of management. Deeper suppression of cortical activity, documented electrocerebral silence and titrable length of time during which such electrocerebral silence can be maintained, make thiopentone the ideal drug for initial management of status epilepticus (1,2). Longer lasting antiepileptic drug regimen can be established during thiopentone induced burst suppression, which can then be tapered and discontinued with minimal chances of recurrence.
Methods: 21 patients ranging from 1½ - 16 years suffering from idiopathic generalized tonic clonic disorder with age of onset 12 months to 2 years were included in the study. All were admitted to pediatric ICU after initial management in the emergency room. Rapid sequence intubation with cricoid pressure was done with thiopentone and succinylcholine. Ventilatory management was with oxygen and air to maintain SaO2 between 95-100%. Additional boluses of thiopentone were administered at 5-30 minute intervals until complete areflexia was achieved, while a continuous intravenous thiopentone infusion was titrated to obtain EEG burst suppression. Serum levels were maintained between 50-100 mcg/ml. Central and arterial lines were inserted in addition to standard ASA monitors. Continuous single channel processed EEGs using cerebral function analyzing monitor and intermittent multichannel electroencephalogram were done during thiopentone infusion and ICU stay. Therapeutic endpoint was absence of electrocerebral seizure activity. Occurrence duration of status epilepticus before and during thiopentone infusion was recorded. After control of clinical and electroencephalographic seizure activity, patients were started on appropriate loading and maintenance infusion of phenytoin and phenobarbitone. Thiopentone infusion was progressively tapered over 24 hours and discontinued once therapeutic serum levels were achieved for these antiepileptic medications.
Results: Out of the 21 patients, 16 showed burst suppression and five showed "flat" record. Two patients in the burst suppression category showed recurrence of seizure activity after being controlled initially and none in the flat one. In these two, EEG seizures recurred earlier than clinical seizures, which were rapidly controlled with increasing the rate of thiopentone infusion. More sustained control of seizure activity was achieved by adding valproic acid to the anti epileptic regimen.
Discussion: Tightly controlled by serum levels, carefully monitored with EEG for therapeutic efficiency, initiating and tapering of thiopentone infusion in ICU setting with mechanical ventilation and hemodynamic monitoring, will allow the physician to establish therapeutic serum levels of conventional antiepileptic agents, reduce the relapse rate, avoid the mortality and long term morbidity associated with this life threatening medical emergency.
References:
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S-135.

THE METHODS OF HUMIDIFICATION DOSE NOT ALTER THE CHANGE OF POSTOPERATIVE BODY TEMPERATURE IN THE PATIENTS UNDERGOING HEAD AND NECK TUMOR SURGERY

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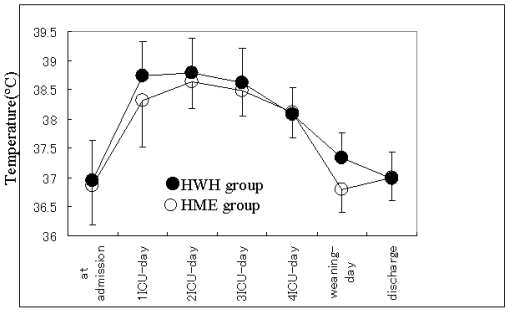
Introduction: Head and neck surgery for malignant neoplastic lesions consists of both tumor resection and reconstruction of removal lesions, and requires postoperative long sedation and mechanical ventilation because of surgical site stability. Moreover, a difficult but important postoperative care is to maintain body temperature because patients have frequent high fever. Thus we investigated that whether the methods of humidification alter the change of postoperative temperature in the patients undergoing head and neck tumor surgery.
Methods: Forty-nine patients admitted to our ICU were studied. They were ventilated with a respirator equipped with either heated water humidifier (HWH: Fisher & Paykel MR410, n=29) or heat and moisture exchanger (HME: PALL BP100PFS, n=20). Axillary temperature was monitored at 3-4 hour interval, and CRP was measured every morning. Both axillary and rectal temperature data were simultaneously obtained from ten patients. We analyzed the data in each subgroup, i.e. age, operation time, operation site, tracheotomy, transfusion, and CRP. Non-repeated measures ANOVA was used to analyze statistical difference between each group, and repeated measures ANOVA was used to analyze statistical difference for intragroup comparisons.
Results: The body temperature significantly increased at 1, 2, 3, 4 ICU-day compared with that at admission, but not at weaning-day (5 ICU-day) and discharge (6 ICU-day). There were good correlations between axillary and rectal temperature (r=0.82). In the HWH group, the body temperature significantly decreased between 4 ICU-day and weaning-day in both without tracheotomy group (from 38.2±0.4 to 37.3±0.5°C, n=12) and with tracheotomy group (from 38.0±0.5 to 37.4±0.4°C, n=17). Likewise, in HME group, the body temperature significantly decreased between 4 ICU-day and weaning-day in both without tracheotomy group (from 38.3±0.4 to 36.7±0.3°C, n=10) and with tracheotomy group (from 38.0±0.4 to 36.9±0.5°C, n=10). However there is no difference in the postoperative body temperature between HME group and HWH group. There were no significant differences in the change of postoperative body temperature in the subgroup of with or without tracheotomy, age, operation time, operation site, transfusion or CRP.
Discussion: We concluded that neither HME nor HWH alter the change of postoperative body temperature in the patients undergoing head and neck tumor surgery. The weaning of mechanical ventilation per se would alter the postoperative body temperature.

Change of postoperative body temperature in the patients undergoing head and neck tumor surgery



S-136.

PRACTICE REDESIGN FOR TIGHT GLYCEMIC CONTROL IN THE INTENSIVE CARE UNIT

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Introduction: Hyperglycemia and insulin resistance are common in critically ill patients, independent of a history of diabetes mellitus. These problems are often compounded by interventions in the intensive care unit (ICU) such as nutritional support and drug therapy. Historically, "loose" glucose control was common practice in order to avoid hypoglycemia. Recent data suggests tighter glucose control may have a profound effect on outcomes in critically ill patients.[1] As part of a Centers for Medicare and Medicaid Services sponsored national demonstration project, we redesigned our practice to maintain tight glycemic control for all patients admitted to the surgical intensive care unit (SICU) postoperatively with an elevated blood glucose .
Methods: All patients admitted to the SICU after surgery were included. From 7/02 to 2/04 we monitored patient records for compliance with tight glucose control protocols and resultant serum glucose levels. Capillary or blood glucose was measured hourly until stable. Glucose results were categorized into three groups: (1) less than 50mg/dL (2) 80mg/dL-150mg/dL and (3) greater than 250mg/dL. Through rapid-cycle improvement methods, a multidisciplinary glycemic control team suggested and implemented changes to improve results. Data was analyzed using chi square analysis with significance at $p<0.05$.
Results: There was a statistically significant improvement in glycemic control after initiation of the protocols (table 1). The number of glucose values less than 50mg/dL increased after initiation of tight glycemic control from 0.46% to 0.54%, but was not statistically significant (p=0.26). The number of values within the desired range (80mg/dL-150mg/dL) increased from 44.6% to 58.1% ($p< 0.01$) and the glucose values greater than 250mg/dL decreased from 8.3% to 3.6% ($p<0.01$).
Discussion: In critically ill patients, normalization of blood glucose levels with intensive insulin therapy has been shown to reduce morbidity and mortality.[1,2] Our data demonstrate that better control of blood glucose level in patients in the ICU is an achievable goal without a significant increased risk of hypoglycemia, which can lead to a lower mortality than in patients who receive conventional insulin therapy.

Glucose values before and after tight glycemic control

Glucose values	Before tight glycemic control	After tight glycemic control	p value
Total glucose readings	12,549	40,736	
Glucose values <50mg / dL	58 (0.46%)	222 (0.54%)	p=0.265
Glucose values = 80-150mg / dL	5,604 (44.6%)	23,668 (58.1%)	p<0.01
Glucose values >250mg / dL	1,038 (8.3%)	1,490 (3.7%)	p<0.01

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S-137.

HEMODYNAMIC PROFILES DURING LIVE DONOR LIVER TRANSPLANTATION SURGERY

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Introduction:
Orthotopic liver transplantation (OLT) utilizing partial liver grafts from live donors has proven to be a viable option in an era of donor organ shortage. Ischemia time and preservation injury are minimized (<2 hours) when live donor liver transplantation (LDLT) is performed.
Methods:
Fifty adult patients, mean age of 50 ±11.5 years, who underwent LDLT between November 2000 and February 2004 were studied. Etiologies were alchohol-induced cirrhosis (n=12), hepatitis B and C cirrhosis (n=11), PSC (n=11), PBC (n=7), nonalcoholic steatotic hepatitis (NASH, n=3) and others (n=6). Intraoperative hemodynamic monitoring included mean arterial pressure (MAP), mean pulmonary artery pressure (mPAP), pulmonary capillary wedge pressure (PCWP) and central venous pressure (CVP). Continuous cardiac output (CO), mixed venous saturation (SvO_2), right ventricular ejection fraction (RVEF), and right ventricular end-diastolic volume (RVEDV) were also measured, together with metabolic parameters: pH, base excess (BE); sodium (Na^+); potassium (K^+); ionized calcium (Ca^{++}); lactate and osmolarity. The Mann-Whitney test was used. $p < 0.05$ was considered statistically significant. All data are presented as mean values ± SD.
Results:
Compared with the baseline, MAP decreased to 72 ± 14 mmHg 5 minutes after reperfusion (III+5). Significant hypotension, defined as MAP ≤ 59 mmHg [1], occurred in 15 % of patients at III+5. In addition, PAP and K^+ remained stable at III+5, while CVP decreases. Average epinepherine doses given at reperfusion was 24 ± 27 mcg.

Table 1: Hemodynamic and Metabolic Profiles During LDLT

	I	I+60	II	III+5	III+60	III+end
CO (l/min)	8.3 ± 2.6	9.4 ± 3.2	8.8 ± 2.4	8.2 ± 2.6	9.4 ± 2.7	9.6 ± 2.7
SvO_2 (%)	84 ± 5	85 ± 5	88 ± 4 *	87 ± 6 *	86 ± 5 *	87 ± 4 *
MAP (mmHg)	75 ± 9	77 ± 10	75 ± 9	72 ± 14 *	72 ± 9	74 ± 9
CVP (mmHg)	11 ± 6	10 ± 4	7 ± 4 *	8 ± 4 *	9 ± 4	9 ± 4
mPAP (mmHg)	20 ± 5	20 ± 5	16 ± 5 *	19 ± 5	20 ± 5	20 ± 4
SVR (dynes·sec·cm^{-5})	721 ± 386	654 ± 320	666 ± 223	700 ± 309	585 ± 250	581 ± 182
Hct (%)	31 ± 5	30 ± 5	28 ± 5 *	29 ± 5	29 ± 5	30 ± 4
HCO_3^-(mmol/l)	21 ± 4	20 ± 3	21 ± 3	20 ± 3 *	21 ± 3	21 ± 3
K^+ (mmol/l)	3.5 ± 0.5	3.6 ± 0.6	3.5 ± 0.4	3.4 ± 0.5 *	3.4 ± 0.4	3.6 ± 0.4
Ca^{++} (mmol/l)	1.1 ± 0.1	1.1 ± 0.2	1.1 ± 0.3	1.2 ± 0.2 *	1.1 ± 0.2	1.2 ± 0.1
Lactate (mmol/l)	1.8 ± 0.9	2.1 ± 1.1 *	6.5 ± 3 *	7.2 ± 3.2 *	6.6 ± 3.7 *	7.2 ± 4.8 *

$p < 0.05$ compared with baseline

Conclusions:
The results of this study show a low incidence of hypotension (15 %), decreasing CVP, and stable mPAP and K^+ values after reperfusion of the donor graft in LDLT recipients. These findings contrast changes described in the "Post Reperfusion Syndrome" (PRS), where hypotension can occur in 29% of patients, and elevations of CVP, PAP and K^+ were observed [2]. Since donor organs for LDLT are from healthy individuals, there should be no hypotension or oxygen delivery issues involving the donor grafts, and preservation/ischemic injury should be minimal. Therefore, one could predict that the incidence of hypotension and PRS may be lower in LDLT, as was shown in this series of patients. Maintaining euvolemia prior to reperfusion may further decrease this reported low incidence of hypotension.
References:
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S-138.

COMPARISON OF FIVE METHODS FOR SECURING ORAL-TRACHEAL TUBE

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Introduction: Accumulating evidence suggests that tracheal tube dislodgment following a successful tracheal intubation may occur at a much higher rate in an emergency setting.[1)] In *Guidelines 2000 for Cardiopulmonary Resuscitation* (American Heart Association), use of a purpose-built commercial device is recommended for securing the tracheal tube, however, there is scant evidence regarding the efficacy of specific devices. In the present study, we performed a comparative study of 5 commonly used methods of securing a tracheal tube by examining the efficacy of each.
Methods: Twelve healthy male volunteers participated as subjects. A half-cut tracheal tube was placed in the mouth of each while lying in a supine position and secured using the 5 experimental methods: A) medical adhesive cloth tape (Johnson&Johnson, Dermicel®, 12-mm width), B) elastic adhesive bandage (Alcare, Elatex®, 50-mm width), C) tape type tube holder (Mallinckrodt, Tracheal Tube Restraint®, 12-mm width), D) screw type tube holder (Laerdal, THOMAS®), and E) string (5-mm width). Thereafter, the tracheal tube was pulled up with a spring balance by the investigator and the scale of the balance mechanism was used as a measurement of maximum force in kilograms before the tube slipped off the mouth of the subject. Three measurements were made for each method with each subject and the results averaged. Further, we applied edible oil on the face to create a situation similar to the presence of saliva, vomit, or blood, and performed the same tests again. Data are shown as mean ± SD, with one-way ANOVA and the Tukey-Kramer method used for multiple comparisons in the statistical analyses. Statistical significance was accepted at $P < 0.05$.
Results: Following are the results of each method without oil: A) 1.4 ± 0.2 kg, B) 2.4 ± 0.3 kg, C) 1.0 ± 0.3 kg, D) 4.4 ± 0.3 kg*, and E) 2.1 ± 0.3 kg (*P<0.05 vs. A, B, C, and E). The following results were obtained with oil: A) 1.0 ± 0.2 kg**, B) 1.9 ± 0.3 kg**, C) 0.9 ± 0.3 kg, D) 4.4 ± 0.3 kg*, and E) 2.0 ± 0.3 kg (*P<0.05 vs. A, B, C, and E, **P<0.05 vs. A and B without oil).
Discussion: Our results demonstrated that the screw type tube holder (D method) was the most reliable for securing the tracheal tube, and that the presence of oil significantly worsened the performance of the medical adhesive cloth tape and elastic adhesive bandage (A and B, respectively). Further, these findings support the recommendations made in *Guidelines 2000 for Cardiopulmonary Resuscitation* and suggest that a screw type tube holder is able to secure an intubated tracheal tube in difficult situations, such as prehospital settings.
References:
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S-139.

PREFFERED HEAD POSITION IN JAPAN DURING RAPID SEQUENCE INDUCTION OF GENERAL ANESTHESIA FOR PATIENTS WITH INCREASED ASPIRATION RISK: AN E-MAIL SURVEY

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Introduction: There has been hardly a consistent recommendation regarding the optimal head position during induction of general anesthesia in an effort to reduce aspiration risk. Among the scanty literatures two positions are recommended for different reasons: head-up and head-down. Proponents of the former argue that head-up position reduces aspiration risk from passive regurgitation by facilitating the gravitational force working in favor of the stomach . Proponents for the head-down position, on the other hand, point out that the risk is reduced, if and when active vomiting occurs, by draining the vomitus away from the trachea and out of the mouth for evacuation. Dr. Sellick who invented the famous Sellick Manuever had recommended this position in his original paper.[1] A previous study in the US showed that most practitioners position their patients flat.[2] By E-mail we have surveyed among current practitioners in Japan in an effort to determine their preferred head positions.
Methods: An E-mail question survey was sent out to anesthesiologists in an academic institution in Tokyo to determine the preferred head position during rapid sequence induction for patients with increased aspiration risk. We did not select those who are with non-M.D. degrees or in residency training. The one-question survey elicited the respondents to choose one of the three possible positions: head-up, flat, or head-down.
Results: Among 43 responses, 36 (84%) indicated that they keep the patients' head position flat; 7 (16%) indicated they raise the head up, and none indicated they keep the head down. Discussion: It is interesting to note that no current major US textbooks in anesthesiology recommend flat head position as the optimal position to reduce the risk for aspiration. Either head up or head down position is recommended in some textbooks for different reasons. Usually for passive regurgitation head up position is in theory better to keep the aspirant in the stomach while for active vomiting head down position is suggested to drain the vomitus out of mouth, and away from the lungs. The survey result may reflect the current controversy or lack of consensus convincing enough to establish a clear guideline for all. This is a very similar finding to the study done in the US.[2]
Conclusion: The majority of current anesthesiologists in Japan do not raise or lower the heads in relation to the patients' feet when they perform rapid sequence induction. Patient's head position does not seem to be a major factor in an effort to reduce the risk of aspiration during induction of general anesthesia.
References:
1. Sellick BA: Cricoid pressure to control regurgitation of stomach contents during induction of anaesthesia. Lancet 2:404-406, 1961.
2. Chee, W, Reed, A: Preferred Head Position during Rapid Sequence Induction. IARS Abstract S92. 2001.

S-140.

IMMEDIATE EXTUBATION AFTER MITRAL VALVE SURGERY: A FIRST EXPERIENCE

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Immediate extubation has become more popular after off-pump or on-pump aortocoronary bypass grafting. However, its use for valve surgery has been limited; only one recent study has presented immediate extubation after aortic valve surgery. We present a prospective audit of immediate extubation after mitral valve surgery using different techniques of peri-operative analgesia.
Twenty patients underwent mitral valve surgery with the object of immediate extubation on the operating table. Patients with normal preoperative coagulation were consented for perioperative epidural analgesia, patients with coagulative disorders (or under full heparinization) or patients who did not consent for epidural catheter insertion were consented for perioperative bilateral single shot paravertebral blocks, followed by patient-controlled analgesia with morphine (PCA) after surgery. In all patients, anesthesia was induced using fentanyl 3-5 µg/kg and propofol 1-2 mg/kg, intubation was facilitated using rocuronium 0.6 mg/kg. Feasability and safety of immediate extubation was evaluated. Pain scores after surgery were compared using rank sum test ($P < 0.05$).
All 15 (preliminary data) patients could be extubated successfully within 15 min after surgery. There was no re-intubation. Patient data, surgery related data are presented in Table 1. Eleven patients had TEA, 4 patients had paravertebral blocks (all because of preoperative anticoagulation). There were no neurological complications or any clinical sign of epidural hematoma. TEA was removed at 52 h (6 h) after surgery at INR lower than 1.5 in all patients. Pain scores immediately after surgery, 2 h po. and 24 h po. were significantly lower with TEA than with paravertebral blocks and PCA at 0.6 (0.9), 0.7 (1.2), 0.6 (0.9) versus 4 (3.5), 3.2 (1.2) and 2.5 (2), respectively. P_{O2} (FiO_2=1) immediately after extubation were significantly higher with TEA than with paravertebral blocks and PCA at 201 (78) versus 101 (45) mmHg; there was no difference concerning P_{CO2} (FiO_2=1) with 49 (5) versus 45 (2) mmHg, respectively.
We conclude that immediate extubation after mitral valve surgery is feasible. Restrictions and concerns about TEA are the same than with other types of surgery and, temporary, full anticoagulation. TEA provides better pain control than paravertebral blocks, especially immediately after extubation with higher arterial oxygen saturations. Immediate extubation after mitral valve surgery is a novel promising path in cardiac anesthesia.
Table 1

	(N=15)
Age (y)	62 (13)
Weight (kg)	63 (18)
Sex (m / f)	6 / 9
TEA / Parav. Block	11 / 4
Ejection fraction (%)	57 (10)
Ischemic time (min)	49 (11)
PO2 (mmHg) po. (FiO2 = 1)	164 (81)
PCO2 (mmHg) po. (FiO2 =1)	49 (5)
Numeric Pain Score (0-10) 0.5 h after surgery	1.4 (2.3)
Numeric Pain Score (0-10) 2 h after surgery	0.7 (1.3)
Numeric Pain Score (0-10) 24 h after surgery	1 (1.5)

S-141.

RAPID SEQUENCE INTUBATION BY NON-PHYSICIAN AIR MEDICAL CREWS: A THREE-YEAR CANADIAN PROVINCE WIDE EXPERIENCE

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Introduction: Rapid Sequence Intubation (RSI) is an airway management tool that has been effectively but not commonly used in the pre-hospital environment. In this study we reviewed the utilization of RSI used in a Canadian provincial air medical transport system over a three-year period.
Methods: Air Medical Crew (AMC) teams consisting of a paramedic and a nurse received intensive, simulator-based training for RSI and advanced airway management. Subsequently all airway interventions by AMCs were prospectively recorded into a database. RSI formed the default airway intervention of choice for this air medical program post training. The population studied involved only those patients >15 years of age and included trauma and non-trauma patients.
Results: The total number of missions carried out by AMCs during the review period was 1274. Trauma accounted for 57% of the primary diagnoses in our patients. 99 patients required advanced airway interventions, with a 99% intubation success rate (98/99). There was one failure to intubate, and this patient was successfully ventilated until arrival at the receiving hospital. RSI was used in 70 patients and endotracheal intubation was successful 99% of the time (69/70). AMCs were the sole airway managers in 74 cases and successfully intubated 100% of patients with an overall first time intubation success rate of 85%. In 25 of the cases non-AMC personnel collaborated in airway management (e.g. ground paramedics, on site MDs, etc.). The most commonly used RSI medications were propofol and succinylcholine. The gum elastic bougie was the most commonly used intubating adjunct. There were no surgical airways performed.
Discussion: Rapid sequence intubation has been introduced into our provincial air medical transport system safely with intubation success rates that are as good as or better than rates previously reported in the literature. RSI by non-physicians is a controversial topic. Our study shows that RSI protocols can be effectively used by non-physician AMCs in achieving endotracheal intubation in critically ill patients. The conclusions of this study are limited to the air medical transport environment and cannot be applied to other pre-hospital settings. Further studies are also needed to review the impact of pre-hospital RSI on patient morbidity and mortality.
References:
Austin P. Air Med J. Jul-Sept 2000, 19:3. p90-97.

S-142.

MANGANESE SUPEROXIDE DISMUTASE NEBULIZATION DOES NOT IMPROVE OXYGENATION IN AN OVINE MODEL OF SMOKE INHALATION INJURY

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Introduction: There is evidence of increased oxygen free radical activity, e.g. superoxide, in association with smoke inhalation injury (1). Since superoxide dismutase converts the reactive superoxide radical to peroxide (2), we hypothesized that nebulization of manganese superoxide dismutase (Mn-SOD) into the airway attenuates pulmonary dysfunction secondary to smoke inhalation injury. The goal of this study was to determine the effect of nebulized Mn-SOD on oxidative stress and gas exchange as well as pulmonary edema formation.
Methods: Fifteen sheep (35±3 kg), were operatively prepared for chronic study. After 7 days of recovery, sheep were randomly allocated to 1) an untreated control group (injured with 4x12 breaths of cotton smoke), 2) an injured group treated with nebulized Mn-SOD (5 mg/kg), and 3) an injured group that received an equivalent volume of the vehicle (saline; n=5 each). Nebulization was performed at 1 h and 12 h after smoke inhalation. Blood gases were analyzed every 2h. After the 24h study period, lung tissue were obtained to determine wet/dry weight ratio and conjugated dienes (CDs), which are lipid peroxidation products indicating oxidative stress. Statistical analysis was performed using two-way ANOVA and Student-Newman-Keuls post hoc comparisons to detect differences within and between groups. Data are expressed as mean ± SEM.
Results: CDs (absorbance units at 233nm) in the Mn-SOD group (1.7±0.1) were significantly lower as compared to saline (2.6±0.1) and control group (3.2±0.3; $P<0.05$ each). However, PaO_2/FiO_2 ratio decreased likewise in all groups. There were no differences in lung wet/dry weight ratio between groups.
Discussion: Although nebulization of Mn-SOD reduced lipid peroxidation products, it failed to reduce the formation of lung edema and to ameliorate gas exchange, thereby limiting its clinical use in the setting of smoke inhalation injury.
References:
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(2) Effects of manganese superoxide dismutase on lung fluid balance after smoke inhalation: J Appl Physiol 78:2161-8, 1995

Economics, Education and Patient Safety

S-143.

CREATING A PATIENT SAFETY CURRICULUM: PURPOSIVE SAMPLING OF PATIENT SAFETY EXPERTS

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Introduction: Redesigning healthcare for patient safety is going to require changing the present healthcare curriculum to focus on patient safety. Purposive sampling of health care education experts produced information which we correlated with truncated internet search results. We determined whether educators believe that patient safety courses should be integrated into the health care education continuum.
Methods: We developed a tool described elsewhere (1) to conduct our purposive interviews, and interviewed more than three dozen state, national, and international experts on patient safety education. We convened an international conference to determine currently available patient safety teaching in health care professional learning institutions. Educator attitudes were probed to assess how likely an integrated curriculum was to be implemented in academic health care centers. We assembled a list of recommendations that were ratified by a modified Delphi method, for teaching patient safety in health care schools and continuing education courses.
Results: Nursing schools are doing more teaching of specific patient safety and tend to be more multidisciplinary. Few medical schools have more than isolated lectures on patient safety. Many healthcare centers already invest deeply in Information Technology (IT), but seamless integration of IT with areas such as medication error and medical records is rare. There was a tendency to wishfully approach IT as a magic solution to complicated system problems. Groups of incoming healthcare underclassmen who are more familiar with IT may help to solve the usability of medical IT. Health care administrators and senior educators believe that there is no need for patient safety curricular overhaul. Interdisciplinary competition and turf wars were frequently given as one reason for the slow development of a patient safety curriculum. The most urgently needed curricular elements are blameless voluntary error reporting, formal teaching of error analysis, team training and simulation. Attitudinal change is needed and is felt to be more important than the learning of factual material. Immediate, honest, documented disclosure of errors by clinicians to patients may prove to be the most cost-effective way to deal with medical errors.
Conclusions: A robust patient safety curriculum for training health care professionals must be multidisciplinary and aim at training the patients and their families as well. An effective "safety culture" requires that a crucial number of senior faculty and administrators buy in to the need for a patient safety based curriculum. Crew resource team training, simulations, and other aspects of a patient safety curriculum that is integrated throughout the entire health care education continuum are needed to make healthcare safer.
References:
http://umdas.med.miami.edu/MPSC/reports%5CSection%2036-5.pdf September 3, 2004.

S-144.

HUMAN FACTORS ON THE CUTTING EDGE: PATIENT SAFETY DURING PEDIATRIC CARDIAC SURGERY

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BACKGROUND:
Pediatric cardiac surgery (PCS) encompasses complex procedures that are highly dependent upon a sophisticated organizational structure, coordinated efforts of team members and high levels of cognitive and technical performance. Medical errors have been attributed to individuals, but this overlooks interactions between individuals and system issues. Little is known about how human factors, such as communication and teamwork contribute to adverse events.
PURPOSE:
We hypothesized that patterns of adverse events and near misses occur during PCS in the operating room, and that they are associated with human factors.
METHODS:
Researchers trained in pediatric cardiac surgical techniques and human factors methodology, observed 300 hours of PCS care from the inception of anesthesia to the patient hand-off in the intensive care unit. Cases varied by type and complexity. Events were classified as major or minor, and the presence or lack of compensatory mechanisms was noted. Events were described as major or minor based on potential patient harm.. An event was considered compensated when a clinical response was used to attentuate adverse event consequences. Complexity scores were calculated using the Aristotle(R) scoring system and outcomes were recorded. Flow diagrams of the surgical care process were created to distinguish frequency of events. This method was used to determine which areas of surgical care needed improvement.
RESULTS:
A total of fifty-five cases were observed over 9 months. Overall hospital mortality was 3%. An average of 1.6 major events occurred per case. Examples of major events included drug overdose, accidental extubation, preparation of cardiopulmonary bypass (CPB) equipment with the wrong blood, bleeding, arrhythmia, ventilation issues, poor myocardial protection, and re-institution of CPB. Major events occurred most frequently during surgical correction (**N=16)** and post-bypass period (**N=17)**. Minor events included delayed blood administration, equipment problems, coordination problems between team members, communication breakdowns, and transport difficulties. Events were found to occur most frequently during the induction of anesthesia period (**N=56)** and during surgical correction (**N=73)**. Compensatory mechanisms consisted of recognition and intervention by the team members, with one exception that arose from blood transfusion safety practices. No uncompensated major events or intraoperative deaths occurred. The Aristotle complexities scores ranged from 6.8 to 22.5, with a mean of 12.1. Case complexity and outcomes were positively correlated ($p<0.0001$ using a t-statistic test). Major and minor events occurred in all types of cases and did not significantly correlate with case complexity or outcome.
CONCLUSION:
Near misses and adverse events occur on a routine basis, and are not routinely recorded. These events are poorly correlated with PCS complexity or outcomes. Event recognition and action by team members was the most important mode of recovery. This data suggests that human factors analysis, team training and safety focused interventions are critical to improve patient outcomes.

S-145.

EASY AND SAFE TECHNIQUE TO REDUCE THE INCIDENCE AND INTENSITY OF EPITAXIS DURING NASOTRACHEAL INTUBATION

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Introduction: Nasotracheal intubation (NTI) is often required during dental and maxillofacial surgery. Nasal bleeding is one of the complications of nasotracheal intubation. We examined whether the insertion of a nasopharyngeal airway lubricated with lidocaine jelly and epinephrine could decrease the incidence and intensity of nasal bleeding during NTI.
Methods: Forty-four (ASA I or II) elective patients (aged 19-64 yr) who were scheduled to undergo NTI were selected for this study. The subjects were randomly assigned into two groups: an Epi (+) group (n = 20), in which subjects received NTI using a nasopharyngeal airway lubricated with lidocaine jelly and with 1:100:000 epinephrine, and an Epi (-) group (n = 20), in which subjects received NTI using a nasopharyngeal airway lubricated with only lidocaine jelly. Anesthesia was induced by propofol (2.0 mg/kg) and fentanyl (2 ug/kg), and muscle relaxation was obtained by administration of vecuronium (0.15 mg/kg). Anesthesia was maintained with 5% sevoflurane in 60% nitrous oxide and 35% oxygen during the NTI. Nasopharyngeal tubes (6.0, 7.0 and 8.0 mm in internal diameter) lubricated with lidocaine jelly with or without epinephrine were inserted into nasopharyngeal airway in the order of its size and placed there for 30 s before the insertion of a nasotracheal tube. Anesthesiologists were blinded for this study, and nasal and pharyngeal bleeding was evaluated by an independent observer as follows: no bleeding, mild bleeding (a little blood on the tip of the nasopharyngeal airway), and moderate bleeding (an obvious blood on the whole airway). Hemodynamic changes during the induction of anesthesia were also recorded.
Results: The two groups were comparable with respect to all characteristics. There was no difficult in intubation due to bleeding. As the airway tube size was increased progressively, the Epi (+) group showed significantly less incidence and less intensity of nasal bleeding than did the Epi (-) group. There were no significant differences in hemodynamic changes between the two groups during the induction of anesthesia.
Conclusion: The results obtained in this study indicate that a nasopharyngeal airway lubricated with lidocaine jelly and 1:100:000 epinephrine helps to reduce the incidence and intensity of nasal bleeding during NTI without an increase in hemodynamic response.

S-146.

AUTOMATED ANESTHESIA INFORMATION MANAGEMENT SYSTEMS AND EPIDURAL CATHETER FOLLOW-UP: A QUALITY IMPROVEMENT SUCCESS STORY

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INTRODUCTION: Identifying patients with epidural catheters (EC) placed in the OR has been problematic at our institution. After the OR, care of EC patients passes to the Acute Pain Service (APS) which develops a list of EC patients who need follow-up. Before this project, the list was generated from multiple sources, all dependent on human intervention. For example, nurses in the post-anesthesia care unit (PACU) wrote the names of EC patients on a board. If names were omitted or patients bypassed the PACU, they were not followed. These patients were subsequently found by the APS during rounds or through requests for follow-up (usually delayed). The human-generated list was replaced by auto-querying an Anesthesia Information Management System (AIMS, Saturn, Drager Medical, Telford, PA) using Crystal Reports software. We hypothesized that automating the creation of the follow-up list would improve our patient care and ease list creation.
METHODS: We used the report writing tool to query the AIMS, generating a daily report of patients whose anesthetic record contained evidence of an EC placement. We compared 3 months of follow-up visits using the new system vs. performance for the same 3 calendar months using the old system in the two prior years. Percentages of ECs billed on time vs. later, and the number of follow-up visits made were tabulated. Results were compared using Chi square analysis.
RESULTS: The AIMS-generated list reduced the incidence of late billing by 71% ($P < .001$), and the incidence of missed follow-up visits by 93% ($P < .001$). 92.7% of patients were seen on POD#1 using the old system vs. 97.5% using the AIMS-generated list ($P<.01$). The time required to compile the daily list was reduced from 58 to 7 minutes.
DISCUSSION: Automatic identification of patients requiring follow-up after EC placement has improved our post-operative care. Prior to this intervention, roughly 7.3% of all patients with ECs were missed for at least the first post-operative day. After the introduction of the AIMS-generated list, the incidence of late follow-up decreased and subsequent follow-up improved. Missed follow-up visits did not fall to 0 for a variety of reasons, including availability of the patients. Automatic generation of the follow-up list succeeded because the AIMS encourages complete reporting by prompting the practitioner to address compliance. Nevertheless, the system as first deployed was not perfect. Initially, patients with an EC as the primary anesthetic, patients anesthetized at a location without the AIMS, and patients for whom the EC insertion was not properly documented were not captured. Subsequent broadening of search criteria improved capture by the AIMS, allowing more timely follow-up care and billing of our patients. Also the amount of time and the task complexity of generating the list have decreased substantially.

S-147.

THE CONTRIBUTION OF PREOPERATIVE EVALUATION TO PATIENT SAFETY IN HIGH-RISK SURGICAL PATIENTS - A PILOT STUDY

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Introduction: Efforts to define the impact of preoperative evaluation for surgical patients have mainly focused on efficiency and cost savings outcomes[1,2]. Few studies have attempted to link deficiencies in preoperative evaluation and perioperative safety. The ASA Task Force on Preanesthesia Evaluation emphasized the need for research in this area[3]. Previous work detected preoperative assessment failures from an incident report database[4]. This study is the first attempt to our knowledge to specifically pilot a tool to capture data on the impact of the preoperative process on patient safety.
Methods: After IRB approval, we identified individuals with one high-risk attribute among all patients seen in the anesthesia preoperative clinic from Jan 1 2002 to Sept 30 2003. High risk attributes were defined as: invasive surgical procedures (major vascular, thoracic, neurosurgery, gastrointestinal, urology); ASA PS 4; high-risk medications (coumadin, heparin, insulin). From this group of approximately 1000 patients, a subgroup of 80 individuals with ≥ 2 high-risk attributes was defined; 49 charts from this subgroup were retrospectively reviewed by one rater. Demographics, evaluation (history, physical exam), preoperative preparation (tests, consults, management of existing conditions), and problems on the day of surgery were captured.
Results: Forty-nine high-risk patient charts were examined. Most patients were ASA class 3 or 4, and had evaluation 7-30 days before surgery. Most evaluation problems involved cardiovascular evaluation, incorrect management of antihypertensives, or failure to follow consultant recommendations. A few charts showed oversights in history, physical examination, or laboratory testing. In at least two instances, the evaluator made significant interventions to improve the patient's condition before surgery. Table 1 summarizes the results.
Discussion: Retrospective review identified preventable failures in preoperative assessment. Certain patients had potential problems averted in the preoperative clinic (dialysis initiated; cardiovascular evaluation initiated by another evaluator after first evaluator omitted; patient with severe pulmonary disease requiring admission). One of the deficiencies of retrospective record review is that some information may not be captured, such as communication breakdown or information loss. This work is preparatory to more comprehensive studies to define the benefits of preoperative evaluation for patient safety and outcomes.
References: 1. Anesth 1996;85:196 2. Anesth Analg 1997;85:1307 3.Anesth 2002:96:485 4. Anaesthesia 2000;55:1173
Funding source: This work was partially supported by grant U18 HS11905 from the AHRQ.

Patient characteristics and preoperative assessment events

Patient demographics	
Total number of patients	49
Gender	M 33 F 16
Age range	34 to 85 yrs
Procedure type	Number of patients
Thoracic	11
Vascular	18
GI	9
Urology	8
Neurosurgery	2
Endocrine	1
ASA Physical Status	Number of patients
2	14
3	19
4	15
not specified	1
Timing of preoperative evaluation (days before surgery)	Number of patients
1-2 days	2
3-7 days	17
7-30 days	29
greater than 30 days	1
Concordance of preoperative evaluator and DOS anesthesiologist	Number of patients
N	48
Y	1
Preoperative evaluation	
Preoperative evaluation content	Number of patients
Incorrect medical history or missing items in history	2
Incomplete physical exam	2
Preoperative preparation: tests and consults	Number of patients
Recommended lab tests or ECG omitted	3
Cardiovascular evaluation inadequate	7
Other subspecialty evaluation inadequate	1
Preoperative preparation: management of existing conditions	Number of patients
Incorrect medication instructions	5
Incorrect device management	1
Other (recommended beta blocker not administered)	2
Day of surgery issues identified	Number of patients
Cardiovascular	2
Potential serious problem averted by preoperative clinic visit	3
No deficits in preoperative evaluation noted	23
Incidents (intraoperative or in PACU)	Number of patients
Airway	2
Cardiovascular	1

S-148.

DEVELOPMENT OF AN INTEGRATED, COMPREHENSIVE AND CONTINUING QUALITY IMPROVEMENT (ICCQI) PROGRAM IN AN ACADEMIC ANESTHESIOLOGY DEPARTMENT; FROM INCEPTION TO ACTION

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Introduction: Quality improvement (QI) has traditionally been limited to Morbidity and Mortality (M+M) and Peer Review. While these are important components of the QI process for Anesthesiology, they face limitations which include a focus on small numbers of adverse clinical outcomes (no denominator), disregard of cost factors, and others. QI development is qualitatively supported by the literature, and advocates a systems-based reporting culture as an excellent means of risk management (1,2,3). Our ICCQI program was developed under the following assumptions: 1. The highest quality care is the most cost effective (4,5). 2. All peri-operative services must be examined (6). 3. The program can approach a real time process. 4. It must be integrated with the hospital CQI process, residency and continuing education programs 5. The program rarely requires Peer Review or disciplinary action. 6. The program enables development of problem solving strategies for the Department that are easily understood and supported by hospital administration. In addition, we hypothesize that an ICCQI program can yield savings that far outweigh its costs.
Methods: In February 2000, Phase 1 was initiated with retrospective review of M+M records. Subsequently (Phase 2), narrative complaints were solicited from all anesthesiology service providers. Based upon these complaints and other verbal reports, we developed a QI encounter form to be used for each Anesthesiology service provided (Phase 3). A database (Microsoft Access ®™) was developed to reflect the QI encounter form and modified to reflect enhancements in the form that developed over time (Phase 4). Intermittent reports and data analysis were shared with the faculty, residents, and hospital administration (Phase 5). In other words, the ICCQI process evolved from a simple accounting of M+M reviews to a comprehensive program of continuing QI that includes assessment, tracking, reporting and reduction of adverse outcomes and delays.
Results: Initial monthly results (July 2000-present) showed a low adverse event rate (4-10%) with major events occurring in less than 1% of cases. Anesthesia equipment failure ranged from 0-3% over the four year period. In those cases where delay was recorded, times averaged between 15 and 48 minutes, with less than 30% related to Anesthesia services. The cost impact of these delays and their elimination was also determined, with analysis of the estimated cost of correction.
Discussion: Given its universal applicability, the QI process is a valuable tool for any Anesthesiology Department. It is a relatively simple and inexpensive way to improve quality of care, it can direct clinical teaching and clinical research within the department, and simultaneously contain and reduce the cost of patient care.
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S-149.

CAN ANESTHESIOLOGISTS REDUCE CARDIAC EVENTS DURING HIGH RISK SURGERY BY IMPLEMENTING BETA BLOCKER THERAPY IN THE PREOPERATIVE CLINIC?

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Introduction: In the last 25 years, great effort has been put forth to establish guidelines to identify patients at risk for poor outcomes after non-cardiac surgery.[1] However, only in the last few years have guidelines been developed that establish methods to decrease this risk by changing perioperative practices.[2] It is clear that cardiac protection using beta blockers (BB) is the most effective way to reduce death and major cardiac morbidity post operatively.[2] This study is an attempt to determine the predicted impact on perioperative cardiac morbidity and mortality that could be achieved with optimal preoperative BB implementation as suggested by the current literature.[3]

Methods: We reviewed >14,000 records (12 months) from our pre-operative clinic. Patients with characteristics placing them at risk for perioperative cardiac morbidity and death who were scheduled to undergo high risk surgery were selected. Risk factors included age ≥70, angina, prior MI, CHF, Stroke, diabetes mellitus and renal failure. 303 patients with ≥1 risk indicators were identified. Patients with 1-2 risk factors were classified as intermediate risk and those with ≥3 risk factors were considered high risk. These classifications are based on the clinical risk scores by Poldermans.[3] We then determined whether these patients were on BB. We hypothetically calculated the projected rates of death or major cardiac events of this group of patients based on results from Poldermans.[3]

Results: We found 88 (34.7%) intermediate risk patients (n=262)on BB. Of those at high risk (n=41) 65.85% were on BB. Based on results from Poldermans, we predicted cardiac event rates shown in the Table.[3] The expected number of events within 30 days of surgery in 303 patients under the observed beta blocker treatment proportions would be 9.4, which would be reduced to 5.4 events if 100% received BB.

Expected # of Cardiac Events Stratified by High and Intermediate Risk Patients on and off BB

	Estimated Event Rate (95% Confidence Interval)	N	Expected Number of Events among N Patients (95% Confidence Interval)
1-2 risk factors			
with β-blocker	1.2% (0.5, 2.8)	262	3.1 (1.4, 7.2)
without β-blocker	2.9% (1.9, 4.9)	262	7.7 (4.9, 12.8)
≥ 3 risk factors			
with β-blocker	5.6% (2.3, 12.4)	41	2.3 (1.2, 5.1)
without β-blocker	12.9% (9.2, 23.9)	41	5.3 (3.8, 9.8)

Discussion: In this pilot study, we predicted that the number of events could be reduced from 3.1 to 1.78 per 100 with 100% BB compliance. Extrapolating this to the estimated 10-12 million patients at risk for cardiac events who undergo surgery yearly in the US presents a huge opportunity for anesthesiologists to improve cardiac event-free survival and operative outcomes.[4]

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S-150.

USING PROBABLISTIC DECISION TREES AND DATA-MINING METHODS OF INTRAOPERATIVE MEDICAL RECORDS TO DETECT AND PREDICT ADVERSE EVENTS

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Introduction

The main reason for healthcare related adverse events is human errors (including adverse events (AE) and near misses (NM)). Identifying and learning from these events is an important goal. Using data-mining technology, we analysed our intropererative medical records (IOEMR) to better understand precursors to AE , and the circumstances possible to avert them. Induction of decision trees is one of the most advanced fields in data mining.

Methods

We used our 21,000 record intraopeartive medical record (IOEMR). We created simulated models based on routine healthcare parameters using the decision-tree generator C4.5. The input of a so-called “flat file” was obtained from existing PICIS databases using classical SQL queries. The output was in the form of a decision tree and was easily converted into *if-then* rules. The trees and rules represent logical functions that can later be “softened” to reflect their uncertainty. The uncertainty inherently contained in the data was quantified by classical Bayesian probability and by the Dempster-Shafer belief theory.

Results

The IOEMR contained 21,000 patient's data which were collected before, during or after the operation in 2004. The data includes 20 parameters such as heart rate, pulse, blood pressure, temperature etc. that are measured every minute. Among 21,000 patients, about 500 of had complications. We used the detailed paramter analysis of these AE to assess which parameters or combination of the parameters led to complications. We randomly picked 70% of the data for training and the 30% of data for testing. The experiments were repeated ten times. We achieved 65 percent accuracy for testing and about 60% for training (average). Attached is the experimental results from our system.

Experiment No	Error Rate Before Pruning (Training)	Error Rate After Pruning (Training)	Error Rate Before Pruning (Testing)	Error Rate After Pruning (Testing)
1	36.7%	36.7%	40.0%	40.0%
2	37.3%	37.3%	40.8%	40.8%
3	35.4%	35.4%	45.4%	45.4%
4	35.6%	35.6%	43.1%	43.1%
5	33.8%	33.8%	41.5%	41.5%
6	36.1%	36.1%	42.3%	42.3%
7	32.7%	32.7%	39.2%	39.2%
8	37.6%	37.6%	38.5%	38.5%
9	34.0%	34.0%	44.6%	44.6%
10	37.6%	37.6%	38.5%	38.5%
Average Error	35.68%	35.68%	41.39%	41.39%
SD	1.717%	1.717%	2.4479%	2.4479%

Discussion

Data mining tools such as decision trees demonstrate that by analyzing the past AEs it is possible to identify and predict the possible adverse events in the future. This might help alert anesthesiologists intraoperatively to prevent adverse events in real time. These tools make it possible to combine the uncertainty of collaborating sources of knowledge and the mechanisms that employ automated reasoning in the perioperative setting.

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S-151.

SOLIDIFYING THE AIRWAY TRAINING EXPERIENCE BY INCORPORATING A STRUCTURED RESIDENT AIRWAY MANAGEMENT CURRICULUM

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Introduction: Fewer than a third(1) of the US's residency programs have an organized curriculum that focuses on airway management planning and follow-through. As the ACGME requires general competency evaluation, it is no longer enough to hope that residents are by chance exposed to airway management situations. (2)
Methods: Every two weeks a different CA-1 will go through the rotation. In December, all CA-1 residents will attend a half-day hands-on airway workshop given at our yearly national conference. Before the formal rotation begins, the CA-1 will be expected to have done 3 awake and 3 asleep fiberoptic intubations, and 3 Fast-Track LMA placements on patients. Additionally, the resident is expected to read through an airway management rotation syllabus. Pre-op assessment, attending-resident discussion, and case management during the rotation focus on the airway. As this rotation focuses on management of all airways, the resident will experience but not be limited to working with patients with difficult airways.(3) Faculty from within the department who have made airway management a specialized interest will be matched up with residents and encouraged to focus the learning process. Finally, during the rotation period, the resident will spend ten hours in our airway management lab learning about less common techniques, improving his/her skills with a flexible fiberoptic bronchoscope, and working on the simulator. Each resident will take his/her skills and build on them as the residency continues past the rotation. As he/she is put into more supervisory roles, s/he will be encouraged to discuss and teach less experienced airway managers as well as non-anesthesia personnel. As the resident progresses, s/he will keep track of procedure data and focus on areas of weakness.
Results: A knowledge test will be administered at the beginning of the residency as well as before and after the rotation. We will use a hands-on evaluation with a computer-guided bronchoscopy program to obtain objective data on the resident's procedural skills. This evaluation will be given before and after the rotation to help determine the extent to which the focused rotation is useful in improving the resident's fiberoptic maneuvering skills. A fully computerized simulator in our airway lab will also be used to assess judgement and adaptability.
Conclusion: An organized airway management curriculum is necessary to ensure a complete airway management education. As the ACGME demands more objective measures of competency, we must adapt the resident training program to meet these needs. We aim to prove that by forming a curriculum through which the resident can learn and solidify an understanding of airway management, we will produce more capable consultants representing our field.
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S-152.

THE EVALUATION OF PATIENT SIMULATOR PERFORMANCE AS AN ADJUNCT TO THE ORAL EXAMINATION FOR SENIOR ANESTHESIA RESIDENTS

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INTRODUCTION: Anesthesiologists increasingly regard realistic patient simulators as invaluable educational and research tools for the study of human performance. However, despite potential benefits for summative evaluations, their use in the assessment of residents' performance and competence is controversial and not well documented (1). Many questions regarding the feasibility, reliability, and validity of simulator-based examinations remain unanswered (2). The present study investigates the potential for assessing clinical performance of senior anesthesia residents with a simulator as compared with the traditional oral examination.
METHODS: After obtaining appropriate IRB approval, 20 final year anesthesia residents from the University of Toronto were enrolled. Two standardized clinical scenarios testing different domains were developed: a resuscitation scenario (RS) and a trauma scenario (TS). All subjects were presented with each scenario using two assessment modalities: oral examination (OE), followed by simulator-based examination (SE) using the SimMan™ Universal Patient Simulator (Leardal ™, Leardal Medical Canada Ltd., Toronto, Ontario, Canada). Two independent examiners scored all performances with a previously validated global rating scale used by the Anesthesia Oral Examination Board of the Royal College of Physicians and Surgeons of Canada (3). Different Royal College examiners were used to rate the oral performances and the simulation performances.
RESULTS: The internal consistency of the rating scale was excellent across scenarios, raters, and assessment modalities: Cronbach's alpha = 0.93 to 0.98. The inter-rater reliability for the total scores was good to excellent across scenarios and modalities: OE: $r = 0.79$* (RS) and 0.86* (TS); SE: $r = 0.88$* (RS) and 0.76* (TS) (*$p < 0.01$). Average total scores for both raters obtained in the OE were then correlated with the corresponding scores obtained during SE. The correlation coefficient reflects the concurrent-related validity of the simulation-based examination compared to the oral examination for each scenario: RS: $r = 0.52$**; TS: $r = 0.50$** (**$p < 0.05$).
DISCUSSION: Clinical performance can be evaluated using simulators with a level of reliability equivalent to the oral examination. The moderate level of concurrent-related validity, in conjunction with relatively high inter-rater reliability suggests that simulator-based assessment may be measuring different but important dimensions of clinical competence compared with the oral examination. Simulators may be considered a useful adjunct to more traditional tests such as oral or written examinations. However, prior to its introduction into an assessment process, future studies need to determine the reliability of the scoring system on a larger scale and to investigate other aspects of its validity. Furthermore, issues of equal accessibility to simulators during training need to be addressed.
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S-153.

IMPROVING ANESTHESIA RESIDENT PERIOPERATIVE PAIN MANAGEMENT EDUCATION FOR SCIATIC NERVE BLOCK FOR ANKLE SURGERY

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Introduction: The search for improved efficiency and patient outcomes in ambulatory surgery has resulted in an increased demand for peripheral nerve blocks (PNB). Adequate perioperative pain control results in early ambulation, short hospital stay, reduced cost, decreased stress and increased patient satisfaction.[1] Therefore, there is need for academic centers to improve knowledge and skills of anesthesia residents with PNBs.[2] The aim of this study was to evaluate a new structured and supervised resident teaching program of sciatic nerve block (SNB) for postoperative analgesia on patient outcomes after ankle surgery.
Methods: A dedicated PNB rotation for anesthesia residents was initiated in February 2002, ensuring proper instruction and supervision in performing SNB for postoperative analgesia.
All blocks were performed on awake patients prior to surgery, using a peripheral nerve stimulator. After IRB approval, retrospective analysis of hospital database from February 2002 to January 2004 identified 79 consecutive patients who underwent ankle surgery, of which 56 received SNB performed by residents during PNB rotation (Education group). Intraoperative Opioid consumption, PACU time, PONV and hospital admission related to pain control or post-anesthesia complications in the education group were compared to a reference group consisting of patients undergoing ankle surgery (prior to new PNB rotation) from January 1st 2001 to June 30th 2001 (Reference group). Statistical analysis was performed using unpaired t-test (* $p<0.01$).
Results: In the reference group, 14 ankle surgeries were performed, of which 0 patients received SNB in the perioperative time period. In the education group, 56 patients received SNB preoperatively. (* $p<0.01$)

group	n	FNB	Intraoperative Opioid (mean ± SD)		PACU time [min] (mean ± SD)	Patient with PONV	Patient with Admission
			Fentanyl (mcg)	Morphine (mg)			
Reference group	14	0/14 (0%)	178 ± 82	1.4 ± 3.6	102.5 ± 39	3 (21%)	14 (100%)
Education group	56	56/79 (71%)	1.3 ± 1.5*	0.4 ± 1.7	39.6 ± 40 *	2 (4%)	1 (2%)*

Conclusion: The implementation of a standardized resident education program of sciatic nerve block for ankle surgery resulted in significantly less intraoperative opioid use, less time in PACU, and fewer number of patients admitted to hospital compared with a control patient group who received SNBs prior to the training program.
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S-154.

A COMPARISON OF ELECTRONIC ANESTHESIOLOGY RESIDENT AND FACULTY EVALUATIONS BEFORE AND AFTER IMPLEMENTATION OF AUTOMATED ELECTRONIC REMINDERS

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Introduction: Regular performance evaluations of resident and faculty physicians in Anesthesiology is a requirement of the Accreditation Council of Graduate Medical Education.[1] Feedback from these evaluations is intended to improve resident performance and faculty teaching skills. [2] It has been shown that less than 75 % of faculty are involved in evaluation at greater than 55 % of institutions.[3] Some institutions have had to resort to punitive measures to improve participation.[3] The purpose of this study was to evaluate the effectiveness of an automated e-mail reminder system to contact residents and faculty regarding incomplete evaluations enhancing the participation in the evaluation process.
Methods: Our institution's Anesthesiology residency has used an electronic evaluation system since March of 2001. In November of 2002, an automated reminder mechanism was implemented to electronically contact residents and faculty via e-mail regarding incomplete evaluations. Two nine-month periods from January 1 to September 30 in 2002 and 2003 were evaluated representing pre and post intervention periods. Data collected contained the rating of residents and faculty in five different categories on five point scales.
Results: The use of electronic reminders resulted in a profound increase in the number of evaluations completed from 1050 to 3761. The number of faculty completing evaluations also was distinctly increased from 40 (61 %) to 66 (100 %). The mean score of resident preop increased from 3.36 to 3.40 (p=0.069). Resident judgment declined from 3.52 to 3.47 (p=0.046). Interpersonal skills declined from 3.75 to 3.61 ($p < 0.001$). Intraoperative management improved from 3.43 to 3.52 (p=0.004). Resident knowledge declined from 3.44 to 3.42 (p=0.229).
Faculty evaluations increased from 244 to 1798 and the number of residents completing evaluations rose from 40 (46 %) to 87 (100 %). Mean scores for demeanor rose from 4.23 to 4.25 (p=0.847). Availability rose from 4.23 to 4.24 (p=0.878). Clinical management increased from 4.12 to 4.22 (p=0.158). Teaching increased from 4.07 to 4.13 (p=0.405). Feedback increased from 3.83 to 4.00 (p=0.024).
Discussion: The electronic reminder system greatly enhanced participation and the number of evaluations completed by both residents and faculty. There was a 358% and 737% increase in the number of resident and faculty evaluations, respectively. The system had a statistically significant impact on the majority of resident performance categories and on the feedback provided to residents by faculty, but the clinical significance of these changes was insignificant.
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S-155.

COMPARISON OF THE PASSING RATES FOR THE AMERICAN MEDICAL GRADUATES AND THE INTERNATIONAL MEDICAL GRADUATES IN ANESTHESIOLOGY WRITTEN AND ORAL BOARD EXAMINATIONS FROM 1990 TO 2003

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Introduction: The passing rates among American medical graduates (AMGs) who took the ABA written and oral board exams for the first time are published annually.[1] Performance by the international medical graduates (IMGs) is derived and compared with those of the AMGs, based on available data and statistics between 1990 to 2003.
Methods: The percentage of the IMGs among the graduating anesthesia residents is assumed to be the percentage for the IMG written exam first takers. From the passing rates for the AMGs and all first takers, the passing rate for the IMGs (among all the IMG first takers) was derived for each year.[2,3] The percentage of the IMGs passing the writen exam among all the successful first takers is assumed to be the percentage of the IMG oral exam first takers in the following year. The passing rate for the IMGs (among all the IMG first takers) for the oral exam was derived for each year.
Results: For the written exams from 1990 to 2003, the IMG first takers represented on average 27% (8-57%) of all first takers. The average passing rate for the IMG first takers was 59% (32-81%), while that for the AMG first takers was 81% (71-90%). For the oral exams from 1991 to 2003, the IMG first takers represented on average 23% (3.6-53.6%). The average passing rate for the IMG first takers was 64% (41-76%), while that for the AMG first takers was 81% (78-84%).
Discussion: The IMG subgroup's passing rates were significantly lower. An average IMG's chance for passing each exam was about 20% lower than that of an average AMG. In addition, the year-to-year variability for the passing rates was much greater for the IMG subgroup. For instance, the IMG first takers' passing rates for the oral exam fluctuated between 41 to 78%, while the AMGs' year to year passing rates ranged only from 78 to 84%.
Conclusion: The calculations show the IMGs' passing rates for both written and oral exams are significantly lower and vary much wider from year to year, compared to those for the AMGs.
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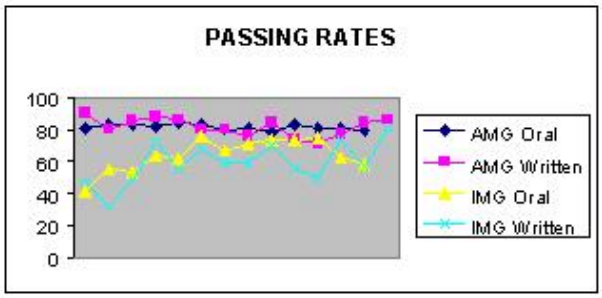

S-156.

WHY IS THE FOREIGN MEDICAL SCHOOL GRADUATES' PASSING RATE LOWER THAN THE US MEDICAL SCHOOL GRADUATES' FOR THE ORAL BOARD EXAMINATION: KNOWLEDGE OR LANGUAGE?

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Introduction: The oral exam passing rate among International medical graduates (IMGs) is much lower than that of the American medical graduates (AMGs).[1] Possible causes are examined for validity.
Methods: By logic, if a statement is true, then the contrapostive of the statement is also true.[2] A contrapositive is constructed by negating and reversing the clauses of the statement. Possible causes are a knowledge deficit and a language difficulty. For each assumed cause, two logical statements are made. By examining the contrapositives, each assumed cause is tested for validity. If the contrapositve is false, then the statements and the assumption must be false.
Results: For the assumption of knowledge as the cause, following statements are valid: 1. If knowledge is the cause, then IMGs' medical training is inadequate. *Contrapositive*: If IMG's medical training is *not* inadequate, then knowledge is *not* the cause. 2. If knowledge is the cause, then the IMGs' passing rate for the written exam is lower. *Contrapositive*: If the IMGs' passing rate for the written exam is *not* lower, then knowledge is *not* the cause. For the assumption of language as the cause, following statements are valid: 3. If language is the cause, then the oral exam tests language skill. *Contrapositive*: If the oral exam does *not* test language skill, then language is *not* the cause. 4. If language is the cause, then English fluency helps passing the oral exam. *Contrapositive*: If English fluency does *not* help passing the oral exam, then language is *not* the cause.
Discussion: The first contrapositive indicates if IMGs'medical training is adequate, then knowledge deficit is unlikely. Demonstrating that IMGs' medical training is adequate eliminates knowledge as the cause. Medical training consists of medical school and residency program. The former is irrelevant to anesthesia training.[3] Residency program could be the main determinant for knowledge problem. The second contrapositive suggests an equal or higher IMGs' passing rate for the written exam eliminates knowledge as the cause. The lower IMGs' passing rate for the written exam prevents elimination. The third contrapositive indicates language is not the cause, if the oral exam does not test language skill. Proving that oral exam does not test language skill would eliminate language as the cause. The fourth contrapositive asserts if English fluency is not helpful, then it is not language. Proving English fluency during the oral exam is not helpful eliminates language as the cause.
Conclusion: Regarding the lower oral exam passing rate by the IMGs, examination of residency programs and candidates' native language would help confirming the causes.
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S-157.

IS THE RESIDENT PERCEPTION OF PERFORMANCE IN THE OSCE A TOOL TO ASSESS DIFFERENCES IN SELF-ASSESSMENT BETWEEN CA-2 AND CA-3 RESIDENTS?

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Introduction: The ACGME recommends the use of the Objective Structure Clinical Examination (OSCE) as a tool to assess the six-core competencies. Beginning in 2002 our department implemented yearly OSCEs for residents. We have thus far conducted two exams each involving 10 different stations providing a live interactive examination in various didactic areas. Five of those areas were common to both tests. Upon completion of each station residents recorded their perceived score using the same scale examiners use. We hypothesized that as the residents become more senior, they would be more proficient at self-evaluation and the ratio between perceived score and actual score (P/A) would be closer to one.
Methods: The stations that were common for the two exams were ACLS, mock oral exam, TEE, regional anesthesia and ethics. The ratios of perceived scores over actual scores were calculated for each resident at each station and for the overall average score. The average ratios were for CA-2 and CA-3 residents were then compared using unpaired t-tests.
Results: A total of 14 residents participated; 7 in year one and 7 in year two. No residents participated in both years and data from both years were combined. The ratios of perceived to actual performance for CA-2 and CA-3 in five areas and average scores with equal weighting is shown in the table below. There was a trend for CA-3 to be better at self evaluation in each area and overall than CA-2s although this did not reach statistical significance.
Conclusions: Self-assessment is an important component in education allowing the trainee to recognize strengths and weakness and promoting efforts to improve knowledge and performance during examinations and clinical practice. Although our small sample size precluded statistical significance, there was a consistent trend for CA-3s to more accurately evaluate their performance than CA-2s which was consistent with our hypothesis. CA-3s presumably have had more extensive testing and self-evaluation experience during their training, which has served to help them assess theirt performance better. We believe that the OSCE exam can be used to evaluate self-assessment and as a tool to help residents develop their own self-assessment skills but further research is clearly needed.

Comparison of ratios between perceived/actual scores between CA-2 and Ca-3 residents

	ACLS	ORAL EXAM	TEE	Regional	Ethics	Overall
CA-2	0.75+/- 0.33	0.20+/- 0	1.07+/-0.75	1.33+/-0.79	1.07+/-0.46	0.89+/-0.12
CA-3	0.99+/- 0.32	0.83+/-0.16	0.97+/-0.33	1.005+/-0.29	1+/-0.14	0.93+/-0.10
p value	0.20	0.21	0.58	0.33	0.69	0.5

S-158.

DEVELOPMENT OF AN INTERNETBASED RESOURCE FOR THE TRAINING OF RESIDENTS IN PRACTICING EVIDENCE BASED MEDICINE

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Introduction: Just in the past 5 years, the number of journals available has gone up ten-fold to more than 4000 currently available.(1) As this trend continues, the education of residents must evolve with it. In order to keep up with new research, expert opinions, and reviews, residents must learn how to best utilize the electronic resources now available to them. As the digital dexterity of the anesthesia residents is quite variable, being able to educate everyone requires developing a curriculum that would bring everyone to a point of proficiency.
Methods: Our department library contains printed as well as computer-assisted resources. As obtaining site licenses for online journals becomes more cost-effective(2), we are charged with evaluating our current reference system. We have analyzed to what extent our residents are using the different library resources with online surveys. As anesthesiology incorporates so many different facets of medicine, the spectrum of resources used is vast. Matching the needs of our residents to the resources that we can offer them will improve efficiency. Finally, we must incorporate a training curriculum into the residency. As the CA-1 class begins their anesthesia training, we plan on assessing each resident's research skill level by giving him/her a set of tasks to complete. These would include specific questions that would require online researching skills. An example would be: "Who were the co-investigators with Mangano when his study on peri-operative ischemia risk was published?"
Fortunately, access to online journals has become easier(3). After an extensive training session, we will re-evaluate their skills with another set of tasks. In addition, we will evaluate ourselves and determine how best to improve the training methods. We have already developed a web-site designed specifically to aid the resident in the library.
Results: Our preliminary data suggest the need for a formalized course introducing residents to the world of digital medical informatics. We aim to prove that with the proper electronic reference tools available, our residents will more effectively be able to find the information they need when searching the literature. As their knowledge base is widened and understanding improved, so too will the care of their patients.
Conclusions: Finding solutions to problems and answers to questions is central to the development of a good resident. As residents do not all have the same level of computer skills, training them requires an organized curriculum. It is our responsibility to train our residents to be able to effectively use the digital resources available to help them become excellent consultant anesthesiologists.
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S-159.

THE COST UTILITY OF CELL SALVAGE BLOOD

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Introduction: Cell salvage blood (CSB) is produced by intraoperative autotransfusion systems that collect, wash, and return blood lost during surgery. Although available since the 1970s, CSB became more popular as concerns regarding viral disease transmission increased in the 1980s. Since then, however, nucleic acid testing has markedly improved the safety of allogeneic blood (1) while obtaining CSB remains expensive (2). The purpose of this study was to determine the cost utility ratio of CSB.
Methods: A decision analysis (Markov) model (3) was created with a spreadsheet (Excel 2002) to calculate the cost utility of CSB in dollars/ quality adjusted life year (QALY) for a hypothetical cohort of 60 yo patients receiving 1 to 4 units of CSB. Cost data were obtained from the literature, as were the disease specific quality-of-life adjustments, transfusion related viral disease transmission rates, hemolytic transfusion reaction rates, and the costs of treating viral and hemolytic complications. Assumptions included a fixed cost for CSB ($623), a one time type and crossmatch fee of $31, a $182/unit fee for packed erythrocytes (PRBC), and liver transplant age eligibility of < 60 yo. Future values were discounted at a rate of 5 percent per year.
Results: The utility of CSB increased as the number of transfused CSB units increased from 1 to 4, but the impact was minimal (from 0.000055 to 0.000089 undiscounted and from 0.000033 to 0.000057 discounted QALY). These utilities corresponded to less than a 47 minute undiscounted and a 30 minute discounted gain in life. The cost utility ratio improved as the number of CSB units transfused increased, but it did not reach the threshold of economic efficiency ($50,000/QALY) until the fourth unit was transfused (figure 1).
Discussion: Despite modeling complication costs, the cost utility ratio of CSB did not become economically efficient until the fourth unit was transfused.

References:
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2. Anesth Analg 2004;98:201.
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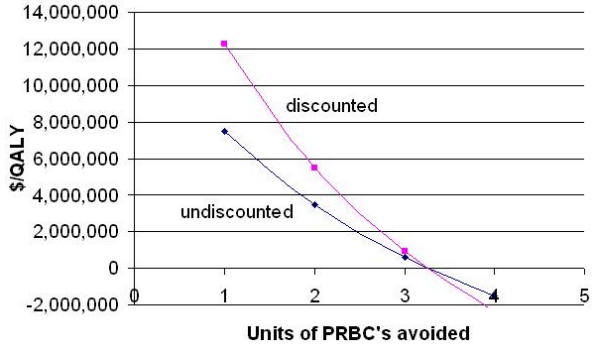

S-160.

THE ECONOMIC IMPACT OF THE FDA DROPERIDOL "BLACK BOX" WARNING ON COSTS OF PERI-OPERATIVE ANTI-EMETIC MANAGEMENT IN A CANADIAN HEALTH REGION

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Introduction: December 2001 the U.S. Federal Drug Administration (FDA) issued a "black box" warning regarding the use of droperidol for the treatment and/or prevention of perioperative nausea and vomiting[1]. Shortly thereafter, a similar warning was issued by Health Canada. Droperidol has been a very effective and economical anti-emetic forming a key strategy in the treatment and prevention of perioperative nausea and vomiting. In Saskatchewan, the use of serotonin antagonist medications, including ondansetron, have very limited application within the provincial formulary. In contrast to most other medications used within the hospital system, the cost of ondansetron could be billed directly to the patient.
Safety concerns expressed regarding the use of droperidol left few options within our formulary for management of patients at risk for perioperative nausea and vomiting. The Pharmacy and Therapeutics Department serving our health region, agreed to bear the cost of ondansetron as a perioperative replacement with use restricted to the OR and PACU effective July 2002.
Methods: Saskatoon Health Region staffs 25 operating rooms across three acute care hospital sites. All surgical specialties are represented within the region. Pharmaceutical Services tracks all medications supplied to each of the operating rooms and post-anesthesia care units. Data is collected and compiled for a fiscal year running April 1 to March 31. The economic cost associated with perioperative anti-emetic management can readily be tracked, and the financial impact related to our response to the safety warnings for droperidol can be assessed.

Results:

Year	**1999-00**	**2000-01**	**2001-02**	**2002-03**	**2003-04**
OR cases	31958	30855	30754	33298	33063
Agent	**Annual expense in Canadian dollars**				
droperidol	6712.91	5312.21	4596.40	1633.50	1240.60
dimenhydinate	2330.51	2404.03	2552.07	3017.94	2782.82
prochlorperazine	191.92	209.22	205.84	290.47	221.49
metoclopromide	2217.97	2696.89	2701.33	3555.69	1944.03
dexamethsone	726.17	885.96	1323.18	2013.96	2964.01
ondansetron	120.75	52.5	36.75	11138.58	33367.59
Total	**12300.23**	**11560.81**	**11415.57**	**21650.14**	**42520.54**

Discussion: The "black box" warning issued initially by the U.S. FDA has repercussions beyond the United States. Though our use of droperidol has markedly diminished, use of droperidol continues. Addition of ondansetron to our formulary has already increased anti-emetic anesthesia costs by 346% despite an increase of only 3% in surgical volume. Anti-emetic synergism using dexamathasone is a recent strategy[2]. Initially combined with low-dose droperidol, its use has continued in conjunction with ondansetron. The "black box" warning applied to droperidol has shifted anti-emetic choices to other agents, primarily ondansetron and dexamethasone associated with a remarkable increase in cost.

References:
1) FDA; Dear Health Care Professional letter, Dec. 4, 2001.
2) Anesth Analg 2000;90:186-194.

S-161.

CREATING AN AUTOMATIC ANESTHESIA ALERT PROCESS USING AN OR SCHEDULING SYSTEM (ORSOS)

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Introduction: Anesthesiologists learn of severe past anesthetic problems during the preoperative evaluation. Many of these anesthetic problems should be identified days in advance in order to optimize care. However, preoperative anesthetic evaluations sometimes occur the day of surgery leaving little time for special preparation. Reliance on the family, patient or medical records immediately prior to surgery may not be adequate due to incomplete knowledge, poor memory or unavailability of charts. If a severe anesthetic problem is identified then it is imperative that such information be passed along to others when the patient comes for future anesthetics. We have developed an "anesthesia alert" system using our OR scheduling system (ORSOS - one of the most frequently used scheduling programs in the US) whereby patients who have had previous anesthetic complications at our institution are automatically identified during all scheduled future surgical procedures.
Methods: All patients with known previous severe anesthetic problems are discussed at the departmental quality assurance meeting. Patients with severe anesthetic problems are classified into 7 categories of anesthesia alerts (difficult airway, difficult intubation, cardiac event, drug reaction, malignant hyperthermia, latex allergy, other). The patient name and anesthesia alert category is then given to the OR scheduler who enters it into the Patient Data screen in ORSOS (version 9.3 - PerSe Technologies Alpharetta, GA). The particular field used is a predetermined field which was previously unoccupied and which will accept alpha characters. The anesthesia alert categories have been permanently added into the codes screen using the utilities dropdown list on the toolbar. The "Anesthesia Alert" category is added to the surgery schedule report (Crystal Reports version 8.5) using a previously open field. This automatically prints an "anesthesia alert" with its associated category every time the particular patient is scheduled for subsequent surgery. The schedule is available for the OR staff to review approximately 2 weeks in advance of the scheduled surgery.
Results: The anesthesia alert system has been used in a large pediatric institution for 14 months. During this time approximately 12,000 general anesthetics have been performed. 18 patients (avg. 6.8 yrs range 28 mos. - 12 years) have been identified. Alert categories include: "airway" (n=2), "intubation" (n=6), "cardiac event" (n=1), drug reaction" (n=3), MH (n=3), latex (n=1), and other (n=2).
Discussion: The need to develop automated anesthesia information management systems (AIMS) to improve patient care is clear (ref). However, these systems are not widely used because of cost and other considerations. The presented "anesthesia alert" system is an attempt to combine critical anesthetic information into the existing OR scheduling system (ORSOS) and to act as a back up to conventional approaches which identify anesthetic problems.
Reference:
Seminars in Anesthesia, Perioperative Medicine and Pain, Vol 23, p 71, 2004

S-162.

LARYNGEAL MASK AIRWAY VS. ENDOTRACHEAL INTUBATION: ESTIMATING THE OVERALL PROCESS COSTS OF GENERAL ANESTHESIA IN ORTHOPEDIC PATIENTS

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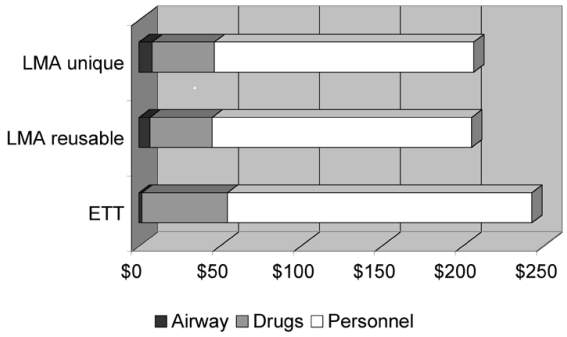
Introduction: Keeping the balance between economics and quality of treatment has become a great challenge for anesthesiologists in these days. Laryngeal Mask Airways (LMA) have become a widely used alternative to the endotracheal tube (ETT). On one hand, the costs per LMA are higher, especially when disposable devices are used. On the other hand, early discharge from PACU and reduced costs for drugs (no relaxant, reduced requirements for maintaining general anesthesia [1] may in fact result in an overall cost advantage of LMA vs. ETT.
Methods: Process costs of LMA vs. ETT were evaluated in a randomized prospective study in adult orthopedic patients (ASA 1-2) scheduled for knee arthroscopy. The study protocol was approved by the Ethics Committee of our university and written consent was obtained from each of the 60 patients enrolled. The patients were randomized for LMA (n=30) or ETT (n=30) and premedicated with 7.5 mg midazolam p.o. 1-2 h before surgery. Anesthesia was induced by injection of 3 µg/kg fentanyl followed by 2-3 mg/kg propofol. If face mask ventilation was successful, the patients of the ETT group received 0.6 mg/kg rocuronium for intubation of the trachea. Anesthesia was maintained with sevoflurane (1 MAC, 40 % oxygen in air). In patients of the LMA group, a Laryngeal Mask (LMA-ProSeal™, San Diego, CA/USA) of appropriate size was placed. All patients received a 100 mg diclofenac supp. To assess the overall process cost, we documented all relevant time points and the amounts of medication used. The consumption of sevorfluran was measured by weighing the vaporizer for sevoflurane before and after surgery. Overall process costs were estimated as the sum of costs of the airway, cost of drugs and personnel costs.
Results: The overall costs of three airways are summarized in the figure. While ETT was cheapest, the costs for both reusable and single use LMA (LMA-unique, no study group, calculated data) were only slightly higher in relation to the overall process costs. In fact, totals were: 207 US$ (LMA-unique), 205 US$ (LMA-reusable), and 242 US$ (ETT).
Discussion: Focusing on the costs of airway alone will not provide a sufficient base for an economic decision. Only the analysis of overall process costs will give the information needed.
References:
1 Cork R et al. Anesth Analg 1994;79:719-727



S-163.

COST AND ANTIEMETIC EFFICACY OF PROPHYLACTIC TRANSDERMAL SCOPOLAMINE VS ONDANSETRON FOR LAPAROSCOPIC GASTRIC BYPASS SURGERY

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Background: Despite advances in antiemetic therapy, postoperative nausea and vomiting (PONV) remains a common complication after surgery. Concerns regarding the high cost of the 5-HT_3 antagonists (e.g., ondansetron) and recent restrictions on the use of traditional antiemetics (e.g., droperidol) has lead to a re-examination of "older" antiemetics. This randomized, double-blinded study assessed the cost, efficacy and safety of transdermal scopolamine vs IV ondansetron when administered for prophylaxis against PONV.
Methods: Following IRB-approval, 78 consenting ASA I-III obese females undergoing laparoscopic gastric bypass procedures were randomly assigned to one of two treatment groups. All patients received premedication with rofecoxib 50 mg po. A "sham" (Group 1) or transdermal scopolamine, 1.5 mg (Group 2) patch, was placed behind the ear at least 60 min before induction of anesthesia. The second study medication consisting of either ondansetron, 4 mg (Group 1), or 2 ml saline (Group 2) administered 20 min prior to the end of surgery. All patients received a standardized general anesthetic and local anesthetics were injected at the incisional site to minimize postoperative pain. The recovery profiles, the incidence of nausea, vomiting/retching, and requirement for rescue antiemetic drugs, as well as side effects were assessed over the 48 h study period. Data were analyzed using ANOVA and chi-square tests, with $p<0.05$ considered significant.
Results: The demographic characteristics were similar in both treatment groups. The recovery times to patient orientation, oral intake, and actual discharge did not differ between the two groups. The incidence of PONV, nausea scores, side effects and need for rescue antiemetics were also similar in both groups during the 48 h study period. However, the drug acquisition costs were US $25.65 and $5.05 for the ondansetron and scopolamine patch, respectively.
Discussion: Ondansetron (4 mg IV) and transdermal scopolamine (1.5 mg) were equi-effective in the prevention of PONV after laparoscopic gastric bypass surgery. However, transdermal scopolamine is more cost-effectiveness for *routine* antiemetic prophylaxis in this high-risk surgical population.

	Ondansetron	**Transdermal Scopolamine**
Number (n)	40	38
Age (yr)	42±10	43±10
Weight (kg)	135±25	124±19
Anesthesia time (min)	120±20	115±23
Propofol (mg)	220±56	250±57
Fentanyl (μg)	205±75	183±69
Time to oral intake (hr)	21±3	21±2
Actual discharge (d)	2±1	2±1
PONV during PACU (n,%)		
Nausea	14,35	11,29
Vomiting	2,5	2,5
Rescue antiemetic	14,35	11,29
PONV from PACU to 24 h (n,%)		
Nausea	22,55	19,50
Vomiting	1,3	2,5
Rescue antiemetic	15,38	17,45
PONV 24-48 h (n,%)		
Nausea	18,45	11,29
Vomiting	2,5	0,0
Rescue antiemetic	16,40	8,21 (p=0.07)
Headache (n,%)	5,13	4,11
Dry mouth (n,%)	2,5	7,18 (p=0.08)
Restlessness (n,%)	3,8	4,11
Dizziness (n,%)	4,10	5,13

S-164.

POINT OF CARE CALCULATION OF ANESTHESIA COST USING A CROSS PLATFORM SPREADSHEET TOOL

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Introduction: The pharmacoeconomic impact of anesthetic choices has become an area of close scrutiny by health care administration. Though the actual cost of the anesthetic pharmaceuticals represents a small portion of the cost of care for a surgical patient, these expenditures are easily tracked using administrative databases. The spectrum of available choice allows for great variety among anesthesiologists in "balancing" anesthetic pharmacology. Change to global anesthesia expenditure must progress one anesthesiologist at a time. Each practitioner must understand the cost of their choice in comparison to their peers. Spreadsheet applications can readily be configured to calculate individual costs[1] and can be easily deployed on a laptop, tablet PC or handheld computer across a variety of operating systems.
Methods: A template was created from a Microsoft Excel spreadsheet allowing institution-specific costs to be calculated based upon the unit price of the medication and the amount used. Formulas were constructed for calculation of costs of bolus doses administered, infusions deployed as well as the total cost of volatile agent used for each case. Allowances for numerous changes of fresh gas flow, percent of agent delivered and intravenous infusion rate allow potential for more accurate tracking of the total anesthetic cost. The interface can be designed to hide much of the calculation and to offer an intuitive approach to use. The prices of pharmaceutical agents are easily changed permitting a simple upgrade to current pricing.
Results: A single sheet was constructed allowing anesthetic cost to be calculated for the most common intravenous agents, most usual infusions and for all volatiles available at our institution. Individual preferences were easily be added to the sheet allowing accurate costs to be generated for each practitioner and anesthetic technique. This original Excel sheet was converted to a format capable of display on a Palm device. The limitation of the screen size prompted reorganization from one page to several pages in order to minimize the need for scrolling across the page. The processing power of the handheld computer resulted in slower calculations as data were entered, but the handheld platform was much easier to use in the OR environment.
Discussion: In order to demonstrate the pharmacoeconomic impact of anesthetic technique, it is necessary to be able to provide each anesthesiologist with the cost of the choices of their anesthetic technique. Readily available tools can compile known formulas and present an interface that is intuitive and that can be easily modified to be useful on a wide range of devices across a variety of platforms.
References:
1) Anesthesiology. 1994 Aug;81(2):514-6.

S-165.

THE IMPACT OF TECHNOLOGY RELEASE ON ACADEMIC PRODUCTIVITY IN THE UNITED STATES

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Introduction: The past two decades have seen a decline in academic productivity in the United States as measured by starter grant applications, and first authorship in leading peer-reviewed journals[1,2]. Although a faculty shortage and greater clinical demands at US institutions, coupled with greater quality and quantity of manuscripts from abroad, are likely significant factors in this decline, the expansion of regulations by agencies including CMS, FDA, ORI, and stricter IRB's may be a contributing factor. Target controlled infusion(TCI) pumps programmed with pharmacokinetic models are a valuable tool in the evaluation of new drugs and in clinical practice. Although this technology was developed jointly in the US and abroad, regulatory hurdles in the US have precluded commercial availability of TCI pumps in the US[3] , whereas they have been readily available overseas (Diprifusor™, Remifusor™). We compared the academic productivity between US and non-US first authors using two new technologies that incidentally both became commercially available in 1996, TCI (available outside US only) and bispectral index (BIS;available worldwide).
Methods: The Medline database was searched for articles in Anesthesiology, Anaesthesia, Anesthesia and Analgesia, BJA, CJA, Acta Anaesthesiologica Scandinavica, and the Journal of Clinical Anesthesia using the key word combinations in Table 1, between 1996 and 2004. Country of origin of the first author's institution was determined.
Results: There were 158 articles published involving TCI, 143 (90%) of which were of non-US origin (Table 2). There were 315 articles involving BIS, 76 (76%) of which involved non-US first authorship.
Discussion: The nine fold greater publication rate from overseas using TCI may be attributed to the availability of easy to use, commercially available TCI infusion pumps, since US based investigators were two and a half times more productive on a relative basis (10% vs. 24%) in academic investigation involving the BIS monitor than with TCI. Regulatory obstacles that thwart technology release in the US may be a significant contributor to the decline of US based academic productivity using new devices.

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2. Declining Proportion of Publications by American Authors in Major Anesthesiology Journals. Anest Analg 2003; 96:513-7.
3. Target-Controlled infusions for Intravenous Anesthetics (Ed). Anesthesiology 2003; 99: 1039-1041.

Table 1

Keywords (Boolean)	**TCI** (OR) **target-controlled infusions** (OR) **CACI** (OR) **computer-assisted continuous infusion**	**BIS** (OR) **bispectral index**
US / non US	**15/143** (10% / 90%)	**76/239** (24% / 76%)

S-166.

END RUN: HOW IT CAUSES UNFORESEEN EFFECTS IN ANESTHESIA

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Introduction
The conversion of paper cognitive artifacts to digital systems is routinely represented as an improvement in healthcare efficiency, flexibility, and reliability. Digitized systems remain vulnerable to the unforeseen effects of automation that have been reported in other high hazard sectors such as nuclear power generation and aviation.
Methods
In the acute care setting, surgeons book cases in operating rooms up to the day before procedures. The anesthesia coordinator (AC) assumes responsibility to assign add-on cases the day before and day of procedures, but adheres to institutional rules intended to be fair to both patients and general surgeons in the queue of add-on cases. The single hard copy of the master schedule previously served as the locus of Operating room needs for orientation, anticipation, prediction, negotiation, and compliance. Control over the physical artifact limited arbitrary action among team members, ensured fair assignment of patients, and optimized resource use.
Results
The recent conversion from physical to digital master schedule has resulted in a number of impediments to team performance that erode team performance. Surgeons at this site have learned that there is no log of edits that have been made to the electronic schedule. Rather than posting to the established "add on" queue, they now schedule cases directly into their assigned operating suite after the schedule has formally closed. This has a number of consequences. Surgeon convenience trumps time in the queue, which is unfair (and potentially detrimental) to patients who wait for unclaimed OR time. OR use becomes suboptimal and thereby increases operating costs. Finally, junior surgeons lose the opportunity to follow scheduled cases in the same rooms.
Discussion
This and related examples demonstrate that IT solutions are vulnerable to the same drivers as physical artifacts and may be more vulnerable to exploitation because they are poorly researched, understood and managed. The short-term solution to this issue is for the vendors of electronic scheduling systems to develop software to restrict access and maintain a log of edits. We anticipate that more useable long term solutions will be identified as a consequence of our ongoing research into how clinicians use cognitive artifacts to support clinical operations.

S-167.

DO ANESTHESIOLOGISTS COMPLY WITH EVIDENCE-BASED LITERATURE GUIDELINES? A MAIL SURVEY OF AMERICAN ANESTHESIOLOGISTS

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INTRODUCTION. Current literature suggests that physician compliance with literature-based care guidelines can vary significantly (1). Little data exist, however, regarding the compliance of anesthesiologists with literature-based evidence or with clinical guidelines. To assess the degree of compliance among American anesthesiologists, we surveyed US anesthesiologists regarding their practice patterns in patients undergoing vascular surgery.
METHODS. After IRB approval, we mailed a survey to a randomly selected group of 2000 anesthesiologists, obtained from the ASA national mailing list. The survey queried respondents about how they would manage an elderly patient with **medical comorbidities** scheduled for **vascular** surgery.
Four versions of this survey were generated by varying the magnitude of vascular surgery (femoral-distal bypass (small) vs. aorto-bifemoral bypass (large)), and severity of medical comorbidities (hypertension, diabetes, prior MI, and moderate stable exertional dyspnea (sick) vs. hypertension alone (healthy)). These variations were then randomly distributed among survey recipients. Survey questions evaluated the propensity for beta blockade, and the heart rate thresholds for doing so. Statistical analysis was performed by two-tailed t-test with $p<0.05$ taken as significant.
RESULTS: 439 completed surveys were received, evenly distributed among the four versions: healthy patient/small operation (n=116), sick patient/small operation (n=106), healthy patient/large operation (n=115), sick patient/large operation (n=102). No differences between groups with respect to years of experience, baseline usage of invasive hemodynamic monitoring, or frequency of vascular cases were found.
On a scale of 1-5 where 1 = never and 5 = always, no difference between groups in the propensity to administer prophylactic beta blockade was found (mean of all groups = 3.7 ± 1.02). However, target heart rates (HR) for use of beta blockers did vary. For "healthy" patients, the preoperative HR triggering beta blockade was 89.1 ± 23 bpm (mean ± SD) for a fem-distal bypass operation, but 81.7 ± 26.3 bpm for an aorto-bifemoral graft procedure ($p<0.05$). This difference persisted for target HRs during and after surgery. No difference in target HRs between "healthy" and "sick" patients receiving the same operation were found.
DISCUSSION: Recent AHA/ACC guidelines recommend beta blockade for high risk patients undergoing vascular surgery (2). Although no target HR is specified, several clinical trials demonstrate benefit at a target HR of 80 bpm (3). We found that anesthesiologists recognize the importance of perioperative beta blockade. However, the threshold heart rate for instituting beta blockade appeared to vary with magnitude of surgery instead of patient comorbidity, and for a fem-distal bypass was approximately 10 bpm higher than that typically used in clinical trials demonstrating cardiac protection. Such information may inform future strategies to promote the use of cardioprotective techniques by anesthesiologists.
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S-168.

PROPHYLACTIC PERIOPERATIVE BETA BLOCKERS: A SURVEY OF CLINICAL FACTORS THAT INFLUENCE PRACTICE

AUTHORS: **J. E. Fiadjoe**, H. Sondhi, R. S. Twersky;
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INTRODUCTION: Despite guidelines by the ACC/AHA, prophylactic perioperative beta blockers (PBB) in noncardiac surgery are still underutilized; few hospitals have protocols to ensure implementation (1-5). Controversy still exists regarding patient selection, timing, duration and responsibility for management. We undertook a survey to further assess current practice patterns of anesthesiologist and identify possible factors aimed at improving compliance.
METHODS: A survey consisting of 10 questions was randomly distributed to 300 attendees at the May 2004 SAMBA meeting.
RESULTS: Sixty-five surveys were returned; response rate 22%. Anesthesiologists practiced in both inpatient (58%) and outpatient (76%) settings. Although 76% reported using PBB, median use was only 15.5%. For inpatient procedures, median use was 62% for vascular and thoracic procedures; 37% for head and neck, GU, Abdominal, intracranial and minimally invasive surgery; 12.5 for orthopedic procedures. The difference for vascular surgery was significant from all others, $p< 0.002$. Among outpatient procedures, median use was 12.5%. PBB use varied among clinical conditions- Median use 62% in patients on chronic ß-Blockers, IHD, HTN; median use 37% in patients > 65 years, PVD and DM; median use 12.5% in compensated CHF, current smoker, CVD, elevated cholesterol, h/o asthma, and CRF. Among anesthesiologists who never use PBB, the most common reasons were limited experience (60%), not familiar with guidelines (33%) and concern about adverse effects (27%). Only 7% felt there was not much evidence to support its use. Respondents that did not have protocols in place (86%) reported a median use of PBB of 15.5% vs. 75.5% among those that did have protocols, $p<0.002$.
Anesthesiologists identified the PCP (51%) and cardiologists (33%) as the preferred responsible providers for administering PBB within one week of surgery. The majority (88%) felt that anesthesiologist should be responsible for administering PBB during perioperative period; for 1-7 days postop 40% surgeons, 30% PCP and 27% cardiologists. For treatment after 7 days postoperatively, PCP 58% and cardiologist 37%. Majority of anesthesiologists selected IV labetalol, metoprolol and esmolol as their preferred drugs for PBB. They did not favor the use of oral PBB. Choice of drug varied by years of experience and type of practice.
DISCUSSION: Multiple clinical factors influence anesthesiologists' use of PBB in inpatients and outpatients. Based on our results, we propose that enhanced education specifically tailored to anesthesiologists that incorporate information outlining the responsibility of physicians, identifying proper clinical conditions, surgical procedures, and preferred drugs for treatment, may result in improved compliance and outcomes.
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S-169.

THE INCIDENCE AND OUTCOME OF PERIOPERATIVE PULMONARY ASPIRATION IN A UNIVERSITY HOSPITAL: A TWO-YEAR RETROSPECTIVE ANALYSIS

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INTRODUCTION: Pulmonary aspiration of gastric contents during the perioperative period has been associated with high morbidity and mortality (1, 2). We evaluated the incidence and consequences of perioperative pulmonary aspiration in the non-obstetric adult population of a tertiary medical center.
METHOD: A 2-year retrospective case analysis using QI data (August 2002 - July 2004) was performed to identify patients who were diagnosed with perioperative pulmonary aspiration. The diagnosis was made when non-respiratory secretions were suctioned from the endotracheal tube or an episode of regurgitation occurred while the patients were unconscious. The pulmonary aspiration was confirmed using chest radiography and/or bronchoscopy. The patients' demography, preoperative condition, perioperative airway management and outcome data were collected through medical record review. Since the data collected was qualitative, no statistical analysis was performed.
RESULTS: A total of 8 cases were identified in 44,400 anesthetic in 2-year period (0.04% / year). There were 7 males and one female with a median age of 59 (26 - 82). The majority of procedures were elective (7): comprising gastrointestinal procedures (2), orthopedics post-trauma (2), plastic (2), and ENT (1). One emergency case was due to perforated colon. None of the cases were assessed as difficult airway. Seven of the 8 patients were considered high risk for aspiration, in 2 of the general endotracheal anesthesia (GETA) cases cricoid pressure was applied. The initial method of anesthesia was IV sedation (MAC) in 4 and GETA in 4. All the incidence of aspiration and regurgitation/vomiting were identified intraoperatively. In the GETA cases, the aspiration was all recognized immediately following induction. In 7 cases, aspiration was occurred after passive regurgitation and in one case after active vomiting. In 4 cases [ASA PS2 (3) & PS3 (1)] the aspiration was minimum with no serious outcome. The other 4 cases [ASA PS3 (3) & PS4 (1)] developed massive aspiration and were admitted to ICU, one (PS4) of whom died post-operatively and the others (PS3) survived with significant post-operative morbidity.
DISCUSSION: Perioperative pulmonary aspiration is rare but still is associated with serious outcome. The incidence (1 in 5,550 anesthesia cases) and the mortality (1 in 44,400) were similar to other reports (1, 2). Severity of the post-operative morbidity is associated with higher ASA class (PS>=3). In half of the cases, the aspiration occurred during MAC, which emphasizes the importance of the strict control of the depth of the IV sedation. All these patients had at least one or two risk factors for aspiration and only in two of them aspiration prophylaxis was applied. Seven out of 8 were male patients, which suggest gender may be a risk factor in pulmonary aspiration.
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S-170.

BISPECTRAL INDEX FOR IMPROVING ANESTHETIC DELIVERY AND POSTOPERATIVE RECOVERY DURING GENERAL ANESTHESIA (META-ANALYSIS)

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Background and Goal of Study: To evaluate whether BIS monitor might improve some measures of patient outcomes or operating suite efficiency.
Methods Published trials were identified by electronic searching in Pubmed and Medline-CDRom between 1990 to January of 2004. After assessing the study quality, only 10 trials involved in meta-analysis.
Results
Monitoring BIS during propofol anesthesia
1) Reduce anesthetic doses (Propofol doses: BIS group: 110.53±22.53 ug/kg/min vs SP group: 110.16±17.73ug/kg/min, P<0.05);
2) Without increasing opioids (Because of different opioids used in different articles, we couldn't consolidate the results. But all articles supported this point of view);
3) Results of Yli (1999) and Lunginbühl (2003) showed muscle relaxants in BIS group and SP group were similar;
4) Time to eye opening (BIS: 6.20±5.31 min, SP: 9.51±12.18 min, P=0.0055), Response to verbal command [Gan (1997) BIS: 6.65 (5.65~7.65) min, SP: 10.47 (9.13~11.80) min, P<0.01], Orientation [Struys (2001) BIS: 7.68±6.2 min, SP: 9.87±38.18, P<0.05] and tracheal extubation (BIS: 7.15±5.37 min, SP: 10.05±12.99 min, P<0.05) were significantly shorter in BIS group.
Monitoring BIS during inhalation anesthesia
1) Reduce anesthetic doses (Sevoflurane doses: Expiratory concentration of sevoflurane BIS: 1.21±0.39% vs SP: 1.43±0.49%, P<0.05; Desflurane MACHour [%h]: BIS: 0.73±0.20 vs SP: 0.88±0.28, P=0.0016);
2) Without increasing opioids (Fentanyl doses: BIS: 136.21±81.38ug, SP: 127.56±86.23ug, P>0.05);
3) But increasing muscle relaxants during inhalation anesthesia (Because of different muscle relaxants used in different articles, we couldn't consolidate the results. But all articles supported this point of view);
4) Time to eye opening(BIS: 6.20±5.31 min, SP: 9.51±12.18 min, P=0.0055), Response to verbal command (BIS: 7.92±3.14 min, SP: 9.1±5.63 min, P<0.05), Orientation [Song (1997) P<0.05] and tracheal extubation (BIS: 6.77±4.21 min, SP: 8.87±6.57 min, P<0.01) were significantly shorter in BIS group.
5) Although, BIS could reduce inhale agent doses, post-operative nausea and vomiting and pain were similar in both groups.
Evidences showed that BIS reduced intra-operative awareness without any markedly post-operative recall were not enough.
Reviewers' Conclusion BIS reduced anesthetic doses during surgery and improved speed of recovery.
References
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S-171.

THE EFFECT OF AGE, GENDER, AND BODY MASS INDEX ON DIFFICULT INTUBATION

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Introduction: Common clinical perception is that gender, older age and higher body mass index (BMI) are associated with an increased likelihood of difficult intubation (DI). However a study predicting DI with reported sensitivity and specificity of 94% and 96% did not find age, sex and BMI to be independent predictors.[1] Either small size or maldistribution of the sample population may cause error in determining predictors. The aim of the study was to examine a large population to determine the effect of age, sex, and BMI on DI.
Methods: This retrospective study examined 30,828 patients requiring elective endotracheal intubation for general anesthesia over 29 months. Difficult intubation was determined at the time of intubation based on the clinical outcome of the intubation. This consisted of 0=no intubation difficulty, 1=moderate difficult with intubation and 2= severe difficulty with intubation, usually a failed intubation. The incidence of age per decade of age and the effect of sex and BMI was then calculated for the "1 "and "2" intubations versus easy to intubate "0". A two-sample t-test compared the mean age, easy versus difficult intubation. Logistic regression evaluated the effect of age on intubation difficulty, fitting regression model with BMI as dependent variable and age as independent variable; a quadratic term established correlation coefficient for BMI and age. (Two-tailed $p<0.05$)
Results: Of 30,828 intubated patients 721(2.3%) were DI, i.e. score of 1 and 2. The mean age of easy "0" intubation was 60.9+/-15.1 vs. DI age of 52.5+/-21.9, $p<0.001$. The DI incidence increased with age, a cumulative odds ratio of 1.22 per decade (95% CI 1.17-1.27,$p<0.001$). The range of decades was from 0-9 years to 90-+ years. Males were more difficult to intubate than females ($p<0.001$), this result was independent of age ($p=0.398$). When all age groups were examined the DI group with a score = 2, there was a weak but positive correlation of BMI with increasing age ($r=0.04$;$p<0.001$).
Discussion: Although our definition of DI was subjective the incidence in our series of 2.3% is comparable to other series. Unfortunately there is no standard definition of DI in the literature or by anesthesia organizations. It is important that a standard definition is developed, preferably one that is clinically relevant. This is the largest series both in numbers and in range of ages, 0-90+ years, in the literature determining that age, sex and BMI does affect DI. In studies determining independent predictors of DI the size, and distribution of the population needs to be stated. Importantly the effects of age, sex and other demographic factors on DI need to be primarily evaluated for that population.
References:
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S-172.

PERIOPERATIVE GLYCEMIC CONTROL AND SURGICAL SITE INFECTION

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Introduction: Surgical site infections (SSIs) account for 14-16% of all hospital acquired infections and are associated with a significant increase in hospital days and cost.[1] Hyperglycemia in the perioperative period has been shown to increase the risk of postoperative infections.[2-3] As part of a Centers for Medicare and Medicaid Services sponsored national demonstration project on surgical site infection prevention, we redesigned our practice for tighter glycemic control throughout the perioperative period as part of an effort to reduce SSIs.
Methods: Patients scheduled for elective hip or knee replacement, coronary artery bypass surgery, valve replacement surgery, thorocotomy, bariatric surgery, and major vascular surgery were included. All patients with a serum glucose in excess of 150mg/dL were started on an insulin infusion to maintain a serum glucose 80mg/dL-150mg/dL. Glucose was checked hourly until stable. The number of cases between SSIs was used as the monitor for infection rates. Glucose values were divided into three categories: (1) below 50mg/dL, (2) 80-150mg/dL, and (3) above 250mg/dL. Data was analyzed using chi square analysis with significance at $p<0.05$.
Results: Prior to initiation of the tight glycemic protocol, no patients had glucose values below 50mg/dL. After aggressive glucose control was instituted, there were 8 glucose values measured below 50mg/dL ($p=0.33$). There was a statistically significant ($p<0.03$) increase in the number of values in the 80-150mg/dL range with tight glycemic control, and a significant reduction the number of patients with values over 250mg/dL ($p<0.02$). The SSI rates fell for each surgical service after initiation of tight glycemic control (Table 1).
Discussion: Diabetes has been demonstrated to be a risk factor for the development of SSIs among selected surgical patients. Recent data suggests that hyperglycemia is an independent predictor of the short-term risk of infection.[2] As part of a program for SSI prevention, improved glucose control in the perioperative period significantly reduced the incidence of SSIs in the orthopedic, cardiothoracic, vascular, and bariatric surgical patients studied.

SSI rates and Glycemic Control

Type of Surgery	Before tight glycemic control	After tight glycemic control
Cardiothoracic Surgery	4.6%	2.5%
Vascular Surgery	1.9%	0.83%
Hip Replacement Surgery	1.0%	0.7%
Knee Replacement Surgery	1.1%	1.0%
Bariatric Surgery	17.9%	5.3%

References:
1. *Infect Control. Hosp Epidemiol* 1996,17(8):552-7
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3. *JParenterEnteralNutr.*1998;22:77-81

S-173.

TIGHT GLYCEMIC CONTROL REDUCES SURGICAL SITE INFECTIONS IN BARIATRIC SURGICAL PATIENTS

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Introduction: The annual incidence of severely obese patients who undergo bariatric surgical procedures has increased significantly over the past few years. More than one-third of these patients have preoperative evidence of diabetes mellitus or impaired glucose tolerance.[1] Hyperglycemia in the perioperative period has been shown to increase the risk of postoperative infections.[2] As part of a Centers for Medicare and Medicaid Services sponsored national demonstration project on surgical site infection (SSI) prevention, we instituted a variable-rate intravenous insulin infusion protocol as part of a program to reduce the incidence of SSIs in bariatric surgical patients.

Methods: All patients scheduled for bariatric surgery were included in the study. Any patient with a serum glucose in excess of 150mg/dL was started on an insulin infusion to maintain a serum glucose between 80mg/dL-150mg/dl. The infusion rate was adjusted based on an hourly evaluation of serum glucose values. The number cases between SSIs was used as the monitor for infection rates. Glycemic control was divided into three categories: (1) below 50mg/dL, (2) 80mg/dL-150mg/dL, and (3) above 250mg/dL. Data was analyzed using chi square analysis with significance at $p<0.05$.

Results: The percent of glucose values in each of the three glucose categories before and after initiation of the tight glycemic control protocol are outlined in table 1. There was a significant reduction ($p<0.01$) in the percent of glucose reading above 250mg/dL following initiation of tight glycemic control. There was a slight increase in the percentage of glucose values in the target range 80mg/dL-150mg/dL ($p=0.41$) as well as values below 50mg/dL ($p=0.91$). The incidence of SSIs prior to tight glycemic control was 23.6% and decreased to 9.7% ($p=0.026$).

Discussion: Diabetes has been demonstrated to be a risk factor for the development of SSIs among selected surgical patients. Recent data suggests that hyperglycemia is an independent predictor of the short-term risk of infection[2]. As part of a program for SSI prevention, improved glucose control in the perioperative period significantly reduced the incidence of SSIs in the bariatric surgical population studied.

Table1. Before and after tight glycemic control

Glucose values	Before tight glycemic control	After tight glycemic control	p value
Glucose value < 50mg/dL	0.11%	0.12%	p = 0.91
Glucose value 80mg/dL - 150mg/dL	59.44%	62.81%	p = 0.41
Glucose value > 250mg/dL	11.27%	0.62%	p < 0.01
Surgical site infections	23.6%	9.7%	p = 0.026

References:
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S-174.

ANESTHESIOLOGIST AS CHANGE AGENT FOR TIGHT INTRAOPERATIVE GLUCOSE CONTROL

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Introduction: Maintaining glycemic control throughout the perioperative period is a clinical challenge. While sliding-scale use of subcutaneous insulin has long been a standard method of glucose control, the use of a variable-rate intravenous insulin infusion is a more effective approach to perioperative diabetic management.[1] However, many anesthesiologists, fearful of patients becoming hypoglycemic under anesthesia, are reluctant to institute tight glycemic control using a continous insulin infusion. As part of a national collaborative to reduce surgical site infections, the Department of Anesthesiology assumed responsibility for maintaining blood glucose values 80mg/dL-150mg/dL throughout the perioperative period. Using rapid-cycle improvement methods to increase compliance with tight glycemic control guidelines, we monitored the efficacy of implementing tight glycemic control with the use of a variable- rate insulin infusion.

Methods: As part of an institutional patient safety initiative, a glycemic control team was convened to improve patient care for patients undergoing surgery. Guidelines and protocols for glycemic control were applied to selected surgical services, and then expanded to all surgical patients. From 7/02 to 2/04 patient records were monitored for compliance with tight glucose control protocols and resultant serum glucose levels recorded. Data was collected before and after initiation of the tight glycemic control protocols. Data was analyzed using chi square analysis with significance at $p<0.05$.

Results: Glucose values before and after institution of tight glycemic control are outlined in table 1. There was a significant increase in the percentage of glucose values measured in the target range of 80mg/dL - 150mg/dL from 44.6% to 57.4% Glucose values measured below 50mg/dL increased from 0.46% to 0.54%, and percent of glucose values over 250mg/dL decreased from 8.5% to 4.1%.

Discussion: There is considerable variation in methods of glycemic control provided by anesthesiologists in the perioperative period. Subcutaneous insulin injection is frequently used for perioperative glycemic management with one-half the usual dose of long- or intermediate-acting insulin given the morning of surgery. This approach can be fraught with problems.[2] Use of an intravenous insulin infusion provides a simple algorithm to maintain glycemic control over a wide range of insulin requirements. Our data support that anesthesiologists using a variable-rate intravenous insulin infusion is a safe and effective means of perioperative glycemic control.

References:
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2. *Diabetes Care* 1992;15:1484-1493

Glucose values before and after tight glycemic control

Glucose values	Before tight glycemic control	After tight glycemic control	p value
Glucose value <50mg/dL	0.46%	0.54%	p=0.23
Glucose values 80mg/dL-150mg/dL	44.6%	57.4%	p<0.01
Glucose value > 250mg/dL	8.5%	4.1%	p<0.01

S-175.

NON-OPEREATING ROOM EMERGENCY AIRWAY MANAGEMENT AND ENDOTRACHEAL INTUBATION OF CRITICALLY ILL PATIENTS BY ANESTHESIOLOGY RESIDENTS

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Introduction: Emergency airway management and tracheal intubation outside of a controlled operating room setting is often required for critically ill patients[1]. At Fairview-University Medical Center (FUMC), the CA-2 anesthesiology resident is responsible for majority of non-operating room endotracheal intubations. We present a study which evaluated indications, medications, difficulty of endotracheal intubation, and complications during non-operating room emergency airway management of critically ill patients.
Methods: After obtaining Institutional Review Board (IRB) approval, all patients requiring emergency tracheal intubation at Fairview-University Medical Center were enrolled. The majority of non-operating room emergent endotracheal intubations are managed by the in-house CA-2 anesthesiology residents, who have completed at least 12 months of clinical anesthesia training. After tracheal intubation of the patient, the anesthesia provider responsible for airway management completed a questionnaire which included the following topics: (1) indication for intubation; (2) type of anesthesia; (3) medications administered; (4) perceived difficulty of intubation; (5) number of attempts at intubation; (6) pre- and post-intubation vital signs; and (7) complications.
Results: Over an approximate 12-month period, the anesthesia care team performed 272 non-operating room endotracheal intubations of which 265/272 were performed by the CA-2 residents and 7/272 by a staff anesthesiologist. Sedative/hypnotics and muscle relaxants were administered 243/272 and 93/272, respectively. Majority of the patients were intubated on the first attempt (86%). Five patients were intubated with an aide of a fiber optic scope.

Indication for Tracheal Intubation		Complications of Tracheal Intubation	
Respiratory failure	175/272 (64%)	Hypertension	39/272 (14%)
Decreased consciousness	53/272 (19%)	Hypotension	53/272 (19%)
Cardiac arrest	25/272 (9%)	Tachycardia	24/272 (9%)
Respiratory arrest	18/272 (7%)	Emesis	10/272 (4%)
Increased ICP	4/272 (1%)	Esophageal intubation	4/272 (1%)

Perceived Difficulty of Intubation		Number of Attempts at Intubation	
Grade 1	165/272 (61%)	1	233/272 (86%)
Grade 2	63/272 (23%)	2	31/272 (11%)
Grade 3	30/272 (11%)	3	6/272 (2%)
Grade 4	14/272 (5%)	4	2/272 (<1%)

Discussion: Critically ill patients may require non-operating room emergency airway management and endotracheal intubations. With proper training and education, our results indicate that CA-2 anesthesiology residents are well prepared to manage emergency airways of critically ill patients in a major university hospital.
Reference:
Nayyar P, Lisbon A. Non-Operating Room Emergency Airway Management and Endotracheal Intubation Practices: A Survey of Anesthesiology Program Directors. *Anesthesia and Analgesia* 1997;85:62-8.

S-176.

IMPROVING ANESTHESIA RESIDENT PERIOPERATIVE PAIN MANAGEMENT EDUCATION FOR SINGLE INJECTION INTERSCALENE BLOCK FOR ARTHROSCOPIC SHOULDER SURGERY

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Introduction: The search for improved efficiency and patient outcomes in ambulatory surgery has resulted in an increased demand for peripheral nerve blocks (PNB). Adequate perioperative pain control results in early ambulation, short hospital stay, reduced cost, decreased stress and increased patient satisfaction.[1] Therefore, there is need for academic centers to improve knowledge and skills of anesthesia residents with PNBs.[2] The aim of this study was to evaluate a new structured and supervised resident teaching program of interscalene block (ISB) for postoperative analgesia on patient outcomes after arthroscopic shoulder surgery.
Methods: A dedicated PNB rotation for anesthesia residents was initiated in February 2002, ensuring proper instruction and supervision in performing ISB for postoperative analgesia.
All blocks were performed on awake patients prior to surgery, using a peripheral nerve stimulator. After IRB approval, retrospective analysis of hospital database from February 2002 to January 2004 identified 258 consecutive patients who underwent shoulder arthroscopy using ISB performed by residents during PNB rotation (Education group). Intraoperative opioid consumption, PACU time, PONV and hospital admission related to pain control or post-anesthesia complications in the education group were compared to a reference group, consisting of patients undergoing shoulder arthroscopy (prior to new FNB rotation) from January 1st 2001 to June 30th 2001 (Reference group). Statistical analysis was performed using unpaired t-test.
(* $p<0.01$)
Results: In the reference group, 76 shoulder arthroscopies were performed, of which 44 patients received ISB in the perioperative period. In the education group, 256 patients received ISB preoperatively. (* $p<0.01$)

group	n	FNB	Intraoperative Opioid (mean ± SD) Fentanyl (mcg)	Morphine (mg)	PACU time [min] (mean±SD)	Patient with PONV	Patient with Admission
Reference group	76	44/76 (58%)	173±88	1.6±2.9	95.5±34	9 (12%)	19 (25%)
Education group	258	256/258 (99%)	1.1±1.6*	0.14±1*	55.5±24 *	34 (13%)	4 (2%)*

Conclusion: The implementation of a standardized resident education program of interscalene nerve block for shoulder arthroscopy resulted in significantly less intraoperative opioid use, less time in PACU, and fewer number of patients admitted to hospital compared with a control patient group who received ISBs prior to the training program.
References:
1- Pavlin DJ. Anesthesia & Analgesia 1998;87:816-826
2- Hanna M. Anesthesiology 2004; 101:A1368

S-177.

THE INTRAOCULAR PRESSURE ALTERATIONS IN ANESTHETIZED PATIENTS UNDER PERCUTANEOUS NEPHROLITHOTOMY

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Introduction:
Percutaneous nephrolithotomy (PCN) is one of the newest treatment methods of nephrolithiasis and it performs under general anesthesia in the prone position. Regarding the effect of prone position on intraocular pressure (IOP) and consequent effect on ocular perfusion pressure (OPP) and probable threat of post-operative visual loss (PVL), this study was carried out to measure the time dependent correlation between IOP and prone position during PCN procedures.
Methods:
After obtaining informed consent, the IOP of 20 patients (18-60 y/o, American society of anesthesiologists physical status I-III) without history of eye disease, ophthalmic surgery or allergy, scheduled for PCN surgery were measured in the status below:
1) Awake patient in supine position (baseline)
2)10 minutes after anesthesia in supine position (supine I)
3)10 minutes after prone position (prone I)
4) End of procedure in prone position (Prone II)
5)10 minutes after returning to supine position (supine II)
The patient head was positioned with a gelatin head holder. The data were analyzed with repeated measures analysis of variances and paired t test.
Results:
The mean values for IOP in successive measurements were significantly different (p=0.000). IOP in supine1 was significantly decreased from baseline IOP (15.42±0.9 to 12.5±0.5 mmHg, P=0.000).
IOP in prone1 (25.5±1.5 mmHg) was significantly higher than both IOP in supine1 (p=0.000) and baseline (p=0.000).
IOP in prone II (38.9±0.9 mmHg) was higher than all the IOP's (p=0.000).
IOP in supine II (13.7±0.4 mmHg) was significantly decreased in comparison with IOP in prone II (p=0.000).
The pulse rate, ETHal, MAP, PIP changes in successive measurements were not significant.
There was a positive linear correlation between IOP and time in prone position.
(r =0.67 P=0.001).
Hemodynamic and ventilatory parameters remained unchanged during the above 5 stages.
Discussion:
IOP decreased after anesthesia and increased significantly after prone position. There was a linear correlation between increasing IOP and duration of prone positioning. IOP was doubled after 2 hours. Therefore precautional efforts and continuous consideration are strongly recommended during long term procedures (more than 2 hours) in prone position anesthetized patients to prevent probable post-operative visual loss.

S-178.

MILD REDUCTIONS IN PREOPERATIVE COGNITIVE AND FUNCTIONAL STATUS ARE ASSOCIATED WITH POSTOPERATIVE DELIRIUM

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Introduction: Postoperative delirium (POD) is common in the elderly and associated with a variety of adverse outcomes.[1,2] However, its predictors after elective, non-cardiac surgery are not well-defined. We hypothesized that even mild reductions of preoperative cognitive and functional status predict POD.
Methods: Following Institutional Review Board approval, patients ≥ 65 y.o. undergoing elective hip or knee arthroplasty were enrolled. Preoperative cognitive and functional status tests included the Mini Mental Status Examination (MMSE), American National Adult Reading Test (AMNART), Adult Verbal Learning Test (AVLT), Controlled Word Association Test (COWAT), and Activities of Daily Living (ADLs). Scores for the AVLT and COWAT were age-adjusted. POD was diagnosed using the Confusion Assessment Method.[3] Data are presented as mean ± S.D. or median (range). p≤0.05 was considered significant using rank sum or two sample T-tests, as appropriate.
Results: Thirty of the first 266 patients (11.3%) developed POD (18/129 male, 12/137 female, p=0.18). MMSE scores, and American Society of Anesthesiologists Physical Status were similar between groups. Patients with POD were older (75.6 ± 6.1 *vs.* 73.4 ± 5.3 years, p=0.04), and more likely to have reduced preoperative functional status (ADL 11 (7-12) *vs.* 12 (9-12) p=0.0003). Although verbal intelligence was comparable in patients with and without POD (AMNART 105.1 ± 7.6 *vs.* 107.5 ± 7.5), those with POD had poorer preoperative age-adjusted auditory verbal memory and verbal fluency (AVLT Delayed Recall 85.9 ± 16.1% *vs.* 95.5 ± 14.1%, p=0.008; COWAT 8.4 ± 2.5 *vs.* 10.0 ± 2.6, p=0.0014).
Discussion: This is the first report associating POD and preoperative, age-adjusted, mild diminution of cognitive status. POD also is associated with subtly reduced preoperative functional status. Further study will determine the cognitive and functional sequelae of POD in the setting of reduced preoperative cognitive and functional status.
References:
1. Br J Anaesth, 73:673-687, 1994.
2. JAGS 48:618-24, 2000.
3. Ann Intern Med, 113:941-948, 1990.

S-179.

GEOGRAPHICAL VARIATIONS IN OXYCODONE EMERGENCY DEPARTMENT VISITS: A REGIONAL STRATIFICATION OF ABUSE LEVEL ESTIMATE IN USA

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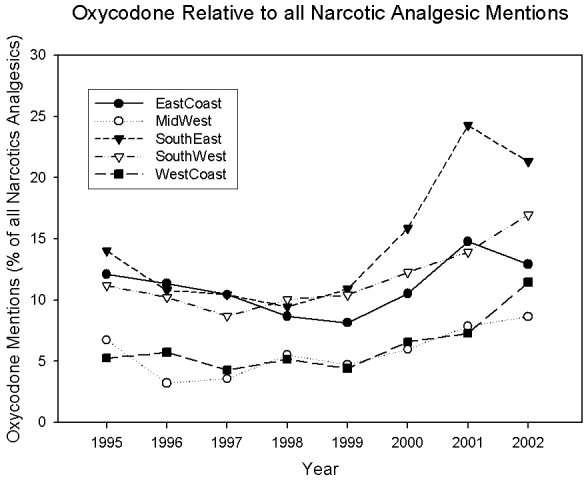
Introduction: Although studies and governmental reports have indicated substantial increases of oxycodone abuse in the U.S., little has been done to examine variations in abuse (*JAMA* 2000; 283:1710-4). We evaluated trends reflecting oxycodone use among 5 regions of the coterminous U.S. compared with all narcotic analgesics.
Methods: Following IRB approval we imported data from the Drug Abuse Warning Network (DAWN). To estimate levels of abuse, we used the number of Emergency Department Mentions (EDM), extracted from the DAWN database. DAWN gathers and maintains data on incidents of drug related problems derived from emergency room visits. EDM related to oxycodone as well as other opioids were extracted from the database over eight years (1995-2002) to facilitate trend comparison across drug categories. Data from 21 metro areas were collapsed into 5 geographic regions: East Coast, Midwest, Southeast, Southwest, and West Coast. To compensate for the overall increase in use and abuse of narcotic analgesics, EDMs for oxycodone were compared to EDMs for narcotic analgesics. To remove effects of population fluxuations values used were indexed per 100,000 persons in each metropolitan area.
Results: We found an increasing trend in all regions of the U.S. from 1999 to 2001 (Figure). The most extreme increase for this period occurred in the Southeast and the East coast. Over this two-year period Southeast EDMs for oxycodone compared to other narcotic analgesics rates doubled from 11.26 to 22.65 and the East coast increased almost as much, 81.6% from 8.14 to 14.78. During the same period the other three regions showed small but steady increases, which extended to 2002. The eastern states (East coast and Southeast) by contrast showed a sharp tapering off/decline from 2001 to 2002.
Discussion: This study clearly indicates regional variations in EDMs and possibly differential abuse levels of narcotics. Although all regions showed an increasing trend, those with the greatest increases, the eastern regions, had truncated trends from 2001 to 2002. This may be due to the heightened interest by the existing legal and regulatory infrastructure, such as the initiation of a comprehensive effort by the DEA in February 2001 to prevent the diversion of OxyContin (a formulation of oxycodone). Additional studies will be required to determine the causes for regional differences in oxycodone abuse.



S-180.

THE INCIDENCE OF DIFFICULT AIRWAYS IN PATIENTS SCHEDULED FOR THYROID SURGERY

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Introduction: Approximately 2% of all patients undergoing general endotracheal anesthesia have airways that are difficult to intubate (1). The importance of identifying and preparing for difficult intubations lies in the fact that failure to intubate and ventilate an apneic patient can be catastrophic. Routine evaluations of patients with difficult airways, including direct visualization of the oropharynx, are imperfect and have low specificity and sensitivity. As the thyroid gland lies directly anterior to the trachea, patients with large thyroid masses might be expected to have a high rate of difficult airways. Interestingly, a recent study showed no increase in the rate of difficult intubations in patients with a thyroid mass (2). This seeming paradox led us to undertake a retrospective study of patients who came to our institution for thyroid surgery in order to determine the incidence of difficult intubations in the presence of thyroid masses and to evaluate factors linked to difficult intubations.
Methods: With Institutional Review Board approval, a retrospective analysis of all thyroid surgeries at our institution from 1/1/03 to 12/31/03 was conducted. Information collected from the medical charts included: age, gender, height, weight, preoperative assessment of airway, notes taken during intubation, and pathology reports of the removed thyroid tissue. The intubation was labeled as difficult when an experienced anesthesia care provider 1) required three or more attempts to accomplish intubation by direct laryngoscopy, 2) failed to accomplish intubation, or 3) used flexible bronchoscopy or a Fastrach LMA for the initial intubation because the patient had a known or suspected difficult airway.
Results: 13.5% of the thyroid surgery patients (25 of 185) presented difficult intubations. Of these 25 patients, 44% were unexpected difficult intubations. Additionally, there was difficulty passing the endotracheal tube in 4 (16%) of the patients, and a smaller tube had to be inserted. This finding is remarkable because previous studies have suggested that thyroid disease does not complicate passage of the tube (2). The weight of the removed thyroid mass was twice as much from the patients with difficult intubations (average of 67 grams per patient) compared to the group with easy intubations (average of 39 grams). Also, 29% of the difficult airway patients had malignant thyroid disease, compared to 8% of the easily intubated patients.
Discussion: This retrospective review shows that the presence of a thyroid mass is a significant risk factor contributing to the difficulty of tracheal intubation, and that difficulty of intubation correlates with the size and the histology of the tumor. Anesthesiologists must be aware of this risk and prepare accordingly.
References:
1) Anesthesiology 1990;73:A1054. 2) Anesth Analg 2004;99:603-6.

S-181.

FREE VITAMINS AND GAIN POSITIVE EMAIL REMINDERS ENCOURAGE OTHER HEALTHY BEHAVIOR ADOPTION AFTER PREOPERATIVE OR PAIN CLINIC VISITS

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Introduction: To determine whether patient compliance for taking vitamins is better with multivitamin, 1 vitamin E tablet, 5 calcium tablets and 2 vitamin C tablets, or with 8 identical tablets which include the same amounts of vitamins and minerals.
Methods: In a randomized double-blinded controlled trial of an educational intervention, 50 preoperative and pain therapy subjects ages 18 yrs-80 yrs of either gender who were not currently taking vitamins, were asked to fill out a computer questionnaire about lifestyle and health. The computer calculated their physiological ages, (RealAge), and gave them recommendations for becoming or staying healthy. Recommendations included nutritional status. We then randomly assigned subjects to one of two groups. The "different" group was given a multivitamin, 2 vitamin C tablets, 5 calcium tablets and 1 vitamin E tablet. All subjects had BP's measured at start and end. All received daily emails written in gain positive language to encourage healthy behaviors. The "same" group was randomly assigned a multivitamin with the overall same vitamin and mineral contact as in the "different" group when 8 tablets were consumed daily. Every 30 days thereafter we met each volunteer to ascertain adherence to the vitamin regimen and to provide refills.
Results: After three months, there was an 80% reported and "counted" compliance of vitamins in the "same" group and a 65% compliance of vitamins in the "different" group ($p \leq 0.029$) Subjects in both groups made additional changes in behavior that fostered health. After 3 months, folate intake increased (self-reported) 451. mcg ($p \leq .00001$), and calcium by 805.5 mg ($p \leq .00001$). We were surprised that subjects adopted other behaviors. By month three, there was an increase per person of 591 calories expended in physical activity per week, a 1.7 % decrease in average saturated fat intake ($p \leq .0002$), a 2.9 g/day increase in flavonoid intake ($p \leq .02$)and -3.5/-0.7 decrease in BP. Sixteen individuals rated their health status more favorably ($p \leq 0.0006$). Of the nine subjects who didn't usually wear seat belts when in a car, seven people reported started doing so regularly.
Discussion: There was an overall compliance of vitamins of 72% for both groups. However, we conclude that there was a higher compliance rate for the subjects who took the identical 8 tablets. Health email tips given to preoperative and pain therapy clinic visitors plus free vitamins may increase calcium, vitamin D and folate intake to recommended levels and motivate other healthy behaviors that reducing care costs greater than the ehealth, vitamin expenses, and even clinic expenses.

S-182.

MEDICAL DEVICE USABILITY ANALYSIS TO EVALUATE INTRATHECAL BACLOFEN OVERDOSE: ADVERSE EVENT CASE STUDY AND NEW EVALUATION METHOD

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A 22 year old female received an overdose of intrathecal Baclofen leading to a respiratory arrest and lasting neurological damage. At present no evidence-based protocol exists for intrathecal Baclofen infusion (IBI). IBI has been well-established as a treatment for spasticity. Complications include local infection, transient hypotonia, and catheter malfunction.
We describe a new method to evaluate medical device related adverse events (AE) and how this method might be used to understand and prevent future AEs. The AE was due to a combination of: (a) miscommunication between resident and attending neurosurgeon; (b) design flaw that prevented the medical device from self-regulation. We present human factors and usability findings relative to design changes that are needed to improve the design of the Baclofen pump.
Methods
We conducted a comprehensive root cause and failure mode analyses of IBI. We interviewed the staff involved and created a precise reconstruction of events. All records (strip charts) produced by the equipment and the patient's chart were analyzed to determine at what point AE occurred. A medical device and human factor usability study was done including evaluating company materials that were submitted for analysis. We reviewed the last 10 years of the FDA medical device AE database. Our study found three types of errors in three primary categories: (1) latent errors that are a result of inconsistent procedures associated with this treatment, (2) person-to-person communication errors, and (3) machine design (human factors) errors. Our findings formed the basis of a new national Protocol that was developed and is now in use in the hospital.
Results
Poor design of the IBI pump and inconsistent procedures by the clinicians led to the AE. Errors occurred in the person-to-person communication and decision-making regarding pump usage. Standard pre-surgery protocols in which team members understand the skill and action levels of team members during this surgery, were not followed. The human-machine error occurred in that the medical device was given instructions (the treatment path to take) that the machine knew was harmful to the patient, but was not designed to alert the physician to this situation. A full usability study of the IBI pump found many design features that were not safe and allowed human error to propagate to an AE.
Discussion
This is a case of patient harm caused by a combination of human error, and machine error, and the interaction between the two. This paper presents the first protocol of its kind to create a set of safety standards for IBI. We suggested design modifications to the medical equipment based on our human factors usability testing. The device is being redesigned based on this input. We hope this new method will help improve the design of medical devices.
References
http://umdas.med.miami.edu/MPSC/human_factor.html

Equipment & Monitoring

S-183.

SPONTANEOUS FRONTAL EMG ACTIVITY DOES NOT INDICATE EEG ACTIVATION

AUTHORS: **W. E. Hoffman**, H. Park, V. Baughman, P. Wheeler;
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Introduction Previous studies show that elevated frontal electromyogram (FEMG) activity can indicate patient arousal(1). FEMG, indicated by increased Response Entropy (RE) in the Datex Ohmeda Entropy module, can increase spontaneously during train of four (TOF) recovery from succinylcholine paralysis and may be related to patient arousal(2). This study evaluated whether increased RE during TOF recovery is related to an increase in State Entropy (SE) of the electroencephalogram (EEG) and patient arousal during painful stimulation.
Methods This study was approved by the institutional review board for clinical research and patient informed signed consent was received. Awake patients undergoing spinal surgery were instrumented for S/5 M-Entropy EEG (Datex Ohmeda Inc, Madison, WI). Anesthesia was maintained in the study with isoflurane 0.8% (n=10) or 1.4% (n=10) during TOF recovery from paralysis with succinylcholine (2 mg/kg), followed by 5s of tetanic ulnar nerve stimulation. RE and SE measures were made awake, during anesthesia with paralysis, 100% TOF recovery, and tetanic stimulation.
Results During anesthesia with 0.8% and 1.4% isoflurane, RE and SE decreased significantly (figure 1). After 100% TOF recovery, RE increased in 5 of 10 patients anesthetized with 0.8% isoflurane and 8 of 10 patients anesthetized with 1.4% isoflurane, indicating FEMG activation. SE did not increase. During tetanic stimulation, RE and SE increased in patients anesthetized with 0.8% isoflurane and RE increased without a change in SE with 1.4% isoflurane. Spontaneous increases in RE during TOF recovery were not correlated with increases in SE during tetanic stimulation.
Discussion Our results show that more than half of the patients produced a spontaneous increase in RE but not SE during TOF recovery and this was not related to depth of anesthesia. SE increased during painful stimulation and this was related to depth of anesthesia. Increased FEMG during TOF recovery from succinylcholine is not an indication that patients will show an elevation in SE or arousal during painful stimulation.
References
1. Eur J Anaesthesiol 1989;6:111-9.
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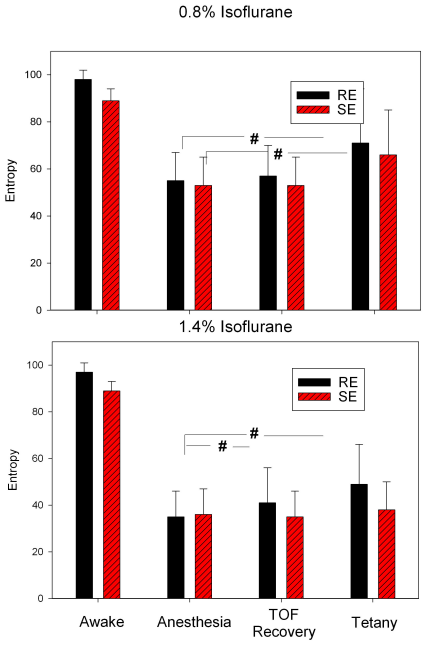

S-184.

CEREBRAL STATE INDEX TO PREDICT PATIENT RESPONSIVENESS DURING SEVOFLURANE ANESTHESIA. A COMPARISON WITH BISPECTRAL INDEX

AUTHORS: **S. S. HO**, M. T. Chan, T. Gin;
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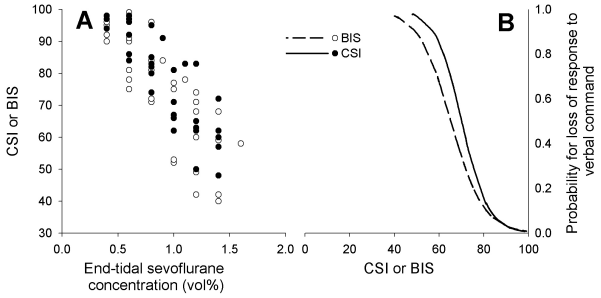
Introduction: The cerebral state index (CSI) is a novel indicator of anesthetic drug effect. It combines several electroencephalographic (EEG) parameters using the adaptive neuro-fuzzy inference system.[1] The purpose of this study is to compare the accuracy of CSI with bispectral index (BIS) to predict patient response during sevoflurane anesthesia.
Methods: This study was approved by ethics committee. Twenty patients (12 F: 8 M), ASA 1-2, aged 20-47 years, scheduled for general surgery gave written informed consents. Patients received increasing concentrations of sevoflurane via a tight fitting face mask, until they lost response to verbal command. CSI was measured by a cerebral state monitor (Danmeter, Odense A/S, Denmark), using Fpz-A1 montage. BIS (version 3.4) was recorded by a right frontal BIS-XP sensor, and was computed online by an A-2000 monitor (Aspect Medical, Newtown, MA). Ten minutes was allowed for equilibration before each step change (0.1%) in sevoflurane concentration. End-tidal CO_2 concentration was maintained at 3.5-4.0 vol%. Patient response was assessed by an blinded observer using the modified Observer's Assessment of Alertness/Sedation (OAA/S) scale.[2] Loss of response was defined as OAA/S score ≤ 2. Patient responses *vs* CSI or BIS were analyzed by logistic regression and sevoflurane concentration *vs* CSI or BIS was tested by nonlinear regression. The ability of CSI or BIS to detect OAA/S level was evaluated by prediction probability (P_K, ranging from 0-1), P_K of 1 indicates perfect prediction. Differences between indices were tested by Mann-Whitney test.
Results: Both CSI and BIS decreased with increasing concentration of sevoflurane (Figure A). The correlation coefficients were -0.83 and -0.79 for CSI and BIS, respectively. The values at which 50% (95% CI) of patients failed to respond to verbal command were 72 (69-75) for CSI and 69 (66-73) for BIS (Figure B). The P_K (±SE) values indicates similar accuracy of CSI (0.89 ± 0.04) and BIS (0.87 ± 0.03) to predict OAA/S scale.
Discussion: During steady state conditions, we found that both CSI and BIS accurately detect the level of consciousness after sevoflurane anesthesia.
Reference:
1. IEEE Trans Syst Man Cybern 1993,23:665-685.
2. J Clin Psychopharmacol 1990;10:244-51.
Figure. Changes of CSI and BIS at different sevoflurane concentration (A). Probability of loss of response to verbal command as a function of CSI and BIS (B).



S-185.

EFFECT OF DEXMEDETOMIDINE ON THE BISPECTRAL EEG INDEX (BIS) AND AUDITORY EVOKED POTENTIAL INDEX (AAI) UNDER PROPOFOL-REMIFENTANYL ANESTHESIA

AUTHORS: **S. She**[1], H. Li[1], M. Mok[2], Y. Chen[1], X. Xu[1], K. Suo[1];
AFFILIATION: [1]Department of Anaesthesiology, The First People's Hospital of Guangzhou, Guangzhou Medical College, Guangzhou, China, [2]Dept of Anesthesia, Taipei Medical University Hospital, Taipei, Taiwan Republic of China.

Introduction: Dexemdetomidine (Dex), a selective alpha-2 adrenergic agonist has been shown to enhance propofol anesthesia. The present study evaluated the effect of Dex on the BIS and AAI in target controlled infusion (TCI) propofol anesthesia.
Methods: Thirty adult patients of ASA class I-II who were scheduled for elective thyroidectomy were monitored with BIS, AAI, ECG, Blood pressure, end-tidal CO_2, and pulse oximeter monitors before and continuously during anesthesia. Anesthesia was induced by TCI with propofol 4 mcg/kg and remifentanyl 1 mcg/kg. After loss of consciousness patient received endotracheal intubation after vecuronium 0.6md/kg i.v.
Remifentanyl was then set at 0.2.mcg/kg/min and propofol infusion (Ct) was titrated to maintain a BIS value at 50. At 10 min after anesthesia stabilized at this state the patients were divided into 2 equal groups in a randomized double blind fashion with Group D (n=15) receiving Dex 0.4 mcg/kg iv administered over 5 min and Group C (n=15) receiving equal volume of normal saline. Values of BIS, AAI, Ct, HR, MAP were recorded every 2 min throughout surgery. At skin closure both agents were turned off and the patient was extubated at the end of surgery.
Results: Before anesthesia the BIS index was (92±2) in Group D and (90±2) in Group C; AAI was (78±2) in Group D and (81±1) in Group C. After the administration of Dex the BIS dropped from (52±2) to (42±16) which necessitated a reduction of propofol Ct from (3.4±0.6) mcg/kg to (2.7±0.8) mcg/kg to maintain the BIS at 50,whereas the AAI stayed at (15±3) before and at (14±5) after Dex. There was a decrease of HR from 78bpm to 65bpm, but no change of MAP after Dex. In Group C both of BIS and AAI remained unchanged after saline placebo injection.
Discussion: BIS index showed a significant decrease with the i.v. administration of Dex 4mcg/kg i.v. While AAI remained unchanged. This raise the interesting question on which hypnotic monitor would be more useful as a guide in propofol infusion by TCI.

S-186.

RELATIONSHIP BETWEEN TRANSCRANIAL MOTOR EVOKED POTENTIALS MONITORINGS (MEPS) AND THE SPINAL CORD HISTOPATHOLOGY AFTER SPINAL CORD ISCHEMIA IN RATS

AUTHORS: **M. Kakinohana**, K. Sugahara, Y. Odo;
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Introduction: Transcranial Motor Evoked Potentials Monitoring (MEPs) also provides a method for monitoring the functional integrity of descending motor pathways during thoracoabdominal aortic replacement surgery. However, there were few studies to investigate the relationship between changes of MEPs and spinal cord histopathology after spinal cord ischemia. In the present experiment using aortic occlusion model in rat (1), we investigate the relationship between changes of MEPs and neurological outcome, including histopathological changes, after spinal cord ischemia.
Materials and Methods: After Animal Care and Use Committee approval (University of the Ryukyus) male SD rats weighing 350 - 400 g were studied. In rats anesthetized ketamine, spinal ischemia (10 min) was induced by the occlusion of thoracic aorta combined with systemic hypotension (40 mmHg). Rats were divided into 3 groups as follows; Group A:6 min of aortic occlusion, Group B:10 min of aortic occlusion, and Group C:12 min of aortic occlusion. MEPs were recorded from the right soleus muscle after transcranial-electrical stimulation (100 - 120 V: 5 train-pulse stimulation) before, during ischemia, after reflow. At 3 days of reperfusion animals were perfusion fixed with 4% paraformaldehide and spinal histopathological changes were determined using Nissl staining following the assessment of neurological outcome. Changes of amplitude in MEPs after aortic occlusion compared with baseline were statistically analyzed using one-way repeated measures ANOVA followed by the Dunnett test.
Results: While MEPs disappeared within 2 min after aortic occlusion, MEPs in all Groups recovered to baseline level 30 min after reperfusion. Althogh the evoked potential waves from MEPs could be identified at 72 hrs of reflow in Group A and B, rats in Group B showed the spastic paraplegia at this time. On the other hand, all rats showed normal motor function at 3 days of reperfusion. Histopathological analysis of the spinal cords in Group B revealed a selective loss of small interneurons in lumbosacral segments. On the other hands, MEPs in Group C showed complete flat at 72 hrs of reperfusion and histopathological analysis revealed complete loss of not only the spinal small interneurons, but also motoneurons in lumbosacral segments.
Comments: Our results suggest that MEPs can not always predict neurological outcome, especially spastic paraplegia, after spinal cord ischemia. According to our histopathological data, whether MEPs can be idetified during the reperfusion periods might depend on the presence of normal spinal motoneurons, but not on the neurological function. We emphasize that MEPs is the better method for detecting spinal cord ischemia, but not for predicting ischemic spinal cord injury.
References
(1) Taira Y & Marsala M. Stroke 1996 ; 27 : 1850 - 1858

S-187.

EVALUATION OF MULTIPLE COMPOUND ACTION POTENTIALS FOR MOTOR EVOKED POTENTIAL MONITORING IN SPINAL CORD SURGERY

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Introduction: Neuromonitoring with somatosensory evoked potentials (SSEP) during spinal cord surgery is limited to the monitoring for spinal sensory function. Motor evoked potentials (MEP) may evaluate motor function at the spinal cord. This study was designed to explore the usefulness of the monitoring of MEP in patients undergoing spinal cord surgery anesthetized with propofol and fentanyl.
Methods: With IRB approval and written informed consent, 85 patients, who were scheduled for spinal cord surgery in whom MEP monitoring was performed, participated in this study. Anesthesia was induced and maintained with propofol and fentanyl.
MEP were obtained (Neuropack, Nihon Kohden, Japan) with train of 4 to 6 stimuli, train rate 500Hz. Current was 400-630V through bipolar capped electrodes 2cm rostral and 3cm lateral to Cz. Multiple compound action potentials for measuring MEP derived from upper limbs (5 points), and lower limbs (5points) by needle electrodes, and anal sphincter muscles by custom-made balloon pressure sensor. During surgery, anesthesia was maintained by target-controlled infusion by propofol and intermittent bolus injection of fentanyl as required. Muscle relaxant, vecuronium, was continuously infused at a rate of 1.5 to 2mg/h to maintain at least three counts of train-of-four counts.
Results: Success rate of MEP are 93.6% for upper limbs, 98.7% for lower limbs, 92.2% for anal sphincter. In 13/85 patients MEP decreased after surgery.
Multiple compound action potentials may effectively detect the MEP decrease. Immobilization of the patient and minimization of the effects of anesthetics are also necessary for MEP monitoring.

S-188.

NEUROMUSCULAR MONITORING WITH ELECTRODES OVER THE ADDUCTOR POLLICIS DOES NOT CAUSE DIRECT MUSCLE STIMULATION

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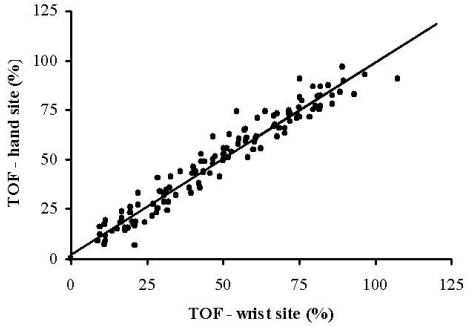
Introduction: Stimulation of the ulnar nerve at the wrist to produce contraction of the adductor pollicis is the standard method of monitoring neuromuscular function. Stimulation over a muscle is believed to cause direct muscle contraction, but evidence for this is lacking. The purpose of this study was to determine if direct muscle stimulation occurred when stimulating over the adductor pollicis in the hand and whether the responses were comparable with those observed with stimulation at the wrist.
Methods: The study included 20 adult patients (ASA I or II) undergoing elective surgery. A pair of standard electrocardiograph (ECG) electrodes was placed over the ulnar nerve, at the wrist. Another pair was applied on both sides of the ipsilateral hand, over the adductor pollicis muscle. Each pair of electrodes was connected alternately to a TOF-Watch stimulator, and an accelerometer was attached to the thumb. Anesthesia was maintained using sevoflurane and fentanyl. Rocuronium 0.6 mg/kg was administered. Train-of-four (TOF) stimulations were applied at the wrist site until maximal blockade, then at the hand site. If a response was recorded at the hand site in the absence of response at the wrist site, direct stimulation was considered to be present. During recovery, both sites were monitored alternately and TOF ratios were recorded.
Results: After rocuronium, 17/20 patients showed no response at both sites, two had responses only with stimulation at the wrist, and one had a response at both stimulation sites. During recovery, there was good correlation of TOF ratios between both sites (Figure), with the hand showing a bias of 0.5% and limits of agreement of ±11.8% compared with the wrist.
Discussion: This study indicates that placing electrodes over a muscle in the hand does not produce direct muscle stimulation as no patient met the criteria for direct muscle stimulation at the hand site. The patient that showed response at both sites was probably resistant to rocuronium. During recovery, both sites could be used interchangeably for monitoring, as there was practically no bias and the 95% limits of agreement could be within the accuracy limits of the accelerometer. Therefore, monitoring of the adductor pollicis by positioning the stimulating electrodes in the hand is an acceptable alternative to applying electrodes at the wrist.

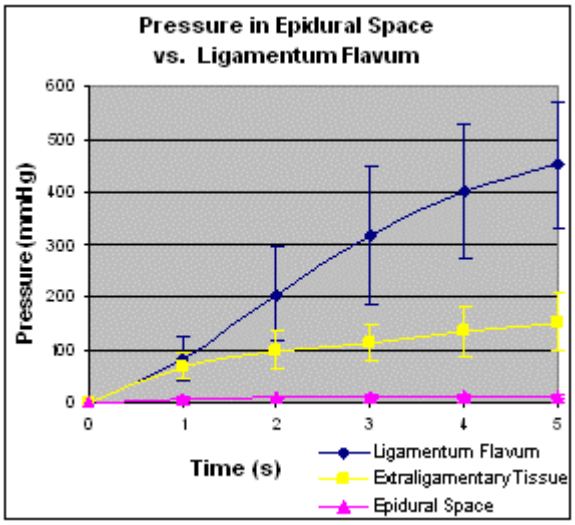


S-189.

UTILIZATION OF THE COMPUFLO® IN DETERMINING THE PRESSURE OF THE EPIDURAL SPACE- A PILOT STUDY

AUTHORS: **O. Ghelber**, R. Gebhard, G. Adebayo, P. Szmuk, C. Hagberg, D. G. Iannucci;
AFFILIATION: University of Texas Health Science Center at Houston, Houston, TX.

Introduction: Proper identification of the epidural space is crucial for efficient and safe epidural anesthesia. However, the current techniques for identification of the epidural space rely on the subjective perception of the operator by the "loss of resistance" to air or saline. The introduction of a method or device that can identify the epidural space with an objective tool could potentially decrease the incidence of side effects and increase the success rate of the procedure and patient safety.[1-3] A novel computerized device, the Compuflo®, was utilized to detect the difference in pressure between the ligamentum flavum and the epidural space.
Methods: Following institutional approval and written consent, 20 adult obstetric patients scheduled to receive epidural anesthesia were enrolled into this preliminary study. Epidural anesthesia was performed using the traditional "loss of resistance" technique. The Compuflo® was attached to the Tuohy epidural needle when the operator initially introduced the needle to a depth of 3cm (baseline pressure), after the operator reached the ligamentum flavum (ligament pressure), and after the operator encountered a "loss of resistance" (epidural space). Measurements of the pressure encountered at the tip of the needle were recorded for at least 5 seconds at each location. After the final pressure reading, the Compuflo® was disconnected from the epidural needle and epidural anesthesia was administered in the usual fashion with 0.2% ropivacaine.
Results: The following mean pressures were calculated: ligamentum flavum, extraligamentary tissue, and epidural space. These pressures are shown as a comparison to time in the graph below. The epidural space exhibited significantly ($p<0.001$) lower pressures than both the extraligamentary tissue and the ligamentum flavum after 1 second of measurement. The extraligamentary tissue exhibited significantly ($p<0.001$) lower pressures than the ligamentum flavum after 2 seconds of measurement.
Discussion: The Compuflo® is able to reliably identify pressure characteristics of the different tissues, including the decrease in pressure of the epidural space in all the cases. Within seconds, the location of the needle can easily be determined, with higher pressures indicative of being in the ligamentum flavum. Further studies are warranted with the use of this device.
References:
1. Anesth Analg 2003; 96:1183-7.
2. Anaesthesia 2002; 57:768-72.
3. Masui 2002; 51:927-30.

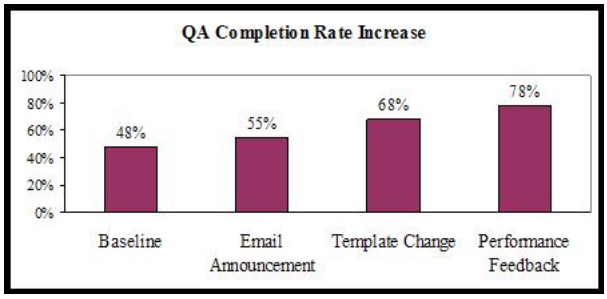


S-190.

QUALITY ASSURANCE DOCUMENTATION: MULTI-STEP PROCESS TO INCREASE COMPLETION RATES

AUTHORS: **M. Vigoda**, F. Gencorelli, S. Lin, D. Lubarsky;
AFFILIATION: University of Miami School of Medicine, Miami, FL.

Introduction: Quality Assurance (QA) documentation is required for healthcare organization accreditation in the United States by the Joint Commission on Accreditation of Healthcare Organizations. QA documentation may also be used as a tool to evaluate performance metrics and improve quality of care. A previous study[1] used an electronic form to document QA at the end of an anesthetic. This form limited the description of QA events to 6 questions, where the default selection was 'no-complication'. We examined the completion rate of QA documentation using a similar but more extensive electronic form with no default response values.
Methods: Using an anesthesia information management system (PICIS, Wakefield, MA), anesthesia providers are able to complete QA documentation electronically at any time during the perioperative period. The completion rates of QA documentation were examined using SQL queries on the AIMS database containing all QA documentation from the past 156 days. The completion rates during four distinct phases (baseline, email notification, template change, and performance feedback) were categorized separately.
1. Baseline: 57 days (11/24/03-01/21/04) - no intervention.
2. Email Notification: 33 days (01/22/04-02/23/04) - notifications sent to all attendings, residents and CRNA's informing them of departmental policy regarding QA completion.
3. QA Template Simplification: 42 days (02/24/04-04/05/04) - modified the steps necessary to complete the form.
4. Performance Feedback: 24 days (04/06/04-04/30/04) - individualized monthly reports sent to all anesthesia residents and CRNA's stating their QA documentation completion rates.
Results: During the baseline period, QA documentation was completed on 48% (n=3016) of cases. After email notification,QA documentation was completed on 55% (n=1909) of cases. After the template simplification, 68% (n=2368) of cases had QA documentation completed. The final stage of performance feedback increased the average QA completion rate to 78% (n=1300).
Discussion: Compliance with departmental protocols was significantly improved as a result of increasing awareness of departmental policy, improving the user interface, and informing users of their most current performance/compliance level.
References:
1. Anesthesiology 1996; 85:977-987.



S-191.

THRESHOLD LEAK VALUE AS DETERMINED BY FDA UNIVERSAL NEGATIVE PRESSURE LEAK TEST

AUTHORS: **J. Tokumine**, K. Sugahara, T. Fuchigami, K. Nitta, H. Tomiyama, E. Okuno;
AFFILIATION: University of the Ryukyus, Nishihara, Japan.

Introduction: FDA universal negative pressure leak test (FDA-LT) is the gold standard of qualitative leak detection in anesthesia machines, with an anesthesia machine considered having passed the test if it has no leak. The amount of leak depends on the pressure in the circuit. Therefore, it is important to know the amount of leak that is the threshold for leak detection by FDA-LT. However, no such threshold value for leak detection has been determined. The aim of this study is to clarify the threshold leak value as a criterion of judgment of FDA-LT.
Methods: We used an anesthesia machine (Aespire, Datex-Ohmeda Co., USA), which had no leak as checked by the soap bubble technique. Before the check, artificial leaks were created in the anesthesia circuit by incorporation of a flow meter, a manometer and a variable restrictor, at the junction of the anesthetic vaporizer and the distal circuit of the anesthesia machine. Artificial leaks ranged from 0 to 100 ml/min at 30 cmH_2O. For FDA-LT, two special suction bulbs (low pressure leak testing device, Datex-Ohmeda Co.) were used. FDA-LT was performed separately with each leakage, and re-inflation time of the suction bulb was measured three times. Re-inflation time was defined as the time that the collapsed suction bulb took to regain its original round shape.
Results: The figure shows the relation between leak volumes and re-inflation times of the suction bulb. The FDA's Anesthesia Apparatus Checkout Recommendations advise to "verify that the bulb stays collapsed for 10 seconds". Therefore, threshold leak value as a criterion of judgment of FDA-LT was calculated at 100 ml/min from the curve.
Discussion: This study revealed the threshold leak value of the FDA-LT, and its quantitative ability to detect leaks. Andrews JJ[1] mentioned that the FDA-LT could detect 30 ml/min of leakage. Our data suggest that a leak of 30 ml/min correlates with a re-inflation time of 31 seconds.
FDA-LT is the gold standard leak test for all anesthesia machines; however, its application on new generation, low-flow anesthesia machines is questionable. From the recent criteria for low-flow anesthesia[2], the allowable upper limit of leakage was 100 ml/min. Therefore, FDA-LT can be applied on low-flow anesthesia machines.

References:
1) Anesth Analg 84: 179-84, 1997
2) J Anesth 13: 166-74, 1999

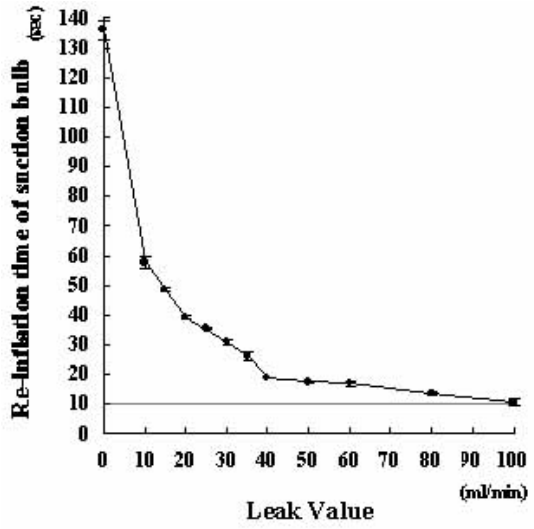


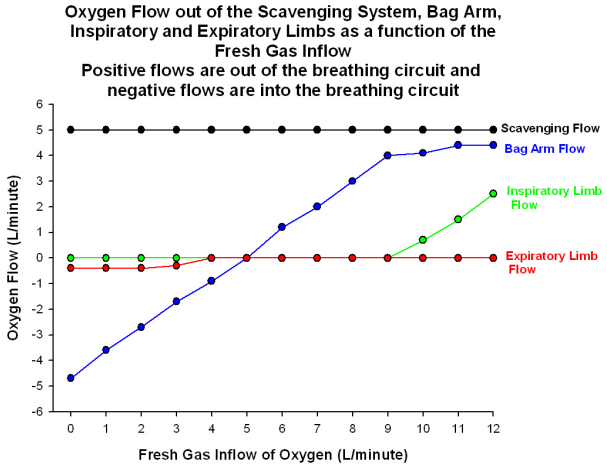
Fig. Relation of leak value and re-inflation time

S-192.

DYNAMICS OF GAS FLOW THROUGH THE DATEX-OHMEDA GMS ABSORBER SYSTEM

AUTHORS: **A. W. Paulsen**, S. Wong;
AFFILIATION: South University, Savannah, GA.

Introduction: Concern over drying of CO2 absorbent and the subsequent production of carbon monoxide following exposure of absorbent material to anesthetic agents, warranted the investigation of gas flow paths through the Datex-Ohmeda GMS absorber when the machine is left on and unused for prolonged periods.
Methods: A Datex-Ohmeda Modulus II Plus anesthesia machine with a GMS absorber was used to investigate all possible fresh gas flow paths resulting from leaving the machine turned-on, with various disposable circuit components in place, with open and closed scavenging systems in operation. Three Michigan Instruments model PF-300 Flow Analyzers were used to measure gas flows in the inspiratory and expiratory limbs and either the bag arm or ventilator connection simultaneously. Data were collected with an open scavenging system and a closed scavenging system set to withdraw 5 l/min of gas from GMS absorber. Both positions of the bag/ventilator switch were examined as well as a fully open and closed APL valve. Data were collected with the breathing bag both in place and off of the bag arm, and with a standard disposable breathing circuit connected and disconnected from the GMS absorber.
Results: With the closed system scavenging flow set to 5 l/min, in the bag mode, APL valve open, all disposable breathing circuit components removed, the fresh gas inflow (FGI) was increased in 1 l/min increments from zero to 12 l/min. At zero FGI, the scavenging system withdrew 300 ml/min of room air through the expiratory limb and 4.7 l/min of room air through the bag arm as illustrated below. Above 9 l/min the fresh gas began to flow out of the inspiratory limb as well as the bag arm.
Discussion: The FG flowing retrograde through the CO2 absorbent while the machine is turned-on but not being used is dependent upon FGI, the type and flow rate of the scavenging system, and the breathing circuit components. Leaving the bag on the bag arm, in the bag mode and the APL valve closed, dry fresh gas will not flow through the absorbent material. The highest flow of dry fresh gas through the CO2 absorber occurs in the bag mode without a breathing bag attached regardless of the scavenging flow or the APL valve setting



S-193.

COMPARATIVE EVALUATION OF A STANDARD MACINTOSH BLADE VS VIEWMAX II BLADE FOR LARYNGOSCOPY AND INTUBATION

AUTHORS: M. Hamza, **S. Armbruster**, B. Ogunnaike, P. F. White;
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Introduction: The availability of a laryngoscope blade that could improve visualization of the glottic structures during tracheal intubation may be helpful in reducing side effects related to laryngoscopy. The Viewmax II laryngoscope blade (Truphatek International Ltd, Israel) is a modified MAC blade with a 30° angle at the tip which incorporates an unmagnified optic side port. These modifications allow for an alternative direct view of the glottis from a position 1 cm behind the left tip of the blade. This study was designed to compare the Viewmax II to the standard MAC-3 blade using a randomized, cross-over study design.
Methods: 41 consenting patients requiring general anesthesia and trachea intubation were enrolled in this study. A standardized preanesthesia airway evaluation was performed. Anesthesia was induced with propofol 2 mg/kg IV and fentanyl 50-100 µg IV, followed by rocuronium 0.6 mg/kg IV. According to the last digit (odd or even) of the patients' ID number, either the standard MAC-3 or Viewmax II blade was initially chosen for laryngoscopy. After viewing the laryngeal structures, the first blade was withdrawn and the other blade was used to repeat the laryngoscopy. A strain gauge handle was used with both blades to measure the peak axial forces applied during laryngoscopy. After viewing the laryngeal structures with the second blade, tracheal intubation was performed. The view of laryngeal structures during the laryngoscopy were classified by the anesthesiologist as: *Grade 1* = most of the glottis is visible; *Grade 2* = only posterior portion of the glottis is visible; *Grade 3* = only the epiglottis is visible; and *Grade 4* = only the soft palate is visible. Finally, the anesthesiologist's preferred blade for tracheal intubation was noted. Data were analyzed using the paired t-test and Chi-square test, * p-value <0.05 vs MAC-3.
Results: The patients' demographic characteristics, peak (max.) force, and anesthesiologist's assessment of the laryngeal view and preferred blade are summarized below (mean±SD).

	MAC-3	Viewmax II
Age (yr)	42±14	41±13
Weight (kg)	79±17	85±28
Thyromental distance (cm)	8.8±1.5	9±1.5
Sternomental distance (cm)	15.5±2.6	15.6±2.5
Max. mouth opening (cm)	4.5±0.9	4.7±0.8
Max. force (kgF)	1.3±1.1	0.8±0.9*
Grading of laryngoscopic view		
Grade 1 (n,%)	28, 68	22, 54
Grade 3 (n,%)	11, 27	9, 22
Grade 3 (n,%)	1, 2	8, 19*
Grade 4 (n,%)	1, 2	2, 5
Preferable laryngoscope blade (%)	48	21*

Discussion: Although less force was applied with the Viewmax blade, this blade was preferred over the MAC-3 blade for tracheal intubation in only 21% of the cases studied. Therefore, the Viewmax II may be more useful as a "backup" blade than as a replacement for the standard MAC blade.

S-194.

A STRATEGY FOR THE DESIGN AND VALIDATION OF PRIORITY-ENCODED AUDITORY ALARM SIGNALS

AUTHORS: **R. McNeer**[1], J. Bohorquez[2], J. Senders[3], A. Varon[1], O. Ozdamar[2], P. Barach[4];
AFFILIATION: [1]University of Miami School of Medicine Department of Anesthesiology, Miami, FL, [2]University of Miami Department of Biomedical Engineering, Miami, FL, [3]Miami Center for Patient Safety, Miami, FL, [4]University of Miami Department of Anesthesiology and Miami Center for Patient Safety, Miami, FL.

Introduction: Most auditory alarm signals (AAS) designed to alert anesthesiologists have an urgency-mismatch. International standards stipulate that AAS should be priority-encoded using an established method. If other strategies are used, then the AAS function must be validated. However, alternative strategies are sparse and there is no standard validation method. We present a multi-disciplinary approach to AAS development that matches AAS acoustical structure and function so that anesthesiologist performance is maximized. We expect for such an approach to facilitate efforts to design effective AAS and improve patient outcomes.
Methods: Three sets of AAS were designed consisting of complex sounds varying along controlled acoustic dimensions: set I-beat period, average pitch, and dissonance; set II-tone overlap and average sound pressure; and set III-tone duration. Eleven subjects rated the AAS for urgency using an established method (see figure legend). Based on the urgency data, five AAS from each set were selected and assembled into three auditory display communication systems (ADCS). Each AAS was mapped based on urgency to one of five priority categories. The channel capacities (T) and signal-to-noise ratios (S/N) were calculated for each ADCS using the method of categorical judgments.
Results: Subjects rated AAS for urgency (figure). The urgency data (Ψ) from set I was plotted against beat period (Φ) and fit to a power equation: $\Psi = 10.7\Phi^{0.35}$ ($R^2 = 0.83$). Data from sets II and III were fit to linear equations. The calculated values T (bits) and S/N were: ADCS I-1.41(+/-0.22) and 1.55; ADCS II-1.71(+/-0.28) and 2.80; and ADCS III-1.30(+/-0.14) and 1.27.

Discussion: The urgency ratings were consistent across subjects. The data from set I appears to follow Steven's power law from psychophysics. This has important implications for better understanding how basic sound properties can influence human perception. With regard to information measures, ADCS II had the highest T and S/N. The acoustical dimensions presented in set II were perfectly aligned while those in set I were not (set III was one-dimensional). These results suggest that the number of acoustic dimensions and dimensional alignment are important in the transmission of urgency information in ADCS. This will likely lead to better designed ADCS.

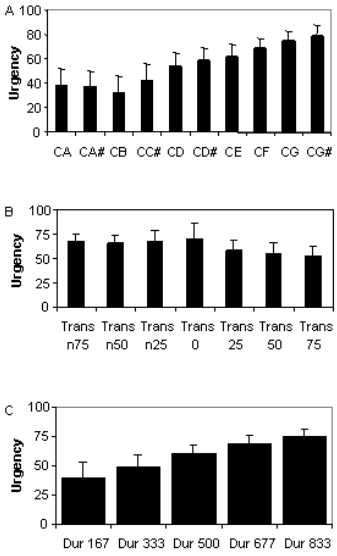


Figure. Urgency rating analysis of AAS sets. Urgency ratings are shown for the chords—set I (A), The melodic intervals—set II (B), and the duration ratios—set II (C). METHODS. Eleven subjects were presented with AAS from each set ten times in block-randomized order. They were instructed to assign a number between 0 and 100 to each of the AAS based on perceived urgency—rating proportional to perceived urgency. Responses were averaged for each AAS per subject and the averages of the means were obtained. Vertical bars are 95% confidence intervals.

References:
IEC 60601-1-8:2003(E);
Human Factors, 1991, 33(2), p. 205-231;
Psychological Review, 1951, 58, p. 446-459;
Psychological Review, 1957, p. 153-181.

S-195.

OXYGEN CONSUMPTION WITH MECHANICAL VENTILATION IN A FIELD ANESTHESIA MACHINE

AUTHORS: **E. N. Javernick**, D. F. Szpisjak, P. Austin;
AFFILIATION: Uniformed Services University of the Health Sciences, Bethesda, MD.

Introduction: Field anesthesia machines (FAM) are compact alternatives to machines used in the fixed hospital setting. They have been designed for remote and austere environments in support of office-based, humanitarian, and military operations. These machines include pneumatically powered ventilators, which are known to rapidly deplete oxygen cylinders (1), and this drive gas consumption rate is inversely proportional to pulmonary compliance (2). This study was done to determine the drive gas consumption rate in a prototype FAM in models of high (HC) and low (LC) pulmonary compliance.
Methods: Drive gas consumption rates were tested using oxygen E cylinders (filling pressure 2000 psig) and the Magellan-2200 FAM (Oceanic Medical Products, Atchison, KS). A semi-closed, circle breathing system was connected to a calibrated test lung (TTL, Michigan Instruments, Grand Rapids, MI) with HC and LC settings of 0.14 L/cm H_2O and 0.020 L/cm H_2O, respectively. Four cylinders were tested for each lung model. FAM fresh gas flow (FGF) was 1 L/min. The ventilator was adjusted to provide a tidal volume (V_T) of 1000 ml, respiratory rate of 10 breaths/minute, and an I:E ratio of 1:2. After verifying ventilator settings, the pipeline supply was stopped, the E cylinder opened, and the time until the low supply pressure alarm sounded was recorded. For calculations, a full E cylinder's pressure and volume were assumed to be 2000 psig and 660 L, respectively. The low oxygen supply pressure alarm threshold was 20 psig. Total oxygen consumed from each cylinder was calculated as 653 L. Between-group comparisons were analyzed using the independent samples t-test. $P < 0.05$ accepted as significant. Data reported as mean (±SD).
Results: The time until the low oxygen supply pressure alarm sounded was longer for the HC lung model than for the LC lung model [41.5 (± 0.58) v. 38.6 (± 1.3) min, $P = 0.007$, table 1). The HC lung model oxygen consumption rate was slower than the LC lung model oxygen consumption rate [14.8 (± 0.22) v. 16.1 (±0.59) L/min, $P = 0.006$).
Conclusion: Drive gas consumption in the Magellan-2200 FAM is inversely proportional to pulmonary compliance. Calculating cylinder duration with data from the LC model underestimates cylinder duration but provides a greater margin of patient safety.

	HC model	LC model	*P*
Alarm time (min)	41.5 (± 0.58)	38.6 (± 1.3)	0.007
Drive gas consumption (L/min)	14.8 (± 0.22)	16.1 (±0.59)	0.006

References:
1. Anesth Analg 2002;95:148-150.
2. Can J Anesth 2004;51:616-620.

S-196.

PATIENTS' CHARACTERISTICS INFLUENCING THE PERFORMANCE OF A LIGHTWAND INTUBATING DEVICE (TRACHLIGHT™)

AUTHORS: **M. Vaillancourt**, J. Lebon, P. Drolet;
AFFILIATION: University of Montreal, Montreal, PQ, Canada.

Introduction: It is important for anesthesiologists to identify patients' characteristics that are likely to influence airway management. Trachlight™ (TL), a lightwand guided intubating device, has been proven effective for intubation of normal or difficult airways.[1,2] Yet, no predictor has been clearly identified to help anticipate how appropriate this device is with regard to patients' specific features. The purpose of this prospective unblinded study is to determine what characteristics, if any, influence the utilisation of the TL, particularly the time and number of attempts needed for tracheal intubation.
Methods: After obtaining approval from the Institutional Review Board and written consent from each participant, patients scheduled to undergo elective surgery with general anesthesia were recruited. Before surgery, morphometric and demographic factors known to be associated with difficult direct laryngoscopy, or believed to influence the utilisation of the TL, were recorded. All patients were paralyzed before intubation with the TL under ambient light by a single experienced investigator. The number of attempts and time needed for intubation were recorded. Failure to intubate was defined as the inability to place the endotracheal tube into the trachea after three attempts. The patient's jaw was lifted after a failed first attempt and room light was turn off if a third attempt was necessary. Correlation coefficients between time or number of attempts and patients' characteristics were calculated.
Results: Two hundred patients were studied. Intubation was successful in 192 patients (96.0%); 93 on first (46.5%), 71 on second (35.5%) and 28 on third attempt (14.0%). Mean time to intubate was 50 seconds (+/- 41.7). Time to intubate and number of attempts increased with weight, body mass index (BMI) and neck circumference (Table). Number of attempts also increased with cutaneous thickness measured at the cricoid cartilage level. Some factors known to be associated with difficult direct laryngoscopy such as Mallampati class, thyromental distance and mouth opening did not influence the performance of the TL.
Discussion: The TL is an effective alternative for endotracheal intubation. Still, multiple attempts and increased time for intubation are associated with heavier patients, larger neck and higher BMI. These characteristics should be taken into consideration to optimize the choice of an airway management device.
References:
1.Anesthesiology 1995;83:509-14.
2.Can J Anaesth 1995;42:826-30.

	Characteristic	Correlation coefficient	95% confidence interval	P value significant (with Bonferroni correction)
Correlation between time to intubate and:	Weight [1]	0.3583	0.2310 to 0.4735	*
	BMI [1]	0.3663	0.2397 to 0.4807	*
	Neck circum-ference [1]	0.3988	0.2753 to 0.5094	*
	Mallampati class [2]	0.1979	0.0567 to 0.3314	ns
	Mouth open-ing [1]	-0.0003	-0.1391 to 0.1385	ns
	Thyromental distance [1]	0.0192	-0.1199 to 0.1575	ns
Correlation between number of attempts to intubate and:	Weight [1]	0.3889	0.2643 to 0.5006	*
	BMI [1]	0.4423	0.3234 to 0.5475	*
	Neck circum-ference [1]	0.4155	0.2937 to 0.5241	*
	Cutaneous thickness [1]	0.2499	0.1141 to 0.3766	*
	Mallampati class [2]	0.1863	0.0447 to 0.3206	ns
	Mouth open-ing [1]	0.0153	-0.1237 to 0.1538	ns
	Thyromental distance [1]	0.0245	-0.1147 to 0.1627	ns

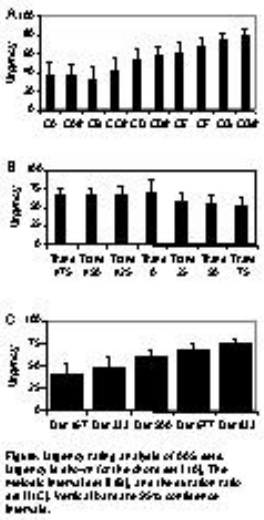
* $p < 0.05$
1.Pearson correlation coefficient
2.Spearman correlation coefficient

S-197.

DESIGN AND VALIDATION OF AUDITORY ALARM DISPLAYS THAT SIGNAL GRADED DEGREES OF URGENCY

AUTHORS: R. McNeer, O. Ozdamar, **P. Barach**;
AFFILIATION: University of Miami, Miami, FL.

Introduction
Most auditory alarm signals (AAS) used to alert anesthesiologists when alarm conditions occur have the problem of urgency-mismatch. International standards stipulate that AAS should be priority-encoded using an established method. If other strategies are used AAS function must be validated. However, alternative strategies are sparse and there is no standard validation method. We present a multi-disciplinary approach to AAS development that matches AAS acoustical structure and function so that anesthesiologist performance is maximized. We expect for such an approach to facilitate efforts to design effective AAS.
Methods
Three sets of auditory symbols were designed using specially designed software (SoundEdit). Each set consisted of complex sounds varying along controlled acoustic dimensions: set I_beat period, average pitch, and dissonance; set II_tone overlap and average sound pressure; and set III_tone duration. 11 subjects rated the AAS for urgency using an established method (1). Based on the urgency data, five AAS from each set were selected and assembled into three auditory display communication systems (ADCS). Each AAS was mapped based on urgency to one of five priority categories. The channel capacities (T) and signal-to-noise ratios (S/N) were calculated for each ADCS using the method of categorical judgments.
Results
Eleven subjects rated AAS for urgency (figure). The urgency data (Ψ) from set I was plotted against beat period (Φ) and fit to a power equation:$\Psi = 10.7\Phi^{0.35}$ ($R^2 = 0.83$). Data from sets II and III were fit to linear equations. The calculated values T (bits) and S/N were: ADCS I-1.41(+/-0.22) and 1.55; ADCS II-1.71(+/-0.28) and 2.80; and (1.30(+/-0.14) and 1.27.
Discussion
Urgency ratings were consistent across subjects. Notably the data from set I appears to follow Steven's power law from psychophysics and has important significance for understanding how basic sound properties can influence human perception. With regard to information measures, ADCS II had the highest T and S/N. Interestingly, the acoustical dimensions present in set II were perfectly aligned while those in set I were not (set III was one-dimensional). These results suggest that the number of acoustic dimensions and dimensional alignment are important in transmission of urgency information in ADCS.
References:
Edworthy J. Urgency Mapping in Auditory Warning Signals. In: Stanton NA ed. Human factors in alarm design. London: Taylor and Francis, 1994.



S-198.

AN EVALUATION OF THE MD-6 CRITICAL DATA VIEWER

AUTHORS: N. Ahluwalia, J. Brock-Utne;
AFFILIATION: Stanford University, Stanford, CA.

Introduction: Anesthesiologists must be vigilant to the hemodynamic changes that occur to their patients. Unfortunately, occasionally the physician has his or her back to the monitors; a Critical Data Viewer (MicroOptical) has been developed and promoted for use in clinical anesthesia. This device relays real time vital sign data directly derived from operating room monitors and places it in front of the practitioner's hand-eye axis via an adjustable color liquid crystal display (LCD) mounted on safety glasses. We evaluated this device at our institution as to its possible clinical applications.
Methods: Twenty anesthesiologists participated in a survey of the MD-6 Critical Data Viewer over a month. Participants included residents at various levels and faculty from different specialties and years of experience. Participants who wore prescription eyewear filled out additional questions. Anesthesiologists tested the viewer during a variety of cases and then were asked to complete a questionnaire. The Critical Data Viewer is a LCD unit that attaches on the temples of goggles and projects a 640 by 480, 60 Hz VGA image in front of either eye. It is clear and unobtrusive, and provides identical data (numeric and waveform) to the primary monitor. The LCD monitor was wired to a control box clipped at the waist, and then connected to the primary monitor via a cable.
Results: The viewer was found to be clinically useful in a variety of situations (20/20) but many found the device too bulky (10/20). It was appropriately sized (13/20) and the monitor was clear (18/20). Of those who wore glasses (13/20), most were able to see the display clearly (12/13) and did not find the additional safety glasses too bulky (6/13). Participants found the device relevant to almost all anesthetic scenarios especially during intubation, extubation, line placement, chart recording, cardiac and neurosurgical cases, and out of operating room procedures. All found the wire connection as a major disadvantage. Most were willing to pay between $500-$1000 for the device (14/20).
Discussion: The optimal placement of monitors and patient is difficult to achieve in current medical practice, and the development of the Critical Data Viewer provides a unique opportunity to bridge that gap. With this device, the anesthesiologist is mobile and able to focus on the clinical scenario while always having objective data in vision. The device interfaces easily with current monitors, and the monitor is clear regardless of the use of prescription eye wear. Many practitioners find this tool useful and are willing to pay between $500-$1000. Improvements should be targeted to overall design to reduce bulkiness. A wireless Critical Data Viewer has the opportunity to become a standard tool for the anesthesiologist in their effort to be more vigilant.
References:
MicroOptical User Guide

S-199.

EVALUATION OF THREE TECHNIQUES OF WARMING INTRAVENOUS FLUIDS

AUTHORS: **J. Satoh**, M. Yamakage, S. Iwasaki, A. Namiki;
AFFILIATION: Sapporo Medical University School of Medicine, Sapporo, Japan.

Introduction: Rapid infusion of unwarmed crystalloid and blood may result in considerable lowering of core temperature which may cause morbid complications. The purpose of the present study was to compare the fluid warming capabilities at different flow rates of IV fluids in three different warming systems during simulated clinical conditions.
Methods: The IV fluid warmers tested were (1) a conventional water bath warmer (Hakko blood warmer HBW-5; Hakko), (2) a novel dry heat plate warmer (Meditemp III; Gaymar), and (3) a well-known IV fluid tube warmer (Hotline HL-90; Level-1). The temperatures of the warmers were set to 37-38, 40-41, and 40-42 degree, respectively. The infusion rate (2-100 mL/min) was controlled by an infusion pump. The IV fluid temperatures were measured with thermocouples and with a temperature monitor at the end of a 1-m tube connected to the warmer. A bottle of acetated Ringer solution at room temperature (21-23 degree) or at ice-cold temperature (4-6 degree) was connected to the IV infusion set of each warmer. The delivered temperature of IV fluids was recorded when it fluctuated less or equal to 0.1 degree for 3 min.
Results: The IV fluid temperature delivered by the water bath warming system increased by increasing the flow rate up to 15-20 mL/min and decreased by increasing the flow rate from 20-30 mL/min to 100 mL/min (Fig. 1). The temperature of the fluid delivered by the dry heat plate warmer system significantly increased by increasing the flow rate within the range studied, and there was no significant difference in the delivered temperature between the room temperature and ice-cold temperature of the IV fluids. The delivered temperature did not depend on the flow rate up to 20 mL/min when the IV fluid tube warming system was used, but the delivered temperature was significantly and fluid temperature-dependently decreased at the high flow rate (over 30 mL/min) tested.
Conclusion: An IV tube warmer is the most effective system for warming IV fluid at rather low flow rate (2-20 mL/min). A dry heat plate warmer is effective for warming IV fluid at rather high flow rate (over 40-50 mL/min). It is important to choose a warmer according to its characteristics.

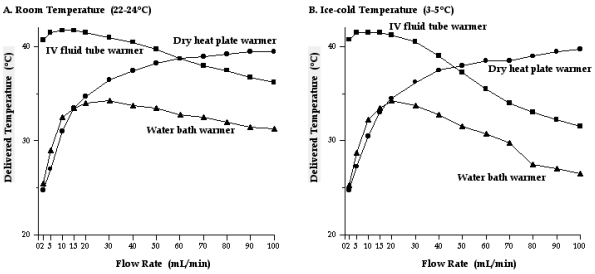


Figure 1 Relationship between flow rate of i.v. fluid and delivered temperature in each temperature of IV fluid [ice-cold (3-5ºC) or room temperature (21-23ºC)] tested. Means of two trials for each warmer.

S-200.

EFFECTS OF A PLASMA SUBSTITUTE HYDROXYETHYL STARCH HESPANDER® ON PLATELET FUNCTION AND BLOOD COAGULABILITY DURING OPERATIONS WITH HEMODILUTIONAL AUTOLOGOUS TRANSFUSION TECHNIQUE

AUTHORS: **J. Satoh**, M. Yamakage, S. Kohro, S. Iwasaki, A. Namiki;
AFFILIATION: Sapporo Medical University School of Medicine, Sapporo, Japan.

Introduction: A hydroxyethy starch plasma substitute Hespander, which is available to use in Japan, is characterized by its low molecular weight (70 kDa) and its low rate of hydroxyethyl substitution (0.5). Therefore, it is expected to have little effect on platelet function and blood coagulation. In the present study, the effects of Hespander on platelet function and blood coagulability were evaluated by the use of a viscometer Sonoclot during urological surgery with hemodilutional autologous blood transfusion (HAT) technique.
Methods: Sixteen patients, who had scheduled to have urological surgery, were enrolled in this study. Anesthesia was induced by propofol (2 mg/kg, iv) and fentanyl 2 ug/kg). After the anesthetic induction, autologous blood was drawn (920 g, mean), and the same amount of Hespander (37 degree) was infused simultaneously. Mean blood pressure, heart rate, base excess, hemoglobin, concentration, PaO2, and body core temperature were measured before HAT, 30 min after HAT, before return of autologous blood, and after return of autologous blood. Parameters of platelet function and blood coagulability by the use of Sonoclot (SonACT, clot rate, and time-to-peak) were simultaneously measured (Figure 1).
Results: Mean blood pressure was slightly but significantly decreased after the hemodilution. Hemoglobin was significantly decreased by 31%. Sonoclot parameters SonACT and time to peak both increased, and the clot rate decreased by the hemodilution (Figure 2). All of the Sonoclot parameters significantly improved by autologous blood transfusion with a concomitant increase in hemoglobin. Total amount of blood loss during the surgery was 1,330 g (mean) and only 2 cases (13%) received homologous blood transfusion. Conclusion: Hespander is useful as a plasma substitute for HAT, and hemodilution-induced impairment of platelet function and blood coagulability can be improved by return of fresh autologous blood transfusion.

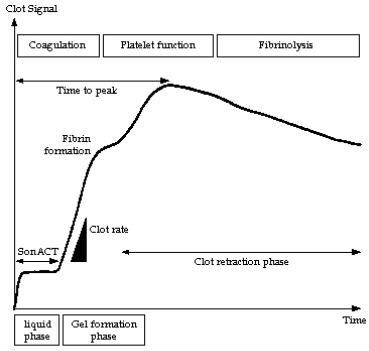


Figure 1. Sonoclot™ signature

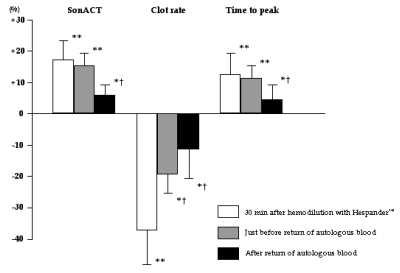


Figure 2. Percent changes in Sonoclot™ parameters in this study

S-201.

A NEW METHOD FOR ESTIMATION OF CORRECTION COEFFICIENT IN SALINE TONOMETRY - APPLICATION OF THEORETICAL REGRESSION EQUATION CALCULATED FROM MODEL EXPERIMENT

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Introduction: Tonometry is a minimally invasive method for estimating gastrointestinal intramural pH (pHi) calculated from the partial pressure of carbon dioxide (PCO2) of saline contained in a balloon within the lumen of the gut. However, this technique takes the long time interval needed for gases to reach equilibrium in saline milieu. To calculate the equilibrium PCO2 from dwell times shorter than the time needed for full equilibration, measured PCO2 is multiplied by dwell time-dependent correction factors. In the present study the regression analysis of the correction factors were conducted on the principle of the carbon dioxide diffusion. Theoretical Basis: Membrane transport model is usually expressed on the basis of osmosis. The state of a solute is related by permeability constant, and the time-dependent change of this state is given by linear differential equation of first order. Therefore, if an experimental setting is assumed that the saline-filled tonometer (TRIP) balloon is placed in a steady-state PCO2 bath filled with the saline, the volume of CO2, which passes through the TRIP balloon membrane, is in proportion to the product of the membrane area (Am) and the PCO2 difference between the bath (PC) and the TRIP balloon (PB).
This principle provides the differential equation:V*dPB/dt = P*Am*(PC-PB)
Where dPB/dt is the rate of CO2 permeation, V is the volume of the TRIP balloon, and P is the permeability constant. Solving this differential equation results in the following mathematical model.
PB/PC = K0 - K0*exp(-t/K1) (K0, K1; constants) (Model 1)
This equation may be interpreted as the particular solution of the general one phase exponential decay model:
PB/PC = K0 + K1*exp(-t/K2) (K0, K1, K2; constants) (Model 2)
Curve fitting programs can be used to obtain the model parameters.
Method: TRIP was inserted in a steady-state PCO2 bath filled with the saline of 37 degreesC. At each equilibrium time, samples of saline were anaerobically aspirated and analyzed on a standard blood gas analyzer. The measurements of PCO2 in the bath (PC) and the TRIP balloon (PB) simultaneously were performed and non-linear regression was calculated according to the two mathematical models (Model 1 and 2).
Results: The theoretical simulation derived from the manufacturer's correction factors showed good-fit (R2 = 0.99, p = 0.0003) in Model 2. Our data (15 samples) were compatible with this regression line. The regression analysis of samples also resulted in the following best-fit equation in Model 2. PB/PC = 1.24 - 0.83*exp(-t/0.017) (R2 = 0.86, p = 0.047) Model 1 regression showed less fitting than Model 2 in both settings.
Conclusion: we successfully calculated time-dependent correction factor for any equilibration period .We emphasized that the equation obtained from the theoretical regression would be helpful to calculate pHi.

S-202.

CLINICAL DATA AND MATHEMATICAL COMPARISON CONCERNING THE EFFICACY OF PREOPERATIVE AUTOLOGOUS BLOOD DONATION AND PERIOPERATIVE BLOOD SALVAGE IN ORTHOPAEDIC PATIENTS

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Introduction: Preoperative autologous blood donation (PAD) and perioperative blood salvage (PBS) have become established blood conservation measures. So far, data on comparing efficacy, i.e. increase/ recovery in/of RBC-mass (+RBC) of either measure is still lacking.
Methods: Prospective analysis in 693 consecutive major orthopaedic surgery patients scheduled for PAD. +RBC due to PAD was calculated by the hct method by calculating patient's estimated blood-volume according to Nadler et al (1), and knowing initial hct (hct init) and hct at given points of time. In parallel, +RBC due to PBS -if no PAD were applied- was calculated according to formulas published elsewhere (2). Salvage of RBC by PBS was set with 30 percent (PBS30). Re-transfusion of RBC together with colloid in order to maintain hct min at pre-set level; thus resulting in maximal allowable blood loss (MABL) substituted. MABL according to either PAD or PBS was calculated according to formulas published elsewhere (2). Statistical analysis was performed by either t-/U-test or ANOVA w/ Scheffé-test or Kruskal-Wallis-test, respectively. Data are given as mean ± SD. Statistical significance was set with $p<0.05$ (*between groups; °within groups).
Results: Tab. 1 summarizes relevant data of this analysis.

n: m / f (%)	693: 282 / 412 (40.5% / 59.5%)		
age (yrs)	62.7 ± 10.8		
estimated blood vol. (L)	4.6 ± 0.8		
RBC mass (L)	1.8 ± 0.4		
hct init (%)	39.2 ± 3.3		
hct preop. (%)	36.9 ± 2.7		
interval PAD to surgery (days)	27.9 ± 10.9		
+RBC w / PABD (ml)	164 ± 11*		
hct min-levels set (%)	18%	21%	24%
+RBC w / PBS30 (ml)	431± 134*	346± 116*	273± 100*
δ +RBC (PBS30 - PAD) (ml)	267 ± 178	183 ± 166	109 ± 156
MABL w / PAD (L)	4.7 ± 1.1*°	3.8 ± 0.9*°	3.1 ± 0.8
MABL w / PBS30 (L)	6.0 ± 1.6*°	4.5 ± 1.3*°	3.4 ± 1.1
δBL (PBS30 - PAD) (L)	1.2 ± 0.8	0.7 ± 0.6	0.3 ± 0.5
PBS30 > PAD: n (%)	670 (96.7 %)	610 (88 %)	495 (71.4 %)

Discussion: Mathematical analysis concerning efficacy (+RBC) of PAD vs. PBS demonstrates PBS superior to PAD, and consequently substituting for blood-/RBC-loss at different hct min-levels; even w/ a PBS-recovery rate of RBC of 30 percent, only. The lower hct min tolerated, the more efficacious is PBS, and the lower the percentage of patients taking advantage from PAD.
References:
1. Surgery 1962; 51: 224 - 232.
2. J Surg Res 1999; 86: 206 - 212. *Erratum* in J Surg Res 2000; 88: 215

S-203.

ACUTE NORMOVOLEMIC HEMODILUTION - ORIGINAL PATIENTS' DATA MATHEMATICALLY ANALYZED

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Introduction: Clinical results and mathematical modeling (MM) concerning efficacy of acute normovolemic hemodilution (ANH) are conflicting. MM of ANH was performed in a 'theoretical model-patient', only. Moreover, quantitative perspectives of dilution-coagulopathy that might limit extent of ANH were not considered. This MA is based on original patients' lab-data and evaluates 1st lab-parameter limiting extent of ANH; 2nd maximal number of ANH-U to be withdrawn until reaching first ANH-limiting lab-parameter at given hct min; 3rd maximal allowable blood-loss (MABL) w/ ANH (maximal number of ANH-U withdrawn) vs. w/o ANH; 4th gender-specific differences concerning these above named perspectives.
Methods: Prospective MA of original lab-data from 207 patients clinically eligible for ANH and undergoing major elective surgery; however, ANH was not applied clinically. Calculating estimated blood-volume, mathematical concept and formula concerning ANH, re-transfusion of ANH-U, and calculating MABL has been described elsewhere (1, 2): Isovolemic exchange of blood vs. an artificial colloid (volume-effect 1.0); applying ANH (500 ml per unit withdrawn) until reaching first limiting parameter (hct min [24, 21,18%], platelets min [plt - 100, 50 per nl], fibrinogen min [fbg - 100 mg per dl]; re-transfusion of ANH-U plus administration of colloid in order to maintain hct min despite ongoing BL until all ANH-U were re-transfused (MABL). Statistical analysis by t-/U-test, ANOVA/Kruskal-Wallis-test. Data are given as mean ± SD. Statistical significance is considered with $p<0.05$ (*between groups; °within group).
Results: Tab. 1 summarizes relevant data. Hct was the dominating parameter limiting ANH, followed by fibrinogen, and the combination of hct plus fibrinogen. Efficacy of ANH, i.e. MABL was statistically significant and clinically relevant higher in males than in females.

tab. 1

	parameter	males : n=52 (25.1%)		females: n=155 (74.9%)		
	hct init (%)	44.5 ± 3.4		40.7 ± 3.7		
	platelets init (p. nl)	257.4 ± 63.8		287.1 ± 68.6		
	fibrinogen init (mg p. dl)	321.1 ± 83.6		345.9 ± 67.9		
		hct min = 24 percent		hct min = 21 percent		hct min = 18 percent
		males	females	males	females	males females
first lab- parameter limiting extent of ANH		hct (24%) 186 (89.9%)		hct (21%) 172 (83.1%)		hct (18%) 121 (58.5%)
		42 (80.8%)	149 (92.9%)	32 (61.5%)	140 (90.3%)	13 (25%) 108 (69.7)
		fibrinogen 100 mg p. dl n = 5 (2.4%)		fibrinogen 100 mg p. dl n = 18 (8.7%)		fibrinogen 100 mg p. dl n = 51 (24.6%)
		4 (7.7%)	1 (0.6%)	11 (21.1 %)	7 (4.5%)	28 (53.8%) 23 (14.8%)
number of ANH-U collected		3.8 ± 1.6 U		5.3 ± 1.7 -U		6.9 ± 1.7 U
at hct min		5.7 ± 1.1*	3.2 ± 1.1*	7.4 ± 1.2*	4.6 ± 1.2*	8.9 ± 1* 6.2 ± 1*
MABL (L) w / ANH		3.7 ± 0.9*°	1.9 ± 0.7*°		2.9 ± 0.9*	6.9 ± 1.2* 4.2 ± 1.0*°
vs. MABL w / o ANH (at hct min)		2.8 ± 0.6*°	1.6 ± 0.6°	5.1 ± 1.1*° 3.7 ± 0.6*°	2.3 ± 0.6*°	4.6 ± 0.7*° 3.1 ± 0.6*°

Discussion: MA of original patients' lab-data reflects maximal possible efficacy of ANH (MABL being substituted by ANH). Hct is the primary parameter limiting the extent of ANH. Overall, ANH is poorly efficacious in substituting for and increasing MABL - at least at usually tolerated hct min in females. ANH is by far more efficacious in males than females. To achieve maximal efficacy of ANH, at least five ANH-U have to be withdrawn in males, and three in females.
References:
1. Surgery 1962; 51: 224 - 232.
2. J Surg Res 1999; 86: 206 - 212. *Erratum* in J Surg Res 2000; 88: 215

S-204.

IS CELL SALVAGE SAFE IN LIVER RESECTION?

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Introduction: Intraoperative cell saving (CS) is a well established, safe, and cost effective method to reduce homologous blood transfusion in orthopedic and vascular surgery (1,2). This should also apply to liver surgery. However, one major concern for its use in hepatic surgery is the retrograde bacterial contamination from bile ducts during resection. In this pilot study we investigated the quality of CS blood in patients undergoing hemihepatectomy with regard to bacterial contamination.
Methods: With written informed consent, six patients undergoing hemihepatectomy or aortobifemoral bypass (control group), respectively, with an intraoperative blood loss of more than 800 ml were included in the study. All patients received intravenous antibiotics according to hospital standard protocol with induction of anesthesia. Blood samples were drawn from the reservoir directly prior to processing in a Haemonetics® Cell Saver 5®, and from the processed blood within 5 minutes after termination of the washing procedure. Microbiological analysis included colony count after cultivation on agar-plates (48 hours; 37° C) in aerobic and anaerobic medium as well as enrichment culture for 6 days.
Results: For results see table below.
Discussion: In the control group all samples were sterile or showed growth of commensal skin microflora (CNS or Propionibacteria) in very low numbers. This is likely to be related to iatrogenic contamination during sample drawing or the inoculation procedure.
In the liver resection group the samples of 3 of 6 patients remained sterile. Two patients showed growth of commensal skin microflora after enrichment culture. In one patient we could not exclude contamination with intestinal flora.
Conclusion: There were no differences in the quality of CS blood between the two study groups regarding microbiological analysis with the exception of one patient with gram positive mixed cultures. These findings are promising and warrant further investigation of cell salvage and processing during liver resection. Before introducing it into clinical practice, however, care has to be taken not to oversee the potential risk of bacterial retransfusion.
References:
1. Chest 1999; 115:113S-121S.
2. Anesth Analg 2002; 95:1312-1317.

Ø: no growth; ae: after enrichment; CNS: coag. neg. staph.; MC: mixed culture; Prop: Proprioni

pat no	vascular surgery CS-reservoir	vascular surgery CS-blood	liver resection CS-reservoir	liver resection CS-blood
1	Ø	Ø	Ø	Ø
2	Ø	Ø	Ø	Ø
3	Ø	Ø	MC ($<10^2$ / ml)	MC ($<10^3$ / ml)
4	Ø	Prop. (ae)	CNS (ae)	CNS (ae)
5	CNS ($<10^3$ / ml)	CNS ($<10^3$ / ml)	Ø	Ø
6	Ø	Ø	CNS (ae)	CNS (ae)

S-205.

CLINICAL EFFICACY OF POST-OPERATIVE AUTOTRANSFUSION OF FILTERED SHED BLOOD IN HIP AND KNEE ARTHROPLASTY

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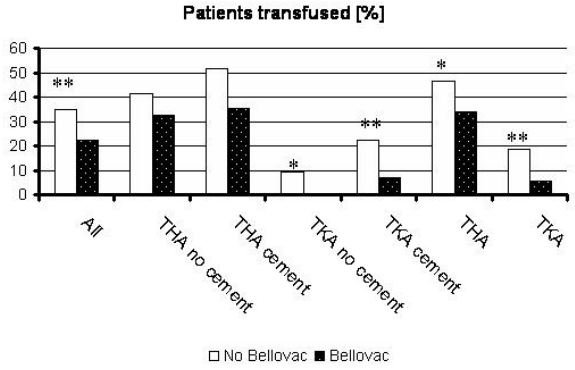
Background
Total knee arthroplasty (TKA) or total hip arthroplasty (THA) regularly results in postoperative requirement of blood transfusion. Because of the disadvantages of allogeneic blood transfusion (ABT) such as the risk of transfusion-associated infections, incompatibility-related transfusion fatalities or immunomodulatory effects, a continuing effort to reduce allogeneic blood transfusion is important. For this purpose we evaluated the effect of reinfusion of drain blood, via a postoperative wound drainage and reinfusion system, on the need for allogeneic blood transfusion.
Methods
Using a prospective observational quality assessment design, we compared 135 patients scheduled for TKA or THA with a historic group of 96 patients. In the study group the Bellovac™ ABT autotransfusion system was used. The shed blood was retransfused either when 500 ml were collected or at most 6 hours after surgery. Compared were the pre-, post- and discharge hemoglobin, as well as the number of allogeneic blood transfusion.
Results
There were no statistical differences between pre-, postoperative and discharge-hemoglobin levels. Autotransfusion reduced the number of patients receiving ABT overall from 35% (control) to 22% (study). The decrease of allogeneic transfusion requirement was most significant after TKA: from 18% to 6% ($p<0.001$) (Figure).
Discussion
We conclude that the Bellovac™ A.B.T. device reduces allogeneic blood transfusions in TKA and THA.



S-206.

A DELAY IN THE PROCESSING OF BLOOD FOR AN ACT: DOES IT REALLY MATTER?

AUTHORS: **B. M. Philip**, J. Brock-Utne, R. Jaffe, H. Lemmens, P. Shuttleworth, S. Hodge;
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Introduction
Activated clotting time, ACT, is a clotting test to monitor heparin anticoagulation. Frequently, in an operating room setting, there is a delay between collecting the blood and performing the ACT measurement. This study attempts to ascertain if the processing of an ACT sample at different times will give different results.
Materials and Methods
Twenty-one patients, ages 18 to 65, undergoing noncardiac surgery, gave written, informed consent preoperatively. Patients were included if they needed an arterial line and if they had normal labs. Twenty milliliters of blood were taken from an arterial line, after withdrawing ten milliliters. Immediately afterwards, one milliliter was placed into two channels each and the calculations were started simultaneously in a Medtronic ACT II machine. Upon completion, an average was taken for that time period. Another set of ACT calculations was then started and the process was repeated ten times per patient.
Each machine used to calculate the ACT measurements was quality controlled per protocol. In order to determine if there was a statistical difference in the ACT after a certain period of time, the first and last ACT averages for each patient were grouped into two, separate categories and a paired t-test was performed.
Results
The mean for the first ACT average for the twenty-one patients was 124 (standard deviation of 21). The mean for the last ACT average was 108 (standard deviation of 20). Using the paired t-test, the p value was highly significant at 0.0046. The average time difference between the first and last sample was 33 minutes.
Discussion
After first being described in 1966, ACT as become the gold standard in measuring heparin anticoagulation. Machines derive an ACT number by rolling blood with an activator of coagulation to form a fibrin clot. A magnet within the channel is then pulled away from a detector and this signals the amount of time required for clot formation, or an ACT. Baseline ACTs usually lie within 70 to 180 seconds.
There exists the possibility of introducing error if there is no standardization in the derivation of lab values. In clinical practice, the ACT blood samples may sit for several minutes before being placed in the machine. No study has ever analyzed the effects of a delay in ACT calculation. Such a delay is likely to occur if the ACT machine is outside the operating room and the anesthesiologist cannot access it readily.
In conclusion, our study shows that there is a statistical difference between the first and the last ACT values ($p = 0.0046$). Thus, processing an ACT should be done almost immediately for every measurement. If one does not follow this recommendation, clinical decision-making could be wrongfully affected.

S-207.

THE COMPARISON OF THE CHANGE IN THE VALUE AND PULSE WAVEFORM OF FOREHEAD-SENSING AND FINGER-SENSING PULSE OXIMETER IN SUPINE AND TRENDELENBURG POSITION

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Introduction: Forehead-sensing pulse oximeter has been reported that it is more effective than finger-sensing pulse oximeter in the patient with peripheral vasoconstriction (1). However, there is a clinical report that forehead-sensing pulse oximeter do not function appropriately (2). We recently have experienced a gynecology surgical case which decreased forehead-sensing pulse oximeter value of "70%" in Trendelenburg position in spite of finger-sensing pulse oximeter showed "98%". To investigate positional influence to the pulse oximeters, we compared the change in the value and pulse waveform of forehead-sensing and finger-sensing pulse oximeter in supine and Trendelenburg position.
Methods: After obtaining written informed consents, 11 healthy adult volunteers were studied. Forehead-sensing pulse oximeter (N-595; Nellcor, US) and finger-sensing pulse oximeter (M-1020A; HP, US) were monitored simultaneously. Pulse waveforms were monitored by a personal computer (PowerBook G3; Apple Computer, US) through MacLab (ADInstuments, US) attached to pulse oximeters. In supine and 5°, 10°, 15°, 20°, 25°, 30° Trendelenburg position, we recorded the values and pulse waveforms of forehead-sensing and finger-sensing pulse oximeter. Data are presented as mean ± SD, repeated measures ANOVA and paired t-test were used to analyze the value change between supine and Trendelenburg position, and p-value < 0.05 was considered statistically significant.
Results: In supine position, the value of forehead-sensing pulse oximeter was 98.2 ± 1.54 %, and finger-sensing pulse oximeter was 99.2 ± 0.87 %. As increased degrees of Trendelenburg position, as the value of forehead-sensing pulse oximeter decreased, and a new top appeared in the pulse waveform. In 30° Trendelenburg position, the value of forehead-sensing pulse oximeter significantly decreased from 98.2 ± 1.54 to 83.6 ± 8.67 % (P=0.0005) in comparison with supine. On the other hand, the change in the value of finger-sensing pulse oximeter was minimum (99.2 ± 0.87 to 99.5 ± 0.69 %, p=0.27), and no pulse waveform changes were recognized.
Discussion: Our results show that forehead-sensing pulse oximeter is not reliable in Trendelenburg position. Since there is no venous valve in the head, forehead peripheral venous pressure rises easily in Trendelenburg position. We presume that the new top in the pulse waveform of forehead-sensing pulse oximeter was a component of forehead peripheral venous waveform. It was detected as peripheral arterial pulse wave by forehead-sensing pulse oxemeter, and the oximeter showed decreased value in Trendelenburg position.
References:
(1) Crit Care Med 31: A72, 2003.
(2) Anesth Analg 98: S92, 2004.

S-208.

PATIENTS' CHARACTERISTICS INFLUENCING THE PERFORMANCE OF THE INTUBATING LARYNGEAL MASK AIRWAY (FASTRACH ™)

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Introduction: It is important for anesthesiologists to identify patients' characteristics that are likely to influence airway management. Fastrach™(FT), an intubating laryngeal mask airway, retains most of the ventilatory features of the classic LMA™ but is designed primarily as a conduit for endotracheal intubation. It has been proven effective for intubation of normal or difficult airways.[1, 2]Yet, no predictor has been clearly identified to help anticipate how appropriate this device is with regard to patients' specific features. The purpose of this prospective unblinded study is to determine what characteristics, if any, influence the utilisation of the FT, particularly the time and number of attempts needed for tracheal intubation.
Methods: After obtaining approval from the Institutional Review Board and written consent from each participant, patients scheduled to undergo elective surgery with general anesthesia were recruited. Before surgery, morphometric and demographic factors known to be associated with difficult direct laryngoscopy, or believed to influence the utilisation of FT, were recorded. All patients were paralyzed before insertion of a FT size # 4 by a single experienced investigator. Then, a normal endotracheal tube (ETT) # 7.0 or 7.5 was inserted blindly through the FT. The number of attempts and time needed for intubation were recorded. Failure to intubate was defined as the inability to place the ETT into the trachea after three attempts. Correlation coefficients between time or number of attempts and studied factors were calculated.
Results: Two hundred patients were studied. Intubation was successful in 196 patients (98%); 168 on first (84%), 24 on second (12%) and 4 on third attempt (2%). Mean time to intubate was 78.1 (+/-56.4) seconds. Time to intubation and number of attempts increased with weight, height and neck circumference (Table). Some factors known to be associated with difficult direct laryngoscopy such as Mallampati class and mouth opening did not influence the performance of the FT but number of attempts increased with thyromental distance.
Discussion: The FT is an effective alternative for endotracheal intubation. Still, multiple attempts and increased time to intubation are associated with heavier, taller patients and individuals exhibiting larger necks. These characteristics should be taken into consideration to optimize the choice of an airway management device.
References:
1.Anaesthesia 1998;53(12):1174-1179
2.Anesthesiology 2001;95(5):1175-1181

	Characteristic	Correlation coefficient	95% confidence interval	P value significant (Bonferroni correction)
Correlation between time to intubate and:	Weight [1]	0.2518	0.1171 to 0.3774	*
	Height [1]	0.2919	0.1596 to 0.4139	*
	Neck circumference [1]	0.3337	0.2044 to 0.4516	*
	Body mass index [1]	0.1015	-0.0378 to 0.2369	ns
	Mallampati class [2]	-0.0248	-0.1671 to 0.1184	ns
	Thyromental distance [1]	0.0824	-0.0570 to 0.2187	ns
	Mouth opening [1]	0.0439	-0.0955 to 0.1815	ns
Correlation between number of attempts to intubate and:	Weight [1]	0.2343	0.0987 to 0.3613	*
	Height [1]	0.3042	0.1728 to 0.4251	*
	Neck circumference [1]	0.3188	0.1884 to 0.4382	*
	Body mass index [1]	0.0763	-0.0631 to 0.2061	ns
	Mallampati class [2]	-0.0296	-0.1717 to 0.1137	ns
	Thyromental distance [1]	0.2187	0.0824 to 0.3469	*
	Mouth opening [1]	0.1227	-0.0164 to 0.2571	ns

1.Pearson correlation coefficient
2.Spearman correlation coefficient
* p<0.05

S-209.

FLEXIBLE AND TAPERED TIP TUBE FACILITATES CONVENTIONAL OROTRACHEAL INTUBATION DONE BY NOVICE INTUBATORS

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Introduction: Orotracheal intubation is the standard technique for airway management, which however is sometimes accompanied by several untoward airway complications. To avoid airway trauma by the tip of the tube during intubation, the Parker Flex-Tip tube (PFT) was developed. The tube has a flexible, tapered tip, and characteristic structure, and passes easily through even a narrow glottis. The shape of PFT facilitates fiberoptic orotracheal intubation and introducer-guided tracheal intubation. However, there has been no report on the efficacy of PFT for conventional orotracheal intubation. In this study, we compared PFT to a standard endotracheal tube (SET) in regard to easiness of passing the tip of the tube through the glottis during conventional orotracheal intubation and incidence of postoperative sore throat and hoarseness.
Methods: One hundred thirty- two patients (66 men and 66 women) scheduled for elective anesthesia using orotracheal intubation were randomized to either PFT or SET. The intubators were classified into three groups according to the experience: two staff anesthesiologists (SA), two inexperienced anesthesiologists (IA) and six anesthesia trainees (AT). The sizes of each tube were 8.0-mm internal diameter (I.D.) for males and 7.5-mm I.D. for females. The tube was selected by a controller and the time required for completion of intubation was measured. Incidence of postoperative airway complications was also investigated.
Results: SET was used in 66 cases, and PFT in 66 cases. In each intubator group (SA, IA, and AT), SET was used in 22 patients (male/female were 11/11) and PFT in 22 patients (male/female were 11/11). No significant differences were found among patient groups. PFT did not reduce the incidence of postoperative airway complications and did not facilitate passing of the tip through the glottis. However, a detailed analysis revealed that PFT decreased the time needed for passing the tip of the tube through the glottis in a novice intubator group (group AT).
Discussion: The features of PFT are designed to minimize or eliminate damage to the airway caused by the tube tip during intubation. It has been reported that the shape of PFT facilitates fiberoptic orotracheal intubation (1) and introducer-guided tracheal intubation (2). In this study, we showed that PFT required less time to be passed through the glottis than SET in group AT in conventional orotracheal intubation. Contrary to our expectation, use of PFT did not decrease the incidence of postoperative sore throat and hoarseness.
Conclusion: We may conclude that the use of PFT (flexible tapered tip tube) is beneficial for novice anesthesia trainees during conventional orotracheal intubation.
References:
(1) Anesthesiology 98: 354-8, 2003.
(2) Anesth Analg 97: 285-288, 2003.

S-210.

RELIABILITY OF THE PULSE OXIMETER PERFUSION INDEX AS AN INDICATOR OF FINGERTIP BLOOD FLOW

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Introduction: During the perioperative period, evaluation of peripheral perfusion would be useful in early detecting decreased circulating volume, thermoregulatory responses or anaphylactoid reactions, and assessing the effects of vasoactive agents. The pulse oximeter perfusion index (i.e., the ratio between the pulsatile and nonpulsatile component of the pulse oximetry signal) has been suggested to reflect changes in peripheral perfusion (1, 2). However, its usefulness in assessing peripheral perfusion has not yet been fully established. In this study, using the laser Doppler flowmetry, we evaluated the reliability of the pulse oximeter perfusion index as an indicator of fingertip skin-surface blood flow.
Methods: With IRB approval and informed consent, we studied seven healthy (ASA-PS I) volunteers (7 males, 27 - 46 yr, Height = 170 ± 4 cm, Body weight = 65 ± 7 kg). Changes in the pulse oximeter perfusion index and fingertip blood flow estimated by the laser Doppler flowmeter were simultaneously measured in the volunteers 1) during stepwise increases (0-160 mmHg) in pressure of the pneumatic tourniquet applied to their upper arms and after its deflation, 2) during immersion of the non-monitored hand in cold (~4°C) water, 3) during the Valsalva test, and 4) during elevation of the monitored arm. ANOVA, contrast, and correlation were used to analyze the data. Data were expressed as mean ± SEM.
Results: 1) In response to the increases in cuff pressure above 20 mmHg, both the perfusion index and the laser Doppler blood flow significantly decreased ($p < 0.05$). Excellent correlation was observed between the changes in the perfusion index and the laser Doppler flow ($r = 0.99$, $p < 0.0001$). 2) In response to the immersion in cold water, both the perfusion index and the laser Doppler blood flow immediately decreased ($p < 0.05$). Excellent correlation was again observed between the changes in the perfusion index and the laser Doppler flow ($r = 0.97$, $p < 0.0001$). 3) Both the perfusion index and the laser Doppler blood flow also significantly decreased ($p < 0.05$) during the Valsalva manuever, and excellent correlation was observed between the changes in the perfusion index and the laser Doppler flow ($r = 0.92$, $p < 0.0001$). 4) In response to the arm elevation, the laser Doppler blood flow greatly decreased ($p < 0.05$), while the perfusion index significantly increased.
Conclusions: The increase in perfusion index during the arm elevation presumably reflected a decrease in the non-pulsatile signal derived from the venous blood. As far as the non-pulsatile signal does not change, the perfusion index appears to serve as a reliable index of fingertip skin-surface blood flow.
References:
1. Clin Exp Pharmacol Physiol 1989; 16:403-15
2. Crit Care Med 2002; 30:1210-3

S-211.

COMBINED INTERNATIONAL MULTI-CENTER PHASE I AND II STUDY ON SAFETY AND PERFORMANCE OF THE AMBU A/S LARYNGEAL MASK

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Introduction: Since the introduction of the LMA, supraglottic airway devices have become an established tool in airway management.[1,2] The Ambu laryngeal mask airway is a new disposable supraglottic airway device similar in design to the LMA-Classic. This multi-center trial was designed to evaluate the performance and safety of the Ambu laryngeal mask in elective surgical patients during positive pressure ventilation.
Methods: Following approval by the local Ethics Committees and written informed consent, 118 (29-30 at each center) patients presenting for elective surgery under total intravenous anesthesia were included. Patients were ASA I/II, Mallampati I/II, aged 18-65 years with a BMI <30 kg/m^2. Propofol was used for induction (2.5mg/kg) and maintenance (12mg/kg/hr propofol) of anesthesia along with a choice of narcotic agent. Patients were ventilated with intermittent positive pressure ventilation, a respiratory rate of 12/min, an inspiratory/expiratory ratio of 1:2, a fresh gas flow of 3L/min in order to maintain CO_2 <45mmHg and SpO_2 ≥95%. Data was collected on size of device, number of insertion attempts, cuff inflation, and oropharyngeal leak pressures. The position of the Ambu laryngeal mask was confirmed with fiberoptic endoscopy and the view recorded. Perioperative and postoperative complications were noted. Patients were examined for sore throat, dysphonia, and dysphagia 1hr and 24hrs postoperatively.
Results: Demographically, patients were 42.8±13.97yrs of age (60.2% female, 39.8% male), 171.2±8.30cm in height, with a BMI of 24.5±3.11kg/m^2 and Mallampati grade I/II (62.9%/37.1%) Patients received a size 3 (0.8%), 4 (51.7%), or 5 (47.5%) Ambu laryngeal mask, according to manufacturer's recommendations. A cuff pressure of 60cm H_2O was accomplished with a volume of 24.3±5.41mL of air. Duration of surgery was 67.0mins (25-250mins). All patients were successfully intubated on the first or second attempt (92.4% and 7.6%, respectively) with an insertion time of 44.9±37.91sec. Oropharyngeal leak pressures were 24.1±5.44cm H_2O. The vocal cords could be visualized by fiberoptic endoscopy in 91.5 % patients and adequate ventilation was achieved in all patients. Complications included blood on the device (8.5%), bucking during removal (0.8%), and minor trauma to the tongue (0.8%), or lips (0.8%). Postoperative complaints 1hr after surgery were sore throat (mild-5.1%, moderate-1.7%), dysphonia (mild-0.8%), dysphagia (mild-2.5%, moderate-1.7%). For complaints 24 hrs after surgery only mild sore throat (2.2%) and mild dysphonia (1.1%) remained.
Discussion: In anesthetized, non-paralyzed patients, the Ambu laryngeal mask is easy and quick to insert. It forms a safe and efficient seal during positive pressure ventilation. Further studies are warranted.
References:
1. Anesth Analg 1996;82:129-33.
2. Anesthesiology 1996;84:686-99.

S-212.

A COMPARISON OF LARYNGOSCOPY TECHNIQUES USING THE VIDEO LARYNGOSCOPE AND THE TRADITIONAL MACINTOSH LARYNGOSCOPE IN POTENTIALLY DIFFICULT TO INTUBATE PATIENTS

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Introduction: The Video Laryngoscope (VL, Karl Storz, Tuttlingen, Germany) is designed to optimize visualization of the airway by projecting an enlarged video image of the laryngeal structures onto a monitor[1]. The purpose of this study is to determine if the VL is useful in patients at risk for difficult intubation, as compared to the traditional Macintosh laryngoscope (ML).
Methods: Following approval by the Institutional Review Board, written informed consent, and randomization, either the VL or ML was used in 100 anesthetized patients that presented with one or more of the following features: (1) history of difficult intubation, (2) morbid obesity (BMI≥35kg/m^2), (3) small mouth opening (<3 cm), (4) limited neck mobility, (5) Mallampati class III, (6) short thyromental distance (<6 cm). The direct view of the laryngeal structures using the Cormack-Lehane (CL) grading system, as modified by Yentis and Lee[2], was noted for all cases. The monitor view was noted for all VL cases. The use of optimal external laryngeal manipulation (OELM) and epiglottis lifting was noted and whether these maneuvers improved the CL grade. The level of difficulty in the performance of intubation and number of attempts were recorded. Postoperative assessment of sore throat, hoarseness, and nausea/vomiting was also conducted.
Results: Demographically, there were no significant differences between the VL and ML groups. All VL cases exhibited a monitor view of ≤2b, as compared to 78% of the ML cases ($p<0.001$). In 98% of the VL cases with a direct view >1, the CL grade improved by ≥1 with the monitor view. OELM was required less often when using the VL, 34% vs. 67% ($p<0.001$). In cases utilizing epiglottis lift, the view was improved in all VL patients as compared to 71% of ML patients ($p<0.01$).
Discussion: The monitor view of the laryngeal structures using the VL is superior in comparison to the traditional ML for potentially difficult intubations. OELM is not as necessary when using the VL. Epiglottis lifting consistently allows a superior view when utilized with the VL. This study suggests that the VL is an effective tool in patients at risk for difficult intubation.
References:
1. J Clin Anesth 2002; 14: 620-6.
2. Anaesthesia 1998; 53: 1041-4.

*p<0.05 were considered significant. Difficult CL are bolded.

	UVIS	MAC	p-value
CL Direct View I:IIa:**IIb:III:IV** (n)	9:9:**14:17:1**	15:15:**9:10:1**	**0.03**
CL Monitor vs. ML View I:IIa:**IIb:III:IV** (n)	30:10:**10:0:0**	15:15:**9:10:1**	**<0.001**
Duration of Laryngoscopy (sec)	26±20.4 (2-90)	25±25.3 (7-150)	0.95
# of attempts 1:2:3	44:3:1	40:4:1	0.72
Assisted/Alternative Device (None:Mild:Moderate:Severe)	2	5	0.24
Difficulty Level	29:11:6:2	20:17:9:4	0.07
Sore Throat	29:14:4:0	23:17:4:4	0.07
Hoarseness	39:7:1:0	35:10:2:1	0.17
Nausea/Vomiting	34:12:1:0	28:16:2:2	0.07

S-213.

EVALUATION OF ALTERNATIVE PULSE OXIMETER MONITORING SITES FOR THE DIFFICULT TO MONITOR SURGICAL PATIENT

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Introduction: In cases of low perfusion, pulse oximeter monitoring on patients' digits can be impossible. Other sites have been investigated, including the forehead, ear and nose.[1],[2],3 However, venous pooling and venous pulsations can cause forehead sensor failure. We identified a population of surgical patients at risk for forehead venous pulsations or pooling and we evaluated alternative monitoring sites.
Methods: 11 IRB-approved adult surgical patients in lithotomy and or trendelenberg were studied. All patients were monitored with Nellcor's N595 (Max-A sensor), Masimo's SET Radical (LNOP Adt sensor) as finger controls and as test sensors the Nellcor N595 MaxFast on the forehead (with a headband), Masimo's SET Radical TC-I on the ear and nose. $Sp0_2$ and pulse rate from all five sensors were continuously logged on computer throughout surgery. Error is defined as difference between test sensors and mean of two digit sensors during stable patient conditions. Data were analyzed using bias (mean error) and precision (standard deviation of error) for each patient, E>7% (percentage of time which error was greater than 7% during stable conditions), sensor failure (E>7% for more than 20 % of surgical duration) and Performance Index (percentage of time which SpO_2 reading is within 7% of control value). Data were compared using paired t-test and Chi-squared test as appropriate, with $p<0.05$ considered significant.
Results: Data are presented as mean (±SD). Mean patient age was 41 (±15) years. Mean surgical length was 94.6 (±43.9) minutes. Bias and precision between digit sensors was ¯0.21 (±0.61) and 0.46 (±0.31) (respectively). Table lists other sensor performance data.
Discussion: This population of difficult to monitor surgical patients (as demonstrated by poor forehead sensor performance), bias and precision of the TC-I was similar whether it was placed in the nose or on the ear. Both ear and nose sites demonstrated small E>7%, indicating a high degree of monitoring reliability for both sites, no failures and better Performance Index than the MaxFast forehead sensor. Our data demonstrates the nose and ear to both be useful sites for Spo2 monitoring of surgical patients who are otherwise difficult to monitor.
References:
1. Anesth Analg 2004; 98; 5S:S10.
2. Anesth Analg 2004; 98; S-92.
3. Anesth Analg 2004; 98; S-94.

Table: Performance characteristics of head sensors. # = p≥0.05 compared with Nellcor Max-Fast sensor.

Sensor	Bias	Precision	E>7% (minutes)	# Of sensor failures	Performance Index
Nellcor MaxFast (Forehead)	-4.77 (±11.7)	3.61 (±5.37)	22.4 (±47.8)	3	76.3
Masimo TC-I (Ear)	-0.3 (±1.0)	0.7 (±0.26)	0.1 (±0.3)	0 #	99.9 #
Masimo TC-I (Nose)	0.2 (±0.8)	0.5 (±0.3)	0 (±0)	0 #	100 #

S-214.

IMPACT OF HEADBANDS ON PERFORMANCE OF 2 FOREHEAD REFLECTANCE OXIMETERS ON DIFFICULT TO MONITOR SURGICAL PATIENTS

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Introduction: Venous pooling and venous pulsations can cause pulse oximeter forehead sensor failure. A recent study compared two pulse oximetry reflectance sensors on patient's forehead.[1] At that time, only Masimo recommended headband use. Shelley reported changed plethysmographic waveforms (more arterial-like) with headband use.[2] We identified a population of surgical patients at risk of forehead venous pulsations or pooling. In this population, we studied the impact of headbands on the performance characteristics of two sensors.
Methods: 19 IRB-approved adult patients in lithotomy and or trendelenberg positions were studied. All patients were monitored with Nellcor's N595 (Max-A sensor), Masimo's SET Radical (LNOP Adt sensor) as finger controls and as test forehead sensors Masimo's SET Radical TF-I sensor and Nellcor's N595 MaxFast. Forehead sensors were secured via manufacturer's headbands. $Sp0_2$ and pulse rate from four sensors were continuously logged on computer throughout surgery. Error is defined as the difference between either of forehead sensors and mean of two digit sensors during stable patient conditions. Data were analyzed using bias (mean error) and precision (standard deviation of error) for each patient and Performance Index (the percentage of time during which a displayed SpO_2 reading is within 7% of control value). Data were compared using paired t-test with $p<0.05$ considered significant.
Results: Data are presented as mean (±SD). Mean patient age was 45.3 (±18) years. Mean surgical length was 76.6 (±41.7) minutes. Bias and precision of digit sensors was ¯0.42 (±0.94) and 0.49 (±0.37) (respectively). Performance Index values were 90.8% for Masimo, and 80.6% for Nellcor. Table below lists forehead sensor performance.
Discussion: Our previous study demonstrated the performance of Masimo's TF-I to be significantly superior to Nellcor's MaxFast.1 This difficult patient population, despite a clear trend towards significance, bias and precision differences didn't reach statistical significance. Headbands may have caused minor performance improvement of the MaxFast sensor. However, Masimo's TF-I demonstrated superior Performance Index; 90.8 (Masimo) vs. 80.6 (Nellcor), theoretically due to Masimo's SET technology. In conclusion we do not recommend the use of forehead reflectance pulse oximetry sensors in this patient population.
References:
1. Anesth Analg 2004 98;5S:S10.
2. Anesth Analg 2004 98;5S:S12.

Table: Performance characteristics of forehead sensors using headbands on each.

	Bias (%)	Precision (%)	E>7% (minutes)	Performance Index
Masimo TF-1	-0.38 ± 1.98	1.37 ± 1.69	7.06 ± 19.41	90.8
Nellcor MaxFast	-3.06 ± 9.17	3.01 ± 4.57	14.89 ± 37.08	80.6
P value	0.15	0.13	0.12	-

S-215.

EFFECT OF BODY POSITION FIXATION DEVICE IN PREVENTING EARLY POSTOPERATIVE ATELECTASIS: EVACUATED BEAN BAG VERSUS CONVENTIONAL FIXATION DEVICE

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Introduction: Lateral decubitus surgeries sometimes result in serious atelectasis in the dependent lung. Recently, a new fixation device (evacuated bean bag) has been used, but its effect on the lung has not been studied. We compared the effects of evacuated bean bag and conventional fixation device in preventing early postoperative atelectasis.
Methods: With institutional review board approval and informed consent from each patient, 75 patients scheduled for hip joint surgery were recruited. After combined epidural-general anesthesia, the body position was fixed using an evacuated bean bag in 41 patients (group E) and conventional fixation device (group N). After surgery and before extubation, radiograph was taken supine position under 66% N_2O inhalation by spontaneous respiration. The radiologist evaluated the pre- and post-operative radiographs for lung volume loss, opacity and atelectasis. The postoperative radiographs were rated as normal, light (volume loss), mild (faint opacity), or severe (dense opacity in over 1/4 or atelectasis).
Results: Normal postoperative radiograph was observed in 7.3% in group E and 14.7% in group N. Light, mild and severe grades were, respectively, 26.8, 31.7 and 34.1% in group E versus 17.6, 38.2 and 29.4% in group N, with no significant differences. However, in cases showing increased opacity, those in group E tended to be diagnosed to be more severe. Among patients rated as severe, the BMI was significantly higher in group N (mean = 26.5) than group E (mean = 21.7). Definitive atelectasis was observed in 10 patients (6 in group E and 4 in group N). Although there was no significant differences in findings depending on the laterality of the dependent lung, radiographs on the next day of surgery tended to show abnormality remaining in the left lung group E and in the right lung in group N.
Discussion: Evacuated bean bag limits thoracic movement in the dependent lung, and was suspected to cause more lung abnormalities than conventional fixation device, but the present study showed no significant differences between the two. Since lung abnormalities were observed even in patients with low BMI, more attention is needed in positioning. The fact that left-right differences were observed on the day after surgery despite no laterality difference in lung findings suggest that since the evacuated bean bag compresses both the thorax and intra-abdominal organs, the left side without the liver is more affected by compression elevating the diaphragm.
Conclusion: We used the new body fixation device (evacuated bean bag) in hip joint surgeries and evaluated the effects on the lung. Although the evacuated bean bag had the same effects as the conventional fixation device, even patients with low BMI showed lung abnormalities. More attention is needed to fix the position with evacuated bean bag.

S-216.

GASTROESOPHAGEAL REFLUX DURING ANESTHESIA AND CONTROLLED VENTILATION WITH SEVEN AIRWAY DEVICES

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INTRODUCTION: The incidence of gastroesophageal reflux with different airway devices has not been determined.
AIM: To investigate the incidence of gastroesophageal reflux with seven airway devices.
METHODS: We evaluated respiratory mechanics during positive pressure ventilation and the incidence of gastroesophageal reflux (GER) with six supraglottic devices or endotracheal tube (ETT). Seventy patients undergoing peripheral surgery under general anesthesia were randomly allocated to seven groups of ten patients ventilated with: perilaryngeal airway (CobraPLA), laryngeal mask airway classic (LMAC), Fastrach, ProSeal, laryngeal tube, cuffed oropharyngeal airway (COPA), and ETT. Anesthesia was induced with propofol. After insertion of the designated device, the lungs were mechanically ventilated (positive pressure ventilation was maintained in a volume mode with a tidal volume of 7 mL.kg-1 and a respiratory rate of 10 breaths/min). Hypopharyngeal pH, peak inspiratory pressures (PIP), leak pressures, pulmonary compliance, end-tidal CO2, and oxyhemoglobin saturation were measured. For the pH monitoring a semi-disposable antimony catheter with external reference electrode (Medtronics Functional Diagnostics Inc. MS, USA) was used. Electrode calibration was made using buffer solutions of pH 1 and 7. The catheter was introduced trans-nasally to the hypopharynx just above the vocal cords under direct vision of a laryngoscope and taped in that position. Examination duration was throughout surgery. All information was digitally recorded and analyzed on a special software. A pH<4 was considered as a reflux event.
RESULTS: Demographic data and preoperative airway assessment tests (Mallampati class, thyro mandibular distance, mouth opening, neck movement and upper teeth examination) were similar among the groups. Twenty-two percent of patients with supraglottic devices had reflux events, with the highest incidence being recorded with the LMAC and COPA (40% each) whereas no reflux was detected with the ETT. Peak inspiratory pressures were lower with LMAC and ProSeal (P = 0.014) and leak pressures were greater with ProSeal (P<0.01) than with the other devices (Table 1). The CobraPLA performed as well as the Fastrach and ProSeal and better than the LMAC, COPA, and laryngeal tube. However, the ProSeal had the highest sealing pressure. Among the supraglottic devices, the lowest incidence (10%) of reflux was recorded with the CobraPLA, Fastrach, and ProSeal.
CONCLUSIONS: The incidence of reflux with the new CobraPLA, the Fastrach and ProSeal was low when compared to the other supraglottic airway devices.

Table 1 - Univariate analysis of pH and ventilation variables

Device Variable	Cobra N=10	LMA clas-sic N=10	Fastrach N=10	ProSeal N=10	Laryngeal Tube N=10	COPA N=10	Tracheal Tube N=10	P
SpO2% baseline	99±1.2	97.7±1.2	98.8±0.8	98.8±1	98.2±1.2	97.7±2.1	99±0.4	0.029
1	98.8±0.8	97.9±1.1	98.3±0.5	98.8±0.6	98.6±0.5	98.1±1.4	98.8±0.9	0.1
2	98.5±0.7	97.3±1.4	98.2±0.8	98.6±0.8	98.5±1	97.9±0.9	98.6±0.7	0.014
EtCO2								
1	38.3±4.4	38.9±4.2	39.2±4	38.9±4.8	38.1±3.9	36.3±4.6	37.1±4.6	0.7
2	37.5±5.4	35.8±3.6	37.9±4	38±4.7	34.9±6	36.6±4.2	34.6±5.1	0.5
pH Average	6.02±1.1	5.5±2.1	6.2±1.2	6.6±1	6.5±0.9	7.1±1.1	6.9±1.3	0.1
Minimum value*	5.5±1.1	5±1.9	5.7±1.2	5.6±1.6	5 ±1.4	4.7±2.1	6.2±1.2	0.3
Episodes of pH<4**	1	4	1	1	2	4	0	0.08
PIP - cmH2O								
1	21.1±6.9	16±2.3	21.3±4.8	24.6±6.2	18.2±2.4	21.8±3.2	22.4±7.4	0.014
2	21.8±7.7	16.5±1.3	22.9±3.4	22±6.9	18.8±5.5	21.5±6	20.8±6.4	0.2
Compliance-mL / cmH2O				43.1±14.		37±20.8		
1	40.9±13.1	42.6±11.5	42±11.8	7	43.4±18.5	37.6±15.	43.8±18.9	0.9
2	42.9±14	40.3±11.7	40.5±11.8	43.4±14. 8	40.4±16.6	7	43.7±16	0.9
Seal pressure-cmH2O	25.6±3.5	23±1.2	23.1±0.9	30.4±6.4	26.1±1.7	25.4±2.2		0.01

S-217.

PRELIMINARY REPORT: INTRAOPERATIVE COMPARISON OF BAIR HUGGER™ WITH VITALHEAT™, A UNIQUE WARMING SYSTEM

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Introduction: The Vitalheat (Dynatherm, Burlingame CA 94010) is a non-invasive device that has been proposed as being able to deliver heat to the thermal core of hypothermic subjects. Heat is applied to the palm of the hand which is encased in a sealed vacuum "mitt". Heat transfer between the warming element and the body is accelerated by the creation of a vacuum around the hand which is thought to open arteriovenous channels (1). Previous studies using similar technology have yielded mixed result (2, 3). The present study compares Vitalheat (a new rendition of the technology) to the Bair Hugger (Augustine Medical, Eden Prairie MN 55344) in their ability to maintain intraoperative body temperature.
Material and methods: Informed consent was obtained from 24 patients ASA1 -2 (Ages 24 to 63 years) undergoing routine general anesthesia (GA) for knee surgery. Patients were given either an upper body Bair Hugger or the Vitalheat mitt after induction of anesthesia. Tympanic temperatures were measured continuously in both ears using Mon-a therm (model 6510) Mallinckrodt, St. Louis, MO 63042). The highest temperature value obtained was recorded at 3 intervals: after the device was placed, at the conclusion of surgery when the devices were removed, and in PACU.
Results: Patient characteristics, duration of anesthesia, and average initial temperatures in both groups were similar. Patients receiving the Bear Hugger were, on average, approximately one half of a degree (0.47 degrees Celsius) warmer than those managed with the Vitalheat device at the conclusion of surgery (See Table 1). This small difference did reach statistical significance. There was a slight trend for the Vitalheat group to appear colder by subjective criteria as well. None of the observed differences between the two groups reached any level of clinical significance. No complications attributable to either device were observed.
Conclusion: Patients warmed with the Bear Hugger demonstrated a small but significantly greater temperature when compared with the Vitalheat warming mitt. The Vitalheat device appeared safe and well tolerated in cases lasting as long as 5 hours. Continued development of the Vitalheat technology is in progress.
References:
1. J. Appl. Physiol. 85: 1643-8, 1998
2. J. Emergency Medicine. 17: 725-730, 1999
3. Anesth Analg. 89: 1541-5, 1999

Table 1: Comparison of Bear Hugger with the Vitalheat warming mitt

	Bear Hugger		Dynatherm		P value
	Mean	SD	Mean	SD	
Age(yr)	41.25	15.57	35.92	13.43	0.38
Sex (M/F)	6/6		5/7		1.00
Weight (kg)	108.67	61.89	84.17	28.99	0.23
1st Temp Reading	36.10	0.44	36.08	0.47	0.89
Last Temp Reading	36.15	0.51	35.68	0.56	0.04
Length Anes/Sur (min)	76.07	48.60	100.92	70.82	0.33
Temp arrive PACU	35.91	0.39	35.58	0.58	0.11
Patient Response (ar/consc/nr)	7/5/0		8/3/1		0.67
Shivering (0/1/2)	10/1/1		7/2/3		0.46
Toes Warm (no/yes)	1/11		3/9		0.59
Toes Cold (no/yes)	11/1		7/5		0.16
Color Face (flush/palid)	12/0		10/2		0.46
Color Hand (flush/palid)	12/0		10/2		0.46

t test or Fisher exact test

S-218.

EFFECT OF WARMING TECHNIQUE ON OUTCOME AFTER MAJOR LAPAROSCOPIC SURGERY: FORCED AIR WARMING VS WARMED AND HUMIDIFIED INSUFFLATION GAS

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Introduction: In the absence of active warming, perioperative hypothermia can occur after major laparoscopic procedures. Administration of heated and humidified insufflation using the Insuflow™ device has been alleged to more effectively maintain core body temperature than dry, room temperature insufflation. However, controversy exists regarding the relative efficacy of this technique compared to external forced air warming. A randomized, sham-controlled study was designed to test the hypothesis that external forced air warming is more effective than warm humidified intraperitoneal insufflation in maintaining core temperature and improving the patient's quality of recovery.
Methods: Thirty-six morbidly obese patients undergoing elective laparoscopic gastric bypass procedures under a standardized anesthetic technique were randomly assigned to either a *Control group* receiving forced air warming and an "inactive" Insuflow device (with room temperature dry carbon dioxide gas insufflation), or an *Experimental group* receiving warmed and humidified intraperitoneal gases with an Insuflow device and a "sham" forced air warming blanket. Esophageal and/or tympanic membrane temperatures were measured at specific time intervals during the perioperative period. Postoperative pain was assessed using an 11-point verbal rating scale, with 0=none to 10=maximal. In addition, postoperative opioid analgesic requirements, incidences of nausea and vomiting, as well as the quality of recovery (using an 18-point questionnaire) were evaluated, with *p<0.05 vs *Control group*.
Results: Compared to the Insuflow group, use of forced air warming was associated with significantly higher intraoperative core body temperatures at the end of surgery. However, at 60 min after surgery in the PACU the tympanic membrane temperatures were not significantly different in the two groups. Postoperative pain scores and opioid analgesic requirements (PCA morphine 47±12 vs 58±16 mg) were significantly lower in the Insuflow (vs forced air) warming group. The Insuflow group also experienced less PONV at 24 h (28 vs 50%) and 48 h (11 vs 22%) after surgery.

	Control Group (Forced air warming)	Experimental Group (Warm humidified insufflation)
Age (yr)	43±10	44±10
Weight (kg)	132±19	129±16
Gender (F/M) (n)	16/2	16/2
Propofol (mg)	179±35	165±27
Fentanyl (μg)	504±265	476±211
Desflurane ave. (end-tidal %)	4.9±1	4.8±1
Surgery time (min)	128±29	132±28
Core body temperature (°C)		
at start of surgery	35.8±0.4	35.8±0.4
at end of surgery	35.9±0.5	35.3±0.7*
Tympanic temperature at 60 min in PACU (°C)	36.3±0.4	35.9±0.7
Time to first pain rescue	46±21	73±44*
Quality of recovery (0-18)		
at 24 h	12 (10-14)	13 (12-14)
at 48 h	15 (14-17)	16 (15-17)
Hospital stay (days)	2 (2-2)	2 (2-2)

Discussion: The Insuflow device would appear to be a useful supplement to forced air warming during major laparoscopic surgery. Although less effective in maintaining core body temperature, the Insuflow improved pain control and reduced the need for opioid analgesics and antiemetics in the postoperative period.

S-219.

COMPARISON OF TWO TYPES OF TRANSCUTANEOUS CARBON DIOXIDE SENSOR IN MICROLARYNGOSURGERY WITH HIGH FREQUENCY JET VENTILATION

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Introduction: In adult patients, measurements of transcutaneous carbon dioxide tension (PtcCO2) for non-invasive assessment of ventilation has not routinely introduced. Hypercarbia is one of the common problems in microlaryngosurgery with high frequency jet ventilation (HFJV). The aim of this study was to evaluate the usability and accuracy of two types of PtcCO2 sensors during HFJV in adult patients.
Methods: With approval of ethical committee and informed consent, eleven (ASA 1 or 2) adult patients aged 19 to 62 years for elective microlaryngosurgery with HFJV via thin tracheal tube (internal diameter; 4.0-6.0 mm) under propofol anesthesia were studied. The heated (42 degrees centigrade) new miniaturized PtcCO2/SpO2 single ear sensor (TOSCA monitor; Linde Medical Sensors, Switzerland) was applied at the ear lobe with a special low ear clip. The heated (42 degrees centigrade) traditional combined PtcCO2/PtcO2 sensor (9900MK2; Koken Medical, Japan) was also applied on the forearm or the chest. PtcCO2 measurements were compared to PaCO2 values analyzed by a calibrate blood-gas analyzer (288Blood Gas System; Ciba-Corning, USA). The simultaneously obtained PtcCO2 (TOSCA), PtcCO2 (9900MK2) and PaCO2 values during HFJV were compared by linear regression analysis. In addition, corresponding data were compared using paired Student t-test and Bland-Altman bias analysis.
Results: A total of 30 paired measurements were correlated in the PaCO2 range 2.9 to 7.2 kPa. No skin lesions occurred. PtcCO2 (TOSCA) values were highly correlated with PaCO2 ($r = 0.87$, $p < 0.01$) during HFJV. PtcCO2 (9900MK2) values were also highly correlated with PaCO2 ($r = 0.89$, $p < 0.01$).
Discussion: The HFJV via thin tracheal tube is a convenient method of ventilation during microlaryngosurgery, since it offers optimal visibility and easy access for surgical instruments into the airway. During HFJV, however, the assessment of carbon dioxide status is a challenge. Capnography values are invalid during HFJV, and an arterial catheter is not always indicated and feasible in microlaryngoscopy. The transcutaneous devices provide an effective method for non-invasive monitoring of PCO2 in situations whereas continuous, precise control of CO2 levels is desired such as perioperative period of microlaryngosurgery with HFJV.
References:
1) Eberhard P, et al. Anesth Anal 2002; 94: S76,
2) Mizushima A, et al. Anesthesiology 2004; 101: A563

S-220.

EVALUATION OF A COMPUTER-CONTROLLED CO_2 INFUSION SYSTEM FOR SPEEDING EMERGENCE FROM ISOFLURANE ANESTHESIA IN PIGS

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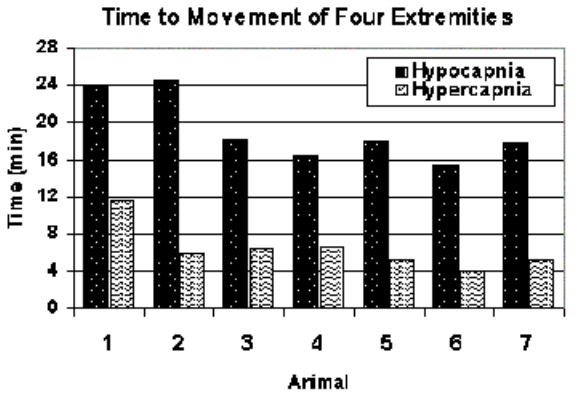
Introduction: Volatile anesthetics can be quickly removed from the lungs by hyperventilation. However, the resulting hypocapnia lowers cerebral blood flow and, thereby, increases emergence time. Studies have shown that infusing CO_2 during hyperventilation can dramatically decrease emergence time [1]. We have developed a feedback controlled CO_2 infusion system that maintains a precise end-tidal CO_2 ($EtCO_2$) level in the presence of hyperventilation.
Methods: The prototype device consists of a computer, CO_2 monitor (Novametrix Medical Systems Inc.), an external timer circuit, and a CO_2 injection valve. The computer runs a Proportional-Integral controller and uses the $EtCO_2$ value to determine the amount of CO_2 to be added to the inspired gas at the start of each breath. The controller's integral and proportional constants are a function of minute volume and respiratory rate.
Seven pigs were maintained at 2 MAC of isoflurane for two hours. The emergence times were compared during hypocapnic ($EtCO_2$=23 mmHg) and mildly hypercapnic ($EtCO_2$=55 mmHg) conditions. Hyperventilation (20 breaths/min) and increased fresh gas flow (10 L/min) were used for both emergence methods. Time to spontaneous breathing and movement of multiple limbs were recorded from the time the vaporizer was turned off. Two hypercapnic and hypocapnic wakeups were done for each animal. The animals were randomized as to which emergence technique was tested first.
Results: The controller kept the $EtCO_2$ at 54.9 ±1.04 mmHg during emergence. The controller had an average rise time (0-95%) of 23. 8 sec. Hypercapnic hyperventilation during emergence reduced the time to movement of all four limbs by 12.7 minutes ($p<0.005$) and time to spontaneous breathing by 14.7 minutes ($p<0.005$). The figure shows the emergence times for all seven pigs.

Discussion: Computer control is an accurate method of maintaining desired $EtCO_2$ during emergence. Maintaining mild hypercapnia during emergence in the presence of hyperventilation significantly decreased the emergence time from isoflurane anesthesia.
References:
1. British Journal Anaesthesia 2003; 91:787-92.



S-221.

AUDIBLE INDICATOR OF EXHALATION IMPROVES DELIVERED TIDAL VOLUME DURING BAG VALVE MASK VENTILATION OF A PATIENT SIMULATOR

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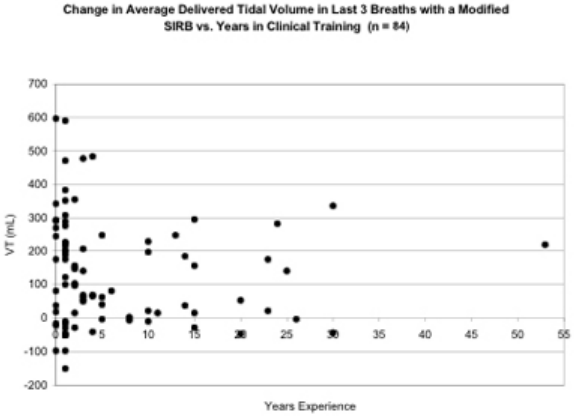
Self Inflating Resuscitation Bags (SIRB), can be misleading because the bag re-inflates even if a patient is not exhaling properly and thus not being properly ventilated. Personnel may not achieve an effective seal with a facemask. A simulator-based study was conducted to determine if an audible indicator of exhalation would improve delivered tidal volume (VT).

Methods: 86 subjects (54m, 32f) with clinical training averaging 6.4 years ± 9.4 years were studied. A reed whistle was added to the exhalation port of a standard adult SIRB as an audible indicator of exhalation. Clinical personnel and residents were randomly assigned to using the SIRB with (modified-SIRB) or without (standard-SIRB) audible feedback modification providing at least 5 breaths to the human patient simulator (HPS). VT delivered by all participants with the standard-SIRB and modified-SIRB was measured.

Results: Average and standard deviation for delivered VT (n = 86) was 486 ± 166 ml with the standard-SIRB and 624 ± 96 ml with the modified-SIRB. The average VT using the modified-SIRB was 138 ml larger than with a standard-SIRB (increase of 28%). Participants who used the standard-SIRB first (n = 43), delivered a VT of 439 ± 180 ml and 614 ± 98 ml with modified-SIRB. Participants using the modified-SIRB first (n = 43), delivered 533 ± 138 ml with the standard-SIRB and 633 ± 95 ml with the modified-SIRB. The increased VT with a modified-SIRB was 175 ml (175/439 = 40%) for participants who started with the standard-SIRB and 100 ml (100/533 = 19%) when the modified-SIRB was used first.

Discussion: The reed whistle produced a louder sound with a larger exhalation and helped participants deliver a more consistent VT. The standard deviation for participants indicates less variability in VT with the modified-SIRB. Percent increase in delivered VT with a modified-SIRB more than doubled, increasing from 19% to 40%, when participants first used the standard-SIRB. This suggests that when the modified-SIRB is used first, learning occurred. Improvement in tidal volume, when using a modifed SIRB, is evident over a wide range of clinical experience (figure).



S-222.

MEASUREMENT OF OXYGEN UPTAKE (VO_2) DURING ANESTHESIA BY A CLOSED CIRCLE VENTILATION SYSTEM WITH BELLOWS SPIROMETER AND PRECISION OXYGEN FLOWMETER

AUTHORS: **H. C. Howard**, S. S. Beroukhim, BSc, D. H. Chien, BSc, A. Rosenbaum, MD, P. H. Breen, MD, FRCPC;
AFFILIATION: University of California Irvine Medical Center, Orange, CA.

Introduction: Despite technological advances, no accurate calibrating measurement of VO_2 is available during anesthesia. Therefore, we have developed an accurate VO_2 measuring system comprised of a closed-circle ventilation circuit, bellows spirometer, and precision oxygen flowmeter. We hypothesized that the VO_2-spirometer will become a standard for measurement and calibration of VO_2 during anesthesia. To validate the system, the VO_2-spirometer was compared with oxygen consumption stoichiometrically generated by ethanol combustion in our previously reported metabolic lung simulator (MLS) (1).

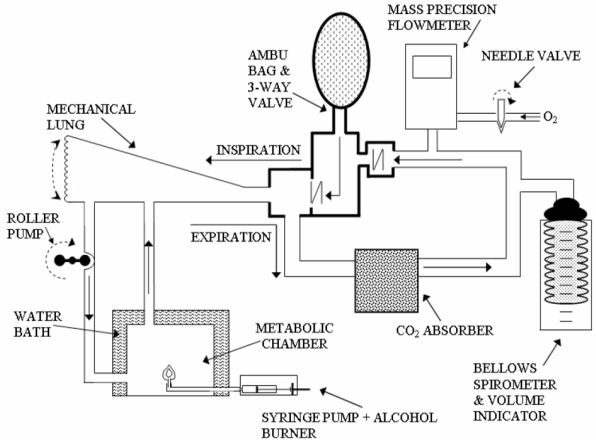
Methods: The VO_2-spirometer (Figure) was composed of an adult 'Ambu' bag, CO_2 absorber, and custom bellows-spirometer. Oxygen was infused into the circuit via a precision mass flowmeter. Prior to manual ventilation, the system was checked for leaks and flushed with 100% O_2. After the MLS had achieved steady state, signaled by stable end-tidal PCO_2 of about 40 mm Hg, the VO_2-spirometer was connected to the MLS and manual ventilation proceeded for 2 minutes at constant tidal volume. Oxygen inflow was adjusted to minimize changes in end-expired bellows spirometer volume. VO_2 was calculated as total infused O_2 over 2 minutes, corrected by any change in spirometer volume. In each experiment, VO_2-spirometer measurements were compared to stoichiometric reference values of VO_2 (50-500 ml/min) generated by 5 different combustion rates of ethanol in the MLS. Five experiments were conducted.

Results: Average percent error for VO_2 was -2.57 ± 4.11% SD. Linear regression analysis showed excellent correlation; slope, Y-intercept, and R^2 were 1.01, -4.79, and 0.99, respectively. Limits of agreement (LOA) ratio analysis demonstrated good agreement between the VO_2-spirometer and stoichiometric values generated by ethanol combustion. The LOA (mean ± 1.96 SD) were 0.97 ± 0.08, where 95% of all points lay within these limits.

Discussion: The VO_2-spirometer is a novel, non-invasive system that provides an accurate calibrating standard for VO_2 measurement during anesthesia. The VO_2-spirometer can also measure VO_2 during oxygen ventilation. We believe that VO_2 will become a vital tool in the assessment of tissue metabolism and detection of critical events during anesthesia (1).

References:
1. Anesthesiology 2004; 100: 1427-1437

Support By: NIH grant HL-42637 and NCRR grant M01 RR00827



S-223.

COMPARISON OF BIS INDEX VALUES TO STATE AND RESPONSE ENTROPY VALUES DURING DESFLURANE ANESTHESIA

AUTHORS: J. Tang, G. Romero, A. Sloninsky, R. Naruse, R. H. Wender, **P. F. White**;
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Introduction: Cerebral monitoring has become increasingly popular in anesthesia for improving the titration of anesthetic drugs. The most recently introduced cerebral monitor is the so-called entropy monitor which provides EEG-derived information about the brain's state (SE) and response (RE) entropy. This study was designed to compare the SE and RE values to the bispectral (BIS) index values at specific time points during general anesthesia.
Methods: 28 patients undergoing laparoscopic surgery were simultaneously monitored using both the BIS (Aspect Medical Systems) and entropy (GE/Datex) monitoring systems. The time to display the initial "baseline" index value was recorded. All patients were premedicated with midazolam 2 mg IV, and induced with propofol 1-2 mg/kg followed by maintenance of anesthesia with desflurane 2-8% in an air/oxygen mixture. Indices were compared at specific time intervals during the perioperative period. The presence of any electrocautery artifact was noted during the surgical procedure. Finally, the ability of the various indices to detect loss of conscious was assessed. Data were analyzed using ANOVA, with $p<0.05$ considered significant.
Results: The BIS and RE values were similar throughout the perioperative period (see Table); however, the SE values at baseline and upon awakening were significantly lower ($p<0.05$). Electrocautery artifacts more frequently interfered with the display of BIS (60%) vs entropy (12%) values. The area under the receiver operating characteristic (ROC) curve was smaller for the SE (0.90±0.04) vs BIS (0.97±0.04) and RE (0.98±0.04) values.

	BIS	RE	SE
Time to display index (sec)	48±37	42±21	42±21
Baseline value (u)	96±4	96±3	88±2*
Ave. value during surgery (u)	41±10	39±12	38±12
Value at end of anesthesia (u)	47±13	46±15	42±13*
Value upon awakening (u)	87±11	90±13	77±15*
Value upon orientation to person and place (u)	93±4	95±3	85±5*

*$p<0.05$ vs BIS
Discussion: SE values were consistently lower than BIS values during the perioperative period. However, the pattern of the changes in the RE and BIS indices were remarkably similar throughout the study. Furthermore, the sensitivity and specificity of the SE value in assessing consciousness was also lower than for the BIS and RE values.

S-224.

CORRELATING BIS AND AEP TO MEASURED PLASMA PROPOFOL CONCENTRATION

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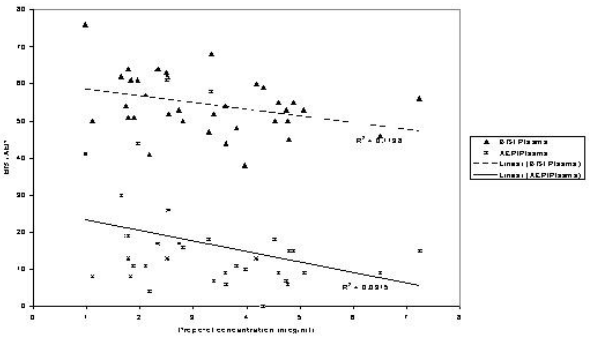
Introduction: Bispectral index (BIS) and the auditory evoked potential (AEP) monitors are approved tools used in assessing the depth of sedation. There is evidence of correlation between BIS and AEP values with calculated effect site propofol concentration (1). There is however, no data comparing AEP and BIS to measured plasma propofol concentration. We determined to establish the correlations between measured plasma propofol concentrations with BIS and AEP.
Method: Following IRB approval and informed patient consent, venous blood samples were taken during steady state period at 60 and 120 min post induction of anesthesia in women undergoing elective total abdominal hysterectomy. All patients received midazolam 0.03 mg/kg, fentanyl 3 mcg/kg bolus and propofol 2 mg/kg followed by a fentanyl 0.03 mcg/kg/min with 70% nitrous oxide in oxygen. Propofol infusion was titrated to maintain a BIS range of 55 to 65. AEP recordings were also noted. Linear regression and t-test were used for statistical analysis and $p< 0.05$ was declared to be significant.
Results: 35 patients had BIS, AEP and plasma propofol concentration measured. The results are shown in graph. Mean (SD) BIS and AEP values during venous blood sampling were 54.4 (7.0) and 16.9 (14.0). The BIS value correlated significantly ($R = 0.34$; $p = 0.04$) to measured plasma propofol concentration compared to the AEP ($R = 0.30$; $p = 0.08$). There was significant correlation between BIS and AEP values ($R = 0.59$; $p < 0.0002$)



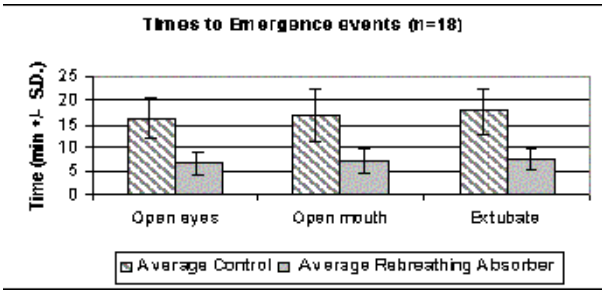
Discussion: Our study suggests an inverse relationship of BIS and AEP values to measured propofol plasma concentration. BIS demonstrated significantly better correlation with plasma propofol concentration than AEP. Despite good correlation with plasma propofol concentration, the AEP did not achieve statistical significance. This may be attributed to the wide range of values obtained from the AEP at measured time points. There was however significant correlation between BIS and AEP at the measured time points.
References
1. Anesthesiology 2003; 99: 802-12

S-225.

CLINICAL EVALUATION OF A DEVICE TO SPEED EMERGENCE FROM INHALED ANESTHESIA

AUTHORS: **D. Sakata**, N. Gopalakrishnan, J. Orr;
AFFILIATION: University of Utah, Salt Lake City, UT.

Introduction: Rapid emergence from a volatile anesthetic is a "trade-off" between hyperventilation to remove volatile anesthetic from the lungs and hypoventilating to maintain normocapnia or slight hypercapnia for elevated blood flow to the brain. We evaluated a device that allows simultaneous hyperventilation and hypercapnia during the reversal process.
Methods: After IRB approval, 18 ASA I patients scheduled to receive anterior cruciate ligament repair surgery were recruited for the study. Patients were randomly assigned to control and experimental groups. All patients received functional femoral nerve blocks. Anesthesia was maintained using 1 MAC of isoflurane and 0.05-0.15 mcg/kg/min of remifentanil.
Emergence was initiated when adhesive wound closure strips were applied. Events were recorded from the time that the isoflurane vaporizer was turned off. Test subjects using the device were hyperventilated by doubling the respiratory rate. Fresh gas flow was increased to 10 L/min in control subjects. The test device was inserted into the breathing circuit of patients in the experimental group. Times to eye and mouth opening in response to command and extubation were recorded.
Results: Using the device, the average time to opening eyes was less by 9.7 minutes (experimental range 4.1 to 11.5 and control range 10.2 to 24.3). Time to respond to an "open your mouth" command was less by 9.5 min (experimental range 4.4 to 11.5 and control range 10.3 to 19.7). Time to extubation was less by 10 minutes (experimental range 5.1 to 12.2 and control range 11.1 to 28.2). For the control, the minute ventilation was kept at an average of 11.7 liters per minute with an average end-tidal carbon dioxide of 29.5 mm of Hg. For the experimental group, the minute ventilation was kept at an average of 14.1 liters per minute with an average end-tidal carbon dioxide of 44.9 mm of Hg.
Discussion: The differences observed in this data set suggest that decreased time to emergence from volatile anesthesia can be effectively achieved by combining hyperventilation with elevated CO_2.

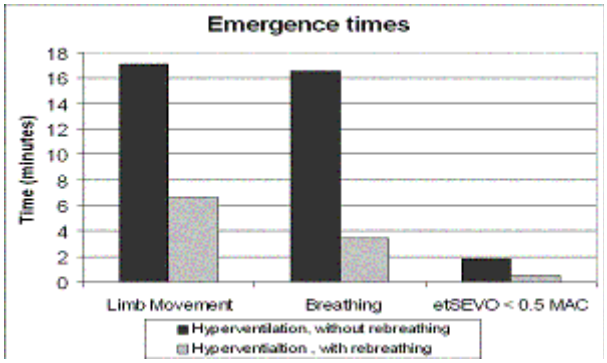


S-226.

EVALUATION OF A DEVICE IN PIGS TO SPEED EMERGENCE FROM SEVOFLURANE ANESTHETIC

AUTHORS: J. Orr, N. Gopalakrishnan, **D. Sakata**, M. Cluff;
AFFILIATION: University of Utah, Salt Lake City, UT.

Introduction: Hyperventilation quickly removes anesthetic gas from the lungs; however, the resulting hypocapnia decreases cerebral blood flow and delays emergence from anesthesia. We tested a device that allows simultaneous hyperventilation and slight hypercapnia during emergence from inhaled anesthesia. It has been previously shown that hyperventilation in the presence of added CO_2 speeds recovery from isoflurane anesthesia. We wanted to determine if hyperventilation in conjunction with increased CO_2 would also be effective when used to remove a lower solubility agent such as sevoflurane. The device is an expandable hose and filter placed between the patient and the Y-piece.
Methods: We compared emergence times from sevoflurane anesthesia with and without the device in 4 pigs. Prior to emergence, each animal was anesthetized at 1.5 MAC of sevoflurane for 2 hours. Time between turning off the vaporizer and return of spontaneous breathing, movement of multiple limbs, and end-tidal sevoflurane less than 0.5 MAC were recorded. Respiratory rate was increased from 10 to 20 breaths per minute and fresh gas flow was raised to 6 l/min during each emergence. The order of testing was randomized to minimize the influence of a prior emergence on subsequent test results.
Results: Average time to spontaneous breathing was 13.2 minutes less using the device. Spontaneous breathing was not observed prior to multiple limb movement in 3 of the animals receiving hyperventilation without the device. Time to movement of multiple limbs was 10.5 minutes less when using the device. The range of emergence times when using the device was 4.4 to 9.6 minutes and 12.8 to 22 minutes without the device. The time to reach end-tidal sevoflurane concentration below 0.5 MAC was 1.3 minutes less when using the device. The figure below shows the time to occurrence for each of the events.
Discussion: Prior studies have shown significant speed-up of emergence using hyperventilation with hypercapnia during reversal of isoflurane anesthetic. These results show that similar benefits are possible when sevoflurane is used.
Reference:
1. British Journal of Anaesthesia 2003; 91:787-92



S-227.

A COMPARISON OF BISPECTRAL INDEX AND ENTROPY DURING GENERAL ANESTHETIC INDUCTION AND EMERGENCE

AUTHORS: **R. G. Soto**[1], I. Rampil[1], R. Smith[2];
AFFILIATION: [1]SUNY Stony Brook, Stony Brook, NY, [2]University of South Florida, Tampa, FL.

Background: Unlike the Bispectral Index (BIS), which relies on a library of data that is compared to a patient's EEG, Entropy relies on the extent of order in signal as measured from the patient's forehead. Specifically, it is based on the concept of spectral entropy, which measures order in the cortical EEG and frontalis EMG. State Entropy (SE) is derived from EEG (0.8 -32 Hz) and Response Entropy (RE) from a combined measure of EEG and EMG activity (0.8 - 47Hz). We sought to compare BIS and Entropy during routine anesthetic induction and emergence with a standardized anesthetic.
Methods: Six consenting adult patients undergoing surgery under general anesthesia were monitored with both BIS and Entropy during both induction and emergence. Induction was standardized to include propofol (2mg/kg) and succinylcholine (1mg/kg). No premedication was given, and all patients were maintained on sevoflurane (ET% 1-1.3) in air and oxygen with fentanyl (2mcg/kg) for pain control. BIS, RE, and SE were monitored every 10 seconds with S5-Collect software (Datex-Ohmeda) from the preoxygenation period through extubation. Data recorded for 1min and 3min during induction and emergence, respectively were compared with a repeated measures analysis of variance and when F statistic was significant, intergroup differences were distinguished using Tukey's HSD post hoc test.
Results: BIS, SE, and RE all decreased similarly with propofol induction. However during emergence, RE preceded both BIS and SE by 30 seconds.
Conclusion: Temporal response of BIS, SE, and RE are similar after induction bolus of propofol, but RE rises earlier than either of the other 2 measures with emergence. This confirms previous findings that suggest that frontalis muscle tone in an unparalyzed patient may be a quicker indicator of return of wakefulness than EEG, or at least that it leads EEG signal by a certain time factor that has yet to be determined (1,2).
References:
1: Soto et al. *Anesth Analg*. Accepted for publication
2: *Acta Anaesthesiol Scand* 2004; 48: 145-15

S-228.

CORRELATION OF SNAP INDEX, BISPECTRAL INDEX, TARGET PROPOFOL EFFECT-SITE CONCENTRATION, PREDICTED PROPOFOL EFFECT-SITE CONCENTRATION AND HEMODYNAMIC PARAMETERS WITH CLINICAL ENDPOINTS DURING COADMINISTRATION OF PROPOFOL AND REMIFENTANIL

AUTHORS: **L. Pei**, Y. Huang, A. Luo;
AFFILIATION: Peking Union Medical College Hospital, Beijing, China.

Background and Goal of Study To compare the Ability of the Bispectral Index (BIS), SNAP Index (SI), target propofol effect-site concentration (CtPROP), predicted propofol effect-site concentration (CePROP), and hemodynamic parameters to measure patient responsiveness during anesthesia with propofol and remifentanil.
Methods Forty patients were randomly allocated to one of four groups (0, 2, 4, 6ng/ml remifentanil) to received graded CePROP and predicted effect compartment controlled remifentanil (CeREMI). At each step, the ability to respond to verbal command using the Observer's Assessment of Alertness/Sedation Scale (OAA/S), eyelash reflex (LOR_{lash}), and electrical titanic noxious stimulus ($LOR_{noxious}$) were compared against BIS, SI, CtPROP, CePROP, Systolic blood pressure (SBp), Diastolic blood pressure (DBp), Mean blood pressure (MBp) and Heart rate (HR). Correlation coefficient and sensitivity/specificity ratio were calculated.
Results and Discussion
BIS, SI, CtPROP, CePROP, SBp, DBp, and MBp correlated well with modified OAA/S. Increasing CeREMI increased BIS and SI values at LOR_{lash} and $LOR_{noxious}$, while decreased CtPROP and CePROP.

Table 1: Correlation Coefficient of different variables with Modified OAA/S

Variables	CeREMI 0ng/ml		CeREMI 2ng/ml		CeREMI 4ng/ml		CeREMI 6ng/ml	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
BIS	0.977	0.001	0.968	0.002	0.958	0.003	0.893	0.016
SI	0.978	0.001	0.942	0.005	0.853	0.031	0.963	0.002
CtPROP	-0.969	0.001	-0.928	0.008	-0.868	0.025	-0.885	0.019
CePROP	-0.924	0.008	-0.869	0.025	-0.852	0.031	-0.891	0.017
MBp	0.897	0.015	0.889	0.018	0.979	0.001	0.934	0.006
HR	0.55	>0.05	-0.632	>0.05	0.377	>0.05	0.170	>0.05

P<0.05 was considered significant

Table 2: Mean BIS values at LOR_{lash} and LOR_{noxi} in different group

	CeREMI 0ng/ml	CeREMI 2ng/ml	CeREMI 4ng/ml	CeREMI 6ng/ml
LOR_{lash}	72.9±10.37**	75.3±8.90**	82.8±7.07**	83.3±7.78**
LOR_{noxi}	43.6±6.55*	56.9±5.65*	68.0±6.20*	72.4±1.42*

*Except for CeREMI 4ng/ml and CeREMI 6ng/ml, Mean BIS values between all other groups were significant, *P<0.05*; **Mean BIS values between every two groups were significant.
Conclusion Although BIS, SI, CtPROP, CePROP were influenced by remifentanil during propofol administration, Correlation coefficients between OAA/S remained accurate.
Reference
1. Struys MM et al. *Anesthesiology* 2003; 99: 802-12

S-229.

VALIDATION OF THE CEREBRAL STATE MONITOR FOR ASSESSING ANAESTHETIC DEPTH

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Introduction: The objective of this study was the validation of a new index, called Cerebral State Index (CSI) during cardiac anaesthesia. The CSI was defined using sub-parameters from the EEG as inputs of an adaptive neuro-fuzzy inference system (ANFIS). The advantage of ANFIS is that it does not assume an underlying mathematical function governing the causal relationship between the EEG values and the clinical state of the patient.
Methods: The study was approved by the local ethics committee. Fifteen patients, (12 male, 3 female, age 60-79 years) scheduled elective cardiac surgery were included in the study. Propofol was the only anaesthetic, administered using a TCI- pump (target 5 ug/ml plasma concentration during 5 min). CSI and BIS was monitored simultaneously and LOC defined as loss of response to a verbal command was assessed. After LOC, surgery was carried out according to the protocol of the department.
Results: Both CSI and BIS showed significant differences between awake and anaesthetised values as shown in the table (mean(SD)). During surgery, both BIS and CSI remained below 60 and in an interview 24 h after surgery none of the patients reported intra operative awareness

	CSI	BIS
Awake	92(5)	94(6)
LOC	55(4)	56(4)

Discussion: The results show that in this population depth of anaesthesia can be measured reliably by using a combination of parameters calculated from the frequency content of the EEG.

S-230.

ANTITHROMBOTIC EFFECTS OF NSAIDS (KETOROLAC, FLURBIPROFEN, ASPIRIN AND SULPYRINE) ON THROMBELASTOGRAPHY (TEG) IN THE PRESENCE OF HEPARIN OR ARGATROBAN

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Introduction: Control of platelet procoagulant activity is an important antithrombotic strategy. We investigated whether NSAIDs (ketorolac, flurbiprofen, aspirin and sulpyrine) blocks platelet-mediated facilitation of clotting on Thrombelastography (TEG) (1).
Methods: After institutional approval and consent, four series (n=10, each) of 8-channel TEG were performed using blood samples from healthy volunteers. In the first series, TEG was performed in the presence of 10 mcL of either normal saline (Control), ketorolac(Ket: final concentration 3 mcg/mL), Ket plus heparin (Hep: 0.1 U/mL), Ket plus Hep plus ADP (8.3mcM/L), Ket plus Hep plus collagen (Col: 10 mcg/mL), Ket plus argatroban (ARG: 0.31mcg/mL), Ket plus ARG plus ADP and Ket plus ARG plus collagen. In the second, third and fourth series, flurbiprofen (FP: 8 mcg/mL), aspirin (Asp: ex vivo blood sample at one hour after oral intake of 660mg) or sulpyrine (Sul: 100mcg/mlL) was used in place of ketorolac, respectively. TEG parameters (R, and angle) were analyzed statistically using one-way ANOVA and Fishers PLSD. P< 0.05 was considered significant. All values are expressed as mean±;SD.
Results: Prolongation of R was seen with addition of Hep or ARG. Although platelet agonists, ADP and Col, shortened R time with Ket and FP in the presence of Hep, they did not produce any shortening of R time with Asp and Sul. Furthermore, although angle clearly increased with Ket and a trend of increase with FP in the presence of Hep with ADP and Col, samples with Asp and Sul were not affected with platelet agonists as shown in Table 1.
Conclusion: Asp and Sul may be more efficacious in blocking platelet procoagulant activity than Ket and FP especially in the presence of heparin anticoagulation.

References:
1) ASA meeting abstract A-162, 2003.

Table. Data of TEG & Statistic analysis using one-way ANOVA and Fisher's PLSD (m±SD)

	R	ANG		R	ANG		R	ANG		R	ANG
Control	5.0±0.5	67.3±2.5	Control	8.2±1.3	75.7±3.4	Control	6.7±1.8	58.3±5.9	Control	5.6±1.6	61.7±4.7
Ket	5.1±0.6	60.1±4.7	FP	7.9±1.3	72.3±5.2	Asp	6.4±1.4	53.8±7.1	Sul	5.4±1.2	59.4±5.6
Ket+Hep	19.8±3.2 *#	29.7±5.5 *#	FP+Hep	28.7±6.0 *#	35.1±8.4 *#	Asp+Hep	21.5±8.6 *#	26.9±7.7 *#	Sul+Hep	20.0±6.7 *#	26.9±6.1 *#
Ket+Hep+ADP	13.2±2.0 *#‡	40.7±7.5 *#‡	FP+Hep+ADP	21.1±5.7 *#‡	39.1±11.1 *#	Asp+Hep+ADP	19.9±8.3 *#	24.9±6.7 *#	Sul+Hep+ADP	18.4±5.7 *#	27.0±3.2 *#
Ket+Hep+Col	13.7±1.4*#‡	39.7±11.3 *#‡	FP+Hep+Col	21.2±6.0 *#‡	39.9±12.8 *#	Asp+Hep+Col	19.2±6.2 *#	27.1±7.6 *#	Sul+Hep+Col	18.9±6.9 *#	27.8±5.3 *#
Ket+ARG	15.5±1.3 *#	36.9±7.5 *#	FP+ARG	29.8±6.2 *#	43.1±4.8 *#	Asp+ARG	14.3±3.4 *#	45.9±3.6 *#	Sul+ARG	14.5±2.1 *#	47.0±1.5 *#
Ket+ARG+ADP	15.3±1.5 *#	37.6±6.2 *#	FP+ARG+ADP	28.3±7.2 *#	43.2±5.1 *#	Asp+ARG+ADP	14.2±3.3 *#	41.2±7.7 *#	Sul+ARG+ADP	13.4±1.6 *#	43.6±4.7 *#
ket+ARG+Col	15.6±1.6 *#	37.4±6.8 *#	FP+ARG+Col	27.3±6.8 *#	44.6±4.6 *#	Asp+ARG+Col	12.9±3.0 *#	45.0±6.4 *#	Sul+ARG+Col	14.3±2.7 *#	46.0±2.9 *#
	*= significant vs. Control(p<0.05),#= significant vs. Ket(p<0.05), ‡=significant vs. Ket+Hep(p<0.05)	*= significant vs. Control(p<0.05),#= significant vs. Ket(p<0.05), ‡=significant vs. Ket+Hep(p<0.05)		*= significant vs. Control(p<0.05),#= significant vs. FP(p<0.05), ‡=significant vs. FP+Hep(p<0.05)	*= significant vs. Control(p<0.05),#= significant vs. FP(p<0.05)		*= significant vs. Control(p<0.05),#=significant vs. Asp (p<0.05)	*= significant vs. Control(p<0.05), #=significant vs. Asp (p<0.05)		*= significant vs. Control(p<0.05),# =significant vs. Sul (p<0.05)	*= significant vs. Control(p<0.05),# =significant vs. Sul (p<0.05)

S-231.

COMPARISON OF NON-INVASIVE "ELECTRICAL VELOCIMETRY" WITH THERMODILUTION METHODS IN DETERMINATION OF CARDIAC OUTPUT

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Introduction: Validated methods in determination of cardiac output (CO) are invasive measurement of thermodilution (TD) via pulmonal artery catheter (PAC) and transpulmonal continous analysis of puls contour (PiCCO). A new non-invasive method called "electrical velocimetry" (EV) determines CO on account of specific time-dependent changes of electrical conductivity on the thoracical surface caused by the cardiac cycle (bioimpedance (1)). This new method might represent an easy-practicable non-invasive procedure in future. In this study its accuracy in comparison with the conventional procedures of TD is investigated in a clinical routine setting.
Methods: After IRB approval 23 intensive care patients (age: 62.4 ± 14.3 years; weight: 80.8 ± 19.1 kg) with clinical need of hemodynamic monitoring by PAC or PiCCO were investigated. In these patients two ECG-electrodes were placed on the neck and lateral thorax on each side for measurement of CO with the EV method by a specific algorhythm (2) with the AESCULON®-monitor (Osypka Medical, Berlin, Germany) additionally to the conventional TD procedure. Mean ± SD of measurements of CO by thermodilution as well as EV and their differences are indicated.
Results: The determination of CO showed comparable values in comparison of TD and EV methods in tendency (Table 1).
Table 1: Comparison of determination of cardiac output by thermodilution with measurement by "electrical velocimetry"

	cardiac output thermodilution	cardiac output electrical velocimetry	differences
Mean ± SD	8.1 ± 2.8 l/min	7.3 ± 2.8 l/min	-0.82 ± 1.78 l/min

Discussion: The new developed method determining the CO by bioimpedance in a non-invasive way of high safety shows sufficient clinical accuracy with invasively measured CO results. Further studies with large numbers of patients are needed for validation of the new non-invasive EV method.
References:
(1) Bernstein DP et al. Crit Care Med 1986; 14 (19): 904-9;
(2) Osypka MJ et al. AACN Clinical Issues 1999 ; 10 (3) : 385-99

S-232.

DETECTING AN INCREASE IN HEART RATE IN CHILDREN USING AN ADAPTIVE CHANGE POINT DETECTION ALGORITHM

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Introduction:
The astute pediatric anesthesiologist uses subtle changes in patient heart rates to monitor changes in anesthesia depth and dictate fluid administration. Clinicians can perceive fluctuations of three to four beats per minute from auditory signals [1]; but may become distracted by simultaneous tasks, as the scope of human attention is finite. To overcome such limitations we attempted to replicate optimum clinician performance in an automated system.
Methods:
Trend heart rate data was collected from 53 children undergoing day care surgery. Clinically detected changes in heart rate, using standard auditory and visual monitoring, were recorded in synchrony with the trend data.
A purpose-built graphical interface was used for post-hoc expert marking of episodes of heart rate increase; graded as definitely or likely significant/ insignificant or artifact using predefined criteria. Following data segmentation, an automated change-point detection algorithm, with adaptive Kalman filtering and a local CUSUM, was used to identify points of increasing heart rate. The relative performance of the algorithm and real-time clinicians was compared against the post-hoc expert review.
Results:
Five cases were excluded due to incomplete data. Results from the remaining sample indicated that the automated trend detection algorithm performed as well as clinicians under test conditions, without a significant increase in the false positive detection rate.

Monitoring Performance	Post Hoc Expert	Automated Algorithm	Real Time Clinician
True HR increase	109	79	80
Missed HR increase	0	30	29
False HR increase	0	27	33

Discussion:
The exponential increase of monitored physiological parameters within the operating room has raised the cognitive burden of anesthesiologists faced with interpreting the resultant streams of data. However by improving computational pattern recognition, knowledge representation, automated reasoning and intelligent communication, human performance could be extended.
Using clinical data recorded from the operating room, we compared the performance of a novel process-monitoring method in detecting patient heart rate increases to that of real-time clinicians and post-hoc graphical review. The automated method seems to describe the signal efficiently; however, it is unlikely to be applicable to all physiological signals without significant tuning. Further work is needed on the classification and organization of change points and the simultaneous integration of multiple signals.
References:
1. MK Molyneux, AK McIndoe, AT Lovell. Anesth Analg 2004;98:A76.

S-233.

QUALITY ASSURANCE DOCUMENTATION: MULTI-STEP PROCESS TO IMPROVE APPROPRIATE TIMING OF QA COMPLETION

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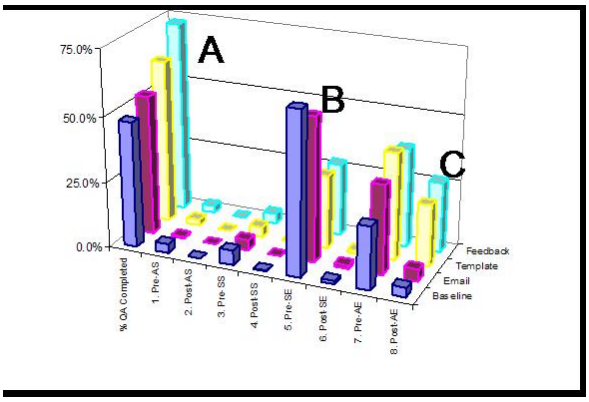
Introduction: Quality Assurance(QA) documentation is required for healthcare organization accreditation by the JCAHO. QA documentation may also be used as a tool to evaluate performance metrics and improve quality of care. Although previous studies have looked at voluntary reporting and electronic scanning of computerized medical records[1], none have considered when during the perioperative period QA documentation is completed. We examined QA documentation timing relative to: Anesthesia Start (AS), Surgery Start (SS), Surgery End (SE), and Anesthesia End (AE).
Methods: Using an anesthesia information management system (PICIS, Wakefield, MA), anesthesia providers are able to complete QA documentation electronically any time after anesthesia care has begun. The completion times of QA documentation were examined using SQL queries on the database containing all QA documentation during a period of 156 days. The completion rate and time of completion during the following four phases were studied.
1. Baseline: 57 days.
2. Email Notification: 33 days-notifications sent to all attendings, residents and CRNAs informing them of departmental policy regarding QA completion.
3. QA Template Simplification: 42 days-modified the steps necessary to complete the QA form.
4. Performance Feedback: 24 days-individualized monthly reports sent to all anesthesia residents and CRNAs stating their QA documentation completion rates.
Results: As the completion rate of QA documentation increased from the baseline through the three interventions ('A'), the following changes were noted in the timing of QA completion:
A. Prior to Surgery End: There was a general decrease in QA completion occurring prior to surgery end ('B').
B. After Surgery End: There was a general increase in QA completion occurring after surgery end ('C').
The most significant changes occurred during the most desirable post-anesthesia end completion time. A value of 3.7% during the baseline period increased slightly to 4.7% after email notification. Template modification and performance feedback then helped to greatly increase the percentage of users filling out QA after anesthesia end time to 23.5% and 26.9%, respectively.
Discussion: Concurrent with the significant increase in the level of QA documentation completion rates as a result of the tiered interventions, there is a significant shift in the documentation completion time towards the desired anesthesia end time. While this trend is encouraging, it is preferable to have all QA documentation completed after anesthesia end.
References:
1. Anesthesiology 1996;85:977-987.



S-234.

EFFECTS OF AGE ON HEART RATE VARIABILITY AND CATECHOLAMINE LEVELS DURING PROPOFOL AND FENTANYL ANESTHESIA

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Introduction: We reported that the elderly patients required propofol more than the younger to maintain the same Bispectral Index (BIS) value (1). The purpose of the present study was in order to elucidate how age affects heart rate variability (HRV) and catecholamine levels.
Methods: Fifty patients (25 patients per group), unpremeditated, ASA physical status 1 [aged 10-29 yr (Group A), aged 60-79 yr (Group B)] scheduled for elective surgery entered the study. After placing routine monitors in the operating room, ECG signals were transmitted to the analysis systems for HRV: the MemCalc/Makin (Suwa Trust, Tokyo, Japan) (2). It provides percentage of the entropy (the randomness of 4 R-R intervals, 0~100 %) and numbers for LF (low frequency; the power from 0.04 to 0.15 Hz) and HF (high frequency; the power from 0.15 to 0.4 Hz) by the maximum entropy method. The ratio of LF/HF was calculated. After 5 minutes of rest, variables including heart rate (HR) and mean blood pressure (MBP) were recorded as baseline control values. Target controlled infusion of fentanyl was then started to achieve the predicted effect-site concentration at 2 ng/ml. The effect-site concentration was predicted using the program of Shafer (3). Patients received propofol at BIS value of 50. All data were expressed as mean ± SD. One-factor ANOVA with Bonferroni correction were used for statistical analysis. $P < 0.05$ was considered to be significant.
Results: Results is shown in the table. Propofol, plasma noradrenaline and dopamine levels of Group B were higher than those of Group A. HR, MBP and HRV did not change.
Discussion: Although the difference of age did not cause the changes of hemodynamics and HRV at BIS value of 50, noradrenaline and dopamine levels of the elderly group increased. Increased catecholamine levels were not likely due to increased sympathetic activity, indicated by increased LF/HF. Therefore, this may suggest that propofol reduces catecholamine levels, but the elderly patients do not inhibit increased catecholamine levels. In summary, the difference of age did not cause the changes of hemodynamics and HRV, but affected catecholamine levels at BIS value of 50.
References:
(1) J Anesth 17:pp470, 2003
(2) Anesthesiology 98:34-40, 2003
(3) Anesthesiology 73:1091-1102, 1990

Group	A	B
Propofol μg/ml	2.4 ± 0.5	3.2 ± 0.8 #
HR bpm	53.4 ± 8.1	65.3 ± 10.1
MBP mmHg	85.2 ± 9.6	96.7 ± 14.8
Noradrenaline pg/ml	142.2 ± 69.3	349.6 ± 206.4 #
Dopamine pg/ml	8.2 ± 3.3	25.8 ± 15.5 #
Entropy %	36.9 ± 10.5	27.4 ± 6.2
HF	368.0 ± 419.3	210.6 ±148.6
LF/HF	2.6 ± 2.1	2.8 ± 1.4

# $p<0.05$ vs. Group A

S-235.

EVALUATION OF HEMODYNAMIC CHANGES DURING HEART DISPLACEMENT IN OFF-PUMP CORONARY ARTERY BYPASS GRAFT SURGERY: COMPARISON OF LOW CARDIAC FUNCTION AND NORMAL CARDIAC FUNCTION USING ESOPHAGEAL DOPPLER ECHOGRAPHY MONITOR

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Background: In off-pump coronary artery bypass (OPCAB) surgery, positioning the heart for anastomosis of the circumflex (Cx) and the posterior descending artery (PDA) can impair cardiac output. The purpose of this study was to evaluate the hemodynamic changes caused by heart displacement in patients undergoing OPCAB surgery using the HemoSonic™ 100 (HS100; Arrow, PA, USA), a new esophageal Doppler echography monitor (EDM). We compared hemodynamic parameters in patients with a low cardiac index (CI) and a normal CI during heart displacement.
Methods: Having obtained IRB approval for this retrospective study, a total of 37 patients undergoing elective OPCAB surgery were reviewed. The patients were divided into two groups: those with a CI of 2.5 or less (Group L, n=11) and those with a CI of over 2.5 (Group N, n=26). We evaluated hemodynamic parameters in each group. The EDM was used to collect hemodynamic variables before (baseline) and after positioning the heart for anastomosis of the left anterior descending (LAD), Cx, and PDA. The data were expressed as mean ± SD. Paired t-tests were used to compare values and $p<0.05$ was considered statistically significant.
Results: The baseline values for cardiac output (CO), aortic blood flow acceleration (Acc; a measure of LV contractility), stroke volume (SV), and left ventricular ejection time (LVET; a measure of preload) were lower in Group L than in Group N. During the Cx and PDA anastomosis, CI, Acc, SV, and LVET decreased more (all $p<0.05$) in Group L than in Group N, but in the LAD position there were no significant differences between Groups L and N in the changes in these parameters.
These hemodynamic changes were transient and returned to baseline after the heart was returned to its anatomical position. There were no complications attributable to the use of the EDM.
Discussion: The results showed that the greater deterioration of CO in Group L was caused by low LV contractility and low SV compared with Group N.
Conclusions: We compared hemodynamic variables in patients with low and normal CI values who were undergoing OPCAB surgery using EDM. We observed a larger deterioration in CO, SV, and Acc in Group L when the heart was dislocated. We conclude that particular care should be taken during the anesthetic management of patients with a low cardiac function during distal anastomosis of OPCAB, especially in the Cx and PDA position.

S-236.

PULMONARY ARTERIAL TEMPERATURE, BUT NEITHER NASOPHARYNGEAL, FOREHEAD DEEP-TISSUE, NOR URINARY BLADDER TEMPERATURE, CLOSELY REFLECTS CHANGES IN BRAIN TEMPERATURE DURING INDUCTION OF PROFOUND HYPOTHERMIA ON TOTAL CARDIOPULMONARY BYPASS

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Introduction: During profound hypothermia, it is essential to monitor body temperatures at several sites to ensure that the organs vulnerable to decreased oxygen delivery actually receive the benefit of the desired degree of hypothermia, assess evenness of cooling, and diagnose hazardous hypothermia. It is thus particularly important to use temperature monitoring sites most likely to reflect brain temperature. In this study, using the jugular venous blood temperature (JVBT) as a standard for brain temperature, we evaluated the accuracy and precision of the pulmonary arterial blood temperature (PABT), nasopharyngeal temperature (NPT), deep-tissue temperature measured at the forehead (FHDTT), urinary bladder temperature (UBT), and fingertip skin-surface temperature (FSST) during induction of profound hypothermia.
Methods: We studied 9 ASA II-IV adult patients with thoracic aortic aneurysms who underwent profound hypothermic cardiopulmonary bypass (CPB) and circulatory arrest for the aortic repair. JVBT, PABT, NPT, FHDTT, UBT, and FSST were recorded every one minute for 20 min before and during cooling on total CPB. Ambient temperature was maintained at ~20°C. JVBT was measured at the level of the right jugular bulb, while PABT in the right pulmonary artery immediately behind superior vena cava (SVC). Hypothermia (17~20°C) was rapidly (~20 min) induced with a separate water bath heat exchanger which was initially set at 10°C. At circulatory arrest, the temperature of the water bath was allowed to rise to 20°C, where it was maintained until rewarming began. The results were analyzed using correlation and Bland and Altman (BA) analyses. ANOVA, Scheffe F test, Fishers Z-transformation, and Student t test were also used for the analyses.
Results: 1) JVBT began to decrease immediately after the start of core cooling, closely matching the PABT ($r = 0.99$, $p<0.0001$). The other four temperatures lagged ($p<0.05$) behind JVBT and PABT; however, NPT ($r = 0.96$), FHDTT ($r = 0.95$), and FSST ($r = 0.92$) followed JVBT and PABT more closely ($p<0.05$) than UBT ($r = 0.87$). The correlation between JVBT and PABT was much stronger ($p<0.05$) than that between JVBT and any of the other four temperatures. 2) In the BA analyses, the offset (study site minus JVBT) was lower for PABT (0.2°C) than for either NPT (1.0°C), FHDTT (1.0°C), BT (2.4°C), or FSST (0.5°C) ($p<0.05$, n=598). The standard deviation of the difference between JVBT and PABT (1.3°C) was much smaller that that for the difference between JVBT and either NPT (2.3°C), FHDTT (2.6°C), BT (4.0°C), or FSST (3.2°C).
Conclusions: During induction of profound hypothermia on total CPB with the heart *in situ*, in spite of nearly ceased pulmonary blood flow, a PA catheter thermistor, presumably because of its placement immediately behind the SVC, provides a reliable measure of the right jugular venous blood temperature and hence brain temperature.

S-237.

HOW DOES THE ARTERIAL KETONE BODY RATIO REFLECT THE HEPATIC VENOUS KETONE BODY RATIO IN NINETEEN PATIENTS UNDDEGOING HEPATIC RESECTION SURGERY

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The arterial ketone body ratio (AKBR:arterial acetoacetate acetoacetate/β-hydroxybutyrate ratio) reflects the hepatic mitochondrial redox potential. It is frequently measured to evaluate hepatic dysfunction and multiple systems organ failure. We compared AKBR to the hepatic venous ketone body ratio (HKBR) to clarify the doubt which exists as to whether AKBR truly represents the ketone body ratio in hepatic venous blood.

This study was approved by our institutional review board and informed consent was obtained from nineteen consecutive patients undergoing hepatic resection surgery. After anesthetic induction, a radial arterial cannula was placed and 7.5-Fr fiberoptic catheters (Opticath Model P7110-EH, Oximetrix) were placed in the pulmonary artery and the hepatic vein. Anesthesia was maintained with nitrous oxide and oxygen with isoflurane. We measured acetoacetate and β-hydroxybutyrate in each patient at one hour intervals while hepatic venous hemoglobin oxygen saturation was stable for a total of 121 sampling points. The results were evaluated with linear regression analysis and p value of 0.05 or less was considered significant.

AKBR was significantly correlated to HKBR ($r=0.824$, $p<0.01$), where AKBR=0.566 Þ HKBR + 0.142. On the linear regression line, HKBR was smaller than AKBR when AKBR was below 0.327. HKBR was larger than AKBR when AKBR was above 0.327. These results show that the differences between AKBR and HKBR largely depend on the value of HKBR. The differences may be related to the ratio in which heopatic venous blood mixes with inferior vena cava blood. It is also possible that the differences were related to the clearance of ketone bodies which may vary depending on the value of HKBR.

These results were obtained during liver resection surgery, but may be applicable in general for the clinical evaluation of liver dysfunction associated with multiple systems organ failure.

Genetics/Genomics

S-238.

XENON ACTS THROUGH INHIBITION OF GLUTAMATERGIC NEUROTRANSMISSION IN *C. ELEGANS*

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Introduction: The mechanism of action of the anesthetic gas xenon is ill-defined. In vitro electrophysiological studies implicate antagonism of several types of postsynaptic ion channels, the most prominent of which is the NMDA subtype glutamate receptor[1], and activation of two-pore domain potassium channels as potential mechanisms of action. Genetic evidence shows that nitrous oxide (N_2O), an anesthetic gas similar to xenon, acts through inhibition of the NMDA receptor in vivo[2]. The goal of this study was to determine the behavioral effects of xenon in the nematode C. elegans and furthermore to test the hypothesis that - like N_2O - the main mechanism of action of xenon is through inhibition of NMDA subtype glutamatergic neurotransmission.
Methods: Well-fed one-day post-L4 adult *C. elegans* animals were transferred by platinum wire to agar pads with no bacteria; the pads were placed into glass chambers containing either a 75%:25% xenon:O_2 mixture or air. After a 10-min incubation period, locomotion was scored over a seven-minute period. The frequency of reversing the direction of locomotion is controlled primarily by glutamatergic neurotransmission. At least 10 animals were scored for each data point or strain.
Results: Xenon produced behavioral effects similar to those seen with N_2O. Like N_2O but unlike volatile anesthetics, xenon did not affect gross locomotion but markedly changed the character of movement. Xenon greatly reduced the frequency of reversals of direction of movement in wild-type worms, an unusual behavioral effect otherwise only seen in worms with reduced glutamatergic neurotransmission (fig.1). The EC_{50} for xenon was 19% ± 0.9%. A mutant lacking the NMDA receptor NMR-1, *nmr-1(ak4)*, was normally sensitive to xenon whereas this mutant is resistant to N_2O. However, the non-NMDA receptor null mutant *glr-1(ky176)*, which is normally sensitive to N_2O, was not significantly affected by xenon. The highly volatile anesthetic resistant mutant *unc-64(md130)* showed a wild-type sensitivity to xenon.
Discussion: Our findings show that the main mechanism of action of xenon in C. elegans is by inhibiting glutamatergic neurotransmission. The sensitivity of the NMDA receptor null mutant to xenon argues that unlike N_2O xenon does not act exclusively through this NMDA receptor; rather a non-NMDA receptor is more central to xenon's action in C. elegans.
References:
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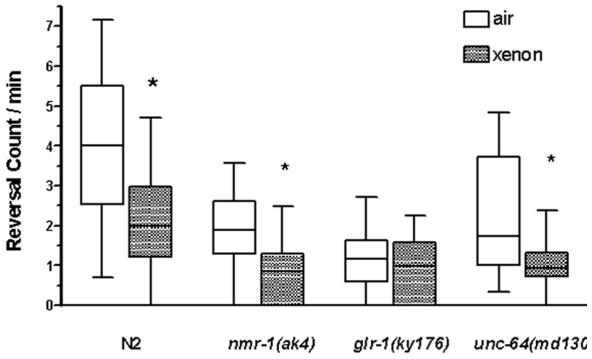
2) PNAS, 101:8791-6 (2004)



S-239.

CYP2C19 FREQUENCIES IN THE SOUTH FLORIDA POPULATION AS DETERMINED BY THE AMPLICHIP CYP450 ASSAY

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Introduction:
It is estimated that 106,000 individuals die per year from non-error adverse effects of medications, which ranks it as the 4th-5th killer in the US (1). These fatalities are believed to be due to interindividual therapeutic response variability, probably related to increased/ decreased drug activity associated with polymorphisms in the cytochrome P-450 metabolic system (CYP). CYP2C19 metabolizes several important drugs, including celecoxib, propranolol and diazepam (2).
To date, there are more than 10 alleles of CYP2C19, however, only *2 and *3 occur with a frequency enough to be considered clinically significant (3). A genotype of *1/ *1 or any combination of *1 and *2 or *3 results in an extensive metabolizer phenotype. Should another combination *2/ *2, *3/ *3 or *2/ *3 occur, the resulting phenotype would be a poor metabolizer.
The purpose of this study was to determine the frequency of *1,*2 and *3 polymorphisms in a predominantly Hispanic population, since most research to date applies to African Americans, Asians and Caucasians and fewer studies have targeted Hispanics (4) (5); the largest minority group in the US.
Method:
Following IRB approval 5ml of blood was taken from 238 patients undergoing surgery. DNA was extracted and processed with the Amplichip CYP450 Assay (Roche Molecular Systems, Inc., Pleasanton, CA).
Results:
The frequency of alleles was *1/ *1 175 patients (73.5%), *1/ *2 57 patients (24%) and *2/ *2 6 patients (2.5%). There were no *3 alleles noted.

Ethnic Group	CYP2C19 *1/ *1	CYP2C19 *1/ *2	CYP2C19 *2/ *2
Hispanic 161/ 238 (67.6%)	118/161 (73.3%)	39/161 (24.2%)	4/161 (2.5%)
Blacks 44/238 (18.5%)	33/44 (75.0%)	10/44 (22.3%)	1/44 (2.3%)
Caucasian 30/238 (12.6%)	22/30 (73.3%)	8/30 (26.7%)	0/30 (0%)
Asian 1/238 (0.4%)	0/1 (0%)	0/1 (0%)	1/1 (100.0%)
Other 2/238 (0.8%)	2/2 (100.0%)	0/2 (0%)	0/2 (0%)

Discussion:
CYP2C19 is known to vary amongst ethnic groups. Genetically, Hispanics are a heterogeneous population. Southwest Hispanics appear to have genotypes similar to Caucasians and Native Americans. By contrast, East Coast Hispanics have a larger proportion of African admixture (6). While Asians have a larger portion of dysfunctional CYP2C19 genes, we did not find this in our South Florida Hispanic population. It appears that there is no significant genetic difference between South Florida Hispanics, Caucasians and Blacks, with reference to the frequency of CYP2C19 polymorphisms (p>.05).
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(6) Am J Hum Genet 69: 1080-1094, **2001.**

S-240.

THE EFFECTS OF ISOFLURANE ON CELL SIGNALING GENES IN THE BASOLATERAL AMYGDALA OF THE RAT

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The basolateral amygdala is a required anatomic substrate for fear conditioning. We propose that volatile anesthetics alter gene expression of proteins responsible for various intracellular and extracellular signaling pathways necessary for formation and consolidation of new memories.
Methods: With IRB approval, 14 rats (9 control and 5 experimental) were exposed in a habituation cage to either oxygen or oxygen containing 2% isoflurane for 15 minutes. Animals were returned to their domicile cage for 6 hours, sacrificed and basal-lateral amygdala removed under RNAase free conditions. Samples were stored in buffer at -80° C then assayed via Affymetrix RAE 230 gene chips (simultaneous measurement of ≈ 16,000 Expressed Sequence Tags). Expression data were standardized, $\log_2$ transformed and the experimental group compared to the baseline control group using 2-tailed t-test. Since these comparisons were intended for hypothesis generation rather than testing, no Bonferroni corrections were used and $p \leq 0.05$ considered significant.
Results: When compared to control, exposure to isoflurane altered expression of 39 genes associated with intracellular and extracellular signaling processes based on the PubMed Gene database. Genes highly down-regulated include Histamine (H1) receptor and Insulin-like growth factor binding protein. Both have been associated with memory formation in the amygdala and hippocampus. Other hormonal receptors with altered regulation included those for cholecystokinin, glucagon, gonadotrophin releasing hormone, LDL, and tachykinin. Substantial up-regulation was noted in adrenergic receptor α1a subunit, interleukin 12b, fibroblast growth factor 23, ryanodine receptor I & II, lysosomal membrane glycoprotein 1, phospholipids scramblase 1, protein phosphatase 3, sperm autoantigen 17 and G-protein Receptor 9, 10, & 30. Of this later list of signaling proteins, to date, only the ryanodine receptor has been linked to memory formation.
Discussion: EST expression is not directly proportional to target protein content because of post transcriptional modifications and feedback control loops present in the translation process. However, gene chip technology provides a window into the dynamics of genomic processes. The mechanism(s) by which volatile anesthetics produce amnesia remain unclear. We chose the basolateral amygdala because of the extensive literature supporting its central role in conditioning, other areas of the CNS may well respond differently to isoflurane. Isoflurane selectively alters expression of specific genes in pathways previously reported to be associated with learning and memory, as well as many other biological pathways. The data also suggests several unexamined, yet potentially interesting targets that may mediate the ability of anesthetics to block memory formation.

S-241.

ISOFLURANE ALTERS TRANSCRIPTION-RELATED GENES IN RAT AMYGDALA

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Introduction: To elucidate how inhaled anesthetics induce amnesia we investigated its effects on the rat amygdala. The amygdala has been described previously as the substrate for fear-associated long term memory (LTM) formation. LTM requires protein synthesis and therefore alterations in specific RNA transcription. We investigated altered transcriptional activity due to isoflurane via gene-chip analysis of total RNA isolated from amygdala.
Methods: We studied 14 rats (9 control, 5 isoflurane) with IRB approval. In a familiar cage we exposed the rats to either oxygen or isoflurane 2.0% steady-state in oxygen for 15min. After 6 hr rats were sacrificed, brains extracted and bilateral baso-lateral nuclei of the amygdala isolated under RNase-free conditions. Poly-A RNA was extracted and studied using Affymetrix RAE230 gene chips (simultaneous measurement of about 16,000 expressed sequence tags, ESTs (roughly equivalent to genes)). Expression data were standardized, log2 transformed and the experimental group compared to the baseline control group using 2-tailed t-test. Since these comparisons were intended for hypothesis generation rather than testing, no Bonferroni corrections were used and $p <= 0.05$ considered significant.
Results: Correlation with the PubMed Gene database revealed 30 transcription-related ESTs which were altered by isoflurane. These ESTs could be divided among specific major functional systems related to transcription. The most prominent group of these genes is associated with the early growth response (EGR) family and its downstream c-JUN pathways (e.g., Egr2, Nab1, Arnt, Cdkn2a, Madh3, Ncoa6, Ptgs2, Yy1). These pathways are known to be involved in LTM and neuronal plasticity. A smaller group of genes changed by isoflurane is related to insulin expression and thus to glucose catabolism. The remaining transcription-related genes with changed expression belong to a wide variety of pathways whose functional relations to isoflurane remains to be determined.
Discussion: The functional effect of isoflurane does not stop at the cell membrane. Isoflurane may exert its effects by altering gene expression in multiple areas of cell function. Isoflurane appears to achieve its selective gene expression with the transcriptional regulators presented here. This may be one of the mechanisms responsible for longer duration side effects following anesthesia.

S-242.

PERINATAL COCAINE EXPOSURE DIFFERENTIALLY REGULATES THE MRNA EXPRESSION OF ßAR SUBTYPES IN THE NEONATAL RAT HEART

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INTRODUCTION: We have previously documented that perinatal cocaine exposure leads to ßAR hyporesponsiveness in neonatal rats at 14 days of age (1). The mechanism for the reduced ßAR inotropic response is unknown. Because both ß-1 and ß-2 ßAR are downregulated (2) while ß-3 ßAR is upregulated in the failing human myocardium (3), we hypothesized that perinatal cocaine exposure might differentially regulate the expression of ßAR subtypes.
METHODS: The study was approved by IACUC of Columbia University. Timed-pregnant (gestational day 0-1) female Sprague-Dawley rats were given saline (Control) or cocaine at 60 mg/kg (Cocaine) in equal volume daily by intragastric administration from gestational day 2 until postpartum day 14. Total RNA was isolated from neonatal rats on postnatal day 14 and used in experiments. RT-PCR was performed using the following primer sets: ß-1 ßAR (S): 5'GCCG ATCTGGTCATGGGA-3'; ß-1 ßAR (AS)5'-GTTGTAGCAGCGGCGCG-3'(440bp);ß-2 ßAR (S) 5'-ACC TCCTCCTTGCCTATCCA-3';ß-2 ßAR (AS) 5'-TAGGTTTTCGAAGAAGACCG-3'(560 bp); ß-3 ßAR (S)5'-AGTGGGACTCCTCGTAATG-3'; ß-3 ßAR (AS)5'-CGCTTAGCTACGACGAAC-3' (444 bp). RT-PCR for ß actin as the housekeeping gene was performed in the same reaction to normalize the data . (ß ACTIN (S) 5'- CGTAAAGACCTCTATGCCAA - 3';ß ACTIN(AS) 5'- AGCCATGCCAAATGTGTCAT - 3' (387bp). Membrane preparation from myocardial tissues were used to determine the protein expression of the different ßAR subtypes by immunoblot. Paired t test was used to compare the signal intensity assessed by densitometry between Control and Cocaine rats. $P<0.05$ was deemed significant.
RESULTS: Three different subpopulations of ßAR were identified by mRNA expression. The expression of ß-1 and ß-2 ßAR mRNA (n=12) was comparable between Control and Cocaine neonatal rat hearts at 14 days of age ($p>0.05$). In contrast, myocardial ß-3 ßAR mRNA (n=12) was reduced in neonatal rats with perinatal cocaine exposure (0.4±0.16) compared to controls (0.6±0.2). Immunodetectable ß-1 and ß-2 ßAR were comparable.
DISCUSSION: Our results indicate that ß-1, ß-2 and ß-3 ßAR are expressed in the neonatal rat heart. Moreover, perinatal cocaine exposure regulates the expression of ßAR in a subtype-selective manner. The observation that ß-3 ßAR are found in the neonatal rat heart suggest that they might have a functional role. We plan to determine the protein expression and the subcellular distribution of the ß-3 ßAR to further elucidate the characterize the myocardial ß-3 ßAR in the neonatal rat heart. In addition, our future experiments will also examine whether the reduced ßAR hyporesponsiveness might be mediated through the ß-3 ßAR and we will explore the possible mechanisms by which perinatal cocaine exposure regulated the expression of ß-3 ßAR.
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S-243.

ACUTE FOOT SHOCK INDUCES DIVERSE TRANSCRIPTIONAL CHANGE IN RAT AMYGDALA

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General anesthesia produces amnesia by mechanisms which are unknown. A useful model of memory formation in anesthesia research is fear conditioning in which an animal learns to associate a neutral stimulus with a noxious one, e.g., a tone with a foot shock (FS). We sought to determine the effects of foot shock on the basolateral amygdala, a region which forms the association between neutral and noxious stimuli.
Methods. With IRB approval, 14 rats (9 control, 5 FS) were studied. Rats were exposed in a familiar cage to either no novel stimuli or to 3 exposures of 3 ma FS, each 2s in duration. Rats recovered for 6 hr, then were then sacrificed, brains extracted, and bilateral baso-lateral nuclei of the amygdala removed under RNAase-free conditions. The polyA RNA was extracted and studied using Affymetrix RAE 230 gene chips(simultaneous measurement of abt. 16,000 ESTs). Expression data were standardized, log2 transformed and the experimental group compared to the baseline control group using 2-tailed t-test. Since these comparisons were intended for hypothesis generation rather than testing, no Bonferroni corrections were used and $p < 0.05$ considered significant.
Results. Pain altered RNA expression in the amygdala. We found widespread, but selective changes in many biological subsystems. Of particular interest, we observed changes in machinery of cell-cell communication, both hormonal and via ligand-gated ion channels. Pain induced down-regulation of opioid growth factor receptor, which represses growth and plasticity and the leptin receptor. Up-regulation was seen in the receptors for thyrotropin releasing hormone, growth hormone, fibroblastic growth hormone, corticotropic releasing hormone, arginine vasopressin, secretin, thyroid hormone, glucocorticoid modulatory element. Pain was also associated with up-regulation ion channels, e.g., potassium channels (Kcna1, Kcnj3, Kcnj4, Kcnj11, Kcnj 13), and glutamate delta 1. Transcription of several voltage gated channels were also modified: chloride channel 2, Sodium 3a and 10a, and potassium channels TWIK2 and Kcnd3.
Discussion. Anesthesia not only produces amnesia, but also modifies the response to pain. By increasing sensitivity to growth-related mediators, the specific genomic changes seen here appear to set the stage for plasticity, in this case, sub-acute adaptation to pain. Better understanding of the genomic response to pain will require measurements of expression over a range of time intervals.

S-244.

ISOFLURANE ALTERS TRANSCRIPTION OF NEURON-RELATED PROTEINS IN RATS

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The intracellular effects of potent inhaled anesthetics have not been extensively explored. It is proposed that certain clinical anesthetic effects such as amnesia requires modulation of genetic transcription and protein synthesis in neurons. We relate here the observed effects of a short exposure of isoflurane on the transcription of expressed sequence tags (ESTs, or genes) in rat amygdala.
Methods. With IRB approval, 14 rats (9 control, 5 isoflurane) were studied. Rats were exposed in a familiar cage to either oxygen, or isoflurane 2.0% inspired in oxygen for 15 min. Rats recovered for 6 hr, then were then sacrificed, brains extracted, and bilateral baso-lateral nuclei of the amygdala removed under RNAase-free conditions. The polyA RNA was extracted and studied using Affymetrix RAE 230 gene chips(simultaneous measurement of abt 16,000 ESTs). Expression data were standardized, log2 transformed and the experimental group compared to the baseline control group using 2-tailed t-test. Since these comparisons were intended for hypothesis generation rather than testing, no Bonferroni corrections were used and $p <= 0.05$ considered significant.
Results. Isoflurane was associated with 674 ESTs changed from baseline, further restriction to those with changes exceeding 20% yielded 213 ESTs whose function was identified using PubMed Gene. Isoflurane up-regulated several subunits of voltage dependent calcium and potassium channels in addition to the TASK1 channel. Expression of receptors for neuropeptide Y/YY, GDNF, leptin, and purines were altered. Solute carriers for glycine were up-regulated whereas those for glutamate were down regulated. Expression of several ESTs involved in neurotransmitter release and cytoskeletal structure (clustering and scaffolding in particular) were altered. The ESTs for several proteins involved in neural plasticity including DLGH3, MOBP, neuregulin 1 were up-regulated and ROBO1 expression was depressed. Complete results will be enumerated on the poster.
Discussion. The effects of isoflurane do not stop at the cell membrane, but rather come to alter genetic transcription in many areas of cell function. Isoflurane alters transcription of a select group of proteins, not a general modulation. In this abstract we outline, from a functional standpoint that transcription of neuron-associated proteins are altered by isoflurane and that these alterations may be relevant to the mechanism of behavioral changes seen during and following exposure to general anesthesia.

S-245.

EXPRESSION PROFILING OF HUMAN ATHEROSCLEROTIC LESIONS TO IDENTIFY MOLECULAR MECHANISM UNDERLYING PLAQUE DESTABILIZATION

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Introduction: Erosion or rupture of atherosclerotic plaques with consecutive exposition of thrombogenic plaque material to the blood stream is the major cause of acute coronary syndromes or infarction. Prevention of plaque-destabilization is of great interest in clinical situations with increased peri-operative stress. Identification of new molecular targets that participate intrinsically in the development of unstable plaque is important for developing new drugs. Here we demonstrate that large scale gene expression analysis of human coronary artery thrombendarterectomy specimens, classified and graded for their potential to trigger thrombus formation, generates reliable results.
Methods: To validate this method we used a DNA-array with 96 genes, which have been shown to take part in the pathogenesis of atherosclerosis. Therefore, human thrombendarterectomy specimens harvested from right coronary arteries with advanced coronary artery disease during CABG surgery were placed in RNA-stabilizing buffer and snap-frozen in tissue freezing medium. Cryosections were stained with cell specific markers and oil-red-o to characterize and grade individual plaques in fibrotic and vulnerable plaques. cDNA was generated from 2 fibrotic stable plaques and 2 prothrombotic unstable plaques and hybridized to GEArrays Q Series Cardiovascular Disease (Bioscience). Spots were visualized with chemiluminescence and normalized to housekeeping genes using Kodak Image station and software (Kodak).
Results: Several genes were strongly expressed in both plaque types, e.g. fibronectin, c-IAP2, ABC-1, PAI-1, HsbpB, M-CSF, integrin beta 5. mRNA levels of a set of genes, whose expression is associated with destabilization of lesions, were more then twofold increased in unstable plaques, e.g. CD44, collagen type III α1 chain, fatty acid binding protein, ICAM-2, osteopontin. Validation of these results using real time PCR and a larger sample size is needed.
Discussion: Although the main pattern of gene expression of most of atherosclerosis relevant genes was unchanged comparing stable with unstable lesions, a subset of genes was >2-fold up-regulated. These genes have previously been shown to be closely related to plaque destabilization. Therefore, large scale expression analysis is a viable method to study changes of gene expression in individual thrombendarterectomy lesions and to identify new targets for drug development. Moreover this method applied to micro-arrays containing ESTs and SNPs could provide new insights in the molecular mechanisms of drug therapies preventing plaque rupture in clinical studies.

Neuroanesthesia

S-246.

ESSENTIAL ROLE OF ERYTHROPOIETIN RECEPTOR UPREGULATION IN ISCHEMIC PRECONDITIONING IN THE RAT RETINA

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Introduction: Retinal ischemic pre-conditioning (IPC) results in complete functional and histological protection from subsequent ischemic damage (1,2). Endogenous protection by IPC provides an ideal model for identifying novel neuroprotective mechanisms (3). Erythropoietin (Epo), a hematopoietic cytokine, also plays a critical role in neuronal survival after ischemic injury (4). We observed in an earlier study that retinal ischemia resulted in pronounced up-regulation of Epo-R and decreased Epo expression in specific retinal cell types (5). Injection of soluble Epo receptor (Epo-R) prior to ischemia neutralized endogenous Epo and exacerbated functional damage (5). Accordingly, we investigated the role of the Epo/Epo-R system in IPC. Methods: Male Sprague-Dawley rats (200-250 g) were were anesthetized with chloral hydrate (450 mg/kg i.p.). For preconditioning, the intraocular pressure was increased to 110 mm Hg for 8 minutes while the opposite eye of each animal served as the non-ischemic control. Ischemia was induced 24 h later (2). Electroretinogram (ERG) was measured and quantitated as we previously reported (2,5). Soluble Epo-R or denatured Epo-R (control) was injected into the vitreous prior to IPC (5). Whole retinal homogenates were collected at 1, 6, and 24 h after IPC for Western blotting and RT-PCR for Epo and Epo-R. Retinal cryosections were prepared for immunohistochemistry. Results: Western blotting showed increased Epo-R protein at 24 h after IPC. Peptide competition experiment proved that the protein bands corresponded to Epo-R (Figure). RT-PCR showed increased Epo-R gene expression at 1 h after IPC. We found no change in expression of Epo after IPC. The injection of soluble Epo-R completely attenuated the protective effect of IPC as measured by the recovery of the ERG b wave after ischemia. Discussion: These results prove conclusively that upregulation of the Epo-R is an essential component of ischemic preconditioning in the in vivo retina. The mechanisms immediately responsible for Epo-R upregulation and those activated downstream require further study.

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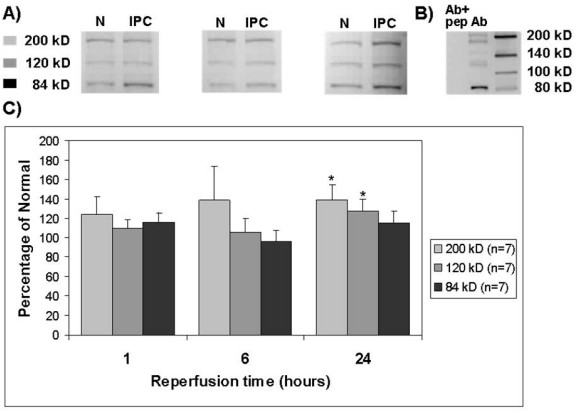

S-247.

DOXYCYCLINE AND MINOCYCLINE INHIBIT CEREBRAL MMP-9 IN A DOSE-DEPENDENT MANNER IN MICE

AUTHORS: **C. Z. Lee**, G. Yang, W. Liu, B. Guglielmo, E. Lin, W. L. Young;
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Introduction: Brain arteriovenous malformations (BAVMs) are a potentially life-threatening disorder of the central nervous system. MMP activity is experimentally associated with abnormal angiogenesis contributing to vascular malformation growth and hemorrhage by destabilizing the vascular wall. We have described greatly increased MMP-9 activity in BAVM tissue removed at surgery[1]. There is growing evidence that MMP inhibition with tetracycline derivatives may be useful in the management of vascular diseases[2]. We have recently demonstrated that doxycycline treatment decreased cerebral angiogenesis, and MMP-9 activities induced by VEGF focal hyperstimulation (via transduction of AdVEGF) in the adult mouse brain[3]. The present study is to determine whether the effect of doxycycline and a more lipid soluble tetracycline derivative, minocycline, on cerebral MMP-9 is dose-dependent using our mouse model with VEGF focal hyperstimulation in the brain.
Methods: mice (n=6 per group) with VEGF gene transduction in the brain were treated with doxycycline or minocycline, respectively. The doses were given at 0.1, 1, 5,10,30,50,100 mg/kg/day through drinking water for 1 week. Brain MMP-9 activities were determined using gelatin zymography, and the mRNA expressions were determined using real time PCR.
Results: mRNA expression was inhibited by doxycycline starting at 10 and further at 50 mg/kg/day, corresponding to 37% and 52% inhibition of the AdVEGF induced MMP-9 (see figure. d: doxycycline; m: minocycline; 5: 5 mg/kg/day, etc.). Minocycline appeared to have more potent effect on MMP-9 mRNA expression, starting at 5 and further at 30 mg/kg/day, corresponding to 38% and 62% inhibition of the AdVEGF induced MMP-9. In a similar pattern but at lower drug dosages, doxycycline started to suppress MMP-9 activity at 1 mg/kg/day, while minocycline with the effect at an even lower dose, 0.1 mg/kg/day.
Discussions: The inhibition of cerebral MMP-9 by doxycycline and minocycline at both gene expression and enzymatic activity levels was dose-dependent. This inhibition on MMP-9 appeared to act at the gene transcription level, and further at the protein translation and / or post-translation levels. The fact that minocycline was more potent than doxycycline in the inhibition of cerebral MMP-9 might be explained by its better lipid solubility, hence better brain penetration.

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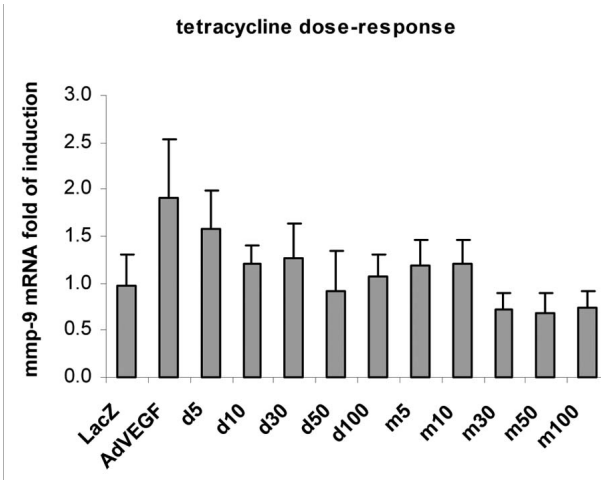

S-248.

PAIN ASSESSMENT IN ADULT POST-CRANIOTOMY PATIENTS: A PRELIMINARY PROSPECTIVE STUDY

AUTHORS: L. C. Berkow, M. Erdek, A. Gottschalk, R. E. Thompson, E. D. White, **M. Yaster**;
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Introduction In 1999 the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) mandated that the relief of pain and suffering become integral in the mission and function of all accredited hospitals and health care settings in the United States. Pain assessment became the "5th vital sign". The purpose of this prospective, clinical trial was to assess the compliance of physicians and nurses in assessing perioperative craniotomy pain.
Methods After obtaining IRB approval and patient consent, data on perioperative pain assessment was obtained in 167 patients undergoing surgical craniotomy. Data was collected pre-operatively and on post-operative day (POD) 0, 1, and 2 via chart review and patient interview by a study nurse practitioner.
Results Prior to surgery, no pain scores were documented in the patient record by either the attending neurosurgeon or the neurosurgical house staff (0/167). Approximately fifty percent of patients (84/167) had a pain score documented in the pre-operative anesthesia assessment and 89% of patients (148/167) had a pain score documented in the pre-operative nursing assessment. On POD#0, pain scores were documented in 70 % (115/167) of postoperative patients by the Intensive Care (ICU) nursing staff but in only 14 % (23/167) of patients by the ICU attending physician. Of the 138 patients who were treated with analgesics on POD#0, only 56 (41%) had a documented pain score by the ICU nursing staff following analgesic intervention. On POD#1, only 2 out of 167 patients had a documented pain score by their attending neurosurgeon, and only 1 of 167 patients had a documented pain score by the neurosurgical house staff. Almost 95 % of patients (158 / 167) had a documented pain score by nursing staff, but only 18 of the 142 patients (13%) who received analgesia on POD#1 had a documented pain score after analgesic intervention. Of the 158 patients assessed for pain by the nursing staff, 38% had 24-hour maximum pain scores > 5, and 20% had a 24-hour maximum pain scores > 7.
Discussion Despite recent JCAHO mandates and hospital policy, pain is incompletely assessed and documented in craniotomy patients perioperatively. A significant number of the patients in the study experienced pain scores at rest of 5 or greater on POD#1. Pain scores were more consistently documented by nursing staff than by neurosurgical attending physicians, neurosurgical house staff, or ICU attending physicians. Some investigators have shown that improvement in pain assessment correlates with improvement in pain management and lowering of pain scores. Future studies will address improving education and training of surgical and nursing personnel which will result in standardized and consistent assessment of pain scores.

S-249.

OROTRACHEAL INTUBATION AND CONTROLLED VENTILATION ALLOWS THE INVESTIGATION OF VOLATILE ANESTHETICS DURING HYPOXIA-ISCHEMIA IN NEONATAL MICE

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Introduction: The recent availability of genetically altered mice has made the species an attractive model in neonatal hypoxia-ischemia research. A frequently used animal model of neonatal brain hypoxia-ischemia (H/I), the Rice-Vannucci model of unilateral common carotid occlusion and hypoxia (1), has therefore recently been modified for neonatal mice. (2) However, this model has not been used to test the effects of volatile anesthetics administered during the hypoxic-ischemic insult. Therefore the present study examined 1) the feasibility of orotracheal intubation, 2) the dose-response of isoflurane on hemodynamic parameters, and 3) the effect of controlled ventilation on mortality in an isoflurane anesthetized modified Rice-Vannucci model in neonatal mice.
Methods: After IACUC approval C57BL6/129T F_1 hybrid mice were studied. Ten day-old mice were anesthetized with 3% isoflurane via nose cone to make a longitudinal 3-4 mm midline neck incision. The trachea was intubated with a 24G catheter and controlled ventilation was started (HSE-Harvard MiniVent ventilator) with 2% isoflurane in oxygen. The right common carotid artery was isolated and cannulated with micro-renathane tubing (n=5) and needle electrodes were placed to record arterial pressure and heart rate (Biopac MP150 system with AcqKnowledge software) during anesthetic depth between 0.5 and 1.5 minimum alveolar concentration of isoflurane. To evaluate mortality during H/I, the right common carotid artery was ligated during isoflurane anesthesia in another group of animals. They were then assigned to either spontaneous ventilation or orotracheal intubation with controlled ventilation (n=6 each) during isoflurane 1.75% anesthesia for a 60 min H/I challenge (10% oxygen in nitrogen), which is consistently survived by unanesthetized animals.
Results: Orotracheal intubation was achieved in all animals in either one (80%) or two attempts (20%). Arterial pressure and heart rate in mechanically ventilated mice was 59±7 mmHg and 578±184 min^{-1} at 0.9% isoflurane, 45±2 mmHg and 604±91 min^{-1} at 1.75% isoflurane, and 29±2 mmHg and 615±24 min^{-1} at 3% isoflurane, respectively. Mortality during 60 min of H/I with isoflurane 1.75% was 100% in spontaneously breathing animals and 0% in intubated and controlled ventilated animals.
Discussion: This study describes a novel neonatal mouse model utilizing endotracheal intubation and controlled ventilation, which was achieved in all animals in one or two attempts. Isoflurane anesthesia during controlled ventilation lead to a dose-dependent decrease in arterial pressure and increase in heart rate. Mortality of anesthetized animals during H/I was reversed from 100% in spontaneously breathing animals to 0% in controlled ventilated animals. Thus, this intubated and ventilated neonatal mouse model seems suitable to examine the effects of volatile anesthetics during H/I in future neuroprotection studies.
References:
1) Ann Neurol 1981;9:131,
2) Behav Brain Res 2003;145:209

S-250.

TRANSDERMAL SCOPOLAMINE REDUCES POSTOPERATIVE NAUSEA AND VOMITING IN PATIENTS AFTER RETOMASTOID CRANINECTOMY WITH MICROVASCULAR DECOMPRESSION CRANIAL NERVES

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Introduction: Postoperative nausea and vomiting (PONV) often occur after Retromastoid Craninectomy with Microvascular Decompression Cranial Nerves. From prior work we observed a high incidence of nausea and vomiting in adults recovering from this surgical procedure despite advances in antiemetic therapy. We had added transdermal scopolamine (TDS) to the antiemetic therapy for the selected patients under going the surgical procedure. The aim of this retrospective study was to assess the effectiveness of TDS on the incidence of PONV in patients following the craninectomy.
Methods: With Institutional Review Board approval, the anesthesia database was searched for craninectomies performed over two years, between January 2000 through December 2002.The search was limited to elective procedures, patient age 18 to 70 years, and American Society of Anesthesiologists (ASA) physical status I to III. The following data were collected: age and gender, total intraoperative fentanyl dose, anesthesia duration and antiemetic administration. Nausea was considered present only if noted as such in the nursing records. Emesis was recorded if retching was noted by nursing staff or vomitus was recorded on the chart. Antiemetic administration alone was not taken to indicate nausea. 99 Medical records including PACU records and anesthesia records were reviewed for the patients undergoing Retromastoid Craninectomy with Microvascular Decompression Cranial Nerves. The occurrence of nausea and vomiting, the request and time for rescue antiemetic medication over 24 hours postoperatively were recorded.
Results: 99 patients met inclusion criteria and were divided into two groups: TDS group (N=33) and no TDS group (N=66). The overall incidence of the PONV in no TDS group was 62 % (41/66) over 24hours postoperatively. PONV occurred only 27% (9/33) in TDS group (27% vs. 62%, $p<0.01$). Differences between TDS and no TDA groups with regard to age and gender, total intraoperative fentanyl dose, anesthesia duration and pre and intraoperatively antiemetic administration were not significant. No serious side effects were noted on the medical records.
Discussion: Nausea and vomiting persist in a high percentage of patients recovering from Retromastoid Craninectomy with Microvascular Decompression Cranial Nerves. The incidence of PONV in TDS group was significant lower than no TDS group. The authors conclude that transdermal scopolamine is a safe and effective antiemetic for this surgical procedure.
References:
1.Postoperative Nausea and Vomiting: A Retrospective Analysis in Patients Undergoing Retromastoid Craninectomy with Microvascular Decompression of Cranial Nerves. Anesthesiology. 99:A314, 2003
2. Transdermal hyoscine and postoperative nausea and vomiting. Anaesthesia 1996; 41: 16-23.

S-251.

THE EFFECT OF DEXMEDETOMIDINE ON STRESS RESPONSE DURING EMERGENCE FROM ANESTHESIA FOLLOWING NEUROSURGERY

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Introduction: During emergence from anesthesia following neurosurgery, early recovery with a reduced stress response is desirable because this enables neurological testing. Dexmedetomidine, an α_2 agonist, has sedative, analgesic and sympatholytic properties and does not cause significant respiratory depression. Patients sedated with dexmedetomidine can easily be aroused into a calm, alert state [1]. Thus, we tested the hypothesis that use of dexmedetomidine perioperatively for anesthesia during neurosurgery would allow rapid emergence from anesthesia with a reduced stress response.
Methods: After written informed consent was obtained, 10 patients scheduled for craniotomy were randomly divided into dexmedetomidine (n=5) and control (n=5) groups. Anesthesia was induced with 3-5mg/kg thiopental and 100μg fentanyl, and then maintained with sevoflurane and intermittent administration of 50μg fentanyl every hour. The concentration of inhaled sevoflurane was adjusted to keep the BIS level between 30-60 during surgery. In the dexmedetomidine group, 1μg/kg dexmedetomidine was administered for 30 min, starting at the time of skin incision, and was thereafter continuously infused at 0.2μg/kg/hr until 10 min after extubation. In the control group, no dexmedetomidine was administered. Arterial blood samples for determination of plasma catecholamine levels were collected at the completion of surgery and 5 min after extubation. The time taken for emergence from anesthesia was defined as the interval between the time at the end of sevoflurane inhalation and the time patients opened their eyes upon a verbal command.
Results: The time for emergence in the dexmedetomidine group appeared longer than in the control group, but the difference was not statistically significant (10.8 ± 8.3 vs. 6.4 ± 2.7 min, mean $\pm$ SD, $P=0.29$). The plasma norepinephrine level was significantly lower in the dexmedetomidine group than in the control group at both time points (at the end of surgery: 53 ± 17 vs. 254 ± 83 pg/ml; 5min after extubation: 116 ± 43 vs. 367 ± 193 pg/ml, mean $\pm$ SD, $P<0.05$). The epinephrine level was not significantly different in the two groups (at the end of surgery: 105 ± 92 vs. 100 ± 42 pg/ml, 5min after extubation: 292 ± 172 vs. 247 ± 111 pg/ml, mean $\pm$ SD).
Discussion: Dexmedetomidine significantly reduced the plasma norepinephrine level but did not affect the plasma epinephrine level at the time of emergence from anesthesia following neurosurgery. The emergence time showed a tendency for prolongation following dexmedetomidine administration. These results suggest that dexmedetomidine may be a useful adjunct perioperatively to attenuate the stress response during emergence from anesthesia following neurosurgery. Further studies will be necessary to clarify the effect of dexmedetomidine on the emergence time, and to determine the most appropriate dose of dexmedetomidine for reduction of the plasma epinephrine level during emergence from anesthesia.
References:
1. J Neurosurg Anesthesiol 16, 126, 2004.

S-252.

GENDER DIFFERENCES IN CEREBRAL BLOOD FLOW VELOCITY AND AUTOREGULATION BETWEEN THE ANTERIOR AND POSTERIOR CIRCULATIONS IN HEALTHY CHILDREN

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Background: There is little information on gender differences in cerebral autoregulation. The goal of this study was to examine differences in cerebral autoregulation between the anterior and posterior cerebral circulations in boys and girls.
Methods: Following IRB approval, healthy children without seizures, syncope, dysautonomia, or other neurologic/cardiac disorders between 10 and 16 years were enrolled. Transcranial Doppler (TCD) ultrasonography was used to measure middle cerebral artery and basilar artery flow velocities (Vmca and Vbas respectively) using standard protocols. Cerebral autoregulation was examined using tilt test methodology. Vmca and Vbas were measured in the supine and sitting upright positions. Non-invasive mean arterial pressure (MAP) was measured and respiratory rate was counted at each position. The vertical distance between the non-invasive blood pressure cuff bladder and the external auditory meatus was used to calculate the approximate MAP at the external auditory meatus (MAPe). The change in Vmca and Vbas in response to the change in MAPe (cerebral autoregulation) was quantified as the autoregulatory index (ARI). An ARI < 0.4 indicates impaired autoregulation whereas an ARI ≥ 0.4 indicates intact cerebral autoregulation. ARI was calculated for the middle cerebral (ARImca) and basilar (ARIbas) arteries. Significance was set at $p < 0.05$. Data are presented as mean ± SD.
Results: 13 boys (12.9 ± 1.7 years) and 13 girls (12 ± 1.4 years) completed the study. Baseline (supine) Vmca was higher in girls compared to boys (89 ± 16 vs. 75 ± 16 cm/s , as was baseline Vbas (59 ± 11 in girls vs. 51 ± 12 in boys ($p < 0.05$). Baseline MAPe was 79 ± 7 mmHg in boys vs. 75 ± 5 in girls ($p<0.05$), and decreased in the sitting upright position to 55 ± 8 in boys and 54 ± 8 in girls ($p=0.47$). All 26 subjects demonstrated intact autoregulation of the anterior and posterior cerebral circulations. However, boys had higher ARImca than girls (boys 0.98 ± 0.03 vs. girls 0.92 ± 0.1), and girls had higher ARIbas than boys (boys 0.92 ± 0.12 vs. girls 0.97 ± 0.06; $p=0.024$).
Conclusions: In this study of 13 boys and 13 girls between 10 and 16 years, girls demonstrated better autoregulation in the basilar artery, and boys demonstrated better autoregulation in the middle cerebral artery. Girls had higher flow velocities in both vessels. For the first time, this study provides normative data on cerebral autoregulation of the anterior and posterior circulation in healthy awake boys and girls according to gender. This information may be useful to clinicians managing children with neurologic disease.

S-253.

EFFECT OF ANAESTHETIC AGENTS ON INTRAOPERATIVE MONITORING OF SOMATOSENSORY EVOKED POTENTIALS - A COMPARISION BETWEEN ISOFLURANE AND PROPOFOL

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Intraoperative monitoring of SSEP provides the ability to monitor the functional integrity of sensory pathways. Anesthetic agents cause significant changes in SSEP and therefore it is essential to quantify these changes in order to make intraoperative recordings of evoked potentials (EP) a useful monitor of neural damage. This study was undertaken to compare and quantify the changes caused by isoflurane to that of propofol on SSEP.
PATIENTS AND METHODS
Fifteen ASA I, II patients undergoing surgery for intracranial mass lesion were consented for the study. Anesthesia was induced with midazolam, fentanyl, propofol, and vecuronium, the anesthesia was maintained with oxygen - air mixture and propofol infusion.
Median and posterior tibial nerves were stimulated and EPs were recorded continuously. Once the steady state of propofol infusion was reached, baseline value of the latency and the amplitude of median nerve (Mo) and posterior tibial nerve (To) SSEP were noted. Isoflurane was added to the inspired gas mixture and EP wave form recorded at an ET isoflurane of 1% noted as M_{ISO-1} or $T_{ISO-1.}$ Nitrous oxide was then substituted for air and EP wave forms were recorded at an ET nitrous oxide of 50% as M_{ISO-N}, $T_{ISO-N.}$ Nitrous oxide was then discontinued and the wave forms recorded when the ET nitrous oxide was negligible were noted as M_{ISO-2} or $T_{ISO-2.}$ The amplitude and latency changes were analyzed statistically.
RESULTS
1% Isoflurane reduced the amplitude of the median nerve SSEP by 40% and prolonged the latency by 5% when compared to propofol. The absolute decrease in amplitude was 2.26 μ V and the increase in latency was 1 msec. The amplitude of posterior tibial nerve waveforms was reduced by 0.25 μV (30%), and the latency were increased by 2 msec (5%) when compared to propofol. The administration of nitrous oxide with isofurane decreased the amplitude of median nerve SSEP by 3.5 μV (63%) and increased their latency by 1.1 msec (7%) as compared to when only propofol was used. Nitrous oxide decreased the amplitude of posterior tibal SSEP by 0.8 μV (56%) and increased their latency by 3 msec (8%). The amplitude of the EP was highest and the latency least when the patients were maintained on propofol infusion.
CONCLUSION
Intraoperative monitoring of median and posterior tibial nerve somatosensory evoked potentials is best recordable with propofol. However with 1 % isoflurane the morphology of the EP wave form is reproducible. The EP wave forms were lost when nitrous oxide is added to isoflurane and hence it is advisable to avoid nitrous oxide when intraoperative monitoring is required. From this study we conclude that TIVA with propofol is a better anesthetic technique when intraoperative monitoring of SSEP is vital for detection of neurological deficits.

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S-254.

EFFICACY OF LOCAL ANESTHETIC TECHNIQUES IN IMPROVING POST-CESAREAN SECTION ANALGESIA-A QUALITATIVE SYSTEMATIC REVIEW

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Introduction: In an attempt to improve the quality of postoperative analgesia local anesthetic techniques, such as, wound infiltration and nerve blocks have been employed in a variety of abdominal operations. However, with the exception of inguinal hernia repair, there is little consensus over their efficacy. The purpose of this qualitative systematic review was to assess the effectiveness of these techniques in improving post cesarean section analgesia.
Methods: The authors independently sought reports of randomized controlled trials examining the effectiveness of wound infiltration and/or nerve blocks, in which post cesarean section pain or the need for supplementary analgesia was an outcome. Electronic search strategies were used to identify eligible studies without language restriction in, MEDLINE (1966-2004), EMBASE (1980-2004) and Cochrane Data Base of Systematic Reviews and Central Register of Controlled Trials 2004. Major text books of anesthesia and journals of the last five years were hand searched for relevant studies. The reference list of retrieved articles was also searched. The last electronic search was conducted in April 2004. Each study was assigned a quality score using the Jadad scale [1].
Results: Eleven* randomized controlled trials were found eligible for inclusion. They were divided into two groups on the basis of their study design. Five trials (n=264) examined the effectiveness of surgical wound infiltration, with single or repeated doses of local anesthetics. The latter being delivered by means of a wound catheter. With the exception of one, all of these studies reported a beneficial effect as denoted by either, reduced visual analogue pain scores or narcotic consumption. Quality scores ranged from 2~4. Another six trials (n=320) were identified which examined the effectiveness of nerve blockade in supplementing post cesarean analgesia. Out of these, five studies carried out bilateral ilioinguinal nerve block and the last one performed abdominal nerves blockade. With the exception of one all other trials examining efficacy of ilioinguinal nerve block found a beneficial analgesic effect. Two studies were able to show a reduction in pain up to 24 hours. The study utilizing abdominal nerves block also reported a significant improvement in postoperative pain as compared to controls. Quality score of these studies ranged from 2~4.
Discussion: Overall the results of this qualitative systematic review suggest that incisional wound infiltration and nerve blocks provide additional post caesarean analgesia. As demonstrated in one of the trials, if movement associated pain had been assessed in other studies as well, improvement in postoperative pain might have been more evident. We recommend further well designed trials to evaluate the effectiveness of these local anesthetic techniques where long acting neuraxial opioids are administered as the primary mode of analgesia.
References:
[1] Controlled Clinical Trials-196;17:1-12.

* Available from authors.

S-255.

IDENTIFICATION OF THE EPIDURAL SPACE-A PILOT STUDY OF A NEW TECHNIQUE

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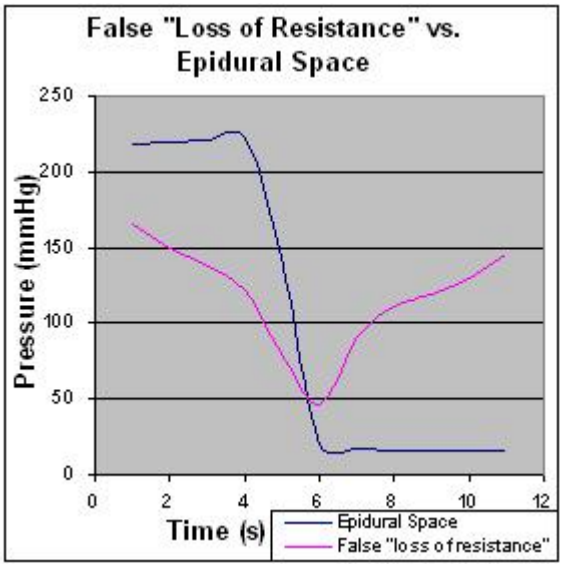
Introduction: The current techniques for identification of the epidural space rely on the subjective perception of the operator by the "loss of resistance" to air or saline. The introduction of a method or device that can objectively identify the epidural space could potentially decrease the incidence of side effects and increase the success rate of the procedure and patient safety.[1,2] The Compuflo® (Milestone Scientific, Inc, Livingston, NJ), a novel, computerized device that integrates a pressure limited infusion and aspirating system, high/low pressure alarms and a mathematical algorithm to calculate the pressure at the end of the needle.
Methods: Following institutional approval and written informed consent, 20 adult obstetric patients scheduled to receive epidural anesthesia were enrolled into this preliminary study. The Compuflo® was utilized to detect the loss of pressure indicative of entering the epidural space. The Compuflo® was attached to the Tuohy needle when the operator initially introduced the needle to a depth of 3 cm. The epidural space was identified when the pressure remained low (within 15 mmHg from original "loss of resistance" pressure of 100 mmHg) for ≥5 seconds, while the pressure in a false "loss of resistance" began to rise within 2 seconds. If the pressure was determined as a false "loss of resistance", the needle continued to be advanced until a true "loss of resistance" was located. After the final pressure reading, the Compuflo® was disconnected from the epidural needle and the epidural catheter was inserted. Epidural anesthesia was administered in the usual fashion with 0.2% ropivacaine.
Results: Pressures were compared for all decreases in pressure below 100 mmHg and categorized as either the epidural space or false "loss of resistance". The mean pressures for the false "loss of resistance" are compared to the epidural space in Figure 1. The epidural space exhibited significantly ($p<0.001$) lower pressures than the false "loss of resistance" within 1 second after the initial drop in pressure. The epidural space was successfully identified in all patients.
Discussion: The Compuflo® is able to reliably identify the epidural space from a false "loss of resistance. Within seconds, the location of the needle can easily be determined. Further studies are warranted with the use of this device.
References:
1. Anesth Analg 2003; 96:1183-7
2. Anaesthesia 2002; 57:768-72. .



S-256.

THE MEDIAN EFFECTIVE DOSE OF INTRATHECAL LEVOBUPIVACAINE FOR CAESAREAN SECTION

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Purpose: To determine the median effective dose of intrathecal L-Bupivacaine for cesarean section using updown sequential allocation study.
Methods: With Hospital Ethics Committee's approval and patients' informed consent, we recruited 30 parturients. A combined spinal epidural was performed in LLD with intrathecal(IT) levobupivacaine 0.5% with a starting dose of 8 mg. A sensory level of T_4 within 10 min after IT dose was required before the operation allowed to start. Efficacy of the IT dose during the operation was assessed using 100-mm VAS score.
1. Success: VAS ≤ 10 mm within the first 45 min of the operation's time, lead to a 0.5 mg decrement for the next patient
2. Failure: VAS >10 mm within the first 45 min of the operation's time or a sensory level of T_4 was not reached within 10 min after IT dose, lead to a 0.5 mg increment for the next patient.
Rescue medication: titration epidural boluses of 5 mL of pre-mixed: 20 mL Lignocaine 1.5% + 2 mL $NaHCO_3$ 8.4% + adrenaline 1/200.000.
Monitoring after completion of CSE:
1. Heart rate, SaO_2 and NIBP
2. Total dose of ephedrine.
3. Sensory level bilaterally to temperature differences using an icepack and motor power according to the Bromage scale.
4. Incision and delivery time.
5. Pain scores (VAS) during the operation.
6. Nausea and/vomiting, shivering and pruritus.
7. Duration of operation.
8. APGAR score at 1 and 5 min
The patient's demographic datas and adverse effects were analyzed using *t*-test. The median effective dose was estimated from the up-down sequences using the method of Dixon and Massey[i]. The sequences were also subjected to Wilcoxon and Litchfield probit regression analyses as back up/sensitivity test.
Result: Two parturients did not have a bilateral sensory level of T_4 at 10 min after IT administration. The mean duration of the surgery was 47.10 ± 11.51 min (30 - 74 min). AGAR scores at 1 and 5 min were 9. The lowest MAP was 75 ± 16 mmHg. The mean dose of ephedrine was 8.7 ± 12.8 mg and the incidence of nausea/vomiting was 7/30.
The ED_{50} of levobupivacaine for LSCS was 7.66 mg (95% CI, 7.46-7.86) using the formula of Dixon and Massey and was 7.62 mg using probit regression analysis.
Conclusion: Determining ED_{50} is useful in parturients with limited cardiac reserve and haemodynamic instability, although it should not be used a single spinal shot but as part of a CSE or other catheter-based technique.
References:
1.Dixon WJ, Massey FJ. Introduction to Statistical Analysis, 4th edition, New York, McGraw-Hill, 1983, pp 423-439

S-257.

SAFETY AND EFFICACY OF HIGH DOSE PCEA FOR LABOR USING ROPIVACAINE

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Introduction: Epidural analgesia for labor is usually as a continuous infusion or patient controlled mode (PCEA). The PCEA parameters usually consist of 3-5 ml of patient controlled boluses with 5-20 minute lock-out intervals, with or without a continuous infusion. These settings require frequent self-administrations, which might lead to patient dissatisfaction. A non- PCEA continuous infusion rate is usually limited to 10-12 ml/hr, often needing extra boluses by anesthesia providers for break-through pain. In this abstract we describe our experience with a PCEA method which utilizes *higher dose boluses* of Ropivacaine with *longer lock-out intervals*, thus requiring less interventions by the anesthesia provider or the patient. The reduced cardiac toxicity and motor blockade of Ropivacaine make it an ideal agent for this purpose.
Methods: We maintain a CQI database in our department on all labor epidural blocks we perform. The database was reviewed by the IRB and is in full compliance with HIPAA regulations. We collected data from 140 parturients who received PCEA (PCEA group), and from a control group of 160 who received a continuous infusion without PCEA (CEI group). All patients received an initial bolus of 10-15 ml of 0.2% Ropivacaine with Fentanyl 100 mcg. Further management in both groups was with Ropivacaine 0.1% plus Fentanyl 2 mcg/ml. The PCEA group received a continuous infusion at 10 ml/hr, and a PCEA dose of 8 ml with lockout interval of 30 min. The continuous group received 10ml/hr; for break-through pain, 10 ml bolus was given by an anesthesia care provider. The following data were collected: 1) maternal age, height and weight, 2) cervical dilatation at the time of epidural activation, 3) number of PCEA boluses delivered, 4) number of boluses delivered by anesthesia provider5) sensory level higher than T6, 6) hypotensive episodes requiring ephedrine administration. Results were expressed as mean (1SD) and analysed using X2 and t-tests.
Results: Maternal demographics were similar in the two groups. There were no high blocks or hypotensive episodes requiring treatment in either group. The number of interventions by the anesthesia provider in the PCEA group were one-half that in the CEI group (table).
Discussion: Our data show that higher doses of Ropivicaine for PCEA are both safe and effective, and that it decreases anesthesia staff involvement significantly.

Demographics and Local Anesthetic Use. Mean (1 SD).

Parameter	PCEA Group	CEI Group	p=
Age	31.3 (5.1)	33.0 (4.4)	0.23
Height (cm)	164.6 (5.8)	164.0 (6.02)	0.53
Weight (Kg)	80.8 (13.0)	79.5 (14.8)	0.64
% Nulliparous	42	33	0.1
Cervical Dilatation (cm)	3.5 (1.4)	3.7 (1.2)	0.2
PCEA boluses	2.7 (2.01)	Not applicable	
Boluses by anesthesia staff	0.5 (0.8)	1.0 (1.2)	0.0001

S-258.

OBSTETRIC OUTCOME OF INTRATHECAL FENTANYL VERSUS EPIDURAL ROPIVACAINE AMONG NULLIPAROUS WOMEN IN EARLY LABOR-A RANDOMIZED PROSPECTIVE TRIAL

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Introduction: Several studies have shown that epidural analgesia with local anesthetics prolongs the first and second stage of labor and increase the incidence of instrumentation delivery in nulliparous women in early labor (cervical dilation <5cm)[1,2]. The purpose of this study is to compare the effect of intrathecal fentanyl {as part of combined epidural technique (CSE) with epidural ropivacaine on the course and outcome of labor in nulliparous women.
Methods: Fifty normal term nulliparous women in early labor (cervical dilation <5cm) were randomized to receive either intrathecal fentanyl 25 µg (single shot spinal through CSE technique) or epidural ropivacaine 0.2% (6cc bolus and continuous infusion at 6cc/ hr through epidural catheter titrated to T-10 level). In the fentanyl group, as the intrathecal analgesia waned off (labor progressed to cervical dilation >5cm), supplemental analgesia was given through epidural 0.2% ropivacaine as needed.
Results: There is increased incidence of instrumentation delivery in ropivacaine group (4% Vs 0%) compared to fentanyl group. There was no significant difference in cesarean deliveries between the two groups (ropivacaine 20% Vs Fentanyl 18%). First and second stage of labor were prolonged in ropivacaine group (794 min & 53 min) compared to Fentanyl group (763 min & 48 min). Both groups had comparable VAS scores at 15 min, and 1 hr post analgesia
Conclusion: We conclude that introduction of subarachnoid narcotic in early labor (cervical dilation <5cm) in nulliparous women provides significant pain relief but does not adversely affect the course and labor outcome either in the form of prolonged labor or increased incidence of instrumentation delivery as compared to epidural local anesthetics.

Reference:
1. Anesthesiology 2004; 100:142-8
2.Am J Obstet Gynaecol 1993; 169: 851-858

Comparison of patients in Fentanyl and Naropin groups

Variable	Fentanyl group (n=49)	Naropin group (n=50)
Maternal age(yr)	26±5	22±5
Maternal weight (lbs)	163±5	160±6
Maternal height (cm	203±35	177±27
Gestation (days)	272±8	272±8
Cervical dilatation on admission (cm)	2±0.9	3±1.3
Cervical dilatation on epidural(cm)	4±0.4	4±0.7

Comparison of course of labor and delivery in patients in Fentanyl and Naropin groups

Variable	Fentanyl group (n=49)	Naropin group (n=50)
Duration of first stage of labor (min)	763±272	794±425
Duration of second stage of labor (min)	48±40	53±41
Spontaneous vaginal delivery	40	38
Lower segment cesarean delivery	9	10
Instrumental delivery	0	2

Data are reported as mean ± 1 SD

S-259.

DOES ADDITION OF BICARBONATE TO LIDOCAINE REALLY IMPROVE THE EFFICACY OF LUMBAR EPIDURAL ANESTHESIA IN CESAREAN SECTION?

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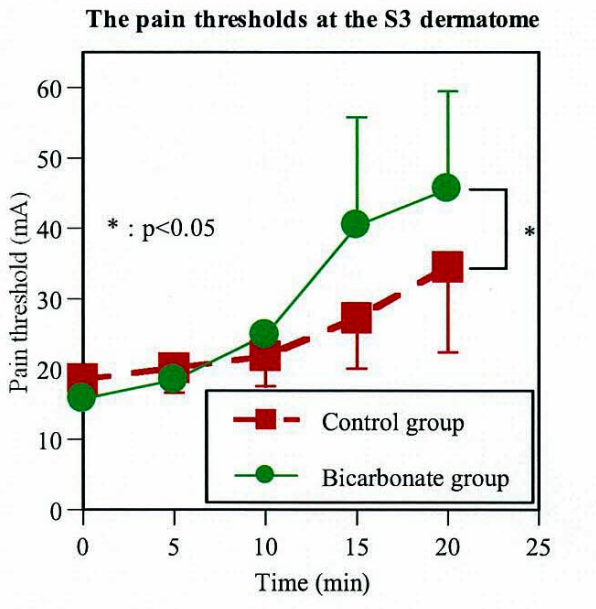
INTRODUCTION: It has been reported that addition of bicarbonate to local anesthetics enhances the efficacy of regional anesthesia and improves the sacral blockade in lumbar epidural anesthesia. In cesarean section, attention should be paid to the inadequate blockade of sacral segments when lumbar epidural anesthesia is performed. We evaluated whether the addition of bicarbonate to lidocaine-epinephrine improved the sacral blockade in cesarean section with lumbar epidural anesthesia.
METHODS: Twenty-eight patients undergoing lumbar epidural anesthesia at L2-3 were divided into two groups and received either 17 mL of 2% lidocaine-epinephrine (1: 200,000) (control group) or 17mL of 2% lidocaine-epinephrine with bicarbonate (bicarbonate group). Two mL of 8.4% sodium bicarbonate was added to 20 mL of 2% lidocaine-epinephrine. The pain threshold response after the repeated electrical stimulation was used to assess sensory blockade at the L2, S1, and S3 dermatomes. The stimulation makes it possible to quantitatively assess the sensory blockade of epidural anesthesia. Motor blockade was evaluated using Bromage scale.
RESULTS: Demographic data were comparable between the two groups. The pain thresholds at the S3 dermatome in bicarbonate group were significantly higher than that in control group (Figure; $p<0.05$). The pain thresholds at the S1 and S3 dermatomes were significantly lower than that at the L2 dermatome within each group ($p<0.01$). No differences in the pain threshold at the L2 and S1 dermatomes and the Bromage scale were found between the groups.
DISCUSSION: We show that the addition of bicarbonate to lidocaine-epinephrine improves the sensory blockade at the S3 dermatome in cesarean section with lumbar epidural anesthesia while the sensory blockade at the S1 segment is not enhanced. We also confirm that the blockade of sacral dermatomes is delayed compared with the L2 dermatome. The addition of bicarbonate to lidocaine-epinephrine is efficacious against the blockade of sacral segments, but adding bicarbonate alone to it may be insufficient for the surgical stimulation because the sensory blockade of S1 dermatome is not adequate and the motor blockade is not enhanced. To overcome the surgical stimulation, additional options also should be considered.



S-260.

STANDING STABILITY DURING CONTINUOUS EPIDURAL ROPIVACAINE/FENTANYL INFUSION AFTER ELECTIVE CESAREAN SECTION

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Introduction: Cesarean section (CS) often complicates deep vein thrombosis, since post-operative analgesia needs capability to walk earlier. There has been debate about the safety of allowing women to walk following regional analgesia because of somatosensory impairment. This study is planned to evaluate standing stability during continuous ropivacaine/fentanyl epidural infusion after elective CS.
Methods: Sixteen ASA physical status 1 or 2 term parturients enrolled this study. All parturients gave informed consent. Anesthesia for CS was performed with combined spinal-epidural anesthesia. An epidural catheter was placed at the Th12/L1 interspace, and spinal anesthesia was performed using hyperbaric bupivacaine 12 mg at the L3/4 interspace. On arriving recovery room, continuous epidural infusion (either 0.2% ropivacaine containing 2.5 mcg/ml fentanyl or 0.2% ropivacaine containing 5 mcg/ml fentanyl) at 5 ml/h was started and continued for 48 hours. Standing stability was assessed with a SYMPACKTM (Nihon Electric Company, Tokyo, Japan) at the day before CS, 24 hours and 7 days after CS. Any woman stood with bare feet and closed legs for one minute with the eyes open and closed. Statistical analysis was used with Friedman's test. A p-value less than 0.05 was considered to indicate significance.
Results: Sway area with the eyes open (0.2% ropivacaine containing 5 mcg/ml fentanyl at 5 ml/h) at 24 hours after CS was significantly higher than 7 days after CS. No woman showed motor blockade of lower extremities at any time using modified Bromage score. Both group had similar VAS score for postoperative pain relief at 24 hour after CS.
Discussion: There has been a continuing scientific debate to whether epidural fentanyl act on spinal or supraspinal sites. A recent study suggests that continuous epidural fentanyl infusion in the presence of local anesthetics acts predominantly spinal mechanism. Although the fentanyl dose of 30 mcg/h is a clinically applicable dose, continuous epidural infusion (0.2% ropivacaine containing 2.5 mcg/ml fentanyl) at 5 ml/h is safe for standing without somatosensory impairment after elective CS.
References:
Anesth Analg; 97: 1428-38, 2003,
Anesth Analg; 97: 1439-45, 2003

S-261.

COMBINED SPINAL-EPIDURAL VERSUS EPIDURAL ANALGESIA: THE INITIAL ANALGESIC METHODS MAY AFFECT THE SUBSEQUENT ANESTHETIC REQUIREMENTS DURING LABOR ANALGESIA USING PATIENT-CONTROLLED INFUSION PUMP

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Introduction: Initial analgesic methods of either initial intrathecal or epidural injection may affect the subsequent anesthetic requirements during labor analgesia. Our aim was to compare epidural anesthetic requirements using a patient-controlled infusion pump following intrathecal versus epidural analgesia.
Methods: Sixty-two nulliparous women who requested labor analgesia were enrolled in this prospective and randomized study. All patients were allocated into two groups: Epidural group received fractionated 11mL of ropivacaine 0.2%; Combined spinal-epidural (CSE) group received intrathecal bupivacaine 2.5mg with fentanyl 25μg. Following these analgesia establishment, an epidural patient-controlled infusion pump (basal infusion=6 ml/h, demand dose=5 ml, lockout interval=10 min) was started with ropivacaine 0.1% with fentanyl 0.0002% in the both groups. All data were analyzed with unpaired t-test. A $p < 0.05$ was considered significant. Data were expressed as mean ± SD.
Results: Maternal age, height and weight, and duration of labor or analgesia were similar between the two groups. However, an hourly infusion dose of ropivacaine (even with exclusion of the initial dose) was significantly less in the CSE group than in the epidural group (9.1 ± 1.8 mg vs. 11.3 ± 4.3 mg, respectively, $p<0.05$). Although a number of hourly effective demands was similar between the two groups, the number of the ineffective demands was smaller in the CSE group (3.4 ± 6.7 times) than that in the epidural group (5.8 ± 9.5 times).
Discussion: A main finding of this study was that initial intrathecal analgesia could reduce subsequent epidural anesthetic requirements during labor when compared with initial epidural analgesia. In addition, this study demonstrated a greater variability in the required dose of anesthetic in parturients receiving initial epidural analgesia than those receiving initial intrathecal analgesia. These advantages of CSE analgesia for labor may be due in part to the facilitated infiltration of epidurally administered anesthetic into the spinal cord.

S-262.

NEURAXIAL VS. SYSTEMIC ANALGESIA FOR LATENT PHASE LABOR ANALGESIA IN NULLIPAROUS PARTURIENTS WITH INDUCTION OF LABOR: EFFECT ON RATE OF OPERATIVE DELIVERY

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Introduction: Studies comparing labor outcome in parturients who received neuraxial *vs*. systemic opioid analgesia suggest early initiation of neuraxial analgesia may be associated with higher operative delivery rates.[1,2] The purpose of this randomized study is to determine if neuraxial compared to systemic analgesia, initiated during early labor in nulliparous women scheduled for induction of labor, increases the incidence of Cesarean delivery.
Methods: Healthy, term, nulliparous parturients with singleton, vertex presentation, scheduled for induction of labor, gave written, informed consent to participate in this IRB-approved study. Parturients who requested analgesia with cervical dilation <4cm were randomized to receive intrathecal fentanyl (IT) or systemic hydromorphone (SYS). Epidural analgesia, followed by patient controlled epidural analgesia (PCEA) was initiated at the 2nd analgesia request. Epidural analgesia followed by PCEA was initiated in Group SYS when the cervix was 4cm or at the 3rd request for analgesia. Parturients who first requested analgesia at cervical dilation ≥4 cm received neuraxial analgesia not dictated by study protocol (observation group (OBS)). Demographic characteristics, incidence of Cesarean delivery, time to complete cervical dilation and delivery (from initiation of analgesia), average verbal rating score for pain (VRSP) between the 1st and 2nd analgesia requests, Apgar scores and cord gases were compared among groups using the χ^2, Mann-Whitney U and Kruskal Wallis tests. $P < 0.05$ was significant.
Results: An interim analysis is presented (N=672). Demographic characteristics were similar among groups, including indication for induction of labor. The cervical dilation at neuraxial analgesia initiation was different. There was no difference among groups in the incidence of Cesarean delivery. Indications for Cesarean delivery were not different, nor was the incidence of operative vaginal delivery. The time from initiation of labor analgesia to complete cervical dilation, and delivery, was shorter in IT compared to SYS, but the duration of 2nd stage was not. Average VRSP was lower in IT. 1- and 5-min Apgar scores were similar among groups, as were umbilical cord gases.
Table.

	IT (N = 270)	SYS (N = 266)	OBS (N = 136)
Cervical dilation at neuraxial analgesia (cm)	2 (0, 3.5)	4 (1, 10)†	4 (4, 8)†
Cesarean delivery (%)	28.5	29.3	22.1
Operative vaginal delivery (%)	22	23.9	15.1
Maximum oxytocin dose (mu/min)	20 (1, 40)	20 (4, 40)	18 (6, 40)
Duration 1st stage labor (min)	337 (70, 1490)	375 (79, 1275)†	243 (16, 768)†‡
Duration 2nd stage labor (min)	92 (7, 313)	88 (7, 411)	97 (10, 300)
Average VRSP	1 (0, 10)	5 (0, 10)†	
Apgar < 7 at 1 min (%)	24	20	17
Apgar < 7 at 5 min (%)	4	2	2
Umbilical artery pH	7.23 (6.93, 7.39)	7.23 (6.87, 7.38)	7.24 (6.97, 7.38)

Data are median (range). †=different from IT. ‡=different from SYS, $P<0.05$.

Discussion: Early labor neuraxial analgesia did not increase Cesarean delivery rate, provided better analgesia and a shorter duration of labor compared to systemic analgesia. Neuraxial labor analgesia need not be withheld until cervical dilation = 4-5 cm. Supported in part by the IARS Clinical Scholar Research Award.
References:
1) Am J Obstet Gynecol 1993;169:851-8.
2) N Eng J Med 1997;337:1715-9.

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S-263.

DELAYED POSTNATAL DEVELOPMENT OF MECHANICAL ALLODYNIA IN NERVE INJURY INDUCED NEUROPATHIC PAIN

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Introduction: Neuropathic pain is thought to be a component of many diverse chronic diseases in children, but little is known of the effects of nerve injury upon the immature nervous system. We have used two established laboratory models of peripheral nerve damage-induced neuropathic pain; the spared nerve injury1 and chronic constriction injury2 in young rat pups to investigate the subsequent development of mechanical allodynia.
Methods: SNI procedure: Under halothane anaesthesia, the tibial and common peroneal nerves were cut and ligated in Sprague Dawley rats and rat pups aged (P) 3, 10, 21, 33 and 60 days (n=6 at each age). Mechanical skin sensitivity in the territory of the sural nerve, adjacent to the denervated foot areas, was tested using von Frey hairs to determine the force required to elicit 50% of maximum response (EF50). Measurements were done on day 1 and weekly for 4 weeks postoperative.
CCI procedure: Under halothane anaesthesia, the sciatic nerve was exposed and loosely ligated with catgut sutures in rats aged (P)10 and 60 days (n=4 at each age). Mechanical sensitivity on the plantar surface of the ipsilateral foot was tested as described above on postoperative days 7, 14 and at 4 weeks after surgery.
Results: Mechanical allodynia, characterised by a fall in EF50 to < 60% of control values was observed in animals that had SNI surgery at P60 and P33 and in those which had CCI at P60. SNI at or below age P21 did not lead to significant mechanical allodynia. Mechanical allodynia did not occur following the CCI procedure at age 10 days.
Discussion: In contrast to studies in mature rodents, nerve injury does not produce mechanical allodynia when it occurs before three weeks of age in the infant rat. Elucidation of the mechanisms involved in compensating for such injury in early life are likely to yield important information for the understanding and treatment of pain and injury at all ages.
References:
1)Decostard & Woolf, Pain 2000, 87;149
2) Bennett & Xie, Pain 1988, 33; 87-107)

S-264.

THE HERBAL MEDICINE SHUCHI-BUSHI REDUCES MECHANICAL ALLODYNIA IN NEUROPATHIC PAIN MOUSE

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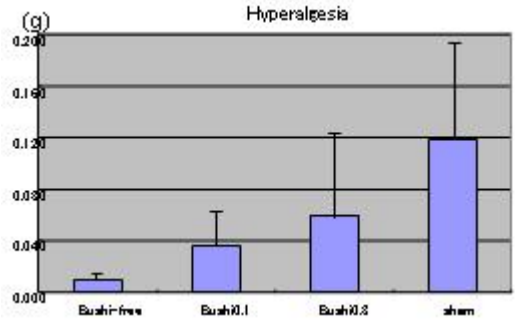
Introduction: Shuchi-Bushi N Powder for Ethical Dispensing (Tsumura Co. ltd., TJ-3022) is an herbal drug of processed aconiti tuber that attenuates its toxicity. It has been used to treat any kind of pain, or diarrhea or virus infection in Japan. However, there was no experimental study of its effects on neuropathic pain. Therefore, we studied the effect of this drug on reduction of pain in mice with neuropathic pain.
Methods: According to Malmberg's method (1), the neuropathic pain model was prepared by unilateral ligation with 9-0 silk suture at section of the sciatic nerve in the mouse (the first day). After the ligation of mouse's sciatic nerve, to investigate whether sciatic surgery was successful or not, we tried von-Fray hair test. Twenty mice with neuropathic pain except sham group were allocated randomly to four groups (each N=5). Sham group: They had no ligation of the sciatic nerve. Bushi-free group: They received only saline. Bushi 0.1 group: They received TJ-3022 0.1g/kg. Bushi 0.3 group: They received TJ-3022 0.3g/kg. TJ-3022 or saline was administered once a day for four days (from the second to fifth days). In the sixth days, we evaluated the extent of mechanical allodynia using a series of von Frey hair. Three cases with von-Fray hair stimuli, "Notice", "Move the hind paw (threshold)", "Hyperalgesia-type response" were evaluated. Data were analyzed by Kruskal-Wallis test. A P value less than 0.05 was statistically significant.
Results: Bushi-free group mice increased responsiveness to mechanical stimuli in the ipsilateral paw. Almost every mouse in the Bushi-free group showed the hyperalgesia-type response by the stimulation of 1.65 von Frey hair, which is most fine filament. Hyperalgesia-type response was not shown by 1.65 filament in the Bushi0.1 and 0.3 groups. TJ-3022 reduced the mechanical allodynia of hyperalgesia type responce (Bushi0.1 group 0.036±0.003g; Bushi0.3 group 0.059±0.064g vs Bushi-free group0.009±0.003g: $p<0.05$). It is likely that Bushi0.3 was more effective than Bushi0.1, but there was no significant difference between two groups (Fig. 1).
Discussion: According to Chinese tradition, Shuchi-Bushi is used to treat sciatic neuralgia in clinical stage in Japan. But there is no academic proof of Shuchi-Bushi's effects on neuropathic pain. Our study clearly shows that Shuchi-Bushi reduced the mechanical allodynia in neuropatic pain model.
Reference:
(1)Pain 76, 215-222 (1998)



S-265.

ESMOLOL AND LANDIOLOL, ULTRA SHORT ACTING BETA-1 BLOCKERS CAN REDUCE PAIN BEHAVIOR IN THE RAT FORMALIN TEST

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Introduction: Systemic administration of Beta blockers have been postulated to have the antinociceptive properties in experimental and clinical studies.
Intravenous esmolol has been reported to possess antinociceptive property in an experimental study[1]. This antinociceptive mechanism, however, has not been clearly understood. We examined the antinociceptive effect of intrathecal esmolol and landiolol in the rat formalin test to investigate their central effect in the modulation of pain.
Methods: Male Splague-Dawley rats (300-350g) were implanted with chronic intrathecal (IT) catheter. Five to Seven days after implantation, rats were divided into four groups for each beta blocker as follows; Saline (control), 1mcg, 3mcg, and 10mcg of esmolol for esmolol group and saline (control), 250mcg, 500mcg, and 750mcg of landiolol for landiolol group. Medications were administered intrathecally 15 min. prior to the formalin injection into the hindpaw with a 30 gauge needle. Pain- related behaviors were quantified by counting the number of flinches for 1 min. period at 1-2 and 5-6 min., and then at every 5 min. up to 60 min. after injection. The data were averaged separately for Phase 1 (0-10min) and Phase 2 (15-60min).
Results: The intrathecal injection of esmolol and landiolol decreased the number of flinches dose dependently in the phase 2, but not in the phase 1. ED50 of phase 2 were 7.4mcg. (Confidencial Interval; 3.97-13.8) and 415mcg (CI;371-463) in esmolol and landiolol respectively.
Discussion: This study suggests that intrathecally administered esmolol and landiolol decrease the nociceptive behaviors in the phase 2, but not in the phase 1 of the rat formalin test. Esmolol may have stronger analgesic potency than landiolol.
References:
1. Can J Anaesth.Jan;48 (1): 59-64,2001

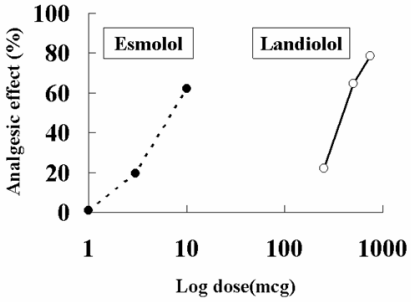

Figure. Dose-Response Curve

S-266.

AN INVESTIGATION OF THE ASSOCIATION BETWEEN PLASMA CONCENTRATION OF STABLE NITRIC OXIDE PRODUCTS, SEVERITY OF EARLY POSTOPERATIVE PAIN AND CHRONIC POST SURGICAL PAIN FOLLOWING BREAST SURGERY

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Introduction: Chronic postsurgical pain (CPSP) following mastectomy is common [1]. Early postoperative pain is the only reliable predictor of CPSP [2]. Nitric oxide plays an important role in nociception [3].
Objectives: a) to compare the effects of two analgesic regimens on perioperative stable nitric oxide products (NOx) and the likelihood of subsequent development of CPSP in this setting; b) to determine the association between perioperative NOx and the likelihood of subsequent development of CPSP.
Methods: Thirty ASA I or II patients undergoing mastectomy were randomized to one of two groups: Group S received a standard prn analgesic regimen (morphine sulphate 0.1 $mgkg^{-1}$ i.m., diclofenac 100 mg, dextropropoxyphene hydrochloride 32.5 mg + acetaminophen 325 mg p.o.); Group A received an aggressive regimen (parecoxib 40 mg i.v. bd followed by celecoxib 200 mg p.o. bd until day 5, acetaminophen 1 g qds, bupivacaine 0.25% 10 ml bd up to 48 h postoperatively through a paravertebral catheter). Visual analogue scale (VAS) pain scores at rest and on movement were systematically recorded up to postoperative day 5. A telephone interview was conducted between 2 and 3 months postoperatively. The McGill Pain Questionnaire was used to characterize pain.
NOx was estimated preoperatively, at end of surgery and at 30 minutes, 2, 4, 12, 24, 48 hours postoperatively and analyzed by chemiluminiscence. Repeated measures ANOVA with Bonferroni's correction, Fisher's exact test and Pearson's correlation was used as appropriate.
Results: 12/15 (80%) patients in group S and no patient in group A developed CPSP. All patients in group S had a McGill pain score $\geq$ 1 at ten weeks postoperatively, whereas only three patients (20%) in group A had a score >1 (explained by numbness). Compared to patients with a McGill score $\geq$ 1, patients with a score of <1 had decreased VAS scores at rest 30 min, 4, 8 and 12 h postoperatively ($p < 0.03$), and on movement at each postoperative time point from 30 min until 96 h ($p < 0.005$). NOx was decreased 12 hours postoperatively compared to baseline (21.0 ± 12.5 vs 30.0 ± 21.6, $p = 0.03$). Although a tendancy to increased NOx in group A compared to group S persisted, this reached statistical significance only at 48 h postoperatively (40.6 ± 20.1 vs 26.4 ± 13.5, $p = 0.04$). NOx was similar in patients who did and those who did not subsequently develop CPSP.
Discussion: Compared with the standard regimen, the aggressive regimen was more effective in providing pain relief with long term benefits. No association between NOx and subsequent development of CPSP could be demonstrated.
References
1. *Pain* 1996; **66:** 195-205.
2. *N Engl J Med* 1997; **336:** 1541-7
3. *Journal of Pain and Symptom Management* 1997; **44:** 225-54

S-267.

DECREASED EXPRESSION OF SODIUM CHANNEL ISOFORM NAV1.7 AFTER INFECTION WITH A RECOMBINANT HERPES VIRUS LEADS TO ALTERED NOCICEPTION IN HYPERALGESIC MICE

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Introduction: Excitable tissues throughout the body employ voltage-gated sodium channels (NaCh) to generate and propagate action potentials. Even though their role appears to be similar in all excitable tissues, at least 9 different NaCh alpha subunit gene products are known to exist. One of several possible explanations for having multiple isoforms performing the same basic function is that different NaCh isoforms may be required for the conduction of different sensory modalities. Our investigation of NaCh isoforms and sensory modalities focused on Nav1.7, a tetrodotoxin-sensitive NaCh suggested to be important in nociception and hyperalgesia by previous studies (1). To elucidate further the role of Nav1.7 in sensory modalities in the peripheral nervous system, a unique approach to decreasing dorsal root ganglion (DRG) neuron protein expression was developed.
Methods: A recombinant non-replicative herpes virus vector (2) was created that encoded anti-sense Nav1.7 mRNA. This virus was then used to infect mouse DRG nociceptors. The mice were then treated with Complete Freund's Adjuvant to induce a hyperalgesic state. Changes in Nav1.7 protein expression level in cryo-sectioned DRG neurons were determined with quanitative confocal immunohistochemistry. In addition, behavioral studies quantified nociceptive behavior (3).
Results: Image analysis demonstrated a significant decrease in Nav1.7 protein expression in small and medium diameter DRG neurons infected with the anti-sense encoding herpes virus construct in both normal and hyperalgesic mice. The hyperalgesic anti-sense infected animals demonstrated an increased latency to hindpaw withdrawal from thermal and mechanical stimuli.
Discussion: This work represents the first demonstration of specific and targeted modulation of sodium channel isoform expression in vivo. In addition, it appears that reduced levels of Nav1.7 in mouse DRG neurons decreases hyperalgesic nociceptive avoidance behavior. On-going and future work will focus on the electrophysiological effects and further define the behavioral consequences of decreased Nav1.7 protein in normal, hyperalgesic and incisional pain paradigms. Ultimately, this novel technique for changing protein expression could become an important diagnostic and therapeutic tool for the treatment of neuropathic pain.
References:
1. *Brain Research* (2000) 854:19-29.
2. *Journal of Virology* (1989) 63: 2861-5.
3. *Pain* (1996) 68:133-140.

S-268.

EFFECT OF DEVELOPMENTAL AGE ON C-FIBRE INDUCED HYPERALGESIA IN THE RAT PUP

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Introduction: Injury or noxious stimulation results in primary hyperalgesia at the site of injury and a surrounding zone of secondary mechanical hyperalgesia mediated by central changes in neuronal sensitivity. Mustard oil and capsaicin are both specific C-fibre stimulants, activating TRPA1(ANKTM1) and VR1 receptors respectively. We aimed to determine if C-fibre induced primary and secondary hyperalgesia varies with developmental age.
Methods: Sprague-Dawley rat pups aged postnatal day (P) 3, 10 and 21 were anaesthetised with halothane in oxygen. A bipolar electrode was placed in the biceps femoris and the flexor reflex electromyogram (EMG) responses to graded plantar hindpaw mechanical stimuli (von Frey hairs) were recorded and analysed. Age adjusted concentrations of inspired halothane were maintained constant for 30 minutes prior to and during recordings. EMG responses were recorded at baseline and following cutaneous application of the C-fibre stimulants mustard oil and capsaicin. The area under the stimulus-reflex response curve was determined for each animal, and subsequent measures expressed as a percentage change from baseline.
At each age, the flexion reflex EMG response to plantar mechanical stimulation was measured in three groups: (i) 100% mustard oil application on the plantar surface of the hindpaw (primary hyperalgesia) (P3:3.5mcl; P10:7mcl; P21:12mcl) or (ii) on the lateral aspect of the hindlimb (secondary hyperalgesia); and (iii) mineral oil application on the hindpaw (control).
Similar experiments were also conducted at P3, P10 and P21 comparing hindpaw injection of capsaicin 0.1% or vehicle.
Results: Primary hyperalgesia was observed at all ages as measured by a significant increase in the reflex response10 minutes following application of mustard oil compared to control. The degree of change increased with age. In contrast, secondary hyperalgesia was only apparent at P10 and P21; at P3 the response to mustard oil did not differ significantly from control.
Secondary hyperalgesia to capsaicin injection was also seen at P10 and P21 as evidenced by a significant increase in reflex response compared with vehicle. At P3 the response to capsaicin did not differ significantly from vehicle.
Discussion: C-fibre induced primary hyperalgesia was demonstrated at all developmental ages, and increased with postnatal age. C-fibre induced secondary hyperalgesia however was not produced in P3 pups by either mustard oil or capsaicin. This suggests that although C-fibre nociceptors are capable of being sensitized by exogenous stimuli and producing primary hyperalgesia early in development, the central nociceptive circuitry required for secondary hyperalgesia matures at a later developmental age.
Supported by ANZCA and Department of Anaesthesia, GOSH

S-269.

EFFECTS OF NEUROPATHIC PAIN ON FORMALIN TEST IN THE RAT: EXPRESSION OF C-FOS PROTEIN IN THE SPINAL CORD AND BEHAVIOR

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<Introduction> The status of neuropathic pain may change the response to noxious stimulation such as inflammation. Recently, it has been reported that chronic-constriction of the sciatic nerve reduces the responsiveness to formalin in rats (1). However, the mechanisms by which neuropathic pain changes the response to formalin are not elucidated and it is unclear whether the similar response occurs in other neuropathic pain models. To clarify changes in neuronal activities in the central pathways, we investigated c-Fos protein (FOS) expression in the spinal cord after an injection of formalin in the hind paw of a rat with segmental spinal nerve ligation (SSNL)-induced neuropathy.
<Methods> Male Sprague-Dawley rats (7w) were used in this study. Under anesthesia, the L5 segmental spinal nerve of one side was tightly ligated according to the model of Kim and Chung (2). In sham-operated animals, the nerve was exposed but no ligature was applied. To confirm tactile allodynia to the plantar aspect, the withdrawal threshold was measured by von Frey filaments. After 4 w of surgery, formalin test was performed. Rats with nerve ligation (the SSNL group), rats with the sham-operation (the Sham group), and naive rat (the Naive group) were used for formalin test (each group: n = 6). After an injection of 50 µl of 5% formalin, the numbers of flinching and biting were counted per 1 min every 5 min. After 60 min of formalin injection, animals were sacrificed and their spinal cords of L4 and L5 segments were isolated for FOS study by immunohistochemistry and the number of FOS per section was counted.
Data: mean ± SD. Statistical analysis: Kruskal-Wallis' test.
<Results> Before formalin test, the withdrawal threshold decreased significantly in the SSNL group (3.9 ± 1.5 g) compared with those in the Sham (11.2 ± 3.0 g, $P < 0.05$) and the Naive (14.8 ± 2.6 g, $P < 0.05$) groups. After 20 min of formalin injection, the numbers of flinching and biting in the SSNL groups (3.0 ± 3.7/min) decreased significantly compared with those in the Sham (6.8 ± 1.6/min, $P < 0.05$) and the Naive (6.2 ± 2.5/min, $P < 0.05$) groups. This significant difference was also observed at 25 and 30 min ($P < 0.05$, respectively). The number of FOS expression in the SSNL group (21.3 ± 6.4/section) was significantly smaller than those in the Sham (38.5 ± 6.9/section, $P < 0.05$) and the Naive (32.2 ± 5.3/section, $P < 0.05$) groups.
<Discussion> FOS study indicates that the decrease in neuronal activities to inflammation pain in the spinal cord after SSNL-induced neuropathy may play an important role in changing in the perception of acute pain.
<References>
(1) Anesth Analg 2003; 97:520-525.
(2) Pain 1992; 50:353-363.

S-270.

THE EFFECT OF EPIDURAL DEXMEDETOMIDINE IS DEVELOPMENTALLY REGULATED IN MODELS OF INFLAMMATORY AND CHEMICAL HYPERALGESIA IN THE RAT PUP

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Introduction: Spinally administered alpha-2 adrenergic agonists provide analgesia in children, but effects in early development have not been evaluated. Significant developmental changes in nociceptive processing, receptor distribution, and descending inhibitory mechanisms1 may influence the response to alpha-2 agonists. Our aim was to assess the response to epidural dexmedetomidine, a selective alpha-2 agonist, at different developmental ages in the rat pup. To do this we have examined: i) awake animals following carrageenan induced inflammation to allow evaluation of analgesic and sedative effects; and ii) anaesthetised animals to allow quantification of responses to threshold and suprathreshold stimuli following mustard oil-induced primary hyperalgesia.
Methods: Rat pups aged 3, 10 and 21 postnatal days (P) were tested. The hindlimb mechanical withdrawal threshold to hindpaw mechanical stimulation (von Frey hairs) was determined at baseline and three hours following experimental hindpaw inflammation with 2% carrageenan.2 Injections were performed under brief halothane in oxygen anaesthesia. Epidural saline or dexmedetomidine (2mcl/g of 0.5-10mcg/ml) was injected and withdrawal thresholds measured at 15-minute intervals, and dose-response curves constructed for the inflamed and contralateral paw. Sedation was assessed by the righting reflex.
In the second series, the withdrawal reflex was measured quantitatively in animals anaesthetised with halothane in oxygen. Following epidural injections of saline or dexmedetomidine (0.1-5mcg/ml), von Frey hairs were applied to the hindpaw, and the electromyogram (EMG) response in the biceps femoris muscle measured. The area under the withdrawal stimulus-response curve was determined prior to and 10 minutes following application of mustard oil to the hindpaw, and the percentage change from baseline calculated. All epidural solutions contained 1% Evans blue and data included if correct placement confirmed.
Results:
At all ages, epidural dexmedetomidine selectively reversed inflammatory hyperalgesia in doses that did not affect the threshold of the contralateral paw or prolong the righting reflex. Higher doses increased the threshold in the contralateral paw and prolonged the righting reflex. The doses of dexmedetomidine required to reverse hyperalgesia or produce sedation were lower at P3 compared to P10 and P21. Epidural dexmedetomidine also produced a dose-dependent reduction in mustard oil evoked hyperalgesia at all ages. Again, effective doses were lower at P3. The maximum epidural dose of dexmedetomidine had no effect when given systemically at any age.
Discussion: The effect of epidural dexmedetomidine is developmentally regulated, as the dose required to reverse hyperalgesia is lower in early life. These effects are achieved at doses that have no effect on contralateral paw baseline nociception. This data has implications for the use and dosing of spinal alpha-2 agonists in neonates and infants.
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S-271.

EFFECT OF INFLAMMATORY AGENTS ON CYTOKINE MRNA PRODUCTION FOLLOWING SPINAL CORD INJURY IN RATS

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Introduction: Activation of the cytokine cascade occurs as a manifestation of the inflammatory response to spinal cord injury (SCI). Currently, methylprednisolone (MP) is the most commonly used anti-inflammatory agent used in spinal cord trauma. Another class of agents that could be beneficial in neurotrauma is cyclooxygenase-2 (COX-2) inhibitors which will antagonize the inflammatory response secondary to COX-2 upregulation. In this study, we sought to compare the effects of COX-2 inhibitor SC76309 and methylprednsiolone (MP) on motor scores and cytokine mRNA production following spinal cord injury (SCI) in rats.
Methods: After approval from the Institutional Animal Care and Use Committee, halothane anesthetized 300 gram female Sprague-Dawley rats underwent laminectomy and exposure of the dura at T6-T8. No lesions were produced in animals in the Saline Control group. SCI was induced by weight drop of a 10 g weight from a height of 5 cm at T7. Animals with spinal cord injury were treated with saline IP, SC-76309A (60 mg/kg) IP, and MP (30 mg/kg IP) immediately after contusion. Four hours after injury, motor scores on a 0-5 scale (0 = complete deficit, 5 = no deficit) were obtained. Spinal cord sections at T7 were processed and an mRNA protection assay was used to measure an array of cytokines, including IL-1 alpha, Il-1 beta, Il-2, IL-6, and TNF. Data were summarized as mean ± sem and compared using a one-way analysis of variance (ANOVA).
Results: Animals in the Saline Control groups had no neurological deficits (motor scores = 5). Animals in the SCI + Saline group had lower motor scores compared to animals in the SCI + SC76309A group (1.083 ± 0.229 vs. 1.833 ± 0.241, $p < 0.05$). SCI + MP animals (1.667 ± 0.310) did not have significantly lower scores compared to SCI + Saline animals. The cytokine mRNAs which were detectable in spinal cord tissue include IL-1 alpha, Il-1 beta, Il-2, IL-6, and TNF. IL-2 mRNA levels were not affected by spinal cord injury. All the other cytokine mRNA levels rose following SCI.. Both SC76309 and methylprednisolone suppressed production of IL-1 beta mRNA and TNF mRNA after injury.
Conclusions: Both SC76309A and methylprednisolone inhibited production of IL-1 beta mRNA and TNF mRNA, confirming their anti-inflammatory effects on the cytokine cascade. Only SCI + SC76309A animals had significant improvement in motor scores compared to the saline injured animals. Further studies are warranted to determine if altering the cytokine cascade with anti-inflammatory agents, such as glucocorticoids and COX-2 inhibitors, offers beneficial effects and neuroprotection following spinal cord injury.

S-272.

DEAFFERENTATION-INDUCED CHANGES IN CHOLINERGIC TRANSMISSION IN PERFUSED SLICES OF RAT SPINAL CORD

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INTRODUCTION: Cholinergic modulation of nociceptive transmission through both nicotinic and muscarinic receptors in the spinal cord represents an important mechanism in pain signaling. The present studies evaluated the effects of chemical and surgical deafferentation of spinal cord neurons on the release of [^{3}H]-acetylcholine ([^{3}H]-ACh) from perfused slices of rat spinal cord.
METHODS: Following IACUC approval, rats from treated and control groups were sacrificed, spinal cords removed, and 300 um slices prepared from regional segments divided into dorsal and ventral sections. Slices were loaded with [^{3}H]-ACh and release induced by perfusion with 30 mM K^+. Chemical deafferentation was accomplished by neonatal capsaicin (50 mg/kg) on postnatal day 2, followed by sacrifice at 6 weeks (1). Spinal nerve ligation was accomplished via the method of Kim and Chung (2). Dorsal rhizotomy was accomplished by surgically cutting dorsal and ventral roots from T_{10}-L_6 with sacrifice 7 days later. Sham groups served as controls.
RESULTS: K^+-evoked release of [^{3}H]-ACh was generally higher from ventral spinal cord slices compared with the dorsal area, independent of spinal segment. Rats treated neonatally with capsaicin demonstrated a significantly decreased K^+-evoked release of [^{3}H]-ACh from dorsal horn but not ventral horn. Likewise, K^+-evoked release of [H]-ACh from dorsal horn spinal cord slices from nerve-injured adult rats was decreased. In contrast, rats subjected to dorsal rhizotomy displayed significantly reduced basal but not K^+-stimulated release of [^{3}H]-ACh from dorsal spinal cord slices compared with controls.
DISCUSSION: The data presented here show that there are regional differences in the release of ACh from spinal cord and that this release can be modulated by chemical or surgical deafferentation. Taken together, these studies also indicate that the source of ACh in the dorsal cord originates mainly from resident somata and their collaterals, interneurons and/or decending terminals, with only very minor contributions coming from primary afferents. These results help to further elucidate the role of ACh in spinal cholinergic signaling, particularly with respect to the effects of nerve injury.
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(2) Pain 50, 355-363, 1992.

S-273.

CONNEXIN 43 MRNA EXPRESSION IN RAT SPINAL CORD WITH NEUROPATHIC PAIN

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Introduction: Gap junction channels function as passageways between two or more cells allowing direct two-way communication of electrolytes, second messengers and metabolites which is dependent on the specific pattern of connexin gene. Connexin 43 (Cx43) is one type of the most abundant connexins in spinal cord. Recent studies have demonstrated that activation of cutaneous C-fibers by capsaicin or sciatic nerve transection increases Cx43 expressions in spinal cord. In this study we investigate the Cx43 mRNA expression in rat spinal cord with chronic constriction injury (CCI) of neuropathic pain.
Methods: After approved by the Animal Care Committee of Guangdong Province, 10 male adult Sprague-Dawley rats were received right sciatic nerve ligation after anesthetized. CCI-induced hyperalgesia were measured with paw withdraw thermal latency (PWTL). On 14 days after operation, Rats were sacrificed and the spinal cord $L_{4/5}$ segment was removed and cut right and left side along the midline. The difference of Cx43 mRNA expression between two sides of spinal cord was analyzed with semi-quantitative RT-PCR according to the expression of β-actin.
Results: Hyperalgesia had developed in the ipsilateral paw, which was still present 14 days after the sciatic nerve ligation compared to the contrallateral (left) side paw. Additionally, the RT-PCR amplified product for Cx43 in right spinal cord was elevated about 3.04% times than that in left spinal cord.
Conclusions: There was a significant increase of Cx43 mRNA expression in spinal cord following sciatic nerve ligation. This implicates that gap junction composed by Cx43 may be involved in the pathophysiologic process and prognosis of neuropathic pain.

S-274.

PERIPHERAL NEUROPATHIC PAIN IS ASSOCIATED WITH REDUCED MU OPIOID RECEPTOR EXPRESSION AND PRE- AND POSTSYNAPTIC ACTION IN THE RAT SPINAL CORD

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INTRODUCTION: Morphine produces antinociception through μ opioid receptor (MOR) activation. Clinical data suggests that some neuropathic pains may be relatively resistant, however, to morphine treatment. Downregulation of MOR density or sensitivity may contribute to such morphine resistance. This study evaluated the effect of the MOR agonist (DAMGO) in two independent partial peripheral nerve injury neuropathic pain models, the spared nerve injury (SNI, Pain 2000;87:149) and the spinal segmental nerve injury (SNL, Pain 1992;50:355) models.
METHODS: The left tibial and common peroneal nerves of adult rats were ligated and severed for SNI and L5 spinal nerve ligated for SNL. Intraplantar complete Freund's adjuvant (CFA) was injected into the hindpaw. 2-3 weeks post surgery (SNI or SNL) or 24 hours post CFA injection the rats were injected intrathecally with MOR agonist (DAMGO), and mechanical threshold assessed. The lumbar spinal cord slices with an attached dorsal root were cut and whole cell patch-clamp recordings were made from lamina II neurons. Primary afferent-evoked monosynaptic excitatory postsynaptic currents (EPSCs) and miniature EPSCs were recorded. Total RNA was extracted from homogenized dorsal root ganglion samples. RNase protection assay (RPA) was performed. Spinal sections were processed for immunohistochemistry using anti-MOR and the ABC technique. Sections were randomly picked from each rat for OD measurement in the superficial dorsal horn using NIH imaging software. Spinal cord slices with attached dorsal roots were prepared. The dorsal root was stimulated using a suction electrode. Two minutes after stimulation, slices were fixed and then processed for immunohistochemistry. The numbers of phophoERK-positive neurons in laminae I-II were counted.
RESULTS: In both the SNI and SNL rat peripheral neuropathic pain models, MOR expression decreases in injured dorsal root ganglion neurons and intrathecal injection of the MOR agonist DAMGO fails to produce analgesia. The normal presynaptic inhibitory effect of DAMGO on both primary afferent-evoked EPSCs and miniature EPSCs in superficial dorsal horn neurons is substantially reduced following SNI and SNL. The two nerve injury models also reduce the postsynaptic potassium channel opening action of DAMGO on lamina II spinal cord neurons.
DISCUSSION: Peripheral nerve injury results in a decrease in MOR mRNA expression in injured small caliber afferents and a consequent decreased presynaptic action of the DAMGO on evoked and miniEPSCs. The nerve lesion also results in a transynaptic loss of the postsynaptic action of DAMGO on the potassium channel in superficial dorsal horn neurons, a change that is restricted to the segmental site of termination of the injured afferents. These alterations, by reducing the efficacy of opioids to produce inhibition in the spinal cord of injured Aδ and C fiber nociceptor evoked responses, may reduce opioid sensitivity in those patients whose pain is generated mainly from injured nociceptor discharge.

S-275.

LIDOCAINE, BUPIVACAINE AND TETRACAINE INCREASE THE RELEASE OF NOREPINEPHRINE IN RAT SPINAL CORD SLICES

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INTRODUCTION: It was reported that lidocaine (Lido) released norepinephrine (NE) in rat spinal cord.(1) The other study demonstrated that alpha-2 adrenoceptor antagonists partially inhibited the antinociceptive effect of spinal Lido and suggested that the NE release played an important role in Lido-induced spinal antinociception.(2) However, it is unclear whether Lido releases NE in a concentration-dependent manner, and whether other local anesthetics have similar effects. Therefore, we investigated the concentration-dependency of NE release by Lido, in comparison with bupivacaine (Bupi) and tetracaine (Tet).
METHODS: Male Sprague-Dawley rats were used. After decapitation, spinal cord was cut transversally into slices. The slices were incubated for 30 min in Krebs solution containing [^{3}H]-norepinephrine ([^{3}H] -NE), gassed with a mixture of 95% O_2 and 5% CO_2 at 37ºC. After incubation, the slices were superfused at 37°C with oxygenated Krebs solution for 90 min. After initial perfusion, 5-min fractions were collected with a fraction collector. The slices were stimulated electrically (3 Hz, 2 ms, 60 mA, for 3 min; S_1) and exposed to local anesthetics (Lido, Bupi, and Tet at 0.1, 0.5, 1, 5 and 10 mM, respectively; S_2). [^{3}H]-NE in collected solution and tissue were counted with liquid scintillator. The effect of local anesthetics on NE release was expressed as the ratio of the fractional release (FR: % of total tissue radioactivity) values for the second (S_2) and the first (S_1) stimulation (FRS_2/FRS_1). Results are presented as mean ± SEM. The data was analyzed using two-way ANOVA followed by Bonferroni's test. $p < 0.05$ was considered significant.
RESULTS: Because of recrystallization, 10 mM of Bupi was not examined. The FRS_2/FRS_1 ratio increased in a concentration-dependent manner in all groups, and there were significant effects of more than 0.5 mM of Bupi and Tet, and more than 1 mM of Lido. Bupi and Tet augmented FRS_2/FRS_1 ratio more strongly than Lido (Figure).
DISCUSSION: The present results showed that local anesthetics increased NE release, and that the effects of Bupi and Tet were more strongly than those of Lido. These results are similar to the potency of local anesthetics, and it is suggested that NE release may contribute to antinociceptive action of local anesthetics.
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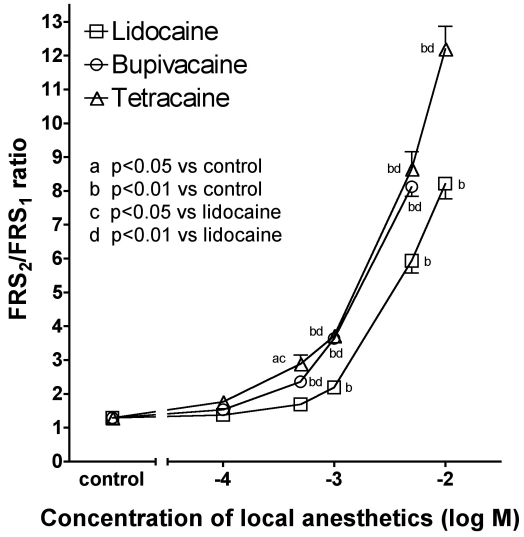

S-276.

K^+_{ATP} CHANNEL OPENERS EXACERBATE NEUROLOGICAL DYSFUNCTION INDUCED BY INTRATHECAL MORPHINE AFTER NON-INJURIOUS INTERVAL OF SPINAL CORD ISCHEMIA IN THE RATS

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Introduction: We have reported that intrathecal (IT) injection of morphine after non-injurious interval of spinal cord ischemia induced transient paraparesis in rats. This effect was reversed by subsequent IT naloxone administration, suggesting that spinal opioid receptor plays an active role in spinal functional dysinhibition initiated by transient spinal ischemia(1). Potassium channels play some role in the analgesic actions of mu-opioid agonists in the spinal cord (2). In this study, we investigate the interaction between K^+_{ATP} channels openers, nicorandil and diazoxide, and morphine on motor function after non-injurious interval of spinal cord ischemia in rats.
Methods: Sprague-Dawley rats were implanted with chronic IT catheter (PE-10) 5 days prior to induction of spinal cord ischemia. Under 1% isoflurane anesthesia, 6 min of ischemia was induced by the placement and subsequent inflation of a 2F Fogarty catheter which was inserted the descending thoracic aorta and combined with systemic hypotension (40mmHg) produced by withdrawal of the blood from the left carotid artery (Taira and Marsara Model). After ischemia, all catheters were removed, incisions were closed, and all rats were allowed to recover from anesthesia. During the reperfusion period the recovery of motor function (motor function index: MDI) was assessed periodically using a 6 point grading scale (6=complete paraparesis, 0=normal motor function). Rats were administered with either 1 or 30 µg of IT morphine (Group M) after 1 hr of reperfusion. 10µg of nicorandil (Group MN) or 200 µg of diazoxide (GroupMD) was administered intrathecally at 90 min after intrathecal injection of morphine. The ED_{50} of each group represents the dosage of morphine associated with 50% probability of resultant transient spastic paraparesis (MDI=5 or 6).
Result: The ED_{50} in Group M was 16.1 µg of IT morphine when behavioral analysis was assessed 3 hrs after reperfusion. This was significantly different from Group MN (ED_{50}=2.9 µg of IT morphine) or Group MD (ED_{50}=4.2 µg of IT morphine).
Discussion: The present study suggests that the opening of K^+_{ATP} channels could enhance the exacerbating effects of IT morphine on neurological outcome after non-injurious interval of spinal cord ischemia in rats. We should be well aware that a combination with K^+_{ATP} channel opener and morphine might exacerbate neurological dysfunction after a spinal cord ischemia.
References:
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2) Anesth Analg. 90:1146-51, 2000

S-277.

BETA RECEPTORS MODULATE THE RELEASE OF [^{3}H]-NOREPINEPHRINE IN RAT SPINAL CORD SLICES

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Introduction: Increasing evidence suggests that β-blocker has antinociceptive effects[1]. There is evidence that stimulation of the noradrenergic neurons of spinal cord is associated with antinociception. No investigation of the effects of the β-blocker on norepinephrine(NE) release has been reported for spinal cord. Thus, we investigated whether β-blocker modulates NE release in rat spinal cord slices.
Methods: The investigation was approved by the Institutional Animal Use and Care Committee. After the SD-rat spinal cord slices were preincubated for 30 min at 37°C in 1 ml oxygenated medium containing 0.1 μM[^{3}H]NE, the slices were superfused at 37°C with oxygenated medium. After an initial perfusion of 90 min, 5-min fractions were collected with a fraction collector. NE release was induced by electrical stimulation (3 Hz, 2 ms, 40 V, for 3 min). The slices were field stimulated for 3 min during the 4th (S_1) and 11th (S_2) 5-min superfusion collection period. Perfusion of drugs was started at the 8th collection period (15 min before S_2) and was maintained until the 14th collection period. Radioactivity of the fraction and of the tissue was measured with liquid scintillation spectrometry. Fractional release (FR in %) was calculated as a percentage of the radioactivity present in the slices at the beginning of the stimulation period. The effect of drugs on evoked release was expressed as the ratio of the fractional release (FR) values for the second (S_2) and first (S_1) stimulation (FRS_2/FRS_1). Drugs were administered between S_2 and S_1 and kept in the perfusion fluid until the end of experiments. The following drugs were used [^{3}H]NE, Propranolol, Alprenolol (β1 and β2 receptor antagonist), CGP20712A (β1 receptor antagonist), ICI118551 (β2 receptor antagonist). Results are expressed as mean ± SD. Data were analyzed using one-way ANOVA followed by Dunnett's test. Statistical significance was set at $p < 0.05$.
Results: Propranolol, alprenolol and CGP20712A significantly reduced the release of [^{3}H]NE. The FRS_2/FRS_1 of propranolol, alprenolol and CGP20712A were decreased from 1.01±0.09 (control) to 0.69±0.13 (1μM, $p<0.05$), to 0.67±0.21 (1μM, $p<0.05$), to 0.60±0.19 (1μM, $p<0.05$) respectively. The FRS_2/FRS_1 of ICI118551was decreased from 1.01±0.09 (control) to 0.90 ± 0.20 (1μM), but there was no significance.
Discussion: Propranolol, alprenolol and CGP20712A inhibited the release of NE in response to neuronal stimulation but, ICI118551 did not inhibit the release of NE. The results obtained from this investigation indicate that β receptors are involved in the modulation of NE release from rat spinal cord. The β1 receptor antagonist is able to reduce noradrenergic neurotransmission and acetylcholine can inhibit the spinal cord NE release via β1 receptors. Although additional studies employing β agonists are need, our findings are of broad relevance to our understanding of spinal noradrenergic mechanisms underlying the control of nociception.
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S-278.

EFFECT OF ORAL CANNABIS EXTRACT WITH DEFINED THC CONTENT ON THE DEVELOPMENT OF SPONTANEOUS PAIN AND HYPERALGESIA AFTER INTRADERMAL CAPSAICIN INJECTION: A PLACEBO-CONTROLLED, RANDOMISED CROSSOVER STUDY IN HUMANS

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Introduction: Analgesic and anti-hyperalgesic properties of cannabinoids have been demonstrated in numerous animal models. However, the data of the few clinical trials with their small and heterogeneous study populations are less convincing. The objective of our study was to investigate the effects of an orally administered standardised cannabis extract on pain response and hyperalgesia induced in healthy volunteers by the intradermal injection of capsaicin.
Methods: After approval by our local ethics committee, healthy female volunteers (n = 16, median age 23 yrs, median BMI 22) were randomised for this double-blind, crossover study. Capsules containing cannabis extract standardised on its Δ9-tetrahydrocannabinol (THC) content (20mg THC each) or active placebo (5mg diazepam) were administered orally together with a standard breakfast. One hundred and fifty minutes after the medication, 20 μl of 0.1% capsaicin were intradermally injected into one forearm. Using an 11-point visual analogue scale (VAS), the initial pain intensity and its decrease were determined at 15 s intervals for the first 2 min, followed by measurements at 2.5, 9, and 15 min after injection. The flare area was assessed by tracing on an acetate sheet 10 min after injection. The hyperalgesic area was determined by pinprick and brush.
Results: Maximum pain intensity was measured immediately after capsaicin injection and disappeared almost completely within 15 min. There was no significant difference in spontaneous pain intensity between the treatment groups, but pain decreased more rapidly under cannabis compared to placebo. Cannabinoid medication had no influence on the flare area or the area of hyperalgesia determined by brush and pinprick testing
Discussion: The intradermal administration of capsaicin, a VR1 receptor agonist, leads to a rapid onset neurogenic inflammation with a local erythema due to the release of neuropeptides from nociceptive nerve endings. The spontaneous pain immediately after capsaicin injection is followed by a secondary mechanical hyperalgesia resulting mainly from central sensitisation. Rukwied et al. described that the hyperalgesia after topically administered capsaicin could be prevented by local pre-treatment of the skin with patches that were soaked with the synthetic cannabinoid WIN 55-212. In our study, however, the intensity of the acute capsaicin-induced pain was not affected by oral pre-treatment with cannabinoids. Only a tendency towards a more rapid decrease of the spontaneous pain was found after cannabis. Thus, in contrast to the animal data, no effect on centrally induced secondary hyperalgesia could be observed in this human model.
Reference:
Rukwied R et al.(2003), Pain 102(3)

S-279.

ACTIVATION OF VANILLOID RECEPTOR (TRPV1) BY PROPOFOL IN RAT DORSAL ROOT GANGLION NEURONS

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Introduction: Propofol is the most commonly used intravenous anesthetic for the induction and maintenance of general anesthesia. One of the most common undesirable effects of propofol during induction of anesthesia is pain at the site of intravenous injection. Excitation of perivascular nociceptors at the site of injection is thought to be responsible for propofol-induced pain. However, very little is known about the mechanisms by which this occurs. The goal of the present study was to investigate the stimulatory effects of propofol on vanilloid receptor (TRPV1), which plays an important role in the pain signal transduction.
Methods: All procedures were approved by the Institutional Animal Care and Use Committee. Lumbar DRG neurons from adult Sprague-Dawley rats were isolated with enzymatic dissociation, and grown in the presence of nerve growth factor. Chinese Hamster Ovary (CHO) cells, which do not express endogenous TRPV1, were transfected with the cDNA for rat TRPV1 using Lipofectamine PLUS reagent and stable cells expressing TRPV1 protein were isolated. The functional integrity of exogenous TRPV1 in CHO cells was confirmed by testing their capsaicin-sensitivity. Changes in intracellular Ca^{2+} were measured using the fluorescent Ca^{2+}-sensitive dye, Fura-2. In all experiments of this study, pure propofol (Sigma Aldrich) was used.
Results: In the presence of 2 mM extracellular Ca^{2+}, application of propofol (10 10 µM to 100 µM) elicited a rapid increase in intracellular Ca^{2+} in small diameter, capsaicin-sensitive DRG neurons. By contrast, capsaicin-insensitive neurons showed little or no Ca^{2+} response upon stimulation with propofol. In Ca^{2+}-free extracellular medium, propofol did not elicit any changes in intracellular Ca^{2+} in DRG neurons, suggesting that Ca^{2+} influx is responsible for propofol's effects. Propofol-induced Ca^{2+} response was sensitive to inhibition by TRPV1 receptor antagonists capsazepine (25-50 µM) and ruthenium red (10 µM). To test the hypothesis that propofol exerts its effects by direct activation of TRPV1, recombinant rat TRPV1 was expressed in CHO cells (CHO-TRPV1). Similar to DRG neurons, propofol induced Ca^{2+} influx in CHO-TRPV1 cells, whereas untransfected CHO cells did not exhibit any Ca^{2+} response. In both DRG and CHO-TRPV1 cells, inhibition of protein kinase C (PKC) with Bisindolylmaleimide-I (BIS-1, 2 µM) decreased the propofol-induced Ca^{2+} response, whereas activation of PKC with phorbol-12-myristate-13-acetate (PMA, 0.2 µM) led to a marked potentiation of the propofol's effect.
Discussion: These results demonstrate that propofol causes direct activation of TRPV1 in both capsaicin-sensitive DRG neurons and in CHO-TRPV1 cells. While propofol's response appears to be partially mediated by its stimulation of PKC, experimental activation of PKC significantly potentiates propofol's effects on TRPV1. These effects of propofol appear similar to capsaicin-induced activation of TRPV1. The molecular mechanisms of TRPV1 activation by propofol and the role of different isoforms of PKC are currently being investigated.

S-280.

NOCISTATIN AMIDE SUPPRESSES LOCOMOTION IN MICE AND ACTS ON A DIFFERENT RECEPTOR FROM NOCICEPTIN

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Introduction: Nociceptin or orphanin FQ (NCP), an endogenous ligand for the orphan opioid receptor-like receptor (ORL1), causes hyperalgesia and allodynia in mice. Nocistatin (NST), derived from the same precursor, antagonises these effects by acting on a different receptor that is still unidentified. (1) NCP is widely distributed in the CNS, with several nervous system effects besides nociception that are not blocked by opioid receptor antagonists. NCP can stimulate locomotion in mice. (2) It is likely that NST also has wider effects as a functional antagonist of NCP. We assessed the effects of synthetic human nocistatin C-terminal heptadecapeptide amide (NSTamide) on spontaneous locomotion in mice, to assess if it had opposite effects to NCP.
Method: Male Swiss albino mice weighing 25 g were used after institutional animal ethics committee approval. NST amide in doses of 0.16 pmol to 2560 pmol was injected into the left intra-cerebral ventricle (icv) in a constant volume of 2 µl artificial cerebrospinal fluid (aCSF). The control group had only aCSF injection. Five minutes after icv injection, the mice were monitored in a NS-AS01 locomotion monitor (Neuroscience Inc, Tokyo) for 30 minutes. We also measured locomotion after co injecting NSTamide 40 pmol with [Nphe^1]nociceptin(1-13)NH_2, (NNN), a specific NCP receptor antagonist.
Results: The cumulative counts of movement over 30 min were increasingly suppressed as NSTamide doses were increased from 0.16 to 40 pmol, with maximal suppression at 40 pmol. There was progressively less suppression as doses were further increased from 40 pmol to 2560 pmol. ANOVA and post hoc tests showed that the locomotion counts with 10, 40 and 160 pmol of NSTamide (243, 237, 247 respectively) were significantly lower compared to aCSF (785 counts). The effect of 40pmol of NSTamide was not blocked by NNN, counts remained significantly lower than with aCSF..
Discussion: NSTamide suppressed spontaneous locomotion in a U shaped dose response curve in mice. This is similar to NST's effect on locomotion (unpublished work), but with maximal suppression at a 4 fold lower dose. This contrasts with NCP's bell shaped response of stimulation at low doses and suppression at high doses.(3) This study also showed that the C terminal carboxylic group was not necessary for NST's effect on locomotion. By inhibiting carboxypeptidase metabolism, such amidation may increase NST's biological stability and potency. C terminal extended peptides, which include precursors of NST, may thus have biological activity. Unlike NCP, NSTamide was not antagonised by NNN, confirming that NSTamide acts at a distinct receptor from ORL1. These effects may be clinically important as they occur at potentially antinoceptive doses of NST.
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S-281.

DIFFERENT INVOLVEMENT OF VR1 AND VRL1 RECEPTOR IN δ AND C FIBER MEDIATED NOCICEPTION IN MOLE RAT

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Introduction: VR1 and VRL1 belong to the larger family of transient receptor potential (TRP) channels[1]. Most of VR1 correspond to unmyelinated C fiber nociceptors of dorsal root gangling and can be activated by noxious thermal stimuli (>43ºC) or the compound capsaicin (8-methyl-N-vanillyl-6_noneamide). While almost all VRL1 expressed by myelinated Aδ nociceptors in DRG that target laminae I and IIi[2]. Although VRL1 shares ~50% sequence identity with VR1, it does not bind capsaicin and activated by noxious thermal stimuli with a threshold of ~52ºC. Our previous evidence shows that African naked mole rat lack of VR1 immunostaining but have abundant VRL1 immunoexpresson on the superficial dorsal horn. The present study is to investigate if VR1 and VRL1 contribute to different types of nociception mediated by Aδ and C nociceptors.
Methods: Anesthetized naked mole rats were tested by foot withdrawal latencies with low heating rate (0.9ºC) and high heating rate (6.5ºC), which preferentially activate Aδ and C nociceptors, respectively[3]. We used capsaicin and low heating rates to selectively activate C fibers which presumably contain VR1 receptor at their cell surface and used DMSO (dimethy-sulfoxide) and high heating rate to selectively activate Aδ fiber which presumably express VRL1 channels.
Results: The studies showed that foot withdrawal latencies of mole rats have no significant changes before and after capsaicin and low rate thermal stimulation, but the latencies clearly decreased after DMSO and high rate heating.
Discussion: The results are consistent with the lack of VR1 receptor but abundant VRL1 and indicate different involvement of VR1 and VRL1 receptor in Aδ and C fiber mediated nociception, specifically VR1 is necessary for C-fiber mediated second slow pain and plays a key role for capsaicin sensitive thermally (43ºC-52ºC) induced hyperalgesia. VRL1 may contributes to Aδ mediated first fast pain and may be important for the hyperalgesia produced by DMSO and intensive thermal stimulation (>52ºC). This supports the hypothesis that first and second pain have different molecular mechanisms.
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S-282.

PARENTERAL NICOTINE REDUCES TOLERANCE TO MORPHINE IN MICE

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Introduction: Nicotine and other nicotinic agonists have been shown to have analgesic actions in animal models and volunteer studies. A single dose of nicotine nasal spray (3mg) given under anesthesia, significantly reduces pain scores and morphine utilization during the first 24 hours after gynecological surgery[1]. The duration of nicotine induced analgesia in that study was surprising given the rapid elimination half life of nicotine (1-2 hours). We hypothesized that nicotine might cause such prolonged analgesia by reducing tolerance to morphine.
Methods: Using a mouse model of postoperative pain[2] approved by the IACUC at our institution, we studied the decrement in analgesia from a chronic infusion of morphine (2mg/kg/hr) over an 18 hour period. After surgery but still under anesthesia, the mice received a single injection of either nicotine 1.5mg/kg, metanicotine 40 mg/kg (EC_{20} analgesic doses) or saline IP. We tested the latency to hind paw withdrawal in response to an infrared heat source placed near the wound. Results are expressed as the percent change from latency at 2 hours after surgery and fit to equations for first order exponential decay.
Results: Tolerance developed to over the 18 hour period in all groups. However, the group that received nicotine retained more analgesic effect after 18 hours then the control group (figure 1a) while the group that received metanicotine had less analgesic effect after 18 hours than the control group (figure 1b).
Discussion: Both nicotine and metanicotine enhance the antinociceptive action of morphine. The broad range nicotinic agonist, nicotine (1.5mg/kg) appears to impede the development of tolerance to morphine. In contrast, the more selective agonist for alpha4 beta2 type nicotinic receptors metanicotine (40 mg/kg) does not reduce, but rather favors the development of tolerance. Positive effects of nicotine on opioid tolerance are not likely to occur due to activation of alpha4 beta2 type nicotinic receptors.
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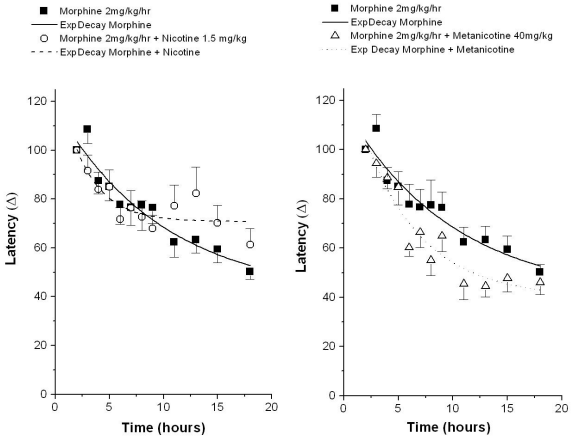

S-283.

CANNABINOID PLASMA LEVELS AND SIDE EFFECTS AFTER ORAL APPLICATION OF CAPSULES WITH CANNABIS EXTRACT OF DEFINED THC CONTENT: A RANDOMISED, ACTIVE PLACEBO-CONTROLLED, CROSSOVER STUDY IN HEALTHY VOLUNTEERS

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Introduction: Capsules of synthetic Δ9-tetrahydrocannabinol (Marinol®) have been approved for the treatment of HIV-wasting syndrome, and also for nausea and vomiting in cancer patients. The low bioavailability of oral cannabinoids due to a significant first-pass-effect and their highly variable gastrointestinal absorption make it difficult to predict dose-related cannabinoid effects in patients. In our study, we therefore investigated the plasma levels of orally administered whole plant cannabis extract and the most common side effects in a homogenous group of healthy volunteers under controlled standardised conditions.
Methods: In a randomized, double-blind, placebo-controlled crossover design, capsules containing cannabis extract standardised on its Δ9-tetrahydrocannabinol (THC) content (20mg THC each) or active placebo (5mg diazepam) were administered orally together with a standard breakfast to healthy female volunteers (n = 16, mean BMI = 25) with no history of drug abuse . Plasma levels of THC, cannabidiol (CBD) and the two active metabolites THC-11OH and THC-COOH were measured before, 2, 4 and 8 hours after administration of the study medication. The major THC side effects, such as sedation, "feeling high", vertigo, dry mouth etc. as well as arterial oxygen saturation, blood pressure, heart rate and body temperature were determined every 60 min for an 8 hrs period by both the proband and an observer using 11-point visual analogue scales (self-rating VAS and observer VAS).
Results: In 12 out of the 16 probands (75%) peak plasma levels of THC and CBD were reached within 2 hrs, in 25% (n = 4) between 2 and 4 hrs after administration showing THC values between 1.29 ng/ml and 7.91ng/ml. The peak values of CBD and the two THC metabolites showed a similar variability. The maximum VAS rating for all side effects was seen at 2.6 hrs after cannabinoid administration and was significantly enhanced compared to baseline and placebo. However, no correlation was found between the magnitude of the subject´s individual plasma level and the intensity of the side effects. Concerning the cardiovascular parameters, only the heart rates were significantly elevated and the systolic blood pressure measurements were slightly diminished in the cannabis group, whereas diastolic blood pressure, body temperature and oxygen saturation remained unaltered.
Discussion: Even under well controlled, standardised conditions, plasma levels and bioavailability of orally administered cannabinoid preparations show high interindividual variability. These results further confirm the clinical observation that cannabinoid effects after enteral administration are not clearly dose-related and may considerably vary. We therefore suggest that the individual dose titration in each subject should be an essential part of future protocols for clinical studies on therapeutic cannabinoid effects.

S-284.

THE EFFECT OF SCIATIC NERVE INJURY ON LYMPHOCYTE SUBPOPULATION OF SPLEEN AND THYMUS IN MICE

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INTRODUCTION: Chronic pain from mononeuropathy is often associated with altered cellular immune function and the need for aggressive control of pain is emphasized to expect better prognosis for an illness. To maintain the optimal performance of immune system, adequate concentration and distribution of lymphocytes are essential. Since various immune cells of thymus and spleen could be affected by chronic pain, we studied the changes in the lymphocyte subpopulations in neuropathic mice through the use of CD4, CD90.2, CD45RB and CD8 markers together with two-color flow cytometry.
METHODS: BALB/c mice (specific pathogen-free, male, 4-6 wks old) were anesthetized and left sciatic nerve was partially transected at the mid-thigh level. For behavioral assessment of mechanical sensitivity, a series of calibrated von Frey filaments were applied to the hind paw on postoperative day 5 and day 18. After confirming tactile allodynia, spleens and thymi were excised aseptically and cell viability was determined by the trypan blue exclusion method. Cells in each group were stained with fluorescein isothiocyanate (FITC)-conjugated anti-mouse CD45RB (B cell marker) and CD4 and phycoerythrin (PE)-conjugated anti-mouse CD90.2 (T cell marker) and CD8. After fixing all samples with 1% paraformaldehyde, stained cells were analyzed by using a FACScan laser flow cytometry system.
RESULTS: The tactile allodynia resulting from sciatic nerve injury was significantly increased compared to the control ($P<0.05$). While none of lymphocyte subpopulations were significantly affected on day 5, the percentages of CD90.2 and CD4 splenocytes and those of CD90.2 and CD8 thymocytes were significantly decreased compared with the control group on day 18 ($P<0.05$).
DISCUSSION: Normal subpopulations of splenic and thymic lymphocytes were changed by neuropathic pain resulting from partial nerve transection in BALB/c mice. Lymphocyte activation could be augmented in the acute stage of a stressful event (1). However, it is known that the immune system is particularly sensitive and supressed under chronic stress (2). We also found decreased T lymphocyte subpopulation in this study. Modified biochemical neurogenic component by activated sensory afferent and sympathetic efferent nerve fibers or increased activation-induced apoptosis of lymphocytes could explain these changes.
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Effect of neuropathic pain on percentage of lymphocytes subpopulations

	Spleen				Thymus			
Percent value(%)	CD90.2	CD45RB	CD8	CD4	CD90.2	CD45RB	CD8	CD4
Control	73.1±6.2	5.0±1.5	14.4±6.4	57.8±6.1	93.3±2.1	0	39.7±15.2	18.7±2.4
Day5	72.6±5.1	4.9±1.4	10.1±3.0	57.0±6.1	90.3±3.4	0	20.8±3.4	66.3±5.1*
Day 18	62.4±9.8*	12.0±4.5*	22.9±9.3*	39.4±6.8*	74.8±7.2*	0	5.4±1.3*	22.9±9.9

S-285.

CLONING, RECOMBINANT EXPRESSION AND PURIFICATION OF PROSTAGLANDIN D2 SYNTHASE, A CSF MARKER PROTEIN: IMPLICATIONS IN SAFE EPIDURAL ANESTHESIA

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Introduction: It is common for 60% of women to receive epidural analgesia for labor analgesia and 90% for caesarean section (1). There is a potential risk of dural puncture in epidural anesthesia or analgesia. Cerebrospinal fluid (CSF) drainage upon dural puncture can cause a "low pressure" headache (2). Accidental dural puncture when trying to locate the epidural space with increased intracranial pressure increases the chance of cerebellar or tentorial herniation due to the loss of CSF (3). Of major concern to anesthesiologists is an unintentional spinal block. Reliable identification/exclusion of CSF is critical to avoid inadvertent subarachnoid injection of local anesthetics during epidural anesthesia. Prostaglandin D2 synthase (PGDS) in brain is produced in choroid plexus, leptomeninges, and oligodendrocytes of the central nervous system, and secreted into the CSF. PGDS is being tested as an immunological marker for the detection of CSF (4). The aim of this study is to make recombinant PGDS (rPGDS) and generate antibodies against this marker. These reagents will be used to develop a rapid bed side diagnostic test kit to detect CSF leaks.
Methods: PGDS cDNA cloned into pDNR-LIB vector was procured from ATCC. The Creator Gene Cloning & Expression System from BD Life Sciences was used to transfer the PGDS gene directly into pLP-PROTet-6xHN bacterial expression vector. *E. coli* BL-21PRO cells were transformed with expression vector and protein expression was induced with anhydrotetracycline. rPGDS was purified using TALON resin. Using "Antigenic Index", a highly antigenic peptide of PGDS was deduced, synthesized and injected into Balb/c mice. Antiserum from immunized mice was used to validate the purified rPGDS. Human CSF samples were also analyzed with antiserum to detect PGDS.
Results: Recombinant pLP-PROTet-6xHN clones containing the transferred PGDS gene were selected by using chloramphenicol. The correct orientation of the cloned PGDS into bacterial expression vector was clarified by DNA sequencing and restriction enzyme digest. Expression of the rPGDS was evaluated by SDS-PAGE and immunoblotting with anti-His tag antibody. The antibodies generated by inoculating PGDS peptide in mice was validated by testing the antiserum against the rPGDS. The antiserum also was able to detect PGDS in Human CSF samples. The results show that PGDS is unique for CSF and can be easily identified (100%) with immunoblotting.
Discussion: Assay of PGDS can evaluate the presence of CSF in biological fluids and may be of great value in safe conduct of epidural anesthesia. rPGDS and its antibodies can be used in different clinical scenarios and can be transferred for coating on to a lateral flow dipstick/ kit for rapid bedside detection of CSF leaks.
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S-286.

MECHANISMS OF MECHANICALLY-INDUCED NOCICEPTOR ACTIVATION AND NOCICEPTOR SENSITIZATION

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Pain arising from mechanical stimuli especially mechanical hyperalgesia remains poorly understood and difficult to manage. Clues about how mechanical forces, whether by direct physical deformation or by osmotic induced shape change produce nociceptor activation have recently emerged. Principally, a member of the ion channel transient receptor potential family (TRP) termed TRPV4 has been shown to be activated by hypotonic - cell stretch conditions. However, TRPV4 does not account for many of the features of mechanically induced pain or hyperalgesia. In order to advance our understanding of mechanical activation of nociceptors, we have initiated the patch-clamp electrophysiologic study of nociceptors (primary cultures of small-diameter dorsal root ganglion DRG neurons) to an alternative mechanical stimulus, hypertonic induced cell shrinkage. Progress in the biophysical characterization of cell-shrinkage induced inward current responses will be presented. In addition, we will discuss progress on our expression-cloning project to isolate a functional ion channel subunit that is activated under cell-shrinkage conditions. Using two-electrode voltage clamp analysis of oocytes injected with *in vitro* transcribed RNA derived from DRG and kidney cDNA libraries, we are isolating candidate cDNA library pools that direct inward current responses to hypertonic stimuli. Finally, we will discuss emerging reports that sub-anesthetic concentrations of volatile anesthetics are associated with increased pain sensation and / or mechanical hyperalgesia. We will present data from our laboratory supporting the hypothesis that volatile anesthetics acting on peripheral nociceptors induce a state of nociceptor sensitization / hyperalgesia.
This work was supported by the Frontiers in Anesthesia Research Award (IARS).

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S-287.

EFFICACY AND SIDE EFFECTS OF IVPCA METHADONE VS HYDROMORPHONE

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Introduction: Methadone is a potent analgesic which has been used previously as a continuous infusion or as an IVPCA in cancer patients with pain refractory to morphine sulfate (1), and as IV intermittent boluses for acute postoperative pain relief, (2, 3, 4). The added NMDA receptor activity of methadone may allow this drug to provide superior pain relief for patients undergoing lumbar laminectomy.
Objectives: to determine the efficacy, equipotency ratio, and side effects of intravenous methadone patient controlled analgesia compared to hydromorphone for postoperative pain control after lumbar laminectomy, (5).
Methods: IRB approved, prospective, randomized, double-blind study, methadone versus hydromorphone IVPCA. Forty healthy adult patients scheduled for single level lumbar laminectomy were included. General anesthesia was standardized. Fentanyl was used for intraoperative and immediate postoperative pain control followed by IVPCA: group A methadone 0.7 mg/mL, group B hydromorphone 0.1 mg/mL with 0 basal rate, and 1 mL PCA bolus every 6 minutes. Data were collected at forty-five minutes, four, eight, twelve and twenty-four hours after initiation of PCA therapy and included pain level (VAS), PCA use, side effects, and patient satisfaction. Use of oral narcotic previous to surgery was also recorded.
Results: Both groups had similar demographic data. Pain levels (VAS), IVPCA use, and side effects were not different for both groups. Patient satisfaction was higher for group A.
Conclusions: IV PCA methadone is an effective and safe technique for acute postoperative pain control after lumbar laminectomy. The equipotency ratio for hydromorphone to methadone when used in an IVPCA for acute postoperative pain control is approximately seven to one, i.e. 0.1mg of hydromorphone produces comparable pain relief as 0.7 mg of methadone given intravenously. Methadone presents additional advantages including higher patient satisfaction and lower cost compared to hydromorphone.

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S-288.

INTRATHECAL MORPHINE AND CONCOMITANT INTRAVENOUS FENTANYL PATIENT CONTROLLED ANALGESIA: A REVIEW OF RESPIRATORY DEPRESSION

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Introduction: Intrathecal (IT) morphine for postoperative analgesia has been associated with respiratory depression for up to 18-24 hours after administration.[1] It is widely accepted that IT morphine and concomitant intravenous opioid patient-controlled analgesia (IV-PCA) is associated with an increased incidence of respiratory depression.[1] We present a retrospective series of 1000 consecutive patients receiving IT morphine and concomitant fentanyl IV-PCA, to examine the incidence of clinically significant respiratory depression.
Methods: A single site, retrospective review of 1000 consecutive patients under the age of 80 (average age 62) undergoing hip arthroplasty using spinal anesthesia with IT morphine was performed. All patients received spinal anesthetics consisting of bupivacaine (12.5 to 17.5 mg) plus morphine sulfate 0.2 mg. Institutional policy prohibits the use of IT morphine in patients 80 years and older because of potential age-related sensitivity to opioids. Beginning in the post anesthesia care unit, all patients received IV-PCA with fentanyl 10 mcg every 6 minutes, as needed, without a basal infusion. De-identified patient information in the database was queried for clinically significant respiratory depression requiring intervention with intravenous naloxone.
Results: No clinically significant respiratory depression requiring naloxone therapy was identified.
Discussion: Respiratory depression is an infrequent complication of both opioid IV-PCA and IT morphine analgesic therapy. The incidence of respiratory depression occurring during combined IT morphine and opioid IV-PCA has not been examined in a large patient series. One dose-finding study of 143 patients showed no respiratory depression with combination therapy[2]. However, respiratory depression is a relatively infrequent complication, and the results from this sample size may not be generalized to larger patient populations. We have identified a large patient cohort in this retrospective analysis of combined treatment demonstrating no clinically significant respiratory depression. Our study suggests that IT morphine sulfate 0.2mg and concomitant opioid IV-PCA without a basal infusion is generally well tolerated with a low incidence of clinically significant respiratory depression.

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S-289.

PAIN EVALUATION IN POSTOPERATIVE PATIENTS USING PATIENT CONTROLLED ANALGESIA

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Introduction: During the last decade Patient Controlled Analgesia (PCA) has replaced intermittent IM injection for postoperative pain treatment. Relatively rapid and wide acceptance of PCA by clinicians has been due to convenience of use and a better pain relief profile than that after an IM injection. An advantage over IM injection, however, does not mean adequate pain relief. Postoperative IV opioid requirements can vary 4 to 10 fold among patients. We hypothesized that significant number of patients receiving IV PCA frequently complain of moderate-to-severe pain.
Methods: Patients expected to receive postoperative IV PCA gave informed consents to participate in this IRB approved study. Subjects were interviewed concerning their pain up to 4 different times during the course of their PCA use and once within 4 hours of stopping the PCA. Subjects were asked to rate the intensity of their pain using a verbal scale of 0 to 10 at 'rest' and after 'activity'. At 'rest' measurement was defined as patient lying in the bed, or sitting in a chair for at least 10 minutes. Activity was defined as 'coughing'.
Results: Sixty subjects (58 Female) were studied. Thirty-four (34) subjects had undergone either a total abdominal hysterectomy, or myomectomy (group 1), 16 had undergone vaginal hysterectomies, or vulvectomy (group 2), and 10 had undergone colectomy, exploratory laparotomy, or a low anterior resection (group 3). PCA was programmed to deliver analgesic every 10 minutes 80% of the times and every 6 minutes 20% of the times. Mean pain score during the first 12 hrs of PCA use was (5.8±3.1) at rest and (6.2±3.5) after activity. During the first 12 hours of being on PCA 70%, and 78% of the subjects had moderate-to-severe pain (VAS ≥ 5) at rest or following activity, respectively. Corresponding values were 34% and 73% for the 12-24 hr period, 40% and 70% for the 24-36 hr period, and 34% and 64% for the 36-48 hr period. Within 4 hours of stopping the PCA 30% and 58% of the subjects had moderate-to-severe pain at rest and following activity, respectively. Satisfaction with pain control was rated as 'good', or 'very good' by 54% of the subjects during the first 12 hr of PCA use.
Discussion: Postoperative pain is not adequately treated in many patients. It is most severe during the first 12 postoperative hours and gradually decreases with time. Approximately 1/3 of the patients continue to have moderate-to-severe pain at rest during PCA use or within a few hours after PCA is stopped. More than half of patients continue to have moderate-to-severe pain following a simple activity. Successful postoperative pain management using PCA is difficult to achieve on a consistent basis unless treatment is individualized.

S-290.

THE ANALGESIC EFFECT OF SELECTIVE COX-2 INHIBITOR, ETODOLAC GIVEN BEFORE VIDEO-ASSISTED THORACOSCOPIC SYMPATHECTOMY FOR THE POSTOPERATIVE PAIN MANAGEMENT

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Introduction: Video-assisted thoracoscopic sympathectomy is a simple, safe, minimally invasive, and effective treatment for palmar hyperhidrosis. Pain therapy is an important aspect in the postoperative care of patients with this benign functional disorder. This study was performed to evaluate the analgesic efficacy of pretreatment with a selective COX-2 inhibitor, etodolac, on postoperative pain after Video-assisted thoracoscopic sympathectomy.
Methods: 28 patients (11 males and 17 females) were studied. The average age of the subjects was 28.1 years. Patients were randomly assigned to 4 groups: Group A; patients who received placebo, dicrofenac 25 mg, etodolac 200 mg, and etodolac 400 mg, at 1h before surgery (n=7 in each group). The procedure was performed with the patient under general anesthesia using one-lung ventilation. A 1-cm incision was made in the third intercostals space below the axilla. An electroresectoscope was then inserted between the ribs. Once the sympathetic trunk at the neck of the ribs was identified, targeted T-2,3 ganglia were electrocoauterized. All procedures were performed by the same surgeons (KM and KK). Postoperative pain was treated with dicrofenac 50 mg suppository. Treatment efficacy was monitored by the visual analogue scale (VAS) and numerical rating scale (NRS), which are established instrument to assess pain intensity. VAS and NRS were recorded at 3h and 12h after surgery. Time to first analgesic medication and the number of postoperative doses of supplemental dicrofenac are also monitored.
Results: No complication was observed in the perioperative period. After sympathectomy, all patients showed the increases in skin temperatures of both palms on thermography (mean 4.6°C) and showed the disappearance of sweating, indicating that sympathectomy was successful. The mean VAS score at 3h after surgery were 63.1 in placebo group, 59.9 in dicrofenac group, 58.6 in 200 mg etodolac group, and 36.6 in 400 mg etodolac group. The mean NRS score at 3h after surgery were 58.6, 60.0, 57.1, and 35.7, respectively. However, there was no statistically significant difference in VAS and NRS at 12h after surgery. The mean time to first medication were 51.4 min, 55.7 min, 63.1 min, and 201.4 min, respectively. There was a significantly greater mean time to the first medication for the 400 mg etodolac group. The number of postoperative medications ranged from 1 to 3. There was no statistically significant difference in the number of postoperative dicrofenac administration between the groups.
Discussion: The preoperative use of 400 mg etodolac reduces acute postoperative pain scores after ETS without an increase in side effects. Our findings indicate that it may help improving the satisfaction rate in Video-assisted thoracoscopic sympathectomy patients .

S-291.

PATIENT-CONTROLLED ANALGESIA (PCA) - AS A METHOD FOR A BETTER POSTOPERATIVE PAIN CONTROL INVESTIGATION IN PATIENTS UNDERGOING TOTAL ABDOMINAL HYSTERECTOMY (TAH)

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INTRODUCTION. Patients, undergoing total abdominal hysterectomy (TAH) experience severe postoperative pain. Using patient-controlled analgesia (PCA) we examined the duration of postoperative intravenous morphine use and tried to optimize the morphine injection route for better pain control with respect to side effects incidence and patients' satisfaction scores.
METHODS. Following IBR approval and written informed consent, 59 non-obese ASA I and II patients undergoing TAH were enrolled in this study. Antiemetic prophylaxis with ondansetrone, 4mg and dexamethasone, 8mg was performed. Patients were operated under spinal anesthesia with bupivacaine, 15mg, and midazolam, 2.5-5mg iv. PCA with morphine was used for 36hr postoperatively in combination with NSAIDs - diclofenac suppository, 75mg twice per day. First group (n = 31) received local anesthetics without additives, second group (n = 28) - with intrathecal morphine (ITM), 0.3mg. Pain severity (VAS, endpoints 0-10), postoperative nausea and vomiting (PONV, 3-rating scale), pruritus (3-rating scale), sedation, respiratory depression, patients' satisfaction (VAS, endpoints 0-10) were evaluated 2, 4, 6, 9, 12, 18, 24 and 36hr postoperatively. PCA morphine consumption was registerd at 6, 12, 24 and 36hr. Peristaltic waves resume was registered. Blood gases were sampled in ITM group 8hr postop. Data was analyzed using Student's test and is reported as mean ± SD.
RESULTS. Spinal anesthesia created an adequate intraoperative pain control in this patients group. Postoperative pain (VAS ≥3) was registered in 58.1% cases in I group vs 0% in II group. Zero episodes of deep sedation or respiratory depression were registered in both groups. Other results atre presented in table.

Groups	PCA morphine consumption, ml		Resume of peristaltic waves, hr	PONV, %		Sedation	Pruritus,%	Patient satisfaction, VAS > 8
	24 hr	36 hr		Nausea, with vomiting	Nausea, without vomiting			
PCA morphine	45,9 ± 9,2	45,9 9,2	20,97 ± 7,4	38.71	6,45	93,5*	16,1	38,7
ITM plus PCA morphine	0,9 ±1,7**	0,9 ±1,7**	23,47 ± 5,9	35.71	7.41	40,0	66,7*	80,0**

* - p value < 0.05, ** - p value < 0.01
DISCUSSION. TAH can be successfully performed under spinal anesthesia in non-obese patients. Morphine consumption in combination with diclofenac lasts 24hr postoperatively. Later NSAIDs provide an adequate pain control (VAS ≤3). Despite higher PONV and significantly higher pruritus incidence, patients' satisfaction scores were significantly higher (p<0.001) in ITM group. We conclude that single intrathecal morphine (0.3mg) injection covers postoperative morphine requirements in patients undergoing TAH.

S-292.

PATIENT CONTROLLED ANALGESIA EVALUATION: DURATION OF USE

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Introduction: During the last decade intravenous patient controlled analgesia (IVPCA) has replaced intermittent IM injection for the management of acute postoperative pain. IVPCA is often used to provide analgesia in postoperative patients unable to tolerate oral intake. In this study we evaluated the relationship between the duration of IVPCA use and the presence of positive bowel sounds as an evidence of ability to tolerate oral intake.
Methods: Patients expected to receive IVPCA postoperatively were asked to participate in this prospective IRB approved study. Patients were visited up to 4 different times during the course of their IVPCA use and once within 4 hr of stopping the IVPCA. IVPCA programming was set by the nursing staff according to surgeons' preferences. Data was analyzed using ANOVA followed by Duncans multiple range test, and linear regression. Data is presented as mean ± SD.
Results: Sixty (60) subjects (58 female) were studied. Thirty-four (34) subjects had undergone either a total abdominal hysterectomy or myomectomy (group 1), 16 had undergone vaginal hysterectomies or vulvectomy (group 2), and 10 had undergone colectomy, exploratory laparotomy, or a low anterior resection (group 3). There was a significant direct relationship between the first record of positive bowel sounds and the duration of PCA use ($r = 0.59$, $p < 0.01$). The duration of IV PCA use and the time to the first notice of positive bowel sounds were significantly longer in group 3.
Discussion: PCA is often used to provide analgesia in postoperative subjects unable to consume orally. Patients are often switched to oral analgesics as soon as oral intake becomes possible. In this study we observed a direct relationship between the occurrence of bowel sounds and the duration of IVPCA use. The duration of IVPCA is not necessarily an indication of severity of postoperative pain.

Table 1

Group	Duration of IVPCA (hr)	Significantly different from groups
1	42 (13)	2,3
2	28 (11)	1,3
3	58 (27)	1,2

Table 2

Group	Mean time to positive Bowel sound (hr)	Significantly different from groups
1	9.9 (6.0)	3
2	5.0 (3.3)	3
3	31.0 (15.6)	1,2

S-293.

EVALUATION OF AFFECT IN POSTOPERATIVE FEMALE PATIENTS RECEIVING IV PCA

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Introduction: Intravenous Patient Controlled Analgesia (IV PCA) has replaced intermittent IM injection for management of acute postoperative pain. Relatively rapid and wide acceptance of PCA by clinicians has been mostly due to convenience of use and better pain relief than IM morphine. Depending on patients' characteristics and surgical procedure, postoperative opioid requirements can vary many folds among patients. This study was designed to evaluate PCA utilization including the affective component of pain.
Methods: Patients expected to receive IV PCA postoperatively were asked to participate in this prospective IRB approved study. Answer to the McGill pain questionnaire were obtained from each patient 12 to 24 hours after being on IV PCA. Patients were also asked to rate the intensity of their pain using a verbal analog scale of 0 to 10 and to describe their pain relief as poor, fair, good, or very good. Data were analyzed using 95% Confidence Interval and student t-test. A $p < 0.05$ was considered statistically significant. Data are reported as mean ± SD.
Results: Fifty-eight (58) female subjects were studied. Thirty-four (34) subjects had undergone either a total abdominal hysterectomy or myomectomy (group 1), 16 had undergone vaginal hysterectomies or vulvectomy (group 2), and the rest had undergone colectomy, exploratory laparotomy, or a low anterior resection (group 3). In approximately half of the patients the presence of pain was described only by words signifying sensory-discriminative dimensions of pain. The most common descriptions were throbbing, cramping, and stabbing pain. In the remaining patients postoperative pain was described by words signifying both sensory and affective dimensions of pain (i.e., tiring). While the number of injections, number of attempts to inject, and the cumulative doses of morphine were higher in patients with affective component of pain, these differences did not achieve statistical significance. In addition, degree of pain relief between those with and without affective components of pain did not differ significantly. Many patients described their pain as annoying or nagging (63%), tiring (29%), or killing (7%). Patients describing their pain as killing used IV PCA for a significantly longer duration (69±31 vs. 41±14 hr), had significantly more cumulative injections and attempts to inject, used significantly more analgesic medication, and had less satisfaction with analgesic treatment.
Discussion: Traditional assessments of postoperative pain do not incorporate affective components. Most female patients receiving IV PCA after surgery described their pain through sensory discriminative components; many of them also described their pain as tiring, annoying, or nagging. These expressions signify that postoperative pain is unpleasant, demands patient's attention, and needs to be individualized. Fixed dosing fails to achieve adequate relief in many patients. Affective component of postoperative pain may need to be evaluated in order to achieve more effective treatment.

S-294.

DOSE-RESPONSE EVALUATION OF MORPHINE ANALGESIA AFTER TOTAL ABDOMINAL HYSTERECTOMY

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INTRODUCTION: Patients undergoing total abdominal hysterectomy (TAH) often experience moderate-to-severe postoperative pain. Morphine is the most commonly used analgesic in the immediate postoperative period. The purpose of this investigation was to evaluate the analgesic dose-response relationship of morphine in TAH patients experiencing moderate-to-severe pain in the immediate postoperative period.
METHODS: Informed consent was obtained from 20 ASA I-III patients scheduled for TAH under general anesthesia. Patients experiencing moderate-to-severe postoperative pain in the PACU were randomly given either morphine 3 mg every 3 minutes (high-dose group, n=10) or alternating doses of morphine 3 mg and placebo every 3 minutes (low-dose group, n=10) in a double blind manner until a maximum of 7 doses, pain was reduced to a mild level, or side effects had developed. Data is presented as mean ±SD.
RESULTS: The time to first complaint of pain occurred in 6.8±7.2 minutes and the time to moderate-to-severe pain occurred at 8.4±7.8 minutes after arrival of the patients to the PACU. The baseline pain intensity prior to the start of the treatment was 7.5±1.9. Three patients in the high-dose group had adequate pain relief following 2 consecutive doses and 2 patients had adequate pain relief following 3 consecutive doses. In the low-dose group one patient had adequate pain relief after a single dose of morphine. The remaining patients received all 7 doses of study drug without adequate analgesic response. Patients receiving morphine every 3 minutes had a significantly greater chance of having adequate pain relief than those receiving alternating doses of morphine and placebo (50% vs. 10%, 95% CI = 3.8% to 76.1%). All patients who achieved adequate analgesia had initial pain scores of 5 to 7. No patient with a baseline pain score of ≥8 had an adequate analgesic response in either group.
CONCLUSION: In our PACU the standard procedure for use of IV morphine is to give 2.5 mg IV doses every 5 minutes until a maximum of 10 mg of morphine is given. A patient may receive more then 10 mg of morphine once re-evaluated by an anesthesiologist. Most of the patients in this study did not have an adequate reduction in pain intensity despite receiving 12 to 21 mg of morphine in a 20 min period. Using small fixed doses along with a cap on the total dose makes successful pain management rather difficult to achieve on a consistent basis. Higher incremental morphine doses, relative to those currently practiced, may be needed for a better analgesic response rate in TAH patients experiencing moderate-to-severe postoperative pain. Adequate dose of an analgesic for a given patient should be based on titration to the effect. The dose needs to be increased until adequate analgesia, or adverse effects results.

S-295.

EFFICACY OF KETOROLAC IN LIEU OF NARCOTICS IN THE OPERATIVE MANAGEMENT OF LAPAROSCOPIC SURGERY FOR MORBID OBESITY

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Background: Prompt recovery of protective airway reflexes, freedom from pain, ability to co operate with respiratory physical therapy, early ambulation and discharge from post anesthesia care unit(PACU) coupled with stable intra operative environment have been desired goals of anesthetic (operative) management of morbidly obese patients. We employed ketorolac in the lieu of narcotics towards this goal and present our subjective and objective data in this study.
Methods: The study was conducted prospectively over a 10 month period. A total of 50 morbidly obese patients undergoing laparoscopic gastric banding or gastric bypass surgery were randomly assigned to two groups of 25 each. Group 1 received IV ketorolac peri operatively in lieu of narcotics, which was continued 24 hours post operatively, while group 2 received peri operative remifentanyl as part of balanced anesthesia. Bispectral index scale (BIS) recording was used in addition to standard monitoring. Pre operative and post operative ventilatory function was recorded using the portable respirometer. All patients were of offered patient controlled analgesia with fentanyl for post operative pain. Assessment of pain intensity using a simple, categorical, verbal rating scale was obtained. Any nausea, vomiting, hypotension, or respiratory depression was recorded. Exclusion criteria included chronic NSAID use, known allergy to aspirin and /or NSAIDS, past medical history of bronchial asthma requiring intubation and renal insufficiency.
Results: While we found no significant difference in the immediate post anesthesia recovery between the two groups, postoperative side effects like pain, nausea and vomiting, requirements for analgesics and anti emetic medications in the PACU, as well as the time spent in the PACU before being discharged to the bariatric care unit were significantly different. Continued administration of ketorolac during the 24 hours post operative period led to improved patient satisfaction and more enthusiastic participation in respiratory physical therapy.
Conclusion: Peri operatively used and postoperatively continued intravenous ketorolac in laparoscopic surgery for morbid obesity provides a stable intra operative environment, early discharge from the PACU and better outcome in this subset of patients
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S-296.

CORRELATION BETWEEN PLASMA CONCENTRATION OF DEXMEDETOMIDINE AND PROLONGED ANALGESIC EFFECT FOR POSTOPERATIVE PAIN FOLLOWING THE EPIDURAL COADMINISTRATION OF DEXMEDETOMIDINE WITH XYLOCAINE IN SURGICAL PATIENTS

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Introduction: The epidural administration of narcotic agents have been widely accepted to use for pain relief.[1] The administration of clonidine (CLO) and dexmedetomidine (DEMD) into intrathecal or epidural space potentiate and prolong the effect of local anesthetic agents.[2] CLO and DEMD exerted on central anesthetic activity which were demonstrated the result from reduction of MAC inhalation anesthetics and also from EEG study in man.[3] To clarify the prolonged action of epidural administration of DEMD with xylocaine, this study is designed to examine the correlation between plasma concentration of DEMD and the duration of analgesic effect for postoperative pain in gynecologic surgical patients.
Methods: 30 patients (ASA=1-2) with informed consent and approved from hospital ethical committee were studied. The patients were divided at random into four groups as follow: group A (control, n=5) received 15ml saline, group B (n=10) received 2mcg/kg DEMD in 15ml saline, group C (n=5) received 1.5% xylocaine 15ml, group D (n=10) received 2.5mcg/kg DEMD in 1.5% xylocaine 15ml respectively. During the study, body temperature, heart rate, blood pressure, ECG, EEG, SpO_2 were monitored. The serum concentrations of norepinephrine, epinephrine and DEMD were measured. Also the duration of postoperative analgesic effect of DEMD with xylocaine was assessed. Between group comparisons were performed by means of an unpaired t-test. Data are expressed the mean values±SD and $P<0.05$ considered statistically significant.
Results: There were no remarkable cardiovascular side effect except transitory decreases of blood pressure and heart rate in group B and group D. Norepinephrine and epinephrine in plasma decreased by 50% in group B and D. DEMD was rapidly absorbed into systemic circulation from the epidural space and it declined in a biexpotnential manner. The C_{max} 439.4±147pg/ml and T_{max} was 15min after the injection of DEMD. The plasma DEMD concentration was maintained for a relative long period. The duration of analgesic effect in group B and D lasted for about 7hrs and it was 7 times longer compared with group A and C.
Discussion: The most striking finding in this study was that DEMD prolonged the analgesic effect of xylocaine when they were administered together epidurally. The same finding was reported that the combined administration of intrathecal CLO and bupivacaine increased the analgesic effect of bupivacaine in knee sugery.[4] Epidural administered DEMD remained in the plasma for a relative long time which was coincided with the other report.[5] We speculate that there is a closed correlation between the prolonged duration of analgesic effect of DEMD with xylocaine and plasma concentration decay of DEMD.
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S-297.

EVALUATION OF THE PERIOPERATIVE ADMINISTRATION OF ROFECOXIB AND EPIDURAL ANALGESIA FOR GASTRIC BYPASS SURGERY

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Introduction: Open gastric bypass surgery can result in considerable postoperative pain. Optimal pain management may be obtained with the utilization of preemptive and multimodal analgesic techniques. The use of NSAIDs with epidural analgesics may provide significant analgesic benefit to patients undergoing gastric bypass surgery. Rofecoxib, a COX-2 specific NSAID, may be more advantageous than conventional NSAIDs because of its lack of platelet inhibition. The goal of this ongoing study is to determine the analgesic efficacy of administering rofecoxib to a preemptive multimodal analgesic technique (epidural fentanyl/bupivacaine) in patients undergoing open gastric bypass surgery.
Methods: Sixty patients scheduled for elective open gastric bypass were randomly assigned to one of two treatment groups. The data presented here is from the first 31 of 60 patients. The preemptive rofecoxib group (n=16) received rofecoxib 50 mg one hour prior to surgery while the control group (n=15) received a placebo. All patients received a thoracic epidural catheter placed prior to induction of general anesthesia. Postoperatively patients were started on a patient-controlled epidural analgesia (PCEA) pump for pain management. Starting 24 h postoperatively, all patients received oxycodone solution 10 mg every 4 hours on a prn basis. In addition, patients in the rofecoxib group received rofecoxib 50 mg on the morning of postoperative day (POD) #1 and POD #2. The study ended 48 hours after the completion of surgery on the morning of POD #3 (after receiving 3 doses of rofecoxib; 1 preoperative and 2 postoperative 50 mg doses). Postoperative efficacy assessments included pain scores, sedation, incidence of nausea and vomiting, patient satisfaction, pulmonary function, opioid use, and length of stay. Pain was recorded on a verbal analog scale (VAS) from 0-10 every 4 hours postoperatively. In addition, patients were asked to quantify their average pain over the past 24 hours and their worst pain over the past 24 hours for POD # 1 and # 2. Ventilatory function was assessed by measuring pulmonary function tests (FEV-1 and FVC), respiratory rate, and oxygen saturation (SpO_2) at baseline in the preoperative holding area, and then at 24, 48, and 72 hours postoperatively. Opiod consumption (epidural fentanyl and oral oxycodone) was recorded for the initial 48 hours after surgery.
Results: There were no differences in demographic variables between the two groups. There was a significant reduction in pain scores at 1 hr. ($p=0.047$), 2 hrs. ($p=0.034$) , and 8 hrs. ($p=0.020$), and 72 hrs ($P=0.021$) postoperatively in the rofecoxib group. Rofecoxib use resulted in a 30% reduction in postoperative oxycodone use.
Discussion: We conclude that Rofecoxib is a powerful adjunct in multimodal analgesic techniques. It significantly reduced postoperative pain in our patients undergoing open gastric bypass surgery.

S-298.

THE EFFECT OF PERIOPERATIVE CELECOXIB ADMINISTRATION ON ACUTE AND CHRONIC DONOR SITE PAIN FOLLOWING SPINAL FUSION SURGERY

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Introduction: Autogenous bone grafts from the ilium are frequently harvested for the purposes of bone fusion in patients undergoing spinal stabilization surgery. Often the pain from the donor site can be more severe than from the laminectomy incision (1). Although this pain usually resolves over a period of several weeks, it may persist and represent a significant source of morbidity (1,2). Donor site pain has been has been reported in up to 39% at 6 months after surgery (2). Prostaglandins are involved in the development of spinal hyperexcitability (3) and upregulation of COX-2 in the CNS may be a target for pain control (4). The preemptive administration of celecoxib significantly reduces postoperative pain and opioid use following spinal fusion surgery (5). The intensity of acute postoperative pain has been associated with a higher incidence of chronic pain (6) In addition, it has been hypothesized that the preemptive administration of COX-2 NSAIDs may thwart the progression of acute to chronic pain (7). This study was designed to examine the effect of pre- and postoperative administration of celecoxib on the incidence of acute and chronic donor site pain in patients undergoing posterior spinal fusion surgery.
Methods: 80 patients undergoing posterior spinal fusion using autologous iliac crest harvest were included in this prospective randomized double-blind study. Patients received either celecoxib 400 mg 1 h prior to surgery followed by 200 mg every 12 h (n=40) or matching placebo capsules (n=40) for the first 5 postoperative days. Patients received PCA morphine for 24 h then acetaminophen/ oxycodone. Pain scores (0-10) and morphine use were recorded every 4 h postoperatively. At 1-year follow-up, patients were evaluated for the presence of donor site pain.
Results: There were no differences in demographic variables, surgical procedures, or operative times between the two groups. Pain scores were significantly ($p<0.01$) lower in the celecoxib group in the PACU, 4, 16, and 20 h after surgery. 24 h morphine use was significantly ($p<0.001$) lower in the celecoxib (93 ± 13 mg) compared to placebo group (135 ± 17 mg). The incidence of chronic donor site pain was significantly ($p<0.01$) lower in the celecoxib group (4/40; 10%) compared to placebo (12/40; 30%).
Discussion: The perioperative administration of celecoxib reduced both the incidence of acute pain and the incidence of chronic donor site pain following spinal fusion surgery.
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S-299.

A SMALL-DOSE PREADMINISTRATION OF PROPOFOL CAN DECREASE PAIN ON INJECTION AT INDUCTION

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Introduction
A lot of research has been done to prevent the injection pain of propofol. The most common method is to premix or preadminister lidocaine[1]; however, both methods require additional cost, and there are problems such as destruction of emulsion[2]. We injected a small-dose of propofol (10-20mg) during peripheral block and noticed that patients preadministered propofol might complain less of pain on injection with an induction dose of 2mg/kg. We designed the study protocol to prove this phenomenon using LCT propofol with or without preadministration and MCT/LCT propofol without preadministration.
Methods
After obtaining the approval of the institutional ethical committee and written informed consent from all patients, we used a randomized, controlled, double blinded method for evaluation. We studied 150 patients, allocated into three groups, which were control, preadministered and MCT/LCT groups. They were given the same size of intravascular catheter, 18-20 gauge and the same fluid, lactate ringer with 5% maltose. For the control group, we administered 2mg/kg of LCT propofol constantly, 1200ml/hr without preadministration. For the preadministerd group, we injected 10 times diluted LCT propofol with saline, 0.1mg/kg, four min (the equilibration time between blood and effect site) before induction and gave a similar to that dose of the control group for induction. For the MCT/LCT group, we gave 2mg/kg MCT/LCT propofol without preadministration. Pain score was evaluated blindly 0 - 3, which corresponded to no pain, mild, moderate and severe pain. The data were analyzed statistically using chi-square, Kruskal-Wallis and Mann-Whitney U test. A P value of <0.05 was accepted as statistically significant.
Results
There was no difference in demographics among the groups. The pain score at induction described in the table and the score of the preadministered group is significantly lower than those of control and MCT/LCT group. The first pain scores of the preadministered group were 0 = 44%, 1 = 52%, 2 = 4% and 3 = 0%, respectively.
Discussion
This is the first report that a small-dose preinjection of propofol is useful to decrease the pain. This method does not need any additional drug except propofol itself. The disadvantage of the method is that 56% of patients may feel mild or moderate pain at the first injection.
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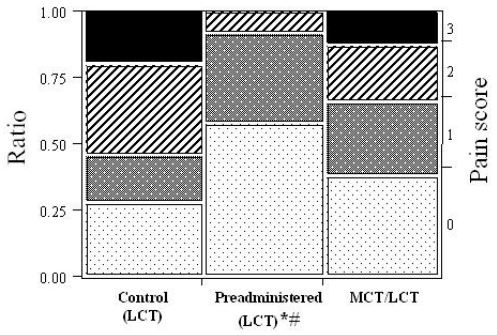

Table; the ratio of pain score for each group.
*P<0.05 v.s control group.
# P<0.05 v.s MCT /LCT group.

S-300.

THE EFFICACY OF "ACUPUNCTURE" IN EXTRA CORPOREAL SHOCK WAVE LITHOTRIPSY(ESWL)

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Introduction: In this study, the efficacy of acupuncture which is noninvasive and devoid of complications has been evaluated and compared with IV sedation in Extra corporeal Shock Wave Lithotripsy (ESWL).
Methods: 100 patients scheduled for ESWL were divided randomly into two groups of fifty (acupuncture and IV sedation). In the first group, acupuncture was carried out with specialized needles (0.30x18mm), two points, one point number 36 from the stomach meridian and an angle of 90 degrees and another point no 60 from the urinary bladder meridian with an angle of 90 degrees 30 minutes before the procedure. In the IV sedation group morphine 0.1mg/kg was injected intramuscularly 30 minutes, and intravenous diazepam 0.1mg/kg one minute before the procedure. The two groups were similar in terms of confounding and interfering factors. Pain (scored in 4 level), blood pressure, heart rate, respiratory rate, and SpO2 were recorded prior to IV sedation or acupuncture, 30 minutes after each, at the beginning of ESWL, 10 minutes after ESWL and at the end of the procedure.
Results: In acupuncture group the pain intensity was less than IV sedation group. (for time3 P =0.019, for time 4 P =0.002, for time 5 P =0.05 .Considering the pain incidence (each pain score except zero), there was a significant difference at time 4(P=0.012). None of the patient's treatment was stopped because of pain and none of the patients experienced complications during operation. Blood oxygen saturation was between 95-100% for all of the patients in this group and recovery time was faster (P<0.0001).
Discussion: Considering the proven efficacy of acupuncture in ESWL, faster recovery and hence discharge economical benefits and the ability to increase the voltage during the technique, it seems to be the ideal preferable choice, particularly for patients with chronic lung and heart disease.

S-301.

MAGNESIUM DECREASES REMIFENTANIL DOSAGE REQUIRED FOR PAIN MANAGEMENT AFTER CARDIAC SURGERY

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Background: Magnesium is known as a noncompetitive *N*-methyl-*D*-aspartate receptor antagonist, preventing the induction of central sensitization from peripheral nociceptive stimulation (1). Administration of IV magnesium sulphate during surgery reduces intra- and postoperative opioid requirements (2) without increased adverse effects (3). It can therefore be used as an adjunct for conventional pain management. Our intention was to evaluate the analgesic effect of co-administration of magnesium gluconate in the postoperative setting after cardiac surgery.
Methods: Analgesia during surgery was achieved with 0.2-0.5 µg/kg/min remifentanil, which was continued into the postoperative period. In addition, shortly after induction of anesthesia, patients were either given magnesium gluconate (n=10; 86,46 mg/kg bolus followed by a continuous infusion of 13,80 mg/kg/h) or placebo (n=10). When the patient was awake, remifentanil was titrated to effect with pain being evaluated by a pain intensity score (PIS) in the intubated patient (range 1-6 with 1 representing no and 6 unbearable pain) and later on by a color VAS scale (range 0-100, i.e. no and worst pain, respectively). A PIS ≥ 3 or a VAS ≥ 30 induced a step increase of remifentanil by 0.01 µg / kg / min. A respiratory rate ≤ 10 caused a decrease by the same magnitude. Apart from VAS score, the remifentanil dosage, time to extubation, and magnesium serum levels were determined. Multivariate analysis and student's t-test were employed as statistical tests.
Results: Immediately after surgery, remifentanil was continued at a dose of 0.05 µg / kg / min in all our patients. Less frequent adjustments because of insufficient pain control had to be made in magnesium treated patients before extubation (4 vs. 11 pts.) Furthermore, magnesium significantly lowered the remifentanil requirement after extubation on average by 20% (P<0.05). VAS score determined during the first 12 hours after extubation significantly decreased in both groups without group differences over time. It dropped in the magnesium group from 15 to 1 and in the control group from 18 to 3 (P>0.05), respectively. Dose reductions due to a respiratory rate ≤ 10 had to be made 11 times in magnesium treated patients as compared to 7 times in controls (P>0.05). The administration of magnesium significantly increased magnesium serum levels immediately after surgery (1.33 ± 0.3 vs. 0.9 ± 0.2, P<0.05) but did not prolong time to extubation (132 ± 15 vs. 129 ± 14 min, P>0.05).
Conclusion: Magnesium gluconate at the dosage we applied effectively reduced the remifentanil requirement for adequate postoperative pain management in patients after cardiac surgery. No serious side-effects were observed with this treatment regimen.
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S-302.

THE EFFECT OF EPIDURAL MORPHINE AND BUPIVACAINE ON BOWEL FUNCTION AND PAIN AFTER GASTRECTOMY

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Introduction: A comparison was made of the effects of postoperative morphine and bupivacaine epidural analgesia with those of intermittent injections of meperidine on postoperative bowel motility and pain after gastrectomies.
Methods: Intramuscular group (N = 20) received intermittent injection of meperidine for the postoperative analgesia. Epidural group (N = 20) received a bolus of epidural 0.5% bupivacaine 10 ml followed by continuous epidural infusion of 0.21% bupivacaine with 0.01% morphine, started at the end of operation with the basal infusion rate of 1 ml/hr, bolus 1 ml, and lockout interval 30 min during 48 hr. We compared the analgesic effect, side effects and restoration of bowel function with first passage of flatus and feces betweeen two groups. Postoperative pain was assessed using the 10 cm visual analog pain scale at rest. Score were taken at 1, 6 hr after operation and 7 AM, 6 PM of the 1st postoperative day and 7 AM of the 2nd postoperative day.
Results: Epidural group revelaed superior analgesia (p<0.005) but had a greater incidence of nausea, pruritus and urinary retention. No significant difference was found in restoration of bowel function between two groups.
Discussion: There was no superior effect of epidural analgesia with morphine and bupivacaine on bowel motility than the effects of traditional intramuscular mepridine administration.
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Incidence (%) of Side Effects *P < 0.05

	Intramuscular	Epidural
Nausea	5	30*
Pruritus	0	55*
Urinary retention	10	25*
Respiratory depression	0	0

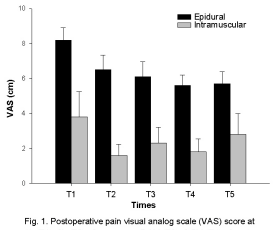

Fig. 1. Postoperative pain visual analog scale (VAS) score at 1h (T1), 6h (T2) after surgery, 7 AM (T3), 6 PM (T4) of postoperative 1 day, and 7 AM (T5) of postoperative 2 day on a scale (cm) from 0 to 10. Epidural bupivacaine and morphine (epidural) compared to intramuscular meperidine (intramuscular). Values are mean +/- SE. p < 0.001 compared with control group.

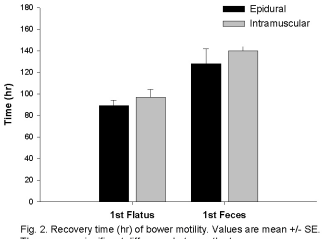

Fig. 2. Recovery time (hr) of bower motility. Values are mean +/- SE. There are no significant difference between the two groups.

S-303.

PAIN MANAGEMENT IN ADULT CRANIOTOMY PATIENTS: A PRELIMINARY PROSPECTIVE STUDY

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Introduction Historically, pain following craniotomy has not been well defined, studied, or treated. The purpose of this prospective, clinical trial was to assess the incidence and intensity of perioperative craniotomy pain and the analgesics used in its treatment.
Methods After obtaining IRB approval and patient consent, data on perioperative pain assessment and treatment was obtained in 167 patients undergoing craniotomy. Data (pain scores, analgesics ordered and administered, and side effects) were collected pre-operatively and on post-operative days (POD) 0, 1, and 2 via chart review and patient interview by a study nurse practitioner.
Results Male and female (M:F 64:103) patients averaging (± SD) 78 ± 20 kg and 52 ± 15 years of age who underwent craniotomy (suboccipital n = 61, frontoparietal n = 99, other n = 8) were studied. Prior to surgery, 32% (53/167) were taking analgesics. All patients received opioids during surgery and 17 % (28/167) received an infiltrative nerve block with 0.25% bupivacaine prior to incision. Of the 158 patients assessed for pain by the nursing staff, 38% had 24-hour maximum pain scores > 5, and 26% had 24-hour maximum pain scores ≥ 7. Ninety-nine percent of patients (165 / 167) were treated with acetaminophen post-operatively. Of these 165 patients, 13% (n = 21) were ordered for potentially toxic amounts of acetaminophen (> 4 g / day). Intravenous opioids were ordered in 124 patients on POD#0 (fentanyl n= 122), 49 patients on POD#1 (fentanyl n = 45), and 8 patients on POD#2 (fentanyl n = 5). The most common order for fentanyl was 25-50 mcg IV to be given as needed (prn). Over a 24-hour period fentanyl administration averaged (± SD) 129 mcg (± 135), 126 mcg (± 128), and 138 mcg (± 116) on POD# 0, 1, and 2, respectively. Patients undergoing suboccipital craniotomy trended toward higher 24-maximum pain scores than patients undergoing frontoparietal craniotomy (p = 0.102, chi-squared test). Sixty-one percent of suboccipital patients reported pain scores ≥ to 7, as compared to 42% of patients undergoing frontoparietal surgery. Approximately 36 percent of patients undergoing frontoparietal craniotomy reported pain scores less than 5, compared to 20 percent of suboccipital patients. However, by POD#1, there was no difference in the percent of patients reporting extreme pain as reported by NP interviewers based on the location of surgery. Side effects included pruritus n=7 and nausea or vomiting n = 70.
Discussion Our data reveal that moderate to severe pain is common following craniotomy and that patients undergoing suboccipital surgery experience more severe pain than patients undergoing frontoparietal surgery. Non opioid and opioid analgesics were prescribed on an as needed basis in doses ranging from inadequate to potentially toxic. Future studies to optimize analgesic therapy are now underway.

S-304.

AGE DIFFERENCE AS RELATED TO THE INCIDENCE AND SEVERITY OF PROPOFOL INJECTION PAIN

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Introduction: Propofol injection pain is a major anesthesia related problem (1), and many studies examining how to decrease the incidence of this issue have been performed (2). However, the precise figure on the incidence and severity of propofol injection pain has not been clarified yet. In the present study, we tried to identify the independent risk factors associated with propofol injection pain.
Methods: Five hundred and thirty consenting patients undergoing elective surgery under general anesthesia were enrolled in this study. Propofol 1-2 mg/kg was injected through either radial cutaneous vein or antecubitus vein for 10-15 seconds. Patients were asked whether or not they felt any pain at the injection site. If pain was experienced, the degree of pain was ranked according to the Ambesh's pain score (none, mild, moderate, and severe) (3). Statistical analysis was performed using multiple logistic regression method and chi-square test. $P<0.05$ was considered significant.
Results: The overall incidence of pain was 48.1%. As a result of multiple logistic regression analysis, we identified age as an independent risk factor for propofol injection pain. The incidence of pain in younger patients below 40 yr (60.4%) was significantly higher than in elderly patients (42.6%). Although the severity of pain was mild in 70.2% of the patients, the incidence of moderate to severe pain was significantly higher in the patients between 13 and 20 yr (50.0%).
Discussion: Although the mechanisms that propofol causes injection pain have not been clarified, we found that age was an independent risk factor associated with propofol injection pain. We concluded that age was related to both incidence and severity of pain, and therefore, measures to alleviate propofol injection pain would be necessary especially in younger patients.

References:
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(3) Anesth Analg 1999; 89: 197

S-305.

EFFECT OF PERI- VS POST-OPERATIVE CELECOXIB ADMINISTRATION ON RECOVERY AFTER MAJOR PLASTIC SURGERY PROCEDURES

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Introduction: The COX-2 inhibitors have become increasingly popular as part of a multimodal approach to pain management. However, pain studies involving these drugs have focused on the immediate perioperative period. This randomized, double-blind, placebo-controlled study was designed to examine the effect of perioperative (vs postoperative) administration of celecoxib for up to 3 days after major plastic surgery.
Methods: 56 healthy consenting patients undergoing plastic surgery (e.g., breast reduction and/or abdominoplasty) procedures utilizing a standardized general anesthetic technique were randomized to one of three treatment groups: (1) *Control group* (n=19) received two placebo pills before and immediately after surgery, as well as one twice/d on postoperative day (POD) #1, #2 and #3, (2) *Postoperative group* (n=18) received two placebo pills before surgery and two celecoxib 200 mg pills immediately after surgery, followed by one celecoxib 200 mg pill twice/d on POD #1, #2 and #3, and (3) *Perioperative group* (n=19) received two celecoxib 200 mg pills before surgery, and two placebo pills immediately after surgery, followed by one celecoxib 200 mg pill twice/d on POD #1, #2 and #3. The assessment tools included verbal analog pain scores (0=no pain to 10=worst pain imaginable), quality of recovery scores (using an 18-point questionnaire), need for rescue analgesic and antiemetic medications, patient satisfaction with their pain management, and resumption of normal activities of daily living, with *p<0.05 vs Control group.
Results: The three study groups were similar with respect to their demographic characteristics. The administration of celecoxib before and after surgery was associated with reduced pain scores and a decreased need for opioid analgesics. Importantly, the quality of recovery improved in the celecoxib groups.

	Control (Placebo)	Postoperative (Celecoxib 400 mg)	Periperative (Celecoxib 400 mg)
Age (yr)	40±12	44±16	43±17
Weight (kg)	68±18	65±13	68±14
Surgery time (min)	147±58	140±68	161±96
Intraoperative sufentanil (μg)	52±26	45±22	47±27
Pain scores (0-10)			
at PACU discharge	4.5 (3-6)	2 (2-4)	3 (2-3)
at 24 h	4.5 (3-7)	3 (2-5)	2 (1-5)*
at 48 h	4 (3-6)	3 (2-6)	3 (1-5)
at 72 h	4 (2-5)	3 (2-4)	1 (1-4)*
Rescue analgesics (n,%)			
in PACU	18, 95	16, 84	14, 74
at 24 h	15, 88	14, 86	13, 77
at 48 h	16, 94	14, 82	13, 77
at 72 h	12, 71	9, 53	9, 53
Quality of recovery (0-18)			
at 24 h	16 (13-18)	17 (16-18)*	17 (17-18)*
at 48 h	16 (15-18)	18 (17-18)*	18 (17-18)*
at 72 h	17 (16-18)	18 (17-18)*	18 (17-18)*
Postoperative nausea and vomiting (n,%)	13,68	6,33	8,42
Patient satisfaction (0-100) with pain management	89±11	96±6*	96±6*

Discussion: Oral celecoxib is an effective analgesic adjuvant in patients undergoing major plastic surgery. Perioperative administration does not provide clinically-significant advantages over postoperative administration alone.

S-306.

A COMPARATIVE STUDY OF PARECOXIB, THIOPENTAL, LIDOCAINE FOR PREVENTION OF PROPOFOL INJECTION PAIN: A DOUBLE BLIND, RANDOMIZED, PLACEBO CONTROLLED STUDY

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Introduction- Intravenous administration of propofol is associated with pain on injection in 28-90% patients. A number of techniques have been tried to minimize propofol-induced pain, with variable results. We compared the efficacy of pretreatment with parecoxib 40mg, thiopental 0.5 mg/kg and lidocaine 0.5mg/kg with control following venous occlusion for prevention of propofol-induced pain.
Method- One hundred and twenty four adult patients, ASA I & II, undergoing elective surgery were randomly assigned into 4 groups of 31 each. Group I received normal saline, group II received lidocaine 0.5mg/kg, groups III received thiopental 0.5mg/kg and group IV received parecoxib 40mg. All pretreatment drugs were made in 2ml and were accompanied by manual venous occlusion for 1 min. Propofol was administered following release of venous occlusion. Pain during administration of pretreatment drug and propofol was assessed with a four point scale: 0 = no pain, 1 = mild pain, 2 = moderate pain and 3 = severe pain at the time of propofol injection. Results were analyzed by comparing two proportions by normal approximation ('Z' test). When the distribution of data was not normal i.e. the data regarding grading of pain Fisher's Exact test was applied. P value < 0.05 was taken as significant.
Results- Twenty-four patients (77%) complained of propofol associated pain in the control group as compared to 12 (39%) each in the groups pretreated with lidocaine and parecoxib, and 1(3%) in the groups pretreated with thiopental (P<0.05). Thiopental pretreatment was more effective in attenuating propofol pain when compared to lidocaine and parecoxib (P<0.05). Pretreatment with lidocaine and parecoxib were equally effective in attenuating propofol pain. Majority of the patients pretreated with parecoxib had moderate to severe pain as compared to mild pain in lidocaine group. Parecoxib pretreatment itself lead to pain (P<0.05).
Discussion- The mechanism propofol pain has been attributed to release of a kininogen from the vein wall with the triggering of a local kinin cascade (1). Non steroidal anti-inflammatory drugs (NSAID) decrease prostaglandin synthesis and inhibit such kinin cascades (2), and thus might reduce the propofol pain. Pretreatment with NSAIDS for propofol pain have yielded varied results. No data is available regarding the efficacy of parecoxib for reducing propofol pain. We observed that parecoxib pretreatment itself lead to pain (P<0.05). Pretreatment with lidocaine 0.5 mg/kg is the second best option for attenuating propofol pain when compared to thiopental 0.5 mg/kg pretreatment (best method) along with venous occlusion for 1 min.
References-
1. Anaesthesia, 62: 202-3; 1989.
2. Goodman and Gillman's the pharmacological basis of therapeutics. 9th ed., 617-57; 1996

S-307.

THE EFFECT OF ADDING LOW DOSE KETAMINE TO STANDARD PRACTICE ANALGESIA AFTER MAJOR SPINE SURGERY IN PATIENTS WITH CHRONIC THERAPEUTIC OPIOID INTAKE

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Introduction: Postoperative pain management is often challenging in patients who undergo major spine surgery for chronic back pain after therapeutic narcotic intake. They have some degree of opioid tolerance mediated by NMDA receptors. We hypothesized that ketamine, a NMDA receptor antagonist will improve analgesia provided by narcotics.
Methods: After institutional approval and informed consent, we prospectively studied 40 ASA I-III adults undergoing lumbar laminectomy and fusion in a randomized double-blinded and placebo controlled clinical trial. Patients were divided into two groups, Group1 received IV ketamine 0.15 mg/kg before incision followed by 2 mcg/kg/min for 24 hours, and Group 2 received saline. All patients had epidural catheters inserted by the surgeon at the end of surgery and bupivacaine 0.1% was infused at 6-12 cc/hour. In addition, they used hydromorphone by IVPCA. Time to first request of analgesia, IVPCA hydromorphone consumption and visual analog scores for 48 hours, time to mobilization, length of hospital stay, pain service interventions and patient satisfaction were followed up by a blinded observer. Central nervous system (CNS) side effects , nausea, vomiting, pruritus, constipation, fever and respiratory/ cardiovascular compromises were also noted by the blinded observer.
Results: Three patients had protocol violations and dropped from the study. Demographics, preoperative pain scores, duration of narcotic intake, anesthesia and surgery, spinal segments operated, intraoperative fentanyl, blood loss and length of incision were similar in both groups. No difference in analgesic outcome was noted between the two groups (Table). Median VAS at rest and movement was > 4 and 6 respectively at all time periods in both groups. CNS side effects were reported in 10 (56%) in Gp 2 and 7 (37%) in Gp 1 (p=0.33). Two patients in Gp 1 reported severe CNS side effects, one of them developed dissociation. PONV was noted in 44% patients in Gp 2 and 32% in gp1 (p=0.64). No difference in the incidence of fever, pruritus, constipation and patient satisfaction was seen between the groups.
Discussion: In this study, IV ketamine, in the dose used as adjuvant to IVPCA hydromorphone and epidural bupivacaine did not improve analgesia in these patients. In spite of multimodal analgesia with ketamine, hydromorphone and epidural analgesia, pain scores remained high in these patients. Side effects were not increased with the addition of ketamine

	Saline Group n=18	Ketamine Group n=19	P-value
Hydromorphone requirement (mg)			
PACU*	1.2 (0.3-2)	1.0 (0.45-2)	0.88
0-8 hours	5.27 (3.47)	5.32 (4.20)	0.97
24 hours	19.36 (13.57)	18.91 (16.49)	0.93
48 hours*	34 (17.91-48.25)	24.22 (16.39-49.05)	0.93
Time to first request for analgesia* (min)	15 (5.5-39.5)	15 (7-55)	0.77
Bupivacaine dose (mg)	375.53 (100.86)	362.68 (136.88)	0.76
Duration of PACU stay (min)*	225 (157.5-267.5)	220 (161.25-240)	0.84
Length of hospital stay (days)*	4 (4-5)	5 (4-8)	0.18
Patient satisfaction scores (0-10 scale)	6.0 (2.58)	5.6 (3.23)	0.68
VAS at physical therapy (0-10 scale)	7 (1.6)	5.3 (3.3)	0.18
No of patients mobilized at 48 hours, n (%)	11 (61%)	9 (47%)	0.61

* Values expressed as median (25%-75%), others as mean (SD)

S-308.

EFFECT OF THE ADDITION OF FENTANYL TO 0.5% ROPIVACAINE FOR INTERSCALENE BRACHIAL PLEXUS BLOCK

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Introduction: Numerous studies assessing the analgesic efficacy of opioids used as adjuncts to local anesthetics have been published, but the results of these studies remain controversial. Several studies (1)-(3) have demonstrated that opioids used to complement the effects of local anesthetics in axillary brachial plexus block prolonged the duration of analgesia. However, few data are available regarding the effects of opioids on interscalene brachial plexus block (4). The aim of this prospective, randomized, double-blind study was to evaluate whether fentanyl administered as an adjunct to ropivacaine in interscalene brachial plexus block prolonged a duration of analgesia.
Methods: Thirty patients scheduled for open shoulder surgery were randomly allocated to 2 groups and received interscalene brachial plexus block of either 20 ml of 0.5% ropivacaine with 2 ml of saline (group R), or 20 ml of 0.5% ropivacaine with 100 μg of fentanyl (group F). Nerve blocks was placed using a nerve stimulator (Stimplex Æ DIG-RC ; B.Braun Melsungen AG, Melsungen, Germany) at a point at which a contraction of the deltoid muscle was obtained, after general anesthesia had been induced. Anesthesia was induced by target-controlled infusion (TCI) of propofol and maintained with propofol TCI and nitrous oxide adjusted to maintain a bispectral index target values of between 40 and 60. Postoperative analgesia consisted of rectal ketoprofen 50 mg, as required. The duration of analgesia (calculated as the time from block placement to first administration of postoperative analgesic) and the total dose of ketoprofen given during 24 hours after block placement were recorded. Values are reported as mean ± SD when applicable. Comparisons were made using the two tailed unpaired Student's t-test, and values of $P < 0.05$ was considered significant.
Results: One patient in group R and one patient in group F were excluded from the results due to postoperative hemorrhaging and the use of ketoprofen for pain not related to the surgery, respectively. Subjects in both groups were similar in age, weight, height, and type of surgery and the duration of surgery. There was no significant difference between the two groups in either the duration of analgesia (512 ± 177 min in group R, and 581 ± 201 min in group F) or the total dose of ketoprofen (mg in group R, and mg in group F).
Discussion: We were unable to show that the addition of fentanyl to ropivacaine for interscalene brachial plexus block prolonged a duration of analgesia. The present study did not suggest clinical relevance of the use of fentanyl as an adjunct to ropivacaine under the study conditions.
References:
(1)Reg Anesth Pain med.2001;26:434-38
(2)Anesth Analg.2000;91:384-7
(3)Br J Anaesth.1996;76:802-5
(4) Br J Anaesth.1995;75:23-26

S-309.

THE INCIDENCE OF POST-OPERATIVE NAUSEA AND VOMITING IN THE 48 HOURS FOLLOWING MAJOR JOINT SURGERY

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Introduction: Post-operative nausea and vomiting (PONV) remains a challenge for inpatient care. Although the overall risk of PONV and that of certain populations (GYN, breast surgery, elderly) is well documented[1], specific "at risk" groups and duration of symptoms in many populations remain unknown. In a recent retrospective study of 90 patients, the overall incidence of PONV for 48 hours following major joint surgery (MJS) was reported to be 42%.[2] The purpose of this study was to prospectively examine the incidence of PONV for up to 48 hours following MJS.
Methods: Following IRB approval of this prospective study, a total of 95 patients undergoing MJS (hip or knee replacement) were analyzed for use of anti-emetics; symptoms of nausea, vomiting, or retching (N/V/R); and average pain scores for 48 hours following surgery. Anesthesia consisted of intrathecal (IT) local anesthetic plus IT morphine for hip replacement and IT local anesthetic with post-operative local anesthetic epidural for knee replacement surgery. In addition, post-operative pain was controlled using 48 hours of IV opioids for both groups. Pain therapy was titrated to patient comfort, achieving an average pain score of <4cm (based on a 10cm visual analog scale) throughout the study period. The incidence was defined both by patients requiring approved therapy for PONV (ondansetron, phenergan, metoclopramide) after complaining of symptoms and by those reporting episodes (>1 hour apart) of N/V/R.
Results: See Table

	Patients Requiring Anti-emetics (N=95)	**Patients Experiencing N/V/R** (N=95)	**Demographics**
Day 0	31%(29)	22%(21)	Male=54
Day 1	18%(17)	58%(55)	Female=41
Day 2	5%(5)	14%(13)	**Average Age**
Overall	47%(45)	65%(62)	53

Discussion: In this incidence study, approximately 65% of individuals undergoing major joint surgery suffered from symptoms of N/V/R and 47% required approved rescue anti-emetic therapy. The first 36 hours post-operatively represent the highest incidence of symptoms necessitating anti-emetic therapy, though patient discomfort continued 48 hours postoperatively. This incidence was higher than expected with an average population age of 52 years.[1] PONV requiring treatment following major joint surgery may be significantly higher than expected based on these findings, and of longer duration (up to 48 hours). This study supports a recent retrospective analysis[2], and suggests patients undergoing MJS may warrant consideration as "at-risk" for PONV and require special consideration for prophylaxis and treatment.
References:
1.) PONV in Regional Anesthesia: A Review. Anesthesiology 2003; 98:530-47.
2.) The Incidence of PONV in the 48 hours Following Major Joint Surgery. IARS Abstract Poster Discussion; S-177: 3/29/2004.

S-310.

THE EFFECT OF INTRA-AND POSTOPERATIVE ADMINISTRATION OF LOW-DOSE KETAMINE AND ORAL CLONIDINE PREMEDICATION ON POSTOPERATIVE ANALGESIA AFTER SPINAL SURGERY

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INTRODUCTION: Subanesthetic ketamine is effective for postoperative pain and reduce morphine consumption.[1, 2] Oral clonidine also has similar analgesic efficacy.[3] The aim of this study is to evaluate the effect of administration both or either intra-and postoperative low-dose ketamine and oral clonidine premedication on postoperative analgesia after spinal surgery.
METHODS: After IRB approval and informed consent, forty-four patients undergoing spinal surgery were allocated randomly to four groups; group C (n = 14): neither ketamine nor clonidine, group K (n = 12): intra and postoperative ketamine alone, group Cl (n = 11): oral clonidine premedication alone, group ClK (n = 7): administration of both ketamine and clonidine. Ninety minutes prior to anesthetic induction the patients in the group Cl and group ClK received clonidine 3 μg/kg orally. During anesthesia the patients in the group K and group ClK received intravenous ketamine (10 mg at induction of anesthesia, and 10 mg/hr during operation). Patients were allowed to use IV-patient controlled analgesia (PCA) which was set a bolus dose of morphine 2 mg (group C and group Cl), or a dose of morphine 2 mg and ketamine 2 mg (group K and group ClK) with a lockout period of 10 min after surgery. If analgesia was not adequate, patient received diclofenac 50 mg rectally. Visual analog scale for pain, morphine requirement, vital signs, nausea, sedation and other side effects were noted for up to post-operative day 2 (POD 2).
RESULTS: Morphine requirement in the group ClK was significantly lower than that in the group C on PODs 1 and 2 ($p < 0.005$), and it decreased significantly in the group K than in the group C on POD 1 ($p < 0.005$). The incidence of side effects and the consumption of NSAIDs did not differ among the groups.

DISCUSSION: This study suggests that the administration intra-and postoperative low-dose ketamine with oral clonidine premedication decreased the morphine requirement for postop-erative pain after spinal surgery.
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1. Can J Anaesth 1996 / 43 (3): 212-5
2. Br J Anaesth 1999 / 83 (3): 393-6
3. Can J Anaesth 1996 / 43 (9): 900-6

S-311.

A RANDOMIZED DOUBLE-BLINDED PROSPECTIVE STUDY COMPARING THE EFFICACY OF CONTINUOUS RADIOFREQUENCY LESIONING TO PULSED RADIOFREQUENCY LESIONING IN THE TREATMENT OF LUMBAR FACET SYNDROME

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Introduction: Lumbar facet joint denervation of the medial branch of the dorsal ramus by continuous radiofrequency lesioning (RF) has been used for over 25 years and has been shown to result in significant pain relief and improved function[1] Pulsed radiofrequency (PRF) is a new technique introduced in an attempt to reduce post-procedure discomfort and neuritis. This is the first study to compare efficacy between the two techniques.
Methods: Fifty patients were randomized to receive either RF or PRF treatment. Inclusion criteria included back pain without radiation below the knee of at least one month duration, reproducible pain, no focal neurological deficits and a negative MRI/CT scan for disc herniation or stenosis. Two separate diagnostic median branch blocks with local anesthetic must have resulted in at least a 50% short term reduction in pain. The RF group received continuous energy delivered at 80ºC for 75 seconds, while the PRF group had energy delivered at 42ºC with a pulse duration of 20 ms at 460.8 kHz and frequency of 2 Hz for 120 seconds. Visual Analogue Scale Pain Assessment (VAS) and Modified Oswestry Low Back Pain and Disability Questionnaire (OWS) were administered at baseline and 3 months post-treatment. Additional questionnaires were completed documenting changes in work status, medication usage, confounding treatments, and complications. Comparisons between groups were assessed using relative percentage improvement. Comparisons between groups and within groups were made of the VAS and OSW using student's t-test and paired t-tests.
Results: Of the 50 patients studied, 26 completed the follow-up evaluation; half received RF and half PRF. In the RF group, the VAS improved at 3 months by an average of 24.7% (SD 50.1), whereas the PRF group improved by 10.6% (SD 45.0). The OWS in the RF group improved by an average of 18.3% (SD 30.7), and the PRF group by 4.1% (SD 44.3). There were no significant differences in the relative improvements between groups in either the VAS (p=0.46) or the OWS (p=0.35). Within the PRF group, comparisons of the relative change at 3 months for both VAS (p=0.21) and OSW scores (p=0.61) were not significant. However, within the RF group, the VAS (p=0.02) and OSW scores (p=0.03) improved significantly at 3 months.
Discussion: This study suggests that there was no significant difference in long-term outcome in the treatment of lumbar facet syndrome between the RF and PRF groups. However, in patients who received RF there was significant improvement in both VAS and OSW at 3 months post-treatment, findings not seen with PRF.
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1) J. Neurosurg 43:448-451, 1975.

S-312.

THE EFFECTS OF CRYOANALGESIA ON POST-THORACOTOMY PAIN

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Introduction: The present study was conducted to determine the efficacy of cryoanalgesia in relieving post-thoracotomy pain in comparison to intravenous meperidine .
Methods: Sixty patients mean age 41 years old entered this clinical trial. Patients were sequentially allocated to two groups: Study group that received cryoanalgesia plus IV Meperidine if needed and Control group that received only IV Meperidine. Pain was measured by Visual Analogue Scale. Pain scoring and measurement of Meperidine consumption were started from recovery room. We measured Meperidine consumption in both groups also measured pain scores till 7th post-thoracotomy day. hypoesthesia, dysesthesia and allodynia recorded during three months after cryoanalgesia.
Results: Pain score was lower in cryoanalgesia group (P value <0.01), and the amount of Meperidine consumption was significantly lower in cryoanalgesia group (P value <0.001). In comparison to dysesthesia and allodynia temporary hypoesthesia is the most common complication of cryoanalgesia (93.3%).
Discussion: The treatment of post-thoracotomy pain remains controversial (1). Conventional methods involve opiates analgesia, administered through parentral routes and nerve block with local anesthetics. Epidural analgesia was used commonly. These methods are not always completely effective and are sometimes accompanied by a number of side effects. Cryoanalgesia, however is not able to provide complete post-thoracotomy pain releif. The area of anesthesia is along the dermatomes treated only, but cryoanalgesia reduces the need for postoperative analgesics (2). In previous studies, effect of cryoanalgesia for relieving pain was lower and its complications has longer duration in comparison to our study and these may be due to several factors:
1 - freezing with unsuitable probes and incomplete freezing of the nerve.
2- long duration of freezing time .
3- freezing of the nerve blindly and only with the use of nerve locator.
but in our technique, we saw the nerves directly when the chest was open, before closure of the thorax. (2, 3, 4)
Cryoanalgesia could safely diminish post-thoracotomy pain and decrease the need for opiates. Cryoanalgesia has not permanent nerve damage.
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S-313.

THORACIC PARAVERTEBRAL BLOCKADE WITH 5% XYLOCAINE FOR CHRONIC PAIN STATES

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Introduction: Thoracic paravertebral blockade (TPB) is a regional anesthesia technique first described in 1905 and recently reviewed in an seminal article by Karmakar[1]. It involves the placement of local anesthetic in proximity to the thoracic vertebral body at the depth of the intervertebral foramen. It is a regional anesthetic technique most commonly utilized for operative thoracic and abdominal procedures. However, TPB has also been utilized for the management of acute and chronic pain states.
Methods: Following IRB approval, we performed 5% lidocaine peripheral nerve blockade at our institution. We report 6 cases of TPB utilizing 5% lidocaine for the treatment of various chronic pain states. In each of these cases, 1.0-2.0 ml of 5% lidocaine was injected at each paravertebral level using radiologic guidance and a Braun Stimiplex stimulator with a 21 gauge 50 or 100 mm Stimuplex needle (B. Braun, Bethlehem, Pa.) with an appropriate ground (2). The endpoint for injection was radiologic confirmation of needle placement and elicitation of a sensory paresthesia either spontaneously or from 0.5-1.0 mA delivered from the stimulator.
Results: (see table).
Discussion: Applications of TPB with local anesthetics for chronic pain states of greater than six months duration include its use for post-thoracotomy pain (3-4). The use of standard neurolytic techniques for TPB has been questioned because of the risk of damage to surrounding tissues and thus limited to patients with a poor prognosis and as a last resort. One review of 7 patients who received 37 neurolytic TPB's with 7% phenol concluded that this technique has limited use (5). While subarachnoid 5% lidocaine is well known to cause occasional prolonged neural blockade (6), we and others have used 5% lidocaine peripheral neural blockade in various chronic pain states without adverse sequelae (7-8). We conclude that 5% lidocaine TPB for chronic pain states is an attractive alternative to other neurolytic techniques because it provides prolonged analgesia without adjacent tissue trauma, neuroma formation and preservation of pulmonary function (9).
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Age/Sex	Diagnosis	# of Treatments	Duration of Analgesia	Patient Satisfied	Treatment Ongoing
44/Female	Post-mastectomy Syndrome	7	10-12 wks	Yes	Yes
86/Male	Post Herpetic Neuralgia	3	4 wks	Yes	No
67/Female	Intercostal Neuralgia	3	12 wks	Yes	Yes
32/Male	Intercostal Neuralgia	3	4-12 wks	Yes	Yes
82/Male	Post-herpetic Neuralgia	2	12+ wks	Yes	No
38/Female	Intercostal Neuralgia	1	5+ wks	Yes	Yes

S-314.

LUMBAR EPIDURAL INJECTION PRACTICES IN THE STATE OF NEW JERSEY

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BACKGROUND: Lumbar epidural injections are performed for acute and chronic pain syndromes, surgical anesthesia and/or postoperative analgesia, and post-dural puncture headaches. These injections are performed in a variety of settings. Some injection complications vary by what is being injected, while others occur independently of the injectate. Consequently, the requirements in terms of environment and location, level of nursing assistance, and monitoring may vary accordingly. This survey was designed to assesss current practice standards of lumbar epidural injections in NJ as they relate to the above. This question was raised because we were being told to do these procedures in areas and under conditions that we felt were substandard.
METHODS: After IRB approval, surveys with pre-addressed stamped envelopes were sent to anesthesia departments of the 88 hospitals in New Jersey listed at njhospitals.com. Departments were queried regarding monitoring, assistance required, and settings that injections are performed. Institutions surveyed that did not perform injections were excluded.
RESULTS: 88 surveys were mailed; 21 were returned (24% response), which is consistent with such surveys (1-2). At 85% of responding institutions, patients requiring lumbar epidural injections are moved to areas where these injections are routinely performed. 100% of responders indicated that injections are performed only in settings where post-procedural vial signs and patient monitoring can be reliably provided for at least twenty minutes. At 90% of responding institutions, lumbar epidural injections are performed in a setting where such injections are done routinely.

Monitoring Requirements:	Local Anesthetic only	Steroid Only	Local Anesthetic Plus Steroid	Epidural Blood Patch
Continuous Pulse-Oximetry	81%	70%	75%	68%
Continuous ECG	62%	60%	65%	53%
NIBP Monitoring	91%	80%	90%	79%
Will Do without IV Access	38%	50%	25%	32%
Will do without an Assistant	43%	35%	35%	26%
Assistant Present Throughout Procedure	57%	50%	60%	68%
Require that Assistant Be Readily Available	14%	30%	20%	26%
Require that Assistant have Familiarity with Procedure	19%	15%	15%	16%
Pre-Op Holding Area	60%	63%	47%	78%
PACU	70%	74%	68%	94%
ER	45%	32%	32%	72%
Intermediate Care Unit (nurse:patient ratio ≤1:4)	50%	47%	47%	50%
Medical/Surgical Ward (nurse:patient ratio ≥1:5)	45%	42%	42%	50%
ICU	70%	63%	58%	72%
Outpatient Clinic	60%	84%	68%	61%

DISCUSSION: Results obtained by this survey demonstrate that only at a small percentage of institutions (15% of responders), epidural injections are not performed in designated areas where injections are routinely performed. Injections are universally performed in settings where post-procedural vital signs can be monitored for at least twenty minutes. Significant variations exist in current practices with respect to monitoring, assistance requirements, and in what settings injections are performed. Noninvasive blood pressure measurement is the most widely used monitor for all injections; continuous pulse-oximetry is employed nearly as commonly. Nonetheless, our survey revealed that at 90% of responding institutions the clinician has the ultimate authority to determine in what setting lumbar epidural injections are performed. These results justify our standard of practice in our institution.
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S-315.

TRAMADOL DEPENDENCE/ABUSE IN PAIN MANAGEMENT FELLOWSHIP TRAINING PROGRAM PRACTICES

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Introduction: Tramadol, an analgesic cogener of codeine, has been used in the US since 1995[1]. Despite its opiate agonist activity, it is not scheduled in the US and has a reported dependence/abuse potential of 1/ 100,000. We previously reported that we discovered 7 patients out of 2,037 active files in our pain management fellowship training program practice that met DSM-IV diagnostic criteria for tramadol abuse[2]. Therefore, we wished to determine if our experience with tramadol is similar to other Pain Programs in the United States.
Methods: Following IRB approval, we surveyed the use of oral and transdermal analgesics in the 99 ACGME Pain Medicine Fellowship Programs at that time. Topics in the survey included: practice demographics, analgesic prescribing habits, rating of tramadol potency versus other analgesics, relationships with pharmaceutical representatives, and evidence of tramadol dependence/abuse in their patient population by using DSM-IV diagnostic criteria for abuse.
Results: We mailed 99 surveys; 34 were returned. Of these 34, one was excluded because the respondent only performed palliative care and one was rejected for incompleteness. The total number of active patients was approximately 100,000 with new patients of approximately 36,200/ year. A total of 84% (27 out of 32 practices) reported concerns with at least one DSM-IV diagnostic criterion of tramadol dependence/abuse. Of the 5 practices that did not report any problems, one of these did not prescribe tramadol. Analgesic potency of tramadol was ranked between propoxyphene and codeine. The estimated total number of patients with tramadol dependence/abuse criteria was 82.
Discussion: Tramadol is marketed as an attractive alternative to other analgesics because it has an analgesic profile similar to morphine[3] without potential for dependence/abuse and is a non-scheduled drug. Our results indicate that tramadol dependence/abuse may be a greater problem than previously recognized. In addition, only a portion of patients in the surveyed practices received tramadol, suggesting the true denominator of patients receiving tramadol is most likely less than the total estimate of active patients. In 1999, a post-marketing survey[4] concluded that tramadol withdrawal was in line with previous estimates. However, dependence/abuse was not considered. Other medications without withdrawal potential are regulated worldwide (i.e., hallucinogens, cannabis, and cocaine). In 2002, the WHO Expert Committee on Drug Dependence[5] recommended keeping tramadol on its "watch list." Finally, proactive MEDWatch reporting revealed tramadol abuse of 10-13 times more than expected, with reports of withdrawal in line with expectations[6]. Further study, including prospective trials, is needed to assess the magnitude of this problem.

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S-316.

THE EFFICACY OF PROPOFOL IN THE TREATMENT OF INTRACTABLE CHRONIC DAILY HEADACHE

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Introduction: Propofol is an intravenous hypnotic anesthetic agent that was used in the acute treatment of refractory headache.1,2
We were interested to determine the short-term and long-term efficacy of IV propofol in the management of intractable chronic daily headache.
Methods: The data were collected retrospectively by reviewing the patient's medical records and headache questionnaires. 50 patients were identified and they underwent 55 treatments with IV propofol. Data on 51 treatments were collected.
All the patients had a diagnosis of refractory chronic daily headache that failed multiple trials with different treatment modalities. 41 patients (82%) had chronic (transformed) migraine with medication overuse.
The patients were treated as an outpatient at our pain and headache clinic. The patients were transferred to the PACU where standard anesthesia monitors and oxygen nasal cannula were placed. 20 mg lidocaine IV was given to ameliorate the burning sensation with IV propofol injection. Then IV propofol 1% (10mg/ml) infusion was started at a rate of 20-30 ml/hour depending on the level of sedation and vital signs for a maximum dose of 200 mg.
Results: There was no difference between the headache score before and after the lidocaine injection. The mean headache score before the propofol infusion was 7.1 and immediately after the infusion was 2.9 with mean difference of 4.2 (95% CI = 3.4-4.9). This was statistically significant with a P value of 0.001 using paired t test. Patients in 19 treatments (37.2%) reported full relief of their headache, while patients in 32 treatments (62.7%) reported more than 50% reduction of their headache.
At 1 month follow up, 32 patients (62.7%, 95% CI = 45.3-76.9) stated that their headache improved in intensity and frequency, while 19 patients (37.2%, 95% CI = 21.9-53.3) stated that their headache is the same and this was not statistically significant (p =0.06 using Pearson Chi square test). 2 patients had headache relief that lasted for 16 weeks; however the average headache relief was 2.3 weeks.
Discussion: The mechanism by which propofol relieves chronic daily headache is unclear. However possible mechanisms include; GABA-A receptor stimulation, NMDA receptor inhibition, sympathetic neuronal activity inhibition, and nitric oxide release.
Our data showed that propofol was effective in the acute treatment for intractable daily headaches, however its long-term efficacy was questionable. We recommend considering the use of propofol to abort intractable daily headache in the emergency room or in a well-equipped headache/pain clinic under the supervision of an anesthesiologist. On the other hand we don't advocate the routine use or the repeated administration of IV propofol for the treatment of chronic daily headaches because of possible development of drug dependency.3

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S-317.

DOES TRANSDERMAL FENTANYL PATCH PRODUCE PERIPHERAL OPIOID ANALGESIA?

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Introduction: Studies demonstrate the presence of peripheral μ opioid receptors (PMOR) in different skin layers.[1] Peripheral analgesia mediated via PMOR has been shown in a variety of settings, most commonly in arthroscopic procedures.[2] The role of PMOR in producing peripheral analgesia after transcutaneous iontophoresis of methadone and intradermal fentanyl injections has been demonstrated.[3,4] The transdermal fentanyl patch (TFP) may offer a direct route to eliciting analgesia via PMOR by accumulation in the skin at the location of patch application. Fentanyl is not absorbed systemically in the first 3-6 hours after TFP application.[5] The present study evaluated the peripheral opioid analgesic effect of TFP using a quantitative sensory testing (QST) method.
Methods: With IRB approval, 12 healthy volunteers (6 male, 6 female) aged 26-66 were enrolled in our prospective, double blind, and placebo controlled study. Subjects were trained in QST using a Thermal Sensory Analyzer (TSAII, Medoc Advanced Medical Systems). Pain threshold for cold and heat, and supra-threshold (100mm visual analog scale (VAS) for pain and unpleasantness after 5 seconds of 48°C) measurements were recorded before and after TFP administration. Subjects served as both control and study group, being administered a TFP (25μg/hr) and placebo patch on opposite forearms for two hours. Blood specimens for fentanyl assay were obtained at baseline and after patch removal. Data comparisons were made using the paired t-test and Wilcoxon matched pairs test.
Results: Baseline testing showed no difference in pain threshold or supra-threshold scores. Cold temperature thresholds decreased by 20.4% for TFP vs. 8.6% for placebo (p=0.069). Heat temperature thresholds and VAS (pain and unpleasantness) were similar for TFP vs. placebo. Sex and hand dominance accounted for no change in pain thresholds or VAS. There were no systemic effects of fentanyl in any subject.

	Fentanyl	Placebo
Cold PT-pre	15.38±8.3	15.86±7.6
Cold PT-post	12.21±8.8	14.49±8.3
	(-20.4%)	(-8.6%)
Hot PT-pre	44.44±3.0	44.57±3.2
Hot PT-post	43.53±3.2	44.05±3.6
	(-2.0%)	(-1.2%)
VASpain-pre	56.87±13.7	57.75±13.5
VASpain-post	64.17±16.1	64.80±17.0
	(+12.8%)	(+12.2%)
VASunpleas-pre	64.50±12.3	66.67±8.9
VASunpleas-post	68.42±18.3	69.13±16.3
	(+6.1%)	(+4.7%)
PT=pain threshold (°C)		Pre= Baseline
VAS=visual analog scale (0-100)		Post=Post-patch removal

Discussion: Our findings suggest no statistically significant analgesia at the site of application of a TFP. We found a trend towards TFP producing analgesia based on cold pain thresholds which was approaching significance. Perhaps with a larger study size, higher dosage of TFP, or prolonged patch application time there could be a proven analgesic effect. [Supported in part by Janssen Pharmaceutica and NIH M01RR10732].
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S-318.

SELECTIVE TRANSFORAMINAL EPIDURAL INJECTIONS FOR RADICULOPATHY IN PATIENTS WITH OR WITHOUT PAST BACK SURGERY HISTORY

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Introduction: To evaluate the efficacy of selective transforaminal epidural steroid injections in patients having radiculopathy with or without past back surgery history
Methods: Between July 2003 and November 2003, total 134 patients with radiculopathy were included in this study. Diagnosis was done previously by X-ray, CT and MRI. 109 patients (Group I) were not taken back surgery before treatment and 25 patients (Group 2) were taken back surgery before treatment and they were referred to our pain management center. Patients in Group 2 had persistent chronic pain after back surgery with MRI showing stenosis, recurrent disc and postsurgical scar -FBSS (failed back surgery syndrome). Fluoroscopy was used for selective transforaminal epidural injection. A 22-gauge Tuohy needle was used to enter anterior epidural space using transformainal approach. Patients were injected 5ml 0.5% lidocaine and 40mg triamcinolone. If the VAS (visual analogue scale) did not reduced less than half of initial VAS one month later, additional selective transformainal injection was done. If the VAS of patient was reduced less than half of initial VAS, we stopped treatment and just followed up. If the VAS of patient was not reduced after the three consecutive treatments, we recommended operation. Initial VAS was checked, and after the last treatment, the VAS was checked.
Results: Groups were comparable with respect to demographic data. There was a significant decrease in VAS after treatments in Group 1 (7.3±2.4 vs 2.4±1.8) and Group 2 (7.9±1.7 vs 3.8±2.4). Average Injection per patient was 1.8 in Group 1 and 2.3 in Group 2. 17 patients of Group 1 (15%) were taken operation after treatment of selective transforaminal epidural steroid injections and 7 patients of Group 2 (28%) were taken re-operation.
Discussion: Selective transforaminal epidural treatment for radiculopathy was more effective in patients without past lumbar operation history than in patients with FBSS. But, the patients with FBSS have also experienced pain relief from selective transforaminal epidural treatment. Selective transformaiminal epidural treatments appear to be effective for patients having low back pain with radiculopathy as well as patients with FBSS.
References:
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S-319.

PARENTERAL NICOTINE FOR POSTOPERATIVE PAIN: AN UPDATE

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Introduction: Nicotine and other nicotinic agonists have been shown to have analgesic actions in animal models and volunteer studies. In a pilot study it has been shown that a single dose of nicotine nasal spray (3mg) given under anesthesia, significantly reduces pain scores and narcotic utilization during the first 24 hours after gynecological surgery[1]. In this study, all subjects were anesthetized with isoflurane and fentanyl. Because low concentrations of isoflurane have been associated with pain enhancement in both animals and humans[2,3], and the increased pain sensitivity can be reversed with nicotine[2], we designed the current trial to determine whether 1) patients anesthetized with isoflurane have more postoperative pain than those anesthetized with propofol, and 2) whether the analgesia associated with nicotine is specific to reversing the hyperalgesia associated with isoflurane anesthesia.
Methods: In a double blind randomized, IRB approved trial, women having gynecological surgery are randomized to one of four groups. Group one is anesthetized with propofol and fentanyl and receives nicotine nasal spray at the end of the anesthetic. Group two is anesthetized with propofol and fentanyl and receives placebo nasal spray. Group three is anesthetized with isoflurane and fentanyl and receives nicotine nasal spray at the conclusion of surgery. Group four is anesthetized with isoflurane and fentanyl and receives placebo nasal spray at the end of surgery. All anesthetic regimens are titrated to a BIS value of 50. The primary outcome variable is pain score during the 24 hours after surgery. Secondary outcome variables are morphine PCA utilization, hemodynamic variables, nausea and sedation.
Results: In this double blind, prospective trial, we have enrolled 25 subject of a projected 80 (20 per group). Preliminary results will be presented at the meeting. In the first 25 subjects, there have been no adverse events and no protocol violations.
Discussion: Parenteral nicotine and other nicotinic agonists have the potential to be used as adjuvant analgesic drugs. Preliminary work has suggested that nicotine nasal spray (3mg) after gynecological surgery with an isoflurane based anesthetic has excellent analgesic efficacy and reduces morphine requirements. The results of our current study will allow us to determine whether the analgesic action of nicotine is specific to isoflurane anesthesia and to address the more basic question of whether the hyperalgesic action of volatile anesthetics that has been reported is clinically relevant. Supported in part by the IARS Clinical Scholar Research Award.
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Pediatric Anesthesia

S-320.

COBRAPLA VS. DISPOSABLE LMA IN PEDIATRIC PATIENTS: A PRELIMINARY COMPARATIVE STUDY

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Background: The CobraPLA® (Engineered Medical Systems, Indianapolis, IN) is a new disposable extraglottic airway. It consists of a breathing tube with a wide distal end; a circumferential cuff is attached proximally to the wide part and serves to seal the distal end from the upper airway. The CobraPLA is manufactured in 8 sizes with 4 of them suitable for pediatric patients (0.5, 1, 1.5, 2). Our goal was to compare the CobraPLA with the LMA Unique in pediatric patients with respect to sealing properties, ease of insertion, positioning within the airway, oropharyngeal irritation, and gastric insufflation.
Methods: 57 ASA I-II, patients, age 0-14 year old, scheduled for short surgeries, were randomly assigned for airway management with either the CobraPLA or LMA Unique. Anesthesia was induced with sevoflurane in 30/70% O_2/N_2O 1 mg/kg of propofol and 1 µg/kg of fentanyl were added. The size of airway was determined according to the manufacturer's recommendation. All patients were mechanically ventilated with a TV of 8 ml/kg at a RR of 20-24 bpm. The following variables were measured: time and ease of insertion, airway sealing pressure at a cuff inflation pressure of 40 and 60 cmH_2O, gastric insufflation, degree of sore throat and dysphonia, and complications (laryngospasm, bronchospasm). *P* values were calculated using unpaired, two-tailed t-test, chi-square test, or Fisher's exact test.
Results: CobraPLA was used in 27 patients and LMA in 30 patients. No differences with regard to time or ease of insertion and number of attempts were found. The CobraPLA had a significantly greater airway sealing pressure at both 40 and 60 cmH_2O cuff inflation pressure (Table 1), and greater peak airway pressure (20 ± 3 vs. 16 ± 6 cm H_2O) and significantly lower gastric gas volumes (7 ± 4 vs. 15 ± 6 ml) than the LMA group.
Discussion: A greater sealing pressure with the CobraPLA allowed for a higher peak airway pressure and a significantly lower gastric gas volume as compared with the LMA group. These results are similar with a study in adults (1). Insertion characteristics of the CobraPLA were similar to the LMA Unique, but airway sealing was superior and there was less gastric inflation.
Reference:
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Table 1. Major Outcomes.

Insertion of airway device	PLA (n = 27)	LMA (n = 30)	*P*
Insertion Time (sec)	19 ± 6	19 ± 70	0.945
Attempts (1 / 2)	24 / 3	30 / 0	0.100
Laryngospasm) (no/yes)	27 / 0	30 / 0	1.000
Bronchospasm (no/yes)	27 / 0	30 / 0	1.000
Maintenance of anesthesia			
Airway Sealing Pressure at 40 cm (cm H_2O)	19 ± 4	15 ± 5	0.003
Airway Sealing Pressure at 60 cm (cm H_2O)	22 ± 4	17 ± 4	<0.001
Peak Airway Pressure at 20 min (cm H_2O)	20 ± 3	16 ± 6	0.003
Removal of airway device and complications			
Blood staining (yes/no)	25 / 1	24 / 5	0.197
Gastric Gas Volume (ml)	7 ± 4	15 ± 6	<0.001
Sore Throat (yes/no)	21 / 1	20 / 2	1.000
Dysphonia (yes/no)	23 / 4	25 / 5	1.000

Data presented as means ± SDs or counts.

S-321.

IMPACT OF NITROUS OXIDE ON PEDIATRIC LMA™ INTRACUFF PRESSURES

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Introduction: The LMA-Classic™ is composed of silicon rubber through which nitrous oxide (N20) and carbon dioxide diffuse to increase intracuff volume and pressure (1,2). Adult studies show a relationship between high LMA cuff volume and postoperative sore throat and dysphagia (3,4). We hypothesize that cuff inflation with water would minimize N2O diffusion into the cuff thereby stabilizing intracuff pressures. This randomized controlled study attempts to determine the impact of N2O on pediatric LMA cuff pressures.
Methods: After IRB approval and parental consent, 10 ASA 1 or 2 pediatric patients undergoing strabismus repair under general anesthesia with LMA were randomized to air versus water into the LMA cuff. Patients received a standard anesthetic including premedication with midazolam, Sevoflorane mask induction with O2:N20 1:2. Intravenous access was obtained to administer standard weight-based doses of atropine, fentanyl, ondansetron, and ketorolac. LMAs were inserted under deep Sevoflorane anesthesia in 100% O2. After stabilization of cuff pressures on 100% O2, anesthesia was maintained with O2:N2O 1:2 and Isoflorane. Ventilation was assisted to maintain EtCO2 < 60 mm Hg, SpO2 > 90%, and airway pressures < 20 cm H2O. LMA intracuff pressure (ICP) was recorded from cuff inflation until deflation via a pressure transducer. Using standard error of mean (SEM) and student T-test p values, the following data from both groups were compared: ICP rate of rise from start of N2O maintenance (time 0) to time of peak ICP (time peak), absolute increase in ICP (time 0 to time peak), and time to achieve peak ICP.
Results: Mean absolute change in ICP from time 0 to time peak was 4-fold higher with air versus water. Time to achieve peak ICP was not different between the groups. ICP rate of rise was 3.9-fold higher with air versus water. Data is presented as mean ± SEM; p<0.05 for both ICP absolute change and slope.

LMA cuff	ICP absolute change (mm Hg)	ICP slope (mm Hg/min)
Air	63.6 ± 9.7	1.99 ± 0.50
Water	15.6 ± 5.4	0.51 ± 0.11

Discussion: We conclude that absolute change and rate of rise in LMA intracuff pressures are lower in water-filled than in air-filled cuffs; this difference is statistically significant. Inflating the LMA cuff with water leads to a more stable intracuff pressure with lower absolute peak pressures.
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S-322.

THE ENDOSCOPICALLY MEASURED EFFECTS OF AIRWAY MANEUVERS AND THE LATERAL POSITION ON AIRWAY PATENCY IN ANESTHETIZED CHILDREN WITH ADENOTONSILLAR HYPERTROPHY

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Introduction: Obstruction of the upper airway is a major challenge for anesthesiologists administering general anesthesia in spontaneously breathing children with adenotonsillar hypertrophy (1-3). Lateral positioning is a simple treatment for obstructive sleep apnea (4-7).
Methods: We examined the effects of body position shifting and common airway maneuvers such as chin lift and jaw thrust on airway patency (stridor score and upper airway dimensions by endoscopy) in anesthetized children scheduled for adenotonsillectomy. Eighteen children aged 1 - 11 yr were anesthetized with sevoflurane. During spontaneous breathing on 5% sevoflurane with 100% oxygen, upper airway dimensions and stridor score were recorded. After baseline recording, chin lift and jaw thrust were performed under both the supine and the lateral decubitus position.
Results: Chin lift, jaw thrust and lateral position increased the airway dimensions and improved the stridor score. Moreover, lateral positioning enhanced the effects of these airway maneuvers on airway patency.
Discussion: Lateral positioning not only improved airway patency, but also increased the effect of airway maneuvers, when using clinical and endoscopical methods. We concluded that lateral positioning combined with airway maneuvers provided better airway patency for anesthetized children with adenotonsillar hypertrophy.
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Effects of airway maneuvers and position shifting on airway dimension and stridor score

	Neutral neck position - supine	Neutral neck position - lateral	Chin lift - supine	Chin lift - lateral	Jaw thrust - supine	Jaw thrust - lateral
Anteroposterior (unit)	0.4 (0.3-0.6)	1.25 (1-1.6) †	1.25 (1.1-1.7) *	1.8 (1.6-2.1)†	1.85 (1.6-2.1) *	2.3 (2-2.6)†
Transverse (unit)	1.65 (1.2-1.8)	2.3 (1.9-2.7)†	2.35 (1.8-2.5)*	2.95 (2.5-3.4)†	2.95 (2.3-3.4)*	3.45 (3-3.7)†
Stridor score	4 (4-4)	3 (2-3)†	3 (2-4)*	1 (1-3)†	2 (1-3)*	1 (1-1)†

S-323.

USE OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE IN CHILDREN WITH POSTOPERATIVE RESPIRATORY FAILURE

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Introduction: Nasal continuous positive airway pressure (NCPAP) has been used to manage acute pulmonary edema in adults and respiratory distress syndrome in newborns. However, few reports have been made on use of NCPAP for postoperative respiratory failure in children. The aim of this study was to determine whether use of NCPAP can improve pulmonary gas exchange and reduce the need for reintubation in children who developed respiratory failure after extubation during postoperative period.
Method: We retrospectively investigated patients < 4 years of age who underwent surgery under general anesthesia and developed respiratory failure after tracheal extubation in our ICU from August 1,2002 to July 31,2004. Since August 2003,we started to use NCPAP for children who developed post-extubation respiratory failure. Before August 2003, physiotherapy alone was provided for respiratory failure before reintubation and patients in this period were served as a control group. We examined whether reintubation was required and whether postoperative pulmonary complications such as atelectasis and pneumothorax occurred. The following data were collected and analyzed: age, gender, weight, ASA physical status, duration of artificial ventilation and ICU stay. Arterial plasma lactate, arterial blood gas analysis and vital signs including blood pressure, heart rate, and respiratory rate were obtained before and after physiotherapy or NCPAP administration. Data were analyzed using Student's t-test.
Results: A total of 734 patients < 4 years of age underwent surgery between August 1, 2002 and July 31, 2004. During this 2-year period, 19 patients (2.6%) developed post-extubation respiratory failure. Ten patients received physiotherapy alone and 9 patients underwent NCPAP. Seven out of 10 patients (70%) who received physiotherapy alone required reintubation whereas none of the NCPAP group required reintubation (P<0.01). Two patients (20%) in the physiotherapy group developed atelectasis, while none in the NCPAP group developed any pulmonary complications (0%) (P<0.01). Mean (±SD) $PaCO_2$ decreased from 60±13 to 58±10 mmHg in patients receiving physiotherapy alone and from 62±16 to 45±6 mmHg in those who underwent NCPAP (P=0.04). Respiratory rate decreased from 62±6 to 59±8 breaths/min in the physiotherapy group and from 60±6 to 28±5 breaths/min in the NCPAP group (P=0.01).
Discussion: Numerous attempts have been made to show that NCPAP is effective for the treatment of obstructive sleep apnea syndrome in children and that it can also be tolerated by children despite its discomfort. However, little has been known concerning the effect of NCPAP on post-extubation respiratory failure in children. In this study, we demonstrated that NCPAP improves gas exchange and vital signs and reduces the need of reintubation in children with postoperative respiratory failure, and that NCPAP can be safely performed without complications such as atelectasis or pneumothorax.

S-324.

DISCHARGE HOME IN THIRTY MINUTES FOLLOWING SEVOFLURANE ANESTHESIA FOR PEDIATRIC OUTPATIENT IMAGING - CAN IT GET ANY BETTER?

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Introduction: The optimal management of pediatric patients for the acquisition of good quality diagnostic imaging has been widely debated. Previous studies have examined both the advantages and adverse effects of general anesthesia versus sedation for this procedure. The advantages of performing pediatric imaging under general anesthesia as opposed to sedation include a quick onset, lack of failure due to patient movement and less incidence of respiratory events[1]. However, no previous study has analyzed the speed of recovery following general anesthesia, which directly impacts efficiency of the MRI suite, patient cost and parental satisfaction. We therefore decided to study recovery and discharge times following sevoflurane anesthesia in our pediatric population for outpatient imaging procedures.
Methods: Sixty-five pediatric patients (ages=2 months to eight years) scheduled for outpatient MRI/CT were included in the study. None of the patients received any premedication. Induction of anesthesia with nitrous-oxide/oxygen and sevoflurane was performed with parental presence in the designated anesthesia induction room. Airway was secured with a LMA (n=60) or endotracheal tube (n=50) as considered appropriate. Anesthesia was maintained with sevoflurane (average end-tidal 2.3%) in oxygen. The following times were noted: discontinuation of sevoflurane, return to baseline level of consciousness, oral intake and discharge home.
Results: Following discontinuation of sevoflurane the documented times expressed as mean ± standard error of mean in minutes were: average time to return to baseline level of consciousness was 10.78 ± 0.56, time to oral intake was 16.48±1.07 and discharge home was 30.01± 1.26.
Discussion: In the past, the management of diagnostic imaging procedures in pediatric population was performed routinely under sedation by non-anesthesiologists. The increased incidence of failure rate due to patient movement, inadequate sedation, adverse respiratory events, residual sedation and adverse respiratory events after discharge has resulted in a recent increase in the involvement of anesthesia providers to aid diagnostic procedures in this patient group. There are several options for the anesthetic management of these cases including the use of total intravenous or inhalational agents. The use of general anesthesia for pediatric imaging has been viewed in the past as costly, associated with high risk and inefficient[2]. Our current study has shown that this is not the case. The physical properties of sevoflurane facilitate a rapid, smooth induction and placement of an intravenous access after induction, both of which were appreciated by the parents. The quick recovery and discharge times were appreciated both by the radiology department and the concerned parents. We therefore conclude that sevoflurane anesthesia is cost-effective and optimal for pediatric outpatient imaging because of the non-existent failure rate, minimal adverse effects, and above all the speed of recovery and discharge.
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S-325.

A THREE YEAR RETROSPECTIVE ANALYSIS OF REINTUBATION IN THE IMMEDIATE POSTOPERATIVE PERIOD IN PEDIATRIC PATIENTS FOLLOWING GENERAL ANESTHESIA

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Introduction: Endotracheal intubation is the most common method used for securing the airway. Complications following intubation range from minor sore throat to major trauma to upper airway and teeth. The need for reintubation (RI) in patients who received general anesthesia (GA) is also a known complication of intubation.[1] However, to date there is only one study that dealt with the factors that led to RI following GA[2] and there is no such study in pediatric patients. The aim of this study is to determine the incidence of RI in pediatric patients undergoing non-cardiac procedures under GA in the immediate postoperative period and distinguish patient characteristics, processes of care and other probable contributing factors leading to RI.
Methods: After obtaining IRB approval, a retrospective review of the charts of patients who were reintubated in the immediate postoperative period (<6 hours) following GA in the past 3 years was done. The following data were collected and analyzed: age, gender, weight, ASA physical status, procedure, perioperative medications, duration of surgery, deep extubation and reason for RI. A descriptive analysis of the demographic data and Chi-square test of the different variables was done. A p value of < 0.05 was considered statistically significant.
Results: There were 12 unplanned RI (incidence: 0.05%; 12/24,000) during the study period. Age of the reintubated patients ranged from 2 months to 7 years. Most patients were ASA physical status II except for 1 ASA I and 4 ASA III. Their weight ranged from 2 to 42 kg. Out of 12 patients, 10 were males, 5 received muscle relaxation, 10 received narcotics, 7 received benzodiazepines and 7 were born premature. Eleven patients had significant upper airway and/or respiratory disease (e.g. obstructive sleep apnea, reactive airway disease, bronchopulmonary dysplasia, bronchitis, gastro esophageal reflux/ aspiration). The duration of procedures was between 9 and 246 minutes. Only 4 patients were extubated in the deeper plane of anesthesia. All were easy intubations. Laryngospasm was the reason for reintubation in 6 patients, apnea in 2, upper airway obstruction in 2, respiratory insufficiency in 1 and seizure in 1. Six patients had adenotonsillectomy and it was a statistically significant variable as was the gender and the use of narcotics.
Discussion: We conclude that the incidence of reintubation in the immediate postoperative period in pediatric patients following GA is low (0.05%). Majority of the reintubated patients had a history significant for upper airway and respiratory diseases. A significant percentage of the reintubated patients were males, had perioperative narcotics and were subjected to adenotonsillectomy. Based on this preliminary study we recommend further studies on this complication in pediatric patients.
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S-326.

INHALATIONAL ANESTHETIC EFFECTS ON EEG COHERENCE IN INFANTS AND CHILDREN

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Introduction: EEG amplitude and synchronization across the brain may reflect cortical activity and level of consciousness. Desynchronized EEG activity signifies arousal whereas greater cortical synchrony is seen with depressed cortical activity.[1] Coherence measures neural synchrony between two electrode locations. Coherence examined locally probes activities of subjacent neural populations. Long-range coherence examines interactions between different cortical areas. In this study, we used a 128-lead geodesic array of electrodes to examine anesthesia effect on EEG coherence.
Methods: Following IRB approval and parental consent, ten children (5 months to 3 years old) undergoing lower abdominal surgery were recruited and randomized to either isoflurane or sevoflurane for maintenance, following sevoflurane induction. The remainder of the anesthetic management was standardized. Continuous 128-lead EEG recording was done following endotracheal intubation until extubation. Data was analyzed in delta (1-4 Hz) and beta2 (20-30 Hz) bands to determine the power, power ratio, coherence, ratio of coherence, and the topographic distribution of each of the variables.
Results: During anesthesia maintenance, delta coherence was greater in the frontal than in the posterior region of the brain. In contrast, beta coherence was greater in the posterior than in the frontal region. Similar to the pattern of frontal dominance in the ratio of delta and beta2 power,[2] the ratio of delta to beta2 coherence also exhibited frontal dominance. A concentration dependent decrease in the spatial average of delta coherence and the ratio of coherence upon emergence was found. In addition, emergence from anesthesia was associated with loss of dominance effects. Beta coherence did not demonstrate a clear concentration dependent effect.
Discussion: Our results illustrate that in infants there are concentration-dependent and region specific changes in EEG coherence. Previous quantitative EEG studies were performed in adults using 19 leads. Our studies provide greater spatial resolution using 128 leads and more accurate spatial correlation since volume conduction is reduced in children.[3] We found anesthesia increased low frequency EEG coherence, particularly in the frontal regions. These are similar to EEG patterns observed during natural sleep.[4,5] Moreover, our findings suggest parallels between the responses of the immature and the adult brain to anesthesia. In one study (n=176, mean age 41.3 years), anesthesia was reported to induce frontal hypercoupling and interhemispheric and anterior-posterior intrahemispheric uncoupling in the low frequency band EEG.[6] We plan to further analyze our data to determine anesthesia effect on long range coherence among different regions of the immature brain. These studies may provide further understanding of the maturation of consciousness and the neurophysiology of anesthesia.

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S-327.

SEDATION WITH KETAMINE AND MIDAZOLAM MINIMIZES HEAT LOSS IN CHILDREN UNDERGOING MRI SCANS

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Introduction: Intravenous sedation with different anesthetic agents is commonly used for MRI in children (1). However, the effects of these agents on thermoregulation have not been evaluated in an environment of heat exchange from exposure to cool rooms and to heat from radiofrequency radiation during scanning. In children under sedation with chloral hydrate, body temperature increased after MRI scans (2). We sought to determine changes in core body temperature after MRI scans in children sedated with ketamine and midazolam.
Methods: With IRB approval, we prospectively studied 7 children who underwent MRI scans sedated with ketamine and midazolam. The mean age was 35 ± 30 months (range, 2 days to 8 years), the mean weight was 14 ± 7 kg (range 4 to 22 kg), and the mean body surface area was 0.58 ± 0.24 m^2 (range 0.25 to 0.84 m^2). The patients were sedated with ketamine (mean dose 30 ± 19 mg; range 2 to 60 mg) and midazolam (mean dose 2.6 ± 1.7 mg; range 0.2 to 5.0 mg) in incremental doses until asleep. After sedation, the patients were covered with a cotton blanket. No heating device was used and the fan was left on in the magnet bore. The tympanic temperatures were measured in the right ear immediately before patients entered the magnet room and upon completion of the MRI scan. The patients were monitored with pulse oximetry, capnography, EKG, and a non-invasive blood pressure monitor while breathing room air. The ambient temperature of the magnet room was 19-20ºC.
Results: The mean pre-scan tympanic temperature was 37.6 ± 0.2ºC; the mean post-scan tympanic temperature was 37.5 ± 0.8ºC. The mean tympanic temperature difference was -0.1 ± 0.7ºC. The mean scan time was 60 ± 36 min and the mean time spent in the magnet room was 71 ± 37 min.
Discussion: Although it has been suggested that sedation augments an inability in some neonates to retain body heat (3), the children in our study had minimal heat loss, reflected by a slight decrease in the mean post-scan tympanic temperature. By causing vasoconstriction, ketamine may have decreased heat loss to the cool magnet room. The absorption of radiofrequency radiation during the scan may have replaced the heat lost. Future studies are required on the thermoregulatory responses to different anesthetic agents during MRI scans.

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S-328.

RECOVERY CHARACTERISTICS AFTER PROPOFOL ANESTHESIA WITH LOW DOSE ROCURONIUM FOR DAY-CASE TONSILLECTOMY IN CHILDREN

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Introduction: Low doses of rocuronium have proved acceptable intubating condition under different anesthesia conditions in children [1,2]. The recovery charactetistics for low dose rocuronium are still not fully described. We compared recovery characteristics as onset time, duration and spontaneus recovery of neuromuscular block during propofol anaesthesia followed by 0.45 and 0.60 mg kg^{-1} rocuronium in children for day case tonsillectomy.
Methods: Sixty children (8-12 old, both sexes, ASA I/II status) were studied in the prospective, randomised, double-blinded study. All children were premedicated with midazolam 0.3 mg kg^{-1} and EMLA was placed on the left fist. Anaesthesia was induced with propofol 2,5 mg kg^{-1} and maintained by continuous infusion of propofol 0.1 mg $kg^{-1}min^{-1}$ and alfentanyl 0.0015 mg $kg^{-1}min^{-1}$ with 50 % oxygen in nitrous oxide. According to randomization schedule the appropriate intravenous bolus of neuromuscular blocking drug was given in thirty children, in standard (0.6 mg kg^{-1}) (R1) or in low-dose (0.45 mg kg^{-1}) (R2). Neuromuscular transmission was monitored by means of acceleromyography with supramaximal train-of-four stimulation of the ulnar nerve with frequency of 1 Hz. Endotracheal intubation was performed at maximal depression of the first twitch (T1). Intubating conditions were assessed using the standard three-point scoring system. After tonsillectomy, infusion of propofol was stoped when 90% control twitch height of TOF was establish. At that time the extubation was carried out. All patients were scored for their clinical recovery by the Steward-scoring system. The data were analysed using the Chi-Square test, the Mann-Whitney U-test and Fisher's exact test. A P-value < 0.05 was considered as statistically significant.
Results: The groups were comparable with respect to age, sex, weight and height as ASA physical status. The mean duration of tonsillectomy was nearly equal in both groups (R1=19 +/- 1.6, R2=18 +/- 1.4 min). Duration of anaesthesia was significantly longer in R1 group (R1=39.2 +/- 0.7, R2=31 +/- 0.5 min) ($p<0.05$). Although the onset time (To) was significantly longer after a low-dose rocuronium (R2=3.1 +/- 0.4; R1=1.3 +/- 0.4 min) ($p<0.05$), no difference was found in the intubating conditions. Clinical duration of the block (T0-T25) was significantly shorter after low-dose rocuronium (R2=10.9 +/- 0.7; R1=18.8 +/- 1.0 min) ($p<0.05$) but recovery index (T25-T75) (R2=13.7 +/- 0.7; R1=14.1 +/- 0.5 min) and recovery time (T75-T90) (R2= 3.3 +/- 0.3, R1= 2.9 +/- 0.2) did not differ between the groups ($p>0.05$).
Discussion: Under continuous propofol-alfentanyl-N2O anaesthesia, low-dose rocuronium in children results in the longer onset time and shorter clinical duration. Spontaneus recovery of neuromuscular block under continous propofol anesthesia in this circumstances is save and clinical acceptable. This technik is recommanded for tonsillectomy in children performed on day case basis where an intubation and shorter clinical duration of block is required.
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S-329.

CONTEXT SENSITIVE PHARMACOKINETICS AND DYNAMICS OF VOLATILE ANESTHETIC AGENTS IN CHILDREN

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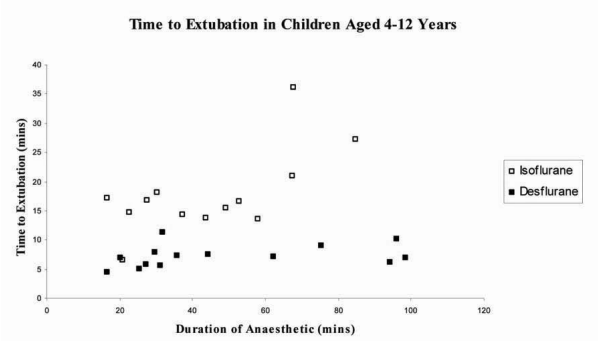
Introduction: We investigated the relationship between anaesthetic duration and the pharmacokinetic and pharmacodynamic recovery from the volatile agents, isoflurane (I) and desflurane (D) in children aged 4 months to 12 years.
Methods: Subjects were randomized according to age (<4 years or >4years) and expected length of operation (<1hour or >1 hour) to receive either I or D. Following induction of anesthesia and endotracheal intubation, the patients were ventilated to normocapnia with a 1.0 MAC agent end-tidal equivalent in oxygen and air. Analgesia consisted of NSAIDs, fentanyl (1-2 mcg/kg) and a regional technique as appropriate. All patient data including end-tidal agent levels were monitored with the Datex AS/3 and saved for later analysis on a laptop PC running the Datex Collect software. The volatile anaesthetic agent was turned off with the last surgical stimulus and the patient was allowed to wake spontaneously with minimal handling. An investigator, blinded to the anaesthetic agent used, observed and timed the patient's emergence events including times to; first gross limb movement, eye opening, establishment of regular breathing pattern, extubation, admission and discharge from PACU.
Results: To date 53 patients have been studied. Mean number of breaths to decrease to 0.5 MAC was less for D (3.2) than for I (9.8). Wake-up times reflect this pharmacokinetic difference (data are median and range (minutes)); in the >4y age group, time to extubation was less for D, 7.20 (4.48-11.35) (<1h); 7.20 (6.30-10.30) (>1h) than I 14.50 (6.57-18.12) (<1h); 27.38 (16.70-36.17) (>1h), see graph. This difference was less clear in the <4y age group, D, 9.06 (4.15-16.33) (<1h); 7.70 (5.56-12.58) (>1h) compared to I, 10.12 (8.53-21.30) (<1h); 13.42 (5.12-18.37) (>1h). Time to discharge from PACU was similar in all groups, median times ranging from 27.40 min to 36.73 min.



S-330.

OPIOID REQUIREMENTS IN CHILDREN UNDERGOING LIVER TRANSPLANTATION

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Introduction: Opioids requirement are reduced in adult patients following liver transplantation.[1] In this study, we reviewed our experience with children undergoing liver transplantation at our institution since April 1998 stimulated by our subjective impression that they required less opioids for postoperative pain control than patients undergoing other major abdominal surgery. The purpose of the study is to examine their requirements for postoperative pain medications.
Methods: The institutional IRB approved the study. We studied patient demographics, fluid/blood product requirement and opioid use during the first 72 postoperative hours. Of 86 pediatric liver transplants performed between April 1998 and September 2003, 39 charts were reviewed. All opioids used were converted to morphine equivalents using the following ratios: 1mg morphine = 10mcg fentanyl = 0.2mg hydromorphone = 1mg oxycodone = 10mg meperidine = 120mg codeine. All data are reported as mean ± standard deviation.
Results: Patient age was between 1 month and 16 years (38 ± 54 months). The most common diagnosis leading to transplant was biliary atresia (74.4%). Estimated blood loss was 45 ± 31.3 cc/kg. Intra-op fluids were 81.6 ± 45.4 cc/kg crystalloid and 42.6 ± 35.4 cc/kg colloid. Intraoperatively, 34/39 and 16/39 patients required transfusion of packed red blood cells (PRBC) and other blood products respectively. Postoperatively, 13/39 patients needed PRBC and 11/39 had other blood products. Patients received 0.37 ± 0.22 mg/kg of morphine equivalent intraoperatively. During the first 72 postoperative hours 0.64 ± 0.44 mg/kg of morphine equivalent was given. All patients received aspirin to avoid vascular thromboses. There was no in-hospital mortality.
Discussion: Following major abdominal surgery, morphine requirement in children is most often greater than 0.015 mg/kg/h.[2] Others have reported adequate post-operative analgesia with 0.01 and 0.04 mg/kg/h of morphine in a variety of surgical procedures.[3] These data would extrapolate to a morphine dose of 0.72 to 2.88 mg/kg over 72 hours which is higher than the 0.64 mg/kg in our patients. This suggests that pediatric liver transplant patients may have a lower analgesic requirement as was reported in adults. Large fluid shifts and transfusions of blood products as evidenced in our patients would lower serum opioid levels and could not explain the lower requirement. In adults, there was no evidence of pharmacokinetics differences between transplant and non-transplant patients. Possible mechanisms for the lower morphine requirement include elevated levels of met-enkephalin, an endogenous opioid; denervation of the liver; and use of high dose corticosteroids. We plan to conduct a prospective study to compare the opioid requirement, opioid pharmacokinetics, and endogenous opioid levels in children undergoing liver transplant and other major abdominal surgery.

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S-331.

RE-EVALUATION OF INTRAOPERATIVE USE OF GLUCOSE SOLUTION IN PEDIATRIC PATIENTS UNDERGOING OUTPATIENT ANESTHESIA

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Introduction: The incidences of perioperative hypoglycemia in pediatric patients remain controversial. Hypoglycemia can occur in pediatric patients fasting for surgery and most of these children remain asymptomatic. The possibility that hypoglycemia may remain undetected during anesthesia has lead many anesthesiologists to routinely use glucose-containing solutions during surgery(1,2). The aim of the present work was to measure the effect of overnight preoperative fasting on blood glucose concentration in children undergoing elective outpatient procedures and to determine the effect of a commonly used concentration of glucose in IV fluids required during surgery.
Methods: Blood glucose concentration was measured in 42 healthy children aged between 2 and 12 years undergoing outpatient surgery and anesthesia. The duration of starvation varied between 6 and 8 hours. The children were randomly assigned to receive either lactated ringer (LR) solution or dextrose 5% in normal saline (D5NS) intraoperatively as maintenance and replacement fluids. Blood samples were taken immediately after induction of anesthesia, but prior to the iv infusion of any fluid, and again at the conclusion of surgery. Blood glucose concentration was assessed by a reflectance meter, SureStepFlex (Lifescan). All patients were unpremedicated. The anesthetic technique consisted of inhalational induction with sevoflurane in nitrous oxide/oxygen followed by initiation of an iv line, endotracheal intubation with or without the use of muscle relaxants and maintenance with sevoflurane in nitrous oxide/oxygen with or without fentanyl analgesia. The volume of fluids infused during surgery was determined on the basis of the child's body weight. For the purpose of this study hypoglycemia was defined as a blood glucose concentration less than 50 mg/dl.
Results: The 2 study groups were comparable for age, sex, weight and duration of anesthesia. None of the patients was noted to be hypoglycemic pre- or postoperatively despite 6-8 hours of starvation. Postoperative blood glucose concentration increased significantly ($p<.0001$) from preoperative levels for both groups of children but the increase in those that received D5NS was significantly greater ($p<.0001$) than those who received LR. In the non-glucose group, mean (+/--SD) blood glucose concentration increased from 91 (+I--15) before surgery to 106 (+/--24) after surgery. The corresponding increase in the D5NS group was from 88 (+I--15) to 238 (+/--66).
Discussion: These data suggest that LR alone is a safe and appropriate fluid for intraoperative fluid therapy in children undergoing outpatient surgery. Intraoperative administration of D5NS invariably results in hyperglycemia. Conclusions drawn from studies made in young inpatients showing hypoglycemia perioperatively may not be applicable to young healthy outpatients.

S-332.

REMIFENTANIL BLOOD LEVELS AND INTUBATING CONDITIONS AFTER INTRANASAL ADMINISTRATION FOLLOWING SEVOFLURANE INDUCTION IN CHILDREN

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Introduction: Intubation without the use of muscle relaxants in children is favored by many anesthesiologists. Attempts at intubation before an adequate depth of anesthesia is achieved can result in coughing or laryngeal spasm. The addition of IV remifentanil (2 mcg/kg) after sevoflurane induction has been shown to allow for rapid tracheal intubation without neuromuscular blocking agents. Nasal administration of remifentanil has been suggested to have similar effect. The remifentanil blood concentrations necessary to obtund the laryngeal response to intubation has not been defined. The goal of this study was to determine the response to intubation, and the blood concentration of remifentanil that is achieved when a fixed dose of remifentanil is administered intranasally following sevoflurane induction in children.
Methods: With IRB approval, 188 children,1-7 yr. of age, were studied. Following an 8% sevoflurane N_2O induction, intranasal remifentanil (4 mcg/kg) or saline was administered. Sevoflurane concentration was then reduced to 5% in oxygen, and ventilation assisted/controlled. A blinded anesthesiologist attempted intubation at 2 or 3 minutes (randomized) and used a validated score to evaluate the conditions for laryngoscopy and response to intubation. Blood samples for determination of remifentanil blood concentrations were collected from 17 children at baseline, 2, 3, 4, and 10 minutes after nasal administration. The blood samples were collected in heparinized syringes, and immediately transferred to a culture tube containing 40 microliter of 50% citric acid to prevent degradation by plasma esterases, and frozen at -80ºC for later analysis by gas chromatography.
Results: Good or excellent intubating conditions were achieved in 68.2% and 91.7% of the children who received intranasal remifentanil at 2 and 3 minutes respectively. This was significantly better than the conditions at three minutes in children who received placebo (23.8%) P=0.006. End-tidal sevoflurane and CO_2 concentrations at the time of intubation were not different among the study groups. All patients had detectable remifentanil blood levels at 2 minutes following intranasal administration. The mean remifentanil plasma concentrations (± SD) at 2, 3, 4, and 10 minutes were 1.0 (0.60), 1.47 (0.52), 1.70 (0.46), and 1.16 (0.36) ng/ml respectively. The observed peak plasma concentration was at 3.47 minutes. The ET_{max} was at 4.76 minutes (95% CI 2.92-9.74). There were no complications associated with the use of intranasal remifentanil.
Discussion: Intranasal administration of the highly lipid-soluble remifentanil results in rapid absorption and similar effects as IV administration. Elimination is fast. This is a useful technique when an anesthesiologist needs to perform tracheal intubation without the use of muscle relaxants in small children who have no accessible veins.
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S-333.

THE USE OF HERBAL REMEDIES AND DIETARY SUPPLEMENTS BY CHILDREN SCHEDULED TO UNDERGO ANESTHESIA: A PRELIMINARY REPORT

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Introduction: Herbal remedies, officially classified by the federal government as dietary supplements, have been gaining popularity in the United States. In 1999, general health interviews indicated that 9.6% to 14% of adults had used some form of herbal remedies/ dietary supplements (HR/DS) in the past year. In a 1998 survey at primary care practices in the Washington DC area, 8% of parents used HR/DS for their child.[1] Some HR/DS may pose a serious health risk if they are taken prior to surgery or anesthesia; yet, surveys of adult presurgical patients have reported a high usage, 22 to 43%. Since there had been no large published surveys of use of HR/DS by children scheduled for anesthesia, we undertook this study.
Methods: A convenience survey was taken of parents or principal caregivers (P/PC) of children admitted from home to undergo anesthesia from September 2002 to May 2004. Survey information included demographics, users of HR/DS in the home, and the child's use of prescribed medications, over the counter medications, large-dose vitamins and HR/DS. Statistical analysis included descriptive summary statistics and the chi-square test for nominal and categorical variables.
Results: Of 501 P/PC approached, 444 completed a survey. Only 11% of P/PC said that anyone involved in the healthcare of their child had ever asked them about the use of HR/DS by their children. Thirty-one per cent of P/PC were using HR/DS for themselves. This significantly correlated with higher levels of education, age (over 40 years) and ethnic background. Thirty-nine children (8.8%) had taken HR/DS in the past; only 9 parents (27%) had discussed this use with a healthcare provider. The most common substance was echinacea, used by 15 children. During the week before scheduled anesthesia, 14 (35% of users) children had taken HR/DS. In addition, 13 children had imbibed herbal teas of an unspecified nature the week before anesthesia. A majority of children (23/39, 59%) were also taking prescribed medications. There was a significant association of a child's use of HR/DS with the use of HR/DS by the parents, the ethnicity of the household (white) and a child's use of large dose vitamins. No association was found with the age of the child.
Discussion: Despite the popularity of HR/DS, healthcare providers still are not asking parents about their child's use of these substances. The majority of parents do not spontaneously share this information. A majority of these children are at risk of a possible prescribed drug and HR/DS interaction. The prevalence of HR/DS in children scheduled for anesthesia is similar to that of children in a primary care setting but less than the published rates for presurgical adult patients.
Reference:
Ambulatory Ped. 2001; 2: 122-125.

S-334.

APOPTOSIS GENE PRODUCTS ARE DETECTABLE IN URINARY EPITHELIAL CELLS FOLLOWING CONGENITAL CARDIAC SURGERY

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Introduction: Apoptosis is a potential mechanism mediating cell death in ischemic renal injury.[1] Apoptosis gene products, which are upregulated following ischemia/reperfusion,[2] are increased in shed urinary epithelial cells in adults with elevated creatinine following major surgery.[3] Bax, BAD, and caspase 8 are pro-apoptotic members of the signaling pathways which terminally activate caspase 3 to induce apoptosis, while Bcl2 is an anti-apoptotic member.[4,5] We obtained urine from children undergoing cardiac surgery to determine whether urinary apoptosis gene products (UAGP) are detectable and explored the relationship between elevated serum creatinine and UAGP abundance.
Methods: The study was approved by the Columbia University IRB. Urine samples were collected after surgery and during the postoperative period. Total RNA was isolated from urine sediments to perform RT-PCR for detection of UAGP (Bax, BAD, caspase 3, caspase 8, and Bcl2) with G3DPH as the housekeeping gene. Data was analyzed by one way ANOVA or unpaired t test, and $p<0.05$ was deemed significant.
Results: We collected 45 urine samples from 23 patients. UAGP were detected in 19 patients. Data from the 10 children (ages 1 week-24 months, median=4 months) who had intraoperative and postoperative samples available are presented. 6/10 patients underwent circulatory arrest. Serum creatinine was normal in all patients both preoperatively and postoperatively. The most abundantly detected UAGP was caspase 3 (0.79 ± 0.28 arbitrary units, $p<0.05$ compared to all other gene products). Circulatory arrest did not influence the relative abundance of UAGP. UAGP were most abundant during the intraoperative period, though there was no significant difference between intraoperative and postoperative UAGP in the 10 patients studied. In those patients who had multiple postoperative samples, there was no change in the relative abundance of UAGP during the first three postoperative days.
Discussion: UAGP were detectable throughout the perioperative period in children undergoing cardiac surgery. None of our patients had abnormal serum creatinine. Therefore, the utility and the optimal timing for the detection of UAGP as early markers of renal dysfunction remain to be determined. Renal failure is one of the major morbidities following cardiac surgery, and the immature kidney may especially be at risk.[6] Early detection of renal failure allows greater opportunity to institute therapeutic measures. As caspase3 was the most abundant UAGP and is the most downstream in the pathways leading to apoptosis, future studies will examine its role as a noninvasive marker to assess perioperative renal function in the pediatric cardiac surgical patient.
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6. Ann Thorac Surg 76, 1443-1449 (2003).

S-335.

THE EFFECT OF REMIFENTANIL OR FENTANYL IN PEDIATRIC DENTAL SURGERY PATIENTS

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Introduction: Opioids provide analgesia and are a significant cause of postoperative nausea and vomiting (PONV). Pediatric patients are at a higher risk for PONV than adults, particularly among school-age children (1,2). Nausea is a subjective finding that is difficult to evaluate in the pediatric population, and therefore will not be assessed. This prospective study compares the incidence of vomiting, a recovery profile, and parent satisfaction for pediatric patients receiving fentanyl or remifentanil, undergoing dental restoration and extractions under general anesthesia.
Methods: With IRB approval and parental consent, children (2-12 yrs; ASA 1-2) who required general anesthesia for dental restoration and extractions were randomly assigned to receive remifentanil (R) 1 mcg/kg IV (over 90 seconds) prior to tracheal intubation, followed by a continuous infusion of 0.2 mcg/kg/min or fentanyl (F) 2 mcg/kg IV prior to tracheal intubation, followed by 1 mcg/kg every 45 minutes during the course of the operation. In both groups, rectal acetaminophen 30 mg/kg was administered, and anesthesia was maintained with sevoflurane at an end-tidal concentration of 1-4% in nitrous oxide/oxygen. The episodes of POV, administration of pain or rescue antiemetic medications, recovery profile, and parent satisfaction scale score were recorded. The parameters assessed within the recovery profile included: 1) the level of consciousness on arrival to the postanesthesia care unit (PACU); 2) an objective pain scale score; 3) adverse events; 4) time to discharge. Comparisons were made using chi-square and two tailed tests. $P < 0.05$ was considered significant.
Results: Data collection is currently in progress and to date, 19 children (11 R; 8 F) have been studied. There were no significant differences in episodes of POV, administration of pain or rescue antiemetic medications between groups. Time to discharge was significantly less in the R group as compared to the F group. Parent satisfaction was not different between groups.
Discussion: The preliminary results of this ongoing study suggest that the use of remifentanil does not appear to decrease the incidence of vomiting when compared to fentanyl. However, there is a trend toward remifentanil decreasing the time to discharge in patients undergoing dental surgery.
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1. Anesth Analg 70:160-167,1990
2. Anesthesiology Clin N Am 20:471-484,2002

Pharmacology - Basic Science

S-336.

INCREASED β_1-ADRENERGIC RECEPTOR DENSITY MAINTAINS LEFT VENTRICULAR EJECTION FRACTION IN AN OVINE MODEL OF CHRONIC HEART FAILURE

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Introduction: β_1-adrenergic receptors (β_1AR) decrease in chronic heart failure (CHF), however, the β_1AR changes that occur during the evolution of CHF are not fully elucidated. We hypothesize that β_1AR density correlates with left ventricular (LV) ejection fraction (EF) during the course of CHF in a sheep model.
Methods: CHF (EF <35% for 2 consecutive weeks) was induced in 12 sheep via microembolization of the circumflex coronary artery.[1] EF, LV end-systolic area, and LV end-diastolic area (LVESA and LVEDA, normalized to body weight) were measured via transthoracic echocardiography to document the progression of CHF for 4 (n=7 sheep) or 12 (n=5 sheep) months. Myocardium was formalin fixed and immunostained with a β_1AR antibody. Myocardium obtained from healthy sheep (n=9) served as controls. From each heart, 12 images of each wall (LV anterior, LV posterior, anterior septum, and right ventricular (RV) free wall) were captured from immunostained sections using a standard upright microscope and camera. Microscopic images were quantified for β_1AR density. Data is presented as the mean ± SEM.
Results: EF measured 50±3% at baseline and decreased to 23±2%* at month-4 and remained unchanged through month-12 (25±2%*) (*p<0.05 compared to baseline). In contrast, LVESA and LVEDA did not stabilize, but progressively increased ~50% from month-4 to month-12*. In the CHF sheep, β_1AR density did not change significantly at month-4, whereas there were marked increases in β_1AR at month-12 in the LV anterior, posterior, and anterior-septal walls compared to controls. In contrast, β_1AR density decreased significantly in the RV free wall of CHF sheep at month-12* as compared to both control and CHF month-4 groups.
Discussion: Unexpectedly, β_1AR density did not correlate with EF in microinfarction-induced CHF. Despite reduced contractility and increased LV dilation, LV β_1AR density remained relatively unchanged at month-4 and increased significantly by month-12 in the CHF sheep. This may represent a compensatory response to the progressive LV dilation for maintaining EF. In contrast, β_1AR changes in the RV did not correlate with those in the LV.
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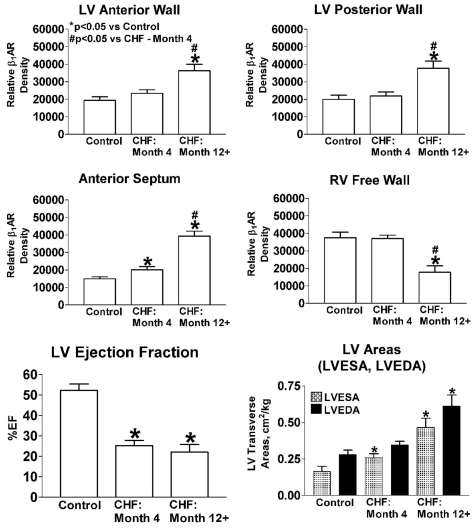

S-337.

MA HUANG AND THE ALPHA (1) SUBTYPE ADRENOCEPTOR IN THE FELINE PULMONARY VASCULAR BED

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Introduction: The purpose of this experiment was to identify the alpha (1)-adrenoceptor subtype(s) utilized by Ma Huang and the role of Ma Huang in the feline pulmonary vascular bed.
Methods: In separate experiments, the effects of phentolamine, the alpha-adrenergic antagonist, prazosin, a selective alpha (1)-adrenoceptor antagonist, BMY 7378, a selective alpha (1)D-subtype adrenoceptor antagonist, 5-methyl-urapidil, the selective alpha (1)A-subtype adrenoceptor antagonist, and chloroethylclonidine, an alpha (1)B-subtype and (1)D-subtype adrenoceptor antagonist, were investigated on pulmonary arterial responses to Ma Huang and other agonist agents in the pulmonary vascular bed of the cat. Lobar arterial perfusion pressure and systemic pressure were continuously monitored, electronically averaged, and permanently recorded.
Results: In the feline vascular bed of the isolated left lower lobe, Ma Huang induced a dose-dependent vasopressor response that was not significantly attenuated following administration of 5-methyl-urapidil. However, the responses to Ma Huang were significantly reduced after administration of phentolamine, prazosin, BMY 7378, and chloroethylclonidine.
Discussion: The results of the present investigation suggest that Ma Huang has potent vasopressor activity in the feline pulmonary vascular bed and that this response may be mediated or modulated by both alpha (1)B-subtype and (1)D-subtype adrenoceptor sensitive pathways.

S-338.

NOREPINEPHRINE AND ALPHA-SUBTYPE RECEPTORS IN THE CAT LUNG

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Introduction: The purpose of this experiment was to identify the role of norepinephrine in the pulmonary vascular bed of the cat and what adrenoceptor subtype(s) is/are utilized by norepinephrine.
Methods: The effects of BMY 7378, the selective alpha (1)D-subtype adrenoceptor antagonist, 5-methyl-urapidil, a selective alpha (1)A-subtype adrenoceptor antagonist, and chloroethylclonidine, an alpha (1)B-subtype and (1)D-subtype adrenoceptor antagonist, were studied on pulmonary arterial responses to norepinephrine and other agonist agents in the pulmonary vascular bed of the cat. The systemic pressure and lobar arterial perfusion pressure were continuously monitored, electronically averaged, and permanently recorded.
Results: Using adult mongrel cats and the pulmonary vascular bed of the isolated left lower lobe, norepinephrine induced a dose-dependent vasoconstrictor response that was not significantly altered after administration of BMY 7378. However, the responses to norepinephrine were significantly attenuated following administration of 5-methyl-urapidil and chloroethylclonidine.
Discussion: The data suggest that norepinephrine has significant vasopressor activity in the feline pulmonary vascular bed and that this response may be mediated or modulated by both alpha (1)A-subtype and (1)B-subtype adrenoceptor sensitive pathways.

S-339.

THE ROLE OF EPHEDRINE IN THE FELINE PULMONARY VASCULAR BED

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Introduction: The purpose of this experiment was to identify the role of ephedrine in the feline pulmonary vascular bed and what adrenoceptor subtype(s) is/are utilized by ephedrine.
Methods: In a university research laboratory and in separate experiments, the effects of phentolamine, the alpha-adrenergic antagonist, prazosin, an alpha (1)-adrenoceptor antagonist, 5-methyl-urapidil, the selective alpha (1)A-subtype adrenoceptor antagonist, chloroethylclonidine, an alpha (1)B-subtype and (1)D-subtype adrenoceptor antagonist, and BMY 7378, a selective alpha (1)D-subtype adrenoceptor antagonist, were analyzed in an attempt to identify any significant effect on pulmonary arterial responses to ephedrine and other agonist agents in the pulmonary vascular bed of the cat. Under constant flow conditions, lobar arterial perfusion pressure and systemic pressure were continuously monitored, electronically averaged, and permanently recorded.
Results: In the isolated left lower lobe of the pulmonary feline vascular bed, ephedrine induced a dose-dependent vasoconstrictor response that was not significantly altered following administration of 5-methyl-urapidil. The vasopressor activity as a result of ephedrine was significantly decreased after administration of phentolamine, prazosin, chloroethylclonidine, and BMY 7378. Further, when the alpha (1)B-subtype and (1)D-subtype adrenoceptor antagonist chloroethylclonidine was given, there was almost complete elimination of the ephedrine-induced vasoconstrictor response.
Discussion: The results of this study suggest that ephedrine causes a dose-dependent vasopressor response in the feline pulmonary vascular bed and that this activity may be mediated or modulated by both alpha (1)B-subtype and (1)D-subtype adrenoceptor sensitive pathways.

S-340.

REGIONAL G PROTEIN ALTERATIONS IN AN OVINE MODEL OF CHRONIC HEART FAILURE

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Introduction: The guanine-nucleotide binding proteins (G proteins) $G_s\alpha$ and $G\alpha_{i\text{-}2}$ regulate cardiac inotropy via receptor-mediated stimulation and inhibition of adenylyl cyclase, respectively. $G\alpha_{i\text{-}2}$ is significantly increased in chronic heart failure (CHF)[1] and may mediate β-adrenergic receptor (βAR) desensitization.[2] The role of the $G_s\alpha$ splice variants in CHF has not been elucidated. We examine the effects of coronary microembolization-induced CHF on cardiac $G_s\alpha$ and $G\alpha_{i\text{-}2}$ protein levels in sheep to determine if alterations comparable to those in humans occur.
Methods: CHF was induced via microembolization of the circumflex coronary artery.[3] Myocardial tissue from the left ventricular (LV) anterior, LV posterior, and right ventricular (RV) free wall was obtained from four CHF sheep (LV ejection fraction <35% for ~20 months) and four healthy control sheep. SDS-PAGE and Western blots were performed with antisera specific for $G_s\alpha$ or $G\alpha_{i\text{-}2}$, with visualization by enhanced chemiluminescence. Autoradiograph band intensity was quantified using densitometry. Data is presented as the mean ± SEM.
Results: The $G_s\alpha$ 45-kDa splice variant ($G_s\alpha_s$) increased 5.7-fold* in the RV free wall but varied in the LV anterior and posterior wall of the CHF sheep compared to controls (*p<0.05). While the $G_s\alpha$ 52-kDa splice variant ($G_s\alpha_l$) increased only slightly in all walls of the CHF sheep, $G\alpha_{i\text{-}2}$ was significantly increased by 3.7-*, 6.4-*, and 1.9-fold in the LV anterior, LV posterior, and RV free wall of the CHF sheep, respectively, compared to controls.
Discussion: In agreement with clinical findings of humans in CHF, our sheep model of CHF exhibited increased $G\alpha_{i\text{-}2}$ levels in all walls of the heart. Diminished adenylyl cyclase activity secondary to increased inhibition by $G\alpha_{i\text{-}2}$ may play a role in the pathophysiological processes of βAR desensitization in CHF. In contrast, $G_s\alpha_s$ and $G_s\alpha_l$ varied by myocardial region. $G_s\alpha_s$ may couple more efficiently to adenylyl cyclase.[4] Thus, the regional decrease in $G_s\alpha_s$ may correlate with LV contractile dysfunction.[3] We speculate that the $G_s\alpha_s$ increase in the RV is a compensatory change associated with RV hypertrophy.

References:
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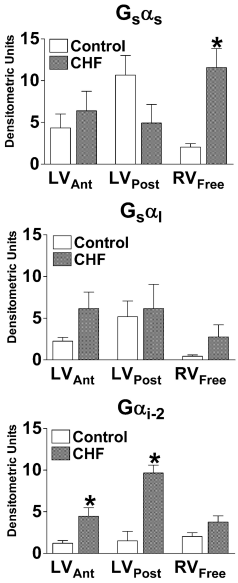

S-341.

EFFECT OF COX-2 INHIBITION ON PERIOPERATIVE CENTRAL AND PERIPHERAL PROSTAGLANDIN E2 IN THE RAT

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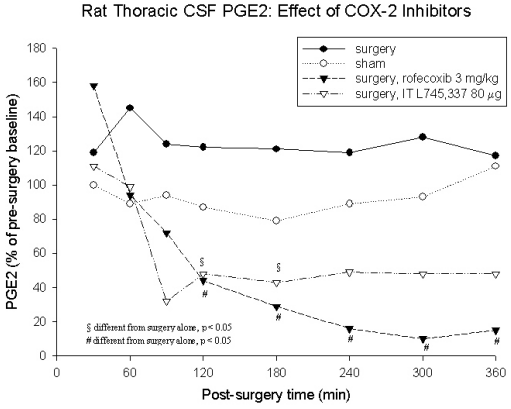
Introduction: Surgical trauma induces local cyclooxygenase-2 (COX-2) upregulation and prostaglandins that sensitize peripheral nociceptors (Anesth Analg 1993;77:362). However, central COX-2 upregulation may also be important, since foot incision in the rat leads to transient increase in spinal COX-2 (Anesthesiology 2004;100:364).The present study examines prostaglandin E2 (PGE2) upregulation in CSF and thoracic tissue over the time course of thoracic muscle incision analogous to surgical exposure for thoracotomy. In addition, the role of systemic and intrathecal COX-2 inhibitor administration in suppressing PGE2 upregulation is examined.
Methods: With animal care committee approval, 300-350 g male Sprague-Dawley rats (n=5/group) were anesthetized with 1.5% isoflurane and microdialysis loop catheters (J Neurosci Meth 1995;62:43) implanted both in the thoracic CSF space (via the cisterna magna) and in the left thoracic subcutaneous space. Following 7 days recovery, baseline microdialysis fluid was collected at 30 min intervals using Ringer's solution infused at 2.5 µL/min via each catheter. Animals were then anesthetized with isoflurane and an incision made in the superficial and deep left thoracic muscles (excluding intercostals) overlying the 3rd to 7th ribs. Microdialysis fluid collection continued during surgery and for 6 hours after the start of surgery in awake animals. Implanted sham unoperated animals were also anesthetized for a similar 30 min time period. In some animals a COX-2 inhibitor was given orally (rofecoxib 3 mg/kg) or intrathecally (L-745,337 80 µg) at start of surgery. Dialysate samples were frozen immediately after collection, and PGE2 assayed by ELISA. PGE2 values over time were compared between drug groups using repeated measures ANOVA.
Results: CSF PGE2 increased in the postsurgical period compared to sham unoperated animals (p=0.042) over the 6 hour collection interval (Figure). Intrathecal L-745,337 reduced CSF PGE2 (p=0.006), as did oral rofecoxib (p=0.001). Tissue PGE2 increased greatly in the postsurgical period (peak increase: 30-fold at 3 h) and that was reduced 70% by oral rofecoxib, but not by intrathecal L-745,337.
Discussion: Surgical incision produces a large increase in local tissue PGE2 and also an increase in CSF PGE2. Systemic COX-2 inhibitor administration decreases both CSF and tissue PGE2, and intrathecal COX-2 inhibitor decreases CSF PGE2. The results indicate that surgery produces both peripheral as well as central inflammatory changes that can be modulated differentially according to the route of administration of COX-2 inhibitor.



S-342.

MEMBRANE EFFECTS OF LANDIOLOL COMPARED WITH THOSE OF ESMOLOL AND PROPRANOLOL

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Introduction: In addition to the interaction with adrenoceptor proteins, classical beta-blockers have been known to interact with lipid bilayers to induce membrane stabilization (1). We studied the membrane effects of landiolol, a new short-acting selective $beta_1$-blocker (2), comparatively with those of selective $beta_1$-blocker esmolol and nonselective beta-blocker propranolol to address one of possible pharmacological mechanisms.
Methods: Each drug was reacted with different liposomal model membranes such as 100 mol% phospholipid (DPPC) liposomes, membrane raft-like liposomes composed of phospholipids (POPC, POPE and sphingomyelin), cerebroside and cholesterol, etc. The changes in membrane physicochemical property were analyzed by measuring fluorescence polarization with DPH, 2-AS, 6-AS, 9-AS and 12-AS which indicate the fluidity of specific regions in membrane lipid bilayers. The relative degree of hydrophobic interaction of beta-blockers was estimated using the capacity factors determined by reversed-phase HPLC (3).
Results: When treating DPPC liposomes with beta-blockers (1 mM for each), landiolol rigidified hydrophobic membrane regions (DPH polarization increased by 6.5 ± 0.3 %, $p < 0.01$) but not esmolol (0.1 ± 0.3 %), whereas propranolol fluidized (decreased by 20.7 ± 0.1 %, $p < 0.01$). Relative AS polarization changes showed that landiolol and esmolol preferentially interacted with membrane core and surface, respectively. All of the drugs much less modified the fluidity of raft-like membranes. In HPLC analysis, esmolol, landiolol and propranolol were retained on ODS solid phase in increasing order of intensity (capacity factor: 1.653 ± 0.024, 1.936 ± 0.032 and 4.775 ± 0.041).
Discussion: While landiolol has been speculated not to possess the membrane activity due to water solubility, it appears to interact with membrane lipids and modify the fluidity unlike hydrophilic esmolol. Different membrane activity between landiolol and propranolol correlates with their different hydrophobic interaction intensity evaluated by HPLC. It is interest to relate the characteristics of landiolol as a membrane-rigidifier and propranolol as a membrane-fluidizer with selectivity and nonselectivity of their beta-blocking properties. Cholesterol and glycosphingolipid forming microdomains in cell membranes have been proposed to function as the rafts for the attachment of functional proteins including G proteins like beta-receptors (4). However, the results on raft-like membranes may suggest that the indirect effect through membrane environmental alteration is less responsible for the mode of beta-blocking action of landiolol. This is the first to report the potent membrane activity of landiolol.
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S-343.

EFFECT OF LANDIOLOL, A NEW ULTRA SHORT-ACTING BETA-BLOCKER, ON MINIMUM ALVEOLAR CONCENTRATION (MAC) IN DOGS

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[Introduction] Landiolol is a short-acting β1blocker that can be used to treat and prevent carsiovascular responses in the perioperative period. It is more potent and has higher cardioselectively than esmolol. Several reports suggest that β-blockers may effect the central nervous system. The effect of β-adrenergic blocker on anesthetic requirement (MAC and BIS) has been investigated. Propranol has no effect on MAC(1), but esmolol may reduce MAC(2). Therefore we investigated whether landiolol given low and high dose could modify the MAC of sevoflurane.
[Method] Four healthy, unpremedicated male beagle dogs (body weight 11.9±1.3kg) were studied. Anesthesia was induced and maintained with sevoflurane in oxygen. MAC was determined by tail clump. All measurements were made after at least 15 minutes of a constant end-tidal sevoflurane concentration. After the induction with sevoflulane, control MAC was determined. Low dose landiolol was determined after continuous intravenous administration of landiolol 30μg/kg/min for 20 miute. Likewise high dose landiolol MAC was determined after administration of landiolol 300μg/kg/min (10 times higher than low dose). After the determination of each MAC, we collected of blood and CSF. Paired analysis with student`s t-t test was used for satatistical analysis and p-value of less than 0.05 was considered as significant.
[Result] No significant changes in MAC were seen in both low and high group (Fig.1). Sevoflurane control MAC was 1.9±0.42, landiolol administration (30μg/kg/min and 300μg/kg/min) were 2.3±0.56 and 2.0±0.34 respectively. CSF concentration of landiolol was approximately 20% of that in blood and depend on blood concentration.
[Discussion] Some study indicats that β-blockers effect on central nerve system (1.3.4). Tanifuji and Eger (1) found no effect of acute and chronic propranolol administration on halothane MAC in dog. They suggested, because propranolol readily crosses the blood-brain barrier, neither acute inhibition of central β-adrenergic receptor nor chronic receptor blockade potential changes in central catecholamine levels influenced volatile anesthetic MAC. Recently there is reported that only in esmolol did not have influence to isofulurane MAC, but decrease isoflurane MAC by administration of alfentanil in human(2). Our results indicate that sevoflurane MAC was not influenced by landiolol administration, and landiolol could pass a blood-brain barrier. It also suggests that landiolol dose not effect the central nervous system.
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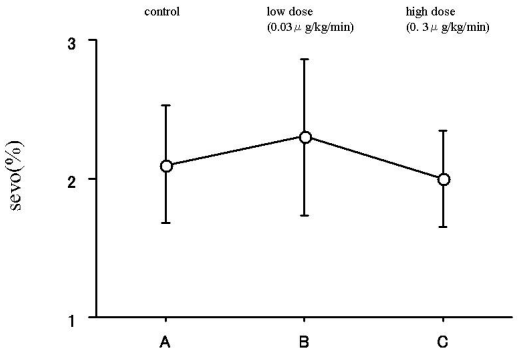

S-344.

MOLECULAR CONFORMATION FOR NICOTINIC CHOLINERGIC ACTION

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Introduction: In each edition of the textbook, *Anesthesia* (Ed. Miller), a rule of 5.9 Angstroms (A) for nicotinic action was cited in its Autonomic Pharmacology chapter. The rule ("the Rule") states that a distance of 5.9 A from the center of a quaternary N atom to the van der Waals extension of an H bond acceptor (HBA) in the vicinity (N-HBAvdw distance) is a conformational feature that imparts nicotinic action. The Rule has been traced to a 1970 publication (based on hand-held Dreiding and CPK models),[1] and validated in the D-ring acetylcholine (Ach) pharmacophoric moiety of vecuronium.[2] Considering the importance of nicotinic drugs, the author reexamined the molecular shape of the compounds cited in the original 1970 publication.[1] Epibatidine, the modern prototype of nicotinic drug researches, was included for comparison.[3,4]
Methods: The molecules were constructed with a molecular modeling software package (Sybyl 9.2, Tripos, St. Louis), run on an SGI Octane workstation. As only low energy conformers may meaningfully represent a molecule, the molecules were subjected to extensive computerized searches for low energy conformers, using the "simulated annealing" and "random search" methods. The search products were energy minimized (MMFF94s), and their N-HBAvdw distances computed.
Results: Nicotine, Cytisine and Anagyrine conformed to the Rule completely, as their lowest energy conformers had an N-HBAvdw distance of exactly 5.8-5.9 A. Epibatidine, Toxifereine 1, Benzoquinonium, and Beta-erythroidine conformed to an N-HBAvdw distance of 5.8-6.0 A with ease, requiring only a small energy penalty of 1.6-2.9 kcal/mol. The lowest energy conformer of Ach did not conform; but 3 other low energy conformers (within 2 kcal/mol) did. Trimethaphan, Strychnine, Lobeline, Muscarone, and d-Tubocurarine did not conform without large (greater than 5 kcal/mol) energy penalty.
Discussion: Ach readily binds to various muscarinic and nicotinic receptors, presumably with several low energy conformations. The energy difference among these conformers is therefore physiologically insignificant barrier. While Nicotine, Cytisine and Anagyrine conform to the Rule with their lowest energy conformers (no barrier), Epibatidine, Toxifereine 1, Benzoquinonium, and Beta-erythroidine did so with insignificant barrier. Other compounds did not conform, because their mechanism of action was misunderstood when the Rule was deduced.[1] For example, Strychnine has a glycine-related mechanism of action irrelevant to the Rule and should not have been included then. In conclusion, nicotinic compounds that bind with an Ach-like moiety conform to Beers & Reich's rule of 5.9 A, while, in cross-validation, compounds that act by different mechanisms of action do not. The Rule may aid screening and development of new nicotinic therapeutics, including analgesics.[4]
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S-345.

A NOVEL METHOD OF MEASURING EXTRACELLULAR GABA LEVELS IN RAT STRATIUM

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INTRODUCTION: Propofol's anesthetic action is hypothesized to act via a GABAergic (γ-aminobutyric acid) pathway. Propofol's behavioral effects (i.e. loss of righting reflex) are altered by GABAA receptor agonists and antagonists (1, 2). We developed a method using high performance liquid chromatography (HPLC) to measure extracellular GABA collected using in-vivo microdialysis. This method was based on two previous methods of determining GABA (3, 4). This technique was evaluated using both in vitro and in vivo measurements. Eventually this technique will allow us to probe putative sites of anesthetic action for changes in extracellular GABA (i.e. during intravenous propofol infusion).
METHODS: In vivo microdialysis samples were collected in adult male Sprague Dawley rats (300-500 gm). While the rats were anesthetized with ketamine and xylazine, a microdialysis probe (CMA / 11-4 mm cutoff 6000 Daltons) was inserted into the right stratium (placement confirmed with brain slices post experiment). The rats recovered for at least 24 hours. Samples were collected in a single rat for four days after the initial surgery. Artificial cerebral spinal fluid (aCSF) was perfused through the microdialysis probe at a rate of 1.5 µl / min. After perfusing for 1 hour to equilibrate the system, four 15 min dialysate samples were collected to establish an extracellular GABA baseline. The aCSF was altered to contain 80 mM KCl or 0.5mM Nipecotic acid (GABA reuptake blocker). After the perturbation, samples were collected to measure GABA recovery. HPLC was performed on the dialysates using a C18 reverse phase column and OPA-sulfite derivation with electrochemical detection. The samples were derivatized at 4 degrees. The percent increase in extracellular GABA was calculated.
RESULTS: Our method of using HPLC to determine extracellular GABA was evaluated using GABase (a collection of two enzymes that convert GABA into succinate). GABase was able to eliminate the GABA signal in both GABA standards and our microdialysis samples (N=3). We also tested two compounds that should increase extracellular GABA in vivo, depolarization (80 mM KCl) and nipecotic acid. Both increased extracellular GABA levels as expected (% increase 13000 (N=12) for depolarization and 1400 (N=16) for nipecotic acid).
DISCUSSION: We developed a new method of determining extracellular GABA using reverse phase HPLC that will allow derivatization to occur at low temperatures. This method was evaluated using both in vitro (GABase) and in vivo (depolarization and nipecotic acid) techniques. The evaluation confirmed that this technique is both robust and stable. This method will enable us in the future to probe different areas of the rat brain to determine the effects of intravenous propofol on extracellular GABA.
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S-346.

IN PRIMARY CULTURED RABBIT MTAL CELLS NH4+-REABSORPTION OCCURS MAINLY THROUGH A ROMK-TYPE CHANNEL

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Introduction: Acute Renal Failure (ARF) is a frequent post-operative complication. Although the cellular pathophysiology of ARF remains ill defined, NH_4^+ has been proposed as a mediator of cellular injury[1]. Since the medullary thick ascending limb (MTAL) plays a crucial role both in NH_4^+-reabsorption by the kidney and in the pathophysiology of ARF, the purpose of this study was to identify apical membrane transporters responsible for NH_4^+-reabsorption in a new model of MTAL cells[2].
Methods: Intracellular pH was used as an indirect measure of NH_4^+/NH_3 transport into these cells and was measured fluorimetrically using BCECF. For studying the NH_4^+-transport pathways in physiologically relevant conditions, experiments were performed in the symmetrical presence of NH_4Cl (4 mM), which acidified the cells to pH_i 6.89. When in this condition blockers of apical NH_4^+-transport were added to the apical superfusion solution, pH_i increased due to a decreased acid (NH_4^+)-loading.
Results: With various drugs acting at different sites the following values (expressed as pH units ± SEM) were observed: bumetanide (0.1 mM) + 0.05±0.01; verapamil (0.1 mM) + 0.04±0.03; Ba^{2+} (2 mM) and Cs^+ (20 mM) + 0.19±0.03; Tertiapin (1 µM) 0.09 ± 0.01; TEA^+ (10 mM) and charybdotoxin (0.1 µM) had no effect on pH_i. These results indicated that the bumetanide-sensitive $Na^+/K^+(NH_4^+)/2Cl^-$-cotransporter mediated only a small part of apical NH_4^+-entry, whereas blocking the apical K^+-channel seemed to block most of NH_4^+-entry. To exclude the involvement of nonspecific cation channels, classical "ammonium-pulse" experiments were performed: exposure of the apical cell membrane to NH_4Cl acidified the cells in controls as well as in the presence of 20 mM K^+. In contrast, when Ba^{2+} , Cs^+ or Tertiapin were present at the luminal side of the epithelium, exposure to NH_4Cl alkalinized the cells. These results indicated that NH_4^+ must have permeated an apical K^+-conductance, rather than an nonspecific cation channel. The pharmacological profile of this apical K^+-conductance pointed towards the involvement of the cloned, tertiapin-sensitive, ROMK-channel. With indirect immunofluorescence the ROMK-protein could be detected in these MTAL cells.
Discussion: These results suggest that the Ba^{2+}-sensitive component of NH_4^+-reabsorption is predominant over $Na^+/K^+(NH_4^+)/2Cl^-$-mediated reabsorption in MTAL cells and that this Ba^{2+}-sensitive component could consist of the permeation of NH_4^+ through the ROMK-channel. These findings are in agreement with the observations in one of the first publications on this subject[3]. However, they are in contrast to the currently accepted concept that NH_4^+-reabsorption occurs mainly via the $Na^+/K^+(NH_4^+)/2Cl^-$-cotransporter and that the Ba^{2+}-sensitive component consists of a K^+/NH_4^+-antiporter[4].
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S-347.

THE ROLE OF GABA RECEPTORS IN THE CAT LUNG BED

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Introduction: The purpose of this study was to identify the role of GABAA and GABAB receptors in the feline pulmonary vascular bed.
Methods: Using adult mongrel cats as the model and in separate experiments, the effects of L-N5-(1-Iminoethyl) ornithine hydrochloride (L-NIO) (nitric oxide synthase inhibitor), glibenclamide (ATP-sensitive K+ channel blocker), meclofenamate (non-selective cyclo-oxygenase (COX) inhibitor), bicuculline (GABAA receptor antagonist), and saclofen (GABAB receptor antagonist), were investigated on pulmonary arterial responses to pinacidil (ATP-sensitive K+ channel activator), bradykinin (nitric oxide synthase inducer), muscimol (GABAA receptor agonist), and SKF-97541 (GABAB receptor agonist).
Results: Under elevated tone conditions in the isolated left lower lobe vascular bed of the cat, muscimol induced a dose-dependent vasodepressor response that was not significantly altered after administration of L-NIO, glibenclamide, meclofenamate, and saclofen. SKF-97541-induced vasodepression was not significantly attenuated following administration of L-NIO, meclofenamate, and bicuculline. Responses to SKF-97541 were significantly attenuated following administration of glibenclamide and saclofen. Responses to muscimol were significantly reduced after administration of bicuculline.
Discussion: The results of this experiment suggest that muscimol and SKF-97541 have potent vasodepressor activity in the feline pulmonary vascular bed and these responses are modulated by respectively GABAA and GABAB receptor sensitive pathways. Further, SKF-97541-induced vasodepression is mediated or modulated by an ATP-sensitive K+ channel.

S-348.

STABLE PLASMA PROPOFOL CONCENTRATION IN THE PORCINE MODEL UNDER THE LONG-TERM COMPLETELY ANHEPATIC CONDITION

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Introduction: Despite the liver has been recognized as a principle organ that catalyzes and eliminates propofol (1), extrahepatic metabolism has been known to contribute to propofol elimination during the anhepatic phase (2,3). To clarify the effects of the completely anhepatic state on hemodynamics, pulmonary gas exchange and clearance of propofol, we established a completely anhepatic porcine model without any blood loss. Herein, using this model, we investigated the changes of circulatory parameters, blood gas analysis and propofol concentration with constant infusion for three hours.
Methods: The principles for care and treatment of experimental animals complied with the national guidelines of the Japanese Ministry of Education, Culture, Sports, Science and Technology (Tokyo, Japan). Piglets, weighing 27-32 kg, were sedated, then we induced anesthesia with oxygen and sevoflurane, using a specially designed mask for long-nosed animals. A few minutes later, the trachea was intubated. Then pancuronium was administered intravenously and the lungs were mechanically ventilated. Anesthesia was maintained with inhaled oxygen with 2.0% sevoflurane and intravenous infusion of propofol of 6 $mg/kg^{-1}/hr^{-1}$. After the carotid, brachial or femoral artery was cannulated for measuring a direct arterial blood pressure and for collecting arterial blood samples, we make a completely anhepatic porcine model by a tourniquet method. All data and samples were measured and collected at time points of non-anhepatic control (C_1), immediate before the initiation of completely anhepatic state (C_2), and 30 (T_{30}), 60 (T_{60}), 90 (T_{90}), 120 (T_{120}), 180 (T_{180}) minutes after the initiation of the completely anhepatic state.
Results: All piglets survived through the three-hour completely anhepatic period without any significant hemodynamic alterations except heart rate. Heart rates in C_2, T_{30}, T_{60}, T_{90}, T_{120}, T_{180} were significantly higher than that in C1 ($p<0.0001$ at all points). Arterial pH, carbon dioxide partial pressure, oxygen partial pressure in blood gas analysis and hemoglobin concentration showed no significant changes. Propofol concentration in mixed venous, arterial and portal venous blood did not show any significant changes through the protocol. In the intergroup comparison, the propofol concentration in portal venous blood was significantly lower than that in mixed venous blood ($P=0.0171$). However, there was no significant difference between the mixed venous blood and arterial blood or between the arterial blood and portal venous blood.
Discussion: In the present study, we showed that constant infusion of propofol anesthesia was stable and safe for the three hours during which the animals were in the anhepatic state in a completely anhepatic porcine model without blood loss. Our findings also suggested that extrahepatic metabolism of propofol during the anhepatic phase might help prevent increases in the blood concentration of propofol.
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S-349.

PROPOFOL ATTENUATES OVALBUMIN-INDUCED SMOOTH MUSCLE CONTRACTION OF SENSITIZED RAT TRACHEA

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Introduction: Althouh propofol has a therapeutic effect on the patients with asthma1), the mechanism involved has not been fully understood. Since ovalbumin (OA) provokes bronchoconstriction by releasing serotonin (5-HT) and acetylcholine (Ach)2), we examined the effects of propofol on OA-induced smooth muscle contraction of rat trachea.
Methods: Male Wistar rats (160-180 g) were used for the experiments. The rats were sensitized by a single intraperitoneal injection of ovalbumin (10 mg) mixed with aluminum hydroxide (10 mg) as adjuvant. Fourteen days later, contractile responses were performed using rat tracheal rings. The effects of propofol on OA-, Ach-, 5-HT- and electrical field stimulation (EFS)-induced contractions were observed.
Results: OA induced contraction in sensitized rat trachea, but not in non-sensitized rat trachea. There were not singnificant differences in Ach-, 5-HT- or EFS-induced contraction between sensitized and non-sensitized trachea. 5-HT potentiated EFS-induced contraction similarly in either sensitized or non-sensitized trachea. Propofol significantly attenuated OA-induced contraction in a dose-dependent manner (IC50 36 ± 11 mM) in sensitized rat trachea. Propofol also attenuated Ach-induced contraction (IC50 78 ± 13 mM), and abolished both 5-HT-induced contraction (IC50 30 ± 8 mM), and the enhancement by 5-HT on EFS-induced contraction in sensitized rat trachea.
Discussion: These results suggest that propofol attenuates OA-induced contraction of sensitized rat trachea mainly by inhibiting the actions of 5-HT.
Conclusion: Propofol attenuates OA-induced smooth muscle contraction of OA-sensitized rat trachea. Propofol is a useful anesthetic agent in patients with airway hypersensitivity.

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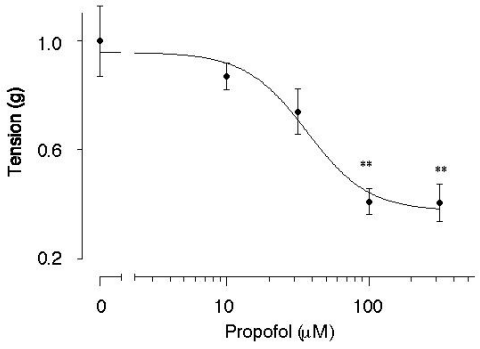

Effects of propofol on OA-induced smooth muscle contraction of sensitized rat trachea
n = 5 - 6, mean ± SEM **P < 0.01 vs propofol 0

S-350.

CHANGES IN CONCENTRATIONS OF FREE PROPOFOL BY MODIFYING THE SOLUTIONS TO REDUCE THE PAIN ON INJECTION

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Introduction: A clinical disadvantage of propofol in a long-chain triglyceride (LCT) emulsion is pain on injection. Propofol in a medium- and long-chain triglycerides (MCT/LCT) emulsion can provide better patient acceptance by reducing the pain. One easy and widely used technique to reduce the pain is to mix lidocaine with propofol before injection. Other techniques are to warm propofol products to body temperature or, conversely, cool them to 4 degrees centigrade and to reduce the pH of the propofol injectate. Since free propofol is thought to cause pain at the site of injection, we determined the concentrations of free propofol in aqueous phases of propofol LCT and propofol MCT/LCT after changing pH or temperature and after mixing with lidocaine.
Methods: In the first series of experiments, 2% lidocaine was added to and mixed with each propofol product (10:1, vol/vol). In the second series of experiments, pH of each propofol product was changed by adding 10% (vol/vol) 5% dextrose in Ringer acetate solution. In the last series of experiments, in which temperature was changed (4, 20, and 36 degree centigrade), propofol products per se were used for dialysis. The propofol preparations were dialyzed for 24 hrs, and the receptor medium was analyzed by HPLC.
Results: The concentrations of free propofol in propofol LCT and propofol MCT/LCT products at 20 degree centigrade were 14.78 ug/mL (mean, n = 5) and 10.37 ug/mL, respectively. Even though the pHs of both lidocaine-mixed propofol products propofol LCT and propofol MCT/LCT were significantly decreased, the concentrations of free propofol in propofol LCT did not change and that in propofol MCT/LCT decreased by only 9%. When the pHs were changes by adding 5% dextrose in acetate Ringer solution, the concentrations of free propofol in propofol LCT and propofol MCT/LCT were significantly decreased by 10% and by 20%, respectively. By decreasing the temperature of the propofol products to 4 degree centigrade, the concentration of free propofol in propofol LCT significantly increased by 12% and that in propofol MCT/LCT slightly but significantly decreased by 8%. Conversely, the concentrations of free propofol in propofol LCT and propofol MCT/LCT were significantly decreased by 26% and by 21%, respectively, by increasing the temperature of the propofol products to 36 degree centigrade.
Conclusion: Since mixing lidocaine can induce instability of an emulsion of a propofol product and warming of a propofol product can rapidly induce microbial growth, injection of lidocaine prior to administration of cool propofol is recommended to reduce the incidence and intensity of pain on injection. The use of propofol MCT/LCT is also recommended for reduction of pain on injection, since the concentrations of free propofol were found to be significantly lower (by 30%~45%) than those in propofol LCT in this study.

S-351.

SMALL CONCENTRATIONS OF PENTOBARBITAL INCREASE EXCITABILITY IN RAT HIPPOCAMPAL NEURONS

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Introduction: Excitation is a characteristic feature of stages II and III of Guedel's classification of anesthetic depth. During emergence from anesthesia excitatory phenomena such as hyperalgesia, sympathetic stimulation, and delirium can occur as patients pass through stages III and II. At these low concentrations of anesthetic, synaptic transmission is enhanced, by mechanisms that are not well understood. In the hippocampus, extracellular field recordings show that synaptic transmission in the CA3-CA1 pathway is enhanced by pentobarbital concentrations that are approximately $1/10^{th}$ those required for anesthesia[1]. Here we have examined the relationship between excitatory postsynaptic (EPSP) slope (as a measure of the stimulus) and the probability of action potential generation during stimulus-response sequences in CA1 hippocampal pyramidal neurons.
Methods: Experiments were performed in an interface tissue chamber on 400 µM hippocampal slices[3] prepared from 20-30 day old male Sprague-Dawley rats. EPSP's were evoked by single pulse stimulation with a bipolar tungsten electrode inserted into the Schaffer collateral pathway. The stimulus amplitude (S.I.) required to evoke a detectable EPSP was determined - the stimulation sequence then repeated for 5-10 traces at increments in amplitude until each stimulus reliably generated an action potential. Intracellular recordings were obtained from CA1 pyramidal neurons with sharp microelectrodes (resistance 50-100 MΩ) filled with 3 M potassium acetate. Effects of pentobarbital (5 µM) were evaluated by measuring intracellular responses to stimulation before and after 30 minutes of drug application (n=10). In selected experiments (n=7), we evaluated the role of HCO_3^{-} [2] by replacing the latter with HEPES in the solution perfusing the slice.
Results: Pentobarbital did not alter spike threshold, resting membrane potential, or EPSP slope. Figure 1 shows that pentobarbital caused the neurons to spike at lower values of EPSP slope (EC_{50}control = 6.4 ± 4 mV/ms, EC_{50}pentobarbital =2.48 ± 2.6 mV/ms, $P<0.01$). In HEPES treated slices, pentobarbital did not shift the stimulus-response relationship.
Discussion: Although there was no observed change in spike threshold, resting membrane potential, or EPSP slope in the presence of pentobarbital, action potential generation occurred at lower values of EPSP slope. These results suggest that low concentrations of pentobarbital are associated with EPSP-spike (E-S) potentiation that is dependent upon HCO3-.
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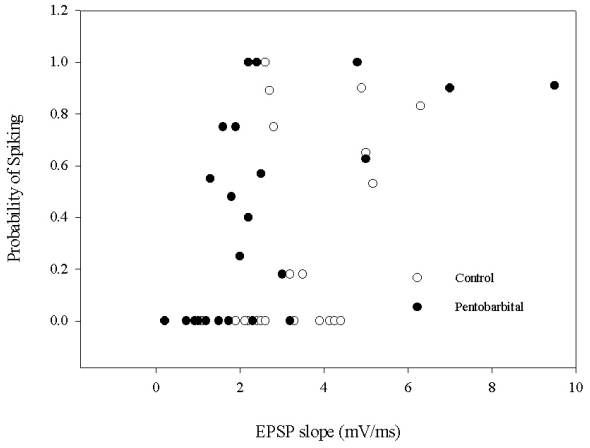

S-352.

ISOFLURANE DECREASES EXTRACELLULAR SEROTONIN LEVELS IN THE MOUSE HIPPOCAMPUS

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Introduction: Alterations in serotonergic neurotransmission in the hippocampus have been linked to depression, anxiety states, as well as changes in arousal and cognition.[1,2] Previously, we reported that propofol can significantly increase extracellular hippocampal serotonin (5-HT) concentrations.[3] However, the effects of volatile anesthetics on hippocampal 5-HT levels are unknown. The purpose of this study was to examine the effects of isoflurane on hippocampal 5-HT levels in mice.
Methods: The study was approved by the institutional animal care and use committee. Adult, male 129/SV mice were used in these experiments. Forty-eight hours prior to the study, each mouse had a probe guide cannula placed in the ventral hippocampus (VHC) under pentobarbital and ketamine anesthesia. On the day of the experiment, a microdialysis probe was inserted into the VHC of the awake mouse and the probe was perfused with artificial CSF at a rate of 0.5 µl/min. Dialysates were collected throughout the study at 20 min intervals for the determination of hippocampal 5-HT levels via high performance liquid chromatography. Once a stable baseline was achieved, the mice were either exposed, via an inhalation chamber, to 1 MAC isoflurane in a 50:50% O_2:air mixture (n=5) or to a 50:50% O_2:air mixture alone (control, n=3) for a period of 80 min. Dialysates for each group were compared to their respective baseline via ANOVA with Dunnett's post-hoc test applied when appropriate. Between-group comparisons were performed using an unpaired t-test. Data are expressed as mean ± SD and $p < 0.05$ was considered statistically significant.
Results: Within 20-40 min of administration, isoflurane produced a significant decrease in hippocampal 5-HT, which lasted throughout the study (Fig. 1). By the end of the study, the extracellular 5-HT level decreased to 37.6 ± 10.5% of the baseline 5-HT level. In the control group, there were no changes in hippocampal 5-HT levels throughout the study.
Discussion: In contrast to propofol[3], isoflurane produces significant decreases in extracellular 5-HT in the mouse VHC. Previously, it has been suggested that isoflurane may alter psychological function in healthy men.[4] It remains to be seen if isoflurane-mediated changes in hippocampal 5-HT are linked to alterations in perioperative mood states or cognitive deficits.

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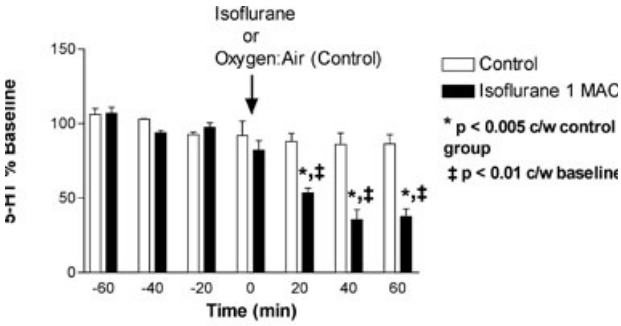

Fig. 1

S-353.

GENERAL ANESTHETICS REGULATE DISTINCT PHOSPHOPROTEIN SUBSTRATES IN MOUSE BRAIN IN VIVO

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Introduction: Although direct effects of general anesthetics on ligand-gated and voltage-gated ion channels and transmitter release resulting in altered synaptic transmission are well-described, their effects on downstream second messenger/protein phosphorylation systems are not. Ketamine, an NMDA receptor antagonist, propofol, a $GABA_A$ receptor agonist, and isoflurane, a $GABA_A$ receptor agonist and Na^+ channel antagonist, have distinct but overlapping mechanisms of action. We characterized these mechanistically-diverse anesthetics by profiling their effects on selected intracellular phosphoproteins *in vivo* in order to identify downstream molecular targets.
Methods: Male C57Bl/6 mice were injected (ip) with ketamine (150 mg/kg in 50 µL saline), propofol (250 mg/kg in 25 µL DMSO), or isoflurane (1300 mg/kg) to induce anesthesia (i.e. loss of righting reflex), or vehicle control. Ten min after injection mice were killed by focused microwave cranial irradiation, which preserves *in vivo* levels of protein phosphorylation. Frontal cortex, striatum (data reported here), and hippocampus were removed, frozen, and analyzed by immunoblotting with phosphorylation site-specific antibodies to 12 sites on 8 selected well-characterized phosphoproteins involved in neuronal signaling.
Results: Ketamine, propofol and isoflurane produced agent- and site-specific effects in striatum. All anesthetics reduced phosphorylation of T183-ERK2, but not T183-ERK1 (MAP kinases), of S897 of the NR1 subunit of the NMDA receptor, and of S831, but not S845, of the GluR1 subunit of the AMPA receptor. Ketamine alone stimulated phosphorylation of T34-DARPP-32, which mediates inhibition of protein phosphatase-1; isoflurane reduced phosphorylation and propofol had no effect on this site. Isoflurane alone reduced phosphorylation of S102-DARPP-32. Propofol and isoflurane, but not ketamine, reduced phosphorylation of S94-spinophilin, a site that regulates cytoskeletal interactions. Only propofol reduced phosphorylation of S133-CREB, a transcription factor implicated in memory. Ketamine inhibited and isoflurane enhanced phosphorylation of S40-tyrosine hydroxylase. Other sites were unaffected by these agents.

Effects of ketamine, propofol and isoflurane analyzed by phosphoprotein profiling

Phosphorylation site/ phosphoprotein	Protein kinase	Con-trol	Ketamine (150 mg/kg)	SE M	Propofol (250 mg/kg)	SE M	Isoflurane (1300mg/kg)	SE M
T183-ERK1	MEK1/2	100	98.6	9.8	93.0	5.4	100.0	19.0
T183-ERK2	MEK1/2	100	68.7*	4.9	52.7*	3.0	66.2*	2.7
S40-Tyrosine hydroxy-lase	PKA	100	89.7*	4.1	99.7	4.3	130.7*	11.6
S94-Spinophilin	PKA	100	89.3	14.4	70.9*	7.6	42.9*	6.2
S133-CREB	PKA	100	101.8	7.1	71.2*	3.2	109.8	6.3
S897-NR1	PKA	100	71.2*	4.4	83.5*	7.0	53.7*	7.0
S102-DARPP-32	CK2	100	106.7	5.1	101.4	4.0	78.6*	3.2
S137-DARPP-32	CK1	100	102.0	11.9	93.7	11.6	102.1	12.8
T75-DARPP-32	CDK-5	100	106.2	7.0	114.7	7.4	93.0	6.9
T34-DARPP-32	PKA	100	301.4*	74.3	90.9	14.7	47.6*	7.5
S845-GluR1	PKA	100	114.1*	1.5	109.5*	2.7	103.6	6.9
S831-GluR1	PKC/CKII	100	84.2*	3.4	72.0*	3.5	56.3*	6.5

6-10 mice/group. *p<0.05 by ANOVA with Newman-Keuls *post hoc* test.
Discussion: These data provide a 'phosphoprofile' of value in identifying novel intracellular signaling targets for both shared and unique actions of these widely-used CNS depressant drugs. Future experiments will apply this approach for identifying downstream effector molecules to additional drugs and brain regions, together with pharmacological and functional characterization *in vitro* using brain slices and reconstituted enzyme systems.
(Supported in part by grant DAMD 17-03-1-0396).

S-354.

THE POTENCY AND DOSE-RESPONSE CURVE OF INHALATION ANESTHETICS: MATHEMATICAL ANALYSIS WITH THE MULTI-UNIT AND MULTI PATH SYSTEM

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The dose-response curve of inhalation anesthetics is steep around the minimum alveolar concentration (MAC). We proposed Multi-Unit and Multi-Path System (MUMPS) as a mathematical model of neural network to explain the steep dose-response curve (1). We successfully demonstrated that the age dependency of MAC is related to the decreased number of the conduction pathways (2). We also showed that the exaggerated anesthetic effects on the spinal cord were related to the structural difference of the neural network between the brain and spinal cord (3). In the current communication, we discuss the neural network with MUMPS which can explain the steep dose-response curves and apparent anesthetic potencies.

Model: We assume that a signal transmission occurs through *m* conduction pathways (Multi-Path) and *n* conduction units (Multi-Unit) in each pathway. Body movement in response to noxious stimuli is prevented when at least one conduction unit of all pathways is blocked by anesthetics. We derived the equations for $EC^{unit}_{50}/EC^{system}_{50}$ and $EC^{system}_{95}/EC^{system}_{50}$ (1). Here, EC^{unit}_{50} and EC^{system}_{50} are the median effective concentrations of anesthetic on the conduction unit and on the whole system, respectively. EC^{system}_{95} is the 95% effective concentration on the whole system.

Results and Discussion: The figure shows the relationship between log (EC_{50}^{unit} / EC_{50}^{system}) and $EC_{95}^{system}/EC_{50}^{system}$ in different combinations of *m* and *n*. The value, log (EC_{50}^{unit} / EC_{50}^{system}), represents a discrepancy of anesthetic potency between conduction units and whole system. This can be a very small number or a large number depending upon the combination of m and n. The value, $EC_{95}^{system}/EC_{50}^{system}$, represents the steepness of the dose-response curve. It becomes 1.2 when the Hill coefficient is around 20. When each conduction pathway has only one conduction unit and *m* increases, this value is always larger than 13.513. When *m* is one and *n* increases, this value will always be larger than 4.321. These findings clearly show that the values *m* and *n* need to be large to have steep dose-response curves with inhalation anesthetics, and that the apparent anesthetic potency on the whole system is not necessarily equal to the potency at the individual effective sites (conduction units).

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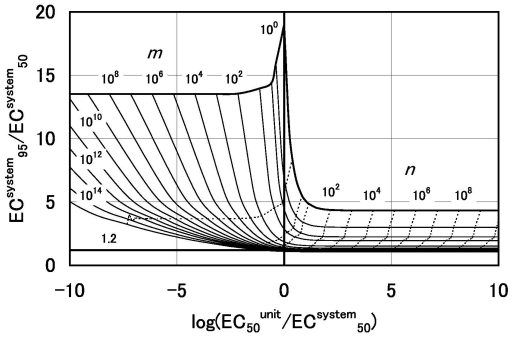

S-355.

BRAIN CHOLINERGIC RECEPTOR SUBUNIT EXPRESSION 48 H AFTER GENERAL ANESTHESIA IN RATS

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INTRODUCTION. General anesthesia and surgery are associated with early cognitive impairment in both young and aged patients (1,2) but the mechanisms are unknown. In the laboratory, we have demonstrated that general anesthesia with isoflurane-nitrous oxide impairs acquisition of spatial memory for days (3). Because brain nicotinic cholinergic receptors (nAChR) are important for working memory and are thought to be involved in anesthetic action, we hypothesized that early post-anesthetic spatial learning impairment may be related to downregulation of brain cholinergic receptor subunit expression. To test this hypothesis, we measured expression of nAChR α4 subunit protein in the cortex and hippocampus 48 h after anesthesia.

METHODS. Six month old male Fisher 344 rats were anesthetized for 4 h with 1.2% isoflurane - 70% N_2O - 30% O_2 (N = 5) whereas control rats received 30% oxygen (N = 4). Rats breathed spontaneously and SaO2 and MAP were measured non-invasively; rectal temperature was controlled. Animals were sacrificed 48 h after anesthesia and the hippocampus and cortex dissected out and processed for Western blotting. Crude membrane extracts were prepared and resolved on 8% gels using SDS-PAGE and then transferred to nitrocellulose. The membrane was blocked and incubated with a commercially available nAChR α4 antibody, followed by incubation with the appropriate secondary antibody conjugated to horseradish peroxidase. Immunoreactive bands were visualized with enhanced chemiluminescence (ECL, Amersham) and quantified by computerized densitometry (relative optical density). Data were analyzed using Student's t-test.

RESULTS. Blood pressure and SaO2 remained well within the normal physiologic range during anesthesia. There was no change in nAChR α4 subunit expression 48 h after general anesthesia in either the cortex or hippocampus (Fig; mean ± SD).

DISCUSSION. At 48 h after general anesthesia with isoflurane-nitrous oxide, at which time young rats have spatial memory impairment (3), there was no change in nAChR α4 subunit expression in either the cortex or hippocampus. Thus, while we can not exclude the possibility that general anesthesia alters expression of other subunits of the receptor or changes nAChR function, our data do not suppport a relationship between post anesthetic spatial memory impairment and downregulation of α4 subunit-containing cortical or hippocampal nicotininic cholinergic receptors.

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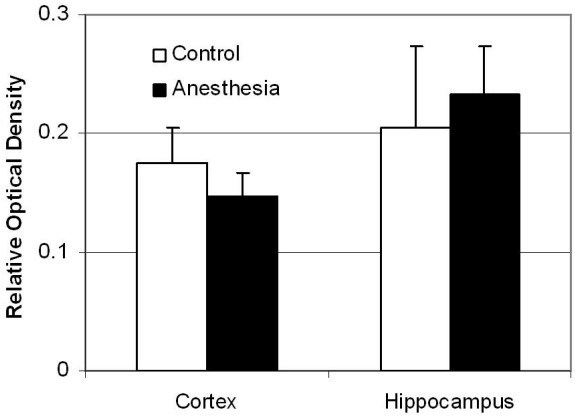

S-356.

TIME-DEPENDENT INHIBITION OF MUSCARINIC SIGNALING BY LOCAL ANESTHETICS IS MODULATED BY PKC

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Introduction: Signaling of several Gq-coupling receptors, such as the LPA- or TXA_2-receptor, is time-dependently inhibited by local anesthetics (LA) [1]. We have previously shown that m1 and m3 muscarinic receptors are affected differently by prolonged exposure to LA: an initial intracellular Gq-dependent inhibition is followed by a subsequent extracellular-mediated increase of muscarinic responses over the following hours [2]. As muscarinic receptors are known to be regulated by proteinkinase C (PKC) activity, we studied possible actions of PKC on this LA effect in order to determine sites and mechanisms of action underlying this muscarinic upregulation by LA.
Methods: Measurement of methylcholine (MCh, at EC_{50})-induced Ca^{2+}-activated Cl^--currents ($I_{Cl(Ca)}$) by 2-electrode-voltage clamp was used to assess the effects of prolonged incubation (10min-48h) with lidocaine (at $^1/_{10}$ of IC_{50} 1.8 or 37 nM) or QX314 (500 µM) on signaling of recombinantly expressed m1 and m3 receptors in *Xenopus* oocytes. Antisense knockdown of Gq and inhibition of PKC by either bisindolymaleimide (BIM, 10 µM) or chelerythrine (CT, 10 µM) have been employed to define sites and mechanisms of action more specifically. Data are normalized to corresponding control responses and shown as mean±sd (n>25).
Results: Inhibition of PKC by either BIM or CT (1h pretreatment) enhanced m1 and m3 signaling by approximately 25% of control response after 48h. Yet, in the presence of lidocaine the PKC antagonists completely abolished the previously described LA-induced increase of muscarinic responses, resulting in time-dependent inhibition (BIM: inhibition of m1 responses to 26.5±7.5% (CT: 36.5±8.9%) and 33.9 ±6.5% (CT: 35.8±9.6%) for m3 receptors, respectively, after 48h of incubation with lidocaine). Extraxcellularly applied membrane-impermeable QX314 did not affect m3 signaling for the first 2h but resulted in an increase of responses after prolonged exposure to the LA (up to 142.5±9.3% of control response after 48h) which again was completely abolished in the presence of BIM/CT.
Discussion: In contrast to our previous assumption the present study clearly shows that muscarinic m1 and m3 signaling in *Xenopus* oocytes is in fact time-dependently inhibited by LA, but masked by PKC-activity. Taking all our data into consideration we hypothesize that prolonged exposure of muscarinic receptors to extracellular LA might result in a change of receptor conformation. Thus, new phosphorylation sites, which are usually not accessible for PKC, may become available. Under these circumstances PKC may provoke upregulation of receptor function instead of expected downregulation. Based on these findings PKC will not always induce predictable effects and not all GPCRs will show time-dependent inhibition by LA.
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S-357.

EFFECT OF VOLATILE ANESTHETICS ON FLASH-EVOKED CORTICAL FIELD POTENTIAL AND MULTIUNIT RESPONSES IN THE RAT

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Introduction: We are searching for the neural correlates of anesthetic-induced unconsciousness. Findings may lead to the design of more specific anesthetic agents and more consistent techniques for monitoring anesthetic depth. Current theories focused on anesthetic drug-receptor interactions alone cannot explain the specific behavioral and phenomenological aspects of anesthetic-induced unconsciousness whose mechanism should be searched at the integrative level of neuronal networks. There is also increasing evidence that general anesthetics in moderate concentrations do not block thalamic information transfer to the cortex but allow the formation of implicit memories [1]. Whereas somatosensory cortical responses are diminished in part due to peripheral mechanisms, certain auditory and visual evoked responses are preserved even at fully suppressed EEG [2]. The question remains what aspects of sensory-evoked cortical activity are preserved vs. suppressed and how these changes may affect cognitive information processing of sensory stimuli during anesthesia. The goal of this study was to determine the effect of volatile anesthetics at concentrations that produce unconsciousness on neuronal responses to visual stimulation in multiple cortical regions involved in processing visual information.
Methods: Experiments have been performed in adult albino rats under graded, steady state levels of anesthesia between 0 and 1.5 MAC of halothane, isoflurane or desflurane. Visual evoked local field potentials (LFP) to monocular flash stimulation were recorded with chronically implanted bipolar electrodes from primary visual (V1), parietal association (PTA), and prefrontal (PF) cortex. Multiunit activity (MUA) responses from neuronal assemblies in V1 were recorded with multi-channel silicone electrode arrays.
Results: Rats lost consciousness as judged by the loss of their righting reflex between 0.5 and 0.7 MAC. The early evoked response (~40 ms) of both LFP and MUA in V1 were preserved up to 1.5 MAC whereas the late components (~200 ms) of MUA were depressed in a concentration-dependent manner. At burst-suppressed EEG, spontaneous LFP bursts occurred in synchrony over all cortical regions, while flash-evoked bursts in PF were delayed by 200 ms relative to the corresponding bursts in V1 and they were not attenuated by the anesthetic.
Discussion: A role for late cortical neuronal activity reflecting recurrent feedback from prefrontal to visual cortex at 200-300 ms in conscious visual perception has been proposed [3,4]. Consistently, our results suggest that volatile anesthetics interfere with the late components of neuronal firing (MUA) in visual cortex in spite of preserved activation (LFP) of the frontal cortex. An interference with recurrent cortico-cortical processing may underlie anesthetic-induced loss of visual consciousness.
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S-358.

PENTOBARBITAL ENHANCES SYNAPTIC PLASTICITY IN RAT HIPPOCAMPUS

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Introduction: Spatial learning and memory in the rat are thought to be correlated with changes in synaptic transmission in the hippocampus, referred to as synaptic plasticity. Since the neurotransmitter, γ-aminobutryic acid (GABA), plays a role in the induction of synaptic plasticity[1], we hypothesized that GABAergic drugs such as pentobarbital may facilitate synaptic changes.
To evaluate the effect of pentobarbital on synaptic plasticity, we have examined the frequency-response relationship for the Schaffer collateral/CA1 pathway in rat hippocampus. Low frequency stimulation causes long term depression (LTD) of the CA1 response while high frequencies evoke long term potentiation (LTP)[2]. The transition frequency (θ) characterizes the change from LTD to LTP - alterations in θ may occur in response to activity-related conditioning[2]. We tested the hypothesis that subanesthetic concentrations of pentobarbital shift the induction of LTP to lower frequencies.
Methods: Protocols were approved by the institutional animal care committee. Experiments were performed on 400 μM hippocampal slices[3] prepared from 20-30 day old male Sprague-Dawley rats in an interface tissue chamber. The Schaffer collateral pathway was stimulated at a frequency of 0.1 Hz with a bipolar tungsten electrode set (3- to 5V) to evoke half maximal population spike (PS) amplitudes recorded with an extracellular microelectrode in the CA1 pyramidal cell layer. The conditioning stimuli (CS) for LTD/LTP in the control conditions (artificial CSF) were single pulse stimulations (900 pulses at 1, 10, 50 and 100 Hz). Waveforms were recorded and analyzed with Labview®-based customized software. Pentobarbital (5 μM) was added to the perfusate for 30 minutes before a 10 Hz CS. PS amplitudes were averaged over 5 minute epochs, 30 minutes before the CS and after 60 minutes of drug washout.
Results: The control frequency-response curve is shown in Figure 1. Results are expressed as mean change ± SD in PS amplitude 60 minutes following the conditioning stimulus. PS amplitude increased 57 ± 18% in pentobarbital-treated slices compared to the control value of 10 ± 20% (*P*=0.003) at a CS of 10 Hz.
Discussion: The results support the hypothesis that subanesthetic concentrations of pentobarbital decrease the CS frequency required to evoke LTP and justify further evaluation of this phenomenon.
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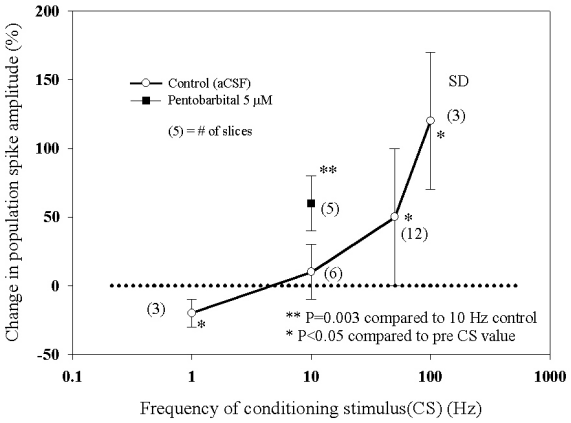

S-359.

THE MEMORY ENHANCING EFFECT OF 0.1% SEVOFLURANE IN RATS IS AMYGDALA DEPENDENT

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Introduction: The amnesic effect of low-dose sevoflurane depends on the functioning of the basolateral amygdala (BLA), a brain site involved with emotion and the modulation of memory consolidation for emotional events **[1].** One study showed a tendency for 0.1% sevoflurane to enhance 24 h memory retention in the rat **[2].** Such a memory enhancing effect has clinical implications for cases of awareness and seems at odds with the idea that all anesthetic agents are potent amnesic agents. Here we determine whether 0.1% sevoflurane exposure in the rat during inhibitory avoidance (IA) training/learning significantly enhances 24 hour memory retention and further whether this effect depends on the BLA, the brain site hypothesized to modulate memory consolidation.
Methods: Following IACUC approval, 30 rats underwent surgery. Ten rats underwent sham surgery as controls and the others received bilateral excitotoxic (NMDA) lesions of the BLA. Following a one week recovery, animals underwent training with a single-trial IA technique (0.3 mA shock/1 sec) during exposure to either air or 0.1% sevoflurane. Memory retention was assessed at 24 hours. Higher retention latency at 24 hours implies better memory. Data (mean +/- SD) are from histology verified hits (n = 4-5 per group).
Results: Sham-operated rats trained during air exposure (n=5) had minimal, if any, 24 h retention of the single trial training experience with a mean retention latency = 35 +/- 25 sec. The mean retention latency (374 +/- 209 sec) of sham-operated rats trained during exposure to 0.1% sevoflurane, however, was significantly greater ($P < 0.001$). This demonstrates sevoflurane's memory enhancing effect. Importantly, this enhancement was not seen in rats with BLA lesions that were trained during 0.1% sevoflurane exposure (latency = 6 +/- 6 sec), as compared with control BLA lesioned rats trained during exposure to air (latency = 14 +/- 7). Additional training in air was then given to these same BLA lesioned rats to control for the possibility that the lesions simply caused a complete inability to learn the IA task. Retention at 24 h markedly improved following this additional training (latency = 582 +/- 38 sec). This shows that these animals were capable of learning and having memory even with a BLA lesion, but that the memory modulating effect of 0.1% sevoflurane was blocked with a specific BLA lesion.
Conclusions: Sevoflurane, at a dose typically encountered by patients emerging from sevoflurane anesthesia (i.e., 0.1%), enhances aversive memory formation. The basolateral amygdala plays a critical permissive role in this memory enhancing effect of sevoflurane.
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Supported by NIH grant #RO1GM065212.

S-360.

DESIGN OF A SPECIFIC INHIBITOR OF PROTEIN PHOSPHATASE-1_I, A REGULATOR OF CELL DEATH ACTIVATED IN GLOBAL CEREBRAL ISCHEMIA

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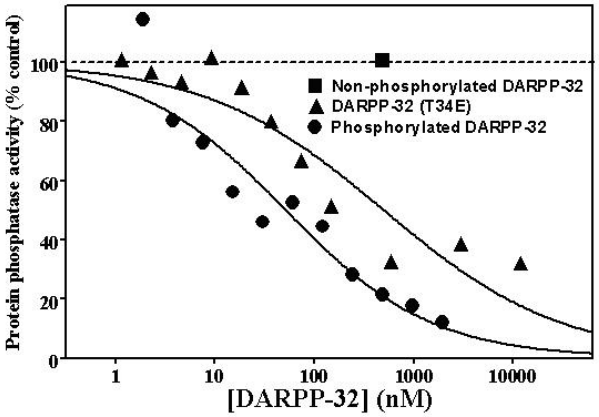
Introduction: Protein phosphatase-1_{IC} ($PP1_{IC}$) is upregulated in global cerebral ischemia following cardiac arrest (1). The catalytic subunit of $PP1_{IC}$ interacts with BAD, Bcl2, and Rb, which upon dephosphorylation by PP1, are involved in initiating apoptosis (2-4). Inhibitors of $PP1_{IC}$ are therefore potential agents to prevent apoptotic cell death in global cerebral ischemia. We therefore designed an inhibitor of $PP1_{IC}$ based on DARPP-32, a specific PP1 inhibitor when phosphorylated on threonine-34 (5).
Methods: The cDNA for human DARPP-32 was used as a template for PCR-mediated site-directed mutagenesis of threonine-34 to glutamate (T34E). DARPP-32(T34E) was further used as a template to produce a truncated mutated DARPP-32(T34E)$^{1-40}$. The cDNA encoding each of these 3 proteins was inserted into an expression vector, expressed in *E. coli*, and the 6His-tagged proteins purified by Ni^{2+}-NTA affinity chromatography. Effects on the activity of the purified catalytic subunit of PP1 were determined using ^{32}P-labelled phosphorylase *a* as substrate (5). Data were fit to sigmoidal concentration-effect curves for determination of IC_{50} values (GraphPad Prism 4.2).
Results: DARPP-32, phosphorylated on threonine-34 by cAMP-dependent protein kinase, inhibited PP1 (IC_{50}=52nM); non-phosphorylated DARPP-32 had no effect. DARPP-32(T34E) also inhibited PP1 (IC_{50}=500nM), but this effect was independent of phosphorylation(Figure). Analysis of the truncated DARPP-32(T34E)$^{1-40}$ is in progress.



Discussion: Reducing ischemic cell death is an important goal in treating global cerebral ischemia following cardiac arrest. Inhibition of the activity of up-regulated $PP1_{IC}$, may prevent the initiation of apoptotic cell death and other ischemic pathophysiology. Design of specific inhibitors of $PP1_{IC}$ based on the active domain of DARPP-32 may be useful in gene therapy or in protein transduction strategies to inhibit pathologically activated $PP1_{IC}$.
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S-361.

EFFECTS OF ISOFLURANE ON THE SARCOPLASMIC RETICULUM OF RAT CARDIOMYOCYTES DURING REOXYGENATION

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Background: Isoflurane inhibits the sequestration of Ca^{2+} by the sarcoplasmic reticulum (SR) Ca^{2+} ATP-ase (1). It also depresses Ca^{2+} release following activation of the SR ryanodine release channel (1,2), which may result in SR Ca^{2+} overload and subsequent enhanced spontaneous Ca^{2+} release (3,4). Both of these mechanisms could account for the remarkable cytosolic Ca^{2+} $[Ca^{2+}]_i$ accumulation that was observed in isoflurane-treated cardiomyocytes after ischemia (5). In order to elucidate the way isoflurane acts on the SR in the course of reoxygenation we applied two blockers of the SR, ryanodine (Rya), and cyclopiazonic acid (CPA), to single ventricular myocytes. Low affinity binding of Rya to the SR Ca^{2+} release channel closes the channel whereas CPA is a specific Ca^{2+} ATP-ase inhibitor.
Methods: After institutional approval, electrically stimulated rat cardiomyocytes were subjected to 30 min of simulated ischemia (external pH: 6.3; pO_2 < 15 mmHg, 10 mM deoxy-glucose) followed by 30 min of reoxygenation in the presence of 10 mM glucose and normal ambient pH. During reoxygenation, the cells were exposed to either air (control group), 2 MAC (0.31 mM) of isoflurane in air, 3 µM Rya, or 10 µM CPA. $[Ca^{2+}]_i$ was investigated using the ratiometric fluorescent dye fura-2. In addition, diastolic cell length was determined.
Results: The $[Ca^{2+}]_i$ increase in the isoflurane group after 30 min of reoxygenation was similar to that seen in Rya treated cells (80% increase from baseline). The rise in CPA treated myocytes resembled the alterations seen in the control group (30% increase, $P < 0.05$ vs. isoflurane and Rya group, ANOVA). There was no difference in $[Ca^{2+}]_i$ between cells treated with CPA and controls. The lower $[Ca^{2+}]_i$ in CPA relative to isoflurane and Rya treated cells, however, neither mitigated hypercontracture (diastolic cell length < 50% of baseline cell length) nor did it improve diastolic relengthening relative to isoflurane and Rya treated cells (80% of baseline cell length vs. 98% in controls, $P < 0.05$, ANOVA).
Conclusion: The action of isoflurane on the SR during reoxygenation appears to be blockade of SR Ca^{2+} release. This can induce SR Ca^{2+} overload with accompanying sudden, spontaneous diastolic Ca^{2+} spillovers and a consecutive rise in $[Ca^{2+}]_i$ (3,4) patricularly when Ca^{2+} efflux from the cell is already impeded by isoflurane (5). Blocking SR Ca^{2+} uptake by CPA did not increase $[Ca^{2+}]_i$ probably because SR Ca^{2+} uptake is already impaired after ischemia (6). Furthermore, hypercontracture, an irreversible cytoskeletal alteration, and impaired diastolic relengthening do not seem to be a mere function of $[Ca^{2+}]_i$ as CPA had no effect on cellular relaxation.
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S-362.

FENTANYL REDUCES THE INFARCT SIZE AND VENTRICULAR ARRHYTHMIA IN A EXPERIMENTAL MODEL OF MYOCARDIAL ISCHEMIA/REPERFUSION INJURY AND CENTRAL SYMPATHETIC OVERACTIVITY IN RABBITS

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Introduction: The cardioprotective effects of opioid drugs are attributed to two distinct mechanisms: a direct effect on the myocardium, in a mechanism of preconditioning-like (1), and a central action, probably by modulating the autonomic nervous system (2). Fentanyl is an opioid-derived drug largely used in the clinical practice, with a favorable hemodynamic profile. Studies using the isolated heart rabbit model demonstrated the cardioprotective actions of fentanyl *in vitro* (3), and suggested that the limitation of ischemic injury is mediated by both delta-opioid receptors and PKC. Although the cardioprotective effects of fentanyl *in vitro* were consistent, while the putative cardioprotection of fentanyl treatment *in vivo* remain unknown.
Objective: The objective of present work is to investigate the cardioprotective effects of fentanyl in a model of ischemia and reperfusion in rabbits. In order to evaluate the protective action of fentanyl, we used the model of central sympathetic overactivity elicited by the intracerebroventricular (i.c.v.) administration of *L*-glutamate.
Methods: New Zealand anesthetized rabbits were treated with saline or fentanyl (5 and 50 µg/kg) and submitted to ischemia and i.c.v. administration of 10 mmol of *L*-glutamate. The period of ischemia was 35 minutes and the reperfusion 120 minutes. We also used in two separated groups naloxone (NAL - 100 µg/kg i.c.v.) and naloxone methiodide (NAL_{METH} - 13 mg/kg i.v.) to differentiate the central and peripheral effects of opioid receptor antagonism. The infarcted area was evaluated by the TTC method, and expressed as the percentage of the area at risk (AI/AR).
Results: The systemic treatment with fentanyl in the doses of 5 and 50µg/kg significantly reduced the total number of ventricular premature complexes during the ischemia (29±6 and 19±7 ($p < 0.01$), respectively) and also during the reperfusion (23±7 and 8.5±4, respectively) when compared with the control group (54±3 during the ischemia and 133±46 during the reperfusion). The pretreatment with NAL i.c.v. abolished the effect of fentanyl during the ischemia, but not during the reperfusion. The systemic pretreatment with NAL_{METH} did not interfere with this effect of fentanyl. Only the dose of 50µg/kg fentanyl reduced the IA/AR from 47±3% in the control group to 25±2% ($p < 0.001$), and the NAL_{METH} blocked this cardioprotective effect.
Conclusions: Our results suggest that the cardioprotective effects of fentanyl treatment involve central and peripheral mechanisms. Moreover, the reduction of infarcted area seems to be related to peripheral receptors, probably in the myocardium, as well as the central nervous system action of fentanyl is related to the reduction in the incidence of premature ventricular complexes.
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S-363.

NICORANDIL REDUCES INTRACELLULAR CALCIUM INCREASE EVOKED BY OXYGEN GLUCOSE DEPRIVATION IN A RAT HIPPOCAMPAL CA1 PYRAMIDAL CELL

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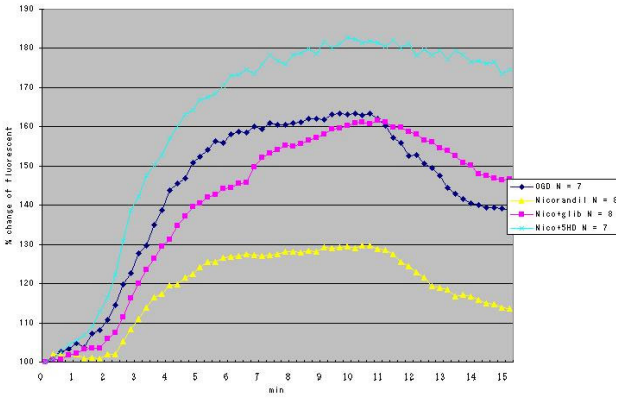
Introduction: The anti-anginal drug nicorandil has been demonstrated to protect myocardium against ischemic injury in both experimental and clinical studies. Recently, several studies showed that nicorandil reduced brain injury in animal models of brain ischemia. Nicorandil seems to protect the organs via activation of ATP-sensitive potassium channels (KATP channels). In addition, mitochondrial KATP channels is related to necrotic and apoptotic neuronal cell death after cerebral ischemia. Multiple intracellular signaling mechanisms underlying ischemic insults, an initial overload of intracellular Ca^{2+} plays a critical role in the neuronal cell death. In this study, we investigated the effects of nicorandil on pathological calcium overload induced by subsequent 10min oxygen glucose deprivation (OGD) in rat hippocampal slices.
Methods: Hippocampal slices were prepared from 14 to 20-d-old Wister rats. After decapitation, hippocampus were rapidly removed and placed in ice-cold artificial cerebrospinal fluid (aCSF). Hippocampal transverse slices approximately 300µm thick were cut with a vibrating slicker. The slices were preloaded with a fluorescent indicator, Oregon Green 488 BAPTA-1, and aCSF bubbled with 95% O2 and 5% CO2 gas mixture for 60min at room temperature. OGD was induced by transferring into a chamber containing of a glucose-free aCSF bubbled with 95% N2 and 5%CO2. The slices were randomly assigned to one of four groups as follows: (1) OGD, (2) nicorandil (0.1mM), (3) nicorandil and glibenclamide (0.01mM), (4) nicorandil and 5-hydroxydecanoic acid (5HD) (0.5mM). After 10min OGD stimulation, slices were recovered in oxygenated aCSF for 5min. Relative changes in the intracellular Ca^{2+} concentration was monitored during 10min OGD and 5min recovery phase.
Results: The intracellular Ca^{2+} concentration of a hippocampal CA1 pyramidal cell was beginning to increase in both nicorandil group and OGD group. Administration of nicorandil, compared maximum intracellular intensity with OGD group dramatically reduced the Ca^{2+} concentration resulting from a subsequent 10min OGD. This effect of nicorandil was abolished by 5HD, a putative mitochondrial KATP channel blocker, and by glibenclamide, a nonselective KATP channel blocker.
Discussion: In our study, nicrandil reduced the intracellular Ca^{2+} overload resulting from a subsequent 10min OGD. 5HD and glibenclamide inhibited this intracellular Ca^{2+} change. This result suggests that opening of KATP channels by nicorandil prevents the intracellular Ca^{2+} overload. Such effect might potentially be attributed to the mechanism of neuroprotection.
References: 1) Teshima et al, 2003, Brain Research 990 45-50



S-364.

ISOFLURANE-INDUCED PRECONDITIONING FOLLOWING GLOBAL AND REGIONAL ISCHEMIA IN ISOLATED RAT HEART INVOLVES ATTENUATION OF ELECTRO-MECHANICAL UNCOUPLING

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Introduction: Ischemia/reperfusion (I/R) injury results in electro-mechanical uncoupling and consequently in deterioration of cardiac function during reperfusion.[1] Protection against I/R injury following anesthetic preconditioning (APC) has not been well characterized. We hypothesized that APC will protect heart against I/R injury by attenuating severity of electro-mechanical uncoupling after global or regional ischemia. In this study, we quantified mean magnitude-squared coherence (MSC) between spectral components of electrograms from two different sites in the ventricle and left ventricular pressure (LVP) to assess the correlation between electrical and mechanical events characterizing cardiac function after APC *ex vivo*.
Methods: Isolated Wistar rat hearts (n=30) in Langendorff mode were perfused at constant pressure of 75 mmHg with crystalloid buffer and were subjected to either 30 min of global or regional ischemia. Bipolar electrograms recorded from the base (RV_1) and the apex (RV_2) of the right ventricle and isovolumic left ventricular pressure (LVP) were simultaneously recorded before, during and 120 min after ischemia. The hearts were untreated (global ischemia/GISC; regional ischemia/RISC), or treated with 30 min isoflurane (GAPC; RAPC, respectively; 0.28 mM). Isoflurane was washed out before ischemia. Another group (SHAM) was not subjected to ischemia nor treated with isoflurane. Data are means ± SD (p<0.05).
Results: Untreated hearts exhibited low levels of coherence during reperfusion. Mean MSC (0-35 Hz) for LVP *vs.* RV_1 and LVP *vs.* RV_2 were 0.21±0.16, 0.20±0.14 for the GISC group and 0.22±0.14, 0.20±0.17 for the RISC group, respectively. In contrast, the isoflurane treated hearts exhibited moderate-to-high levels of mean MSC throughout reperfusion of 0.48±0.14, 0.46±0.14 for the GAPC group and 0.44±0.16, 0.42±0.14 for the RAPC group. The SHAM hearts had mean MSC of 0.77±0.15, 0.77±0.16.
Discussion: The dissociation between left ventricular contraction and right ventricular depolarization following both global and regional ischemia was decreased in the isoflurane treated groups compared to untreated hearts. The results demonstrate that APC significantly attenuates electro-mechanical uncoupling following ischemia.
References:
1. Am J Physiology 283: H44-52, 2002.
Acknowledgments: Supported in part by grant No. 0360042Z (EN) from the American Heart Association-Greater Midwest Affiliate and PO1GM066730 (ZJB) from the National Institutes of Health.

S-365.

IMPROVED SPATIAL MEMORY PERFORMANCE AFTER ISOFLURANE-NITROUS OXIDE ANESTHESIA IN YOUNG ADULT RATS

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INTRODUCTION. Clinical studies indicate that general anesthesia and surgery are associated with early cognitive impairment in both young and aged patients but that impairment persists for up to three months only in the elderly (1,2). In the laboratory, we have demonstrated that general anesthesia with 1.2% isoflurane-70% nitrous oxide-30% oxygen (ISO+N_2O) impairs acquisition of spatial memory for days in both young and aged rats but that aged rats remain impaired for at least 2 weeks after anesthesia (3,4). The present study was designed to test the hypothesis that this lasting impairment is age-dependent such that spatial memory is intact 2 weeks after anesthesia in young rats.
METHODS. Six-month-old rats were randomized to anesthesia for 2 h with ISO+N_2O or 1.8% isoflurane-30% oxygen (ISO)(N = 10 per group). Rats were anesthetized in a chamber, intubated, and mechanically ventilated; SaO2 and MAP were measured non-invasively and rectal temperature was controlled. Control rats (N = 10) breathed 30% oxygen spontaneously. Rats recovered for 2 weeks and then were tested daily for 14 d on a 12-arm radial maze to assess acquisition of spatial memory. Data were analyzed with a repeated-measures ANOVA or a 1-way ANOVA followed by Dunnetts test, as appropriate.
RESULTS. Blood pressure and SaO2 were similar in the anesthetized groups and well within the physiologic range. In each group, performance improved over the 14 d of testing, indicating learning across trials. There were no differences between the control and the anesthesia groups in number of correct choices to first error or time to complete the maze. Neither was there a main effect of group for total number of errors ($P > 0.05$). However, the group by day interaction was significant ($P < 0.05$), reflecting improved performance during the later days of testing in the ISO+N_2O group compared to the controls.
DISCUSSION. In contrast to the impairment we observed previously in aged rats (3,4), the maze performance of young adult rats is improved 2 weeks after general anesthesia with ISO + N_2O. This suggests that the long term effects of ISO+N_2O anesthesia on spatial memory are age-dependent.
References:
1. Lancet 1998; 351: 857-61
2. Anesthesiology 2002; 96: 1351-7
3. Anesthesiology 2004; 100: 309-14
4. Anesth. Analg 2004; In Press

S-366.

TWENTY FOUR HOURS OF SLEEP DEPRIVATION ATTENUATES HALOTHANE MINIMUM ALVEOLAR CONCENTRATION IN RATS

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Introduction: Sleep deprivation precipitates adverse physiological effects and may even cause death. (1) Recent data suggested that sleep deprivation potentiates the ability of inhaled anesthetic agents to induce a loss of righting reflex. (2) It is known that minimum alveolar concentration (MAC) of volatile agents is influenced by numerous physiological factors but there are no reports on the effects of sleep deprivation on MAC. We tested the hypothesis that MAC of inhaled anesthetic agent is attenuated in sleep-deprived rats. Using a blinded, crossover randomized control design we compared the MAC of halothane in rats with and without sleep deprivation.
Methods: Rats were randomly allocated into two groups. One rat from each group was put into a Rechtschaffen deprivation apparatus. (1) Sleep deprivation was provided by rotation of a disc over water when continuous computerized EEG and EMG monitoring detected sleep. The study included four phases with an initial seven days of adaptation, followed by a 24 hr period of ad libitum activity (Group ND rats) or sleep deprivation (Group DN rats). Then it was followed by five days of recovery, and a crossover of 24 hr periods during which Group DN rats were ad libitum and Group ND rats were sleep deprived. MAC for halothane was measured on the morning before and after each 24 hr period.
Results: Following 24 hr of sleep deprivation halothane MAC decreased by 26.4±4.4% for all rats (P<0.01 Vs baseline for MAC). (Table 1) These changes were not significantly different between groups. Halothane MAC returned to original values in all rats after adequate sleep.
Discussion: Our results demonstrate that 24 hr of sleep deprivation attenuates halothane MAC in rats. This imply that adequacy of pre-anesthesia sleep may affect anesthetic potency. An important question is whether sleep deprivation also has such effects on human. Our results might be of clinical importance to humans requiring inhalation general anesthesia, particularly the critically and terminally ill patients who might be suffering from profound sleep disturbance because of pain, grief, discomfort, and therapeutic interventions.
References:
(1). Science. 221:182-184, 1983
(2). Anesthesiology 97:906-11, 2002.

Changes in halothane minimum alveolar concentration (MAC) before and after sleep deprivation

Group	MAC (%)		
	before sleep deprivation	after sleep deprivation	after adequate sleep
ND	1.36 ± 0.10	1.05 ± 0.13*	Not measured
DN	1.37 ± 0.11	1.03± 0.10*	1.35 ± 0.04**

Values represents mean ± standard deviation
* Differs from values before sleep deprivation; p<0.01, Student's t-test.
** Differs from values after sleep deprivation; p<0.01, Student's t-test.

S-367.

EFFECTS OF NOCICEPTIN/ORPHANIN FQ ON RESPIRATION-RELATED NEURONS IN THE ROSTORAL VENTROLATERAL MEDULLA; AN IN VITRO STUDY IN NEWBORN RAT

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Introduction: Nociceptin/orphanin FQ (N/OFQ) is the endogenous agonist of the orphan opioid receptor-like receptor (NOP receptor, previously termed ORL1 receptor). Our previous study showed that N/OFQ acts as a neuromodulator to reduce respiratory frequency (fR) in the medulla oblongata (1). However, mechanisms for N/OFQ-induced fR reduction have not yet been elucidated. In the present study, using *in vitro* newborn rat preparations, we examined the role of N/OFQ in the modulation of respiration-related neurons in the rostral ventrolateral medulla (RVLM) that is thought to be an important area for respiratory rhythm generation.
Methods: This study was approved by the Animal Care Committee of the Hokkaido University Graduate School of Medicine. The brainstem-spinal cord from 3-day-old Wistar rats was isolated and perfused with artificial cerebrospinal fluid (27.5 °C) equilibrated with 95% O_2 and 5% CO_2 at pH 7.4. Respiratory activity was recorded from the C4/C5 ventral roots. The unit activity of inspiratory (Insp) neurons and pre-inspiratory (Pre-I) neurons in RVLM was recorded extracellularly. Pre-I neurons fire in pre- and usually also during post-inspiratory phase. N/OFQ 30 nM was administered for 10 min through the recording chamber by means of a perfusion system. Each preparation was once exposed to N/OFQ. Firing frequency of C4 activity (bursts/min) was regarded as fR. Intraburst frequency (spikes/s) in Insp neurons was calculated from the inspiratory time and the number of spikes. In Pre-I neurons, the number of spikes at the pre- and post-inspiratory phase was analysed. All data are presented as mean (SD). Statistical significance was evaluated using ANOVA followed by Dunnett's test (P<0.05).
Results: The unit activity was recorded from 20 Insp neurons and 8 Pre-I neurons. Application of N/OFQ resulted in a synchronous decrease in the burst rates of Insp neurons and of C4 activity (fR) [6.7 (1.5) min^{-1} to 3.0 (2.0) min^{-1}; P<001], while intraburst frequency in Insp neurons increased significantly [9.1 (4.2) to 10.4 (5.3) spikes/s; P<0.05]. Application of N/OFQ caused an decrease of fR [7.5 (1.2) min^{-1} to 3.5 (2.0) min^{-1}; P<001] as well as a Pre-I neuronal burst rate [7.2 (1.3) min^{-1} to 3.1 (2.3) min^{-1}; P<001]. In Pre-I neurons, N/OFQ significantly decreased the number of spikes at the pre-inspiratory phase [3.7 (2.8) to 1.2 (1.5) spikes; P<0.05] and post-inspiratory phase [7.8 (2.7) to 3.6 (5.2) spikes; P<0.05].
Discussion: N/OFQ suppressed burst activities of Pre-I neurons. Pre-I neurons are suggested to be primary rhythm generating neurons, which have pacemaker properties (2). The present results suggest that N/OFQ-induced fR reduction is caused by the inhibitory effects on the central respiratory rhythm generated by Pre-I neurons.
References:
(1) Br J Anaesth 91:385-9 2003
(2) Prog Neurobiol 59: 583-634 1999

S-368.

COMPLEMENT ACTIVATION FOLLOWING ENVIRONMENTAL EXPOSURE TO ANESTHETICS

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Introduction: Allergic drug reactions can affect anesthetic and surgical outcomes. Several studies have implicated the complement system in these reactions. However, in many of these studies it is difficult to separate the role of the anesthetic from that of the surgical treatments in generating allergic responses. Hence, previous studies have focused on the role of antibodies in drug reactions while the complement system has not been extensively investigated.
Investigating immune reactions following environmental anesthetic exposure could help to identify the role of complement in allergic drug reactions. Previous studies have shown that cytochrome P450 2E1 (CYP2E1) IgG autoantibodies have been found in persons chronically exposed to halogenated volatile anesthetics[1], while further studies have shown significantly higher CYP2E1 IgG4 subclass autoantibodies in exposed patients with liver injury from an allergic response to the anesthetic when compared to those without injury ($p < 0.001$) [2]. Finding IgG4 subclass antibodies is important since these antibodies in combination with antigen can activate the classical complement pathway by engaging the complement component 1, thus connecting the adaptive immune response and the complement system.
Methods: To uncover the role of complement in anesthetic-induced allergic drug reactions, sera from four experimental groups were studied: Control persons (pre-employment sera, CON, N=43), anesthetic hepatitis patients (AH, N=24), pediatric anesthesiologists (exposed to high levels of anesthetic gases, SPA, N=44) and general anesthesiologists (exposed to lower levels of anesthetic gases, JHU, N=44). IgG1 and IgG3 levels were measured using a human IgG subclass ELISA Kit while complement components C3a, C4a and C5a levels were measured using human complement component ELISA Kits.
Results: Total IgG3 levels were significantly elevated in AH patients (2.2 ± 1.0 mg/ml) compared to CON (1.7 ± 0.9 mg/ml, $p < 0.05$), SPA (0.9 ± 0.8 mg/ml, $p < 0.001$) or JHU 1.0 ± 0.6 mg/ml, $p < 0.001$), while total IgG1, although higher than reported values in all groups were significantly different between AH (18.9 ± 7.0 mg/ml) and SPA (10.0 ± 8.7 mg/ml, $p < 0.01$). Conversely, significantly elevated levels of classical complement pathway C4a, common pathway C3a and terminal complement pathway C5a were seen in environmentally exposed persons ($p < 0.001$) when compared to the AH group, while lower exposure to anesthetics (JHU) induced significantly higher levels of C3a and C4a ($p < 0.001$) when compared to the higher exposure (SPA) group.
Conclusions: Environmental exposure to volatile anesthetics and IgG autoantibodies in conjunction with immune complexes may activate the complement system through the classical pathway. In susceptible AH persons, IgG4 CYP2E1 autoantibodies and IgG3 are formed which also trigger the classical complement pathway further depleting complement components, and may result in liver injury.
References:
[1]ANA 94:243-9, 2002,
[2]Anesthesiology Suppl, 2004.

S-369.

PROPOFOL ACTIVATES ENOS IN CULTURED BOVINE AORTIC ENDOTHELIAL CELLS

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Introduction: Endothelial cells play a major role in regulating vascular tone, through the production of vasoactive mediators, including endothelium-derived nitric oxide (NO). One of the side effects of propofol is that it causes a dose-dependant decrease in blood pressure, due in part to decreased systemic vascular resistance(1). The goal of the present study was to determine the effect of propofol on eNOS activation in cultured bovine aortic endothelial cells.
Methods: Bovine aortic endothelial cells (EC) were maintained in Dulbecco s modified Eagle s (DME) medium and F12 medium supplemented with 5% fetal bovine serum, 100 units/ml penicillin and 100 µg / ml streptomycin, in a humidified atmosphere containing 5% CO2. Cells were exposed to clinically relevant concentrations of propofol, and lysed for Western Blot analysis. Activation of eNOS was studied using specific anti-phospho eNOS antibodies (pS-1177 and pT-495). Similarly, Akt activation was evaluated using and anti-phospho Akt (pS-473) antibody. Relative amounts of phosphorylated protein was quantified by densitometry and expressed as percentage of the control. Blots were controlled for equal amounts of total eNOS and total Akt.
Results: Propofol induced a time- and dose-dependent activation of eNOS, marked by increased phosphorylation at Serine 1177 and decreased phosphorylation at Threonin 495. Because serine 1177 is a substrate for Akt, we determined whether propofol induced Akt activation and found an increased Akt phosphorylation at serine 473 in propofol-treated cells.
Discussion: Our results show for the first time that propofol activates a nitric oxide-generating pathway in aortic endothelial cells. This is in agreement with previous studies indirectly showing that propofol stimulates NO release by endothelial cells(2). Moreover, the peak of Akt activation precedes eNOS activation, in favor of a role for Akt in propofol-induced eNOS phosphorylation.

References:
1. CNS Drugs 2003;17:235-272.
2. Br J Pharmacol 1993;109:6-7.

S-370.

FENTANYL ATTENUATES ANTIGEN-INDUCED CONTRACTILE RESPONSES OF SENSITIZED RAT TRACHEA

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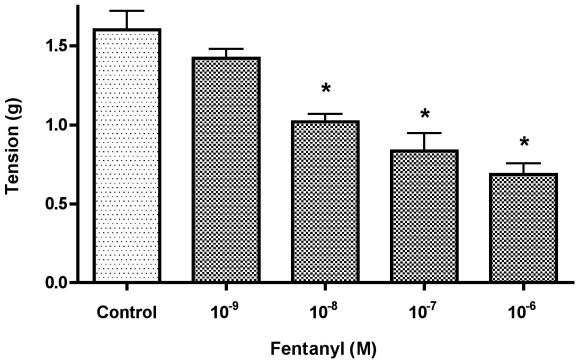
Introduction: Fentanyl attenuates contractile responses to electrical field stimulation (EFS) in isolated airways (1). On the other hands, antigen-induced contractile responses are mediated by serotonin and acetylcholine (2). However, it is not clear whether fentanyl attenuates the antigen-induced contractile responses. Thus, this study was carried out to determine the effects of fentanyl on antigen-induced contractile responses of sensitized rat trachea.
Methods: Studies were conducted under guidelines approved by our Animal Care Committee. Male Wistar rats weighing 150-200 g were used. The rats were sensitized by a single intraperitoneal injection of 10 μg ovalbumin (OA) mixed with 10 mg aluminum hydroxide as adjuvant. Fourteen days later, the rats were exsanguinated under anesthetized with intraperitoneal pentobarbital, and the trachea was rapidly isolated. The trachea was chopped into 3-mm-wide rings. The resting tension was adjusted periodically to 0.5 g during equilibration period. The tissues were challenged by the addition of OA at a final concentration of 50 μg / ml. First, we examined the effect of fentanyl (0.001 - 1 μM) on the contraction induced by OA. Second, 0.1 μM tetrodotoxin was added 30 min before addition of OA, and the ring tension was measured. Third, we examined the effect of 1μM fentanyl on the contraction induced by OA in the presence of tetrodotoxin. Data were expressed as mean ± SE. Statistical significance was determined using ANOVA.
Results: The contraction induced by OA was 1.6 ± 0.12 g. Fentanyl concentration-dependently attenuated the OA-induced contraction of sensitized rat trachea. Tetrodotoxin attenuated the contraction induced by OA (0.90 ± 0.05 g), and fentanyl had no further effect on the contraction in the presence of tetrodotoxin (0.95 ± 0.05 g).
Discussion: Cholinergic nerves on smooth muscle mediate the contractile response to EFS in isolated trachea, and this response is abolished by tetrodotoxin (1). In the present study, when cholinergic nerves were blocked beforehand by tetrodotoxin, fentanyl had no effect on the OA-induced contraction. It suggests that the attenuation by fentanyl is the inhibition of cholinergic nerves on the smooth muscle.
Conclusion: Fentanyl attenuates the antigen-induced contractile responses of sensitized rat trachea. This mechanism involved is the inhibition of cholinergic nerves on the smooth muscle.
References:
1) Anesthesiology 53:93-100, 1980.
2) British J. Pharmacology 126:312-316, 1999.



Effect of fentanyl on the OA (50 μg/ml) -induced contraction of the sensitized rat tracheal rings. n = 6, mean ± SE, * $P < 0.001$, vs Control.

S-371.

THE ROLE OF CYCLOOXYGENASE IN THE FELINE PULMONARY VASCULAR BED

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Introduction: Although there are extensive data on the roles of cyclooxygenase 1 and cyclooxygenase 2 enzymes in temperature, coagulation, and inflammatory modulation, there is little, if anything, known of the function of these enzymes in regulating tone in the pulmonary vasculature. Therefore, the purpose of this investigation was to elucidate the roles of cyclooxygenase 1 and 2 in the feline pulmonary vascular bed.
Methods: In a university research laboratory and in separate experiments, the effects of arachidonic acid, prostaglandin E1, the thromboxane mimic U46619, angiotensin II, and norepinephrine, were analyzed before and after administration of selective cyclooxygenase 1 and 2 inhibitors.
Design: Prospective vehicle controlled study
Subjects: Intact chest preparation; adult mongrel cats
Results: In the first part of our experiments, Western blot analysis demonstrated cyclooxygenase 1 and 2 protein expression. Under constant flow conditions, lobar arterial perfusion pressure and systemic pressure were continuously monitored, electronically averaged, and permanently recorded. In the isolated left lower lobe of the feline pulmonary vascular bed under low tone conditions, arachidonic acid, prostaglandin E1, the thromboxane mimic U46619, angiotensin II, and norepinephrine induced a dose-dependent vasoconstrictor response. After either administration of the cyclooxygenase 1 inhibitor SC 560, or the cyclooxygenase 2 inhibitor nimesulide, arachidonic acid-induced vasopressor responses were significantly attenuated while the prostaglandin E1, U46619, angiotensin II, and norepinephrine-induced vasopressor responses were not significantly altered.
Conclusion and Discussion: The results of the present study suggest that arachidonic acid has potent vasopressor activity in the feline pulmonary vascular bed and that this response is mediated or modulated by both a cyclooxygenase 1 and cyclooxygenase 2 sensitive pathway. The cyclooxygenase 1 and cyclooxygenase 2 enzymes have different characteristics. Cyclooxygenase 1 is constitutive, it synthesizes prostanoids that mediate homeostatic functions, and is especially important in the kidney, gastric mucosa, platelets, and vascular endothelium.[1] Cyclooxygenase 2 is inducible (in most tissues), synthesizes prostanoids that mediate inflammation, pain, and fever, and is induced mainly at sites of inflammation by cytokines.[1] However, cyclooxygenase 2 is also constitutively expressed, primarily in the brain and kidney.[1] Future investigation is necessary to better elucidate the roles of cyclooxygenase 1, cyclooxygenase 2, and arachidonic acid in the human pulmonary vascular bed as they pertain to the complex pathophysiological conditions associated with pulmonary hypertension.
Reference:
[1] DuBois RN, et al. *FASEB J*. 1998;12:1063-1073.

S-372.

ANTINOCICEPTIVE EFFECTS OF DEXMEDETOMIDINE IN THE CONTROL OF INFLAMMATORY PAIN

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Introduction: Dexmedetomidine is a novel alpha2-adrenoceptor agonist, which is 8 fold more selectivefor this receptor than clonidine. Recently some studies suggest that dexemedetomedine may be useful in anesthesia for its sedative and analgesic effects without induce significant respiratory and cardiac depressions. The mechanism underlying the analgesic effect of dexmedetomidine remains uncertain. It is known that the activation of alpha2-adrenoceptor releases nitric oxide (NO) from endothelial cells. But the mechanisms involved in the antinociceptive effect of dexmedetomidine are not completely understood.
Objective: The main objective of the present study is to investigate the antinociceptive effect of dexmedetomidine in two different model of pain. We also evaluated if the antinociceptive effect of dexmedetomidine is dissociated from its sedative effects, and the possible participation of NO-cGMP pathways in this effect.
Methods: Thermal sensitivity was determined using latency to withdrawal of the hind paw from radiant heat in Wistar male rats. The acid acetic writhing test was used to evaluate the antinociceptive effect of dexmedetomidine on inflammatory pain in male Swiss mice. Dexmedetomidine was intraperitoneally (i.p.) injected at the doses of 10, 30 and 50 mcg/kg, in the hot plate model, and the latency either to forepaw licking or to jumping was recorded by means of an electronic timer started and stopped by a foot switch. In the writhing test, dexmedetomidine (0.5 to 5.0 µg/kg, i.v.) were administrated 5 min before the acid acetic 0.7% (10 ml/kg), and after 5 min the Stretching movements, consisting of arching of the back, development of tension in the abdominal muscles, elongation of the body and extension of forelimbs, were counted during 10 min. The doses of dexmedetomedine used in the present study were deprived of sedative effects as previously accessed by rota rods test.
Results: Dexmedetomidine had no analgesic activity in the hot-plate test in the doses used in this study. In the other hand, dexmedetomidine attenuated the writhing response induced by acetic acid in mice in the doses of 2 and 5 µg/kg.
Conclusions: Dexmedetomidine showed a potent analgesic effect in mice submitted to a classical model of inflammatory pain in mice, the precise mechanism this specific antinociceptive effect are under investigation in our laboratory.

S-373.

ISOFLURANE ELEVATES INTRACELLULAR CALCIUM IN BOVINE CHROMAFFIN CELLS VIA A MECHANISM THAT IS SOMEWHAT DIFFERENT THAN THAT OF ETOMIDATE

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Introduction: GABA is the primary inhibitory neurotransmitter in the adult brain. Chromaffin cells in adrenal medulla are known to express functional $GABA_A$ receptors with properties similar to their neuronal counterparts; these $GABA_A$ receptors play a role in the changes observed in catecholamine levels during anesthesia and surgery. We have shown that activation of the $GABA_A$ receptors leads to cellular excitation in chromaffin cells due to the depolarized anion equilibrium potential resulting from the absence of the K^+/Cl^- co-transporter [1]. Clinically relevant concentrations of etomidate, an intravenous anesthetic agent, directly activated $GABA_A$ receptors and depolarized chromaffin cells. This depolarization activated voltage-dependent Ca^{2+} channels thereby stimulating catecholamine release[2]. Our goal was to determine whether isoflurane, an inhalational agent, mimicked this response and to explore the functional consequences of this activation.
Methods: Imaging experiments with the Ca^{2+}-indicator dye fura-2 was used to monitor $[Ca^{2+}]_i$. Bovine adrenal chromaffin cells were superfused with a variety of drugs to determine their effects on $[Ca^{2+}]_i$.
Results: Isoflurane elevated $[Ca^{2+}]_i$ in chromaffin cells at clinically relevant concentrations (0.3 to 2 mM). Removal of extracellular Ca^{2+} or blockade of voltage-dependent Ca^{2+} channels prevented the elevation of $[Ca^{2+}]_i$ by isoflurane. Bumetanide, an Na^+-K^+-$2Cl^-$ co-transporter blocker, decreased the elevation of $[Ca^{2+}]_i$ by isoflurane. Unlike etomidate, the elevation of $[Ca^{2+}]_i$ by isoflurane was only partially blocked by selective $GABA_A$ antagonist bicuculline (100 µM). *In vivo,* chromaffin cells are activated by ACh released by splanchnic neurons, which induces catecholamine release. When isoflurane was co-applied with ACh or nicotine, isoflurane significantly reduced the ACh- or nicotine-mediated responses.
Conclusions: Our data indicate that isoflurane directly activates $GABA_A$ receptors and depolarizes chromaffin cells. This depolarization activates voltage-dependent Ca^{2+} channels, which stimulates catecholamine release. The underlying mechanism is somewhat different from that of etomidate since bicuculline only partially blocks the actions of isoflurane but it completely blocks the actions of etomidate. Our data suggest that circulating catecholamines may be elevated when isoflurane is applied. However, unlike etomidate and $GABA_A$ agonists, isoflurane reduces the ACh-induced elevation of $[Ca^{2+}]_i$ in chromaffin cells. These results suggest that isoflurane may alter catecholamine secretion in chromaffin cells. During surgery, surgical stimulation will increase sympathetic discharge, resulting in an increase in catecholamine release mediated by ACh. Isoflurane may regulate ACh's actions in chromaffin cells.

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(This work was in part supported by the grant from the Brain Research Foundation of the University of Chicago to Z Xie).

S-374.

EFFECTS OF TOTAL INTRAVENOUS ANAESTHESIA (TIVA) ON THE CYTOKINE BALANCE DURING MINIMAL SURGICAL STRESS PROCEDURES: A COMPARISON BETWEEN SCHISTOSOMAL AND NON-SCHISTOSOMAL PATIENTS

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Introduction: The postoperative immunosuppression is a combined result of surgery, stress and anesthesia[1]. In health, there is equilibrium between pro- and anti-inflammatory cytokines called the cytokine balance. The choice of the anesthetics may modify it [2]. The liver is a principal site of cytokine synthesis and clearance. Schistosomiasis *mansoni* is a disease which is accompanied by disturbances in cytokine levels and immune system secondary to hepatic affection [3]. The aim of our work is to compare the cytokine balance between normal and schistosomal patients using TIVA during urosurgical endoscopic procedures.
Methods: This study was conducted on 20 male patients (ASA class I-II), admitted at the Urology Department, Theodor Bilharz Research Institute. Patients were divided into two groups of 10 patients each: control group and schistosomal group. Anesthesia was induced and maintained with propofol-sufentanil. Four venous blood samples were obtained: before induction of anesthesia, fifteen minutes after induction before and start of the procedure, one hour after anesthesia and 24 hours afterwards. Specific estimation of the following parameters was done: Interleukin 1- beta (IL-1β), Tumor necrosis factor alpha (TNF-α), Interleukin-8 (IL-8), Interferon gamma (IFN-γ), Interleukin-1 receptor antagonist (IL1-ra), TNF binding protein (TNF BP-1), cortisol and prolactin.
Results: IL-1β showed a statistically significant increase after 24 hours in the schistosomal group compared to pre-induction level as well as in comparison with the control group ($p < 0.01$). TNF-α showed a statistically significant decrease 15 min. and 1 hour after anesthesia in comparison to the 24 hrs sample ($p < 0.05$) in the schistosomal group. IL-8 and IFN-γ did not show any statistically significant change. IL-Ira and TNF BP-1 showed a highly statistically significant rise 24 hours after anesthesia in comparison to all previous samples in both groups. No statistically significant difference was present within both groups as regards the cortisol level. Serum prolactin was highly elevated ($p < 0.001$) 15 min. and 1 hour after anesthesia in both groups, yet being still in the clinically acceptable range. We found a positive correlation between TNF-α with its antagonist TNF BP-1 by 15 minutes and 24 hours in the control group also between IL-1β and its antagonist IL1-ra in the schistosomal group at 15 minutes and 1 hr.
Discussion: This study shows that anesthetics probably seem to have an immunomodulatory response on their own, and the choice of the drug has substantial implications on the patient's outcome after surgery. The use of TIVA with propofol might offer a better chance for patients with neoplastic, septic or immunocompromised conditions such as schistosomiasis.
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S-375.

EFFECT OF ISOFLURANE ANESTHESIA ON PERIOPERATIVE CSF PROSTAGLANDIN E2 (PGE2) IN THE RAT

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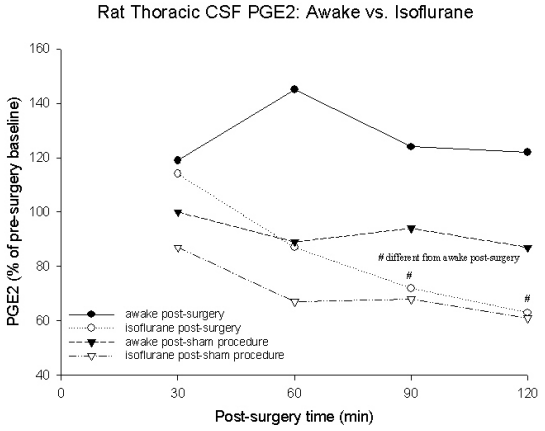
Introduction: In cats, pentobarbital anesthesia reduces prostaglandin E2 (PGE2) in cisternal cerebrospinal fluid (CSF) (J Neurochem 1984;43:1642). Both ether and isoflurane anesthesia reduce PGE2 in rat brain (Agressologie 1989;30:473; Can J Anesthes 1995;42:1031). However, it is not known how general anesthetics affect PGE2 concentrations during and immediately after surgery. Using a rat model of thoracic muscle incision, we monitored thoracic CSF PGE2 during and after surgery in awake rats and in rats remaining anesthetized with isoflurane after surgery.
Methods: With animal care committee approval, 300-350 g male Sprague-Dawley rats (n=5/group) were anesthetized with 1.5% isoflurane and a microdialysis loop catheter (Marsala et al, J Neurosci Meth 1995;62:43-53) implanted in the thoracic CSF space (via the cisterna magna). Following 7 days recovery, baseline microdialysis fluid was collected at 30 min intervals using Ringer's solution infused through the catheter at 2.5 µL/min. Animals were then anesthetized for 30 min with 1.5% isoflurane and an incision made in the superficial and deep left thoracic muscles (excluding intercostals) overlying the 3rd to 7th ribs. Microdialysis fluid collection continued during surgery and for 90 min after the end of surgery in awake animals or animals continuing to receive 0.8% isoflurane. Sham unoperated animals were also anesthetized for 30 min (equivalent to surgery duration) and were awake or on 0.8% isoflurane for 90 min afterwards. Dialysate samples were frozen immediately after collection, and PGE2 was assayed by ELISA. The PGE2 values over time were compared between drug groups using repeated measures ANOVA.
Results: In animals who received isoflurane only during thoracic surgical incision, CSF PGE2 increased during surgery and in the postsurgical period ($p=0.042$) compared to sham unoperated controls (Figure). In operated animals maintained on isoflurane, CSF PGE2 concentrations decreased over the 90 min postsurgical period compared to awake operated animals ($p=0.030$).
Discussion: Surgical thoracic muscle incision produces an increase in CSF PGE2, which is suppressed by isoflurane anesthesia. Although the results suggest that central inflammatory changes associated with surgery may be influenced by isoflurane anesthesia, it is still not known what the effect would be with other general anesthetics or spinal anesthesia. Such information is important when interpreting data from studies evaluating the effects of interventions to modulate the inflammatory response during surgery.



S-376.

WITHDREW

S-377.

WITHDREW

S-378.

DECREASED PH AND LIDOCAINE ARE PREREQUISITE FOR EMULSION INSTABILITY OF PROPOFOL-LIDOCAINE MIXTURE

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INTRODUCTION: A previous study has demonstrated time-dependent, physicochemical instability of propofol-lidocaine (P-L) mixture, which is frequently used clinically to alleviate pain associated with IV injection (1). Although *p*H value of such mixture is reported to be less than propofol alone (2), effects of decreased *p*H on emulsion stability remains undetermined. This study was designed to determine whether the mechanism for emulsion instability of P-L mixture is attributed to reduced *p*H, lidocaine or both.
METHODS: 1% propofol 20 mL (Diprivan™, AstrtaZeneca, Osaka, Japan) was mixed with 2% lidocaine hydrochloride 2 mL (Xylocaine™, AstrtaZeneca, Osaka, Japan). In a separate mixture of the same contents, titration was performed with sodium hydroxide (NaOH) to achieve a similar *p*H to that of 1% propofol alone (*p*H7.9). Lastly, hydrochloric acid (HCl) was mixed with 1% propofol to obtain a *p*H value similar to that of the P-L mixture (*p*H6.2). The *p*H values of these preparations and 1% propofol alone (n=6 each) were determined by a *p*H meter, and, propofol concentrations were measured by gas chromatography (GC) at times 0 and 24 h after preparation. Furthermore, lidocaine concentrations were determined in the aqueous phase of the P-L mixture with or without NaOH by equilibrium dialysis at time 24 h (n=5). All data are expressed as mean±SD, and paired or unpaired *t*-tests were used for statistical analysis. A *P* value less than 0.05 was considered to be significant.
RESULTS: A *p*H value in the mixture with 40 mg lidocaine was lower than that of 1% propofol alone, as shown in table 1. Propofol concentration in the mixture decreased significantly at time 24 h (71.0±1.7%) compared with time 0 (100%). However, P-L mixture with NaOH (*p*H7.9) and propofol with the addition of HCl (*p*H6.2) were macroscopically stable and their propofol concentrations were unchanged over time. Lidocaine concentration in the aqueous phase of the mixture with NaOH was significantly less than that without titration (Table 1).
Table 1

	*p*H	Propofol at 24 h (%)	Lidocaine in aqueous phase (mg / mL)
P-L	6.18±0.03	71.0±1.7	1.70±0.06
P-L+NaOH	7.71±0.01	100.9±2.1	0.53±0.01
P+HCl	6.21±0.04	100.2±2.8	-
P	7.88±0.15	97.2±2.2	-

CONCLUSIONS: These results suggest that both decreased *p*H and lidocaine greater than a certain concentration in the aqueous phase are prerequisite for emulsion instability of the P-L mixture.
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S-379.

THE EFFECTS OF PHOSPHODIESTERASE-III INHIBITORS ON SEVOFLURANE-INDUCED IMPAIRMENT OF RAT DIAPHRAGMATIC FUNCTION

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Introduction: Diaphragmatic contractile dysfunction is thought to contribute to acute respiratory failure. Several animal in vivo studies have demonstrated that volatile anesthetics cause diaphragmatic dysfunction using a whole body model (1). The first aim of the current study was to compare the impairing effect of halothane and sevoflurane on diaphragmatic contractile functions under unfatigued and fatigued conditions using rat isolated muscle strips. Cyclic adenosine monophosphate (cAMP)-elevating agents (ex. dopamine, dobutamine, isoproterenol) have been shown to increase diaphragmatic contractility (2). The second purpose of the current study was to determine whether milrinone and olprinone, phosphodiesterase-III inhibitors (cAMP elevating drugs), can improve sevoflurane-induced impairment of diaphragmatic contractile function.
Methods: After approval of the institutional animal care review board, diaphragmatic twitch characteristics and tetanic contractions were measured before and after muscle fatigue, which was induced by repetitive tetanic contraction with or without exposure to halothane (1-3 MAC) or sevoflurane (1-3 MAC), according to experimental protocols described previously (3). Disphragmatic functions were further assessed with exposure to 3 MAC sevoflurane in the presence and absence of milrinone (1.5 microg/mL), or olprinone (0.02 microg/mL). The cAMP concentrations in the fatigued diaphragm exposed to sevoflurane in the presence of milrinone or olprinone were also measured. Data were statistically analyzed using ANOVA followed by Dunnet test or using repeated-measures ANOVA. $P < 0.05$ was deemed statistically significant.
Results: Halothane (1-3 MAC) or sevoflurane (1-2 MAC) did not induce a direct inotropic effect under unfatigued and fatigued conditions. Sevoflurane at 3 MAC enhanced fatigue-induced impairment of twitch and tetanic tensions. Clinically relevant concentrations of olprinone but not milrinone improved the sevoflurane-induced augmentation, accomapnied by restoration of diaphragmatic cAMP levels.
Discussion: Although we are unable to give satisfactory explanation for additive effect of fatigue and sevoflurane on diaphragmatic contractile dysfunction, the free radical-producing capacity of sevoflurane may contribute to sevoflurane-intensified impairment of contractility after fatigue. Accumulation of cAMP is probably involved in the positive inotropic effect on the fatigued diaphragm via activation of calcium ion pumps on sarcoplasmic reticulum, an increase in the inward calcium ion current, alteration of intracellular calcium ion exchange, sodium-potassium transportation, and myosin phosphorylation .
Conclusion: Our findings suggest that sevoflurane has a greater decreasing effect on diaphragmatic contractility after fatigue than halothane, and that clinical dose of olprinone surmounts the disadvantage of sevoflurane in various conditions where diaphragmatic fatigue is predisposed. However, we are unable to simply extrapolate our in vitro findings to the clinical settings.
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S-380.

EFFECTS AND MECHANISM OF ACTION OF VOLATILE ANAESTHETIC AGENTS ON THE FOETAL-PLACENTAL VASCULATURE

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Objectives: This study examined the effects of volatile anaesthetic agents on isometric tension development and both direct and NO-mediated relaxation in isolated human chorionic plate arterial rings, in response to the vasoconstrictor prostaglandin F2α and the endothelium-independent vasodilator sodium nitroprusside.
Setting: Anaesthesia Research laboratory within a University Department.
Subjects: Quadruplicate *ex vivo* human chorionic plate arterial rings.
Interventions: ***Series I*** examined the effects for isoflurane on constriction produced by prostaglandin F2α, and on endothelium-independent vasodilation produced by sodium nitroprusside. ***Series II*** examined the effects for halothane on constriction produced by prostaglandin F2α, and on endothelium-independent vasodilation produced by sodium nitroprusside. ***Series III*** examined the effects for sevoflurane on constriction produced by prostaglandin F2α, and on endothelium-independent vasodilation produced by sodium nitroprusside. ***Series IV*** examined the potential for inhibition of NO synthesis inhibitor L-NAME to attenuate sevoflurane induces chorionic plate arterial vasodilation
Measurements and Main Results: Neither isoflurane nor halothane altered prostaglandin F2α mediated vasoconstriction or NO-mediated vasodilation. Isoflurane did not directly vasodilate pre-constricted human chorionic plate arterial rings. In contrast, halothane did directly vasodilate pre-constricted human chorionic plate arterial rings. Sevoflurane attenuated Prostaglandin F2α mediated vasoconstriction, but did not alter nitroprusside mediated vasodilation. Sevoflurane directly vasodilated pre-constricted human chorionic plate arterial rings. Inhibition of NO production did not alter the vasodilator activity of sevoflurane.
Conclusions: Isoflurane does not appear to have significant vasoactive effects in the foetal-placental circulation. In contrast, sevoflurane and halothane cause potent placental arterial vasodilation. The altered vasorelaxation induced by sevoflurane appears to be independent of nitric oxide.

S-381.

WITHDREW

S-382.

EFFECTS OF ONDANSETRON ON THE ROCURONIUM-INDUCED PARTIAL NEUROMUSCULAR BLOCKADE

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Introduction: Ondansetron, a 5-HT_3 receptor antagonist, is widely used for the prevention of postoperative nausea and vomiting. Many drugs interact with neuromuscular blocking drugs and often enhance the induced block. There are several studies about the interaction of 5-HT receptor and smooth muscle. It may also blocks the nicotinic acetylcholine receptor based on other animal study. This study was designed to investigate the effects of ondansetron on rocuronium-induced neuromuscular blockade on the rat hemidiaphragm preparation.
Methods: After institutional ethical committee approval. Male Sprague-Dawley rats (200 g, n=40) were randomly allocated into control group (C, n=10), ondansetron 1 μg/ml group (O_1 n=10), 10 μg/ml group (O_{10} n=10), 100 μg/ml group (O_{100} n=10). Animals were anesthetized with 40 mg/kg of thiopental sodium intraperitoneally and the hemidiaphragm with phrenic nerve was dissected and mounted in a bath containing 100 ml of oxygenated Krebs' solution at 32°C. The phrenic nerve was stimulated at the supramaximal intensity by stimulator through isolation unit and twitch responses were measured by precalibrated force displacement transducer and recorded. After stabilization of twitch response, 300 μg of rocuronium was added to the solution. When stable 3-5 twitches were obtained after the first dose, each dose of ondansetron was administered.
Results: There was no difference between C, O_1, O_{10} and O_{100}.
Discussion: The potency of rocuronium is not increased by usual dose of ondansetron in clinical situation. But used in conjunction with other muscle relaxant potentiating drugs or used in high dose, ondansetron may affect neuromuscular transmission.

S-383.

THE EFFECTS OF LEVETIRACETAM ON ANAESTHETIC-INDUCED HYPERALGESIA IN THE RAT

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Introduction:
Excitation, commonly observed during emergence from anesthesia, may be associated with delirium, seizures, cardiovascular instability and hyperalgesia. The mechanism of anesthetic excitation is not well understood and at present, therapy is limited to managing the undesirable manifestations. Preventative therapy would potentially offer a major advantage over current clinical management.
Levetiracetam, a novel antiepileptic pyrrolidone, presents a pharmacological profile that may be suitable for blunting the excitatory stage of anesthesia. Here we have examined the influence of pretreatment with levetiracetam on the enhancement of nociceptive reflexes induced with sedative doses of pentobarbital, propofol, and midazolam.
Methods:
Resting measurements of the latency to hindpaw withdrawal (PWL) from noxious heat were made and then repeated after intraperitoneal (i.p.) injection of saline or one of three doses of levetiracetam (100, 200, 500 mg/kg). Nociceptive withdrawal reflexes were then enhanced by i.p. injection of pentobarbital (30 mg/kg), propofol (30 mg/kg), or midazolam (1.9 mg/kg). PWL was measured by an observer blinded to the levetiracetam treatment, every ten minutes, starting 5 minutes after the sedative injection, until 65 minutes had elapsed. Sedation scores and the presence or absence of the righting reflex were recorded after each PWL measurement. The values for each animal were averaged over time. For each sedative/anesthetic, levetiracetam treatment groups were compared by ANOVA with the saline controls, applying Dunn's correction for multiple comparisons.
Results:
Levetiracetam did not alter PWL in the unsedated animals (P=0.11) or influence the sedation scores or righting reflex profiles after anesthetic drug administration. The three anesthetic/sedative drugs reduced nociceptive reflex thresholds by 20-30% of control values. Levetiracetam (500 mg/kg) reduced the hyperreflexia associated with pentobarbital and propofol (PWL decreased 10% and 13% respectively; P<0.05). Despite levetiracetam pretreatment, midazolam was associated with a 23% decrease in PWL, not different from saline controls (P=0.33).
Discussion:
Levetiracetam blunted the hyperreflexia associated with pentobarbital and propofol without any demonstrable effects on pre-anesthetic nociceptive reflexes or depth of sedation. These results support further investigation into the potential role of levetiracetam in the prevention of drug-induced excitation.

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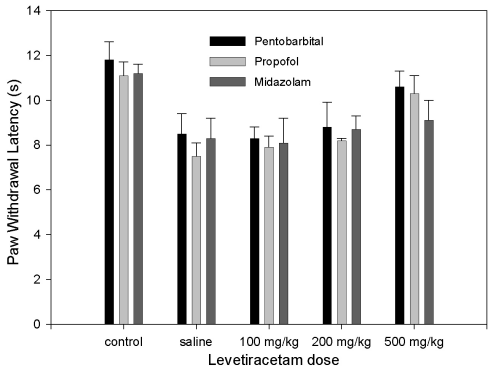

S-384.

LOCAL ANESTHETICS INHIBIT SIGNALING OF HUMAN NMDA RECEPTORS EXPRESSED RECOMBINANTLY IN *XENOPUS LAEVIS* OOCYTES VIA PROTEIN KINASE C

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Introduction: NMDA-receptor activation contributes to postoperative hyperalgesia. Studies in volunteers have shown that intravenous local anesthetics (LA) prevent the development of hyperalgesic pain states. One potential explanation for this beneficial effect is the inhibition of NMDA receptor activation. Therefore, we studied the effects of LA on NMDA receptor function.
Methods. The human NR1A/NR2A NMDA receptor was expressed recombinantly in *Xenopus laevis* oocytes. Peak currents were measured by voltage clamp in Mg^{2+}- and Ca^{2+}-free, Ba^{2+}-containing Tyrode´s solution. Holding potential was -70 mV. Oocytes were stimulated with glutamate/glycine (at EC_{50}) with or without 10 min prior incubation in bupivacaine, levobupivacaine, S-(-)-ropivacaine, or lidocaine (all at 10^{-9} - 10^{-4} M), procaine (10^{-4} M), R-(+)- ropivacaine (10^{-4} M), QX314 (permanently charged, $5x10^{-4}$ M) extracellularly or intracellularly, or benzocaine (permanently uncharged, $5x\ 10^{-3}$ M). We also determined the effect of the protein kinase C (PKC) inhibitors chelerythrine ($5x10^{-5}$ M), Ro 31-8220 (10^{-7}M), calphostin C ($3x10^{-6}$ M) and the effect of PKC activation with phorbolester (10^{-6} M).
Results. Non-injected oocytes were unresponsive to agonist application, but oocytes expressing NMDA receptors responded with inward currents. All LA inhibited responses to agonists concentration-dependently. The inhibition was reversible and stereoselective. Intracellular QX314 inhibited responses to 66% of control, but extracellular QX314 was without effect. Benzocaine reduced responses to 33% of control. PKC inhibitors had no additional inhibitory effect above to that of bupivacaine. There was no stimulating effect of PKC activator phorbolester when incubated with bupivacaine
Discussion. All tested LA inhibited concentration-dependently the activation of human NMDA receptors. This effect might play a role in the reduced hyperalgesia and opiate tolerance observed after systemic administration of LA. The effect is independent of the charge of LA; site of action is intracellular. The mechanism of action seems to be via inhibition of PKC.
Supported in part by the 2004 Ben Covino Reserach Award, sponsored by AstraZeneca, Sweden

Pharmacology - Clinical

S-385.

EFFECT OF LOW-DOSE DROPERIDOL ON THE QT INTERVAL DURING GENERAL ANESTHESIA: A PLACEBO-CONTROLLED STUDY

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Background: An FDA-imposed "black box" warning mandates additional ECG monitoring when droperidol is used for antiemetic prophylaxis because of its alleged potential for producing QT prolongation. However, the effects of low-dose droperidol on the QT interval have not been previously studied. Therefore, we designed a randomized, double-blind placebo-controlled study to evaluate the effect of small-doses droperidol (0.625 and 1.25 mg IV) on the QT interval when used for antiemetic prophylaxis during general anesthesia.
Methods: Sixty ASA 1-2 outpatients undergoing otolaryngologic procedures with a standardized general anesthetic technique were enrolled in this IRB-approved study. After anesthetic induction and prior to the surgical incision, patients were administered either saline, droperidol 0.625, or droperidol 1.25 mg IV in a total volume of 2 ml. A standard ECG lead II was recorded immediately before and every minute after the injection of the study medication during a 10-min observation period. The QTc (QT interval corrected for heart rate) was evaluated from the recorded ECG strips. Any abnormal heart beats or arrhythmias during the operation or the subsequent 3 h monitoring interval were also noted.
Results: Droperidol, 0.625 and 1.25 mg IV, prolonged the QT interval by an average of 15±40 and 22±41 msec, respectively (vs 12±35 msec with saline) at 3-6 min following IV administration during general anesthesia. There were no statistically-significant differences among the three study groups with respect to the mean QTc prolongation >10% of the baseline value. However, the two patients in each of the droperidol groups had QTc prolongation lasting >60 msec during the 10 min observation period. Importantly, there were no ectopic heart beats observed on the ECG rhythm strip during the 3 h observation period.

	Saline	Droperidol 0.625 mg	Droperidol 1.25 mg
Number (n)	20	20	20
Age (yr)	47±14	45±16	45±15
Weight (kg)	82±22	81±16	77±21
QT interval before injection (msec)	406±28	400±56	396±46
QTc before injection (msec)	439±28	435±27	426±47
QTc at 10 min after injection (msec)	446±35	449±40	444±52
QTc ≤ baseline at 10 min (n, %)	10, 50	6, 30	8, 40
QTc prolongation 0-10% at 10 min (n, %)	8, 40	11, 55	10, 50
QTc prolongation 10-25% at 10 min (n, %)	2, 10	3, 15	2, 10
Mean maximum Δ QT_c (msec)‡	12±35	15±40	22±41
Maximum QT_c prolongation (msec)	58	120	133
ECG rhythm disturbances (n)	0	0	0

Discussion: Use of droperidol, 0.625-1.25 mg IV, for antiemetic prophylaxis during general anesthesia was associated with a small but clinically-insignificant prolongation of the QTc interval. Furthermore, there was no evidence of any cardiac rhythm disturbances during or after surgery.

S-386.

WITHDREW

S-387.

EFFECTS OF DEXMEDETOMIDINE INFUSION FOR SEDATION IN PEDIATRIC BURN PATIENTS

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Introduction: Dexmedetomidine (DEX) is a highly selective alpha-2 agonist which provides sedation and analgesia in critically ill patients. Advantages of DEX include favorable pharmacokinetics, attenuation of sympathetic response, and lack of side effects seen with other ICU sedation regimens. A potential disadvantage of alpha-2 agonists is hyperglycemia resulting from inhibition of insulin secretion. We report on dose requirements, tachyphylaxis, drug withdrawal, respiratory depression, and blood glucose trends in a group of pediatric ICU burn patients on DEX infusion.
Methods: We performed a retrospective chart review of twenty one patients (13 male, 8 female) placed on DEX infusion because of failure achieve adequate sedation with our standard regimen of opioids and benzodiazepines. The mean (±SEM) age was 4.9± 1.2 years (range 0.7-17), burn size was 32.0± 4.7% TBSA (range 6-94), and weight was 23.4± 4.3kg (range 10-72). DEX infusion was initiated at 0.2 mcg/kg/hr; fifteen patients received loading dose of 1 mcg/kg. DEX was titrated to achieve adequate sedation. Blood glucose levels on DEX infusion were compared to levels off DEX infusion (1 patient on insulin infusion was excluded).
Results: The average duration of DEX infusion was 9.9± 1.2 days (range 1-21). The dose ranged from 0.2-2.4 mcg/kg/hr. The mean maximum dose was 1.1± 0.1 mcg/kg/hr; mean dose was 0.5± 0.2 mcg/kg/hr. Level of sedation was rated by nursing staff as "good" or "very good" in all patients on DEX infusions. Dose requirements decreased over time for all patients. Infusions were weaned over 12-24 hours without evidence of rebound hypertension. Of the fourteen patients receiving ventilatory support at the initiation of DEX infusion, four were extubated and the rest were partially weaned during the infusion. Clinical evidence of respiratory depression was absent. Blood glucose levels averaged 121.2 mg/dl (range 99.9-146.4) while on DEX infusion and 117.1 mg/dl (range 98.3-149.3) while off.
Discussion: DEX infusion provided adequate sedation in our critically ill pediatric burn patients at a mean dose nearly 60% greater than the maximum dose of 0.7 mcg/kg/hr cited in the literature. However, there was no evidence of tachyphylaxis; dose requirements decreased rather than increased over time. A relatively rapid wean did not result in rebound hypertension, which can occur with discontinuation of clonidine. DEX is an alternative that lacks the respiratory depression associated with other ICU sedation regimens. Stimulation of alpha-2 receptors located on pancreatic beta cells is known to inhibit insulin secretion(1,2), and cause hyperglycemia which can have detrimental effects on critically ill patients (3). DEX infusion did not appear to significantly affect blood sugar levels in our patients despite high dose and duration of infusion.
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S-388.

THE EFFECT OF LOW DOSE DEXMEDETOMIDINE ON SEDATION AND INTERNAL CAROTID ARTERY BLOOD FLOW

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Introduction: Dexmedetomidine(Dex) is a new alpha2-agonist. This study was to evaluate the effect of low dose Dex on sedation and internal carotid artery blood flow in Chinese patients without cardiovascular disease.
Methods: Thirty young healthy adults (16 male and 15 female) were randomly divided into 2 equal groups, In Group D (n=15), a loading dose of dexmedetomidine 0.4 μg/kg i.v. was given in 5 minutes followed by intravenous infusion of dexmedetomidine 0.4μg/kg /h over 30 minutes while in Group C (n=15), equal volume of normal saline was given as control. The MAP, HR, SpO2, end-tidal PCO_2, Bispectral EEG Index (BIS), Auditory Evoked Potential Index (AAI), OAA/S scale, Ramsay sedation scale were monitored before and continuously during Dex infusion. In addition, the diameter, blood flow velocity, blood flow of common carotid artery and internal carotid artery were measured with AU4 color Doppler. The above parameters were recorded at the time before dexmedetomidine infusion (T_0), after loading dose (T_1), and at 5, 10, 15, 20, 25, and 30 minutes ($T_{2\sim6}$) after continuous infusion.
Results: Demographic data of the patients in both groups were comparable. After the loading dose and during continuous infusion of dexmedetomidine BIS and AAI decreased by 17.0%~30.9% and 30.1%~43.4% (P<0.05) compared with baseline value respectively, the OAA/S and Ramsay scale also decreased significantly (P<0.05), which showed an obvious sedative effects of Dex. The blood flow velocity, blood flow of common carotid artery showed an initial increase (P<0.05) then reutrned to normal in 15 minutes after the loading dose of Dex The blood flow velocity and blood flow of the internal carotid artery decreased by 17%~21% (P<0.05~0.01) at T_5 and T_6 compare with T_0. Dexmedetomidine infusion also produced HR and MAP decrease of 15.2% and 19.8% respectively (P<0.05),which however were not clinically significant. No respiratory depression was observed.
Conclusion: Low dose dexmedetomidine (0.4μg/kg loading dose followed by 0.4μg/kg/h continuous infusion) produces sedation accompanied by decrease of the blood flow of the internal carotid artery in Chinese.

S-389.

THE OPTIMAL DOSAGE OF ALFENTANIL FOR ATTENUATING HEMODYNAMIC CHANGES DURING ENDOTRACHEAL INTUBATION

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Introduction: [1]Alfentanil is an opioid often used during direct laryngoscopy. [2]The various methods have been used to prevent or minimize the increase of blood pressure and heart rate to endotracheal intubation. The purpose of this study was to investigate an optimal dosage of alfentanil for attenuating hemodynamic change.
Methods: Sixty patients aged 20-60 years, scheduled for elective surgery requiring endotracheal intubation, were assigned to four groups of fifeen. Anesthesia was intravenously induced with propofol (2 mg/kg) followed by vecuronium (0.1 mg/kg), and 2 minutes later (at 1 minute before intubation), group 1 (control group) received no alfentanil, and groups 2, 3, and 4 received 10, 20, or 30μg / kg alfentanil, respectively. The hemodynamic changes (systolic blood pressure, mean arterial blood pressure, diastolic blood pressure and heart rate) were measured at preinduction, postinduction (immediately before intubation), intubation, and postintubation (1 minute, 2 minute, 3 minute, 4 minute, and 5 minute after intubation).
Results: The hemodynamic changes in the group 2, 3, and 4 were significantly lower than in the control group 1 ($p<0.05$), but the incidence of hypertension was higher in the group 1 and 2 at 1, 2, and 3 minutes after intubation ($p<0.05$). The incidence of bradycardia and hypotension was higher in the group 4 ($p<0.05$).
Discussion: In this study, the authors suggest that the recommended dosage of alfentanil for attenuating hemodynamic changes during endotracheal intubation is about 20μg / kg.
References:
[1] Anesthesia 2001; 56: 319-25
[2] Br J Anesth 1982; 54: 1185-9

S-390.

DEXMEDETOMIDINE SEDATION FOR AWAKE FIBEROPTIC INTUBATIONS

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Introduction: The rationale for intubation under topical anesthesia (awake intubation) is that it preserves the patency of the airway and the patient's drive to breathe where the ability to intubate and/or ventilate the patient after inducing pharmacologic apnea is uncertain. Nevertheless, some sedation is generally given to make the procedure easier for the patient and the anesthesiologist. The challenge is to give enough sedation to prevent unpleasant memories of the intubation without compromising respiratory function. The commonly used agents, benzodiazepines and narcotics, can cause significant respiratory depression. The alpha-2 agonist dexmedetomidine provides sedation without suppressing respiratory drive (1) making it an attractive agent for awake intubations. Two case reports of its use for awake fiberoptic intubations have been published (2,3). This study was undertaken to provide a reliable and reproducible technique for awake fiberoptic intubations using dexmedetomidine for sedation.
Methods: After IRB approval and informed consent seven patients underwent awake fiberoptic intubations. Premedication included midazolam (0.02 mg/kg), glycopyrrolate (0.2 mg), and fentanyl (0-1 mcg/kg). An infusion of dexmedetomidine was started in the holding area at 0.7 mcg/kg/hr. Topical anesthesia applied in the operating room included Hurricaine spray to the posterior oropharynx, 2% lidocaine gel to the base of the tongue, and transtracheal injection of 3-4 ml of 4% lidocaine. Fiberoptic intubation was then performed.
Results: The patients included four women and three men. The average weight was 113 kg (range 53-210 kg). Indications for awake intubation included a history of difficult intubation in two patients, severe cervical spine disease in three patients, and a combination of poor mouth opening/short thyromental distance and Mallampati class IV airways in two patients. The average time for intubation was 139 seconds (range 15-300 seconds), and all the intubations were successful on the first or second attempt. Blood pressure and heart rate varied less than 15% from baseline during and after the intubations. There were no instances of desaturation or the need for airway support. The average duration of dexmedetomidine infusion prior to intubation was 23 minutes (range 7-46 minutes). Six of the patients had no recall of the intubation, and the seventh patient did not consider the memory unpleasant. The average satisfaction score on a scale of one to ten was 8.9. All seven patients were willing to have the same procedure again if they needed to be intubated in the future.
Discussion: Dexmedetomidine is a useful sedative agent for awake intubations, providing excellent patient cooperation and satisfaction. Starting the infusion in the holding area induced adequate sedation without requiring a bolus dose of dexmedetomidine which has been associated with significant hemodynamic effects in previous studies.
References:
1. Anesthesiology 1992; 77:1125.
2. Can J Anesth 2003; 50:607.
3. J Clin Anesth 2003; 16:124.

S-391.

A NOVEL USE OF DEXMEDETOMIDINE: THYROPLASTY SURGERY

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Introduction: Laryngeal framework surgery (thyroplasty) restores phonation in patients who have unilateral vocal cord paralysis. A wedge-shaped silastic prosthesis is inserted into the thyroid ala on the affected side to medialize the paralyzed cord. The key to the procedure's success lies in the appropriate sizing and placement of the prosthesis[1]. The most effective way to ensure optimal post-operative phonation is to have the patient phonate intraoperatively after the prosthesis has been inserted so that necessary adjustments in prosthesis size and location can be made. Thus, the anesthetic goal is to provide a quiet operative field during the neck dissection that precedes the placement of the prosthesis, and then to have the patient awake and phonating for assessment of the repair. Previous reports have described multiple anesthetic techniques. These include straight local anesthesia[2], local with sedation[3] (such as midazolam with flumazenil reversal), and general anesthesia.[4] None of these choices is perfect, since local or local with sedation can leave the patient uncomfortable during the neck dissection, and the general anesthetic (and even the midazolam sedation) can leave the patient too drowsy to follow commands. We present our experience using dexmedetomidine for these procedures. This short-acting α_2 agonist provides adequate analgesia and anesthesia during the initial phase of the operation while allowing for a cooperative and comfortable patient when voice analysis is necessary.
Methods: Two patients underwent thyroplasty procedures using the following anesthetic technique: 2 mg of midazolam was given as a premedicant. In the operating room, infusions of dexmedetomidine (0.7 mcg/kg/hr) and propofol (100 mcg/kg/min) were started. No bolus of dexmedetomidine was given. The propofol was tapered off over ten minutes.
In the first case, an LMA was placed and the dexmedetomidine infusion was continued along with an amnestic (.5-.6 MAC) level of sevoflurane. Once the prosthesis was seated, the LMA was removed, and the dexmedetomidine infusion was decreased to 0.3 mcg/kg/hr. The patient phonated immediately upon command.
In the second case, the propofol was tapered off without LMA placement, and the patient was kept comfortable with the dexmedetomidine alone. Once the surgeon was ready to test phonation, the infusion was again decreased to 0.3 mcg/kg/hr. The patient followed commands immediately.
Discussion: Like the intraoperative wake-ups needed for some craniotomies and spinal instrumentations, thyroplasties require the patient to be comfortable during the initial dissection and awake and interactive when the repair is being evaluated. The rousable state of sedation in patients on dexmedetomidine infusions along with the analgesic properties of this drug make it a useful agent for these procedures.
References:
1. *Anaesthesia* 1998; 53:1199.
2. *J Laryngol Otol*. 1996; 110:111.
3. *Can J Anaesth* 1995; 42:813. 4. *Br J Anaesth* 2000; 85:547.

S-392.

TREATING PONV ONDANSTRON PROPHYLAXIS FAILURES: A COMPARISON OF REDOSING WITH ONDANSTRON VS. GRANISETRON

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Introduction:
Patients at risk for postoperative nausea and vomiting (PONV) are routinely given prophylactic treatment with a selective 5HT3 antagonist (1). Should prophylaxis fail, one option is the administration of a repeat dose of the same 5HT3 antagonist. However, it has been suggested that repeating the same 5HT3 antagonist for PONV may be no better than administering placebo(2).
In chemotherapy patients, crossover from ondansetron to granisetron has been shown to successfully alleviate chemotherapy induced nausea and vomiting (CINV) symptoms after ondansetron failure (3). The aim of this study was to determine if patients who experienced PONV despite prophylactic ondansetron for PONV would respond favorably to treatment with granisetron.
Methods:
After IRB approval and informed consent, 250 ASA I & II females ages 18 to 64, undergoing general anesthesia for surgery were enrolled in this three arm, prospective, double blind, randomized trial comparing ondansetron 4mg, granisetron 0.1mg, and granisetron 1.0mg for breakthrough PONV in patients who had received prophylactic ondansetron 4mg 30 minutes prior to extubation. If a patient had PONV within 4 hours, they were randomized and followed for 30 minutes. Randomized patients were classed into 3 outcome groups (Improved-no further treatment; Improved-further treatment needed and PONV not improved).
Results:
A total of 243 patients completed the study. 88 patients required PONV rescue (36.2%). 37 patients had vomiting (15.2%).
Groups were similar demographically. Patients with a history of PONV during prior surgeries benefited from repeat 5HT3 dosing ($p<.05$*), regardless of which drug was given as a second dose. There was no difference in the rescue rate between 0.1mg and 1.0mg of granisetron. Data for crossover are noted in Table 1.

Drug	Number Randomized (n)	*Improved-No further treatment	*Improved-Needed further Tx	*Failure
Ondansetron 4 mg	30	(17/30) 56.7%	(5/30) 16.7%	(8/30) 26.7%
Granisetron 1.0 mg	30	(18/30) 60.0%	(7/30) 23.3%	(5/30) 16.7%
Granisetron 0.1 mg	28	(19/28) 67.9%	(5/28) 17.9%	(4/28) 14.3%

Discussion:
While Kovac(2) found no benefit to repeating a 5HT3 antagonist we noted a statistically significant benefit for patients who had overall improvement (with and without further treatment) vs. failure ($p<0.05$*). This benefit was agent independent. Of note was that granisetron 0.1mg and 1.0mg appeared to have the same efficacy for rescue (post-hoc analysis).
While no clear benefit was noted for crossing over agents this study was powered as a pilot and would appear to justify a larger study.
References:
1. Anesthesia Analgesia Vol.72:751-5, **1991**.
2. Journal of Clinical Anesthesia Vol. 11,6;453-459, **1999**.
3. British Journal of Cancer Vol. 85:1099-1101, **2001.**

S-393.

EFFECT OF MULTIPLE DOSE ORAL CYCLOOXYGENASE-2 (COX-2) INHIBITOR ADMINISTRATION ON CENTRAL AND PERIPHERAL PROSTAGLANDIN E2 (PGE2) RESPONSE TO TOTAL HIP REPLACEMENT

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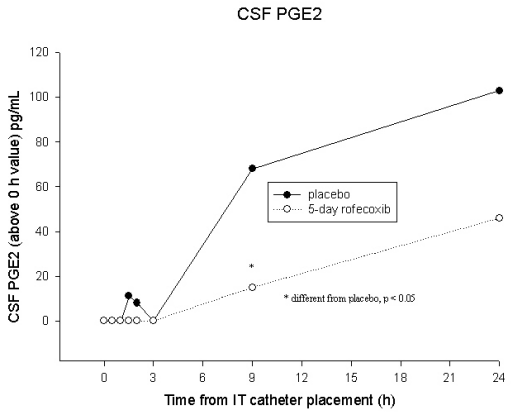
Introduction: Surgical trauma induces COX-2 upregulation and subsequent synthesis of prostaglandins that locally sensitize peripheral nociceptors and mediate central sensitization (Anesth Analg 1993;77:362). Recently, investigators have recognized cyclooxygenase-2 (COX-2) inhibition in the central nervous system as one component of the overall effect of COX-2 selective inhibitors in reducing pain (Nature 2001;410:425; Nature 2001;410:471). The objective of the present study is to determine if there is CSF and peripheral PGE2 upregulation during hip replacement surgery, and to evaluate the effect of oral COX-2 inhibitor administration as evidenced by PGE2 suppression.
Methods: Following IRB approval, patients were randomized to 2 groups (n=6/group). Group one received rofecoxib 50 mg PO each morning for 4 days prior to surgery and on the day of surgery 1-2 hr preoperative. Group two received placebo 50 mg PO each morning for 4 days prior to surgery and on the day of surgery 1-2 hr preoperative. Intrathecal catheters were placed prior to surgery, and fentanyl/ bupivacaine infused intrathecally during and after surgery. CSF, plasma and hip drain fluid were periodically collected for 24 hours after start of surgery. PGE2 concentrations were assayed using ELISA. Groups were compared with repeated-measures ANOVA.
Results: Administration of 50 mg rofecoxib for 5 consecutive days prior to surgery reduced CSF PGE2 at later times after surgery, compared to patients receiving placebo (Figure). There was no difference in CSF PGE2 between groups at 0 h (start of surgery). At 9 h from start of surgery, CSF PGE2 was not different from baseline level for the 5-day rofecoxib group (15 ± 20 pg/mL), while values increased by 68 ± 15 pg/mL for the placebo group. Hip drain fluid PGE2 was suppressed with 5-day rofecoxib. At 9 h, hip drain PGE2 was 34,500 ± 7175 pg/mL for the placebo group, but only 6,609 ± 1660 pg/mL for the 5-day group (p=0.006). Plasma PGE2 was insensitive to group, and was approximately 100-fold less than hip drain PGE2.
Discussion: Total hip arthroplasty increases PGE2 in hip drain fluid and CSF, and 5-day rofecoxib administration reduces hip drain (peripheral) and CSF (central) PGE2. These data indicate that perioperative oral dosing of the COX-2 inhibitor rofecoxib has both central and peripheral actions that may play a substantial role in affecting analgesia and other postoperative outcomes.



S-394.

GENDER DIFFERENCES IN THE ALTERATIONS OF ANALGSIC LEVEL WHEN RANITIDINE IS ADMINISTERED WITH MORPHINE

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Introduction: Morphine is metabolized to morphine-6-glucuronide (M6G) and morphine-3-glucuronide (M3G). M6G is a potent agonist and a contributor to the analgesia produced by morphine while M3G is inactive in humans. Since M6G contributes to the analgesic effect of morphine, we were interested in whether altering the amount of M6G produced in an individual will result in alterations in analgesia.
Methods: After institutional review board approval, 5 male subjects and 5 female subjects have been enrolled out of a planned 20 total subjects (10 male/ 10 female) within the age range of 18-40 in this two-period crossover study. During one study session, subjects receive 50 mg of ranitidine IV 30 minutes before the study session. Ranitidine has been shown in both in vitro and in vivo studies to inhibit the formation of M3G and to enhance the production of M6G.[1] This is followed by a target controlled infusion of morphine to achieve a fixed plasma concentration of 10 ng/mL of morphine, which is maintained for a period of 1 hour while assessments of subjects response to a noxious stimulus (pressure algometry) are made. The target concentration of morphine was increased to 50 ng/mL and held for 1 hour while the measurements are repeated. At the end of this session, measurements of response to stimuli and morphine and metabolite concentrations are made during the washout period. In the crossover session, each subject receives a saline infusion at the beginning of the study rather than the ranitidine dose. The target concentration levels and the effect measures are replicated in both sessions.
Results: The area under the algometry response curve (AUEC) for the first five male subjects showed an increased level of analgesia (greater AUEC) when ranitidine was administered prior to the morphine infusions in four out of the five males. The AUEC for the first five female subjects showed a decreased level of analgesia (smaller AUEC) when ranitidine was administered prior to morphine infusion. The one male subject who did not show the same result as the other males had a very low initial baseline algometry reading, which may have elevated his AUEC for the control period.
Discussion: The results indicate that administration of ranitidine produces an opposite effect on the level of analgesia experienced by men and women. The plasma concentration of morphine and its metabolites will be assessed by interaction modeling to discover whether this difference is due to alterations in these levels.
Reference:
1. Aasmundstad TA, Storset P. Human Exp Toxicol 1998; 17: 347-52.

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S-395.

RANDOMIZED, DOUBLE BLIND STUDY OF THE EFFECT OF INTRA-OPERATIVE HIGH DOSE REMIFENTANIL AND LOW DOSE NALAXONE ON POSTOPERATIVE MORPHINE REQUIREMENT

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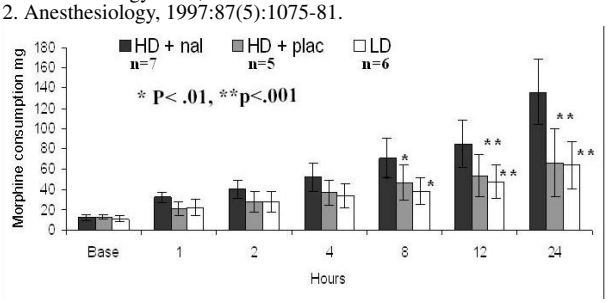
Introduction: Intraoperative high-dose opioid use increases the postoperative morphine usage. [1] In vitro work and animal studies have demonstrated that low dose antagonist reduces the development of tolerance possibly due to up-regulation of receptors. Further a clinical study demonstrated that low-dose naloxone infusion decreased postoperative morphine requirement.[2] We hypothesized that low dose bolus of naloxone can decrease the postoperative opiate requirement by producing up-regulation of receptors.
Objectives: 1.To establish the influence of intraoperative remifentanil infusion rate (high vs. low) on postoperative opiate requirements. **2**.To assess the effect of a low-dose naloxone bolus on post-operative opiate requirement in the high-dose remifentanil group.
Method: Patients 18-70 years of age undergoing elective abdominal hysterectomy were enrolled. The exclusion criteria were: BMI >35, ASA >3 and regular opioid use within past week. Eighteen consented patients were ramdomized to one of the groups: 1)Intraoperative low-dose remifentanil infusion (0.05µg/kg/min) (LD). 2) Intraoperative high-dose remifentanil (0.2µg/kg/min) and placebo at the end of surgery (HDP). 3) Intraoperative remifentanil high-dose (0.2 mcg/kg/min) and intravenous bolus of nalaxone 0.02 mcg/kg at the end of surgery (HDN). End of the surgery 7.5 mg of morphine was administered and Morphine PCA was commenced. Morphine consumption and VRS pain score were obtained at 1, 2, 4, 8, 12 and 24 hrs following surgery. Data was analyzed using MANCOVA, followed by ANCOVA at each time point with Tukey-Kramer adjusted p-value for post-hoc pairwise comparisons.

Results: The morphine consumption was significantly higher in HDN compared to the LD and HDP at 8, 12 and 24 hours. LD and HDN were not different. The morphine consumption at measured time points is expressed in the figure1. The p values represent comparison of HDN versus HDP and LD. The VRS was not different between the groups at any measurement points.
Discussion: Contrary to our hypothesis, extremely low-dose bolus of naloxone has increased morphine consumption for comparable pain relief. Either the agonist-antagonist combination or sequence of administration may have caused this effect via oligomeric receptor mechanism. Study of these mechanisms might further clarify the issue.
References:
1.Anesthesiology.2000;93:409-417.
2. Anesthesiology, 1997:87(5):1075-81.



S-396.

THE EFFECT OF NSAIDS ON SPINAL FUSION

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Introduction: Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used in clinical medicine to manage post-operative pain, specifically in patients undergoing spinal fusion surgery. Despite their routine administration, there have been concerns about possible deleterious effects on bone healing. However, most of the supporting studies did not study NSAIDs in human subjects, and administered NSAIDs over several weeks to months at doses greater than that approved for acute pain.
Methods: We retrospectively analyzed the data of 434 patients undergoing single or bi-level instrumented posterior spinal fusion using autologous iliac crest bone graft by the same surgeon. Patients received perioperative ketorolac (20-240 mg/d), celecoxib (200-600 mg/d), rofecoxib (50 mg/d) or no NSAIDs in the 5 consecutive days following surgery. Postoperatively, all patients received patient-controlled analgesia morphine for the first 24 hours following surgery and then acetaminophen/oxycodone tablets. Non-union was evaluated at 1 year following surgery via radiographic analysis.
Results: There were no significant differences in demographic variables, surgical duration, smoking history, or number of vertebral levels fused among the groups. A total of 48 patients (11%) developed non-union postoperatively. There were no significant differences in the incidence of non union among the rofecoxib (9 out of 124 patients; 7.3%), celecoxib (5 out of 60 patients; 8.3%), or no NSAID (11 out of 130 patients; 8.5%) groups. The incidence of non-union in the ketorolac group (23 out of 120 patients; 19.2%) was significantly (P<0.001) higher than that for the no NSAID group. This represents approximately a 2.5-fold increased likelihood of developing non-union with ketorolac administration. However, low-dose ketorolac (20-110 mg/d) administration resulted in 3 out of 50 patients (6%) developing non-union, which was not significantly different than that for the no NSAID group. Patients receiving high-dose ketorolac (110-240 mg/d) had a significantly (P<0.0001) higher incidence of non-union (20 out of 70 patients; 29%) when compared to no NSAID users. This represents approximately a 4.3-fold increased likelihood of developing non-union with high-dose ketorolac administration. Also, among those patients that developed non-union, there was a significantly (P<0.001) higher incidence between smokers and non-smokers, as well as one level fusions versus two level fusions.
Conclusion: This retrospective study revealed that short-term perioperative administration of rofecoxib (50 mg/day), celecoxib (200-600 mg/day) and low-dose ketorolac (20-110 mg/day) did not increase the rate of non-union for spinal fusion surgery. In contrast, higher doses of ketorolac (120-240 mg/d), a history of smoking, and two level vertebral fusions did result in a significantly higher incidence of non-union following spinal fusion surgery.

S-397.

THE EFFECT OF FENTANYL DURING BISPECTRAL INDEX GUIDED SEVOFLURANE-FENTANYL ANESTHESIA ON AUTONOMIC NERVOUS ACTIVITY AND POST OPERATIVE PAIN

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Introduction: The minimum alveolar concentration to blockade adrenergic response to surgical incision of sevoflurane is reduced with increasing concentrations of fentanyl[1]. The aim of this study was to compare the different effect site concentration(Ce) of fentanyl administered using target-controlled infusion (TCI) on autonomic nervous (ANS) activity during sevoflurane anesthesia and post operative pain. The depth of anesthesia was titrated to target the bispectral index (BIS) value between 40 and 50 using sevoflurane for maintaince of anesthesia.
Method: With IRB-approval, 20 unpremedicated ASA I-II female patients scheduled for gynecological abdominal surgery were randomized to one of the two groups: in Group 1 fentanyl Ce was maintained at 3.0 ng/ml (n=10) and in Group 2 at 1.5 ng/ml (n=10). Anesthesia was induced with 5% sevoflurane deep breath inhalation with 100% oxygen after the TCI of fentanyl was initiated. . After induction of anesthesia, sevoflurane was adjusted to maintain a BIS between 40 and 50. Patients of the both groups were awakened between 1.5 and 2.0 ng/ml of fentanyl Ce. Thereaftere, intravenous fentanyl patient controlled analgesia (PCA) was started. Continuous BIS (A-1050, Aspect Medical System) and heart rate variability (HRV) (Tarawa, Suwa Trust) recording were started before induction of anesthesia. Spectral analysis of HRV was assessed as an index of ANS activity: Low-frequency component (LF:0.04~0.15Hz), High-frequency component(HF:0.15~0.4Hz), and LF/HF ratio. Prince Henry Score (PHS), the pain visual analogue scales (VAS) at rest and at movement. The number of demand for bolus PCA were recorded. Appropriate statistical analysis were performed. P <0.05 was considered significant.
Result: There were no differences in demographic data between the groups. End-tidal sevoflurane concentrations were lower in Group 1 than in Group2 (1.2±0.1% vs. 1.5±0.2%, p<0.05). LF, HF, and LF/HF were lower in Group 1 than in Group 2 (LF; 34.2±14.5 vs. 137.3±108.2, HF; 24.8±14.6 vs. 57.1±45.7, LF/HF; 1.8±0.4 vs. 2.6±0.4, respectively, p<0.05). PHS at 6hr was lower in Group 1 than Group 2 while PHS at 0, and 18 hr was not different. The pain VAS at rest at 6hr was lower in Group 1 than Group 2 (21.0±15.9 vs. 43.0±19.4, p<0.05). The pain VAS at rest at 18hr, and the pain VAS at movement at 6, 18hr were not different between the groups. The number of demand for bolus of PCA at 6 was lower in Group 1 than in Group 2 (5.7±6.9 vs.20.0±33.4, p<0.05), but that at 18hr was not different between the groups (8.9±8.0 vs.25.5±36.2).
Discussion: The higher fentanyl Ce with sevoflurane anesthesia suppress the intraoperative ANS, and shift the balance of the ANS toward sympathetic suppression when the BIS value was maintained at the same level during various combination of sevoflurane with fentanyl anesthesia. Higher fentanyl may improve postoperative pain relief.
Reference:
1 Anesthesiology 1999;90:398-405

S-398.

FENTANYL EFFECT-SITE CONCENTRATION NECESSARY DURING AND AFTER OPEN REDUCTION AND INTERNAL FIXATION OF MANDIBULAR FRACTURE

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Introduction: As the effect-site concentration (ESC) can accurately determine the drug effect, optimal drug delivery can be achieved by pharmacokinetic analysis. However, there have been few reported pharmacokinetic evaluations of fentanyl administration during the postoperative period. The aims of this study are twofold: Firstly, to calculate the ESC of fentanyl during and after the operation of mandibular fracture, and secondly, to evaluate the relationship between the intra-operative ESC of fentanyl and that at the first required administration of postoperative analgesics.
Methods: 18 patients (ASA/PS 1/2) undergoing open reduction and internal fixation of mandibular fracture were enrolled in this study. General anesthesia was induced and maintained with propofol and fentanyl without any inhaled anesthetics. Propofol was infused with the target-controlled infusion (TCI) system (Diprifusor) during the operation to maintain the Bispectral Index (BIS) in a range from 40 to 60. Fentanyl was injected repeatedly as necessary to maintain a stable heart rate. After the operation, the patients were observed in the ward. The estimated blood concentration and ESC of fentanyl during and after anesthesia were calculated by pharmacokinetic simulation analysis with Shafer's parameter set until the patients received the analgesics for postoperative pain management up to 48 hours after the operation.
Results: The minimal ESC of fentanyl during the operation 1.31 ng/ml in median. All the patients required postoperative analgesics, and the average time of the first required administration was 139 minutes after the operation. The ESC of fentanyl at the first required postoperative analgesic administration was 0.64 ng/ml in median, but was widely distributed from 0.27 to 1.12 ng/ml. The median ESC of fentanyl during surgery was best correlated to that at the first required postoperative administration among the analyzed variables, but this correlation between them (r=0.294) was not statistically significant.
Discussion: Patients exhibit large individual differences in fentanyl requirements both during and after surgery. However, those that require higher fentanyl ESCs with proper titration during surgery have also been found to require analgesics at higher fentanyl ESCs. This phenomenon has prompted the hypothesis that the fentanyl dosage for postoperative pain management should be tailored to individuals using strategies such as patient-controlled analgesia. In this study we were unable to show any correlation between the ESC of fentanyl necessary during surgery for mandibular fracture and that for postoperative pain management. This may have been due to the change in the nociceptive stimulation from higher levels during the surgery to lower levels postoperatively. Even in this situation, however, it seems reasonable, both from an ethical and an economic perspective, to tailor the fentanyl dosage for postoperative pain management to individuals using strategies such as patient-controlled analgesia.

S-399.

AMPOFOL ADMIXED WITH LIDOCAINE VS DIPRIVAN FOLLOWING IV LIDOCAINE: A COMPARISON OF PAIN ON INJECTION

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Introduction: Ampofol, a low-lipid formulation of propofol, has been reported to possess the same pharmacologic profile as Diprivan in comparative clinical studies (1,2). However, these preliminary studies suggested that Ampofol was associated with more pain on injection than Diprivan. This randomized, double-blind study was designed to compare Ampofol admixed with 0.33% lidocaine to the "gold standard," namely IV lidocaine followed by Diprivan®.
Methods: 158 outpatients undergoing surgical procedures under general anesthesia participated in this study. All patients received midazolam, 20 μg/kg IV, for premedication. Induction of anesthesia consisted of either 1 ml of 1% lidocaine followed by Diprivan, 2 mg/kg in the *Control group*, or 1 ml of saline followed Ampofol, 2 mg/kg (mixed with 0.33% lidocaine) in the *Experimental group*. Assessments included time to onset of unconsciousness, severity of pain on injection of propofol (0=none, 1=mild, 2=moderate and 3=severe), and recall of pain on injection at the time of discharge.
Results: The two treatment groups were comparable with respect to demographic characteristics, use of adjunctive drugs and time to onset of anesthesia. The incidence and severity of injection pain was identical in the two study groups. Although over 50% of the patients in both groups experience mild-to-severe pain on injection of propofol, only 11% recalled experiencing any pain on injection when questioned in the postoperative period.

	Diprivan (Control)	Ampofol (Experimental)
Age (yr)	50±17	51±16
Weight (kg)	78±17	81±21
Gender (M/F) (n)	31/47	36/44
Midazolam (mg)	1.5±0.3	1.5±0.3
Fentanyl (μg)	38±6	39±8
Propofol (mg)	150±25	152±30
Desflurane (ave. % ET)	4.5±1.7	4.4±1.6
Onset of hypnosis (sec)	57±23	62±28
Pain on injection (n,%)		
None	36, 44	32, 41
Mild	27, 33	22, 29
Moderate	12, 15	16, 21
Severe	6, 7	7, 9
Recalled injection pain (n,%)	9, 12	8, 10

Discussion: Ampofol admixed with 0.33% lidocaine is an effective alternative to IV lidocaine followed by Diprivan for minimizing pain on injection of propofol.
References:
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(2) Song et al, Anesthesiology 2004; 100: 1072-5.

S-400.

PROPOFOL IN AN EMULSION OF LONG- AND MEDIUM-CHAIN TRIGLYCERIDES REDUCES THE INCIDENCE AND INTENSITY OF PAIN ON INJECTION IN ADULTS

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Introduction: This study was designed to assess 1) whether 1% propofol in a mixture of medium- and long- chain triglycerides emulsion (propofol MCT/LCT) entails less incidence and less intensity of injection pain than a commonly used 1% propofol emulsion with LCT (propofol LCT) and 2) whether the pre-administration of fentanyl resulted in less incidence and less intensity of propofol-induced pain in adult patients undergoing elective surgery.
Methods: 1) A total of 100 patients received either 20 ml of propofol LCT with 2 ml of normal saline (NS) (Group I; n = 20)/with 2 ml of 2% lidocaine (II; n = 20), or 20 ml of propofol MCT/LCT with 2 ml of NS (III; n = 20)/with 2 ml of 2% lidocaine (IV; n = 20)/without any additional solution (V; n = 20) into a dorsal vein of the hand for induction of anesthesia. 2) A total of 80 patients received either propofol LCT (I; n = 20), fentanyl + propofol LCT (II, n = 20), propofol MCT/LCT (III, n = 20), or fentanyl + propofol MCT/LCT (IV; n = 20) via the hand dorsal vein. Fentanyl (2 ug/kg) in Groups II and IV was infused 3 minutes prior to propofol administration. Pain at the injection site was graded as none, mild, moderate, or severe. Induction time and changes in hemodynamics during the anesthetic induction were also measured.
Results: 1) Group I receiving propofol LCT with NS had a significantly higher incidence of pain on injection compared to the other four groups (75% vs. 20~35%). Also the intensity of pain in Group I was severer that that in the other groups. There were no significant differences among Group III~V in the incidence and intensity of pain. There were no differences among all the groups in the anesthetic induction time (38~44 s) and hemodynamics during the induction. 2) Group I which received propofol LCT had a significantly higher incidence of pain at the injection site compared with the other three groups (70% vs. 20~30%). Also the intensity of pain in Group I was more severe than of the other groups. Anesthetic induction time in Groups II and IV which received fentanyl prior to propofol was significantly shorter than the other two groups. Tracheal intubation-induced hemodynamic changes in Groups II and IV were attenuated by fentanyl.
Conclusion: With regard to pain on injection, propofol MCT/LCT offers a significant advantage over standard propofol so that a premixture of lidocaine is not necessary. Pre-administration of fentanyl can reduce the incidence and intensity of pain on injection of propofol LCT similar to the new propofol MCT/LCT, and is recommended for use in patients, especially those who have cardiovascular complications.

S-401.

THE KINETICS OF PROPOFOL TRANSFER INTO BREAST MILK

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Introduction: Lactating women undergoing operations requiring general anesthesia are advised to pump and discard their breast milk for 24 hours after the procedure. Data on propofol transfer into breast milk are very limited. (1) The present study determined the pharmacokinetics of propofol transfer into breast milk in order to provide anesthesia caregivers with clinically relevant information regarding the safety of breast milk after propofol administration.
Methods: Three lactating women participated in this study after providing written institutionally approved informed consent. Patients were premedicated with midazolam, 30 μg/kg IV, five minutes before induction of anesthesia with fentanyl, 1.5 μg/kg IV, and propofol, 2.5 mg/kg IV. Anesthesia was maintained with potent volatile anesthetics. Breast milk and blood were collected before drug administration. Milk was then collected using an electric breast pump at 5, 7, 9, 11, and 24 hours after drug administration. Venous blood samples were collected at regular intervals up to 7 hours after drug administration. Plasma and milk propofol concentrations were measured by high performance liquid chromatography with fluorescence detection. (2,3) Propofol plasma pharmacokinetics were modelled with SAAM using a standard 3-compartment model. The pharmacokinetics of propofol transfer into breast milk were modelled simultaneously with the plasma pharmacokinetics using the cumulative amount of the drug in milk just as urinary drug excretion is modelled, albeit with a pharmacokinetic delay to describe the transfer.
Results: Plasma propofol pharmacokinetics were consistent with those reported by others (Table). (4) In the 24 hours of milk collection only 0.04 (± 0.04)% of the propofol dose was collected in milk, representing less than 0.05% of the propofol Cl_E with a pharmacokinetic delay of approximately 6 h (Table).
TABLE . Propofol pharmacokinetic parameters, Mean ± S.D.
Volumes (L/kg)
Clearances (L/min/kg) Milk Delay

V_C	V_F	V_S	V_{SS}	Cl_F	Cl_S	Cl_E	% Cl_E	(min)
0.2	0.3	1.8	2.3	0.05	0.03	0.02	0.04	362
±0.1	±0.2	±0.4	±0.6	±0.03	±0.01	±0.01	±0.04	±96

Discussion: Consistent with the reports of others for methohexital, meperidine, and diazepam, (5) the amount of propofol excreted into breast milk in the first 24 hours after induction of anesthesia provides insufficient justification for interruption of breast feeding.
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S-402.

ANALYSIS OF POST-MORTEM BLOOD THIOPENTAL CONCENTRATIONS AFTER EXECUTION BY LETHAL INJECTION

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Introduction: Lethal injection is currently the prevalent method employed in the United States to inflict the death penalty. The goals of the procedure are twofold: to cause the death of the inmate, and to do so in a humane fashion. The substances used to achieve lethal injection are, in sequence, sodium thiopental, a neuromuscular blocker (usually pancuronium bromide), and potassium chloride. Anesthetic depth is not assessed prior to the administration of the neuromuscular blocker, and the personnel performing the procedure are not trained in general anesthetic techniques. The administration of neuromuscular blockers prevents determination of whether past lethal injections achieved and sustained adequate anesthetic depth. In order to begin to understand the pharmacokinetic features of thiopental in lethal injection procedures, the Oklahoma lethal injection protocol and autopsy reports were obtained and post-mortem thiopental blood concentrations were analyzed.
Methods: Approval for this research was obtained from the local IRB. Data from 46 lethal injection procedures conducted in Oklahoma were reviewed (data from two female individuals were not available). Blood was drawn from the femoral artery and thiopental was quantified by the Oklahoma Office of the Chief Medical Examiner. Information regarding the Oklahoma lethal injection protocol was provided by the Warden of the Oklahoma State Penitentiary. Data were analyzed by the unpaired *t* test and the two-tailed P value is reported.
Results: The Oklahoma lethal injection protocol employs two intravenous lines; in the study population thiopental and potassium were injected into the left arm and a neuromuscular blocker (either vecuronium, pancuronium, curare, or succinylcholine) was injected into the right arm. The mean thiopental level was 12.1 μcg/ml, with a range of 1.4 μcg/ml to 64.6μcg/ml. Over time, epochs of high and low levels of thiopental were observed. 83% of the lethal injection procedures were conducted on either a Tuesday or Thursday; thiopental levels from Tuesday executions were higher than those from Thursday executions (P=.0010).
Discussion: Clinical studies suggest that patients emerge from unconsciousness when the blood concentration of thiopental is approximately 7 μcg/ml(1) and that a blood concentration in the range of 39-42 μcg/ml is suitable for surgical anesthesia(2). The wide range of thiopental levels in the femoral artery after lethal injection raises the possibility of inconsistent delivery and/or distribution within the circulatory system. The difference between thiopental levels from Tuesday and Thursday executions may relate to the practice in Oklahoma of using different execution teams on those days.
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S-403.

THE IMPACT OF ENDOGENOUS STEROIDAL HORMONES ON THE PHARMACOKINETICS OF ORAL MORPHINE: A POPULATION ANALYSIS

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Introduction: Gender related differences have been documented in the analgesic effect received from morphine in both human and animal studies. Pharmacodynamic factors have been investigated to explain these differences, but pharmacokinetic factors could also differ between males and females. Morphine and steroid hormones are both metabolized by a similar pathway and different levels of steroid hormones have been shown to alter the metabolism of other drugs (1,2,3). This study investigates the effect of covariates such as subject demographics and biochemical data, including steroid hormone level, on the pharmacokinetics of oral morphine in post-menopausal women.
Methods: Plasma concentration levels of morphine from thirty-one (31) female subjects at least 60 years old were modeled using a population pharmacokinetic approach (WinNonMix, Pharsight Corp, Mountain View CA) after a standardized dose of 0.5 mg/kg morphine sulfate. Circulating plasma gonadal steroid hormone, estradiol and progesterone, levels were measured prior to the administration of morphine. The data was initially modeled with a one-compartment, first order pharmacokinetic model with no lag time and with no covariates. Systematically, the covariates were added to the model. Adjusting the model for the individual covariates of age or endogenous steroid levels reduced the error in the pharmacokinetic model.
Results: The covariate adjustments that provided the largest error reduction were estrogen and progesterone. The greatest error reduction was found using progesterone alone as a covariate for V/F, volume of distribution divided by bioavailability.
Discussion: The results showed that systemic levels of progesterone affect the early term pharmacokinetics of oral morphine in post-menopausal women, likely effecting the oral bioavailability. If this correlation applies also to the level of analgesia experienced in elderly women, the dosing regimen of morphine may need to be adjusted in respect to the women's progesterone level.
Supported by NIH R03AG16509-01
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S-404.

PRINGLE MANEUVER OF SEVERAL TIMES DECREASES LIVER METABOLISM

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INTRODUCTION: Propofol is an intravenous anesthetic agent with a short duration of action. Metabolism of propofol is very immediate, and it is metabolized in liver 60-80%. Therefore Pringle maneuver, hepatic artery and portal vein clamp technique at the same time, which gives hepatic blood flow influence may change metabolic rate of propofol. In this study, we examined the influence that several times Pringle maneuver gave hepatic metabolism by measuring blood propofol concentration.
METHODS: Twelve ASA physical status 1-2 patients undergoing pancreaticoduodenectomy or hepatectomy were involved in this study. Anesthesia was induced with thiopental 4-5 mg/kg and maintained with isoflurane (0.5%), 50% N2O, and continuous epidural mepivacaine injection. Inserts two kinds of Swan-Ganz catheters in pulmonary artery and right hepatic vein (Edwards Lifesciences, 774HF75, D750HF75) from the right internal jugular vein in a fluoroscopy. After stability of hemodynamics, we stopped isoflurane administration and started continuous infusion of propofol (6 mg/kg/h) for four hours. We divided cases into following three groups; the Pringle maneuver number of times; 0 times (Pringle(-)); once (Pringle(+)), more than twice (Pringle(2+)). In each cases we collected blood from radial artery after stopping dosage and measured propofol blood concentration for 1, 2, 3, 5, 10, 15, 20, 30, 45, 60, 90, 120 min. The data were presented as average value and standard deviation (mean±SD) and analyzed with two-way ANOVA followed by Bonferroni's test. A probability of less than 5% was considered to indicate significance.
RESULT: Hemodynamics in Pringle maneuver did not change, and the effective hepatic blood flow in Pringle maneuver decreased to 40%. There was no significant difference of propofol concentration just after stopping dosage between three groups. In the Pringle(-) and Pringle(+) groups, propofol concentration decreased immediately. In the Pringle(2+) group, propofol concentration decreased at same as other groups to one minute, however, two minutes later, the propofol concentration decreased slowly ($p < 0.05$) in comparison with other groups. The blood propofol concentration 120min in Pringle(2+) group and the values after five minutes of other group were about the same.
CONCLUSION: The results suggested that Pringle maneuver of several times inhibited liver metabolism.
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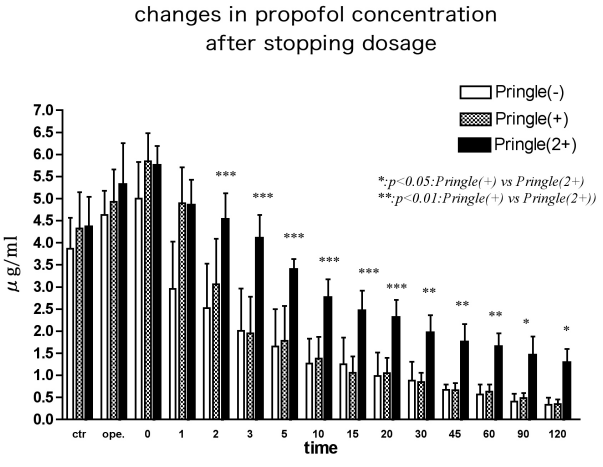

S-405.

OPIOID-VOLATILE ANESTHETIC PHARMACODYNAMIC SYNERGY: A RESPONSE SURFACE ANALYSIS OF SEVOFLURANE AND REMIFENTANIL INTERACTIONS IN VOLUNTEERS

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Introduction: Response surface methodology has proven useful in the characterization of the synergistic interaction between opioids and intravenous hypnotics.(1) The aim of this study was to extend this analysis method to the characterization of the interaction between opioids (remifentanil) and inhaled hypnotics (sevoflurane).
Methods: After obtaining IRB approval and informed consent, sixteen healthy adult male and female volunteers were enrolled. Volunteers received a computer controlled infusion of remifentanil (0-80 ng/mL) and inhaled sevoflurane (0-7 %) at various target concentration pairs spanning the entire clinical spectrum. After reaching steady-state drug levels, the Observers Assessment of Alertness/Sedation (OAAS) was measured, followed by the volunteers response to a series of random experimental pain stimuli (pressure algometry, electrical tetany, and thermal stimulation). Inadequate anesthesia (i.e., a responder) was defined as a withdrawal movement or a 20% increase in heart rate.
Response surface interaction models, as described by Greco (2) were constructed for sedation (OAAS) and analgesia (pressure algometry, electrical tetany and thermal stimulation) using MATLAB to fit a non - linear regression model (pain stimuli) or logistic regression model (OAAS).
Results: The response surfaces constructed from the pooled data of all sixteen volunteers adequately described the data. Representative surfaces are shown for OAAS (Figure 1) with correlation coefficient of 0.81. The response surfaces showed considerable synergy for all effect measures.
Discussion: Remifentanil decreased the amount of sevoflurane necessary to produce sedation and analgesia. It appears that remifentanil not only synergistically affects sevoflurane induced immobility to noxious stimulation, but also has a synergistic effect on sevoflurane produced sedation. These models may be useful in expanding the clinical utility of a previously described pharmacodynamic drug display system of inhalation anesthetics. (3)

References:
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(2) *Pharmacol Rev* 1995;47 (2): 331-85**.**
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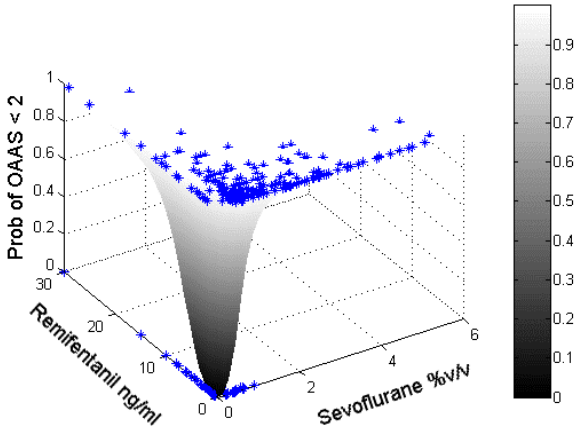

S-406.

THE PHARMACOKINETICS AND PHARMACODYNAMICS OF PROPOFOL DURING CARDIOPULMONARY BYPASS

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Background: In general, a drug's pharmacokinetic effects reflects its unbound fraction, because only drug not bound to plasma protein is able to pass through various membranes and reach target sites within tissues. We have previously reported that a significant increase in the unbound concentration of propofol with no alteration in the total propofol concentration occurred during CPB 1). The similar increase of the unbound concentration of propofol would be expected to occur at its target site in the brain. The purpose of this study was to estimate pharmacokinetics and pharmacodynamics of propofol during CPB by measuring the unbound fraction of propofol and EEG burst suppression ratio which is accepted measure of propofol's effect.
Methods: In 10 patients undergoing cardiac surgery with CPB, after induction of anesthesia with propofol, vecuronium and fentanyl, propofol was infused continuously at a rate of 6mg/kg/h during surgery. Plasma propofol concentration and burst suppression ratio were measured at the predetermined following times:(1) 30 minutes after the infusion of propofol,(2) just before the administration of heparin after sternotomy, (3) 30 minutes after the start of CPB,(4) 60 minutes after the start of CPB. Propofol concentration was measured by high performance liquid chromatography. The unbound fraction of propofol was estimated via equilibrium dialysis.
Results: There were no significant differences of the total concentration of propofol (n=10, p=0.19) and BIS score (n=10, p=0.17) between before and during CPB. After the start of CPB, the unbound fraction of propofol in blood increased by 2-fold during CPB. Burst suppression values became significantly greater than baseline values (n=10, p<0.002).
Conclusion: The efficacy of propofol was enhanced by the increase of unbound fraction during CPB.

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S-407.

PILOT SAFETY, TOLERABILITY, AND PHARMACOKINETIC HUMAN TRIAL OF PROPOFOL LINGUAL SPRAY

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Introduction: There is no entirely satisfactory method for producing relatively brief periods of light-to-moderate preprocedural sedation, even in medically supervised inpatient or ambulatory settings. The variability of orally administered sedatives in onset, duration and effectiveness is well known, while intravenous sedation mandates advanced levels of clinical skill and supervision. To develop a practical alternative, we tested whether propofol, when titrated via lingual spray, possesses the safety advantages of orally administered sedatives, while producing the necessary profile of rapid onset and titratability. Lingual spray delivery was chosen because of the tongue's high degree of vascularity, allowing for rapid systemic uptake of appropriately formulated hydrophobic drugs.
Methods: Following local Ethics Committee approval, a pilot proof of principle study was conducted, focusing on safety, tolerability, and blood level response, following administration of a spray formulation containing propofol. This was a single-center, double-blind, placebo-controlled, dose escalating, and randomized trial, conducted in 12 fasting, healthy adults of both genders. After initial screening, propofol (20 mg IV) was administered by bolus intravenously. At three day intervals thereafter, a single administration of between 100 and 300 uL propofol formulation was sprayed lingually via unit dose actuator, and blood obtained for later propofol concentration analysis (HPLC-FL method; >LOQ (limit of quantitation) = > 2.5 ng/mL) over the next 3 hours. Safety was assessed via vital signs, S_aO2, $P_{tc}CO_2$, oral mucosal examination, and subjective tolerability.
Results: One subject was eliminated following IV dosing, due to protocol violation. All other subjects completed the study, without any treatment associated serious adverse events, or subjective intolerance to the lingual spray. All subjects rapidly achieved blood levels in excess of 100 ng/mL after IV bolus, without any episodes of apnea. Similarly, following spray administration, all subjects achieved significant blood levels ($p < 0.005$, *t*-test) without any episodes of apnea, desaturation, or other serious adverse events. All spray subjects, at all spray doses, achieved blood levels within 15 min. Bioavailability from spray propofol could be documented as early as 4 min following lingual spray administration.
Conclusions: These data establish that propofol is rapidly bioavailable following lingual spray administration. Our pilot subjective and objective data indicate that lingual spray administation is safe and well tolerated. With these principles established, work in progress is designed to optimize the propofol lingual spray formulation, with respect to the most relevant pharmacokinetic parameters (T_{max}, C_{max} and AUC).

S-408.

DETERMINING THE OPTIMAL NICARDIPINE INFUSION RATE FOR MAINTAINING HEMODYNAMIC STABILITY DURING GENERAL ANESTHESIA

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Introduction: Nicardipine, an IV calcium-channel blocking drug, has been used to control hyperdynamic responses during the perioperative period. This placebo-controlled, randomized, double-blind study was designed to evaluate the effect of three different "basal" infusion rates of nicardipine on the anesthetic and analgesic requirements, hemodynamic stability, blood loss, and early recovery profile after major abdominal surgery procedures.
Methods: 21 consenting patents undergoing major surgical procedures were randomized to one of four treatment groups. All patients received midazolam, 20 µg/kg IV, for premedication. Induction of anesthesia consisted of propofol 1.75 mg/kg IV) in combination with sufentanil, 0.2 µg/kg IV. After tracheal intubation, anesthesia was initially maintained with desflurane, 4% ET, in combination with nitrous oxide 60% in oxygen. A study drug infusion containing either saline (Control), nicardipine 2.5, 5 or 10 mg/h was initiated prior to skin incision. The assessments included average end-tidal desflurane concentration, total dosage of opioid analgesic medication, need for cardiovascular adjuvants during surgery, and intraoperative blood loss. The effect of the study medication on the emergence times and need for postoperative analgesic and antiemetic drugs was also assessed. Values are means ±SD, with p-value <0.05 (*).
Results: The four groups were comparable with respect to their demographic characteristics. Although use of a nicardipine infusion reduced intraoperative blood loss and perioperative blood pressure values, it failed to facilitate the recovery process.

	Control	Nicardipine infusion (mg/h)		
	(saline)	2.5	5	10
Age (yr)	59±14	51±19	54±12	37±9
Weight (kg)	91±22	84±23	93±30	86±12
Anesthesia time (min)	169±74	172±66	187±114	201±74
Sufentanil dosage (µg)	95±21	91±43	75±38	71±35
Desflurane conc. (ave. ET%)	4.9±2.1	5.0±1.7	4.3±1.1	3.8±0.8
Nicardipine dosage (mg)	0	7±4	13±7	22±13
Antihypertensive rescue drug (%)	30	20	16	0*
Sympathomimetic rescue drug (%)	23	10	0	50*
Intraoperative blood loss (ml)	640±276	500±204	363±103	444±145
MAP on arrival in PACU (torr)	99±29	73±36	62±42*	55±39*
HR on arrival in PACU (bpm)	95±20	95±15	90±20	95±13
Opioid analgesic rescue medication (%)	60	50	40	85
PACU discharge time (min)	89±35	88±30	91±41	87±40

Discussion: Nicardipine infusion produced dose-dependent cardiovascular depression during and after surgery. A nicardipine infusion rate of 2.5-5 mg/h is recommended for controlling acute intraoperative hyperdynamic responses and minimizing blood loss during major surgical procedures.

S-409.

RENAL PRESERVATION WITH FENOLDOPAM IN PATIENTS UNDERGOING MAJOR SURGICAL PROCEDURES

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Introduction: Acute renal failure (ARF) is a serious and costly complication that results in prolonged hospitalization and a 5.5-fold increased risk of dying (1,2). Animal models of ARF consistently demonstrate the benefits of dopamine adrenergic agonists (DAAs) in the prevention and management of ARF (3). DAAs are thought to mediate their renoprotective effects by enhancing renal blood flow (RBF) and natriuresis, as well as maintaining glomerular filtration rate (GFR) via stimulation of DA1 receptors (4). In human studies, the nonselective DAA, dopamine, has failed to demonstrate any consistent or reproducible benefits in preventing or treating ARF. This lack of benefit may be attributed to dopamine's simultaneous activation of DA-2 and alpha-1 adrenergic receptors which counteract its DA-1 receptor-mediated actions (5). Fenoldopam is a selective DA-1 receptor agonist that has been shown to enhance RBF and maintain GFR (6). In our study, we examined the potential renoprotective effects of fenoldopam in patients undergoing surgical procedures.
Methods: A total of 114 patients undergoing major surgery for abdominal aortic aneurysm (AAA) repair, vascular reconstruction, trauma, orthopedic reconstruction, or abdominal surgery comprised the study group. Fifty-seven patients received fenoldopam at variable doses perioperatively up to 48 hours post-operatively. Fifty-seven patients matched for type of surgery, APACHE score, age, race, gender, and baseline renal function served as controls. ARF was defined as an increase of 25% in serum creatinine or absolute increase in serum creatinine of 0.5 mg/dl over baseline.
Results: ARF occurred in 8 (14%) patients receiving fenoldopam and in 17 (30%) controls (p=0.02). One patient receiving fenoldopam required dialysis, while 4 controls required dialysis. Length of stay (LOS) was 9.8 $\pm$ 8.7 days in the fenoldopam group and 11.7$\pm$ 9.5 days in the control group (p=0.08). Total hospital charges were $19,475 in the fenoldopam group and $23,101 in the control group.
Discussion: The selective DA-1 receptor agonist, fenoldopam, is beneficial in preventing ARF in patients undergoing surgical procedures and its use is associated with decreased hospital costs.
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S-410.

PERIOPERATIVE BETA BLOCKADE FOR HIGH RISK SURGERY: COMPLIANCE WITH CLINICAL PRACTICE GUIDELINES

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Introduction: Some patients who undergo high risk surgery are at an increased risk for perioperative cardiac complications. Risk factors can identify those most susceptible and recent studies have shown that beta-adrenergic blocking drugs administered in the perioperative period can reduce the incidence of these cardiac complications and improve long term survival.[1] However, studies have also shown that a large percentage of patients who should benefit from beta blockers (BB) do not receive them in the perioperative period.[2] The purpose of this pilot study was to determine how closely current guidelines are followed in our institution.
Methods: We reviewed records of 14,200 patients seen in our preoperative clinic over a 12 month period. We identified 2300 patients with clinical risk factors that predicted a possible adverse cardiac outcome as outlined by Boersma.[1] These risk factors included age $\geq$70, current angina, prior myocardial infarction, congestive heart failure, prior cerebrovascular event, diabetes mellitus and renal failure. We found 303 patients with at least 1 risk factor who were undergoing high risk surgery as outlined by the ACC/AHA guidelines.[3] These were further divided into 2 groups based on $\geq$3 (high risk) vs. 1-2 risk factors (intermediate risk). We then determined whether these patients were taking a BB. Additionally, for those on a BB we evaluated whether their heart rate (HR) was controlled to the degree suggested by the current literature (i.e. $\leq$ 70 beats/min).
Results: See Table

Beta Blocked Patients with and without HR Control and Non- Beta Blocked Patients

	Intermediate Risk Group (n=252)	**High Risk Group** (n= 41)
No Beta Blocker	164 (65%)	14 (34%)
Beta Blocker w/o HR control (>70/min)	44 (17%)	15 (36.5%)
Beta Blocker with HR control ($\leq$ 70/min)	44 (17%)	12 (29%)

Discussion: Multiple recent publications show that administration of BB in the perioperative period reduces cardiac mortality in patients at risk who are undergoing non-cardiac surgery. With this study we identified that a majority of patients who are predicted to benefit from administration of BB are not receiving these medications. Additionally, we have shown that of those who are on BB, the majority do not have their heart rates controlled to the degree that has been recommended in the literature. This presents an opportunity for anesthesiologists to have a major impact on operative outcomes through implementation and optimization of beta blocker therapy during the pre-operative visit.
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S-411.

SUBANESTHETIC SEVOFLURANE PREFERENTIALLY INHIBITS HUMAN EMOTIONAL MEMORY

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Introduction: Sevoflurane amnesia in the rat depends on the functioning of the basolateral amygdala **[1].** Given the amygdala's role in modulating memory for emotional material **[2],** the animal work predicts sevoflurane amnesia in humans will depend not only on the dose of sevoflurane administered, but also on the emotional intensity of the stimuli that are to be remembered. Thus, with sevoflurane memory of emotional stimuli should be suppressed to a greater degree than memory of neutral stimuli. Such a dissociation would implicate the amygdala as a key site mediating sevoflurane amnesia. We examined this possibility using the subsequent memory paradigm in volunteers.
Methods: Following IRB approval and informed consent, 27 volunteers (aged, 18-29) were randomized to receive steady-state subanesthetic doses of either: 0.0, 0.1, 0.2 or 0.25% expired sevoflurane concentrations while watching a series of 36 slides from the international affective picture system (IAPS). Slides were displayed for 6 s each and immediately following each slide the subjects rated their emotional reaction to it on a scale of 1 (neutral) to 4 (very emotional). Subjects returned at 1 week for recall and recognition memory testing. No anesthesia was given during memory testing. Main drug effects on memory were assessed with ANOVA and post-hoc t-tests; dose-by-emotional rating memory effects were assessed using ANCOVA.
Results: Overall mean (+/- SD) recall in the placebo group was 6.8 +/- 3.6 slides. Sevoflurane significantly reduced mean total recall at the 0.2% (3.5 +/- 2.1 slides), and the 0.25% (3.2 +/- 2.5 slides) doses ($p < 0.05$, for both). Most importantly, with slide recognition the dose-by-emotional rating interaction was significantly different from placebo only at the 0.25% sevoflurane dose ($p < 0.05$). Mean percent of neutral slides recognized was not significantly different between placebo = 28 +/- 24 and 0.25% sevoflurane = 29 +/- 14. However, mean percent of emotional slides recognized was significantly different between placebo = 78 +/- 18 and 0.25% sevoflurane = 41 +/- 38% ($p < 0.05$).
Conclusions: The dose of sevoflurane causing amnesia in humans for long-term recall of contextual information is in the range of 0.2 to 0.25%. This is similar to results obtained from the rat inhibitory avoidance model **[3]**. Most importantly, sevoflurane at 0.25% specifically interferes with memory of emotional material, more so than it does for memory of neutral material. This is consistent with the theoretical framework whereby the basolateral amygdala is a key neuroanatomic site mediating anesthetic-induced amnesia and suggests sevoflurane may help prevent cases of awareness by preferentially blocking recall of emotionally laden information.
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S-412.

INTRAOPERATIVE LOW DOSE INFUSION OF PROSTAGLANDIN E1 CAN REDUCE POSTOPERATIVE CORE TEMPERATURE ELEVATION AND THE INCIDENCE OF POSTOPERATIVE SHIVERING IN PATIENTS WITH PROLONGED HEAD-NECK SURGERY

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Introduction: A regulated elevation in core temperature (Tc) setpoint occurs normally after surgery. The association between Tc elevation and duration of surgery, and the cytokine response suggests that early postoperative fever is a manifestation of perioperative stress. Infusion of Prostaglandin E1 (PGE1) was reported to inhibit proinflammatory cytokines production during open cardiac surgery. The aim of this study is to investigate whether PGE1 could reduce postoperative Tc elevation and the incidence of postoperative shivering after prolonged head-neck surgery.
Method: After obtaining approval from Department of Anesthesiology and written informed consent, 40 patients undergoing elective head-neck surgery were enrolled in the study. All patients were divided randomly into control group (saline 0.3 ml/kg, n=20) and PGE1 group (0.0125 μg/kg/min, n=20). Anesthesia was performed with inhaled anesthetics (nitrous oxide and isoflurane) and intravenous fentanyl throughout a surgery. All patients were actively warmed by the Forced-Air Warming system during surgery. Tc was measured using thermocouples in the urinary bladder. Postoperatively, all patients were admitted to the postanesthetic care, and shivering was assessed and recorded every 15 min using a five-point scale, with a score greater than zero defined as the presence of shivering. Setpoint of Tc was defined when shivering resolved. The setpoint of postoperative Tc and the incidence of postoperative shivering was analyzed by unpaired t-test and chi-square analyses, respectively.
Results: Although intraoperative Tc was gradually increasing in all patients, any significant differences could not be found at any time points between both groups. However, the rate of increase of postoperative Tc was more rapid in the control than in PGE1, and there was significant difference in the setpoint of Tc between control and PGE1(39.2± 0.2 in the control and 38.4 ± 0.2 in PGE1, $P<0.05$). The incidence of postoperative shivering was less in PGE1 (45 %) than in control (100 %).
Discussion: This study demonstrated that intraoperative low dose infusion of PGE1 could reduce the incidence of postoperative shivering after prolonged head-neck surgery. We speculated that this effect might be associated with reduction of the setpoint of Tc resulted from inhibiting proinflammatory cytokines production by intraoperative infusion of PGE1.

S-413.

AMERICAN GINSENG REDUCES WARFARIN'S ANTICOAGULANT EFFECT: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Ginseng is a most commonly used herb in the U.S. Surgical patients often concurrently take herbal supplements. Herbals like ginseng have the potential to interact with medications that have a narrow therapeutic index, such as warfarin, a commonly used anti-coagulant in orthopedic surgery (1, 2). We conducted this double-blind, randomized, placebo-controlled trial to evaluate the interactions between American ginseng and warfarin.
Methods: With approval from the IRB, 9 men and 11 non-pregnant women were enrolled in this study. The mean age ± S.D. was 27.8 ± 6.7 yr (range, 18-45). All subjects received oral warfarin 5 mg each day for 3 consecutive days during week 1. Beginning week 2, subjects were randomly assigned to receive either oral American ginseng 1.0 g or placebo twice daily for 3 consecutive weeks. During week 4, all subjects again received oral warfarin 5 mg each day for the first 3 consecutive days. International normalized ratio (INR) and warfarin plasma level were measured. Subjects were also instructed to record their daily diet throughout the study period.
Results: Using a HPLC method, we found that the total ginsenoside content in the American ginseng was 5.19%. The constituent split was as follows (percentages): ginsenoside Rb_1, 1.93; Rb_2, 0.20; Rc, 0.61; Rd, 0.42; Re, 1.68; and Rg_1, 0.35. The peak INR decreased significantly following 2 weeks of ginseng as compared to changes following placebo (ginseng vs. placebo difference -0.19, 95% CI -0.36 to -0.07; $P < 0.01$). INR area under the curve (AUC), peak warfarin plasma level and warfarin AUC were also significantly reduced in the ginseng group as compared to changes in the placebo group ($P < 0.01$). Peak INR and peak warfarin plasma level were positively correlated ($P < 0.001$). There were no statistically significant differences in the vitamin K intake between the two groups ($P = 0.70$) or over time ($P = 0.62$). No adverse effects of clinical importance were observed in this study
Discussion: Because of the narrow therapeutic index of warfarin, it is crucial to keep its anti-coagulant effect in a target range. The use of warfarin, however, is complicated by potential drug-drug or drug-herbal interactions (3). Our data suggest that American ginseng reduces the anti-coagulant effect of warfarin. Thus, anesthesiologists should be aware of possible ginseng-warfarin interactions during perioperative care.
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S-414.

COMPARISON OF ISOFLURANE VS SEVOFLURANE ON MYOCARDIAL PROTECTION IN ULTRA-FAST-TRACK ANESTHESIA FOR OFF-PUMP CABG

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Introduction: Volatile anesthetics provide protection against myocardial ischemia by pharmacologic preconditioning. So far, studies have focused on the effects and outcome of volatile anesthetics and not on comparing different agents. In this randomized, prospective study, we compare the cardioprotective propensities of sevoflurane versus isoflurane in OPCABG with the hypothesis that sevoflurane offers superior myocardial protection..
Methods: Forty patients undergoing OPCABG with TEA and ultra-fast-track anesthesia were randomized in two groups of 20 patients. Anesthesia was maintained with either 1 MAC of sevoflurane or 1 MAC of isoflurane. Troponine-T, CK-MB, regional wall motion abnormalities and ejection fraction, time to extubation, respiratory functions and hemodynamic stability were compared.
Results: All patients were successfully extubated in the operating room with minimal post-operative pain up to 72h after surgery. Troponine-T and CK-MB levels, immediately after surgery, 3, 12, 24, 48 and 72h after surgery, were not statistically different between the two volatils agents. (Table 1) Hemodynamic stability during surgery and preservation of ejection fraction were equally not different between the two groups. Time to extubation was significatively quicker with sevoflurane than with isoflurane.
Dicussion: Our study shows that sevoflurane and isoflurane protect the heart against ischemic damage in the same way during OPCAB. They do not differ in providing hemodynamic stability or maintenance of contractile function during and after aortocoranry grafts. As expected, recovery from anesthesia was quicker with sevoflurane, without causing any difference in post-operative respiratory function.
Conclusion: In conclusion, sevoflurane and isoflurane provide equal myocardial protection during OPCAB. Both volatile agents can be used to immediate extubation, keeping in mind that isoflurane has to be stopped earlier because of its longer washout period.
TABLE 1

	Sevoflurane (N=20)		**Isoflurane (N=20)**	
	Troponine-T	CK-MB	Troponine-T	CK-MB
Immediately	0 (0.08)	-	0 (0.03)	-
3h post-op	0.03 (0.09)	21.55 (7.47)	0.03 (0.05)	20.70 (10.12)
12h post-op	0.08 (0.10)	18.25 (14.45)	0.07 (0.85)	22.80 (53.25)
24h post-op	0.19 (0.30)	19.90 (11.64)	0.15 (1.43)	19.10 (81.96)
48h post-op	0.11 (0.21)	16.70 (4.20)	0.12 (1.50)	15.90 (54.15)
72h post-op	0.29 (0.45)	15.20 (3.82)	0.09 (0.17)	16.75 (18.18)

*Values are presented as median, in parentheses are standard deviation.

S-415.

CAN LANDIOLOL, A NOVEL SHORT ACTING BETA-BLOCKER, PREVENT TACHYCARDIA DURING INTUBATION IN GENERAL ANESTHESIA?

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Objective: Tracheal intubation often causes transient tachycardia and hypertension. In patients at risk for ischemic heart disease, many physicians consider to use some kind of treatment such as infusion of opioids or esmolol to attenuate these hemodynamic responses[1,2]. We designed this study to assess the landiolol, a novel short acting beta-blocker, can prevent harmful tachycardia event during tracheal intubation in the general anesthesia.
Methods: After institutional approval, 30 patients undergoing elective non-cardiac surgeries were included in this study. Exclusion criteria included: (1) under 18 or over 85 years old; (2) baseline heart rate < 60 bpm; (3) present treatment with antihypertensive or antiarrhythmic drugs. The protocol was designed as double blind study. Patients were randomly allocated into three groups. Group NS received 2ml of saline, group LA received 5mg of landiolol in 2ml of saline, and group FE received 0.1mg of fentanyl. Two minutes after patients received drugs, general anesthesia was induced with 2mg/kg of propofol and 0.1mg/kg of vecuronium. Heart rate and blood pressure were recorded at prior to drug administration, two minutes after administration, immediately after intubation, and five minutes after intubation.
Results: There was no difference in demographic data between the groups. Changes of heart and mean blood pressure were shown in table 1 and 2. At the time immediately after intubation, there was 21% increase of heart rate from baseline in group NS. On the other hand, 3.7% and 5.3% increase of heart rate were observed in group LA and FE, respectively. Only fentanyl could prevent increase of mean blood pressure, but decreased 27% at 5 minutes after intubation. Changes of blood pressure were similar in group NS and LA.
Conclusion: Infusion of 5mg of landiolol successfully prevented tachycardia during tracheal intubation without excessive decrease in blood pressure. These results suggest that because of its ultra-short acting and higher cardioselectivity than esmolol, landiolol may valuable to prevent undesirable response during intubation.
References:
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S-416.

IN-VITRO CALCIUM BINDING CAPACITY OF CITRATE IN ANTICOAGULANT PRESERVATIVE IN BLOOD COLLECTION BAGS

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Introduction: The binding of ionized calcium (Ca^{2+}) by citrate during massive transfusion can cause ionized hypocalcemia and severe hemodynamic instability. This is especially true during liver transplantation when there is little or no hepatic function, leading to citrate accumulation in the blood (1-2). To maintain Ca^{2+} at physiologic range under these conditions, the appropriate amount of calcium supplementation to offset the binding of citrate in various blood products should be known. Our previous study showed that slightly more than 400 mg $CaCl_2$ (dihydrate) added to a unit of fresh frozen plasma (FFP) can keep the Ca^{2+} within normal physiologic range (3). To further estimate the calcium binding capacity in a unit of whole blood and in other blood components, we studied the calcium binding capacity of the anticoagulant preservative in standard blood collection bags.
Methods: Blood collection bags containing CPD or CPDA-1 anticoagulant were obtained from our local blood bank. Each of these standard blood collection bags contains 63 ml anticoagulant. These bags are considered identical because each contains the same amount of citrate. To measure the calcium binding capacity of the anticoagulant in a collection bag, Plasmalyte (Baxter) was added to the bag to a total volume of 300 ml. The initial pH of this mixture was quite acidic and was adjusted to a pH of 7.4 at 37°C. Aliquots of 6 ml of the mixture were transferred to test tubes, and $CaCl_2$ (dihydrate) (10%, American Regent Laboratories, Inc.) was added to each test tube in 2 mg increments. Therefore, each test tube represents 100 mg increments of $CaCl_2$ mixed with a unit of anticoagulant. The samples were analyzed on a blood gas machine (ABL System 625, Radiometer Copenhagen) to measure Ca^{2+} as well as other parameters.
Results: Ten experiments were performed, which generated smooth and reproducible titration curves representing dose dependent increases in Ca^{2+} levels as more $CaCl_2$ was added to the anticoagulant mixture. Based on an excellent polynomial curve fitting through the data points, about 700 mg $CaCl_2$ is required for each unit of anticoagulant to maintain a Ca^{2+} level of 1.1 mmol/L (physiologic range 1.05-1.3 mmol/L).
Discussion: In our previous study, about 400 mg $CaCl_2$ was needed in a unit of FFP to obtain a Ca^{2+} level within the physiologic range (3). The extra 300 mg $CaCl_2$ required for a unit of anticoagulant in this study represents the calcium binding capacities in other blood components from a unit of whole blood - the platelet and packed red blood cells (PRBCs). Therefore, during liver transplant, rational calcium supplementation should also be considered for rapid transfusion of platelet and PRBCs.
References:
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S-417.

DOES PRIMING ENHANCE THE ONSET OF A SUBSEQUENT DOSE OF VECURONIUM?

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Introduction: Onset of neuromuscular block (NMB) produced by a nondepolarizing muscle relaxant can be hastened by preadministration of a small (priming) dose of the same agent. The priming dose should be efficacious without causing any discernible muscle weakness (1). We have investigated the effect of two priming doses of vecuronium on the speed of onset of the second dose of vecuronium. A constant total (priming + the second) dose of vecuronium (25 $\mu g \bullet kg^{-1}$) was selected to produce an incomplete NMB.
Methods: After approval by the local IRB, 30 adult non-obese patients scheduled for elective surgery consented to participate. Following iv administration of 1-2 mg midazolam and fentanyl 3-5 $\mu g \bullet kg^{-1}$, anesthesia was induced with propofol 2-3 $mg^2 kg^{-1}$ and maintained with propofol infusion (100-150$\mu g \bullet kg^{-1^2}min^{-1}$) and 66% N_2O in oxygen. Oral endotracheal intubation was performed following topical application of lidocaine (4%, 3 mL). Ventilation was controlled to maintain normocapnia. The thumb on one hand was abducted (preload 250 to 300 g) and connected to a force transducer. Trains of four supramaximal stimuli at 2 Hz were applied to the ulnar nerve at the ipsilateral wrist and repeated at 12 s intervals. The elicited contractions of the thumb were recorded. Following 25 min of stimulation (stabilization period), vecuronium (in $\mu g \bullet kg^{-1}$) was injected iv to three groups of 10 patients each. Either a single dose (Group 1: 0+25) or two doses separated by four min interval were injected, Group 2: (5+20) and Group 3: (10+15). The mean strength of T_1 during the five minutes immediately preceding the first injection of vecuronium was denoted as 1.0. Onset time (mean± SD) was estimated as time difference between the time of injection of the second dose (Groups 2 and 3) or of the single dose (Group 1) and the time the lowest T_1 was attained.
Results: In Group1, the minimal T_1 (0.17± 0.15) was established at 4.7± 0.6 min after the bolus injection. In Group 2, minimal T_1 after the second dose was 0.11± 0.07 at 4.6± 0.9 min, while in Group 3, minimal T_1 was 0.13± 0.09 at 3.7± 0.8 min. The onset time in Group 3 was significantly shorter (P = 0.019) than the onset time in either Group 1 or Group 2. At the moment of the second injection, T_1 and T_4/T_1 in Group 2 were 0.99± 0.03 and 0.98± 0.03, while in Group 3 the values were reduced to 0.85± 0.21 and 0.72± 0.23, respectively. Four of the ten patients in Group 3 had T_4/T_1 below 0.7.
Discussion: A priming dose that does not cause a measurable NMB does not hasten the onset of action of a subsequent dose of vecuronium.
References:
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S-418.

SUCCINYLCHOLINE - MIVACURIUM INTERACTION: ANOTHER PERSPECTIVE

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INTRODUCTION: Succinylcholine (SCH) may first be used and then continue with mivacurium (MIV) during short lasting procedures (1). MIV has also been suggested as pretreatment before SCH (2). Conflicting results arises from earlier studies on SCH-MIV interaction (3 - 4). The aim of the following study is to revisit this interaction.
MATERIAL AND METHODS: Consenting patients (n= 45) with no clinical contraindication for SCH, anesthetized with intravenous agents were randomly assigned either to group **1** receiving MIV 100 $\mu g.Kg^{-1}$. In group **2,** SCH 1 $mg.Kg^{-1}$ was used, and at 50%, spontaneous recovery MIV 100 $\mu g.Kg^{-1}$ was administered. For group **3,** MIV 10 $\mu g.Kg^{-1}$ pretreatment followed by the same regime as group 2. Using electromiography, maximal effect (MAX), onset time (OT), and clinical duration (DUR) for MIV assessed. C*orrected MAX* (**cMAX**) was considered as the remaining block (50%) subtracted from actual effect in groups 2 and 3, and speed of action (**SA**) as the ratio between MAX or cMAX and OT (% / sec, sec / %) Analysis of variance and Student-Neuman-Keuls used for statistical comparison,
RESULTS: During the sequence, MIV showed a significantly increased MAX and reduced OT without effects on DUR, **SA** and **cMAX** Pretreatment, doesn't add any further change (Table 1).
DISCUSSION: Interaction between SCH and MIV depends upon the order and timing of administration. Using MIV before worn off effect of SCH made that remaining blockade is not usually accounted for final block. To avoid distortions, **cMAX** and **SA** was calculated, and neither one were significantly modified. These results clarify previous data obscured by statistics, showing a faster action by MIV if SCH is previously administered (5 - 6). As 50% blockade was already present, the actual net block for MIV almost halved, in accordance to an antagonistic action already described (4). DUR seems related to the interval between drugs, with no change reported after 90% recovery (5) and a statistically reduction if MIV is administered during 95% SCH block (1), but these reports are neither sustained by present findings.
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Table 1.-Mean ± standard deviation. (♣) = speed of action. cMAX = corrected maximal effect

	1) MIV-BOL	2) SCH-MIV	3) MIV-SCH-MIV	SIG
MAX (%)	93.3 ± 4.3	98.2 ± 4.5	97.9 ± 3.7	1) vs=2.- 3.-
cMAX (%)		48.2 ± 4.5	47.9 ± 3.7	p=0.843
ONSET (sec)	279.8 ± 48	136.2 ± 26	158.2 ± 45	1) vs= 2.- 3
sec / % ♣	3.01 ± 0.58	2.85 ± 0.79	3.36 ± 1.13	p=0.226
% / sec ♣	0.34 ± 0.08	0.37 ± 0.09	0.33 ± 0.11	p=0.483
DUR (min)	14 ± 5	15.2 ± 8.8	15.8 ± 5	p=0.889

S-419.

TWITCH STRENGTH AND FADE IN MYASTHENIA GRAVIS SIMULATED IN A MODEL OF NEUROMUSCULAR TRANSMISSION

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Introduction: Although myasthenia gravis is caused by a reduction in postsynaptic acetylcholine (ACh) receptors at the motor end plates, the disease is also characterized by fade on repetitive stimulation (1). In normal human muscle, repetitive stimulation produces a decrease in the quantal content of ACh (2). The goal of our study was to simulate the impact of a decreased stimulus-induced release of ACh in the presence of decreasing number of the postsynaptic receptors (R). The first and the fourth twitch elicited by a repetitive stimulation pattern (TOF, four stimuli at 2 Hz) are labeled T_1 and T_4. We postulated that the amount of ACh released by the fourth stimulus and the resulting initial concentration of ACh, $[A]_4$, are equal to, or smaller than, the corresponding amount and the concentration, $[A]_1$, produced by the first stimulus, *i.e.,* $[A]_4 \leq [A]_1$.
Methods: The previously published model of neuromuscular transmission (3) was modified by (*a*) decreasing the concentration of R, [R], below that in normal subjects ($[R]_{normal} = 7.75 \cdot 10^{-5}$ M), (*b*) constant $[A]_1$ ($= 7.75 \cdot 10^{-6}$ M), but decreasing $[A]_4$, and (*c*) twitch strength of either T_1 or T_4 calculated identically from the peak concentration of the Rec with both binding sites occupied by ACh. The rate of ACh hydrolysis and the binding affinities of ACh for R were those reported in the model (3). T_1, T_4 and T_4 / T_1 were simulated for the diminishing R and $[A]_4$, alone or in combination.
Results: A decrease in [R] to less than $0.3 \cdot [R]_{normal}$, with $[A]_4 = [A]_1$, diminish both T_1 and T_4. However, T_4 / T_1 remains constant at 1. A decrease in $[A]_4$ below $0.8 \cdot [A]_1$, with $[R] = [R]_{normal}$, diminishes T_4 and T_4 / T_1. When both [R] and $[A]_4$ are diminished together, T_1 decreases slightly, whereas T_4 and T_4 / T_1 decrease markedly.
Discussion: The simulations demonstrate that a decrease in [R] by itself is not associated with fade, even though both T_1 and T_4 are diminished at $[Rec] \leq 0.3 \cdot [R]_{normal}$. Twitch fade, defined by either $T_4 < T_1$ or T_4 / $T_1 < 1$, is simulated only for $[A]_4 < [A]_1$. Twitch fade is more pronounced, if both [R] and $[A]_4$ are diminished. The simulations suggest that muscle weakness and fade observed in patients with myasthenia gravis may be due to a combination of a diminished number of the postsynaptic receptors and a diminished release of ACh elicited by repetitive stimulation.

References:

(1) Mann R *et al*: Anesthesiology 93: 346, 2000.
(2) Kamenskaya MA *et al*: Arch Neurol 32: 510, 1975.
(3) Nigrovic V, Amann A: J Pharmacokinet Pharmacodyn 30: 23, 2003.

S-420.

NEUROMUSCULAR BLOCKADE IN SURGERY INVOLVING FACIAL NERVE MONITORING - A SYSTEMATIC REVIEW

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Introduction:
Intraoperative monitoring of facial nerve function during neurotologic and middle ear surgery allows early detection of surgical nerve damage and reduces the incidence of postoperative nerve dysfunction. Surgeons often request avoidance of neuromuscular blocking agents. This is based on the hypothesis that the use of neuromuscular blockers can make the facial muscles unresponsive to nerve stimulation. Anesthetic management is challenging in these patients because simultaneous monitoring of evoked potentials may limit the use of inhalational agents. Muscle groups differ in their response to neuromuscular blocking agents. Facial muscles recover earlier than the muscle groups supplied by ulnar nerve.
Methods:
Reports of clinical studies examining the facial nerve function during various degrees of peripheral neuromuscular blockade were sought systematically using Medline database from 1966-2004 without language restriction. Abstracts, letters of correspondence and unpublished observations were not considered for the review. Two authors read all selected articles independently and consensus was subsequently achieved. Search terms such as facial nerve monitoring, neuromuscular blockade, otologic surgery and middle ear surgery were used. The following data were obtained; number of patients, type of surgery, anesthetic technique, muscle relaxant used, type of peripheral nerve and facial nerve monitoring and facial muscle response during various degrees of neuromuscular blockade as measured by ulnar nerve stimulation.
Results:
Six studies were found involving 102 patients. Two studies were done in middle ear surgeries and 4 others were studied in acoustic neuroma resections. Atracurium was used in 5 studies and pancuronium was used in one study. Neuromuscular blockade monitoring was done in five studies using ulnar nerve train-of-four stimulation and compound muscle action potential (CMAP) in one study. Facial nerve monitoring was done using accelerometer in 2 studies and facial electromyography (EMG) in 4 studies.
CMAP of facial nerve was also done in one study. One study showed that with 100% neuromuscular blockade no facial nerve response was measured in 31% of patients, whereas another study did not find any suppression of facial nerve response even complete block. Facial nerve EMG response was detectable in all patients in 2 studies with 75% ulnar blockade. One of these studies has shown that mean stimulation threshold to obtain facial muscle response was increased in patients with 75% block compared to 0% block. None of the studies have shown any impairment of facial nerve monitoring with 50% block.
Discussion:
During surgeries involving facial nerve monitoring use of non-depolarizing muscle relaxants are not contra-indicated as part of standard anesthesia technique. However it is advisable to monitor the ulnar nerve TOF and avoid 100% neuromuscular blockade. Partial neuromuscular blockade (50 - 75 %) does not affect the intra-operative facial nerve monitoring.

S-421.

SUCCINYLCHOLINE ALSO HAVE A BIPHASIC ONSET TIME

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INTRODUCTION: Biphasic onset time for rocuronium has been postulated without supporting data (1) and also denied by others (2). Objective and proper methodology have demonstrated that some nondepolarizing muscle relaxants (NDMR) have two different phases during onset time (3 - 4). The aim of the present trial is to define if such an action is also present when succinylcholine (SCH) is used.
MATERIAL & METHODS: After institutional consent, 20 adult patients were anesthetized with propofol and nitrous oxide. They were 45 ± 15 years, 69 ± 11 Kg., 13 female and 7 males, any of them having clinical evidence to contraindicate SCH. Standard monitoring was used, and SCH 1 mg.Kg^{-1} administered for intubation. Time to 80% blockade, maximum effect and onset time were assessed by electromyography. Velocity and speed of action were derived as the ratio between fractional block and time: for the ***initial*** period (up to 80%), ***final*** phase (between 80% and maximal block) and ***global*** onset time (from drug injection to maximum effect) and expressed as ***% / seconds*** and **seconds / %** respectively. Analysis of variance and Student-Neuman-Keuls with 0.05 level for significance were used for statistical comparison.
RESULTS: Final period of onset time was significantly slower than the initial phase. Global velocity and speed were intermediate. (Table1).
DISCUSSION: According to present results, SCH also follow the pattern of a biphasic onset as NDMR do (3 - 4). Although some observations have not been originally discussed in this way, when pharmacodynamic data for SCH are closely examined and recalculated, a biphasic onset time very similar to present results is noticed (2.93 and 0.55 %/sec and 0.34 and 1.8 sec/% for initial and final phases respectively) (5). Classical mechanisms to explain onset time (1) do not support this type of findings, instead of that, speculations can be made among timing differences in the association constant between muscle relaxants molecules to various receptors population (6), as a possible cause.

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2) Br J Anaesth (1992) 65: 269.
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4) Anesth Analg (2004) 98: S.1037.
5) Br J Anaesth (2000) 85: 251.- 6) Biochemistry (1980) 19: 5344

Table 1: ♦ seconds ♣ % / sec * sec / %)

	80%♦	MAX(%)	ONSET ♦	(1)INI-TIAL	(2)FINAL	(3)GLO-BAL	SIG
SCH	37±14	99±0.8	69±15	2.57±1.4♣	0.715±0.3	1.53±0.5	1)vs=2-3 2) vs= 3
				0.462±0.17*	1.67±0.73	0.698±0.16	2)vs=1-3

S-422.

ROCURONIUM BIPHASIC SPEED OF ONSET CHARACTERIZATION: TWO DIFFERENT PHENOMENA?

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INTRODUCTION: Three quarters of the receptors must be occluded before neurotransmission begins to fail, 0.8 occupancy for 50% reduction of twitch, and over 90% before all junctions fail (1 - 2). To clinical characterize this concepts the following trial was undertaken.
MATERIAL & METHODS: During intravenous and nitrous oxide anesthesia (patients n= 23), an initial dose of rocuronium was used by priming technique (60 + 340 µg.Kg^{-1},). Neuromuscular block for priming and main dose (MAX), time to 80% blockade and onset time were assessed by electromyography. *Velocity* was calculated as the ratio between time and fractional blockade ***(sec / %)*** during the ***initial*** phase of onset (up to 80%), ***final*** period (80% to maximal block) and ***global*** velocity (drug injection to maximal effect). After 25% spontaneous recovery, a second dose (100 µg.Kg^{-1}) was administered. New maximal effect was corrected for the remaining 75% block and corresponding velocity calculated. T test, analysis of variance and Student-Neuman-Keuls with $p<0.05$ significance level used for statistical comparison.
RESULTS: No statistical difference between initial and second dose was found for MAX. Onset time was significantly shorter after the second dose, but global velocity was statistically slower, as in the range to final speed for the first administration. The later in turn, was significantly slower in comparison to both initial (biphasic onset time) and global velocity (Table 1).
DISCUSSION: According to previous statement (1 - 2) actual 80% and MAX lies between 80 and 90% blocked receptors. Due to similar effect and speed, number and type of receptors occupied during the first slow final and second global period should probably be the same, and possible different from the initial receptor group responsible for early 80% fast blockade. Differences among receptors can be structural or functional as pre and post-synaptic receptors may not have the same binding specificities (3). Only prejunctional suppressive action is used to explain the priming effect (4). Sensitivity for the relevant segment of receptors responsible for the fast initial phase, can varied with time and molecules concentration (non stationary) (5) to the next slower period, conforming two different phenomena.

REFERENCES:
1) J Physiol 1967, 191: 59.
2) Anesthesiology 1977, 46: 94.
3) J Physiol 1988, 403: 425.
4) Anesthesiology 1986, 65: 480.- 5) Anesthesiology (1994) 81: 59.

Table 1.- ¶) Statistically slower vs initial and global (*) NS between 1st final and 2nd global

	PRIMING (%)	80%BLK(sec)	MAX (%)	ONSET (sec)	INITIAL (sec/%)	FINAL (sec/%)	GLOBAL (sec/%)
1st dse	8±5	87±45	94±5	204±75	1.09±0.5	9.96±6 ¶*	2.2±0.8
2nddse			93±5	154±43			10.1±5.5*
.p=			0.420	0.009		0.923*	0.0001

S-423.

ROCURONIUM: CORRELATION BETWEEN FRACTIONAL MOLAR CONCENTRATION, ONSET TIME AND MAXIMAL BLOCKADE

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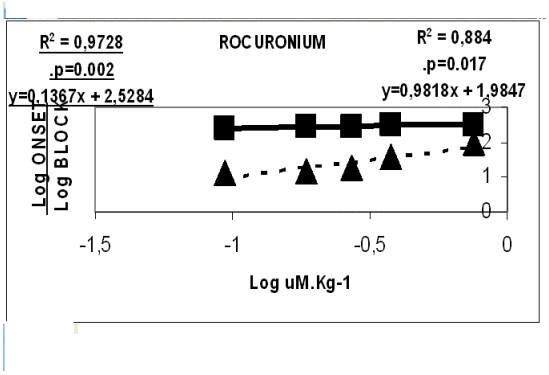
INTRODUCTION: Sub-paralyzing doses for muscle relaxants (**MR**) have the same onset time (**OT**) (1). Onset depends on molecular size (2 - 3). An excellent correlation between doses and square root of time has been described (4). Good correlation between molar potency for rocuronium (**ROC**) and time to partial effect has been stated (5), but no studies correlated fractional molar potency and OT and maximal blockade (**MAX**) for ROC, which is the aim of present trial.
MATERIAL & METHODS: During elective induction with intravenous agents and nitrous oxide, patients randomly received 0.34, 0.68, 1, 1.38 or 2.8 x ED_{50} ROC. MAX and OT were assessed by electromyography. Speed of action (**SA**) was considered as the ratio between OT and MAX (*sec/%*). Molar concentration (**µM.Kg^{-1}**) for doses, square root (**V^2**) and logarithmical (**Log**) transformation were used to correlate data. Analysis of variance, Student-Neuman-Keuls and $p<0.05$ were used for statistical comparisons.
RESULTS: No statistical difference was noticed among OT for the five doses. MAX ranged between 14 and 92% directley related to dose, without full paralysis. Good and significant correlation between V^2µM.Kg^{-1} and V^2OT and V^2MAX (R^2 =0.926, 0.962 and p= 0.008, 0.009 respectively) was found and also for Logµ M.Kg^{-1} and LogOT and LogMAX (Fig 1).
DISCUSSION: OT for low doses MR is not statistically different up to ED_{95} and inversely related to ED_{50} (1).To the opposite we found longer OT related to gradual increase of fractional ED's, as SA to every greater MAX was slower. Good correlation has been described between molar concentration of equipotent doses of various MR including ROC and OT (5). Actual results show that good and statistical correlation also exists between molar concentration of fractional ED's and their increasingly respective OT. Logarithms and V^2 can be use interchangeable for this type of calculations.
REFERENCES:
1) Anaesth Pharmacol Rev 1993, 1: 34.
2) Br J Anaesth 1978, 50: 361
3) Anesthesiology 1982, 67: 247.
4) Anesthesiology 1976; 45: 370.- 5) Anesthesiology 1999; 90: 425



S-424.

VECURONIUM AND ATRACURIUM ONSET TIME AND SPEED OF ACTION: A RESTRICTIVE METHOD FOR ASSESSMENT

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INTRODUCTION: Neither speed of action (**SA**) or onset time (**OT**) for equipotent doses of vecuronium (VEC) and atracurium (ATR) are supposedly statistically different (1 - 2). Potency, final blockade and variability can influence onset (3). The present trial reassess **OT** and **SA** for both muscle relaxants in two matched groups for final block, a restricted method which previously demonstrated that ATR is faster than VEC (3).
MATERIAL & METHODS: During intravenous and nitrous oxide induction, consenting patients received either VEC or ATR. Time to 80% blockade, maximum effect (MAX) and onset time were assessed by electromyography. Only patients with 91 and 92% final block were matched. Age, gender and weigh were also matched. ***Velocity (% / sec)*** were calculated as the ratio between fractional block and time, during ***initial*** phase (up to 80% block), ***final*** period (between 80% and MAX) and ***global*** velocity (from drug administration to MAX) (2). Analysis of variance, Student-Neuman-Keuls and T test were used for statistical comparison with $p<0.05$ as significance level.
RESULTS: Patients received 0.99 ± 0.11 and 0.929 ± 0.13 x ED_{95} of VEC and ATR (p= 0.385) (n= 7 e/a) respectively. Poor correlation was found between **OT** and block (R^2= 0.319 and 0.250, p= 0.328 and 0.253 for VEC and ATR respectively). No significant differences were found between groups. *Final* speed was statistically slower and *initial* velocity faster (biphasic onset speed) (Table 1).
DISCUSSION: Time to a fraction of final blockade, when the later is restricted to a range, is nearly constant and reproducible (3). For comparison to other investigations, sample size, anthropometric data and sub paralyzing block were kept similar, and a narrower and more restricted range for final block (1%) employed. Halogenated agents were avoided and a third drug excluded. Velocity was used for an expanded and more comprehensive comparison. **OT** during previous studies is showed as standardized curves (3) and any additional numerical data included in order explaining a shorter **OT** for ATR. Actual controlled method couldn't demonstrate statistically differences neither on **OT** or **SA** between equipotent doses of VEC and ATR. Biphasic **OT** as previously described (2) is sustained by present results.
REFERENCES: 1) Br J Anaesth (1986) 58: 620.- 2) Anesth Analg (2004) 98: S.1037.- 3) Anesth Analg (1993) 77: 574.

Table 1.- ((*) seconds.- (♣) % / sec)

	80%*	MAX(%)	ONSET*	*INITIAL*♣	FINAL♣	GLOBAL♣
VECURONIU	273±58	91.5±0.5	482±57	0.303±0.05	0.061±0.02	0.192±0.02
ATRACU	281±72	91.5±0.5	407±72	0.306±0.10	0.107±0.05	0.232±0.05
SIG (p=)	0.813	1.000	0.052	0.945	0.068	0.094

S-425.

THE EFFECT OF ISOFLURANE ON DISTRIBUTION OF CRYSTALLOID SOLUTIONS IN HUMANS

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Introduction: The current view is that fluid retention and postoperative tissue edema during surgery are caused by surgical trauma or mechanical ventilation and not by the administration of an anesthetic per se. However, our research group has conducted two recent studies in sheep [1, 2] that have demonstrated that the combination of isoflurane anesthesia and mechanical ventilation significantly alters the disposition of an infused fluid during anesthesia. In one of these studies[2], isoflurane was singled out as the cause for reducing urinary excretion and instead increasing peripheral fluid accumulation. We hypothesize that the same results will be found in humans.
Methods: Eleven volunteers of both sexes were included and assigned either to an awake or an isoflurane-anesthetized protocol during which they received 25 mL/kg of 0.9 % saline during 20 minutes. Plasma volume measurements were performed using indocyanine green dye. Arterial blood was frequently sampled for massbalance- and volume kinetic analysis [3] of the fluid distribution for the entire experiment of three hours. Hemodynamic parameters were in both protocols measured using ECG and a non-invasive bloodpressure device. Cardiac output was measured using a CardioQ-doppler esophageal catheter. Hormones pertinent to fluid distribution were also measured .
Results: All subjects tolerated the study protocols well. The subjects in the anesthetized group made less urine than in the awake group. On the average the awake group made 795 mL of urine and the anesthetized 575 mL. Volume kinetic analysis showed extremely good curve-fitting. The elimination rate constant (kr) was decreased in the anesthetized protocol.
Discussion and conclusion: Preliminary results in humans are in accordance with previous results found in sheep. Inhalation anesthetic agents may have inhibitory effects on urine output and may contribute to redistribution of infused fluids interstitially.

References:
1. Anesthesiology, 2002. 96(2): p. 442-9.
2. Anesthesiology, 2003. 98: p. 670-81.
3. Anesthesiology, 1997. 87(2): p. 204-212.

Regional

S-426.

LONG-TERM EVALUATION OF MOTOR FUNCTION FOLLOWING INTRANEURAL INJECTION OF ROPIVACAINE USING WALKING TRACK ANALYSIS IN RATS

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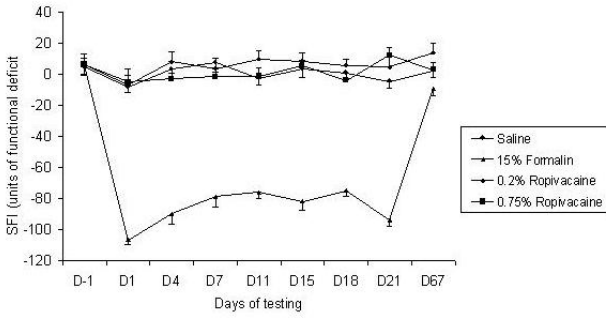
Introduction: There is a paucity of data regarding neurologic function following nerve injury. Motor dysfunction has been reported after intraneural injection of local anesthetics (1). Our objective was the long-term evaluation of motor function following intraneural injection of ropivacaine in rats using the sciatic function index (SFI) (2), derived from walking track analysis.
Methods: Rats were randomly assigned to one of four groups of 13 animals each. A needle was inserted under magnification into the left sciatic nerve and 0.2 ml of normal saline, 15% formalin, 0.2 or 0.75% ropivacaine were injected intraneurally. The right side was sham operated. Walking track analysis was performed preoperatively and on days 1, 4, 7, 11, 15, 18, 21 and 67 following the intraneural injection. At the end of the experiment (day 67) a semiquantitative evaluation of neuropathologic changes was performed by three independent observers.
Results: Animals belonging to the saline and ropivacaine (0.2 and 0.75%) groups had no detectable impairment of motor function at any timepoint. In contrast, rats belonging to the formalin group had a complete loss of motor function immediately after the intraneural injection (Figure 1) which persisted until day 21 and returned to normal by day 67. Important changes (score = 2) with excellent inter-observer agreement were seen only in the Formalin group. This applied to both axonal degeneration and Schwann density evaluations.
Discussion: The strength of this study design is that it provides sequential information about dynamic motor function following nerve injury. In addition, each animal acted as its own control. Foot prints remained normal on the sham operated side proving that SFI is not sensitive to non nervous factors such as skin clips or muscle incision. SFI does not assess, however, the sensory component following nerve injury. Because motor function is last to return (compared to sensory function), dynamic assessment of motor function may better characterise recovery from nerve injury**.** These findings suggest that intraneural injection of ropivacaine at concentrations routinely used in clinical practice had no deleterious effect on sciatic nerve motor function in the rat model as assessed by the SFI.

References:
1. *Br J Anaesth* 1992; **69:** 433-8
2. *Experimental Neurology* 1982; **77:** 634-43

Fig 1. SFI profile following intraneural injections of saline, 15% formalin, 0.2 and 0.75% ropivacaine. Data are mean (SD). *p < 0.001 refers to comparisons to baseline.



S-427.

MINIMUM CONVULSIVE DOSES OF BUPIVACAINE, LEVOBUPIVACAINE, DEXTROBUPIVACAINE AND ROPIVACAINE IN CATS

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Introduction: Bupivacaine is a racemic mixture of optical isomers, levobupivacaine (S(-) bupivacaine) and dextrobupivacaine (D(+) bupivacaine). Although precise relative anesthetic potencies of bupivacaine, levobupivacaine, dextrobupivacaine, and ropivacaine, another long acting local anesthetic, are remain uncertain, they are thought to be roughly equal(1,2). On the other hand, it is demonstrated that levobupivacaine and ropivacaine are weaker but dextrobupiovacaine is stronger than bupivacaine in cardiotoxicity. However, accurate minimum convulsive doses of these local anesthetics with the same model and animals have not been investigated yet. We studied the minimum convulsive dose of bupivacaine (n = 6), levobupivacaine (n = 5), dextrobupivacaine (n = 6) and ropivacaine (n = 5) in the cats.
Methods: Brain electrodes were chronically implanted in the cortex, amygdala, hippocampus and midbrain reticular formation of the cats under halothane anesthesia. One week after the implantation, the cats were anesthetized with halothane and a laryngeal mask airway was inserted. While anesthesia was maintained with 0.5% halothane and 5mcg· kg^{-1} fentanyl in oxygen under mechanical ventilation for 30 min, 0.25% levobupivacaine, 0.25% bupivacaine, 0.25% dextrobupivacaine, or 0.25% ropivacaine was infused intravenously at a rate of 1mg· kg^{-1}· min^{-1}. The cortical, amygdala and hippocampal electroencephalograms, reticular multi-unit activity were continuously monitored. The blood samples when convulsions were induced were taken and the serum concentrations of these local anesthetics were assayed with HPLC system. All data were expressed as mean ± SD. Statistical comparison among groups was performed with one-way ANOVA followed by Fisher's PLSD. P<0.05 was considered statistically significant.
Results: The minimum convulsive doses of levobupivacaine, ropivacaine, bupivacaine, and dextrobupivacaine were 13 ± 3 mg· kg^{-1}, 13 ± 4 mg· kg^{-1}, 11 ± 2 mg· kg^{-1}, 9 ± 1 mg· kg^{-1}, respectively. The minimum convulsive dose of dextrobupivacaine was significantly lower than those of levobupivacaine and ropivacaine. The minimum convulsive dose of bupivacaine tended to be lower (but not statistically significant) than those of levobupivacaine and ropivacaine.
Discussion: Convulsive potencies of levobupivacaine and ropivacaine are significantly weaker than that of dextrobupivacaine. Bupivavaine is likely to be a stronger convulsant than levobupivacaine and ropivacaine based on the assumption that bupivacaine, levobupivacaine, and ropivacaine is roughly equivalent in anesthetic potencies.

References:
(1)Anaesthesia, 56, 331-341, 2001
(2)Br J Anaesth. 76, 300-307, 1996

S-428.

SYMPATHETIC BLOCK WITH ADDITION OF DEXMEDETOMIDINE TO A LOCAL ANESTHETIC IN DOGS

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BACKGROUND: The aim of this study is to examine the duration and magnitude of vasodilative effect induced by sympathetic block with the addition of different concentrations of dexmedetomidine to mepivacaine.
METHODS: Mean arterial pressure (MAP), heart rate (HR), and right and left brachial artery blood flow (BABF) were measured before and after cervicothoracic sympathetic block (CSB) used as sympathetic block in dogs. The experimental protocol was designed as follows: 1) Group 1: left SGB using 0.5% mepivacaine 1 ml (n = 6), 2) Group 2: left SGB using the addition of dexmedetomidine 0.5 microgram to 0.5% mepivacaine 1 ml (n = 6), 3) Group 3: left SGB using the addition of dexmedetomidine 5 micrograms to 0.5% mepivacaine 1 ml (n = 6).
RESULTS: MAP showed no significant changes throughout the study in the groups 1 and 2. In the group 3, MAP significantly decreased after CSB (baseline, 130±8 mmHg; peak at 70 min after CSB, 118±10 mmHg; $p<0.05$). HR showed no significant changes throughout the study in all groups. In the group 1, left CSB increased left BABF significantly from 5 min through 50 min after the block (baseline, 100%; peak at 10 min after CSB, 176±28%; $p<0.01$). In the group 2, left CSB induced a significant increase of left BABF from 5 min through 90 min after the block (baseline, 100%; peak at 80 min after CSB, 176±45%; $p<0.01$). The values of left BABF after CSB in the group 2 were significantly higher than those in the group 1 from 60 min through 90 min after CSB ($p<0.05$). In the group 3, left CSB decreased right BABF (baseline, 100%; peak at 10 min after CSB, 60±8%; $p<0.01$) and left BABF (baseline, 100%; peak at 10 min after CSB, 72±19%; $p<0.01$).
CONCLUSION: Sympathetic block with the addition of dexmedetomizine to local anesthetics prolongs the duration of vasodilation. However, the addition of higher dose of dexmedetomidine decreases in BABF after sympathetic block because of systemic vasodilative effect of dexmedetomidine.

S-429.

VALDECOXIB EFFICACY AND SAFETY WITH LOCAL ANESTHETIC IN CONTINUOUS FEMORAL CATHETER INFUSION IN TOTAL KNEE REPLACEMENT SURGERIES

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Introduction: Postoperative pain is commonly under-treated after orthopedic surgery[1,2]. It has been suggested that a combination of regional anesthetic techniques with COX-2 inhibitors can significantly reduce postoperative pain and the need for opioid analgesics [3]. This may lead to early rehabilitation and improved functionality of the affected limb. The aim of this double-blind study is to evaluate the analgesic efficacy and safety of valdecoxib (Bextra®) in conjunction with continuous administration of local anesthetic in patients undergoing total knee replacement surgery (N=120). Our hypothesis is that compared to a placebo, the use of the local anesthetic with valdecoxib will reduce postoperative opioid requirements and speed the recovery of the affected limb.
Methods: After institutional IRB approval, patients undergoing knee replacement surgery were consented and randomly assigned to one of four groups (Group 1: placebo PO + placebo infusion, N=7; Group 2: placebo PO + ropivacaine infusion, N=8; Group 3: valdecoxib PO + placebo infusion, N=9; Group 4: valdecoxib PO + ropivacaine infusion, N=7). Patients received valdecoxib (40 mg) or placebo 30-60 minutes before surgery and 20mg PO twice a day for three days. All patients received a femoral block preoperatively (20cc 2% lidocaine and 10cc 0.5% ropivacaine) by nerve stimulation technique using the Arrow® StimuCath™ system. Postoperatively, patients were connected to the I-Flow® ON-Q™ Continuous Nerve Block system (0.9% NaCl placebo or 0.1% ropivacaine). Further, patients had PCA morphine access for the first 24 hours with oral opioids thereafter. Nerve block systems were removed on POD3.
Results: There were no technical problems with femoral catheter placement or postoperative infusion. There were no statistical differences between any of the groups for the intensity of post-operative pain (p=0.55), morphine consumption (p=0.87), or length of stay (p=0.29). However, group 3 demonstrated greater ranges of motion on POD1 (p=0.07), and Groups 3 and 4 demonstrated better levels of pain control compared to Group 2 from late POD1 through POD3 (p=0.003). There were no differences between the groups with respect to the incidence of side effects.
Discussion: Our preliminary findings suggest that patients receiving valdecoxib had superior pain relief at the end of POD1 and improved function. However, all patients required large amounts of morphine on POD1. We suspect this is due to surgical compression dressings as well as the lack of a sciatic block to treat posterior knee pain. Although our pilot study demonstrated that 0.1% ropivacaine provides adequate pain relief while maintaining muscle strength, it is possible that this concentration still has an effect on quadriceps strength as demonstrated by differences between groups 3 and 4 for early mobilization.

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S-430.

THE INFLUENCE OF UNILATERAL SPINAL ANESTHESIA ON DEEP SEDATION

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Introduction: The aim of this study is to evaluate whether unilateral spinal anesthesia may alter the susceptibility to the sedatives compared to conventional bilateral spinal anesthesia.
Methods: Sixty patients undergoing elective knee surgery were enrolled this prospective, randomized, double blind study and divided into three groups(n=20 in each). After induction of spinal anesthesia in the lateral position, the position was maintained for 15 min in U (unilateral) group or turned supine immediately in B (bilateral) group. In the control group, patients were sedated without preceding spinal anesthesia. Sedation was performed by a blind anesthesiologist and doses of midazolam needed to deep sedation were recorded.
Results: The doses of midazolam administered to the point of deep sedation were 0.13, 0.08 and 0.15mg/kg in U, B and the control goup.
Discussion: The effect of unilateral spinal anesthesia on the susceptibility to the sedatives was decreased compared to conventional bilateral spinal anesthesia.

S-431.

THE EFFICACY OF "PERICONAL ANESTHESIA" IN TIME CONSUMING VITREORETINAL OPERATIONS

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Introduction: Patients with ophthalmic disease scheduled for surgery are mostly elderly and have associated advanced systemic cardiovascular disease and high risk factors for general anesthesia (G.A), besides the increased medical coasts. Retrobulbar injection, the most commonly used local anesthesia (L.A) for ocular surgery has its own vision and life threatening complications. We prospectively evaluated the efficacy of periconal anesthesia (peribulbar, periocular) in time consuming vitreoretinal operations.
Methods: In this study, we prospectively studied 72 patients who were operated for viterectomy and retinal reattachment surgery with periconal anesthesia .The L.A mixture consisted of 4 ml 2% lidocaine, 4ml 0.75% bupivacaine and 150 units of hyalurinidase. With a sharp, fine 27 G x 20 needle. L.A mixture was injected from 2 sides, first inferotemporal and second superonasal of the orbital rim. The adequacy of the periconal anesthesia was evaluated preoperatively on the basis of globe akinesia and anesthesia based on four grades (IV, III operable and I, II inadequate for surgery). The cooperation of the patients on injection and during surgery were classified to three grades (E = Excellent, S = Satisfactory and P = Poor). We evaluated onset and duration of anesthesia and akinesia and complications.
Results
The demographic data from 72 study patients shows:
44 women, 28 men ages from 39 to 84 (mean = 66.16 years)
The operation time was 55-240 minutes (mean = 113.78)
Considering anesthesia and akinesia 71 patients were in group III and IV.
Considering the operation, 71 patients (99%) were cooperating sufficiently in the beginning of the surgery.
IOP was without any change during operation because there was no pain and strain.
The surgeon's satisfaction was incredibly more than retrobulbar .There was no complication due to insufficient anesthesia.
Discussion: Our results show that periconal anesthesia can be effectively used for time consuming vitreoretinal operations. It has low rate of complications and is very well tolerated by the patients and may be preferred for local anesthesia especially in scleral bucking procedures in patients with high myopia.

S-432.

EFFECTS OF INTRATHECAL EPINEPHRINE ON INTRAOPERATIVE BLOOD LOSS AND VASOPRESSOR USE DURING RADICAL PROSTATECTOMY

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Introduction: We recently observed that intrathecal epinephrine (EPI) use may reduce blood loss and vasopressor use during radical retropubic prostatectomy (RRP) performed by one surgeon. This effect may be via an extra-spinal mechanism, however, reports on these benefits are sparse.
Methods: We prospectively evaluated two consecutive groups of patients undergoing RRP with combined spinal-epidural anesthesia. Groups-I (n=20) and -II (n=20) received intrathecal isobaric bupivacaine 0.5% 2.5-3.0 ml while Group-II only received EPI 150 mcg. Epidural "top-ups" consisted of lidocaine 2% for all patients. Hypotension (systolic < 85 mmHg) was treated with either intermittent boluses (40 mcg) or continuous phenylephrine infusion. Autologous blood donation of 2 units was encouraged in all patients. Estimated blood loss (EBL), fluid (crystalloid+colloid) requirements, and the number of autologous or packed red blood cell (PRBC) units transfused were recorded. Using historical data it was estimated that 20 patients in each arm would be needed to detect a difference in EBL of > 0.5 L between the groups with 80% power. Students t and Fishers exact tests were performed. For non-normally distributed data the Mann-Whitney U test was done.
Results: The two groups did not differ in demographic data or mean blood loss (Table). The need for intermittent boluses of phenylephrine did not differ between the two groups (6/20 vs. 5/20, P=0.72) as was the need for continuous phenylephrine infusion (3/20 vs. 7/20, P=0.27), respectively. The proportion of patients with an EBL > 1.5 L did not differ between groups I or II, 3/20 vs. 6/20, P=0.45, respectively. Patients in group-II, however, received PRBCs more often than group-I patients (P=0.047, Table).

Conclusions: These preliminary data do not support an important role for intrathecal EPI to reduce intraoperative blood loss or vasopressor requirements in patients undergoing RRP with combined spinal-epidural anesthesia.

Patient and Intraoperative Characteristics			
	Group I - No EPI (n=20)	Group II - EPI (n=20)	P value
Age, yr.	56±9	57±6	0.69
Height, cm	177±8	175±8	0.40
Weight, kg	85±13	83±12	0.65
Preop Hb, gm / dl	14.4±1.1	14.2±1.2	0.49
EBL, L	1.3±0.6	1.4±0.7	0.94
Cryst + Coll, L	4.8±1.1	5.4±1.1	0.06
Autologous, n	0 (0-2)	0 (0-2)	0.54
PRBCs, n	0 (0-2)	0 (0-4)	0.047

Data are mean SD or median (range).

S-433.

SLAB COMPOSITE APPROACH TO MAGNETIC RESONANCE NEUROGRAPHY SCANS OF THE BRACHIAL PLEXUS

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Introduction: Magnetic resonance neurography is a method by which nerves can be selectively highlighted. We explored a variety of approaches by which to display 3D brachial plexus information from MRI data sets using commercially available software. We developed a frontal slab composite approach that creates a quasi-3D reconstruction effect of the entirety of the brachial plexus.
Methods: With IRB approval, magnetic resonance neurography scans of the brachial plexus were performed in ten volunteer subjects. MR neurography imaging was performed on a GE 1.5 Tesla MR scanner with 9.0 software and HighSpeed gradient platform using a phased array torso coil. Coronal STIR and T1 oblique saggital sequences of the brachial plexus were obtained using 4-6 mm slices (no interslice gap). Saturation bands were applied, which enabled better signal suppression over patient induced subclavian artery flow and respiratory artifacts. Multiple software programs were explored for possible display and manipulation of the MRI images. Automatic segmentation (which depends on distinguishing different grey levels) of these programs was inadequate to separate the subtle differences of the nerves from the surrounding tissue, and required supplemental manual segmentation, complete or partial, in nearly all cases. There was a significant amount of variation between individuals in terms of their brachial plexus anatomy.
Results: Educational materials created include: (1). *Animated GIFs* (oblique views). Fly-through views of the stack of images were created with colorized nerves and vessels. (2) *3D model.* An AVI movie of the brachial plexus illustrates the 3-D effect of tilting and rotation on the relative position of the vessels, bone, and nerves, upon use of different angles of approach to the brachial plexus. (3) *Composite frontal slabs* (coronal views), which are enhanced 2D frontal view projections of the underlying coronal slices onto a single slice. This prominent highlighting makes possible a composite quasi 3-D rendering effect for the totality of the brachial plexus. Each composite slab image was created from an average of ten sequential coronal view data sets. Using the layering and mask tools in Photoshop, the areas of interest (bones, nerves, vessels) were cropped appropriately. Blending between the layers was done to create smooth transitions. The structures of interest were enhanced (using the dodge and burn tool) or colorized.
Discussion: Image-processed slab composite quasi-3D MR neurographic scans of the brachial plexus are superior to conventional MR scans, and have educational value in illustrating the complexity and individual variation of the brachial plexus. Anatomical landmark information relevant to the performance of infraclavicular plexus block is presented.
References:
Filler AG, Hayes CE, Kliot M, Winn HR, Bell BA, Tsuruda JS. Magnetic resonance neurography. Lancet 1993; 341: 659-661.

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S-434.

CLINICAL EXPERIENCE WITH ULTRASOUND GUIDED INFRACLAVICULAR BRACHIAL PLEXUS BLOCK

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Introduction: Ultrasound (US) guidance has been used during the past 6 years to perform infraclavicular brachial plexus blocks (ICBPB) in our institution (1). The aim of this study was to analyze retrospectively all of the ICBPB performed over a 21 month period obtained from our database developed using an automated intraoperative anesthesia record keeping system (Saturn, Drager , Telford , PA).
Methods: Data for all patients receiving US guided ICBPB were analyzed to determine the rates of successful blocks, failed blocks necessitating conversion to general anesthesia, requirement for local anesthesia supplementation and/or larger than usual dose of sedation, and complications.
Results: A total of 829 patients (mean age of 38±14 and male: female ratio of 4:1) received blocks for surgery of the hand, forearm or arm lasting 159 ± 127 minutes. All blocks were performed by residents who were directly supervised by attending physician holding the US probe in place to guide them. In six patients (0.7%) the block was converted to general anesthesia (GA); block failed in 3 (0.35%), positional discomfort despite a working block occurred in 2 (0.25%) approximately 2.5 hours after the start of surgery, and block combined with GA was planned for the one patient. Propofol (314±625 mg) was used in 34 patients (4.1%) in addition to the routine sedation dose of fentanyl, 50-100 µg and midazolam, 1-2 mg given immediately before administering the block. Two of these patients required local anesthetic infiltration by surgeon and propofol was used in another 32 patients despite good sensori-motor block because of use of a microscope necessitating absolute immobility (7), positional discomfort, patient anxiety and anesthesiologist preference were the reasons. Vascular puncture occurred in 8 (1%) patients but were all inconsequential. None of the patients had inadvertent intravascular injection, signs of local anesthetic toxicity, or complaints suggestive of peripheral nerve injury.
Discussion: Our overall failure rate was about 1%; this fact and the lack of significant complications suggest that this technique is effective, reliable and safe. In contrast the best reported success rate with a nerve stimulator technique is 86 % (2) significantly lower than ours (99%) Attending physician experience appears to be a factor in the success rate, as we noted a moderate correlation between the two.
Reference
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S-435.

NO NEED FOR NEUROSTIMULATION IN ULTRASOUND-GUIDED INFRACLAVICULAR BRACHIAL PLEXUS BLOCK

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Introduction: Ultrasound guidance (USG) for infraclavicular blocks provides real time visualisation of the advancing needle and local anesthetic distribution, minimising the risk of complications and decreasing procedural time. Neurostimulation is often combined with USG, but its benefit has never been formally evaluated. Therefore, we conducted a prospective randomised study comparing the speed of execution and quality of USG infraclavicular block with and without neurostimulation.
Methods: 72 patients scheduled for hand or forearm surgery were randomised to receive lateral infraclavicular block with either USG alone (Group U) or USG combined with neurostimulation (Group US). The anesthetic solution consisted of 0.5 $ml \bullet kg^{-1}$ of lidocaine carbonate 1.5%, bupivacaine 0.125% and epinephrine 1 :200 000 (final concentrations). In group U, local anesthetic was deposited in a U-shaped distribution posterior and to each side of the axillary artery. In group US, a single injection was made after obtaining a distal motor response with a maximal stimulating current of 0.5 mA, and the spread of local anesthetic artery was recorded. Block onset and quality were quantified with a verbal analogue scale at 5-minute intervals for 30 minutes. Patients were contacted 1 week after their surgery to evaluate the incidence of pneumothorax and neuropathy.
Results: Procedure times were significantly shorter in group U compared to group US (3.1 VS 5.2 minutes, p=0.006). Thirty minutes after injection, 86% of patients in group U had a complete block compared to 57% in group US (p=0.007). Block supplementation rates were 26% in group US VS 8% in group U (p=0.049). Block failure occurred in one patient in group US due to inability to obtain a distal stimulation after 20 minutes. Complication rates were low, and included 3 arterial punctures (1 in group US and 2 in group U), and one patient in each group with transient neuropathy.
Discussion: The results of this prospective study confirm the advantages of ultrasound-guided deposition of local anesthetic for infraclavicular blocks. In group U, it was not necessary to visualize the cords of the brachial plexus in order to obtain a successful block. In both groups, spread of the anesthetic solution postero-lateral to the axillary artery predicted a successful block. In contrast, anterior distribution of the local anesthetic correlated with incomplete block in group US. In conclusion, USG infraclavicular block is more rapidly performed and gives a block of better quality when neurostimulation is not used as the end-point for injection.

S-436.

MEASURING THE DISTANCE FROM THE SKIN TO THE EPIDURAL SPACE BY COMPUTED TOMOGRAPHY IS BENEFICIAL TO PREDICT THE EPIDURAL DEPTH IN LOWER THORACIC AND LUMBER EPIDURAL ANESTHESIA

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Introduction: We investigated whether computed tomography (CT) was useful to predict the depth of the epidural space.
Method: 82 surgical patients who had preoperative CT examination and agreed to receive epidural anesthesia (EA) were studied. EA was performed by two of authers at the interspace between the T10-L4, using either median or paramedian approach. Actual distance from the skin to epidural space (AD) was measured by marking on the Tuohy needle. Distance from the skin to the epidural space in the midline (MD), 1.5cm lateral to the midline on the skin to epidural space (PD) and the distance from the skin to the supraspinous ligament in the midline (DSSL) were measured from CT. MD and PD and also height and weight and body mass index (BMI) were compared with AD.
Result: In patients received median approach (n = 36), there were significant correlation between AD with MD ($r^2 = 0.982$, $p < 0.001$), DSSL ($r^2 = 0.416$, $p < 0.001$), BW ($r^2 = 0.455$, $p < 0.001$) and BMI ($r^2 = 0.577$, $p < 0.001$). The relationship between AD and MD was described by the regression equation: AD = 1.075 x MD. In patients received paramedian approach (n = 46), there were significant correlation between AD with PD ($r^2 = 0.952$, $p < 0.001$), MD ($r^2 = 0.949$, $p < 0.001$), DSSL ($r^2 = 0.416$, $p < 0.001$), BW ($r^2 = 0.196$, $p = 0.002$) and BMI ($r^2 = 0.153$, $p = 0.005$). The relationship between AD and MD, AD and PD were described by the regression equation: AD = 1.23 x PD, AD = 1.23 x MD.
Discussion: There are several studies using the CT to predict the depth of epidural space [1] . But there are few studies [2] describe the prediction using paramedian approach. In this study measuring the distance from the skin to the epidural space usind CT is the good predictor of the epidural depth in both median and paramedian approach of lower thoracic and lumber EA.

References:
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S-437.

RELATIONSHIP OF PERINEURAL NERVE LOCATION AND NERVE STIMULATION PARAMETERS: A RAT SCIATIC NERVE MODEL

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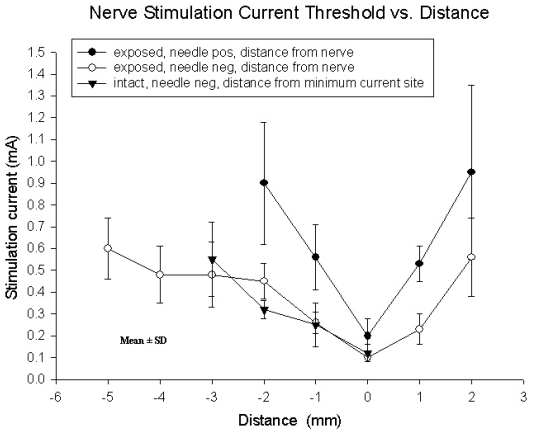
Introduction: Percutaneous nerve stimulation (PNS) is utilized by anesthesiologists to locate a peripheral nerve for local anesthetic block. However, PNS criteria for approximating nerve location vary considerably among individual clinicians (Reg Anesth Pain Med 2000;25:356). This animal study was designed to quantitate the relationship of PNS current to perineural needle distance using the rat proximal sciatic nerve.
Methods: With animal care committee approval, adult male rats were briefly anesthetized with 1.5% isoflurane. The dorsal muscle pocket covering the sciatic nerve was opened, leaving the nerve undisturbed. An insulated 27 g hypodermic needle, was positioned at various distances lateral to the 1-mm diameter single-fascicle proximal nerve. A nerve stimulator (1 Hz, 0.2 ms pulse width) was connected to the needle for monopolar stimulation. Stimulation current was increased until a barely perceptible twitch was produced in the ipsilateral hindlimb digits. With microscopic visualization, the needle was randomly moved to different locations on either side of the nerve (touching ventral muscle floor), to the top surface of the nerve, and also inside the nerve. Both needle positive (anodal) and negative (cathodal) currents were used. After the initial mapping experiments, another group of animals were used to determine nerve stimulation thresholds while percutaneously advancing the needle.
Results: With exposed nerve, current stimulation thresholds were lower with cathodal than anodal stimulation (Figure). Mean stimulation threshold at the nerve surface (0 mm) was 0.10 mA, with the needle tip negative. Thresholds increased symmetrically with increasing distance from the nerve. In 50 microscopically-aimed attempts, it was not possible to penetrate the nerve, and only when the nerve was fixated with forceps was it possible to insert the needle tip inside the nerve. Mean cathodal threshold inside fascicle was 0.10 mA. With percutaneous needle advancement it was also possible to attain a 0.10 mA cathodal stimulation threshold (mm on graph refers to distance along advancing needle trajectory), and the increase in current threshold with increasing distance from the nerve was similar for both exposed and intact nerve.
Discussion: For the rat sciatic nerve, stimulation thresholds decrease progressively as the stimulating needle approaches the nerve, achieving a minimum of 0.1 mA with either exposed or intact nerve. This model can provide insight into the appropriateness of PNS current criteria used clinically.



S-438.

FASCIAL SPLITTING INJECTION IN A PORCINE MUSCLE MODEL

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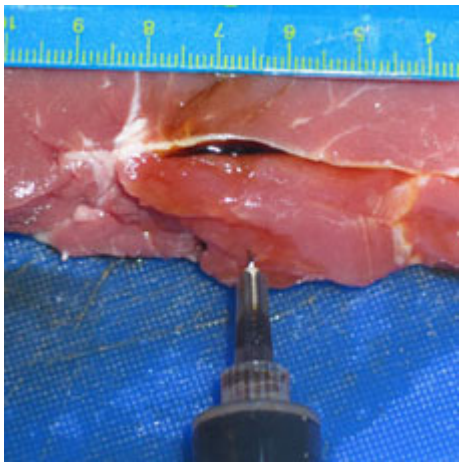
Introduction: The success of regional anesthesia depends on the proximity of local anesthetics to nerves. As some nerves are embedded in a muscular fascia, splitting of this muscular fascia and injection within the fascia surrounding nerves ideally places local anesthetic. The aim of the study was to develop a model to test needles in their ability to split muscular fascia.
Methods: We used fresh cut pork loin/sirloin chops (Costco Wholesale) from serial cuts. The muscular fascia between the muscles was clearly visible. We injected 2-3 mls soy sauce using a 22-gauge Quincke and a 22-gauge Gertie Marx needle. Injections were placed 1 cm below the cut surface. A successful fascial splitting was indicated by a visible separation of fascial layers and a leakage of soy sauce between the layers. We tested every needle on three different chops.
Results: The thickness of the muscular fascia was 1.0 ± 0.1 mm. With the Quincke needle 7 of 9 attempts were successful and with the Gertie Marx needle 5 of 5. The length of splitting was 28 ± 8 mm.
Discussion: As the size of human and pork muscular fasciae is comparable, porcine muscle provides a valuable model for testing fascial splitting. Small side port needles may be advantageous over tip cut needles.



S-439.

THE SUCCESS RATE AND EFFICIENCY OF INFANT SPINAL ANESTHESIA IN AN ANESTHESIA RESIDENCY PROGRAM

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Introduction: Despite decreases in complications such as hypoxemia, bradycardia and apnea, infant spinal anesthesia (SA) is underutilized in comparison to general anesthesia.(1) Reasons cited include technical difficulty in performing the block and high reported rates of block failure.(2) In order to determine the level of expertise required to successfully utilize infant SA, we examined the ability of various anesthesia practitioners to successfully perform lumbar puncture and the time required to induce subarachnoid block.
Methods: Since 1977, clinical data concerning all infants undergoing spinal anesthesia at the University of Vermont are prospectively entered into the Vermont Infant Spinal Registry (VISR). Since July 1992, success rate and the time required to complete the spinal anesthetic and the level of training of the practitioner performing the spinal (resident, pediatric vs. non-pediatric specialist attending) was recorded. Performance time was calculated for residents during their first five infant spinals (Group I), their 6th through 10th spinals (Group II), their 11th through 15th spinals, and all spinals performed beyond the first 15 (Group IV). Performance times among the four experience groups were examined for significant differences using analysis of variance (ANOVA); pair-wise comparison of differences between individual groups were tested using Student's t-testing with Bonferroni's correction for multiple comparisons.
Results: A total of 564 infant spinals with complete data were performed. 422 cases had anesthesiology resident participation and 142 were performed by an attending working alone. Lumbar puncture (LP) was performed successfully in 99.2% of cases. Residents were successful in performing LP in 360/422 (85.3%) of cases; the attending assisted after the resident had been unsuccessful in 62/422 (14.6%), successfully obtaining LP in 420/422 (99.5%) of cases. LP's attempted by an attending pediatric anesthesiologist alone were successful in 100/102 (98.0%) and non-specialist attending anesthesiologists were successful in 40/40 (100%). The average time taken to perform SA for cases involving residents (9.9 ± 6.1 min) was not significantly different from that for attending anesthesiologists working alone (10.5 ± 7.2 min, p=NS). The average time to perform SA declined as residents became more experienced: Group I (10.9 ± 6.9 min); Group II (10.1 ± 6.2 min); Group III (9.7 ± 5.4 min); Group IV (8.0 ± 4.0 min; Group I v. II and I v. III, p=NS; Group I v. IV, P<0.05). The average time to perform SA for pediatric anesthesiologists (10.4 ± 7.1 min) was not significantly different than that for non-specialist attending anesthesiologists (10.3 ± 7.7 min).
Discussion: Infant spinal anesthesia can be performed efficiently and with the expectation of a high degree of success, even in an anesthesia training program. The block is typically established in approximately 10 minutes regardless of the level of training.
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S-440.

IMPROVING ANESTHESIA RESIDENT PERIOPERATIVE PAIN MANAGEMENT EDUCATION OF FEMORAL NERVE BLOCK FOR ANTERIOR CRUCIATE LIGAMENT (ACL) RECONSTRUCTION

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Introduction: The search for improved efficiency and patient outcomes in ambulatory surgery has resulted in an increased demand for peripheral nerve blocks (PNB). Adequate perioperative pain control results in early ambulation, short hospital stay, reduced cost, decreased stress and increased patient satisfaction.[1] Therefore, there is need for academic centers to improve knowledge and skills of anesthesia residents with PNBs.[2] The aim of this study was to evaluate a new structured and supervised resident teaching program of femoral nerve block (FNB) for postoperative analgesia on patient outcomes after ACL reconstruction surgery.
Methods: A dedicated PNB rotation for anesthesia residents was initiated in February 2002, ensuring proper instruction and supervision in performing FNB for postoperative analgesia.
All blocks were performed on awake patients prior to surgery, using a peripheral nerve stimulator. After IRB approval, analysis of hospital database from February 2002 to January 2004 identified 227 consecutive patients who underwent ACL reconstruction using FNB performed by residents during PNB rotation (Education group). Intraoperative opioid consumption, PACU time, PONV and hospital admission related to pain control or post-anesthesia complications in the education group were compared to a reference group, consisting of patients undergoing ACL reconstruction (prior to new FNB rotation) from January 1st 2001 to June 30th 2001 (Reference group). Statistical analysis was performed using unpaired t-test (* $p<0.01$).
Results: In the reference group, 97 ACL reconstructions were performed, of which 68 patients received FNB in the perioperative period. In the education group, all 227 patients received FNB preoperatively. (* $p<0.01$)

group	n	FNB	Intraoperative Opioid (mean ± SD)		PACU time [min] (mean ± SD)	Patient with PONV	Patient with Admission
			Fentanyl (mcg)	Morphine (mg)			
Reference group	97	68 / 97 (70%)	137 ± 96	1 ± 2.8	97.4 ± 40	12 (14%)	24 (25%)
Education group	227	227 / 227 (100%)	1.8 ± 1.5*	0.3 ± 1.6*	65.5 ± 29 *	28 (12%)	2 (1%)*

Conclusion: The implementation of a standardized resident education program of femoral nerve block technique for ACL reconstruction resulted in significantly less intraoperative opioid use, less time in PACU, and fewer number of patients admitted to hospital compared with a control patient group who received FNBs prior to the training program.

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S-441.

COMPARISON OF REGIONAL ANESTHESIA VERSUS GENERAL ANESTHESIA FOR OUTPATIENT ANESTHESIA: A META-ANALYSIS OF RANDOMIZED CLINICAL TRIALS

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Introduction: Ambulatory surgery is growing in popularity worldwide. It remains unclear if regional (RA) or general anesthesia (GA) offers a superior profile for ability to bypass or reduce PACU stay, reduce side effects, and hasten patient recovery from the ambulatory surgery unit (ASU). Thus, we performed this meta-analysis to determine if there is an optimal technique for ambulatory anesthesia.
Methods: MEDLINE and other databases were searched for randomized controlled trials comparing RA to GA for ambulatory anesthesia. Search terms included Ambulatory surgical procedures, Outpatient, Spinal anesthesia, Intrathecal, Subarachnoid, Epidural anesthesia, Extradural, Peridural, Nerve block, Axillary, Brachial, Interscalene, Infraclavicular, Femoral, Sciatic, Popliteal, and Lumbar. Outcomes were extracted from these articles, and meta-analysis performed.
Results: Sixteen RCTs enrolling a total of 782 patients were included. Meta analysis was performed for all regional techniques and then separated for central neuraxial (CNB) and peripheral nerve block (PNB) techniques. In general, RA increased PACU bypass, decreased pain scores, need for postoperative analgesics, and risk of nausea while slightly increasing anesthesia induction time. Despite these advantages, neither PACU nor ASU times were significantly affected by use of RA. Subgroup analysis revealed similar findings except PNB decreased PACU time vs GA, whereas CNB increased ASU stay vs GA and did not reduce risk of nausea.

Outcome	N	Difference or Odds Ratio (95% CI) for RA vs GA
Anesthesia induction time	531	7.6 (4.2-11) more min for RA*
PACU bypass	365	16 (7-36) more likely with RA*
PACU time	652	-6.6 (-15 to 2) min
PACU time	258	-26 (-40 to -13) less min with PNB*
Nausea	704	0.31 (0.15 to 0.65) less likely with RA*
VAS pain	458	-16 (-23 to -10) mm less pain with RA*
Need for ASU opioids	561	0.21 (0.1 to 0.4) less likely with RA*
ASU time	753	22 (-1 to 45) min
ASU time	545	32 (13 to 51) more min with CNB*

*=$p<0.05$
Discussion: Meta analysis indicates several potential advantages for RA such as increased PACU bypass, decreased nausea, and postoperative pain. All of these factors have been proposed to reduce duration of ASU stay, thus it is curious that use of RA did not reduce ASU time and even increased it for CNB. Other factors such as a negative bias amongst medical personnel or use of unsuitable discharge criteria may explain this discrepancy.

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S-442.

DOSE-RESPONSE STUDY OF EPIDURAL BUPIVACAINE AND ROPIVACAINE FOR LABOR ANALGESIA

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Introduction: We conducted a prospective randomized double-blind study using traditional dose-response methodology to formally determine the dose-response curves for ropivacaine and bupivacaine for labor epidural analgesia, and then ascertain their relative potencies from the ED50 values.
Methods: With Ethics Committee approval and written informed consent, eligible ASA I or II term nulliparous parturients in active labor with cervical dilation ≤ 5 cm who had not received systemic opioid analgesia within 2 h, were recruited when they requested epidural analgesia. 250 women (25 subjects per dose group) were randomized to receive one of either Bupivacaine (B10 mg, B15 mg, B20 mg, B30 mg, B40 mg) or Ropivacaine (R15 mg, R20 mg, R30 mg, R45 mg, R60 mg) in a 20-ml volume in their lumbar epidural to initiate analgesia. Pain scores were obtained at 5-min intervals for 30 min, followed by 10-min assessments until patient's request for additional analgesia. If VAPS improved to ≤ 25% baseline within 30 min and sustained for ≥ 15 min: study dose was considered *effective* or ìsuccessî. Otherwise, if analgesia was obtained from a ìrescueî (5 ml epidural 0.25% bupivacaine) given at 30 min or second ìrescueî at 40 min: study dose was considered *ineffective* or ìfailureî. If all the above failed: considered a technical failure of epidural catheter and case excluded. Time to onset of analgesia, duration of analgesia, sensory and motor block, and any adverse maternal or fetal side effects were noted. Individual dose-response curves for bupivacaine and ropivacaine were plotted and ED50 and ED95 determined by logistic regression and probit analysis. Other data were compared using ANOVA, Kruskal-Wallis and Chi-square tests, with $p < 0.05$ considered significant.
Results: Physical and obstetrical demographics were similar. Parallel dose-response curves were fitted to the data: ED50 were 17.2 (95% CI 14.2 to 21.0) mg for bupivacaine, and 20.2 (95% CI 16.3 to 25.1) mg for ropivacaine, respectively, giving a potency ratio of 1.17 (95% CI 0.89 to 1.56). There was a trend towards a shorter onset time and a longer duration of analgesia with increasing doses of both drugs.
Figure 1. Probit-log dose-response plot for bupivacaine and ropivacaine. $R^2 = 0.83$, $r = 0.91$
Bupivacaine:
ED_{50} 17.2 (95% CI 14.2 to 21.0) mg
ED_{95} 72.2 (95% CI 46.1 to 112.9) mg
Ropivacaine:
ED_{50} 20.2 (95% CI 16.3 to 25.1) mg
ED_{95} 84.8 (95% CI 55.7 to 129.0) mg
Discussion: Using traditional dose-response methodology to plot dose-response curves, we have demonstrated ropivacaine to be equi-potent to bupivacaine (relative potency ratio of 1.17, 95% CI 0.89 to 1.56) when used for epidural analgesia during the first stage of labor.
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S-443.

THE INCIDENCE OF COMPLICATIONS ASSOCIATED WITH INFANT SPINAL ANESTHESIA IN THE VERMONT INFANT SPINAL REGISTRY

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Introduction: Young infants and neonates are at particularly high risk for anesthesia complications in the perioperative period.(1) Previous smaller studies of spinal anesthesia in infants have demonstrated a low incidence of complications such as bradycardia, hypoxia etc. (2,3) We prospectively recorded data on a very large population of patients to determine the incidence of complications associated with this technique.
Methods: All infants undergoing spinal anesthesia at the University of Vermont are entered into the Vermont Infant Spinal Registry (VISR). Patient demographic data, details of the anesthetic management and the presence of any complications are recorded as the case progresses.
Results: 1364 patients have been entered into the registry. A wide variety of surgical procedures were performed including inguinal hernia repair (764 pts), circumcision (60 pts), exploratory laparotomy (52 pts), pyloromyotomy (106 pts), and gastroschisis repair (20 pts). The average dose of hyperbaric tetracaine was 0.54 mg/kg. The incidence of complications was very low. Most patients remained stable in room air. 47 patients (4.1%) received supplemental oxygen. Oxygen desaturation was noted in six patients (0.5%). In 55 patients (4.8%) the spinal level was higher than intended. 20 of the patients with high spinals received supplemental oxygen and increased vigilance. In nine patients (0.7%) the spinal level was high enough to require either bag/mask ventilation (four patients) or endotracheal intubation (five patients). Four of these patients were extubated in the OR at the end of the procedure. The final patient was undergoing gastroschisis repair and was returned to the NICU undergoing mechanical ventilation. The average dose of tetracaine for the patients with a high spinal was 0.55mg/kg, which was not different from the population as whole (Student's t test, p=0.856). Bradycardia (HR<100) was noted in 23 patients (2.0%). Seven patients received atropine for bradycardia. One patient was intubated and received brief cardiac massage while the atropine was administered. This patient was extubated at the conclusion of the procedure and no complications were observed in followup. The average dose of tetracaine for the patients with bradycardia was 0.60 mg/kg, which was similar to the group as a whole (Students t test p=0.182). Significant hypotension was not observed and no patient required treatment with a vasopressor.
Discussion: Spinal anesthesia in infants can be performed safely with a very low rate of complications. This study group included a very large number of patients including infants undergoing complicated major surgery. The vast majority of patients remained stable without supplemental oxygen. A small number of patients required active intervention such as bag/mask ventilation or endotracheal intubation. The occurrence of these complications was not predictable based on the dose of local anesthetic utilized.
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S-444.

A COMPARISON STUDY OF BUPIVACAINE PRECEDED BY EITHER CHLOROPROCAINE OR LIDOCAINE FOR INFRACLAVICULAR BLOCKADE

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Introduction: The need for ever faster regional blocks led us to compare the duration and speed of onset of a chloroprocaine-bupivacaine local anesthetic (LA) solution versus a lidocaine-bupivacaine LA solution.
Methods: A prospective, randomized, double-blind study was conducted with two groups (n = 15 each) of ASA I or II patients having forearm or hand surgery under infraclavicular block. The block was facilitated by titration of IV midazolam sedation. Localization of the block was considered adequate if the Palmaris Longus or Flexor Digitorum Superficialis were stimulated at 0.3 milliamps. Onset of motor block (assessed every 15 seconds) was when the patient was unable to lift the upper extremity from the table. Group 1 patients received a solution containing 18 ml of 3% chloroprocaine, 2 ml of 8.4% sodium bicarbonate and 50 mcg of epinephrine, followed by 20 ml of a solution containing 0.5% bupivacaine and 50 mcg epinephrine. Group 2 patients received a similar solution except 2% lidocaine was substituted for the 3% chloroprocaine. Motor block was checked at the end of surgery and again before discharge. Pain scores and analgesic medication usage in the PACU were also assessed.
Results: The block was successful (i.e., motor block with satisfactory surgical analgesia) in 13 of 15 group 1 patients and 13 of 15 group 2 patients. The distribution of onset times of motor block in both groups showed central peaks and large right skews. The mean onset time in group 1 was 2.8 minutes and in group 2 was 9.8 minutes. The log-rank test of differences in times to motor block for Groups 1 and 2 was significant ($P<0.001$). Survival data reveals that if an infraclavicular block were performed on 1000 people, on average (with 95% confidence interval), 76 (4-229) people in group 1 and 357 (130-594) people in group 2 would have to wait at least 10 minutes for a successful block; and 0 (0-0) people in group 1 and 93 (23-366) people in group 2 would have to wait at least 20 minutes for a successful block. One patient (in group one) had pain (2/10) in the PACU and received one Percocet. Her pain was 0/10 at time of discharge.
Discussion: Regional blocks are used for upper extremity procedures because they supply excellent perioperative analgesia. However, infraclavicular blocks are perceived to take effect slowly and occasionally fail. Adding a fast acting LA, especially chloroprocaine, permits rapid assessment of the adequacy of the block, allowing for efficient conversion to GA if necessary.
Conclusion: a chloroprocaine-bupivacaine LA mixture was found to be significantly faster and equally reliable in establishing an infraclavicular block compared to a lidocaine-bupivacaine LA mixture. Both mixtures afforded a solid long lasting base for successful upper extremities procedures.

S-445.

SAFETY AND EFFECTIVENESS OF CONTINUOUS POPLITEAL FOSSA BLOCKS WITH LEVOBUPIVACAINE IN CHILDREN UNDERGOING SINGLE LIMB FOOT AND ANKLE SURGERY

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Introduction: We sought to determine the safety and effectiveness of continuous posterior fossa blocks (CPFB) for postoperative analgesia in children undergoing single limb foot and ankle surgery using levobupivacaine administered as a continuous infusion with or without intermittent bolus injections. **Methods:** After IRB approval, 53 consented patients, < 21 years old, undergoing unilateral foot and ankle surgery were randomized into one of two groups. Group A (n=27) received CPFB with 0.25% levobupivacaine as a continuous infusion rate of 0.4mg/Kg/Hr. Group B (n=26) received CPFB with 0.25% levobupivacaine administered at a basal rate of ≤ 2ml/Hr with intermittent q 6 Hr bolus injections equivalent to a levobupivacaine dose of 0.4mg/Kg/Hr x 6 up to a maximum bolus of 20 mls. CPFB catheters were placed under general anesthesia. Patients received an initial injection of 1 ml/kg of 0.25% Levobupivacaine in 1:200,000 epinephrine solution up to a maximum dose of 25 mls. CPFB infusion was started in the PACU and was discontinued after 48 hours or just prior to discharge. Plasma levels of levobupivacaine were determined 30 and 60 minutes after the initial injection and 6 hours after starting CPFB. Patients in group B also had a levobupivacaine level determination 30 minutes following the first postoperative injection. Pain scores were recorded every 4 hours. Pain management surveys were distributed to all patients. Efficacy of CPFB was determined by evaluating the average pain and daily worse pain scores and assessing the total daily dose of analgesic medications used. Adverse reactions/ complications related to the CPFB were recorded. **Results:** Study groups were similar with respect to age, sex, weight and surgical procedure performed. 85 % of patients in both groups underwent saphenous or femoral nerve blocks at the end of surgery. Postoperative pain control was satisfactory in all study patients as determined by low mean pain scores, limited use of postoperative parenteral analgesic medications and patient willingness to undergo repeat CPFB. Plasma levels of bupivacaine were low (<1.3 mg/L) (Table 1). No complications related to CPFB were identified.
Conclusions: CPFB in children controlled postoperative pain following single limb foot and ankle surgery. Plasma levels of levobupivacaine using CPFB were low, even after initial and repeat bolus injections of 0.25 % levobupivacaine

Table 1: Plasma Levels of Levobupivacaine (mg/L) with CPFB (Mean ±SD).

	30 min after initial bolus	60 min after initial bolus	6 hrs after CPFB	Post-bolus CPFB
Group A	0.06 (± 0.067)	0.03 (± 0.032)	0.051 (± 0.226)	N / A
Group B	0.08 (± 0.103)	0.04 (± 0.042)	0.23 (± 0.139)	0.48 (± 0.285)

S-446.

ACUTE INTRAVASCULAR VOLUME EXPANSION WITH RAPIDLY ADMINISTERED A LOW-MOLECULAR WEIGHT DEXTRAN UNDER EPIDURAL AND SPINAL ANESTHESIA

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Introduction: There is relative hypovolemia throughout the development of hypotension induced by epidural or spinal anesthesia (ESA). Volume loading results in hemodynamic stability and hemodilution in patients who develop hypotension during ESA. A low-molecular weight dextran (Dextran 40, DEX) is a colloid that was commonly used for volume resuscitation. However, the impact of acute preoperative volume loading with DEX on circulating blood volume (CBV) has not been investigated sufficiently and the hemodilution that can be achieved with rapid administration of DEX is unknown in patients under ESA. The purpose of the study was to evaluate the variation in the expansion of CBV in patients under ESA after clinically allowable rapid infusion of DEX and lactated Ringer's (LR) solution.
Methods: After institutional review board approval, informed, written consent was obtained from 33 (ASAPS I-II) patients undergoing elective surgery. Patients with anemia, limitation of cardiac or pulmonary function, untreated hypertension, and coagulation disorders were excluded. Epidural anesthesia (ropivacaine 0.5%) or spinal anesthesia (bupivacaine 0.5%) was given to all patients before the induction of general anesthesia. The patients were randomly allocated to receive either 10mL/kg of 10% Dextran 40 (n=17, DEX) or LR solution (n=16, LR). Each fluid was administered in 30 minutes immediately after ESA. In both groups of patients, hypotension was treated promptly with a 5-mg IV bolus of ephedrine repeated if hypotension persisted. Hemoglobin, hematocrit, blood glucose value, and levels of serum electrolytes were measured before and immediately after hemodilution. Pre-hemodilution CBV was estimated using height and body weight. Post-hemodilution CBV is calculated from the ratio (pre/post) of hemoglobin concentration and estimated pre-hemodilution CBV. Values were reported as median (range). Statistical significance ($P < 0.05$) was determined using unpaired Student's t-test for comparison of parametric data, and Fisher's exact test for comparison of nonparametric categorical data.
Results: The hemodynamic profile and demographic variables were similar between the two groups. Percent decrease of hemoglobin values from baseline were a median (range) of 20.1% (14.0 to 26.3) and 9.6 (2.6 to 15.3) (P less than .001) in DEX and LR groups, respectively. The median volume expansion immediately after 10 ml/kg infusion of each solution were 16.7 ml/kg (10.8 to 23.4) and 7.3 (1.7 to 13.9) (P less than .001) in DEX and LR groups, respectively.
Discussion: Recently, attention has been focused on the administration of colloid solutions immediately after ESA for the treatment of hypotension. Furthermore, a colloid solution is the more logical choice in reducing intraoperative blood loss by hemodilution. In this preliminary study, DEX was more effective than LR solution in pronounced hemodilution and acute volume expansion during ESA, although the actual CBV was unknown. We concluded that DEX was the beneficial solution for relative hypovolemia during ESA.

S-447.

IS EPIDURAL ANALGESIA SAFE IN PEDIATRIC PATIENTS UNDERGOING THOROCOTOMY FOR EMPYEMA?

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Introduction: Epidural analgesia is becoming increasingly popular among pediatric anesthesiologists for augmentation of general anesthesia and providing postoperative pain management. Although infection at the site of catheter insertion is considered an absolute contraindication, there is no consensus regarding insertion of epidural catheter in patients with localized infection such as empyema.[1,2] This study was undertaken to assess the safety of epidural catheter placement in a high risk group of children who had empyema and underwent surgical decortication at our institution.
Methods: After the approval of Institutional Review Board, medical records of children with empyema who underwent surgical decortication from February 2000 to May 2002 were reviewed. Epidural analgesia was administered to 32 patients for post operative analgesia. Abstracted variables included patient demographics, vital signs, body temperature during and within 24 hours of catheter insertion, laboratory values, culture reports, days the epidural catheter was in place, indication for epidural catheter removal, complications (e.g., epidural abscess or hematoma), and presence of antibiotic coverage.
Results: Fifty-nine patients underwent surgical decortication during the study period. Of these, epidural catheter was inserted in 32 patients for postoperative analgesia. Age of the patients ranged from 6 months to 18 years. Average maximum temperature within 24 hours of catheter insertion was 37.9^0C. Average duration of use of epidural catheter was 2.2 days. None of the catheters were removed for catheter related complications. All the patients who presented for surgery were on broad spectrum antibiotic coverage.
Discussion: Abscess at the site of epidural catheter placement is a very serious complication, but fortunately it is rare. Although epidural abscesses have been reported in patients with no obvious predisposing factors,[3] it is more common in patients with immunodeficiency and cancer and in situations where the catheter is used for long term. Placement of epidural catheter in a febrile patient with a serious localized infection such as empyema has been controversial. Some anesthesiologists decline to insert an epidural catheter in patients with signs of infection. Hence we chose to study a high risk group of children who were often febrile at the time of catheter insertion. In this limited review, there was no evidence of increased risk related to epidural catheter placement and usage in spite of the serious localized infection at the time of catheter insertion. However, all the patients who were subjected to insertion of epidural catheter had perioperative broad spectrum antibiotic coverage. Based on our observation it could be assumed that epidural analgesia is a safe mode of providing pain relief even in patients with localized infection like empyema, provided they are on broad-spectrum antibiotic coverage. More studies are needed in this regard.

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