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AWIC Special Reference Brief:

Swine Anesthesia and Analgesia, 2000-2010

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Disclaimers

About this Document

This bibliography updates and revises the Anesthesia chapter in AWIC's "Information Resources on Swine in Biomedical Resesarch 1990-2000," AWIC Resource Series No. 11, February 2000 (online: http://www.nal.usda.gov/awic/pubs/swine/swine.htm).

Citations in this chapter were selected from a variety of medical, agricultural, and biological databases. They include articles primarily from peer reviewed journals, proceedings, and book chapters. Documents were published between the years of 2001 to 2010.

Citations that include NAL call numbers may be available at the National Agricultural Library (NAL). Guidelines and information on how to request materials that are included in the collection of the National Agricultural Library (NAL) may be found on the Request Library Materials page at http://www.nal.usda.gov/services/request.shtml.

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This document represents only one chapter in our extensive series on Swine in Biomedical Research. More chapter revisions are currently underway and will be released when completed. It was felt that with the increased depth of coverage on swine and the importance of this large model, information should be released in chapters as completed and not withheld as a final product. The next chapter will cover the use of swine as cardiovascular models, another important area of current research.

Introduction: Anesthesia and Analgesia Selection

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Selection of a proper anesthetic and analgesic regimen for swine used in biomedical research is one of the most important aspects of the experimental procedure. One key issue is ensuring that pain and distress associated with an experimental procedure, such as surgery, is adequately controlled. For example, the use of preemptive analgesia in surgical protocols has been shown to reduce the length of the postoperative recovery and the number of postoperative analgesic administrations that have to be performed in swine. But of equal importance is ensuring that the agents selected do not interfere with the goals of the research. Veterinarians and research personnel should consider the physiologic effects of the anesthetics and analgesics when designing the experimental protocol. An educated team based approach to the design of invasive research projects is a good way to ensure success. Ensuring that the protocol is adequate to control pain and distress and that a research complication does not occur requires knowledge of the effects of these agents within the porcine species. In many cases the effects of these pharmacologic agents will be different in other species when making comparisons. The selection of manuscripts in this section will provide guidance in adhering to these humane and scientific principles.

Anesthesia and Analgesia

Aagaard, S., J.R. Larsen, J.S. Berg, E. Sloth, and J.M. Hasenkam (2007). **Does the pre-ischaemic administration of sevoflurane reduce myocardial stunning? A porcine experimental model.** *Acta Anaesthesiologica Scandinavica* 51(5): 577-81. ISSN: 0001-5172.

Abstract: BACKGROUND: In a porcine model, the cardioprotective effect of sevoflurane was studied with regard to the preservation of myocardial contractility (myocardial stunning) after a myocardial ischaemic insult. METHODS: Twenty-seven pigs were randomized to receive either a dual 4% sevoflurane inhalation period as a supplement to pentobarbital anaesthesia or pentobarbital anaesthesia only before a 15-min ischaemic insult on the left anterior descending coronary artery. The ischaemic period was followed by 180 min of reperfusion. Myocardial contractility was assessed by myocardial sonomicrometry. RESULTS: A significant difference was found between the sevoflurane group and the control group at 5 min of reperfusion. However, subsequently, there was no overall difference between the two groups. CONCLUSION: Sevoflurane administered as a pre-ischaemic bolus does not provide long-term improvement of the myocardial contractility. However, it can be speculated that sevoflurane may induce an early improvement in contractility.

Descriptors: anesthetics, inhalation administration and dosage, methyl ethers administration and dosage, myocardial contraction drug effects, myocardial stunning prevention and control, hypnotics and sedatives administration and dosage, models, animal, monitoring, physiologic, pentobarbital administration and dosage, random allocation, sus scrofa, time factors.

Abu Huwaij, R., S. Assaf, M. Salem, and A. Sallam (2007). **Potential mucoadhesive dosage form of lidocaine hydrochloride: II. In vitro and in vivo evaluation.** *Drug Development and Industrial Pharmacy* 33(4): 437-48. ISSN: 0363-9045.

Abstract: The aim of this study was to develop a controlled release buccal mucoadhesive delivery system for systemic delivery of lidocaine hydrochloride as a model drug. In vitro release and buccal permeation as well as in vivo permeation of LDHCL patches were evaluated. The drug release and the permeability of the drug through porcine buccal mucosa were evaluated using Franz diffusion cell. In vivo evaluation of patches was carried out on rabbits as an animal model. Patches were designed in two fashions, bi-layer (BLP; LDHCL, carbopol, glycerin, pentration enhancer, and Tween 20 as the first layer; and EVA as the second layer) and triple layer (TLP; LDHCL, carbopol and glycerin as the first layer; carbopol, glycerin, pentration enhancer and pluronic F-127 as the middle layer; and EVA as the third layer) patches, respectively. Presence of oleic acid as PE in the formulation significantly enhanced the in vitro permeability of LDHCL ($p<0.05$), while propylene glycol monolaurate as PE suppressed it ($p<0.05$). The in vivo evaluation in rabbits showed that TLP had significantly higher Cmax and AUC0-8 ($p<0.05$) than BLP. Furthermore, TLP showed a well-controlled drug plasma concentration over 6 hr which was significantly longer than BLP ($p<0.05$). Patches were well adhered to buccal mucosa of the rabbits over the 8-hr study period. It was postulated that the hypothetical release mechanism of the drug and oleic acid from TLP was controlled by their diffusion through the swollen polymer network and micelled gel.

Descriptors: anesthetics, local pharmacokinetics, drug carriers chemistry, excipients chemistry, lidocaine pharmacokinetics, mouth mucosa drug effects, acrylates, adhesiveness, administration, buccal, anesthetics, local chemistry, area under curve, biological availability, delayed action preparations, diffusion, excipients pharmacology, glycerol, laurates pharmacology, lidocaine chemistry,

mouth mucosa metabolism, oleic acid pharmacology, permeability, polysorbates, polyvinyls, propylene glycols pharmacology, rabbits, swine.

Adetunji, A. and A. Ajao (2001). **Comparison of extradural injections of lignocaine and xylazine in azaperone-sedated pigs.** *Veterinary Journal* 161(1): 98-99 . ISSN: 1090-0233.
NAL Call Number: SF601.V484
Descriptors: swine, lidocaine, injection, xylazine, azaperone, anesthesia, heart rate, body temperature, efficacy, respiration rate.

Ajadi, A.R., T.A. Olusa, O.F. Smith, E.S. Ajibola, O.E. Adeleye, O.T. Adenubi, and F.A. Makinde (2009). **Tramadol improved the efficacy of ketamine-xylazine anaesthesia in young pigs.** *Veterinary Anaesthesia and Analgesia* 36(6): 562-566. ISSN: 1467-2987.
DOI: 10.1111/j.1467-2995.2009.00496.x
NAL Call Number: SF914 .V47
Abstract: To evaluate the influence of premedication with tramadol on xylazine -ketamine anaesthesia in young pigs. Prospective, randomized, blinded cross -over study. Ten young Niger hybrid pigs: mean weight 6.1 pl 0.6 kg. Pigs were anaesthetized twice. Xylazine (2.5 mg kgp#), ketamine (25 mg kgp#) and atropine (0.04 mg kgp#) were administered by intramuscular (IM) injection, 5 minutes after either tramadol (5 mg kgp#) (treatment XKT) or saline (treatment XKS). Time to loss of righting reflex (TLRR), duration of antinociception, duration of recumbency (DR) and recovery times (RCT) were recorded. Quality of induction of anaesthesia including ease of endotracheal intubation was assessed using a subjective ordinal rating score of 1 (worst) to 4 (best). Heart, pulse and respiratory rates, arterial oxygen saturations and rectal temperatures were determined over 60 minutes. Antinociception was assessed by the pigs' response to artery forceps applied at the interdigital space. Data were compared with Student's t-test, Mann-Whitney's test or analysis of variance (anova) for repeated measures as appropriate and are presented as mean pl standard deviation. The quality of anaesthetic induction was significantly better and duration of antinociception significantly longer ($p < 0.05$) in treatment XKT (3.1 pl 0.7 score; 43.7 pl 15.5 minutes) than in treatment XKS (2.8 pl 0.6 score; 32.0 pl 13.3 minutes). TLRR, DR and RCT did not differ significantly ($p > 0.05$) between treatment XKT (2.1 pl 0.8, 65.8 pl 17.0 and 13.2 pl 6.7 minutes) and treatment XKS (2.1 pl 1.3, 58.0 pl 14.8 and 10.3 pl 5.6 minutes). Physiological measurements did not differ between the treatments. Tramadol improved the quality of anaesthetic induction and increased the duration of antinociception in xylazine-ketamine anaesthetized young pigs without increasing duration of anaesthesia, nor causing additional depression of the physiological parameters measured.
Descriptors: ketamine, swine, xylazine, piglets, anesthesia , analgesia, veterinary drugs, general anesthetics, analgesics, preanesthetic medication, opium alkaloids, drug evaluation, combination drug therapy, drug synergism, intramuscular injection, depth of anesthesia, analgesic effect, biomarkers, hemodynamics, breathing, thermoregulation, reflexes, tramadol-, endotracheal-intubation, Internet-resource.

Alexander, K., J.R. Del Castillo, N. Ybarra, V. Morin, D. Gauvin, S. Authier, P. Vinay, and E. Troncy (2007). **Single-slice dynamic computed tomographic determination of glomerular filtration rate by use of Patlak plot analysis in anesthetized pigs.** *American Journal of Veterinary Research* 68(3): 297-304. ISSN: 0002-9645.
NAL Call Number: 41.8 Am3A
Abstract: OBJECTIVE: To compare glomerular filtration rate (GFR) as estimated from Patlak plot analysis by use of single-slice computed tomography (CT) with that obtained from clearance of plasma inulin in pigs. ANIMALS: 8 healthy anesthetized juvenile pigs. PROCEDURES:

All pigs underwent precontrast, whole-kidney, helical CT; postcontrast single-slice dynamic CT; and postcontrast, whole-kidney CT for volume determination. On dynamic images, corrected Hounsfield unit values were determined for each kidney and the aorta. A Patlak plot for each kidney was generated, and plasma clearance per unit volume was multiplied by renal volume to obtain whole-animal contrast clearance. Mean GFR determined via inulin clearance (Inu-GFR) was measured from each kidney and correlated to mean GFR determined via CT (CT-GFR) for the left kidney, right kidney, and both kidneys by use of linear regression and Bland-Altman analyses. RESULTS: CT-GFR results from 7 pigs were valid. Total and right kidney Inu-GFR were correlated with total and right kidney CT-GFR (total, R(2) = 0.85; right kidney, R(2) = 0.86). However, left kidney CT-GFR was poorly correlated with left kidney Inu-GFR (R(2) = 0.47). Bland-Altman analysis revealed no significant bias between Inu-GFR and CT-GFR for the left kidney, right kidney, or both kidneys. CONCLUSIONS AND CLINICAL RELEVANCE: CT-GFR as determined by use of a single-slice acquisition technique, low-dose of iohexol, and Patlak plot analysis correlated without bias with Inu-GFR for the right kidney and both kidneys (combined). This technique has promise as an accurate CT-GFR method that can be combined with renal morphologic evaluation.

Descriptors: anesthesia, general veterinary, glomerular filtration rate veterinary, swine physiology, tomography, spiral computed veterinary, contrast media pharmacokinetics, glomerular filtration rate physiology, inulin metabolism, iohexol pharmacokinetics, kidney physiology, kidney radiography, reproducibility of results, tomography, spiral computed methods.

Alexson, S.E., M. Diczfalusy, M. Halldin, and S. Swedmark (2002). **Involvement of liver carboxylesterases in the in vitro metabolism of lidocaine.** *Drug Metabolism and Disposition the Biological Fate of Chemicals* 30(6): 643-7. ISSN: 0090-9556.

NAL Call Number: RM300.A1D7

Abstract: Although lidocaine has been used clinically for more than half a century, the metabolism has still not been fully elucidated. In the present study we have addressed the involvement of hydroxylations, deethylations, and ester hydrolysis in the metabolism of lidocaine to 2,6-xylidine. Using microsomes isolated from male rat liver, we found that lidocaine is mainly metabolized by deethylation to N-(N-ethylglycyl)-2,6-xylidine, and N-(N-ethylglycyl)-2,6-xylidine is mainly metabolized to N-glycyl-2,6-xylidine, also by deethylation. However, 2,6-xylidine can be formed both from lidocaine and N-(N-ethylglycyl)-2,6-xylidine, but not from N-glycyl-2,6-xylidine, in an NADPH-independent reaction, suggesting that the amido bond in these compounds can be directly hydrolyzed by esterases. To test this hypothesis, we incubated lidocaine, N-(N-ethylglycyl)-2,6-xylidine, and N-glycyl-2,6-xylidine with purified liver carboxylesterases. Rat liver microsomal carboxylesterase ES-10, but not carboxylesterase ES-4, hydrolyzed lidocaine and N-(N-ethylglycyl)-2,6-xylidine to 2,6-xylidine, identifying this esterase as a candidate enzyme in the metabolism of lidocaine.

Descriptors: anesthetics, local metabolism, carboxylic ester hydrolases metabolism, lidocaine analogs and derivatives, lidocaine metabolism, microsomes, liver metabolism, carboxylesterase, hydrolysis, hydroxylation, microsomes, liver enzymology, rabbits, rats, species specificity, swine.

Allaouchiche, B., R. Debon, J. Goudable, D. Chassard, and F. Duflo (2001). **Oxidative stress status during exposure to propofol, sevoflurane and desflurane.** *Anesthesia and Analgesia* 93(4): 981-5. ISSN: 0003-2999.

Abstract: We evaluated the circulating and lung oxidative status during general anesthesia established with propofol, sevoflurane, or desflurane in mechanically ventilated swine. Blood samples and bronchoalveolar lavage fluid (BAL) specimens were respectively performed via an internal jugular vein catheter and a nonbronchoscopic BAL for baseline oxidative activity measurements:

malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione peroxidase (GPX). A 4-h general anesthesia was then performed in the three groups of 10 swine: the Propofol group received 8 mg x kg(-1) x h(-1) of IV propofol as the sole anesthetic; the Desflurane group received 1.0 minimum alveolar concentration of desflurane; and the Sevoflurane group received 1.0 minimum alveolar concentration of sevoflurane. We observed significantly larger levels of MDA in plasma and BAL during desflurane exposure than with the other anesthetics. We also observed smaller concentrations of circulating GPX and alveolar GPX. We found a significant decrease for MDA measurements in the plasma and the pulmonary lavage during propofol anesthesia. We also found larger values of GPX measurements in the serum and the pulmonary lavage. No significant changes were observed when animals were exposed to sevoflurane. No significant changes were found for circulating concentrations of SOD during exposure to all anesthetics. In this mechanically ventilated swine model, desflurane seemed to induce a local and systemic oxidative stress, whereas propofol and sevoflurane were more likely to have antioxidant properties. IMPLICATIONS: Superoxide is an unavoidable byproduct of oxygen metabolism that occurs in various inflammatory reactions. Inhalation of volatile anesthetics under mechanical ventilation induces an inflammatory response. We evaluated the bronchoalveolar and systemic oxidative stress in swine during exposure to propofol and newer volatile anesthetics. Desflurane induces more lipid peroxidation than do the other anesthetics.

Descriptors: anesthetics, inhalation pharmacology, anesthetics, intravenous pharmacology, bronchoalveolar lavage fluid chemistry, isoflurane pharmacology, methyl ethers pharmacology, oxidative stress drug effects, propofol pharmacology, antioxidants metabolism, glutathione peroxidase metabolism, isoflurane analogs and derivatives, lipid peroxidation drug effects, malondialdehyde blood, pulmonary alveoli drug effects, pulmonary alveoli metabolism, superoxide dismutase blood, swine.

Allaouchiche, B., F. Duflo, R. Debon, J.P. Tournadre, and D. Chassard (2001). **Influence of sepsis on minimum alveolar concentration of desflurane in a porcine model.** *British Journal of Anaesthesia* 87(2): 280-3. ISSN: 0007-0912.

Abstract: The effect of sepsis on the minimum alveolar concentration of desflurane (MAC(DES)) in humans and other animals has not been reported previously. The aim of this study was to test the hypothesis that sepsis might alter MAC(DES) in a normotensive septic porcine model. Twenty-four young healthy pigs were premedicated with ketamine 10 mg kg(-1)i.m and then anaesthesia was established with propofol 3 mg kg(-1) and the trachea was intubated. Baseline MAC(DES) in each pig was evaluated by pinching with a haemostat applied for 1 min to a rear dewclaw. MAC(DES) was determined by changing desflurane concentrations stepwise until purposeful movement appeared. Pigs were randomly assigned to two groups of 12 animals: the saline group received a 1 h i.v. infusion of saline solution while the sepsis group received a 1 h i.v. infusion of live Pseudomonas aeruginosa. Epinephrine and hydroxyethylstarch were used to maintain normotensive and normovolaemic haemodynamic status. In both groups, MAC(DES) was evaluated 5 h after infusion. Significant increases in heart rate, cardiac output, mean pulmonary artery pressure and pulmonary vascular resistance occurred in the sepsis group. MAC(DES) was 9.2% (95% confidence interval (CI) 6.8-10.6%) for the saline group and 6.7% (95% CI: 4.7-10.4) for the sepsis group ($P<0.05$). These data indicate that MAC(DES) is significantly decreased in this normotensive hyperkinetic septic porcine model.

Descriptors: anesthetics, inhalation pharmacokinetics, bacteremia metabolism, isoflurane pharmacokinetics, pulmonary alveoli metabolism, bacteremia physiopathology, disease models, animal, hemodynamic processes drug effects, isoflurane analogs and derivatives, swine.

Allaouchiche, B., F. Duflo, J.P. Tournadre, R. Debon, and D. Chassard (2001). **Influence of sepsis on sevoflurane minimum alveolar concentration in a porcine model.** *British Journal of Anaesthesia* 86(6): 832-6. ISSN: 0007-0912.

Abstract: Sevoflurane is widely used in anaesthetic protocols for patients undergoing surgical procedures. However, there are no reports on the influence of sepsis on minimum alveolar concentration of sevoflurane (MAC(SEV)) in animals or in humans. The aim of this study was to test the hypothesis that sepsis could alter the MAC(SEV) in a normotensive septic pig model. Twenty young, healthy pigs were used. After they had received 10 mg kg(-1) of ketamine i.m. for premedication, anaesthesia was established with propofol 3 mg kg(-1) and the trachea was intubated. Sevoflurane was used as the sole anaesthetic agent. Baseline haemodynamic recording included electrocardiography, carotid artery blood pressure and a pulmonary thermodilution catheter. Baseline MAC(SEV) in each pig was evaluated by pinching with a haemostat applied for 1 min to a rear dewclaw. MAC(SEV) was determined using incremental changes in sevoflurane concentration until purposeful movement appeared. Pigs were assigned randomly to two groups: the saline group (n = 10) received a 1-h i.v. infusion of sterile saline solution while the sepsis group (n = 10) received a 1-h i.v. infusion of live Pseudomonas aeruginosa. Epinephrine and hydroxyethylstarch were used to maintain normotensive and normovolemic haemodynamic status. In both groups, MAC(SEV) was evaluated 5 h after infusion. Significant increases in mean artery pulmonary pressure, filling, epinephrine and vascular pulmonary resistances occurred in the sepsis group. MAC(SEV) for the saline group was 2.4% [95% confidence interval (CI) 2.1-2.55%] and the MAC(SEV) for the sepsis group was 1.35% (95% CI 1.2-1.45%, P<0.05). These data indicate that MAC(SEV) is significantly decreased in this normotensive septic pig model.

Descriptors: anesthetics, inhalation pharmacokinetics, methyl ethers pharmacokinetics, pulmonary alveoli metabolism, sepsis metabolism, swine metabolism, analgesics, anesthetics, intravenous, ketamine, models, animal, premedication, propofol.

Notes: Comment In: Br J Anaesth. 2001 Jun;86(6):746-9.

Allison, C.P., R.C. Johnson, and M.E. Doumit (2005). **The effects of halothane sensitivity on carcass composition and meat quality in HAL-1843-normal pigs.** *Journal of Animal Science* 83(3): 671-678. ISSN: 0021-8812.

NAL Call Number: 49 J82

Abstract: Objectives of this study were to determine the incidence of halothane sensitivity in pigs that are homozygous normal at the ryanodine receptor nucleotide 1843 (HAL-1843-normal) and the relationships between halothane sensitivity and carcass composition or meat quality. In Exp. 1, piglets (Lines A, B, C, and D; n = 168, 170, 168, and 169, respectively) were obtained from mating a HAL-1843-normal sire line to four HAL-1843-normal dam lines. In Exp. 2, piglets from Lines A and B (n = 87 and 90, respectively) were included with piglets (Lines E, F, G, and H; n = 94, 92, 89, and 89, respectively) obtained from mating four HAL-1843-normal sire lines to a single HAL-1843-normal dam line. Pigs were subjected to 3% halothane at approximately 9 wk of age. In Exp. 1, limb rigidity, blotching of the skin, and muscle tremors were visually assessed, and based on these criteria, halothane sensitivity (HS) was observed in 48% of the pigs. To better characterize this response, a scoring system was developed and used in Exp. 2. Using this system, 25, 42, and 33% of the pigs in E and 40, 33, and 27% of the pigs in Line G were categorized as HS-low (HS-L), HS-intermediate (HS-I), and HS-high (HS-H), respectively. In Lines F and H, 13 and 18% of the pigs were HS-I, and 0 and 2% were HS-H, respectively. No consistent effects due to HS were observed in carcass composition or meat quality; however, when a subset of pigs from Exp. 2 were subjected to more extensive handling and transportation before slaughter, ultimate pH was lower and drip loss was higher in LM from HS-H compared with HS-L pigs (P < 0.05; n = 71). These results demonstrate that some pigs are sensitive to halothane

anesthesia even in the absence of the known HAL-1843 polymorphism. Additionally, halothane sensitivity may be associated with inferior pork quality under adverse antemortem conditions.
Descriptors: pig carcasses, pork, meat quality, carcass composition, halothane, ryanodine receptors, piglets, homozygosity, anesthesia, genetic polymorphism, stress tolerance, abiotic stress, malignant hyperthermia.

Allison, C.P., A.L. Marr, N.L. Berry, D.B. Anderson, D.J. Ivers, L.F. Richardson, K. Keffaber, R.C. Johnson, and M.E. Doumit (2006). **Effects of halothane sensitivity on mobility status and blood metabolites of HAL-1843-normal pigs after rigorous handling.** *Journal of Animal Science* 84(4): 1015-1021. ISSN: 0021-8812.
NAL Call Number: 49 J82
Abstract: The objective of this study was to determine if HAL-1843-normal pigs that respond abnormally to halothane anesthesia were more likely to become nonambulatory (NA) when subjected to rigorous handling than pigs that exhibit a normal response to halothane. After a 1,100-km transport, pigs exhibiting low (HS-L; n = 33), intermediate (HS-I; n = 10), and high (HS-H; n = 47) sensitivity to halothane were moved through a 36.6-m long aisle that was 2.1 m wide at each end and 0.6 m wide in the middle 18.3 m. Ten groups of 8 pigs were briskly moved down the aisle and back 4 times, receiving a minimum of 1 electrical prod per pass (8 prods/pig). Before testing, rectal temperature was measured, open-mouth breathing and skin discoloration were visually evaluated, and a blood sample was collected from each pig. After the test, the pigs were returned to their pens, and the same measurements were taken immediately posttest and 1 h posttest (no blood at 1 h posttest). Pigs that were HS-H were more prone to becoming NA compared with HS-L pigs ($P < 0.02$). Regardless of halothane status, a greater number of pigs exhibited open-mouth breathing and skin discolorations immediately posttest than at the pretest or 1 h posttest times ($P < 0.05$). No differences were observed in blood metabolites between the different halothane sensitivity categories. However, pigs that became NA had elevated blood levels of creatine phosphokinase, lactate, glycerol, nonesterified fatty acids, ammonia, and urea nitrogen before testing ($P < 0.05$). Collectively, these data suggest HS-H pigs are more susceptible to becoming NA than HS-L. The elevated pretest blood metabolites of NA pigs suggest that they were in a hypermetabolic state that predisposed them to becoming NA.
Descriptors: swine, blood chemistry, animal handling, malignant hyperthermia, halothane, anesthesia, genotype, genetic variation, animal transport, body temperature , breathing, skin, color, downer animals, urea nitrogen, glycerol, lactic acid, ammonia, free fatty acids, creatine kinase.

Almubarak, A., K. Clarke, and T.L. Jackson (2005). **Comparison of the Bain system and Uniflow universal anaesthetic breathing systems in spontaneously breathing young pigs.** *Veterinary Anaesthesia and Analgesia* 32(5): 314-21. ISSN: 1467-2987.
NAL Call Number: SF914 .V47
Abstract: OBJECTIVE: To compare minimum fresh gas flow (V(min)) requirements and respiratory resistance in the Uniflow and Bain anaesthetic breathing systems used in the Mapleson D mode. Animals Seven pigs, aged 8-12 weeks, anaesthetized for ophthalmic surgery. MATERIALS AND METHODS: Anaesthesia was maintained with halothane delivered in oxygen using a (Mapleson D) Bain breathing system. The V(min) that prevented re-breathing was found, and peak inspiratory (PIP) and peak expiratory (PEP) pressures measured. The fresh gas flow (V(f)) was then increased to V(min) + 50%, then V(min) + 100%, and respiratory pressures re-measured. A heat and moisture exchanger (HME) was inserted at the endotracheal tube and the procedure repeated. The breathing system was then exchanged for a Uniflow and the protocol repeated. After final disconnection from the breathing system, the animals' peak inspiratory and

expiratory flows, tidal, and minute volumes (Vm) were measured over five respiratory cycles. RESULTS: The V(min) (L minute(-1); mL kg(-1) minute(-1)) required to prevent rebreathing in the Uniflow system [8.1(mean) +/-1.7 (SD); 332 +/- 94] was significantly greater than the Bain system (6.5 +/- 1.1; 256 +/- 64). At V(min), PEP with the Uniflow (3.5 +/- 0.1 cm H(2)O) was significantly higher than the Bain system (2 +/- 0.7 cm H(2)O), but PIP values did not differ (Uniflow -0.6 +/- 2.1 cm H(2)O; Bain system -0.2 +/- 0.6 cm H(2)O). With both systems, PEP increased significantly ($p < 0.001$) with each increase in V(f): Uniflow system 4.2 +/- 0.4 (V(min) + 50%) and 5.5 +/- 0.5 cm H(2)O (V(min) + 100%); Bain system 2.8 +/- 0.7 (V(min) + 50%) and 3.5 +/- 0.7 cm H(2)O (V(min) + 100%). Insertion of the HME did not alter pressures. The mean tidal volume was 6.4 +/- 1.6 mL kg(-1); mean Vm was 184.9 +/- 69.8 mL kg(-1) and mean respiratory rate was 28 +/- 5 breaths minute(-1). In one pig breathing with the Uniflow system PEP rose sharply; respiratory and heart rates increased, and ventricular dysrhythmias occurred. When the system was changed and V(f) reduced, physiological variables became normal. CONCLUSION: The study discredited the hypothesis that the two breathing systems behave similarly. Values for V(min) and PEP were higher with the Uniflow system. Increasing V(f) increased PEP with both systems. Insertion of an HME did not affect respiratory pressures. CLINICAL RELEVANCE: The Uniflow used in Mapleson D mode is not suitable for anaesthesia in young spontaneously breathing pigs.

Descriptors: anesthesia, inhalation veterinary, laboratory physiology, respiration, artificial veterinary, swine physiology, anesthetics, inhalation administration and dosage, newborn physiology, equipment design, halothane administration and dosage, pulmonary gas exchange, respiration, artificial instrumentation, swine surgery.

Ansley, D.M. (2006). **Is anesthesia good for you? Timing is everything!** *Canadian Journal of Anaesthesia; Journal Canadien D'Anesthesie* 53(7): 643-5. ISSN: 0832-610X.

NAL Call Number: RD78.68.C4

Descriptors: anesthesia adverse effects, swine, time factors.

Language of Text: French.

Arulmani, U., S. Gupta, A.M. VanDenBrink, D. Centurion, C.M. Villalon, and P.R. Saxena (2006). **Experimental migraine models and their relevance in migraine therapy.** *Cephalalgia an International Journal of Headache* 26(6): 642-59. ISSN: 0333-1024.

Abstract: Although the understanding of migraine pathophysiology is incomplete, it is now well accepted that this neurovascular syndrome is mainly due to a cranial vasodilation with activation of the trigeminal system. Several experimental migraine models, based on vascular and neuronal involvement, have been developed. Obviously, the migraine models do not entail all facets of this clinically heterogeneous disorder, but their contribution at several levels (molecular, in vitro, in vivo) has been crucial in the development of novel antimigraine drugs and in the understanding of migraine pathophysiology. One important vascular in vivo model, based on an assumption that migraine headache involves cranial vasodilation, determines porcine arteriovenous anastomotic blood flow. Other models utilize electrical stimulation of the trigeminal ganglion/nerve to study neurogenic dural inflammation, while the superior sagittal sinus stimulation model takes into account the transmission of trigeminal nociceptive input in the brainstem. More recently, the introduction of integrated models, namely electrical stimulation of the trigeminal ganglion or systemic administration of capsaicin, allows studying the activation of the trigeminal system and its effect on the cranial vasculature. Studies using in vitro models have contributed enormously during the preclinical stage to characterizing the receptors in cranial blood vessels and to studying the effects of several putative antimigraine agents. The aforementioned migraine models have advantages as well as some limitations. The present review is devoted to discussing various

migraine models and their relevance to antimigraine therapy.
Descriptors: analgesics administration and dosage, disease models, animal, migraine disorders drug therapy, migraine disorders physiopathology, serotonin agonists administration and dosage, vasodilator agents administration and dosage, treatment outcome.

Ashley, Z., B. Jugg, R.F. Brown, C.E. Kenward, J. Platt, P. Rice, and F.M. Harban (2002). **Effects of inhaled nitric oxide on the anesthetized, mechanically ventilated, large white pig.** *Inhalation Toxicology* 14(11): 1175-85. ISSN: 0895-8378.
NAL Call Number: RA1199.4.A54I53
Abstract: Inhalation of nitric oxide (NO) results in selective pulmonary vasodilation, which may be beneficial in the treatment of acute lung injury. However, NO has toxic effects, and it is important to monitor the effects and fate of inhaled NO. Under intravenous general anesthesia, large white female pigs were instrumented, ventilated with intermittent positive pressure ventilation (IPPV, FiO(2) 0.3; TV 10 ml kg(-1); RR 20 bpm; PEEP 3 cm H(2)O) and monitored for 24 h. Following a period of stabilization, groups were exposed to air (control), or to 10, 40, or 80 ppm NO, delivered via the endotracheal tube in each inspiratory breath. At regular intervals throughout the 24-h period, physiological measurements and arterial blood, plasma, and urine samples were collected. Inhalation of NO acted specifically on the pulmonary vasculature, as no alterations in systemic blood pressure were observed. Administration of NO at 80 ppm resulted in a decreased mean pulmonary artery pressure, decreased pulmonary wedge pressure, and increased methemoglobin and plasma/urine nitrate levels. At post mortem, congestion of the alveolar capillary network was noted in this group. In addition increases in plasma/urine nitrate levels were also observed in the 40 ppm group. In contrast, no significant alterations were observed in the 10 ppm group, compared to the control group. Therefore, 10 ppm inhaled NO is a dose that induced no pathological changes in normal healthy lungs and may be of use as a therapeutic adjunct in the management of acute lung injury.
Descriptors: anesthesia, general, disease models, animal, nitric oxide toxicity, swine, vasodilator agents toxicity, administration, inhalation, capillaries drug effects, capillaries pathology, dose response relationship, drug, hemodynamic processes drug effects, nitric oxide administration and dosage, no observed adverse effect level, pulmonary alveoli blood supply, pulmonary alveoli drug effects, pulmonary alveoli pathology, respiration, artificial, vasodilator agents administration and dosage.

Baker, T.F., M. Torabinejad, S.F. Schwartz, and D. Wolf (2009). **Effect of intraosseous anesthesia on control of hemostasis in pigs**. *Journal of Endodontics* 35(11): 1543-1545. ISSN: 0099-2399.
Online: http://dx.doi.org/10.1016/j.joen.2009.07.017
NAL Call Number: RK351
Abstract: Introduction: Intraosseous anesthesia is used to deliver anesthetic into cancellous bone adjacent to the root apices. No study has assessed the effect of this anesthetic technique on hemostasis. The purpose of this study was to compare the amount of bleeding from soft tissue and bone in pig jaws after preoperative intraosseous or infiltration anesthesia with 2% lidocaine containing 1:50,000 epinephrine. Methods: Twelve pigs were divided into 3 groups. The first group received infiltration anesthesia on one half of the jaw and no anesthesia on the other half. The second group received intraosseous anesthesia on one half of the jaw and no anesthesia on the other half. The third group received infiltration anesthesia on one half of the jaw and intraosseous anesthesia on the second half. Blood was collected during flap reflection to measure the volume of soft tissue bleeding. Osteotomies were then prepared with blood collected from the surgical site to measure the volume of osseous bleeding. Results: The median soft tissue blood loss observed in animals receiving infiltration anesthesia (1.14 mL) was significantly less as compared with animals

that received no anesthesia (4.49 mL) or intraosseous anesthesia (2.45 mL). Compared with median hard tissue blood loss observed in animals without anesthesia (1.51 mL), significantly less blood loss was observed in animals receiving either infiltration anesthesia (0.67 mL) or intraosseous anesthesia (0.76 mL). Conclusions: Infiltration anesthesia resulted in significantly less soft tissue bleeding (p=.004) as compared with no anesthesia. Infiltration and intraosseous anesthesia resulted in significantly less osseous bleeding than the use of no anesthetic (p<.001). The volume of blood loss for each animal was shown to be below the maximum safe volume of blood loss for a single procedure.
Descriptors: anesthesia, anesthetics, epinephrine, hemorrhage, hemostasis, jaws, lidocaine, pharmacodynamics, surgery, techniques, teeth, pigs.

Bako, A. and G. Bilkei (2004). **A clinical trial on the effects of a neuroleptic analgesia in piglet castration [Tierschutzgerechte Ferkelkastration in Neuroleptanalgesie**. *Tierarztliche Umschau* 59(6): 340-344. ISSN: 0049-3864.
NAL Call Number: 41.8 T445
Descriptors: stress, body weight, castration, ketamine, liveweight gain, neuroleptics, ketamine, acepromazine, piglets, pigs.
Language of Text: German, Summary in English.

Banaszczyk, M.G., A.T. Carlo, V. Millan, A. Lindsey, R. Moss, D.J. Carlo, and S.S. Hendler (2002). **Propofol phosphate, a water-soluble propofol prodrug: in vivo evaluation.** *Anesthesia and Analgesia* 95(5): 1285-92, Table of Contents. ISSN: 0003-2999.
Abstract: After a single IV injection of the water-soluble propofol prodrug propofol phosphate (PP) in mice, rats, rabbits, and pigs, propofol was produced rapidly (1-15 min), inducing dose-dependent sedative effects. In mice, the hypnotic dose (HD(50)), lethal dose (LD(50)), and safety index (defined as a ratio: LD(50)/HD(50)) were 165.4 mg/kg, 600.6 mg/kg, and 3.6, respectively. Propofol was produced with half-lives of 5.3 +/- 0.6 min in rats, 2.1 +/- 0.6 min in rabbits, and 4.4 +/- 2.4 min in pigs. The maximal concentration was dose and species dependent. The elimination half-life was 24 +/- 12 min in rats, 21 +/- 16 min in rabbits, and 225 +/- 56 min in pigs. Propofol generated from PP produced pharmacological effects similar to those described in the literature. We found a correlation between PP dose and duration of sedation with propofol concentrations larger than 1.0 microg/mL, which produced somnolence and sedation in rats and pigs. Adequate sedation and, at large enough doses, anesthetic-level sedation were produced after the administration of PP. Overall, PP, the water-soluble prodrug of propofol, seems to be a viable development candidate for sedative and anesthetic applications. IMPLICATIONS: Propofol phosphate, a water-soluble prodrug of the widely used IV anesthetic propofol, was developed and evaluated in mice, rats, rabbits, and pigs after IV injection. The results of the study clearly demonstrate the feasibility of the prodrug approach to achieve sedative and anesthetic levels of propofol in laboratory animals; this warrants further evaluation in humans.
Descriptors: anesthetics, intravenous pharmacokinetics, prodrugs pharmacokinetics, propofol pharmacokinetics, anesthetics, intravenous administration and dosage, anesthetics, intravenous toxicity, dose response relationship, drug, half life, lethal dose 50, mice, musculoskeletal equilibrium, pain measurement drug effects, prodrugs administration and dosage, propofol administration and dosage, propofol toxicity, rabbits, rats, rats, sprague dawley, swine.

Barel, C., M. Belkhiria, B. Bui Xuan, J. Descotes, P. Chevalier, M.C. Gagnieu, F. Arnal, P. Tsibiribi, and Q. Timour (2003). **Ropivacaine combined with various anti-arrhythmic drugs results in mild alterations in myocardial contractility in pigs.** *Canadian Journal of Anaesthesia; Journal Canadien D'Anesthesie* 50(10): 1031-4. ISSN: 0832-610X.

NAL Call Number: RD78.68.C4
Abstract: PURPOSE: The present study was undertaken following the observation of a marked decrease in myocardial contractility after ropivacaine in a patient on amiodarone, in order to investigate the cardiovascular effects of combining ropivacaine with anti-arrhythmic drugs (AARD). METHODS: Anesthetized domestic pigs were treated with disopyramide, flecainide, atenolol, amiodarone, diltiazem or nicardipine at a dose leading to blood levels obtained in treated patients, then received 1 mg*kg(-1) ropivacaine. Blood pressure (BP), left venticular (LV) dP/dt max, sinus heart rate, and intraventricular conduction time were measured before and following the administration of AARD, and following ropivacaine at different time points. RESULTS: All tested AARD induced the expected hemodynamic and electrophysiologic effects. Following ropivacaine, a 20 to 35% decrease in LV dP/dt max of prolonged duration was observed with amiodarone only. A brief 10 to 20% decrease in mean BP was observed in all animals, except those treated with nicardipine who sustained an important and prolonged decrease in BP. All other variables were not significantly affected. DISCUSSION: The combination of ropivacaine with AARD was always associated with a slight drop in LV dP/dt max. The effect on mean BP was slight, except with nicardipine. Clinicians should be aware of the interactions of ropivacaine with AARD, especially amiodarone and nicardipine.
Descriptors: amides pharmacology, anesthetics, local pharmacology, myocardial contraction drug effects, amiodarone pharmacology, analysis of variance, anti arrhythmia agents pharmacology, disopyramide pharmacology, drug interactions, heart rate drug effects, hemodynamic processes drug effects, prospective studies, random allocation, swine.

Basu, S., D.K. Mutschler, A.O. Larsson, R. Kiiski, A. Nordgren, and M.B. Eriksson (2001). **Propofol (Diprivan-EDTA) counteracts oxidative injury and deterioration of the arterial oxygen tension during experimental septic shock.** *Resuscitation* 50(3): 341-8. ISSN: 0300-9572.
NAL Call Number: RC86
Abstract: PURPOSE: Human septic shock can be replicated in the endotoxaemic pig. Endotoxaemia causes a multitude of events, including reduced PaO(2) and increased lipid peroxidation. This study was designed to evaluate the possible effects of a commonly used anaesthetic drug with known antioxidant properties (propofol) during porcine endotoxaemia. METHODS: Ten pigs were anaesthetised and given a 6 h E. coli endotoxin infusion. The animals received, randomly, a supplementary continuous infusion of propofol emulsion (containing 0.005% EDTA) or the corresponding volume of vehicle (controls). Pathophysiologic responses were determined. Non-enzymatic (by measuring plasma 8-iso-PGF(2 alpha) and enzymatic (by measuring plasma 15-keto-dihydro-PGF(2 alpha)) lipid peroxidations were evaluated. Plasma levels of the endogenous antioxidants alpha- and gamma-tocopherols, were also analysed. RESULTS: Endotoxaemia increased plasma levels of 8-iso-PGF(2 alpha) (1st-4th h) and 15-keto-dihydro-PGF(2 alpha) (1st-4th h) significantly more in controls than in the propofol+endotoxin group. PaO(2) was significantly less affected by endotoxin in the propofol treated animals (2nd-4th h). Mean arterial pressure (4th-6th h) and systemic vascular resistance (6th h) were reduced significantly more by endotoxin among the propofol-treated animals. Vitamin E (alpha-tocopherol) increased in all animals, significantly more in the propofol+endotoxin group (1/2-6th h) than in the control group. CONCLUSIONS: Propofol reduced endotoxin-induced free radical mediated and cyclooxygenase catalysed lipid peroxidation significantly. The implication is that propofol counteracts endotoxin-induced deterioration of PaO(2).
Descriptors: anesthetics, intravenous therapeutic use, dinoprost analogs and derivatives, endotoxemia physiopathology, escherichia coli infections physiopathology, lipid peroxidation drug effects, oxidative stress drug effects, propofol analogs and derivatives, propofol therapeutic use,

shock, septic blood, shock, septic drug therapy, vitamin e physiology, dinoprost blood, f2 isoprostanes blood, inflammation therapy, radioimmunoassay, swine, vitamin e blood.

Bataille, G., B. Minvielle, J. Boulard, M. Bouyssiere, and P. Chevillon (2002). **Evaluation of the welfare of pigs during carbon dioxide anaesthesia [Evaluation du bien-etre des porcs, lors de l'anesthesie au CO2**. *Techni Porc* 25(5): 31-36. ISSN: 0181-6764.
NAL Call Number: SF391.T4
Descriptors: abattoirs, anesthesia, animal behaviour, carbon dioxide, EU regulations, heart rate, slaughter, distress, welfare.
Language of Text: French, Summary in English.

Bauer, A., H. Baschnegger, V. Renz, U. Brandl, P. Brenner, E. Thein, B. Reichart, M. Schmoeckel, and F. Christ (2007). **Comparison of propofol and isoflurane anesthesia in orthotopic pig-to-baboon cardiac xenotransplantation.** *Xenotransplantation* 14(3): 249-54. ISSN: 0908-665X.
Abstract: BACKGROUND: Orthotopic pig-to-baboon xenogeneic heart transplantation (oXHTx) is the only accepted preclinical animal model for cardiac xenotransplantation. We compared the hemodynamic stability of a propofol- and isoflurane-based anesthetic regimen during oXHTx. METHODS: Hearts from 12 hDAF or hCD46 transgenic pigs (Sus scrofa; body weight 7 to 32 kg) were transplanted into baboons (Papio anubis and Papio hamadryas; body weight 9 to 26 kg) in the orthotopic life-supporting position. Animals received a propofol-based intravenous regimen or inhalation anesthesia with isoflurane. Analgesia was achieved with fentanyl in both groups. Systemic hemodynamic variables were measured before, during and after cardiopulmonary bypass (CPB) and the need for inotropic or vasoactive pharmacological support was compared before and after CPB. RESULTS: Global hemodynamic variables [i.e. heart rate, mean arterial pressure (MAP) and cardiac output] were not significantly different in propofol-anesthetized baboons compared to baboons anesthetized with isoflurane. Baboons anesthetized with isoflurane showed a trend towards less pharmacological support required to achieve an adequate MAP of >60 mmHg after CPB (propofol: epinephrine 0.13 [0.05; 0.16] and norepinephrine 0.15 [0.02; 0.16] microg/kg/min vs. isoflurane: epinephrine 0.05 [0.02; 0.08] and norepinephrine 0.06 [0.02; 0.19] microg/kg/min; no significant difference). CONCLUSIONS: Propofol and isoflurane appear to provide equal hemodynamic stability in orthotopic cardiac pig-to-baboon xenotransplantation prior to the start of CPB. The trend of a reduced catecholamine support needed after CPB, however, suggests that isoflurane may be the preferred drug for maintenance of anesthesia in this primate model.
Descriptors: anesthetics, inhalation pharmacology, anesthetics, intravenous pharmacology, heart transplantation methods, isoflurane pharmacology, propofol pharmacology, transplantation, heterologous methods, anesthesia, general methods, anesthesia, general veterinary, blood pressure drug effects, central venous pressure drug effects, disease models, animal, heart rate drug effects, papio, sus scrofa.

Baumann, B. and G. Bilkei (2002). **Castration of piglets under general anaesthesia [Saugferkelkastration in Narkose**. *Agrarforschung* 9(1): 8-13. ISSN: 1022-663X.
NAL Call Number: S469.S9A37
Descriptors: acepromazine, anesthesia, castration, ketamine, liveweight gain, piglets, surgery, pigs.
Language of Text: German, Summary in English; French.

Baumert, J.H., K.E. Hecker, M. Hein, M. Reyle Hahn, N.A. Horn, and R. Rossaint (2005). **Effects of xenon anaesthesia on the circulatory response to hypoventilation.** *British Journal of Anaesthesia* 95(2): 166-71. ISSN: 0007-0912.

Abstract: BACKGROUND: Circulatory response to hypoventilation is aimed at eliminating carbon dioxide and maintaining oxygen delivery (DO(2)) by increasing cardiac output (CO). The hypothesis that this increase is more pronounced with xenon than with isoflurane anaesthesia was tested in pigs. METHODS: Twenty pigs received anaesthesia with xenon 0.55 MAC/remifentanil 0.5 microg kg(-1) min(-1) (group X, n=10) or isoflurane 0.55 MAC/remifentanil 0.5 microg kg(-1)min(-1) (group I, n=10). CO, heart rate (HR), mean arterial pressure (MAP) and left ventricular fractional area change (FAC) were measured at baseline, after 5 and 15 min of hypoventilation and after 5, 15 and 30 min of restored ventilation. RESULTS: CO increased by 10-20% with both anaesthetics, with an equivalent rise in HR, maintaining DO(2) in spite of a 20% reduction in arterial oxygen content. Decreased left ventricular (LV) afterload during hypoventilation increased FAC, and this was more marked with xenon (0.60-0.66, P<0.05 compared with baseline and isoflurane). This difference is attributed to negative inotropic effects of isoflurane. Increased pulmonary vascular resistance during hypoventilation was found with both anaesthetics. CONCLUSION: The cardiovascular effects observed in this model of moderate hypoventilation were sufficient to maintain DO(2). Although the haemodynamic response appeared more pronounced with xenon, differences were not clinically relevant. An increase in FAC with xenon is attributed to its lack of negative inotropic effects.

Descriptors: anesthesia methods, anesthetics, inhalation, cardiac output drug effects, hypoventilation physiopathology, xenon, analysis of variance, echocardiography, transesophageal, isoflurane, models, animal, random allocation, swine.

Baumert, J.H., K.E. Hecker, M. Hein, S.M. Reyle Hahn, N.A. Horn, and R. Rossaint (2005). **Haemodynamic effects of haemorrhage during xenon anaesthesia in pigs.** *British Journal of Anaesthesia* 94(6): 727-32. ISSN: 0007-0912.

Abstract: BACKGROUND: It was hypothesized that xenon would stabilize mean arterial pressure (MAP) in haemorrhagic shock, recovery, and volume resuscitation, because a higher MAP has been observed with xenon, when compared with isoflurane anaesthesia. The responses to haemorrhage and subsequent volume replacement were therefore compared between xenon and isoflurane anaesthesia, in pigs. METHODS: Pigs were randomized to anaesthesia with xenon 0.55 MAC (group Xe, n=9) or isoflurane 0.55 MAC (group Iso, n=9), each with remifentanil 0.5 microg kg(-1) min(-1). MAP, heart rate, cardiac output (CO), and left ventricular fractional area change (FAC) were collected at control (1), after haemorrhage (20 ml kg(-1)) (2), after 10 min of recovery (3), after volume replacement (4), and 30 min later (5). Data were analysed by two-way repeated measures anova. RESULTS: Blood loss decreased MAP (Xe: 103 [21] to 53 [24] mm Hg; Iso: 92 [18] to 55 [14] mm Hg) and CO (Xe: 4.1 [0.8] to 2.6 [0.5] litre min(-1); Iso: 5.1 [1.1] to 3.8 [1.2] litre min(-1)), in spite of significant tachycardia. MAP and CO recovered to about 75% of control, and subsequent volume replacement completely reversed symptoms in both groups, but increased FAC only with xenon. CONCLUSION: Haemodynamic response to acute haemorrhage appeared faster with xenon/remifentanil than with isoflurane/remifentanil anaesthesia. In particular MAP decrease and short-term recovery were more marked with xenon (P<0.02). In the xenon group, volume replacement increased FAC compared with control and isoflurane (P<0.02).

Descriptors: anesthetics, inhalation pharmacology, blood loss, surgical physiopathology, hemodynamic processes drug effects, xenon pharmacology, blood pressure drug effects, hypovolemia etiology, hypovolemia physiopathology, isoflurane pharmacology, swine.

Baumert, J.H., M. Reyle Hahn, K. Hecker, R. Tenbrinck, R. Kuhlen, and R. Rossaint (2002). **Increased airway resistance during xenon anaesthesia in pigs is attributed to physical properties of the gas.** *British Journal of Anaesthesia* 88(4): 540-5. ISSN: 0007-0912.

Abstract: BACKGROUND: In this study we investigated the effects of the physical properties of xenon on respiratory mechanisms in pigs. METHODS: With institutional approval, 10 female pigs (mean 25.2 (SD 2.5) kg) were anaesthetized with thiopental, remifentanil, and pancuronium. Gas flow and pressure were recorded continuously at the proximal end of the tracheal tube during constant flow ventilation for control, with 100% oxygen (control), followed by 1.5% isoflurane in 70/30% nitrogen/oxygen, 1.0% isoflurane in 70/30% nitrous oxide/oxygen, and 70/30% xenon/oxygen in random order. Compliance (C) and resistance (R) were calculated using a single compartment model. Resistance was corrected for gas viscosities eta and also for densities pho and viscosities eta as (pho*eta)(1/2) to compare assumptions of laminar and mixed flow in the airways. RESULTS: With constant flow ventilation, xenon increases inspiratory pressure compared with other gas mixtures. There were no significant differences in resistance, corrected for laminar or mixed flow, between the gas mixtures. Xenon anaesthesia did not affect compliance. CONCLUSIONS: The increase in airway pressure observed with xenon anaesthesia is attributed completely to its higher density and viscosity. Therefore, determination of airway resistance must take into account the physical properties of the gas. Xenon does not exert any major effect on airway diameter.

Descriptors: airway resistance drug effects, anesthetics, inhalation pharmacology, xenon pharmacology, anesthetics, combined pharmacology, anesthetics, inhalation chemistry, isoflurane pharmacology, nitrogen pharmacology, nitrous oxide pharmacology, respiratory mechanics drug effects, swine, viscosity, xenon chemistry.

Bein, B., E. Cavus, V. Doerges, K.H. Stadlbauer, P.H. Tonner, M. Steinfath, and J. Scholz (2005). **Arginine vasopressin reduces cerebral oxygenation and cerebral blood volume during intact circulation in swine a near infrared spectroscopy study**. *European Journal of Anaesthesiology* 22(1): 62-66. ISSN: 0265-0215.

Descriptors: arginine vasopressin (AVP), pharmacology, cardiovascular system: transport and circulation, nervous system: neural coordination, methods and techniques, near ir spectroscopy, laboratory techniques, spectrum analysis techniques, cerebral blood volume, cerebral oxygenation.

Belanger, M.P., N. Askin, K. Bandali, W.J. Wallen, and C. Wittnich (2003). **Circulating awareness of adverse effects of propofol.** *Journal of the American Veterinary Medical Association* 223(6): 781-2. ISSN: 0003-1488.

NAL Call Number: 41.8 Am3

Descriptors: anesthetics, intravenous adverse effects, animals, newborn physiology, propofol adverse effects, respiration drug effects, swine physiology, acidosis chemically induced, acidosis veterinary, blood gas analysis veterinary, fatal outcome, hemodynamic processes drug effects, safety, swine diseases chemically induced.

Belliotti, T.R., T. Capiris, I.V. Ekhato, J.J. Kinsora, M.J. Field, T.G. Heffner, L.T. Meltzer, J.B. Schwarz, C.P. Taylor, A.J. Thorpe, M.G. Vartanian, L.D. Wise, T. Zhi Su, M.L. Weber, and D.J. Wustrow (2005). **Structure-activity relationships of pregabalin and analogues that target the alpha(2)-delta protein.** *Journal of Medicinal Chemistry* 48(7): 2294-307. ISSN: 0022-2623.

NAL Call Number: RS403.A1J6

Abstract: Pregabalin exhibits robust activity in preclinical assays indicative of potential antiepileptic, anxiolytic, and antihyperalgesic clinical efficacy. It binds with high affinity to the alpha(2)-delta subunit of voltage-gated calcium channels and is a substrate of the system L neutral

amino acid transporter. A series of pregabalin analogues were prepared and evaluated for their alpha(2)-delta binding affinity as demonstrated by their ability to inhibit binding of [(3)H]gabapentin to pig brain membranes and for their potency to inhibit the uptake of [(3)H]leucine into CHO cells, a measure of their ability to compete with the endogenous substrate at the system L transporter. Compounds were also assessed in vivo for their ability to promote anxiolytic, analgesic, and anticonvulsant actions. These studies suggest that distinct structure activity relationships exist for alpha(2)-delta binding and system L transport inhibition. However, both interactions appear to play an important role in the in vivo profile of these compounds.
Descriptors: amino acid transport system l metabolism, analgesics chemical synthesis, anti anxiety agents chemical synthesis, anticonvulsants chemical synthesis, calcium channels metabolism, gamma aminobutyric acid analogs and derivatives, gamma aminobutyric acid chemical synthesis, amines antagonists and inhibitors, amines metabolism, analgesics chemistry, analgesics pharmacology, anti anxiety agents chemistry , anti anxiety agents pharmacology, anticonvulsants chemistry, anticonvulsants pharmacology, brain metabolism, cho cells, cricetinae, cricetulus, cyclohexanecarboxylic acids antagonists and inhibitors, cyclohexanecarboxylic acids metabolism, leucine antagonists and inhibitors, leucine metabolism , mice, mice, inbred dba, protein binding, protein subunits metabolism, rats, structure activity relationship, swine, gamma aminobutyric acid chemistry, gamma aminobutyric acid metabolism, gamma aminobutyric acid pharmacology.

Bernards, C.M., D.D. Shen, E.S. Sterling, J.E. Adkins, L. Risler, B. Phillips, and W. Ummenhofer (2003). **Epidural, cerebrospinal fluid, and plasma pharmacokinetics of epidural opioids (part 1): differences among opioids.** *Anesthesiology* 99(2): 455-65. ISSN: 0003-3022.
Abstract: BACKGROUND: The pharmacokinetics of epidurally administered drugs has been the subject of many studies, yet drug concentration in the epidural space has never been measured. This study was undertaken to characterize the epidural, cerebrospinal fluid, and plasma pharmacokinetics of epidurally administered opioids on the basis of measurement of drug concentration in each of these compartments after epidural administration. METHODS: Morphine plus alfentanil, fentanyl, or sufentanil were administered epidurally in anesthetized pigs. Microdialysis was used to sample the epidural space and the cerebrospinal fluid for measurement of opioid concentration over time. Plasma samples were obtained from the central venous plasma and the epidural venous plasma. These data were used to calculate relevant pharmacokinetic parameters, including mean residence time, elimination half-lives, areas under the concentration versus time curves, clearance, and volume of distribution for each opioid in each compartment. RESULTS: Some of the more important findings were that the cerebrospinal fluid and plasma pharmacokinetics of the opioids did not parallel their epidural pharmacokinetics and that their hydrophobic character governed multiple aspects of their lumbar epidural pharmacokinetics. CONCLUSIONS: The findings indicate that the spinal pharmacokinetics of these drugs are complex and, in some ways, counterintuitive. Also, the bioavailability of opioids in the cerebrospinal fluid and epidural space is determined primarily by their hydrophobicity, with less hydrophobic drugs having greater bioavailability.
Descriptors: analgesia, epidural, analgesics, opioid pharmacokinetics, adipose tissue metabolism, analgesics, opioid blood, analgesics, opioid cerebrospinal fluid, chemistry, physical, dose response relationship, drug, gas chromatography mass spectrometry, injections, intravenous, injections, spinal, molecular weight, regional blood flow physiology, solubility, solvents, spinal cord blood supply, swine, tissue distribution.

Bernards, C.M., D.D. Shen, E.S. Sterling, J.E. Adkins, L. Risler, B. Phillips, and W. Ummenhofer (2003). **Epidural, cerebrospinal fluid, and plasma pharmacokinetics of epidural opioids (part 2): effect of epinephrine.** *Anesthesiology* 99(2): 466-75. ISSN: 0003-3022.

Abstract: BACKGROUND: The ability of epinephrine to improve the efficacy of epidurally administered drugs is assumed to result from local vasoconstriction and a consequent decrease in drug clearance. However, because drug concentration in the epidural space has never been measured, our understanding of the effect of epinephrine on epidural pharmacokinetics is incomplete. This study was designed to characterize the effect of epinephrine on the epidural, cerebrospinal fluid, and plasma pharmacokinetics of epidurally administered opioids. METHODS: Morphine plus alfentanil, fentanyl, or sufentanil was administered epidurally with and without epinephrine (1:200,000) to pigs. Opioid concentration was subsequently measured in the epidural space, central venous plasma, and epidural venous plasma, and these data were used to calculate relevant pharmacokinetic parameters. RESULTS: The pharmacokinetic effects of epinephrine varied by opioid and by sampling site. For example, in the lumbar epidural space, epinephrine increased the mean residence time of morphine but decreased that of fentanyl and sufentanil. Epinephrine had no effect on the terminal elimination half-life of morphine in the epidural space, but it decreased that of fentanyl and sufentanil. In contrast, in the lumbar intrathecal space, epinephrine had no effect on the pharmacokinetics of alfentanil, fentanyl, or sufentanil, but it increased the area under the concentration-time curve of morphine and decreased its elimination half-life. CONCLUSIONS: The findings indicate that the effects of epinephrine on the spinal pharmacokinetics of these opioids are complex and often antithetical across compartments and opioids. In addition, the data clearly indicate that the pharmacokinetic effects of epinephrine in spinal "compartments" cannot be predicted from measurements of drug concentration in plasma, as has been assumed for decades.

Descriptors: adrenergic alpha agonists pharmacology, analgesia, epidural, analgesics, opioid pharmacokinetics, epinephrine pharmacology, vasoconstrictor agents pharmacology, analgesics, opioid blood, analgesics, opioid cerebrospinal fluid, anesthetics, local pharmacology, area under curve, epidural space metabolism, injections, intravenous, injections, spinal, microdialysis, posterior horn cells drug effects, receptors, adrenergic, alpha 2 agonists, spinal cord metabolism, swine.

Bethune, C.R., C.M. Bernards, T. Bui Nguyen, D.D. Shen, and R.J. Ho (2001). **The role of drug-lipid interactions on the disposition of liposome-formulated opioid analgesics in vitro and in vivo.** *Anesthesia and Analgesia* 93(4): 928-33. ISSN: 0003-2999.

Abstract: Although liposome encapsulation prolongs the duration of action of epidurally administered drugs, little is known about how liposome encapsulation affects opioids differently, or about how lipid content of liposomes alters the bioavailability of epidurally-administered opioids. To address these issues, morphine, alfentanil, fentanyl, and sufentanil were loaded into D-alpha-dipalmitoyl phosphatidylcholine multilamellar liposomes, and incorporation efficiency and in vitro release rates were determined. We then determined epidural morphine and sufentanil liposomes, at two different lipid/opioid ratios, in vivo in a pig model in which epidural and intrathecal spaces were continuously sampled via microdialysis. Liposome encapsulation efficiency was significantly more for sufentanil (100%) than for the other opioids (25%-30%). The in vitro release rate was slowest for morphine, intermediate for fentanyl and alfentanil, and fastest for sufentanil. In vivo, morphine was released more slowly than sufentanil. It is most important to note that increasing the lipid content of morphine liposomes increased the proportion of drug reaching the intrathecal space. In contrast, increasing the lipid content of sufentanil liposomes did not alter intrathecal movement but did decrease movement into plasma. Therefore, increasing drug hydrophobicity and lipid content of the liposomes modulates drug distribution in vivo. IMPLICATIONS: The degree of interaction between opioids and lipid bilayers in liposome-formulated opioids dictates the rates at which epidurally-administered drugs distribute into the intrathecal compartment and blood in potentiating analgesic effects.

Descriptors: analgesics, opioids, administration and dosage , pharmacokinetics, chemistry, area

under curve, drug carriers, kinetics, lipids, liposomes chemistry, microdialysis, models, chemical, morphine, sufentanil, swine.

Bina, S., G. Cowan, J. Karaian, S. Muldoon, P. Mongan, and R. Bunger (2006). **Effects of caffeine, halothane, and 4-chloro-m-cresol on skeletal muscle lactate and pyruvate in malignant hyperthermia-susceptible and normal swine as assessed by microdialysis.** *Anesthesiology* 104(1): 90-100. ISSN: 0003-3022.

Abstract: BACKGROUND: Skeletal muscle fibers from malignant hyperthermia (MH)-susceptible humans and swine are markedly more sensitive to ryanodine receptor (RyR1) agonists than those from normal individuals. Reproducible shifts in the dose-response of skeletal muscle to caffeine and halothane are the basis of the current in vitro diagnostic caffeine-halothane contracture test. In an attempt to develop a less invasive MH diagnostic test, the authors determined the effects of RyR1 agonists (caffeine, 4-chloro-m-cresol [4CmC], and halothane) on the adductor muscle with respect to the lactate-pyruvate (L/P) system that was percutaneously dialyzed using a microdialysis technique in homozygous MH-susceptible compared with normal swine. METHODS: Animals were anesthetized (ketamine-propofol) and artificially ventilated. Sets of six CMA/20 microdialysis catheters were implanted; each catheter was perfused with different RyR1 agonist concentrations. After a 30-min equilibration after implantation, one of the catheters was perfused (2 microl/min) with vehicle (0.9% saline or lipid emulsion), and the other five were perfused with caffeine (1-64 mM), 4CmC (0.1-8 mM), or halothane (prepared in lipid emulsion; 10-500 mM). Outflow dialysate fractions collected at 10-min intervals and L/P parameters were measured enzymatically. RESULTS: Only in the MH-susceptible group did all RyR1 agonists increase dialysate L/P in a dose-dependent manner. The dose-effect relations were most prominent with 4CmC. With the halothane lipid emulsion, data scatter was high compared with that of the caffeine group and especially the 4CmC group. There were no signs of global muscle rigidity, systemic hypermetabolism, or a clinical MH episode during microdialysis RyR1 perfusion. CONCLUSIONS: The authors data demonstrate that the in vivo muscle microdialysis of the porcine L/P system reveals distinct differences between MH-susceptible and MH-normal muscle, especially in response to highly specific RyR1 agonists such as 4CmC. The microdialysis L/P technique seems to have an MH diagnostic potential in the clinical setting.

Descriptors: anesthetics, inhalation pharmacology, caffeine pharmacology, central nervous system stimulants pharmacology, cresols pharmacology, halothane pharmacology, lactic acid metabolism, malignant hyperthermia metabolism, muscle, skeletal metabolism, pyruvic acid metabolism, anesthesia, general, anesthetics, dissociative, anesthetics, intravenous, blood gas analysis, creatine kinase blood, dose response relationship, drug, electrolytes metabolism, glucose metabolism, ketamine, malignant hyperthermia genetics, microdialysis, muscle, skeletal drug effects, propofol, ryanodine receptor calcium release channel drug effects, swine.

Bina, S., S.M. Karan, E.W. Lojeski, P.D. Mongan, and S.M. Muldoon (2001). **Prolonging viability of swine muscle biopsy specimens in malignant hyperthermia testing**. *Anesthesia and Analgesia* 93(3): 781-786 . ISSN: 0003-2999.

Descriptors: animal care, methods and techniques, muscular system: movement and support, physiology, caffeine halothane contracture test, diagnostic method, malignant hyperthermia testing, skeletal muscle viability.

Binder, R., W. Hagmuller, P. Hofbauer, C. Iben, U.S. Scala, C. Winckler, and J. Baumgartner (2004). **Castration of male piglets (1): aspects of animal welfare and methods of anaesthesia [Aktuelle Aspekte der Kastration mannlicher Ferkel 1. Mitteilung: tierschutzrechtliche Aspekte der Ferkelkastration sowie Verfahren zur Schmerzausschaltung bei der chirurgischen Kastra-**

tion. *Wiener Tierarztliche Monatsschrift* 91(7): 178-183. ISSN: 0043-535X.
NAL Call Number: 41.8 T345
Descriptors: anesthesia, animal welfare, boar taint, castration, European Union, piglets, regulations, surgery, pain, distress, alternative methods.
Language of Text: German, Summary in English.

Bird, A.P., J.R. Faltinek, and A.H. Shojaei (2001). **Transbuccal peptide delivery: stability and in vitro permeation studies on endomorphin-1.** *Journal of Controlled Release Official Journal of the Controlled Release Society* 73(1): 31-6. ISSN: 0168-3659.
NAL Call Number: RS201.C64J68
Abstract: The purpose of this study was to investigate the feasibility of buccal delivery of a model peptide, endomorphin-1 (ENI), using stability and in vitro permeation studies. ENI is a recently isolated mu-opiate receptor agonist with high selectivity and specificity for this receptor subtype. Stability studies were conducted in various buffers and the drug was shown to be stable in both acidic and basic buffer systems. In the presence of full thickness porcine buccal epithelium, ENI was unstable with only 23.4+/-15.7% intact drug present after 6 h. The region responsible for this degradation was found to coincide with the major barrier region of the buccal epithelium as delineated through stability experiments in the presence of partial thickness buccal epithelium. Various peptidase inhibitors were used to isolate the enzyme(s) responsible for this degradation. Diprotin-A, a potent inhibitor of dipeptidyl peptidase IV, provided significant inhibition of the degradation of ENI in the presence of buccal epithelium. In vitro permeation studies revealed that the permeability coefficient of ENI across porcine buccal epithelium was 5.67+/-4.74x10(-7) cm/s. The enzymatic degradation of ENI was found not to be rate limiting to the drug's permeation across buccal epithelium, as diprotin-A did not increase the permeation of ENI. Sodium glycocholate as well as sodium taurocholate were also ineffective in enhancing the permeation of ENI across porcine buccal epithelium.
Descriptors: analgesics, opioid administration and dosage, oligopeptides administration and dosage, administration, buccal, algorithms, analgesics, opioid chemistry, analgesics, opioid pharmacokinetics, buffers, chromatography, high pressure liquid, drug delivery systems, drug stability, endopeptidases metabolism, mouth mucosa drug effects, mouth mucosa enzymology, oligopeptides chemistry, oligopeptides pharmacokinetics, permeability, protease inhibitors pharmacology, solutions, swine.

Birtoiu, I.A., R. Badea, P.M. Sirbu Boeti, and C. Efrimescu (2008). **Different anesthesia protocols used for experimental swine surgery**. *Lucrari Stiintifice Universitatea De Stiinte Agricole a Banatului Timisoara, Medicina Veterinara* 41: 526-529. ISSN: 1221-5295.
Descriptors: anesthesia, experimental surgery, surgery, surgical operations, pigs.

Blaze, C.A. and M.M. Glowaski (2004). ***Veterinary Anesthesia Drug Quick Reference***, London, UK: W.B. Saunders\Elsevier Science., x + 324 p. ISBN: 0721602606.
Descriptors: anesthesia, case studies, diagnosis, dosage, drugs, electrocardiograms, pharmacology, resuscitation, cats, cattle, dogs, ferrets, goats, horses, pigs, rabbits, sheep.

Boccara, G., J. Eliet, Y. Pouzeratte, C. Mann, and P. Colson (2003). **Pre-emptive lidocaine inhibits arterial vasoconstriction but not vasopressin release induced by a carbon dioxide pneumoperitoneum in pigs.** *British Journal of Anaesthesia* 90(3): 343-8. ISSN: 0007-0912.
Abstract: BACKGROUND: We assessed the preventive effects of i.v. or i.p. lidocaine

administration on increases in vascular resistance produced by carbon dioxide pneumoperitoneum and related this to vasopressin release. METHODS: Carbon dioxide pneumoperitoneum (14 mm Hg intra-abdominal pressure) was performed in 32 anaesthetized young pigs and monitored using a pulmonary artery catheter. Animals received lidocaine 0.5% (0.5 mg kg(-1)) i.v. (n=9) or 2 ml kg(-1) i.p. (n=9) or saline (n=5) 15 min before the pneumoperitoneum and were compared with a control group (n=9). RESULTS: I.V. and i.p. lidocaine inhibited increases in mean systemic vascular resistance induced by the pneumoperitoneum [2109 (SD 935) and 2282 (895), respectively, vs 3013 (1067) dyne s(-1) cm(-5) in the control group]. Cardiac output was increased. Plasma lidocaine concentrations were threefold higher after i.p. administration than after i.v. administration. After pneumoperitoneum insufflation, plasma lysine-vasopressin concentrations increased in all groups (control 74%, saline 65%, i.p. lidocaine 57%, i.v. lidocaine 74%). CONCLUSIONS: I.V. and i.p. lidocaine blunted systemic vascular responses to carbon dioxide pneumoperitoneum in pigs, but without influencing vasopressin release.

Descriptors: anesthetics, local administration and dosage, carbon dioxide physiology, lidocaine administration and dosage, lysine vasopressin blood, pneumoperitoneum, artificial methods, vascular resistance drug effects, vasoconstrictor agents blood, arteries physiology, blood pressure drug effects, cardiac output drug effects, heart rate drug effects, injections, intraperitoneal, injections, intravenous, lidocaine blood, pneumoperitoneum, artificial adverse effects, swine, vasoconstriction drug effects.

Bogdanski, R., M. Blobner, H. Fink, and E. Kochs (2003). **Effects of xenon on mesenteric blood flow.** *European Journal of Anaesthesiology* 20(2): 98-103. ISSN: 0265-0215.

Abstract: BACKGROUND AND OBJECTIVE: The effects of xenon on mesenteric vascular resistance have not been investigated. Because human beings anaesthetized with xenon show good cardiovascular stability, we believed that the agent would have little or no effect on vascular resistance in the splanchnic bed. We determined the effects of different inhaled xenon concentrations on mesenteric blood flow and mesenteric oxygen consumption in pigs sedated with intravenous propofol. METHODS: Twenty-three minipigs were instrumented with transit time flow probes around the pulmonary and superior mesenteric arteries as well as with pulmonary artery and portal venous catheters. A 14 h recovery was allowed followed by recordings of baseline values. Xenon was then randomly administered in 0.30, 0.50, and 0.70 end-tidal fractions. RESULTS: The administration of xenon resulted in an 8% (not dose dependent) decrease in mean arterial pressure (from 99 +/- 15 to 91 +/- 19 mmHg; P < 0.05), a 20% decrease in calculated systemic oxygen consumption (from 0.23 +/- 0.07 to 0.19 +/- 0.04L min(-1); P < 0.01), a 20% reduction in mesenteric oxygen delivery (from 41 +/- 12 to 33 +/- 11 mL min; P < 0.001), a 37% reduction in mesentericmetabolic rate of oxygen (from 11.3 +/- 3.6 to 7.1 +/- 3.2 mL min(-1); P < 0.01) and an 8% decrease in mesenteric artery blood flow (0.22 +/- 0.07 to 0.20 +/- 0.07 L min(-1); P < 0.05) in a dose-dependent fashion. Heart rate, cardiac output, systemic vascular resistance, mesenteric vascular resistance, mesenteric oxygen extraction fraction and portal lactate concentration were not significantly altered by xenon. CONCLUSIONS: Xenon inhalation in the propofol-sedated pig had no measurable effects on mesenteric vascular resistance. This finding may partly explain the well-known cardiovascular stability observed in patients anaesthetized with xenon. Although mesenteric artery blood flow and mesenteric oxygen delivery decreased during xenon administration, unchanged mesenteric oxygen extraction fraction and portal lactate suggest that metabolic regulation of the splanchnic circulation remained unaltered.

Descriptors: anesthetics, inhalation pharmacology, splanchnic circulation drug effects, xenon pharmacology, anesthetics, intravenous therapeutic use, blood pressure drug effects, cardiac output drug effects, central venous pressure drug effects, heart rate drug effects, oxygen consumption drug effects, propofol therapeutic use, swine, swine, miniature blood, vascular resistance drug effects.

Boissevain, I. and H. Vrieselaar (2006). **Gillen als een... [Screaming like a.....]**. *Tijdschrift Voor Diergeneeskunde* 131(24): 925. ISSN: 0040-7453.
NAL Call Number: 41.8 T431
Descriptors: anesthesia veterinary, clinical competence, pain veterinary, swine physiology, vocalization, animal, anesthesia contraindications, Netherlands, pain etiology, pain prevention and control, vaccination adverse effects, vaccination veterinary.
Language of Text: Dutch.

Bollen, P.J.A., A.K. Hansen and A.K.O. Alstrup (2010). ***The Laboratory Swine.***, 2nd edition, :CRC Press/Taylor & Francis: Boca Raton, FL, xiii, 124 p.: col. ill.; 24 cm. p. ISBN: 9781439815281.
NAL Call Number: SF407.S97.B66 2010
Descriptors: handbooks, manuals, inhalation anesthesia, injectable anesthesia, monitoring, neuromuscular blocking agents, postoperative pain, euthanasia.
Notes: Laboratory animal pocket reference series.

Bonome Gonzalez, C., F. Alvarez Refojo, C. Fernandez Goti, B. Fernandez Rosado, H. Aymerich, and J. Belda Nacher (2001). **Hipertermia maligna en un cerdo anestesiado con desflurano. [Malignant hyperthermia in a pig anesthesized with desflurane]**. *Revista Espanola De Anestesiologia y Reanimacion* 48(2): 81-4. ISSN: 0034-9356.
Abstract: A large-white pig that had not been genetically selected to develop malignant hyperthermia (MH) during anesthesia nevertheless suffered an episode of severe MH after repeated exposure to increasing concentrations of desflurane. MH is a hypermetabolic alteration that may develop in susceptible patients who have inhaled certain drugs or agents that act as triggers. Early identification and appropriate treatment are essential to reduce the likelihood of death associated with this severe alteration. We report a case of late-developing MH triggered by low concentrations of inhaled desflurane.
Descriptors: anesthetics, inhalation adverse effects, isoflurane administration and dosage, isoflurane analogs and derivatives, malignant hyperthermia veterinary, malignant hyperthermia etiology, swine.
Language of Text: Spanish.

Bose, S., W.R. Ravis, Y.J. Lin, L. Zhang, G.A. Hofmann, and A.K. Banga (2001). **Electrically-assisted transdermal delivery of buprenorphine.** *Journal of Controlled Release Official Journal of the Controlled Release Society* 73(2-3): 197-203. ISSN: 0168-3659.
NAL Call Number: RS201.C64J68
Abstract: The objective of this study was to explore the electrically assisted transdermal delivery of buprenorphine. Oral delivery of buprenorphine, a synthetic opiate analgesic, is less efficient due to low absorption and large first-pass metabolism. While transdermal delivery of buprenorphine is expected to avoid the first-pass effect and thereby be more bioavailable, use of electrical enhancement techniques (iontophoresis and/or electroporation) could provide better programmability. Another use of buprenorphine is for opiate addiction

therapy. However, a patch type device is subject to potential abuse as it could be removed by the addict. This abuse can be prevented if drug particles are embedded in the skin. The feasibility of doing so was investigated by electro-incorporation. Buprenorphine HCl (1 mg/ml) in citrate buffer (pH 4.0) was delivered in vitro across human epidermis via iontophoresis using a current density of 0.5 mA/cm(2) and silver-silver chloride electrodes. Electroporation pulses were also applied in some experiments. For electro-incorporation, drug microspheres or particles were driven into full thickness human skin by electroporation. It was observed that the passive transdermal flux of buprenorphine HCl was significantly enhanced by iontophoresis under anodic polarity. The effectiveness of electro-incorporation seemed inconclusive, with pressure also playing a potential role. Delivery was observed with electro-incorporation, but the results were statistically not different from the corresponding controls. **Descriptors:** analgesics, opioid administration and dosage, buprenorphine administration and dosage, electroporation, iontophoresis, skin metabolism, administration, cutaneous, biological transport, buprenorphine pharmacokinetics, swine.

Boyd, J.J., J.V. Kytta, J.V. Aittomaki, P.H. Rosenberg, T.A. Seppala, and T.T. Randell (2006). **Cardiovascular changes after naloxone administration in propofol-sedated piglets during opioid overdose.** *Acta Anaesthesiologica Scandinavica* 50(10): 1271-6. ISSN: 0001-5172. **Abstract:** BACKGROUND: Naloxone is an opioid receptor antagonist. Even when used in modest doses, it has been associated with serious cardiopulmonary side-effects. In this experimental porcine study, we examined the cardiac effects of naloxone during an opioid overdose. METHODS: Cardiac parameters, changes in the left ventricular compliance and the magnitude of catecholamine release were evaluated in eight spontaneously breathing piglets under propofol sedation. Cardiac parameters were recorded every 30 s and transthoracic echocardiography was used for the continuous assessment of cardiac performance. Respiratory arrest was induced by morphine (8 mg/kg). Ten minutes after morphine administration, naloxone (80 microg/kg) was injected intravenously. Every 5 min, arterial blood gases were measured and, every 10 min, a sample for the analysis of plasma catecholamines was drawn. RESULTS: There were no statistically significant changes in left ventricular ejection fraction and no signs of pulmonary hypertension. There was a statistically significant increase in the mean arterial pressure immediately after naloxone administration and in norepinephrine concentration before naloxone administration. After naloxone administration, the plasma catecholamine levels decreased in all but one animal. Two animals developed cardiac arrest (pulseless electrical activity and ventricular fibrillation) shortly after receiving naloxone. Although they were both administered naloxone prematurely due to hypoxic bradycardia, naloxone could have contributed to the development of ventricular fibrillation. CONCLUSION: Naloxone did not cause changes in ejection fraction or mean pulmonary artery pressure in hypoxic and hypercarbic conditions. After naloxone administration, the plasma catecholamine levels returned to baseline in all but one animal, and two animals developed cardiac arrest. **Descriptors:** analgesics, opioid toxicity, cardiovascular physiology drug effects, naloxone pharmacology, overdose, propofol pharmacology, carbon dioxide blood, catecholamines blood, disease models, animal, electrocardiography drug effects, hydrogen ion concentration, partial pressure, swine.

Bozeman, W.P. and A.H. Idris (2005). **Intracranial pressure changes during rapid sequence intubation: a swine model**. *Journal of Trauma Injury Infection and Critical Care* 58(2): 278-283. ISSN: 1079-6061 .

Descriptors: methods and techniques, nervous system: neural coordination, pharmacology, head injury, craniocerebral trauma, injury, paralysis, nervous system disease, arterial pressure monitor, laboratory equipment, intracranial pressure monitor, laboratory equipment, rapid sequence intubation, laboratory techniques, animal model, cerebral metabolism, drug regimen, hemodynamic parameters, intracranial pressure.

Brull, R., V.W. Chan, C.J. McCartney, A. Perlas, and D. Xu (2007). **Ultrasound detects intraneural injection.** *Anesthesiology* 106(6): 1244; Author Reply 1247. ISSN: 0003-3022.
Descriptors: anesthetics, local administration and dosage, nerve block adverse effects, peripheral nerves injuries, peripheral nerves ultrasonography, swine.
Notes: Comment On: Anesthesiology. 2006 Oct;105(4):779-83.

Buehner, E., U.C. Pietsch, A. Bringmann, C. Foja, P. Wiedemann, and S. Uhlmann (2010). **Effects of propofol and isoflurane anesthesia on the intraocular pressure and hemodynamics of pigs**. *Ophthalmic Research* 45(1): 42-46. ISSN: 1423-0259 (Electronic). 0030-3747 (Linking).
DOI: 10.1159/000317060
Abstract: To determine the conditions under which anesthetized pigs can be used in acute noninvasive investigations of ocular hydro- and hemodynamics, the intraocular pressure (IOP) of adult pigs was recorded under the following conditions: (1) after intravenous injection of propofol plus ketamine; (2) during inhalation of isoflurane, and (3) 2 h after topical administration of bimatoprost or (4) timolol. Propofol/ketamine and isoflurane induced significant decreases in the IOP. The pulsation of the ophthalmic artery appeared at a significantly higher IOP in animals anesthetized with isoflurane than in those anesthetized with propofol/ketamine. Bimatoprost and timolol did not significantly decrease the IOP within 2 h after topical administration. It is concluded that different techniques for the acute noninvasive investigation of ocular hydro- and hemodynamics are applicable in anesthetized pigs. To test the effects of antiglaucoma agents, investigation periods longer than 2 h are required. We recommend the use of intravenous propofol/ketamine anesthesia rather than isoflurane anesthesia in future experiments using pigs.
Descriptors: adult pigs, noninvasive investigations, ocular hydro- and hemodynamics, intraocular pressure, propofol, ketamine, isoflurane, topical administration,bimatoprost, timolol.

Cai, W.Z., Y.J. Li, B.T. Cai, C.H. Zeng, Y. Wang, and B.D. Luo (2003). **Effect of occlusive wound dressing supplemented with antiphlogistic and analgesic agents on plasma beta-endorphin in hot and humid environments: a study in pigs.** *Di Yi Jun Yi Da Xue Xue Bao; Academic Journal of the First Medical College of PLA* 23(7): 699-701. ISSN: 1000-2588.
Abstract: OBJECTIVE: To study the changes of plasma beta-endorphin (beta-EP) in pigs with traumatic injury after occlusive wound dressing supplemented with antiphlogistic and analgesic agents in hot and humid environments (HHE). METHODS: Traumatic models were established in 10 pigs, 5 of which received antiphlogistic- and analgesic-supplemented occlusive dressings of the wounds (experiment group, EG), while the rest pigs were assigned to control group (CG) to receive routine wound management. The pigs in both groups were then exposed to artificial HHE and at different time points during the exposure, the plasma beta-EP level, respiratory frequency and heart rates were measured respectively. RESULTS: The plasma beta-EP concentration of EG was significantly lower than that of CG ($P < 0.01$) after the injury, but in both groups, the levels before the injury were similar to those mea-

sured at hour 8 during HHE exposure and at hour 24 following the injury. The variation range of the respiratory frequency and heart rates during HHE exposure were significantly smaller in EG than CG (P <0.01). CONCLUSION: This supplemented occlusive wound dressing can help restrain the peak of plasma beta-EP level and the variation range of respiratory frequency and heart rates of pigs exposed to HHE.
Descriptors: analgesics administration and dosage, occlusive dressings, beta endorphin blood, heart rate, heat, humidity, respiration, swine.

Carvalho, A.R., F.C. Jandre, A.V. Pino, F.A. Bozza, J.I. Saluh, R. Rodrigues, J.H. Soares, and A. Giannella Neto (2006). **Effects of descending positive end-expiratory pressure on lung mechanics and aeration in healthy anaesthetized piglets.** *Critical Care London, England* 10(4): R122.
Abstract: INTRODUCTION: Atelectasis and distal airway closure are common clinical entities of general anaesthesia. These two phenomena are expected to reduce the ventilation of dependent lung regions and represent major causes of arterial oxygenation impairment in anaesthetic conditions. In the present study, the behavior of the elastance of the respiratory system (Ers), as well as the lung aeration assessed by CT-scan, was evaluated during a descendent positive end-expiratory pressure (PEEP) titration. This work sought to evaluate the potential usefulness of the Ers monitoring to set the PEEP in order to prevent tidal recruitment and hyperinflation of healthy lungs under general anaesthesia. METHODS: PEEP titration (from 16 to 0 cmH2O, with a tidal volume of 8 ml/kg) was performed, and at each PEEP, helical CT-scans were obtained during end-expiratory and end-inspiratory pauses in six healthy, anaesthetized and paralyzed piglets. The distribution of lung compartments (hyperinflated (HA), normally- (NA), poorly- (PA), and non-aerated areas (N)) was determined and the tidal re-aeration was calculated as the difference between end-expiratory and end-inspiratory PA and NA areas. Similarly, the tidal hyperinflation was obtained as the difference between end-inspiratory and end-expiratory HA. The Ers was estimated on a breath-by-breath basis from the equation of motion of the respiratory system during all PEEP titration with the least squares method. RESULTS: HA decreased throughout PEEP descent from PEEP 16 cmH2O to ZEEP (ranges from 24-62% to 1-7% at end-expiratory and from 44-73% to 4-17% at end-inspiratory pauses) whereas NA areas increased (30-66% to 72-83% at end-expiratory and from 19-48% to 73-77% at end-inspiratory pauses). From 16 to 8 cmH2O, Ers decreased with a correspondent reduction in tidal hyperinflation. A flat minimum of Ers was observed from 8 to 4 cmH2O. For PEEP below 4 cmH2O, Ers increased associated with a rise in tidal re-aeration and a flat maximum of the NA areas. CONCLUSION: In healthy piglets under a descending PEEP protocol, the PEEP at minimum Ers presented a compromise between maximizing NA areas and minimizing tidal re-aeration and hyperinflation. High levels of PEEP, greater than 8 cmH2O, reduced tidal re-aeration but enlarged hyperinflation with a concomitant decrease in normally aerated areas.
Descriptors: anesthesia, general, lung physiology, positive pressure respiration methods, pulmonary gas exchange physiology, respiratory mechanics physiology, animals, newborn, lung compliance physiology, swine.

Chen, X., M. Yamakage, and A. Namiki (2002). **Inhibitory effects of volatile anesthetics on K+ and Cl- channel currents in porcine tracheal and bronchial smooth muscle.** *Anesthesiology* 96(2): 458-66. ISSN: 0003-3022.
Abstract: BACKGROUND: K+ and Ca2+-activated Cl- (ClCa) channel currents have

been shown to contribute to the alteration of membrane electrical activity in airway smooth muscle. This study was conducted to investigate the effects of volatile anesthetics, which are potent bronchodilators, on the activities of these channels in porcine tracheal and bronchial smooth muscles. METHODS: Whole-cell patch clamp recording techniques were used to investigate the effects of superfused isoflurane (0-1.5 minimum alveolar concentration) or sevoflurane (0-1.5 minimum alveolar concentration) on K+ and ClCa channel currents in dispersed smooth muscle cells. RESULTS: Isoflurane and sevoflurane inhibited whole-cell K+ currents to a greater degree in tracheal versus bronchial smooth muscle cells. More than 60% of the total K+ currents in tracheal smooth muscle appeared to be mediated through delayed rectifier K+ channels compared with less than 40% in bronchial smooth muscle. The inhibitory effects of the anesthetics were greater on the delayed rectifier K+ channels than on the remaining K+ channels. Cl- currents through ClCa channels were significantly inhibited by the anesthetics. The inhibitory potencies of the anesthetics on the ClCa channels were not different in tracheal and bronchial smooth muscle cells. CONCLUSIONS: Volatile anesthetics isoflurane and sevoflurane significantly inhibited Cl- currents through ClCa channels, and the inhibitory effect is consistent with the relaxant effect of volatile anesthetics in airway smooth muscle. Different distributions and different anesthetic sensitivities of K+ channel subtypes could play a role in the different inhibitory effects of the anesthetics on tracheal and bronchial smooth muscle contractions.

Descriptors: anesthetics, inhalation pharmacology, bronchi drug effects, chloride channels drug effects, muscle, smooth drug effects, potassium channels drug effects, trachea drug effects, 4 aminopyridine pharmacology, charybdotoxin pharmacology, electrophysiology, isoflurane pharmacology, methyl ethers pharmacology, muscle, smooth cytology, patch clamp techniques, swine.

Chini, E.N., T.F. Keller, Y.S. Prakash, C.M. Pabelick, and G. Sieck (2002). **Effect of halothane on cADP-ribose-induced Ca(2+) release system in tracheal smooth muscle.** *Anesthesiology* 97(4): 1022-4. ISSN: 0003-3022.

Descriptors: adenosine diphosphate ribose pharmacology, anesthetics, inhalation pharmacology, calcium metabolism, halothane pharmacology, muscle, smooth metabolism, trachea metabolism, 8 bromo cyclic adenosine monophosphate pharmacology, aniline compounds, fluorescent dyes, heparin pharmacology, microsomes drug effects, microsomes metabolism, muscle, smooth drug effects, ruthenium red pharmacology, signal transduction drug effects, swine, trachea drug effects, xanthenes.

Cohen, S., N. Parvizi, E.J. Mulder, H.A. Van Oord, F.H. Jonker, G.C. Van Der Weijden, and M.A. Taverne (2001). **Effects of morphine and naloxone on fetal heart rate and movement in the pig.** *Journal of Applied Physiology* 90(4): 1577-83. ISSN: 8750-7587.

NAL Call Number: 447.8 J825

Abstract: To test the hypothesis that an increasing opioid tonus is involved in decreases in fetal heart rate (FHR) and movement (FM) during late gestation, we studied the effects of intravenous bolus injections of morphine (1 mg) and naloxone (1 mg) on FHR and FM in the fetal pig. Twenty-one fetuses (1 per sow) were catheterized at 90-104 days of gestation (median 100 days). Recordings of FHR (electrocardiograph or Doppler-derived signals) and FM (ultrasonography) were made from 15 min before to 45 min after treatment. Morphine administration significantly decreased FHR, but it increased FHR variation and forelimb movements (LM). LM were clustered, and this stereotyped behavior has never before been

observed in any mammalian fetus. Naloxone administration increased gross body movements and FHR without significant changes in FHR variation. It is concluded that FHR and motility are under opioidergic control in the pig fetus. Both morphine and naloxone induce hypermotility, suggesting that naloxone does not act as a pure opioid antagonist in the fetal pig.
Descriptors: analgesics, opioid pharmacology, fetal movement drug effects, heart rate, fetal drug effects, morphine pharmacology, naloxone pharmacology, narcotic antagonists pharmacology, analgesics, opioid administration and dosage, injections, intravenous, morphine administration and dosage, naloxone administration and dosage, narcotic antagonists administration and dosage, swine.

Coppens, M.J., L.F. Versichelen, G. Rolly, E.P. Mortier, and M.M. Struys (2006). **The mechanisms of carbon monoxide production by inhalational agents.** *Anaesthesia* 61(5): 462-8. ISSN: 0003-2409.
Abstract: Carbon monoxide can be formed when volatile anaesthetic agents such as desflurane and sevoflurane are used with anaesthetic breathing systems containing carbon dioxide absorbents. This review describes the possible chemical processes involved and summarises the experimental and clinical evidence for the generation of carbon monoxide. We emphasise the different conditions that were used in the experimental work, and explain some of the features of the clinical reports. Finally, we provide guidelines for the prevention and detection of this complication.
Descriptors: anesthetics, inhalation chemistry, carbon monoxide chemistry, absorption, adolescent, anesthesia, closed circuit, calcium compounds chemistry, child, preschool, gas scavengers, isoflurane analogs and derivatives, isoflurane chemistry, methyl ethers chemistry, middle aged, oxides chemistry, sodium hydroxide chemistry, swine.

Cornick Seahorn, J.L. (2001). ***Veterinary Anesthesia***, Woburn, USA: Butterworth-Heinemann., x + 318 p. ISBN: 0750672277.
Descriptors: anesthesia, anesthetics, dosage, equipment, inhaled anesthetics, injectable anesthetics, local anesthesia, monitoring, pain, patient care, pharmacology, preanesthetic medication, resuscitation, veterinary products, birds, Camelidae, cats, dogs, horses, mammals, pigs, reptiles, ruminants.
Notes: The Practical Veterinarian .

Costea, R., A. Tanase, L. Ionita, C. Copaescu, I. Girjoaba, J. Mocanu, and D.S. Drugociu (2009). **Inhalatory anaesthesia in pigs for laparascopic surgery [Anestezia inhalatorie la porc in interventiile chirurgicale laparoscopice**. *Lucrari Stiintifice Medicina Veterinara, Universitatea De Stiinte Agricole Si Medicina Veterinara "Ion Ionescu De La Brad" Iasi* 52(11(1)): 503-505. ISSN: 1454-7406.
Descriptors: anesthesia, inhalation, laparoscopy, pigs.
Language of Text: Romanian, Summary in English.

Court, M.H. (2001). **Acetaminophen UDP-glucuronosyltransferase in ferrets: species and gender differences, and sequence analysis of ferret UGT1A6.** *Journal of Veterinary Pharmacology and Therapeutics* 24 (6): 415-22. ISSN: 0140-7783.
NAL Call Number: SF915.J63
Abstract: The principal objective of this study was to determine whether ferrets glucuronidate acetaminophen more slowly compared with other species, and if so investigate the

molecular basis for the difference. Acetaminophen-UDP-glucuronosyltransferase (UGT) activities were measured using hepatic microsomes from eight ferrets, four humans, four cats, four dogs, rat, mouse, cow, horse, monkey, pig and rabbit. Gender differences between male and female ferret livers were explored using enzyme kinetic analysis. Immunoblotting of microsomal proteins was also performed using UGT-specific antibodies. Finally, the exon 1 region of UGT1A6, a major acetaminophen-UGT, was sequenced. Glucuronidation of acetaminophen was relatively slow in ferret livers compared with livers from all other species except cat. Gender differences were also apparent, with intrinsic clearance (Vmax/Km) values significantly higher in male compared with female ferret livers. Furthermore, Vmax values correlated with densitometric measurements of two protein bands identified with a UGT1A subfamily-specific antibody. No deleterious mutations were identified in the exon 1 or flanking regions of the ferret UGT1A6 gene. In conclusion, like cats, ferret livers glucuronidate acetaminophen relatively slowly. However, unlike cats, in which UGT1A6 is encoded by a pseudogene and dysfunctional, there are no defects in the ferret UGT1A6 gene which could account for the low activity.

Descriptors: acetaminophen pharmacokinetics, analgesics, non narcotic pharmacokinetics, ferrets metabolism, glucuronosyltransferase metabolism, microsomes, liver enzymology, amino acid sequence, cattle metabolism, dna primers, dogs metabolism, glucuronosyltransferase genetics, glucuronosyltransferase immunology, haplorhini metabolism, horses metabolism, immunoblotting veterinary, mice metabolism, microsomes, liver immunology, molecular sequence data, polymerase chain reaction veterinary, rabbits metabolism, rats metabolism, species specificity, swine metabolism.

Crandall, C.S., S. Kerrigan, R.L. Aguero, J. Lavalley, and P.E. McKinney (2006). **The influence of collection site and methods on postmortem morphine concentrations in a porcine model.** *Journal of Analytical Toxicology* 30(9): 651-8. ISSN: 0146-4760.

NAL Call Number: RA1221.J6

Abstract: This study was to determine the relationship of antemortem to postmortem morphine concentrations in heart and femoral blood in a porcine model following acute intravenous opiate overdose. The study involved 20 swine; each was sacrificed 10 min after injection of 2 mg/kg body weight of morphine. Drug concentrations were assayed from vitreous humor and blood isolated from the femoral vein and artery and left and right ventricles at various times postmortem. Comparisons were made between antemortem and postmortem values to determine agreement and reliability. Both free and total postmortem values varied significantly among animals, sampling sites, and over time. Free postmortem values were generally higher in comparison with antemortem values, whereas postmortem total morphine values were similar to or slightly lower than antemortem values. The effect of time on postmortem values was small. These results demonstrate a significant amount of variability in free and total morphine measurements both over time and within and between sites. Furthermore, a comparison of antemortem to postmortem values demonstrates a lack of consistency relative to the dose of morphine administered. Concentrations of morphine in the femoral vein were typically the lowest observed. This observation is not surprising given the transformation that occurs prior to the drug reaching the femoral vein. Values associated with diffuse tissues, relative to femoral veins, demonstrate more stochastic variation.

Descriptors: analgesics, opioid blood, blood specimen collection methods, morphine blood, narcotics blood, postmortem changes, analgesics, opioid pharmacokinetics, femoral artery,

femoral vein, forensic medicine, heart ventricles, morphine pharmacokinetics, narcotics pharmacokinetics, research design, swine.

Crystal, G.J. and M.R. Salem (2003). **Isoflurane causes vasodilation in the coronary circulation.** *Anesthesiology* 98(4): 1030. ISSN: 0003-3022.
Descriptors: anesthetics, inhalation adverse effects, coronary circulation drug effects, isoflurane adverse effects, vasodilation drug effects, swine.
Notes: Comment On: Anesthesiology. 2002 Jun;96(6):1465-71.

Dahse, T., J. Wennek Klose, M. Listing, C. Fleck, and H. Oelschlager (2006). **In-vitro-Untersuchungen zum Phase-1-Metabolismus des Fomocain-Derivats Oe 9000 mit Schweineleberhomogenaten. [In vitro investigations of phase I metabolism of the fomocaine derivative Oe 9000 with pig liver homogenates]**. *Pharmazie, Die* 61(11): 943-51. ISSN: 0031-7144.
Abstract: 2,2'-[4-(4-Phenoxymethylphenyl)butylimino]diethanol (Oe 9000) is a new, highly potent local anaesthetic related to fomocaine. It displays a long duration of action, low toxicity and is superior to fomocaine with regard to aqueous solubility and efficacy. In view of the development of new application forms, e.g. for the treatment of postoperative pain, the elucidation of the biotransformation of the drug is required. Therefore, experiments with 10000 x g supernatants and microsomes from pig liver homogenates were conducted. Using specifically synthesized reference compounds six phase I metabolites could be identified by LC-MS. Apart from the predominating oxidative desamination of the compound, that led after redox reactions to the corresponding butyric acid and butanol derivatives, oxygenation of the exocycle, oxidative N-desalkylation, and N-oxidation were observed. Thus, with the exception of one compound only metabolites are generated, that are expected to have no local anaesthetic activity due to their reduced basicity.
Descriptors: anesthetics, local metabolism, ethanolamines metabolism, liver metabolism, phenyl ethers metabolism, biotransformation, chromatography, gas, indicators and reagents, mass spectrometry, nitric oxide chemistry, spectrophotometry, ultraviolet, swine.
Language of Text: German.

de Groot, H. (2007). **Onderzoek naar verdoofd castreren van biggen van start. [Swine castration with anesthesia investigation begins]**. *Tijdschrift Voor Diergeneeskunde* 132(11): 446-7. ISSN: 0040-7453.
NAL Call Number: 41.8 T431
Descriptors: anesthesia veterinary, legislation, veterinary, orchiectomy veterinary, swine surgery, netherlands, orchiectomy methods.
Language of Text: Dutch.

Deacon, C.F., A. Plamboeck, S. Moller, and J.J. Holst (2002). **GLP-1-(9-36) amide reduces blood glucose in anesthetized pigs by a mechanism that does not involve insulin secretion.** *American Journal of Physiology. Endocrinology and Metabolism* 282(4): E873-9. ISSN: 0193-1849.
Abstract: Glucagon-like peptide 1 (GLP-1) is a potent anti-hyperglycemic hormone currently under investigation for its therapeutic potential. However, due to rapid degradation by dipeptidyl peptidase IV (DPP IV), which limits its metabolic stability and eliminates its insulinotropic activity, it has been impossible to assess its true efficacy in vivo. In chloralose-anesthetized pigs given valine-pyrrolidide (to block endogenous DPP IV activity), the

independent effects of GLP-1-(7-36) amide on glucose and insulin responses to intravenous glucose were assessed, and the metabolite generated by DPP IV, GLP-1-(9-36) amide, was investigated for any ability to influence these responses. GLP-1-(7-36) amide enhanced insulin secretion (P < 0.03 vs. vehicle), but GLP-1-(9-36) amide was without effect, either alone or when coinfused with GLP-1-(7-36) amide. In contrast, GLP-1-(9-36) amide did affect glucose responses (P < 0.03). Glucose excursions were greater after saline (121 +/- 17 mmol x l(-1) x min) than after GLP-1-(9-36) amide (73 +/- 19 mmol x l(-1) x min; P < 0.05), GLP-1-(7-36) amide (62 +/- 13 mmol x l(-1) x min; P < 0.02) or GLP-1-(7-36) amide + GLP-1-(9-36) amide (50 +/-13 mmol x l(-1) x min; P < 0.005). Glucose elimination rates were faster after GLP-1-(7-36) amide + (9-36) amide (10.3 +/- 1.2%/min) than after GLP-1-(7-36) amide (7.0 +/- 0.9%/min; P < 0.04), GLP-1-(9-36) amide (6.8 +/- 1.0%/min; P < 0.03), or saline (5.4 +/- 1.2%/min; P < 0.005). Glucagon concentrations were unaffected. These results demonstrate that GLP-1-(9-36) amide neither stimulates insulin secretion nor antagonizes the insulinotropic effect of GLP-1-(7-36) amide in vivo. Moreover, the metabolite itself possesses anti-hyperglycemic effects, supporting the hypothesis that selective DPP IV action is important in glucose homeostasis.

Descriptors: anesthesia, blood glucose metabolism, insulin secretion, peptides pharmacology, antigens, cd26 metabolism, chloralose, glucagon blood, glucagon like peptide 1, glucagon like peptides, infusions, intravenous, kinetics, metabolic clearance rate, peptide fragments administration and dosage, peptide fragments blood, peptide fragments pharmacology, peptides administration and dosage, peptides pharmacokinetics, protease inhibitors pharmacology, protein precursors blood, pyrroles pharmacology, swine, valine pharmacology.

del Castillo, J.R., V. Laroute, P. Pommier, C. Zemirline, A. Keita, D. Concordet, and P.L. Toutain (2006). **Interindividual variability in plasma concentrations after systemic exposure of swine to dietary doxycycline supplied with and without paracetamol: a population pharmacokinetic approach.** *Journal of Animal Science* 84(11): 3155-66.

NAL Call Number: 49 J82

Abstract: Anorexigenic substances released during infection may hinder the therapeutic efficacy of in-feed antibiotics. Paracetamol (acetaminophen; PARA) inhibits the anorexia of infection and seems to improve the clinical efficacy of doxycycline (DOX) against bacterial respiratory disease in swine herds. In order to verify whether PARA selectively stimulates intake of DOX-medicated feed in diseased pigs, we documented the pharmacokinetics (PK) of DOX when coadministered with PARA and examined the effect of in-feed PARA on the interindividual variability in plasma concentrations after systemic exposure to in-feed DOX in swine herds with respiratory disease. Systemic exposure to DOX was measured with the area under the curve (AUC) of its plasma concentrations over time. First, a rich-sampling PK study of in-feed and i.v. DOX (10 mg/kg of BW) and PARA (30 and 10 mg/kg of BW, respectively) was performed on 5 pigs. The PK profiles of in-feed DOX were used in mathematical simulations to determine 5 optimal sampling times for the farm-based population PK study. A randomized, blind, parallel PK study was performed in 2 herds with bacterial respiratory disease, where liquid feed was fortified with DOX alone (5 mg x kg of BW(-1) x meal(-1)) or combined with PARA (15 mg x kg of BW(-1) x meal(-1)). Medicated meals were given twice, 12 h apart, to group-housed growing pigs (n > 50 pigs x treatment(-1) x herd(-1), totaling 215 pigs). Plasma concentrations of DOX and PARA were measured with HPLC. At variance with our expectations, PARA decreased (P = 0.069) mean AUC of in-feed DOX and did not decrease its variability (P > 0.34). Mean AUC of DOX increased

with feed intake and with initial exposure to DOX, and was greater in sick animals. Therefore, symptomatic PARA-induced improvement in bacterial respiratory disease control with DOX is more likely caused by its analgesic/antipyretic effects than by its orexigenic effect. Interindividual variation in the AUC of DOX was large in pigs given group medication, even when sufficient feeding space was allowed and the amount of feed offered was greater than their requirements. Therefore, future studies to improve the efficacy of group antibiotic therapy should focus on feeding behavior characteristics as well as biopharmaceutical properties of medicated feeds.

Descriptors: acetaminophen pharmacokinetics, analgesics pharmacokinetics, anti bacterial agents pharmacokinetics, doxycycline pharmacokinetics, swine metabolism, acetaminophen blood, acetaminophen pharmacology, analgesics blood, anti bacterial agents blood, anti bacterial agents pharmacology, appetite drug effects, area under curve, doxycycline blood, doxycycline pharmacology, drug interactions, feeding behavior drug effects, respiratory tract infections drug therapy, respiratory tract infections microbiology, respiratory tract infections veterinary, swine diseases drug therapy.

Delahaut, P., P. Brasseur, and M. Dubois (2004). **Multiresidue method for the detection of tranquillisers, xylazine, and a b-blocker in animal production by liquid chromatography-tandem mass spectrometry.** *Journal of Chromatography A* 1054(1-2): 373-378. ISSN: 0021-9673.

NAL Call Number: QD272.C4J68

Descriptors: drug residues, tranquilizers, anesthetics, beta adrenergic antagonists, high performance liquid chromatography, mass spectrometry, swine, liver, kidneys, skeletal muscle, pork, food contamination, xylazine.

Notes: In the special issue: Food science / edited by M. Careri and K. Robards.

Demestiha, T.D., I.N. Pantazopoulos, I. Dontas, N.A. Valsamakis, P.P. Lelovas, and T.T. Xanthos (2010). **Refined induction of anesthesia with remifentanil after bolus propofol administration in Landrace/Large White swine**. *Lab Animal* 39(10): 319-24. ISSN: 0093-7355 (Print). 0093-7355 (Linking).

NAL Call Number: QL55.A1L33

Abstract: The authors report a prospective randomized blind study in which they used a refined anesthetic technique in male Landrace/Large White swine (n = 125 pigs, 19 +/- 2 kg, 10-15 weeks old). The animals were first premedicated with ketamine, midazolam and atropine and then given a dose of 1, 2, 3, 4 or 5 mug remifentanil per kg body weight (dose amounts were randomly assigned) after a bolus dose of propofol. The authors assessed the intubation conditions (e.g., jaw relaxation and other parameters) 20 min after premedication and then 5 min after anesthesia induction. All animals that received each of the different remifentanil dose amounts were successfully intubated in less than 30 s. No animal developed apnea during intubation or experienced substantial reductions in heart rate or blood pressure (> 25%) between the two time points (20 min after premedication and 5 min after anesthesia induction). Overall intubation conditions were significantly better in animals that received 5 mug remifentanil per kg body weight than in animals that received other dose amounts ($P < 0.001$). The average time to intubation was significantly shorter for animals that received 5 mug remifentanil per kg body weight than for animals that received any of the other dose amounts ($P < 0.001$). The authors concluded that for this study, 5 mug remifentanil per kg body weight resulted in excellent intubating conditions in this swine breed.

Descriptors: male Landrace, refined anesthetic technique, ketamine, midazolam, atropine, intubation .

Di Stasi, S.M., A. Giannantoni, P. Navarra, R. Massoud, D. Zavaglia, P. Bertucci, G. Vespasiani, and R.L. Stephen (2003). **The stability of lidocaine and epinephrine solutions exposed to electric current and comparative administration rates of the two drugs into pig bladder wall.** *Urological Research* 31(3): 169-76. ISSN: 0300-5623.
NAL Call Number: RC870 .U76
Abstract: Intravesical electromotive administration of local anesthetics is clinically successful but electrochemistry, cost and effectiveness limit the choice of drugs to diluted lidocaine HCl 4% mixed with epinephrine. These studies address the stability of lidocaine and epinephrine both over time and when exposed to electric current, i.e. transport rates with passive diffusion and electromotive administration. The drug mixture used was 50 ml lidocaine 4%, 50 ml H2O and 1 ml epinephrine 1/1000. For stability, the solution was placed either in bowls for 7 days or in a two chamber cell with the donor compartment (drugs) separated from the receptor compartment (NaCl solution) by a viable pig bladder wall. This was subjected to 30 mA for 45 min. Stability was measured with mass spectrometry. The cell was also used to determine transport rates with passive diffusion and currents of 20 mA and 30 mA, over 20, 30 and 45 min. Drug measurements in both compartments and bladder were made with HPLC. Lidocaine remained stable throughout the 7 days, epinephrine on day 1 only and both drugs were stable with 30 mA for 45 min. Comparing 20 mA and 30 mA with passive diffusion, there were significant differences in 6/6 donor compartment lidocaine levels, 4/6 receptor compartment levels and 6/6 bladder tissue levels and also in 6/6 epinephrine donor levels and 6/6 tissue levels. The combination lidocaine and epinephrine remains stable for 1 day and when exposed to 30 mA for 45 min. Electric current accelerates the transport of lidocaine and epinephrine.
Descriptors: anesthetics, local administration and dosage, anesthetics, local chemistry, epinephrine administration and dosage, epinephrine chemistry, lidocaine administration and dosage, lidocaine chemistry, urinary bladder metabolism, anesthetics, local pharmacokinetics, biological transport, diffusion, drug combinations, drug stability, electricity, epinephrine pharmacokinetics, lidocaine pharmacokinetics, solutions, swine.

Diaz Del Consuelo, I., F. Falson, R.H. Guy, and Y. Jacques (2005). **Transport of fentanyl through pig buccal and esophageal epithelia in vitro: influence of concentration and vehicle pH.** *Pharmaceutical Research* 22(9): 1525-9. ISSN: 0724-8741.
NAL Call Number: RS1
Abstract: PURPOSE: To validate pig esophageal epithelium as a model for the permeability barrier of the buccal mucosa, the transport of fentanyl across the two tissues was compared in vivo. METHODS: The epithelia were separated by immersing the excised mucosae into an isotonic saline solution at 60--65 degrees C. Fentanyl was delivered as the citrate salt at a concentration of 1 or 2 mg/mL buffered at one of four pH values (between 6.0 and 7.4). RESULTS: Across both barriers, drug transport increased proportionally with concentration as expected. However, drug flux was not linearly related to the unionized fraction of the drug; indeed, fentanyl delivery was significant even when 98.5% of the drug was in the ionized form. CONCLUSIONS: Buccal and esophageal fluxes were very similar under all conditions suggesting that the esophageal epithelium is a representative tool for buccal transport studies in vitro.

Descriptors: analgesics, opioid pharmacokinetics, esophagus metabolism, fentanyl pharmacokinetics, mouth mucosa metabolism, cheek, hydrogen ion concentration, swine.

Diaz del Consuelo, I., F. Falson, R.H. Guy, and Y. Jacques (2007). **Ex vivo evaluation of bioadhesive films for buccal delivery of fentanyl.** *Journal of Controlled Release Official Journal of the Controlled Release Society* 122(2): 135-40.
NAL Call Number: RS201.C64J68
Abstract: The goals of this work were (i) to develop bioadhesive films for the buccal delivery of fentanyl, and (ii) to evaluate their performance in vitro using the pig esophageal model. Films were made with polyvinylpyrrolidone (PVP) of two different molecular weights: PVP K30 and PVP K90. Delivery of fentanyl was determined across full-thickness mucosa and across heat-separated epithelium (where the permeability barrier was shown to be located). The influence of film pH was investigated, and it was found that fentanyl permeation increased with increasing pH (i.e., when a higher percentage of the unionized fraction of drug was present). However, at the pH values studied, fentanyl was predominantly ionized suggesting that transport pathways offering a hydrophilic, or polar, environment across the mucosa were available. The transport rates achieved from the PVP films providing the highest delivery suggest that a buccal system of only 1-2 cm(2) in surface area could achieve a therapeutic effect equivalent to a 10 cm(2) transdermal patch, with a much shorter lag-time.
Descriptors: analgesics, opioid chemistry, drug carriers, fentanyl chemistry, povidone chemistry, adhesiveness, administration, buccal, analgesics, opioid administration and dosage, analgesics, opioid metabolism, chemistry, pharmaceutical, diffusion chambers, culture, drug compounding, esophagus metabolism, fentanyl administration and dosage, hydrogen ion concentration, kinetics, molecular weight, mucous membrane metabolism, permeability, solubility, swine.

Diemunsch, P.A., T. Van Dorsselaer, K.D. Torp, R. Schaeffer, and B. Geny (2002). **Calibrated pneumoperitoneal venting to prevent N2O accumulation in the CO2 pneumoperitoneum during laparoscopy with inhaled anesthesia: an experimental study in pigs.** *Anesthesia and Analgesia* 94(4): 1014-8, Table of Contents. ISSN: 0003-2999.
Abstract: Nitrous oxide (N2O) accumulates in the CO2 pneumoperitoneum during laparoscopy when N2O is used as an adjuvant for inhaled anesthesia. This may worsen the consequences of gas embolism and introduce a fire risk. In this study, we quantified the pneumoperitoneal gas venting necessary to prevent significant contamination by inhaled N2O. Four domestic pigs (26-30 kg) were anesthetized and ventilated with 66% N2O in oxygen. A CO2 pneumoperitoneum was insufflated and maintained at a pressure of 12 mm Hg. Each animal underwent three experimental conditions, in random sequence, for 70 min each: 1) no pneumoperitoneal leak, 2) leak of 2 L every 10 min (12 L/h), and 3) leak of 4 L every 10 min (24 L/h). Every 10 min, pneumoperitoneal gas samples were analyzed for fractions (FPn) of N2O and CO2. Without leaks, FPnN2O increased continually and reached 29.58% +/- 3.15% at 70 min. With leaks of 2 and 4 L every 10 min (12 and 24 L/h), FPnN2O reached a plateau of <10% after 30 min. We conclude that calibrated pneumoperitoneal venting of 12 or 24 L/h is enough to prevent the constitution of potentially dangerous pneumoperitoneal gas mixtures if venting is constant. IMPLICATIONS: External venting calibrated at four or eight initial pneumoperitoneal volumes per hour with compensation by fresh CO2 is sufficient to prevent nitrous oxide buildup of more than 10% in the pneumoperitoneum during laparoscopy with inhaled general anesthesia if venting is constant.

Descriptors: anesthetics, inhalation pharmacokinetics, carbon dioxide administration and dosage, laparoscopy, nitrous oxide pharmacokinetics, pneumoperitoneum, artificial methods, anesthesia, inhalation, diffusion, swine.

Dingley, J., G.P. Findlay, B.A. Foex, J. Mecklenburgh, M. Esmail, and R.A. Little (2001). **A closed xenon anesthesia delivery system.** *Anesthesiology* 94(1): 173-6. ISSN: 0003-3022.
Descriptors: anesthesia, closed circuit instrumentation, anesthetics, inhalation administration and dosage, xenon administration and dosage, equipment design, swine.

Duke, A.M., P.M. Hopkins, J.P. Halsal, and D.S. Steele (2004). **Mg2+ dependence of halothane-induced Ca2+ release from the sarcoplasmic reticulum in skeletal muscle from humans susceptible to malignant hyperthermia.** *Anesthesiology* 101(6): 1339-46. ISSN: 0003-3022.
Abstract: BACKGROUND: Recent work suggests that impaired Mg(2+) regulation of the ryanodine receptor is a common feature of both pig and human malignant hyperthermia. Therefore, the influence of [Mg(2+)] on halothane-induced Ca(2+) release from the sarcoplasmic reticulum was studied in malignant hyperthermia-susceptible (MHS) or -non-susceptible (MHN) muscle. METHODS: Vastus medialis fibers were mechanically skinned and perfused with solutions containing physiologic (1 mm) or reduced concentrations of free [Mg(2+)]. Sarcoplasmic reticulum Ca(2+) release was detected using fura-2 or fluo-3. RESULTS: In MHN fibers, 1 mm halothane consistently did not induce sarcoplasmic reticulum Ca(2+) release in the presence of 1 mm Mg(2+). It was necessary to increase the halothane concentration to 20 mm or greater before Ca release occurred. However, when [Mg(2+)] was reduced below 1 mm, halothane became an increasingly effective stimulus for Ca(2+) release; e.g., at 0.4 mm Mg(2+), 58% of MHN fibers responded to halothane. In MHS fibers, 1 mm halothane induced Ca(2+) release in 57% of MHS fibers at 1 mm Mg(2+). Reducing [Mg(2+)] increased the proportion of MHS fibers that responded to 1 mm halothane. Further experiments revealed differences in the characteristics of halothane-induced Ca(2+) release in MHS and MHN fibers: In MHN fibers, at 1 mm Mg(2+), halothane induced a diffuse increase in [Ca(2+)], which began at the periphery of the fiber and spread slowly inward. In MHS fibers, halothane induced a localized C(2+)a release, which then propagated along the fiber. However, propagated Ca(2+) release was observed in MHN fibers when halothane was applied at an Mg(2+) concentration of 0.4 mm or less. CONCLUSIONS: When Mg(2+) inhibition of the ryanodine receptor is reduced, the halothane sensitivity of MHN fibers and the characteristics of the Ca release process approach that of the MHS phenotype. In MHS fibers, reduced Mg(2+) inhibition of the ryanodine receptor would be expected to have a major influence on halothane sensitivity. The Mg dependence of the halothane response in MHN and MHS may have important clinical implications in circumstances where intracellular [Mg(2+)] deviates from normal physiologic concentrations.
Descriptors: anesthetics, inhalation pharmacology, calcium metabolism, halothane pharmacology, magnesium physiology, malignant hyperthermia metabolism, muscle, skeletal metabolism, sarcoplasmic reticulum metabolism, caffeine pharmacology, central nervous system stimulants pharmacology, cytosol metabolism, magnesium metabolism, muscle fibers drug effects, muscle fibers metabolism, muscle, skeletal drug effects, ryanodine pharmacology, sarcoplasmic reticulum drug effects.

Egan, T.D., S.E. Kern, K.B. Johnson, and N.L. Pace (2003). **The pharmacokinetics and pharmacodynamics of propofol in a modified cyclodextrin formulation (Captisol) versus propofol in a lipid formulation (Diprivan): an electroencephalographic and hemodynamic study in a porcine model.** *Anesthesia and Analgesia* 97(1): 72-9, Table of Contents. ISSN: 0003-2999.

Abstract: The currently marketed propofol formulation has a number of undesirable properties that are in part a function of the lipid emulsion formulation, including pain on injection, serious allergic reactions, and the support of microbial growth. A modified cyclodextrin-based formulation of propofol (sulfobutyl ether-beta-cyclodextrin) has been developed that may mitigate some of these formulation-dependent problems. However, reformulation may alter propofol's pharmacologic behavior. Our aim in this study was to compare the pharmacokinetics and pharmacodynamics of propofol in the currently marketed lipid-based formulation with those of the novel cyclodextrin formulation. We hypothesized that the pharmacokinetics and pharmacodynamics of the propofol in cyclodextrin would be substantially similar to those of the propofol in lipid. Thirty-two isoflurane-anesthetized animals were instrumented with pulmonary artery, arterial, and IV catheters and were randomly assigned to receive either propofol in lipid or propofol in cyclodextrin by continuous infusion. Arterial blood samples for propofol assay were collected. The processed electroencephalogram, heart rate, mean arterial blood pressure, and cardiac output were measured continuously. The propofol formulations were compared by using model-independent analysis techniques. Combined kinetic/dynamic models were also constructed for simulation purposes. There were no significant differences in the pharmacokinetics or pharmacodynamics of the two propofol formulations. The simulations based on the combined pharmacokinetic/pharmacodynamic models confirmed the substantial similarity of the two formulations. The hypothesis that the propofol-in-cyclodextrin formulation would exhibit pharmacokinetic and pharmacodynamic behavior that was substantially similar to the propofol-in-lipid formulation was confirmed. IMPLICATIONS: A modified cyclodextrin-based formulation of propofol has been developed that may mitigate some of the problems associated with propofol in lipid emulsion. However, reformulation of propofol may change its clinical characteristics. This study in a pig model showed that the novel propofol formulation was substantially similar to the lipid emulsion propofol formulation.

Descriptors: anesthetics, intravenous pharmacokinetics, anesthetics, intravenous pharmacology, electroencephalography drug effects, hemodynamic processes drug effects, propofol pharmacokinetics, propofol pharmacology, anesthetics, intravenous administration and dosage, blood pressure drug effects, cardiac output drug effects, chromatography, gas, cyclodextrins, excipients, heart rate drug effects, infusions, intravenous, lipids, propofol administration and dosage, swine.

Eijck, I., C. van der Peet Schwering, M. Kiezebrink, and A. Vink (2007). **Effect van verdoofd castreren van biologische biggen op de dieren- artskosten en arbeidsbelasting van de varkenshouder. [Effect of castration of organic swine with anesthesia on the veterinary cost and physical work load of the pig farmer]**. *Tijdschrift Voor Diergeneeskunde* 132(12): 476-9. ISSN: 0040-7453.

NAL Call Number: 41.8 T431

Abstract: We studied the costs of the veterinarian and physical work load for the farmer of anaesthetizing piglets before surgical castration compared with castration without anaesthesia on seven organic pig farms . Based on experiences from farmers and veterinarians in Norway

a protocol 'Castration with anaesthesia' was formulated. This protocol was tested on the Experimental Farm at Raalte and then applied on six organic pig farms. By means of video recording it was measured how much time it takes to castrate and anaesthetize the piglets. The veterinarian anaesthetized the piglets with lidocaine. The work load for the farmer was measured by scoring the physical load for the back and the upper limbs. It took 142 and 81 seconds per litter, respectively, to castrate and anaesthetize the piglets. The waiting time between anaesthesia and castration varied from 10 to 20 minutes on the six farms. Based on these measurements, it was calculated that the costs of the veterinarian (excluding call out fee) of anaesthetizing piglets are Euro 1.73 per litter with five boars. The costs of lidocaine are Euro 0.25 per litter with five boars. The costs per kg organic pig meat are Euro 0.012. The farmers and their veterinarians were asked to react on some theses. They all agreed that the pig farmer should perform the anaesthesia with lidocaine. Anaesthetizing piglets before castration did not affect the physical load for the back and the upper limbs of the pig farmer.
Descriptors: anesthesia, local veterinary, anesthetics, local administration and dosage, animal husbandry economics, animal husbandry methods, lidocaine administration and dosage, orchiectomy veterinary, swine surgery, anesthesia, local economics, anesthesia , local methods, norway, orchiectomy economics , orchiectomy methods, swine physiology, time factors.
Language of Text: Dutch.

Eleveld, D.J., A. De Haes, J.H. Proost, and J.M. Wierda (2003). **A pharmacokinetic-pharmacodynamic model for neuromuscular blocking agents to predict train-of-four twitches.** *Journal of Pharmacokinetics and Pharmacodynamics* 30(2): 105-18. ISSN: 1567-567X.
NAL Call Number: RM1
Abstract: The train-of-four (TOF) stimulation pattern consists of 4 stimuli (T1, T2, T3, and T4) at 2 Hz, and is used in daily anesthesiological practice to determine the degree of relaxation caused by muscle relaxants. At a surgical levels of relaxation the degree of relaxation can be estimated by counting the number of "measurable" or "visible" muscular reactions to the 4 stimuli in the TOF stimulation pattern (TOF count). During recovery relaxation can be estimated by calculating the TOF ratio (T4/T1). Bartkowski and Epstein described a pharmacokinetic-pharmacodynamic (PK-PD) model to predict TOF ratio by modifying and extending the PK-PD model as described by Sheiner to use a hypothetical distributed effect compartment described by a median equilibration rate constant and a dispersion parameter. We extended the Bartkowski and Epstein PK-PD model to simulate all four TOF twitches by including EC50 terms for T2 and T3. We fit this model to data from the pig and compared the results to fitted models using separate PD models for each TOF twitch (extended Sheiner model). The extended Bartkowski and Epstein model fit the twitch height data from all four TOF twitches better than the extended Sheiner model and has fewer parameters.
Descriptors: anesthesia, models, biological, neuromuscular blocking agents pharmacokinetics, neuromuscular blocking agents pharmacology, computer simulation, reproducibility of results, sensitivity and specificity, time factors.

Elowsson, P., K. Norlen, and S. Jakobson (2001). **Continuous positive pressure ventilation during epidural blockade--effects on cardiac output distribution.** *Acta Anaesthesiologica Scandinavica* 45(1): 95-103. ISSN: 0001-5172.
Abstract: BACKGROUND: It has been shown that when cardiac output (CO) decreases

during continuous positive pressure ventilation (CPPV), its regional distribution adapts with a favouring of vital organs. Does epidural blockade modify this adaptation? METHODS: Regional blood flows were assessed by the microsphere technique (15 microm) in 17 anaesthetised pigs during spontaneous breathing and CPPV with 8 cm H2O end-expiratory pressure (CPPV8) before and after epidural blockade. The block was induced at either the Th6-7 (Thep) or the L6-S1 (Lep) level with 1 ml of lidocaine 40 mg x ml(-1). RESULTS: When Lep was combined with CPPV8, mean arterial pressure and CO decreased significantly, and they decreased even more when combined with Thep. In contrast, the relative perfusion of the central nervous system, heart and kidneys remained stable during the four conditions studied. The adrenal perfusion during CPPV8 was obviated by epidural blockade. The absolute and relative perfusion of the skeletal muscle decreased during epidural blockade. The administered doses of epidural lidocaine did not affect blood flow in the spinal cord. CONCLUSIONS: The locally mediated nutritive vasoregulation of vital organs outweighed the sympathetic blockade induced by epidural blockade. During Thep blockade the animals were less capable of responding to the haemodynamic changes induced by CPPV8, probably due to the blockade of the cardiac part of the sympathetic nervous system.
Descriptors: analgesia, epidural, cardiac output physiology, positive pressure respiration, adrenal glands blood supply, blood cell count, blood gas analysis, hemodynamic processes physiology, microspheres, regional blood flow physiology, respiratory mechanics, swine.

Emmerich, I.U. and F.R. Ungemach (2003). **Arzneimittel zur Allgemeinanasthesie des Schweines. [Drugs for general anaesthesia in pigs.]**. *Tierarztliche Praxis Ausgabe G, Grosstiere/Nutztiere* 31(6): 352-355. ISSN: 1434-1220.
NAL Call Number: SF603.V43
Descriptors: anesthesia, azaperone, drug residues, ketamine, legislation, metomidate, thiopental, pigs.
Language of Text: German.

Ennis, M., E. Nehring, and C. Schneider (2004). **Adverse reactions to drugs: in vitro studies with isolated cells.** *Inflammation Research Official Journal of the European Histamine Research Society [Et Al.]* 53(Suppl 2): S105-8. ISSN: 1023-3830.
NAL Call Number: RS122.A3
Abstract: OBJECTIVE AND DESIGN: Drug-induced adverse reactions can be allergic or pseudoallergic in nature, in this study the histamine releasing ability of 4 radiographic contrast media and 2 opioid analgesics was tested on a variety of mast cell containing cell suspensions. MATERIAL: Mast cell containing cell suspensions were obtained from porcine lung, liver, kidneys and heart, as well as rat lung and rat peritoneal lavage. TREATMENT: Cells were incubated for 10 min with Angiographin (amidotrizoate), Hexabrix (ioxaglate), Rayvist (ioglycate) or Telebrix (ioxithalamate) all 10-500 microl/ml or with levomethadone (0.1-5 mM) or pethidine (0-10 mM). METHODS: Histamine was measured using an automated fluorometric method and percentage histamine release calculated. RESULTS: All agents caused histamine release from porcine cells and rat lung cells. However, rat peritoneal mast cells were refractory to the action of pethidine. Cardiac cells were the most sensitive to the radiographic contrast media but the least sensitive to the opioid analgesics. CONCLUSIONS: The data indicate that mast cells isolated from animal models can provide an indication of those agents likely to induce an adverse pseudoallergic reaction. However, these data should be used together with those obtained from human mast cells, in vivo animal

experiments as well as studies using human volunteers and clinical trials as advocated in the Marburg Model. Copyright 2004 Birkhauser Verlag, Basel

Descriptors: analgesics, opioid adverse effects, contrast media adverse effects, hypersensitivity pathology, liver cytology, mast cells drug effects, analgesics, opioid immunology, analgesics, opioid pharmacology, bronchoalveolar lavage, cell line, contrast media pharmacology, histamine release drug effects, histamine release immunology, hypersensitivity immunology, kidney cytology, lung cytology, mast cells immunology, mast cells secretion, myocardium cytology, peritoneal lavage, radiography instrumentation, rats, rats, sprague dawley, swine.

Errando, C.L., C. Sifre, S. Moliner, D. Lopez Alarcon, J.C. Valia, F. Gil, and C.M. Peiro (2004). **Utilizacion de ketamina para anestesia subaracnoidea durante hipovolemia. Estudio experimental preliminar en cerdos.** *Revista Espanola De Anestesiologia y Reanimacion* 51(1): 3-11. ISSN: 0034-9356.

Abstract: OBJECTIVES: To assess whether subarachnoid ketamine has fewer hemodynamic effects than lidocaine in normal and hypovolemic pigs and to determine whether or not the effects of ketamine are dose-dependent. METHODS: Thirty pigs were randomly allocated to receive subarachnoid administration of lidocaine 2 mg x kg(-1), ketamine 1 mg x kg(-1) or ketamine 2 mg x kg(-1), in a situation of either normal or reduced blood volume. The pigs were assigned to six groups: group L2 (2% lidocaine 2 mg x kg(-1), normovolemia), group L2H (2% lidocaine 2 mg x kg(-1), hypovolemia), group K1 (ketamine 1 mg x kg(-1), normovolemia), group K1H (ketamine 1 mg x kg(-1), hypovolemia), group K2 (ketamine 2 mg.kg(-', normovolemia), and group K2H (ketamine 2 mg x kg(-1), hypovolemia). To induce hypovolemia 30% of the calculated blood volume was withdrawn from each pig. The subarachnoid space was catheterized, and invasive measurements of hemodynamic variables (derived from arterial, central venous and pulmonary artery catheter monitoring) were obtained. Variables were recorded at baseline and 5 and 15 min after drug injection in the normovolemic groups, and at baseline after inducing hypovolemia and 5 and 15 min after drug injection in the hypovolemic groups. RESULTS: In the normovolemic pigs no significant differences were detected between groups. In hypovolemic pigs differences were observed in heart rate and arterial pressure between the ketamine 1 mg x kg(-1) and lidocaine 2 mg x kg(-1) groups ($P < 0.05$). The decreases in heart rate and arterial pressure were less marked in the ketamine group. Mixed venous oxygen saturation and cardiac index deteriorated to a lesser degree in both ketamine groups than in the lidocaine groups ($P < 0.05$). CONCLUSIONS: Racemic ketamine administered by subarachnoid injection in hypovolemic pigs produces less deterioration in hemodynamic variables than does lidocaine. Hemodynamic changes caused by ketamine were not dose-dependent. These findings may be of interest, given the increased use of ketamine in neuroaxial anesthesia and analgesia and perhaps the possible use of neuroaxial ketamine in hypovolemic patients.

Descriptors: anesthesia, spinal, anesthetics, dissociative administration and dosage, hypovolemia physiopathology, ketamine administration and dosage, hemodynamic processes, random allocation, risk factors, swine.

Language of Text: Spanish.

Notes: Comment In: Rev Esp Anestesiol Reanim. 2004 Jan;51(1):1-2.

Fahlman, A., E.J. Bosi, and G. Nyman (2006). **Reversible anesthesia of Southeast Asian primates with medetomidine, zolazepam, and tiletamine.** *Journal of Zoo and Wildlife Medicine Official Publication of the American Association of Zoo Veterinarians* 37(4): 558-61. ISSN: 1042-7260.

NAL Call Number: SF601.J6

Abstract: Medetomidine (0.02-0.06 mg/kg) in combination with zolazepam-tiletamine (0.8-2.3 mg/kg) were evaluated for reversible anesthesia in four species of Southeast Asian primates: Bornean orangutan (Pongo pygmaeus pygmaeus), Bornean gibbon (Hylobates muelleri), long-tailed macaque (Macaca fascicularis), and pig-tailed macaque (Macaca nemestrina). Twenty-three anesthetic procedures of captive-held and free-ranging primates were studied in Sabah, Malaysia. The induction was smooth and rapid. Respiratory and heart rates were stable throughout anesthesia, whereas body temperature and systolic arterial blood pressure decreased significantly. Atipamezole at five times the medetomidine dose effectively reversed anesthesia, with first signs of recovery within 3-27 min.

Descriptors: anesthetics, combined administration and dosage, hylobates physiology, macaca fascicularis physiology, macaca nemestrina physiology, pongo pygmaeus physiology, adrenergic alpha agonists administration and dosage, adrenergic alpha antagonists administration and dosage, anesthesia recovery period, anesthetics, combined adverse effects, animals, wild, heart rate drug effects, imidazoles administration and dosage, medetomidine administration and dosage, respiration drug effects, species specificity, tiletamine administration and dosage, time factors, zolazepam administration and dosage.

Fannelop, T., G.O. Dahle, K. Matre, L. Segadal, and K. Grong (2004). **An anaesthetic protocol in the young domestic pig allowing neuromuscular blockade for studies of cardiac function following cardioplegic arrest and cardiopulmonary bypass.** *Acta Anaesthesiologica Scandinavica* 48(9): 1144-54. ISSN: 0001-5172.

Abstract: BACKGROUND: Neuromuscular blockade should, for ethical reasons, not be allowed in animal experiments unless the use is strongly motivated. Beforehand, the anaesthetic protocol must be documented without muscle relaxation in the species studied. Documentation is difficult to obtain from the scientific literature. When focusing on cardiac function over time, in particular, the ideal anaesthetic protocol should cause no or minor alterations in cardiac variables. METHODS: We intended to document an anaesthetic protocol involving ventilation with N(2)O combined with loading doses and continuous infusions of pentobarbital, fentanyl and midazolam in seven pigs by applying potentially painful stimuli every 15 min for 7 h. Subsequently, left ventricular global and regional function was studied with conductance catheter and strain rate imaging by echocardiography in eight pigs with pancuronium included. RESULTS: Pigs without pancuronium were completely immobilized and unresponsive to potentially painful stimuli and sternotomy, with no accumulation or degradation of anaesthetic agents. With pancuronium included, left ventricular preload gradually decreased together with reduction of cardiac index from 3.52 +/- 0.14 at 2 h to 2.84 +/- 0.11 L min(-1). m(-2) (+/-SEM) after 7 h of observation. Preload recruitable stroke work decreased after 7 h, whereas peak systolic strain in the anterior left ventricular wall and load-independent indices of diastolic function were not significantly altered. CONCLUSION: In specific experimental protocols, the anaesthetic protocol described could allow the use of muscular paralysis in young domestic pigs, for instance when involving hypothermic cardiopulmonary bypass, cardioplegic arrest and reperfusion.

Descriptors: anesthesia, cardiopulmonary bypass, heart physiopathology, heart arrest,

induced, neuromuscular blockade, adjuvants, anesthesia, anesthesia, inhalation, anesthetics, intravenous, cardioplegic solutions, fentanyl, hemodynamic processes drug effects, hydrocortisone blood, midazolam, monitoring, intraoperative, myocardial contraction drug effects, myocardial reperfusion, nitrous oxide, pentobarbital, research design, swine, ventricular function, left drug effects.

Fedder, A., R. Dall, S. Laurberg, and S.A. Rodt (2004). **Epidural anaesthesia with bupivacaine does not cause increased oedema in small gut anatomoses in pigs.** *European Journal of Anaesthesiology* 21(11): 864-70 . ISSN: 0265-0215.

Abstract: BACKGROUND AND OBJECTIVE: Epidural analgesia is widely used for abdominal surgery due to the properties of 'stress-free' anaesthesia and superior pain control. Nevertheless, sympathomimetics are known to antagonize inflammation. The present study was performed to investigate if epidural local anaesthetics caused increased local oedema formation. METHODS: Thirty Dansk Landrace pigs were randomized into three groups: epidural bupivacaine, epidural morphine or intravenous (i.v.) fentanyl. All animals were anaesthetized with isoflurane and i.v. midazolam and received an identical fluid regimen. Six small bowel resections were performed over a 3-h period and during the following 3 h the anastomoses were resected. Primary end-points were water content in small bowel and mesentery samples before and after gut anastomosis, lymph flow and urine production. RESULTS: The water content in the small bowel samples was not changed by surgery or by the different anaesthetic protocols. In the mesenteric tissue, there was a highly significant increase in water content of the postanastomotic samples compared to pre-anastomotic samples ($P < 0.001$) and a significant time treatment interaction was revealed ($P < 0.05$) suggesting an increase in oedema formation in the epidural local anaesthetic group. Lymph flow did not change during the experiments and there were no significant differences between the groups ($P = 0.80$). The mean total urine output was 44% higher in the epidural morphine group compared to the local anaesthetic group ($P = 0.17$). CONCLUSIONS: Surgery did not increase gut wall water content, but acute oedema formation resulted in the peri-resectional mesenterial tissue, more prominently so in the bupivacaine group.

Descriptors: anesthesia, epidural methods, anesthetics, local adverse effects, bupivacaine adverse effects, edema etiology, intestine, small surgery, mesentery drug effects, analgesics, opioid administration and dosage, analysis of variance, anastomosis, surgical methods, anesthetics, intravenous administration and dosage, anesthetics, local administration and dosage, body fluids drug effects, bupivacaine administration and dosage, edema chemically induced, fentanyl administration and dosage, hemodynamic processes drug effects, mesentery surgery, morphine administration and dosage, swine, time factors, urine.

Fiege, M., F. Wappler, R. Weisshorn, M.U. Gerbershagen, K. Kolodzie, and J.S. Am Esch (2005). **Phosphodiesterase-iii-inhibition with amrinone leads to contracture development in skeletal muscle preparations of malignant hyperthermia susceptible swine**. *European Journal of Anaesthesiology* 22(4): 283-288. ISSN: 0265-0215.

Descriptors: pharmacology, tumor biology, biochemistry and molecular biophysics, muscular system: movement and support, malignant hyperthermia, neoplastic disease, general anesthesia, clinical techniques, contracture development, bath concentration.

Fiege, M., F. Wappler, R. Weisshorn, M.U. Gerbershagen, and J.S. Am Esch (2002). **Dibucaine is not a trigger of malignant hyperthermia in anesthetized susceptible swine.** *Anesthesiology Abstracts of Scientific Papers Annual Meeting*(2001): Abstract No. A-1016.
Descriptors: metabolism, muscular system: movement and support, pharmacology, dibucaine, Malignant hyperthermia (MH), hyperthermia, metabolic disease, body temperature, hemodynamics .
Notes: Meeting Information: 2001 Annual Meeting of the American Society of Anesthesiologists, New Orleans, LA, USA; October 13-17, 2001.

Fiege, M., F. Wappler, R. Weisshorn, M.U. Gerbershagen, and J.S. Am Esch (2002). **Effects of theophylline on anesthetized swine susceptible for malignant hyperthermia in-vivo.** *Anesthesiology Abstracts of Scientific Papers Annual Meeting*(2001): Abstract No. A-1015.
Descriptors: metabolism, pharmacology, theophylline, hyperthermia, metabolic disease, anesthesia, clinical techniques, body temperature, hemodynamics, abstract.
Notes: Meeting Information: 2001 Annual Meeting of the American Society of Anesthesiologists, New Orleans, LA, USA; October 13-17, 2001.

Field, M.J., P.J. Cox, E. Stott, H. Melrose, J. Offord, T.Z. Su, S. Bramwell, L. Corradini, S. England, J. Winks, R.A. Kinloch, J. Hendrich, A.C. Dolphin, T. Webb, and D. Williams (2006). **Identification of the alpha2-delta-1 subunit of voltage-dependent calcium channels as a molecular target for pain mediating the analgesic actions of pregabalin.** *Proceedings of the National Academy of Sciences of the United States of America* 103(46): 17537-42. ISSN: 0027-8424.
NAL Call Number: 500 N21P
Abstract: Neuropathic pain is a debilitating condition affecting millions of people around the world and is defined as pain that follows a lesion or dysfunction of the nervous system. This type of pain is difficult to treat, but the novel compounds pregabalin (Lyrica) and gabapentin (Neurontin) have proven clinical efficacy. Unlike traditional analgesics such as nonsteroidal antiinflammatory drugs or narcotics, these agents have no frank antiinflammatory actions and no effect on physiological pain. Although extensive preclinical studies have led to a number of suggestions, until recently their mechanism of action has not been clearly defined. Here, we describe studies on the analgesic effects of pregabalin in a mutant mouse containing a single-point mutation within the gene encoding a specific auxiliary subunit protein (alpha2-delta-1) of voltage-dependent calcium channels. The mice demonstrate normal pain phenotypes and typical responses to other analgesic drugs. We show that the mutation leads to a significant reduction in the binding affinity of pregabalin in the brain and spinal cord and the loss of its analgesic efficacy. These studies show conclusively that the analgesic actions of pregabalin are mediated through the alpha2-delta-1 subunit of voltage-gated calcium channels and establish this subunit as a therapeutic target for pain control.
Descriptors: analgesics therapeutic use, calcium channels metabolism, pain drug therapy, pain metabolism, gamma aminobutyric acid analogs and derivatives, amino acid sequence, arginine genetics, arginine metabolism, autoradiography, base sequence, calcium channels chemistry, calcium channels genetics, calcium channels, n type metabolism, cell line, cercopithecus aethiops, constriction, pathologic, formaldehyde, ion channel gating drug effects, mice, mice, transgenic, mutation genetics, pain genetics, protein binding, protein subunits chemistry, protein subunits genetics, protein subunits metabolism, swine, gamma aminobutyric acid metabolism, gamma aminobutyric acid therapeutic use.

Fischer, S., D. Renz, J. Kleinstuck, W. Schaper, and G.F. Karliczek (2004). **In-vitro-Effekte von Anasthetika auf die Blut-Hirn-Schranke. [In vitro effects of anaesthetic agents on the blood-brain barrier]**. *Anaesthesist, Der* 53(12): 1177-84. ISSN: 0003-2417.

Abstract: BACKGROUND: The blood-brain barrier (BBB) forms a selective barrier between blood and brain and regulates the passage of most molecules. Pathological conditions such as ischemia lead to breakdown of the BBB. Vascular endothelial growth factor (VEGF) has been shown to be responsible for hypoxia-induced hyperpermeability of the BBB in vivo as well as in vitro. To eliminate factors which alter the permeability of the BBB in vivo, an in vitro model was used to test the effects of intravenous and volatile anesthetics on the permeability and on VEGF expression during normoxia and hypoxia. METHODS: The in vitro model of the BBB consisted of primary cultures of porcine brain microvascular endothelial cells (BMEC). The permeability was measured by the paracellular passage of [3H]inulin across the BMEC monolayer and the expression of VEGF was determined by northern blot analysis. RESULTS: All intravenous and volatile anesthetics tested (etomidate, ketamine, fentanyl, propofol, midazolam, sodium-gamma-hydroxybutyrate as well as halothane, enflurane, isoflurane, sevoflurane, desflurane) did not alter the permeability of the BBB or the expression of VEGF in vitro. Hypoxia (2 vol%) increased the permeability and the VEGF expression significantly which was not altered in the presence of the anesthetics. CONCLUSION: The in vitro model represents a suitable model of the BBB to investigate direct effects of anesthetics on functions of the BBB independent of hemodynamic factors.

Descriptors: anesthetics pharmacology, blood brain barrier drug effects, anesthetics, inhalation pharmacology, anesthetics, intravenous pharmacology, anoxia metabolism, blotting, northern, cell membrane permeability drug effects, cell survival drug effects, cells, cultured, endothelial cells drug effects, endothelial cells metabolism, swine, vascular endothelial growth factor a biosynthesis.

Language of Text: German.

Fredriksen, B. and O. Nafstad (2006). **Surveyed attitudes, perceptions and practices in Norway regarding the use of local anaesthesia in piglet castration.** *Research in Veterinary Science* 81(2): 293-295. ISSN: 0034-5288.

DOI: 10.1016/j.rvsc.2005.11.003

NAL Call Number: 41.8 R312

Abstract: The last two years piglet castration in Norway has been performed by veterinarians and with the use of anaesthesia. In order to evaluate this new policy, veterinarians and pig producers were asked to fill out a questionnaire regarding their experiences with the new castration practices. The answers showed that the piglets were most often castrated using a combination of subcutaneous and intratesticular administration of lidocaine with adrenaline at an average age of 10 days. The effect of the anaesthesia was regarded as good by 54% of the veterinarians and 19% of the producers. Post-operative complications were rare. The overall evaluation showed that two-thirds of the veterinarians, but only one-third of the pig producers were satisfied or very satisfied with the implemented policy. However, while two-thirds of the pig producer had a negative attitude to the policy before it was implemented, only one-third were dissatisfied after two years experience.

Descriptors: piglets, castration, national surveys, farmers' attitudes, farmers, veterinarians, anesthesia, questionnaires, lidocaine, epinephrine, postoperative complications, livestock production, Norway.

Friton, G.M., H. Philipp, T. Schneider, and R. Kleemann (2003). **Investigation on the clinical efficacy and safety of meloxicam (Metacam) in the treatment of non-infectious locomotor disorders in pigs.** *Berliner Und Munchener Tierarztliche Wochenschrift* 116(9-10): 421-6. ISSN: 0005-9366.

NAL Call Number: 41.8 B45

Abstract: The clinical efficacy and safety of meloxicam (Metacam 20 mg/ml) in the treatment of non-infectious locomotor disorders in pigs was investigated in a randomised double-blind, placebo controlled, multi-centre field study. A total of 220 pigs were examined, 211 pigs were suitable for evaluation. Treatment was performed on Day 1 with meloxicam (0.4 mg meloxicam/kg) or placebo by intramuscular injection. If necessary, treatment was optionally repeated on Day 2. Clinical examinations were conducted daily from Day 1 (immediately prior to initiation of therapy) to Day 4. The primary parameter, mean "Clinical Lameness Score" (CLS, a sum of the scores of "Lameness at Rest" and "Lameness at Walk"; range 2 to 11) improved from 6.8 and 6.3 on Day 1, to 3.5 and 4.7 on Day 4 in the meloxicam and placebo groups respectively ($p < 0.001$). At the final examination mean changes from baseline for CLS (Day 1) were 3.25 for meloxicam treated animals and 1.7 for placebo treated animals ($p < 0.001$). Behaviour score and feed intake improved during the study period with statistically significant differences in favour of meloxicam at all time points after initiation of therapy. Significantly fewer pigs received a second treatment in the meloxicam group than in the placebo group, 46% versus 73% ($p < 0.001$). A 'very good' or 'good' clinical efficacy assessment was recorded in 83% of the meloxicam cases compared to 42% of the placebo controls at the final examination ($p < 0.001$). No adverse events were reported due to the use of meloxicam. Furthermore safety of meloxicam in pregnant sows was demonstrated. It is concluded that intramuscular injection of meloxicam (Metacam) at a dosage of 0.4 mg/kg is efficacious and safe for the treatment of non-infectious locomotor disorders in pigs.

Descriptors: analgesics, non narcotic therapeutic use, lameness, animal drug therapy, pain veterinary, swine diseases drug therapy, thiazines therapeutic use, thiazoles therapeutic use, analgesics, non narcotic adverse effects, double blind method, injections, intramuscular veterinary, pain drug therapy, safety, thiazines adverse effects, thiazoles adverse effects, treatment outcome.

Fritz, H.G., M. Holzmayr, B. Walter, K.U. Moeritz, A. Lupp, and R. Bauer (2005). **The effect of mild hypothermia on plasma fentanyl concentration and biotransformation in juvenile pigs.** *Anesthesia and Analgesia* 100(4): 996-1002. ISSN: 0003-2999.

Abstract: Therapeutic hypothermia may alter the required dosage of analgesics and sedatives, but no data are available on the effects of mild hypothermia on plasma fentanyl concentration during continuous, long-term administration. We therefore assessed in a porcine model the effect of prolonged hypothermia on plasma fentanyl concentration during 33 h of continuous fentanyl administration. Seven female piglets (weight: 11.8 +/- 1.1 kg) were anesthetized by IV fentanyl (15 microg . kg(-1) . h(-1)) and midazolam (1.0 mg . kg(-1) . h(-1)). After preparation and stabilization (12 h), the animals were cooled to a core temperature of 31.6 degrees +/- 0.2 degrees C for 6 h and were then rewarmed and kept normothermic at 37.7 degrees +/- 0.3 degrees C for 6 more hours. Plasma fentanyl concentrations were measured by radioimmunoassay, cardiac index by thermodilution, and blood flows of the kidney, spleen, pancreas, stomach, gut, and hepatic artery by a colored microspheres technique. Furthermore, in an additional 4 pigs, temperature dependency of hepatic microsomal cytochrome P450 3A4 (CYP3A4) was determined in vitro by ethylmorphine N-demethylation.

Plasma fentanyl concentration increased by 25% +/- 11% (P < 0.05) during hypothermia and remained increased for at least 6 h after rewarming. Hypothermia reduced the cardiac index (41% +/- 15%, P < 0.05), as well as all organ blood flows except the hepatic artery. A strong temperature dependency of CYP3A4 was found (P < 0.01). Mild hypothermia induced a distribution and/or elimination-dependent increase in plasma fentanyl concentration which remained increased for several hours after rewarming. Consequently, a prolonged increase of the plasma fentanyl concentration should be anticipated for appropriate control of the analgesia/sedatives during and early after therapeutic hypothermia.
Descriptors: analgesics, opioid pharmacokinetics, fentanyl pharmacokinetics, hypothermia metabolism, analgesics, opioid blood, biotransformation, blood gas analysis, blood glucose metabolism, blood pressure drug effects, cytochrome p 450 enzyme system metabolism, electrocardiography drug effects, fentanyl blood, hemodynamic processes drug effects, lactic acid blood, liver metabolism, microsomes, liver drug effects, microsomes, liver enzymology, mixed function oxygenases metabolism, oxygen blood, swine.

Fudge, M., R. Coleman, and S. Parker (2002). **A minimally invasive percutaneous technique for jugular vein catheterization in pigs.** *Contemporary Topics in Laboratory Animal Science* 41(1): 38-42. ISSN: 1060-0558.
NAL Call Number: SF405.5.A23
Descriptors: swine, jugular vein, blood sampling, animal anatomy, anesthesia, animal welfare, laboratory techniques, animal use refinement, propofol, cannulation, laboratory mammals.

Galagudza, M., J. Vaage, and G. Valen (2006). **Isoflurane and other commonly used anaesthetics do not protect the isolated buffer perfused mouse heart from ischemia-reperfusion injury.** *Clinical and Experimental Pharmacology and Physiology* 33(4): 315-9. ISSN: 0305-1870.
NAL Call Number: QP1.C55
Abstract: 1. Some anaesthetic agents such as barbiturates and opioids possess cardioprotective properties in rats, rabbits, dogs and pigs. The purpose of this study was to evaluate the effects of some commonly used anaesthetic agents (pentobarbital, isoflurane and a mixture of midazolam, fentanyl and fluanisone) on the tolerance of the isolated mouse heart to ischaemia-reperfusion injury. 2. The isolated, Langendorff-perfused hearts were subjected to 45 min of global ischaemia followed by 60 min of reperfusion. Left ventricular pressures, heart rate and coronary flow were measured and infarct size was determined using triphenyltetrazolium staining. 3. There were no differences in haemodynamic variables during reperfusion between groups. Infarct size was not influenced by the choice of anaesthesia. 4. None of the anaesthesia protocols exerted significant protective effects on the ischaemic-reperfused isolated mouse heart performance. In mice, isoflurane as well as pentobarbital, opioids and benzodiazepines may be safely used for anaesthesia without a risk of protective side-effects in isolated mouse heart studies.
Descriptors: anesthetics, inhalation pharmacology, isoflurane pharmacology, myocardial reperfusion injury prevention and control, anticoagulants pharmacology, heart function tests, heparin pharmacology, mice, mice, inbred c57bl, myocardial infarction pathology, myocardial reperfusion injury pathology, myocardium pathology.

Gamperl, A.K., T.W. Hein, L. Kuo, and B.A. Cason (2002). **Isoflurane-induced dilation of porcine coronary microvessels is endothelium dependent and inhibited by glibenclamide.** *Anesthesiology* 96(6): 1465-71. ISSN: 0003-3022.

Abstract: BACKGROUND: Isoflurane has been reported to cause dose-dependent constriction in isolated coronary microvessels. However, these results are inconsistent with data from in situ and in vivo heart preparations which show that isoflurane dilates the coronary vasculature. To clarify the direct effects of isoflurane on coronary tone, we measured the response of isolated porcine resistance arterioles (ID, 75 +/- 4.0 microm; range, 41-108 microm) to isoflurane in the presence and absence of adenosine triphosphate-sensitive and Ca2+-activated potassium channel blockers and also after endothelial removal. METHODS: Subepicardial arterioles were isolated, cannulated, and pressurized to 45 mmHg without flow in a 37 degrees C vessel chamber filled with MOPS buffer (pH = 7.4). After all vessels developed spontaneous (intrinsic) tone, dose-dependent (0.17-0.84 mm; approximately 0.5-2.5 minimum alveolar concentration) isoflurane-mediated effects on vessel ID were studied in the presence and absence of extraluminal glibenclamide (1 microm; an adenosine triphosphate-sensitive channel blocker) or iberiotoxin (100 nm; a Ca2+-activated potassium channel blocker) or before and after endothelial denudation using the nonionic detergent CHAPS (0.4%). Vessel ID was measured using an inverted microscope and videomicrometer, and vasomotor responses were analyzed by normalizing changes in arteriole ID to the dilation observed after exposure to 10-4 m sodium nitroprusside, which causes maximal dilation. RESULTS: Isoflurane caused dose-dependent dilation of all coronary arterioles. This vasodilation was 6.0 +/- 0.7 microm at an isoflurane concentration of 0.16 mm (approximately 0.5 minimum alveolar concentration) and 25.3 +/- 2.1 microm at 0.75 mm (approximately 2.5 minimum alveolar concentration). These values represent 18.1 +/- 1.7% and 74.1 +/- 3.3%, respectively, of that observed with 10-4 sodium nitroprusside (34 +/- 3 microm). Glibenclamide, but not iberiotoxin, exposure affected arteriolar dilation in response to isoflurane. Glibenclamide caused a downward displacement of the isoflurane dose-response curve, reducing isoflurane-mediated dilation by an average of 36%. Denuded arterioles showed a marked (approximately 70%) reduction in their ability to dilate in response to isoflurane. CONCLUSIONS: The authors conclude that isoflurane dilates coronary resistance arterioles in a dose-dependent manner, and that this dilation is partially mediated by adenosine triphosphate-sensitive channels and is highly dependent on the presence of a functioning endothelium.

Descriptors: anesthetics, inhalation pharmacology, coronary vessels drug effects, endothelium, vascular physiology, glyburide pharmacology, isoflurane pharmacology, potassium channels physiology, vasodilation drug effects, adenosine triphosphate pharmacology, coronary vessels physiology, dose response relationship, drug, microcirculation drug effects, swine.

Notes: Comment In: Anesthesiology. 2003 Apr;98(4):1030.

Garcia Aguado, R., F. Gil, J.a. Barcia, J. Aznar, F. Hostalet, J. Barbera, and F. Grau (2000). **Prophylactic percutaneous sealing of lumbar postdural puncture hole with fibrin glue to prevent cerebrospinal fluid leakage in swine**. *Anesthesia and Analgesia* 90(4): 894-898. ISSN: 0003-2999.

Descriptors: methods and techniques, headache, cerebrospinal fluid (CSF) leakage, percutaneous lumbar postdural puncture hole sealing, alternative to an epidural blood patch.

Gerbershagen, M.U., F. Wappler, M. Fiege, R. Weisshorn, P.a. Alberts, F. Von Breunig, and J.S. Am Esch (2002). **In vitro effects of 4-chloro-3-ethylphenol in skeletal muscle preparations from malignant hyperthermia susceptible and normal swine**. *European Journal of Anaesthesiology* 19(2): 135-140. ISSN: 0265-0215.
Descriptors: pharmacology, 4-chloro-3-ethylphenol, diagnosis, malignant hyperthermia, (Malignant Hyperthermia (MeSH)), genetic disease, muscle disease, muscle biopsy, examination method.

Gerritzen, M., M. Kluivers Poodt, H. Reimert, V. Hindle, and E. Lambooij (2008). **Castration of piglets under CO2-gas anaesthesia.** *Animal an International Journal of Animal Bioscience* 2(11): 1666-1673. ISSN: 1751-7311.
DOI: 10.1017/S1751731108002887
NAL Call Number: SF1 .A45
Abstract: It has become common practice in pig fattening production systems to castrate young boar piglets without the use of anaesthesia. In this study, we examined whether or not CO2 gas is capable of inducing an acceptable anaesthetic state during which castration can be performed. The first step was to identify the most promising CO2/O2 mixture. Based on the results from this first experiment, a mixture of 70% CO2 + 30% O2 was chosen for further investigation as a potential anaesthetic during the castration of young piglets. Thereby, it was established whether the duration and depth of anaesthesia were acceptable for castration where the animal has to be insensible and unconscious. Physiological effects were assessed based on electroencephalogram (EEG) and electrocardiogram (ECG) measurements, blood gas values and behavioural responses. During the induction phase, the only typical behaviour the piglets exhibited when exposed to the 70/30 gas mixture was heavy breathing. All piglets (n = 25) lost consciousness after approximately 30 s according to the EEG. Heart rate decreased slowly during the induction phase, a serious drop occurred when piglets lost their posture. Immediately after this drop, the heart rate neared zero or showed a very irregular pattern. Shortly after loss of posture, most animals showed a few convulsions. None of the animals showed any reaction to castration in behaviour and/or on the EEG and ECG. On average, the piglets recovered within 59 s, i.e. EEG returned to its pre-induction pattern and piglets were able to regain a standing position. After 120 s, heart rate returned to pre-induction levels. In order to explore the usage range of CO2 concentration, 24 piglets were exposed to 60% CO2 + 20% O2 + 20% N2 for up to 30 s after loss of consciousness (as registered on EEG), and castrated after removal from the chamber. Sixteen of the 24 animals showed a reaction to the castration on the EEG. To establish the maximum time piglets survive in 70% CO2 + 30% O2, five piglets were placed in this mixture for 3 min. Two of them died. After that, four piglets were placed in this mixture for 2 min after unconsciousness, one died after 2 min. It was concluded from this study that it is possible to anaesthetise piglets with a mixture of 70% CO2 + 30% O2, but that there are limits to its safety in terms of CO2 concentration and duration of exposure. Before implementation for practical use, further research is essential to assess the limits of gas concentration and exposure times.
Descriptors: piglets, males, castration, methodology, anesthesia, general anesthetics, carbon dioxide, drug formulations, oxygen, intranasal administration, depth of anesthesia, unconsciousness, adverse effects, biomarkers, heart rate, breathing, arrhythmia, seizures, death, animal welfare.

Giorgi, M., S. Bertini, G. Soldani, and M. Giusiani (2001). **Comparison of HPLC and GC-MS methods for determination of embutramide (a component of Tanax or T-61) in biological specimens.** *Journal of Analytical Toxicology* 25(5): 323-7. ISSN: 0146-4760.
NAL Call Number: RA1221.J6
Abstract: Tanax or T-61, a euthanasia solution commonly used in veterinary medicine, has been often involved in suicide attempts (humans) and malicious intoxications (animals). For forensic reasons, the identification of one or more of the three components (embutramide, mebenzonium iodide, and tetracaine hydrochloride) of Tanax is needed to confirm the hypothesis of intoxication. This study was performed with new high-performance liquid chromatographic and gas chromatographic-mass spectrometric methods to identify embutramide in biological matrices (blood, liver, kidney) from different animal species. The good sensitivity and specificity of both methods recommend their use in toxicological analysis in both human and veterinary medicine.
Descriptors: amides blood, anesthetics blood, chromatography, high pressure liquid methods, gas chromatography mass spectrometry methods, substance abuse detection methods, amides administration and dosage, cats, drug administration routes, drug combinations, euthanasia, active veterinary, horses, kidney chemistry, liver chemistry, quaternary ammonium compounds administration and dosage, rabbits, rats, reproducibility of results, sensitivity and specificity, sheep, species specificity, swine, tetracaine administration and dosage.

Goldmann, K., M. Kalinowski, and S. Kraft (2005). **Airway management under general anaesthesia in pigs using the LMA-ProSeal: a pilot study.** *Veterinary Anaesthesia and Analgesia* 32(5): 308-13. ISSN: 1467-2987.
NAL Call Number: SF914 .V47
Abstract: OBJECTIVE: Evaluation of the LMA-ProSeal for positive pressure ventilation (PPV) in the pig. STUDY DESIGN: Prospective observational study. ANIMALS: Twelve German country pigs, weighing 25-62 kg. METHOD: Lungs of pigs were mechanically ventilated under general anaesthesia using the LMA-ProSeal. The ease of insertion, number of attempts and total time until placement of the LMA-ProSeal and gastric tube were recorded. Bronchoscopy was performed to determine the position of the LMA-ProSeal and to detect signs of aspiration. Ventilation variables and the leak airway pressure (P(leak)) were measured. An arterial blood gas sample was taken to determine the adequacy of ventilation. RESULTS: The airway was secured in all pigs within 39 +/- 19 seconds (27-51). Different sizes of LMA-ProSeal were used; up to 30 kg: size 3, up to 43 kg: size 4; and above 43 kg: size 5. In all but one animal the P-LMA and gastric tube were inserted at the first attempt. In nine animals gastric fluid was drained through the gastric tube. There was no evidence of aspiration in any animal. The mean [+/-SD (95%CI)]P(leak) was 28.8 +/- 7.5 cm H(2)O (24.06-33.60) and normal ventilation was achieved in all animals. CONCLUSIONS: The results of this study indicate that the airway of pigs weighing 25-62 kg can be secured safely and reliably with the sizes 3, 4 and 5 LMA-ProSeal. CLINICAL RELEVANCE: Endotracheal intubation in pigs can be difficult so there is a risk of hypoxemia in the apnoeic animal. With the LMA-ProSeal the airway can be secured rapidly, safely and reliably. Use of the Standard-LMA under PPV can be associated with gas leakage into the stomach and the subsequent risk of gastric distension and regurgitation. Both the ability to drain the stomach and the high P(leak) of the LMA-ProSeal could contribute to improved protection against aspiration under PPV.

Descriptors: anesthesia, general veterinary, animals, laboratory physiology, laryngeal masks veterinary, respiration, artificial veterinary, swine physiology, equipment design, pilot projects, prospective studies , respiration, artificial instrumentation.

Gonzalez, A. (2004). **Anaesthesia in pigs for procedures in farming [Anestesia del cerdo para procedimientos en la granja.]**. *SUIS*(3): 32-34.
Descriptors: anesthesia, pig farming, pigs, equipment, methods.
Language of Text: Spanish.

Gonzalez, A. and I. Cruz (2005). **Anaesthesia of pigs in hospital conditions [Anestesia del cerdo en condiciones de hospital.]**. *SUIS*(16): 34-37.
Descriptors: anesthesia, surgical operations, techniques, induction, maintenance, postoperative anesthesia.
Language of Text: Spanish.

Gopalakrishnan, N.A., D.J. Sakata, J.A. Orr, S. McJames, and D.R. Westenskow (2007). **Hypercapnia shortens emergence time from inhaled anesthesia in pigs.** *Anesthesia and Analgesia* 104(4): 815-21.
Abstract: BACKGROUND: Anesthetic clearance from the lungs and the circle rebreathing system can be maximized using hyperventilation and high fresh gas flows. However, the concomitant clearance of CO2 decreases PAco2, thereby decreasing cerebral blood flow and slowing the clearance of anesthetic from the brain. This study shows that in addition to hyperventilation, hypercapnia (CO2 infusion or rebreathing) is a significant factor in decreasing emergence time from inhaled anesthesia. METHODS: We anesthetized seven pigs with 2 MACPIG of isoflurane and four with 2 MACPIG of sevoflurane. After 2 h, anesthesia was discontinued, and the animals were hyperventilated. The time to movement of multiple limbs was measured under hypocapnic (end-tidal CO2 = 22 mm Hg) and hypercapnic (end-tidal CO2 = 55 mm Hg) conditions. RESULTS: The time between turning off the vaporizer and to movement of multiple limbs was faster with hypercapnia during hyperventilation. Emergence time from isoflurane and sevoflurane anesthesia was shortened by an average of 65% with rebreathing or with the use of a CO2 controller ($P < 0.05$). CONCLUSIONS: Hypercapnia, along with hyperventilation, may be used clinically to decrease emergence time from inhaled anesthesia. These time savings might reduce drug costs. In addition, higher PAco2 during emergence may enhance respiratory drive and airway protection after tracheal extubation.
Descriptors: anesthesia recovery period, anesthesia, inhalation instrumentation, hypercapnia physiopathology, anesthetics, inhalation, carbon dioxide metabolism, equipment design, hypercapnia metabolism, hyperventilation metabolism, hyperventilation physiopathology, isoflurane, methyl ethers, swine, time factors.

Graham, J.S., F.M. Reid, N.A. Niemuth, S.M. Shumaker, and J.D. Waugh (2004). **Effects of three anesthetic regimens on bioengineering methods conducted on ventral abdominal skin of weanling swine**. *Journal of Toxicology Cutaneous and Ocular Toxicology* 23(2): 105-118. ISSN: 0731-3829 .
NAL Call Number: RL803.J67
Descriptors: swine model, anesthesiology, methods and techniques, pharmacology, toxicology, blister, integumentary system disease, therapy, anesthesia treatment, clinical techniques, therapeutic and prophylactic techniques, laser doppler perfusion imaging, clinical techniques,

diagnostic techniques, imaging and microscopy techniques, laboratory techniques, reflectance colorimetry, laboratory techniques.

Greene, S., G. Benson, W. Tranquilli, and K. Grimm (2004). **Effect of isoflurane, atracurium, fentanyl, and noxious stimulation on bispectral index in pigs.** *Comparative Medicine* 54(4): 397-403. ISSN: 1532-0820.
NAL Call Number: SF77 .C65
Abstract: The study reported here was done to determine the relationship between anesthesia depth and bispectral index (BIS) in stimulated pigs. Isoflurane minimal alveolar concentration (MAC) was determined using the tail-clamp method in 16 Yorkshire/Landrace-cross pigs with mean +/- SEM weight of 27.7 +/- 1.76 kg. One week later, BIS, ECG, heart rate, arterial blood pressure, esophageal temperature, end-tidal CO2 tension and isoflurane concentration, arterial pH, PaO2, PaCO2, plasma bicarbonate concentration, and base excess were determined at each of five isoflurane MAC-multiples: 0.8, 1.0, 1.3, 1.6, and 2.0. Six treatments were studied: isoflurane; isoflurane and atracurium; isoflurane, atracurium, and fentanyl; isoflurane with noxious stimulation; isoflurane and atracurium with noxious stimulation; and isoflurane, atracurium, and fentanyl with noxious stimulation. The noxious stimulus during BIS measurement was the same as that for MAC determination. Each pig was studied three times (n = 8), and order of MAC-multiples and treatments was randomized. Data were evaluated by use of general linear model analysis of variance and linear regression analysis, with statistical significance set at $P < 0.05$. Significant differences in BIS values were identified between MAC-multiples within each treatment and between treatment 3 compared with treatments 2 and 4. Significant differences also were observed within and between treatments for heart rate, arterial blood pressure, and PaO2. Use of BIS appears reliable for identification of light versus deep anesthesia, but is of limited use for discrimination between isoflurane MAC-multiples of 1 and 1.6. We conclude that, compared with other treatments, atracurium and noxious stimulation had no significant effect on BIS.
Descriptors: swine, depth of anesthesia, anesthetics, isoflurane, atracurium, fentanyl, laboratory equipment.

Grossherr, M., A. Hengstenberg, T. Meier, L. Dibbelt, K. Gerlach, and H. Gehring (2006). **Discontinuous monitoring of propofol concentrations in expired alveolar gas and in arterial and venous plasma during artificial ventilation.** *Anesthesiology* 104(4): 786-90. ISSN: 0003-3022.
Abstract: BACKGROUND: Analyzing propofol concentration in expired alveolar gas (cPA) may be considered as a convenient, noninvasive method to follow the propofol concentration in plasma (cPPL). In the current study, the authors established procedures to measure cPA and cPPL for the assessment of their relation in two animal models during anesthesia. METHODS: Expired alveolar gas and mixed venous and arterial blood were simultaneously sampled during continuous application of propofol for general anesthesia to three goats and three pigs. Propofol infusion rates were varied to modify plasma concentrations. cPA, sampled cumulatively over several respiratory cycles, was quantified by thermal desorption gas chromatography-mass spectrometry. cPPL was determined using reversed phase high-performance liquid chromatography with fluorescence detection. RESULTS: cPA ranged from 0 to 1.4 and from 0 to 22 parts per billion in goats and pigs, respectively, at cPPL of 0-8 microg/ml. The relation between cPA and cPPL was linear; however, the slopes of the regression lines varied between animals. CONCLUSION: Propofol can be quantified in expired

alveolar gas. The results stress the role of marked species-specific variability.
Descriptors: propofol pharmacokinetics, pulmonary alveoli metabolism, respiration, artificial, breath tests, goats, lung metabolism, species specificity, swine.

Grossini, E., C. Molinari, A. Battaglia, D.A. Mary, F. Ribichini, N. Surico, and G. Vacca (2006). **Human placental lactogen decreases regional blood flow in anesthetized pigs.** *Journal of Vascular Research* 43(2): 205-13. ISSN: 1018-1172.
Abstract: In 22 pigs anesthetized with sodium pentobarbitone, changes in blood flow caused by infusion of human placental lactogen into the left renal, external iliac, and anterior descending coronary arteries were assessed using electromagnetic flowmeters. In 17 pigs, infusion of human placental lactogen whilst keeping the heart rate and arterial pressure constant decreased coronary, renal and iliac flow. In 5 additional pigs, increasing the dose of human placental lactogen produced a dose-related decrease in regional blood flow. The mechanisms of the above response were studied in 15 of the 17 pigs by repeating the experiment of infusion. The human placental lactogen-induced decrease in regional blood flow was not affected by blockade of cholinergic receptors (5 pigs) or of alpha-adrenergic receptors (5 pigs), but it was abolished by blockade of beta2-adrenergic receptors (5 pigs). The present study showed that intra-arterial infusion of human placental lactogen primarily decreased coronary, renal and iliac blood flow. The mechanism of this response was shown to be due to the inhibition of a vasodilatory beta2-adrenergic receptor-mediated effect.
Descriptors: anesthesia veterinary, placental lactogen pharmacology, regional blood flow drug effects, adrenergic alpha antagonists pharmacology, adrenergic beta antagonists pharmacology, atropine pharmacology, butoxamine pharmacology, cholinergic antagonists pharmacology, coronary circulation drug effects, hemodynamic processes drug effects, iliac artery drug effects, kidney blood supply, pentobarbital, phentolamine pharmacology, swine.

Grund, F., O. Tjomsland, I. Sjaastad, A. Ilebekk, and K.A. Kirkeboen (2004). **Pentobarbital versus medetomidine-ketamine-fentanyl anaesthesia: effects on haemodynamics and the incidence of ischaemia-induced ventricular fibrillation in swine.** *Laboratory Animals* 38(1): 70-8. ISSN: 0023-6772.
NAL Call Number: QL55.A1L3
Abstract: The present study was performed to compare haemodynamic variables at baseline and the incidence of ventricular fibrillation during the early phase of ischaemia in swine during pentobarbital or medetomidine-ketamine-fentanyl anaesthesia. Twenty-two swine (mean +/- SD: 29+/- 3 kg) were anaesthetized with sodium pentobarbital (induction with 36 mg/kg intraperitoneally, and maintenance with 5-20 mg/kg/h intravenously [i.v.]) and 6 swine (27+/- 3 kg) were anaesthetized with ketamine and fentanyl (premedicated with medetomidine 0.1 mg/kg and ketamine 10 mg/kg intramuscularly, induction with ketamine 20 mg/kg and fentanyl 0.025 mg/kg i.v., and maintenance with ketamine 20 mg/kg/h and fentanyl 0.025 mg/kg/h i.v.). After a stabilization period of 30 min, the left anterior descending coronary artery (LAD) was occluded for 10 min. Haemodynamic data and occurrence of ventricular fibrillation were recorded. The ischaemic area was measured by fluorescing microspheres. Swine anaesthetized with medetomidine-ketamine-fentanyl had significantly lower heart rate, myocardial contractility, peak left ventricular pressure, arterial blood pressure, aortic blood flow, myocardial blood flow and cardiac index at baseline, than swine anaesthetized with pentobarbital. Whereas none of the swine anaesthetized with pentobarbital fibrillated during the LAD occlusion, ventricular fibrillation occurred in 83% of the animals

anaesthetized with medetomidine-ketamine-fentanyl (P< 0.001). No significant difference was found in size of ischaemic area between the two groups. Thus, we show a depression in haemodynamic variables at baseline and a higher incidence of ventricular fibrillation during the early phase of ischaemia in swine anaesthetized with medetomidine-ketamine-fentanyl compared to swine anaesthetized with pentobarbital.
Descriptors: anesthesia adverse effects, anesthesia veterinary, anesthetics adverse effects, hemodynamic phenomena drug effects, swine diseases chemically induced, ventricular fibrillation veterinary, constriction, coronary vessels, fentanyl adverse effects, ischemia complications, ketamine adverse effects, medetomidine adverse effects, pentobarbital adverse effects, swine, ventricular fibrillation chemically induced.

Gucbrin, C., F. Bayle, S. Debord, J.C. Poupelin, M. Badet, S. Lemasson, and J.C. Richard (2007). **Viscoelastic properties of lungs and thoracic wall of anesthetized mechanically ventilated piglets.** *Veterinary Anaesthesia and Analgesia* 34(5): 331-338. ISSN: 1467-2987.
DOI: 10.1111/j.1467-2995.2006.00336.x
NAL Call Number: SF914 .V47
Abstract: To investigate the viscoelastic properties of lungs and thoracic wall in piglets. Prospective experimental study. Six piglets weighting 30 kg. Animals were tracheotomized, anesthetized and mechanically ventilated under controlled conditions. After control measurements of the mechanical properties of the lung of the pigs had been taken, acute lung injury (ALI) was induced by saline lavage. Lung and thoracic wall tissue resistance (R), which reflects viscoelastic properties and/or time constant inequalities, were determined by using a rapid airway occlusion technique during constant flow inflation ([graphic removed]), at constant tidal volume. [graphic removed] was varied from 0.1-0.2 to 1.2 L secondp# on a single breath. Multiple data sets of R of lung (RL) and thoracic wall (Rw) to inspiratory time (TI = VT/ [graphic removed]) were fitted to a model whose prediction equation was R = R[1 -exp(-TI/s)], where R and s are the 'viscoelastic' resistance and time constant, respectively. Subscripts L and W are used to represent lung and theracic wall, respectively (RL, RW, sL, sW). Two more sets of physiological measurements were then taken - the first under zero end-expiratory pressure (ZEEP) and the second under a positive end-expiratory pressure (PEEP) of 10 cmHO. Data of R adequately fitted to the prediction equation in all instances. In control, R,L was 15.3 (10.7-22.6) cmHO Lp# secondp# (median, interquartile range), s,L 3.3 (1.9-5.5) seconds, R,w 6.5 (2.2-10.3) cmHO Lp# secondp# and s,w 2.9 (1.1-4.3) seconds. In ALI, R,L significantly increased to 129.6 (105.9-171.3) cmHO Lp# secondp# on ZEEP but not significantly decreased to 48.9 (17.8-109.6) cmHO Lp# secondp# with PEEP. The corresponding values of s,L were 7.1 (5.1-11.6) and 4.4 (3.1-5.5) seconds. The values pertaining to thoracic wall did not change significantly among conditions. Viscoelastic properties of the lung and thoracic wall in piglets can be described by a viscoelastic model. Values of parameters of this model were markedly increased in ALI and decreased with PEEP. AGRICOLA
Descriptors: piglets, acute lung injury, mechanical ventilation, modeling respiratory system, viscoelastic behavior.

Gutzwiller, A. (2003). **Castration of piglets under local anaesthesia [Castration de porcelets sous anesthesie locale.]**. *Revue Suisse D' Agriculture* 35(2): 65-67. ISSN: 0375-1325.
Descriptors: animal welfare, castration, lidocaine, local anesthesia, local anesthetics, pain,

piglets, potency, restraint of animals, surgery.
Language of Text: French, Summary in German; English.

Gutzwiller, A. (2003). **Castration of piglets under local anaesthesia [Kastration von Ferkeln unter Lokalanasthesie.]**. *Agrarforschung* 10(1): 10-13. ISSN: 1022-663X.
NAL Call Number: S469.S9A37
Descriptors: adverse effects, animal welfare, castration, local anesthesia, local anesthetics, pain, piglets, testes, vocalization, pigs.
Language of Text: German, Summary in English; French.

Haga, H.A. and B. Ranheim (2005). **Castration of piglets: the analgesic effects of intratesticular and intrafunicular lidocaine injection.** *Veterinary Anaesthesia and Analgesia* 32(1): 1-9. ISSN: 1467-2987.
NAL Call Number: SF914 .V47
Abstract: OBJECTIVE: The aim of this study was to evaluate the analgesic effect of intratesticular and intrafunicular lidocaine for the surgical castration of piglets and to investigate the degree of nociception induced by lidocaine injection. STUDY DESIGN: Prospective controlled experimental study. ANIMALS: Forty-seven male Norwegian landrace piglets with normal testicular anatomy, aged 22 (+/-2.6 SD) days and weighing 7.4 +/- 1.4 kg. MATERIALS AND METHODS: Anaesthesia was induced and maintained using halothane delivered in oxygen. End-tidal halothane was stabilized at 1.3% for 20 minutes before mean arterial blood pressure (MAP) pulse rate and electroencephalography (EEG) monitoring began. After 5 minutes of data collection, scrotal skin was desensitized with lidocaine before either an intrafunicular (IF) (n = 15) or an intratesticular (IT) (n = 16) lidocaine injection was made. Pigs in the control group (n = 16) did not receive lidocaine. Ten minutes later, a scalpel and an emasculator were used to cut the funiculus spermaticus. The MAP, pulse rate and EEG were monitored continuously for 5 minutes after castration. RESULTS: During castration, MAP increased significantly, while pulse rate and EEG theta power fell significantly more in control, compared with the IT or IF groups. EEG alpha power fell more in the control group than in the IF group. No significant differences were found between the IF and IT groups. EEG, MAP and pulse rate responses to castration in the control group were significantly larger than the response to lidocaine injection. CONCLUSION/CLINICAL RELEVANCE: Injecting lidocaine into the funiculus spermaticus or into the testes is effective in reducing signs of nociception caused by castration. Lidocaine injection is less noxious than castration without local anaesthetic.
Descriptors: anesthetics, local administration and dosage, castration veterinary, lidocaine administration and dosage, swine physiology, anesthesia, general veterinary, animals, newborn, castration methods, electroencephalography veterinary, heart rate, injections, pain measurement veterinary, prospective studies, swine surgery, testis, treatment outcome.

Haga, H.A., B. Ranheim, and T. Framstad (2002). **Sedation, anaesthesia and analgesia of pigs [Sedasjon, anestesi og smertebehandling av gris.]**. *Norsk Veterinaertidsskrift* 114(2): 254-259. ISSN: 0332-5741.
Descriptors: anesthesia, analgesics, caesarean section, castration, drug residues, hysterectomy, neuroleptics, ovariectomy, regulations, postoperative pain control.
Language of Text: Norwegian.

Haga, H.A., A. Tevik, and H. Moerch (2001). **Electroencephalographic and cardiovascular indicators of nociception during isoflurane anaesthesia in pigs**. *Veterinary Anaesthesia and Analgesia* 28(3): 126-131. ISSN: 1467-2987.
NAL Call Number: SF914 .V47
Descriptors: anesthesia, anesthetics, isoflurane, blood pressure, electroencephalograms, isoflurane, pulse rate, nociception .

Haga, H.A., A. Tevik, and H. Moerch (2002). **Motor responses to stimulation during isoflurane anaesthesia in pigs**. *Veterinary Anaesthesia and Analgesia* 29(2): 69-75. ISSN: 1467-2987.
NAL Call Number: SF914 .V47
Descriptors: anesthesia, anesthetics, isoflurane, pharmacodynamics, reflexes, stimulation, stimuli, breed, Norwegian Landrace, male, female.

Halloy, D., C. Cambier, N. Kirschvink, and P. Gustin (2004). **Evaluation experimentale de la fonction pulmonaire chez le porc experimental assessment of pulmonary function in pigs**. *Annales De Medecine Veterinaire* 148(2): 91-96. ISSN: 0003-4118.
NAL Call Number: 41.8 An78
Descriptors: respiratory system, respiration, systematic anesthesia, esophageal balloon, laboratory techniques, impulse oscillometry, laboratory techniques, pulmonary function, experimental assessment, blood partial pressure.
Language of Text: French.

Haney, M.F., G. Johansson, S. Haggmark, and B. Biber (2002). **Method of preload reduction during LVPVR analysis of systolic function: airway pressure elevation and vena cava occlusion.** *Anesthesiology* 97(2): 436-46. ISSN: 0003-3022.
Abstract: BACKGROUND: A graded preload reduction during analysis of the left ventricular pressure-volume relationship (LVPVR) is required for derivation of end-systolic elastance (Ees) and preload recruitable stroke work (PRSW). The authors aimed to measure serial changes in these systolic function parameters before and during planned circulatory interventions using two different methods of preload alteration: a positive airway pressure plateau (APP) and inferior vena cava occlusion (IVCO). METHODS: In eight animals, measurements were made at 38 degrees, 30 degrees, 32 degrees, 34 degrees, and posthypothermia 38 degrees C. In an additional eight animals, isoflurane, adrenaline, and aorta occlusion (balloon catheter occluder) were administered in series, each with a preintervention control measurement. Left ventricular volume was measured by conductance. Paired measurements of the systolic function parameters Ees and PRSW, each derived with two preload methods, were analyzed for bias. RESULTS: Circulatory alterations were achieved with the temperature, isoflurane, adrenaline, and aorta occlusion interventions. Measured changes in Ees and PRSW from control to intervention showed a strong correlation and no significant bias for APP in relation to IVCO. The APP-derived absolute values for Ees and PRSW demonstrated a consistent positive bias compared with IVCO. CONCLUSION: The APP method for preload reduction during LVPVR analysis detected changes in Ees and PRSW during the circulatory interventions in this model that were not different than those detected using another preload reduction method, IVCO. APP and IVCO are not interchangeable methods for preload reductions during LVPVR absolute quantitation of systolic function, and each needs to be used serially.
Descriptors: anesthetics, inhalation pharmacology, isoflurane pharmacology, stroke volume

drug effects, systole drug effects, analysis of variance, hemodynamic processes drug effects, swine.

Harikrishnan, V.S., S.J. Shenoy, and P.R. Umashankar (2006). **Anaesthetic regimen for coronary stenting in porcine model** . *Indian Veterinary Journal* 83(5): 486-489. ISSN: 0019-6479.
NAL Call Number: SF604.I45
Descriptors: pharmacology, cardiovascular system: transport and circulation, methods and techniques, coronary stenting, laboratory techniques, experimental surgical techniques, blood pressure, heart rate, temperature range, anesthetic regimen.

Harikrishnan, V.S. and P.R. Umashankar (2006). **Long duration anaesthesia for experimental surgical procedures in pigs**. *Indian Veterinary Journal* 83(11): 1173-1175. ISSN: 0019-6479.
NAL Call Number: SF604.I45
Descriptors: anesthesia, drug effects, inhaled anesthetics, injectable anesthetics, pharmacodynamics, preanesthetic medication, surgery, pigs.

Hart, L.A., M.W. Wood, and H.Y. Weng (2005). **Effective searching of the scientific literature for alternatives: search grids for appropriate databases**. *Animal Welfare* 14(4): 287-289. ISSN: 0962-7286.
NAL Call Number: HV4701.A557
Descriptors: information studies, veterinary medicine: medical sciences, animal care, animal welfare, scientific literature, biomedical research, compliance, animal testing, database resource, alternatives, laboratory animal information, analgesia, anesthesia, animal models.

Harvey Clark, C.J., K. Gilespie, and K.W. Riggs (2000). **Transdermal fentanyl compared with parenteral buprenorphine in post-surgical pain in swine: a case study**. *Laboratory Animals (London)* 34(4): 386-398. ISSN: 0023-6772.
NAL Call Number: QL55.A1L3
Descriptors: animal care, behavior, nervous system: neural coordination, pharmacology, buprenorphine hydrochloride, fentanyl hydrochloride, transdermal, cost effective method, analgesiometry, pain assessment, detection method , analgesia, animal welfare, post surgical pain, thoracotomy .

Hayashi, M., S.G. Penheiter, T. Nakayama, A.R. Penheiter, D.O. Warner, and K.A. Jones (2006). **Halothane does not inhibit the functional coupling between the beta2-adrenergic receptor and the Galphas heterotrimeric G protein.** *Anesthesiology* 104(4): 754-62. ISSN: 0003-3022.
Abstract: BACKGROUND: This study investigated whether halothane affects the functional coupling between the beta2 adrenergic receptor and the alpha subunit of its cognate stimulatory heterotrimeric guanosine-5'-triphosphate (GTP)-binding protein (Galphas). The authors hypothesized that halothane does not affect isoproterenol-promoted guanosine nucleotide exchange at Galphas and hence would not affect isoproterenol-induced relaxation of airway smooth muscle. METHODS: Halothane effects on isoproterenol-induced inhibition of calcium sensitivity were measured in permeabilized porcine airway smooth muscle. Galphas nucleotide exchange was measured in crude membranes prepared from COS-7 cells transfected to transiently coexpress the human beta1 or beta2 receptor each with human short Galphas. A radioactive, nonhydrolyzable analog of GTP, [S]GTPgammaS, was used as the reporter for nucleotide exchange at Galphas. RESULTS: Halothane

(0.75 mm, approximately 2.8 minimum alveolar concentration [MAC] in pigs) did not affect isoproterenol-induced inhibition of calcium sensitivity. Isoproterenol caused a time- and concentration-dependent increase in Galphas nucleotide exchange. Halothane, even at concentrations of 1.5 mm (approximately 5.6 MAC), had no effect on basal Galphas nucleotide exchange in the absence of isoproterenol, whereas halothane inhibited isoproterenol-promoted Galphas nucleotide exchange in both the beta1-Galphas and beta2-Galphas expressing membranes. However, the effect was significantly greater on beta1-Galphas coupling compared with beta2-Galphas coupling, with no effect on beta2-Galphas coupling at 2.8 MAC halothane. CONCLUSION: Halothane does not inhibit the biochemical coupling between the beta2 receptor and Galphas and hence does not affect the inhibition of calcium sensitivity induced by isoproterenol. Therefore, halothane should not affect the efficacy of beta2 agonists, as suggested by studies of in vivo animal models of asthma.
Descriptors: anesthetics, inhalation pharmacology, gtp binding protein alpha subunits, gs drug effects, halothane pharmacology, receptors, adrenergic, beta 2 drug effects, cos cells, calcium metabolism, cercopithecus aethiops, dose response relationship, drug, gtp binding protein alpha subunits, gs physiology, guanosine 5' o 3 thiotriphosphate metabolism, guanosine diphosphate metabolism, isoproterenol pharmacology, receptors, adrenergic, beta 2 physiology, swine.

He, F., H.L. Jia, G. Liu, Y.P. Wang, J. Feng, and R.X. Zhuo (2006). **Enzymatic synthesis and characterization of novel biodegradable copolymers of 5-benzyloxy-trimethylene carbonate with 1,4-dioxan-2-one.** *Biomacromolecules* 7(8): 2269-73. ISSN: 1525-7797.
NAL Call Number: QD380
Abstract: Enzymatic ring-opening copolymerization of 5-benzyloxy-trimethylene carbonate (BTMC) and 1,4-dioxan-2-one (DON) was investigated for the first time. Immobilized porcine pancreas lipase (IPPL) on silica particles was selected to perform the copolymerization. A series of novel biodegradable copolymers with different compositions were characterized by (1)H NMR, (13)C NMR, and GPC. The influences of reaction conditions such as polymerization time and catalyst concentration on the yield and molecular weight of the copolymers were also studied. The copolymerizations of different monomer feed ratios were carried out in bulk at 150 degrees C with 4.5 wt per thousand IPPL as a catalyst for 24 h. With the increase of the BTMC molar feed ratio from 20% to 79%, the M(n) of the resulting copolymers increased from 5600 to 63400. Water uptake and static contact angle experiments showed that the hydrophilicity of copolymers could be improved with increasing DON content in the copolymers. Moreover, the in vitro drug release rate (ibuprofen as the model drug) of the resulting copolymers also increased along with the DON content in the copolymers.
Descriptors: analgesics, non narcotic chemistry, dioxanes chemistry, ibuprofen chemistry, lipase chemistry, polymers chemical synthesis, biocompatible materials, biodegradation, environmental, delayed action preparations chemical synthesis, delayed action preparations chemistry, magnetic resonance spectroscopy, polymers chemistry, swine.

Heavner, J.E. (2001). **Local anesthetic toxicity and milrinone.** *Canadian Journal of Anaesthesia; Journal Canadien D'Anesthesie* 48(5): 512-3. ISSN: 0832-610X.
NAL Call Number: RD78.68.C4
Descriptors: anesthetics, local antagonists and inhibitors, anesthetics, local toxicity, milri-

none pharmacology, swine.
Notes: Comment On: Can J Anaesth. 2000 Nov;47(11):1114-8.

Heavner, J.E. (2002). **Cardiac toxicity of local anesthetics in the intact isolated heart model: a review.** *Regional Anesthesia and Pain Medicine* 27(6): 545-55. ISSN: 1098-7339 .
Abstract: An editorial in 1979 by George Albright about sudden cardiac arrest after regional anesthesia spawned an era of intense research focusing on what local anesthetics do to the heart and how they do it. The ultimate goal of the research was to bring to the clinician long-acting local anesthetics that are less cardiotoxic than ones available before 1979, bupivacaine and etidocaine, in particular. In this article, I will review results of studies of local anesthetic cardiotoxicity using the intact mammalian heart in vitro published after the Albright editorial through 2001.
Descriptors: amides adverse effects, anesthetics, local adverse effects, arrhythmia chemically induced, bupivacaine adverse effects, lidocaine adverse effects, amides pharmacology, anesthetics, local pharmacology, bupivacaine pharmacology, calcium channels drug effects, electrocardiography, heart conduction system drug effects, lidocaine pharmacology, potassium channels drug effects, rabbits, rats, stereoisomerism, swine.

Hecker, K.E., J.H. Baumert, N. Horn, M. Reyle Hahn, N. Heussen, and R. Rossaint (2003). **Minimum anesthetic concentration of sevoflurane with different xenon concentrations in swine.** *Anesthesia and Analgesia* 97(5): 1364-9. ISSN: 0003-2999.
Abstract: In a previous study, we described a partial antagonism of xenon (Xe) in combination with isoflurane. One hypothetical explanation suggested that Xe and isoflurane probably induced anesthesia via different pathways at the neuronal level. This warranted investigating the combination of Xe with other inhaled anesthetics to examine the relationship between Xe and volatile anesthetics in general. We therefore investigated the influence of Xe on the minimum alveolar concentration (MAC) of sevoflurane. The study was performed in 10 swine (weight 30.8 kg +/- 2.6, mean +/- SD) ventilated with xenon 0%, 15%, 30%, 40%, 50%, and 65% in oxygen. At each Xe concentration, various concentrations of sevoflurane were administered in a stepwise design. For each a supramaximal pain stimulus (claw clamp) was applied. The appearance of a withdrawal reaction was recorded. The sevoflurane MAC was defined as the end-tidal concentration required to produce a 50% response rate. At each Xe concentration, the animals' responses to the pain stimulus were categorized and a logistic regression model was fitted to the results to determine sevoflurane MAC. Sevoflurane MAC was decreased by inhalation of Xe in a linear manner from 2.53 with 0% Xe to 1.54 with 65% Xe. In contrast to Xe and isoflurane, the anesthetic effects of Xe and sevoflurane appear to be simply linear. IMPLICATIONS: We investigated the influence of the anesthetic gas, xenon, on the minimum alveolar concentration (MAC) for the volatile anesthetic sevoflurane. The study was performed in 10 swine ventilated with fixed xenon and various concentrations of isoflurane. The sevoflurane MAC is decreased by inhalation of xenon in a linear relationship.
Descriptors: anesthetics, inhalation administration and dosage, methyl ethers administration and dosage, xenon administration and dosage, algorithms, blood gas analysis, drug interactions, hemodynamic processes drug effects, logistic models, potassium blood, pulmonary alveoli metabolism, pulmonary gas exchange drug effects, respiration, artificial, sodium blood, swine.

Hecker, K.E., N. Horn, J.H. Baumert, S.M. Reyle Hahn, N. Heussen, and R. Rossaint (2004). **Minimum alveolar concentration (MAC) of xenon in intubated swine.** *British Journal of Anaesthesia* 92(3): 421-4. ISSN: 0007-0912.

Abstract: BACKGROUND: The minimum alveolar concentration (MAC) is a traditional index of the hypnotic potency of an inhalational anaesthetic. To investigate the anaesthetic as well as the unwanted effects of xenon (Xe) in a swine model, it is useful to know MAC(Xe). METHODS: The study was performed using ten swine (weight 27.8-35.4 kg) anaesthetized with halothane and Xe 0, 15, 30, 40, 50 and 65% in oxygen. With each Xe concentration, various concentrations of halothane were administered in a step-by-step design. For each combination, a supramaximal pain stimulus (claw clamp) was applied and the appearance of a withdrawal reaction was recorded. The MAC(Xe) with halothane was calculated using a logistic regression model. RESULTS: During stable ventilation, haemodynamics and temperature, MAC(Xe) value was determined as 119 vol. % (95% confidence limits 103-135). CONCLUSION: MAC(Xe) in swine was calculated by extrapolation of a logistic regression model. Its theoretical value is 119 vol. %.

Descriptors: anesthetics, inhalation pharmacokinetics, xenon pharmacokinetics, anesthesia, closed circuit, anesthetics, combined pharmacology, dose response relationship, drug, halothane pharmacology, intubation, intratracheal, logistic models, pain threshold drug effects, swine.

Hecker, K.E., M. Reyle Hahn, J.H. Baumert, N. Horn, N. Heussen, and R. Rossaint (2003). **Minimum alveolar anesthetic concentration of isoflurane with different xenon concentrations in Swine.** *Anesthesia and Analgesia* 96(1): 119-24, Table of Contents. ISSN: 0003-2999.

Abstract: For patients requiring a fraction of inspired oxygen more than 0.3, the use of xenon (Xe) as the sole anesthetic is limited because of its large minimum alveolar anesthetic concentration (MAC) of 71%. This warrants investigating the combination of Xe with other inhaled anesthetics. We therefore investigated the influence of Xe on the MAC of isoflurane. The study was performed in 10 swine (weight, 28-35 kg) ventilated with Xe 0%, 15%, 30%, 40%, 50%, and 65% in oxygen. For each Xe concentration, various concentrations of isoflurane were administered in a step-wise design. For each combination, a supramaximal pain stimulus (claw-clamp) was applied, and the appearance of a withdrawal reaction was recorded. The isoflurane MAC was defined as the end-tidal concentration required to produce a 50% response rate. At each Xe concentration, the responses to the pain stimulus were categorized, and a logistic regression model was fitted to the results to determine isoflurane MAC. Isoflurane MAC was decreased by inhalation of Xe in a nonlinear manner from 1.92% (95% confidence interval, 1.70%-2.15%) with 0% Xe to 1.17% (95% confidence interval, 0.75%-1.59%) with 65% Xe. Although this indicates partial antagonism of the two anesthetics, a combination of Xe with isoflurane may prove valuable for patients requiring a fraction of inspired oxygen more than 0.3. IMPLICATIONS: We investigated the influence of the anesthetic gas xenon on the minimum alveolar anesthetic concentration (MAC) for isoflurane (another anesthetic gas). The study was performed in 10 swine ventilated with fixed xenon and various concentrations of isoflurane. The isoflurane MAC is decreased by inhalation of xenon in a nonlinear relationship.

Descriptors: anesthetics, inhalation pharmacology, isoflurane pharmacology, pulmonary alveoli metabolism, xenon pharmacology, anesthetics, inhalation metabolism, blood gas anal-

ysis, drug interactions, hemodynamic processes drug effects, isoflurane metabolism, logistic models, pain measurement drug effects, pulmonary gas exchange drug effects, swine.

Heid, A. and U. Hamm (2009). **[Alternativen zur betaubungslosen Ferkelkastration: Stand der Forschung zur Verbraucherakzeptanz der Alternativen.] Consumer acceptance of alternatives to piglet castration without anaesthesia**. *Fleischwirtschaft* 89(12): 93-98. ISSN: 0015-363X.
NAL Call Number: 280.38 F62
Descriptors: anesthesia, animal welfare, boar taint, castration, consumer attitudes, consumers, piglets, pigs, immunocastration.
Language of Text: German, Summary in English.

Heim, K., J. Morrell, A. Ronan, and A. Tagliaferro (2002). **Effects of ketamine-xylazine and isoflurane on insulin sensitivity in dehydroepiandrosterone sulfate-treated minipigs (*Sus scrofa domestica*).** *Comparative Medicine* 52(3): 233-237. ISSN: 1532-0820.
Online: http://openurl.ingenta.com/content?genre=article&issn=1532-0820&volume=52&issue=3&spage=233&epage=237
NAL Call Number: SF77 .C65
Abstract: Isoflurane and ketamine-xylazine (KX) combinations are widely used veterinary anesthetics, KX being the particularly common agent for immobilizing swine. Results of previous studies indicate that KX and xylazine suppress insulin release. The steroid hormones, dehydroepiandrosterone (DHEA) and its sulfated form, dehydroepiandrosterone-sulfate (DHEAS), have variable effects on insulin sensitivity in animals. We evaluated the effect of DHEAS on plasma glucose and insulin concentrations in female Yucatan swine under KX and isoflurane anesthesia. A 2 x 2 factorial design was used. Twenty-four 17-week-old gilts were randomly assigned to receive vehicle (placebo) or DHEAS as part of an ongoing study. The KX was given intramuscularly to all animals prior to blood sample collection at weeks two and four. At week three, all animals received isoflurane by inhalation. During KX anesthesia, mean insulin concentration in DHEAS-treated and control groups approximated half the postisoflurane values ($P < 0.001$). While under isoflurane, the DHEAS group had significantly higher mean plasma insulin concentration and mean insulin-to-glucose ratio, compared with values for controls ($P < 0.05$). These findings are consistent with changes in insulin values following DHEAS treatment observed previously in nonanesthetized swine. The effect of DHEAS treatment was absent in animals under KX anesthesia. These results suggest that KX significantly decreases plasma insulin concentration and blunts DHEAS-associated insulin resistance in female minipigs.
Descriptors: miniature swine, anesthesia, isoflurane, ketamine, xylazine, blood glucose, insulin, blood plasma, metabolic diseases, androsterone, lipid metabolism, laboratory mammals.

Heinritzi, K., M. Ritzmann, and W. Otten (2006). **Alternativen zur Kastration von Saugferkeln, Bestimmung von Katecholaminen sowie Wundheilung nach Kastration von Saugferkeln zu unterschiedlichen Zeitpunkten. [Alternatives for castration of suckling piglets, determination of catecholamines and wound healing after castration of suckling piglets at different points of time]**. *DTW. Deutsche Tierarztliche Wochenschrift* 113(3): 94-7. ISSN: 0341-6593.
NAL Call Number: RM300.A1D7

Abstract: According to the applicable animal welfare legislation, the surgical castration of pigs is allowed up until the age of 4 weeks, without anaesthesia. According to the european guideline (2001/93/EG) it is only permitted in the first week after birth. The investigation should show, whether the castration of young piglets takes a milder course and to what extent stress reactions occur in different age groups. The healing process of castration wounds in piglets that were castrated at the age of four days progressed more rapidly and with less complications than those piglets that were castrated at 28 days of age. The catecholamine levels in younger piglets rose significantly after the operation, while these levels virtually stayed the same in piglets castrated at 28 days. As alternatives to castration without anaesthesia, several methods are in discussion: (1) Castration under general anaesthesia can only be practiced by a veterinary surgeon. The sole use of Azaperon and Ketamine has insufficient pain sedating effect. Isofluran anaesthesia is apparatively extravagant. (2) CO2-Anaesthesia in piglets leads to high strain. (3) Castration under local anaesthesia must be practiced by a veterinary surgeon. The application and the pain after the castration are not taken into consideration. (4) Jung boar fattening up until the slaughtering weight of 80 kg is not transformable, because of boar taste. (5) The breeding of slaughter pigs with little boar taint is not yet transformable. (6) Sperm sexing is not and will not, in the near future, be mature for practice. (7) Immunocastration is an active immunisation against GnRH. The immunological elimination of GnRH suppresses the development of sex hormones, such as testosterone, as well as the substance responsible for boar taint, Androstenone. To consider is the acceptance of the consumer. The preparation has the same effect in humans as it has in swine. "Self injections" have the same effect in humans as it has in swine. "Self injections" are therefore risky.
Descriptors: anesthesia veterinary, animal welfare, catecholamines blood, orchiectomy veterinary, swine surgery, wound healing physiology, age factors, animals, newborn, animals, suckling surgery, orchiectomy methods, pain prevention and control, pain veterinary, pain measurement veterinary, swine blood, swine physiology.
Language of Text: German.

Hellebrekers, L.J. and A. van Nes (2004). **Castratie van biggen onder verdoving? [Castration of swine with anesthetics?]**. *Tijdschrift Voor Diergeneeskunde* 129(14-15): 491. ISSN: 0040-7453.
NAL Call Number: 41.8 T431
Descriptors: anesthetics, local administration and dosage, castration veterinary, pain veterinary, swine surgery, animal welfare, castration methods, odors prevention and control, pain prevention and control.
Language of Text: Dutch.

Heltne, J., M. Farstad, T. Lund, M. Koller, K. Matre , S. Rynning, and P. Husby (2002). **Determination of plasma volume in anaesthetized piglets using the carbon monoxide (CO) method.** *Laboratory Animals* 36(3): 344-350. ISSN: 0023-6772.
NAL Call Number: QL55.A1L3
Abstract: Based on measurements of the circulating red blood cell volume (VRBC) in seven anaesthetized piglets using carbon monoxide (CO) as a label, plasma volume (PV) was calculated for each animal. The increase in carboxyhaemoglobin (COHb) concentration following administration of a known amount of CO into a closed circuit re-breathing system was determined by diodearray spectrophotometry. Simultaneously measured haematocrit (HCT) and haemoglobin (Hb) values were used for PV calculation. The PV values were compared

with simultaneously measured PVs determined using the Evans blue technique. Mean values (SD) for PV were 1708.6 (287.3) ml and 1738.7 (412.4) ml with the CO method and the Evans blue technique, respectively. Comparison of PVs determined with the two techniques demonstrated good correlation (r=0.995). The mean difference between PV measurements was -29.9 ml and the limits of agreement (mean difference +/- 2SD) were -289.1 ml and 229.3 ml. In conclusion, the CO method can be applied easily under general anaesthesia and controlled ventilation with a simple administration system. The agreement between the compared methods was satisfactory. Plasma volume determined with the CO method is safe, accurate and has no signs of major side effects.
Descriptors: piglets, anesthesia, blood volume, blood plasma, carbon monoxide, hemoglobin, biomarkers, dyes, adverse effects, hematocrit, dilution, hemoglobin value, spectrophotometry, volume determination, carboxyhemoglobin, Evans blue.

Hewson, C.J., I.R. Dohoo, K.A. Lemke, and H.W. Barkema (2007). **Canadian veterinarians' use of analgesics in cattle, pigs, and horses in 2004 and 2005.** *Canadian Veterinary Journal, The; Revue Veterinaire Canadienne, La* 48(2): 155-64. ISSN: 0008-5286.
NAL Call Number: 41.8 R3224
Abstract: Anecdotal evidence suggests that many veterinarians may not use analgesics in livestock for routine surgical procedures or painful disease states. To investigate this, we conducted a national mail survey of a random sample of 1431 Canadian veterinarians (response rate, 50.1%). Questions primarily concerned veterinarians' analgesic usage for common surgeries and medical conditions in beef and dairy cattle, pigs, and horses, and attitudes toward pain management. More than 90% of veterinarians used analgesic drugs for equine surgeries, for cesarean section in sows and cows, and for bovine claw amputation and omentopexy. However, in these and other categories, the analgesics used were often inadequate, and many veterinarians did not give analgesics to young animals. When castrated, < 0.001% of piglets received analgesia, compared with 6.9% of beef calves and 18.7% of dairy calves < or = 6 mo of age, 19.9% of beef calves and 33.2% of dairy calves > 6 mo of age, and 95.8% of horses. Respondents largely agreed that there are no long-acting, cost-effective analgesics available for use in livestock (median rating 8/10; interquartile range 4-9), and that the long or unknown withdrawal periods of some drugs outweighed the benefits of using them (median rating 7/10; interquartile range 4-9). The results indicate an urgent need for veterinarians to manage pain in livestock better. Continuing education would help, as would an increase in the number of approved, cost-effective analgesic drugs with known withdrawal periods.
Descriptors: analgesics therapeutic use, pain, postoperative veterinary, perioperative care veterinary, veterinarians psychology, veterinary medicine statistics and numerical data, adult, cattle surgery, horses surgery, middle aged, pain, postoperative prevention and control, perioperative care methods, perioperative care statistics and numerical data, questionnaires, swine surgery, veterinary medicine methods.

Hiltebrand, L.B., V. Krejci, and G.H. Sigurdsson (2004). **Effects of dopamine, dobutamine, and dopexamine on microcirculatory blood flow in the gastrointestinal tract during sepsis and anesthesia**. *Anesthesiology Philadelphia* 100(5): 1188-1197. ISSN: 0003-3022.
Descriptors: anesthesia, animal models, blood flow, cardiac output, digestive tract, dopamine, sepsis, septic shock model, pigs.

Hirabayashi, G., T. Mitsui, T. Kakinuma, Y. Ogihara, S. Matsumoto, A. Isshiki, and W. Yasuo (2003). **Novel radiator for carbon dioxide absorbents in low-flow anesthesia.** *Annals of Clinical and Laboratory Science* 33(3): 313-9. ISSN: 0091-7370.
NAL Call Number: RB37.A1A5
Abstract: During long-term low-flow sevoflurane anesthesia, dew formation and the generation of compound A are increased in the anesthesia circuit because of elevated soda lime temperature. The object of this study was to develop a novel radiator for carbon dioxide absorbents used for long durations of low-flow sevoflurane anesthesia. Eleven female swine were divided into two groups comprising a "radiator" group (n = 5) that used a novel radiator for carbon dioxide absorbents and a "control" group (n = 6) that used a conventional canister. Anesthesia was maintained with N2O, O2, and sevoflurane, and low-flow anesthesia was performed with fresh gas flow at 0.6 L/min for 12 hr. In the "control" group, the soda lime temperature reached more than 40 degrees C and soda lime dried up with severe dew formation in the inspiratory valve. In the "radiator" group, the temperature of soda lime stayed at 30 degrees C, and the water content of soda lime was retained with no dew formation in the inspiratory valve. In addition, compound A concentration was reduced. In conclusion, radiation of soda lime reduced the amounts of condensation formed and the concentration of compound A in the anesthetic circuit, and allowed long term low-flow anesthesia without equipment malfunction.
Descriptors: anesthesia, closed circuit instrumentation, anesthesia, inhalation, anesthetics, inhalation, carbon dioxide analysis, water, absorption, body temperature, calcium compounds, chromatography, gas , ethers analysis, ethers metabolism, hydrocarbons, fluorinated analysis, hydrocarbons, fluorinated metabolism, methyl ethers, oxides, sodium hydroxide, swine, temperature.

Hodgkinson, O. (2007). **Practical sedation and anaesthesia in pigs.** *In Practice* 29(1): 34-39. ISSN: 0263-841X.
NAL Call Number: SF601.I4
Descriptors: swine, sedation, sedatives, anesthesia, anesthetics.

Hodgson, D.S. (2007). **Comparison of isoflurane and sevoflurane for short-term anesthesia in piglets.** *Veterinary Anaesthesia and Analgesia* 34(2): 117-24. ISSN: 1467-2987.
NAL Call Number: SF914 .V47
Abstract: OBJECTIVES: To compare isoflurane (ISO) and sevoflurane (SEVO) short-term anesthesia in piglets during castration. STUDY DESIGN: Prospective, randomized study. ANIMALS: A total of 114 male piglets aged 6-10 days, body weight 1.3-5.0 kg. METHODS: Piglets were randomly selected from multiple litters and randomly assigned to being anesthetized with ISO or SEVO prior to castration. To calculate appropriate doses for induction and maintenance of anesthesia, a square root of time model was used, with calculations based on metabolic size and attainment of 1.3x minimum alveolar concentration. The equipotent target alveolar concentration of ISO was 1.82% and for SEVO 4.03%. After doses were calculated, a table listing piglet weights and agent requirements was produced. Anesthetics were delivered via liquid anesthetic injection into a previously developed rebreathing inhaler that was filled with oxygen prior to use. Piglets were anesthetized, castrated and allowed to recover prior to return to the sow. Times for induction, recovery and total time to standing were recorded, and end-tidal carbon dioxide (Pe'CO2) tensions were measured by capnography immediately after mask removal. Each response variable was

analyzed in sas using the Proc Mixed procedure, with piglet weight and days of age as covariates. Castration problems and mortality were assessed relative to unanesthetized littermates. RESULTS: There were no statistically significant differences in age, weight or total anesthetic time between the anesthetics. Induction time was shorter, recovery time longer, and Pe'CO2 lower with ISO. No morbidity or mortality was associated with either group. CONCLUSION AND CLINICAL RELEVANCE: Isoflurane and SEVO, delivered in a novel inhaler, provided economical, safe, rapid anesthetic induction and maintenance. Optimal conditions were provided for castration and recoveries were brief and smooth. Statistically significant differences in times would be of minor clinical importance. The cost of anesthesia was much less with ISO than with SEVO.

Descriptors: anesthesia, inhalation veterinary, anesthetics, inhalation administration and dosage, isoflurane administration and dosage, methyl ethers administration and dosage, nebulizers and vaporizers veterinary, swine physiology, anesthesia, inhalation instrumentation, animals, newborn physiology, animals, newborn surgery, orchiectomy veterinary, postoperative complications, prospective studies, pulmonary alveoli metabolism, swine surgery, treatment outcome.

Hodgson, D.S. (2006). **An inhaler device using liquid injection of isoflurane for short term anesthesia in piglets.** *Veterinary Anaesthesia and Analgesia* 33(4): 207-213. ISSN: 1467-2987.
DOI: 10.1111/j.1467-2995.2005.00258.x
NAL Call Number: SF914 .V47

Abstract: To test a novel inhaler for administering isoflurane (ISO) anesthesia to piglets during castration and other surgical procedures of short duration. Prospective, randomized study. Fifty-seven male piglets aged 6-10 days, body weight 1.1-3.5 kg. An inhaler was developed which consisted of a mask, center body with open-close valve, vaporization chamber with wick and injection port, and a rebreathing bag. Liquid ISO required for induction of anesthesia and surgery was calculated, based on a desired alveolar ISO concentration of 1.82%. Dose was calculated using a square root of time model and metabolic size (B.W.[superscript 0].[superscript 75]). For practical use the calculated dose was expressed in relation to scale weight (kg). Isoflurane was delivered into the liquid injection port, followed by oxygen to fill the rebreathing bag and initiate vaporization. After the mask was fitted over the piglet's nose, the sliding open-close valve was opened to allow respiratory flow to move gases in and out of the inhaler and rebreathing bag. Fifty-seven male piglets received anesthesia prior to castration. Morbidity and mortality were assessed relative to unanesthetized litter mates. Induction, recovery and total anesthetic times were measured. End-tidal CO[subscript 2] was measured immediately after mask removal by capnography. Costs of equipment and anesthetic agent were calculated. Mean induction time was rapid, 47.5 * left-pointing-double-angle *8.7 seconds, generally with minimal or no struggling. Surgery usually lasted less than 30 seconds and was always completed prior to the 120 seconds allotted for induction and surgery. Anesthesia was adequate and recovery time was 122 * left-pointing-double-angle * 44 seconds. Total time from start to standing was 260 * left-pointing-double-angle * 51 seconds. The end-tidal CO[subscript 2] was 5.2 * left-pointing-double-angle * 1.1 kPa (39.4 * left-pointing-double-angle * 8.4 mmHg). No morbidity or mortality was associated with either group. Inhaler construction costs were below $100, and liquid ISO cost ranged between $0.02 and $0.03 per piglet. Isoflurane delivered in a novel inhaler has the potential to provide economical, safe, rapid anesthetic induction and safe, smooth recovery in piglets.
Descriptors: anesthesia, castration, isoflurane, novel inhaler, piglets, surgery.

Holmstrom, A. and J. Akeson (2003). **Cerebral blood flow at 0.5 and 1.0 minimal alveolar concentrations of desflurane or sevoflurane compared with isoflurane in normoventilated pigs.** *Journal of Neurosurgical Anesthesiology* 15(2): 90-7. ISSN: 0898-4921.

Abstract: Whether desflurane and sevoflurane have clinical advantages over isoflurane in neuroanesthesia is much debated. A porcine model was used for comparison of desflurane and sevoflurane with isoflurane with respect to their cerebrovascular effects. The minimal alveolar concentration (MAC) of each of the three agents was first determined in a standardized manner in six domestic juvenile pigs to enhance comparison reliability. Six other pigs were then anesthetized with isoflurane, desflurane, and sevoflurane, given in sequence to each pig in an even crosswise order with the first agent also used to maintain anesthesia during surgical preparation. Cerebral blood flow (CBF) was calculated from the clearance curve of intraarterially injected 133Xe. The mean arterial pressure (MAP) was invasively monitored. The estimated cerebrovascular resistance (CVRe) was calculated by dividing MAP with CBF, thereby approximating the cerebral perfusion pressure with MAP. For both MAC levels, the trend for CBF was desflurane > isoflurane > sevoflurane, and the trend for MAP and CVRe was sevoflurane > isoflurane > desflurane. Statistical comparison of desflurane and sevoflurane with isoflurane with respect to CBF and MAP revealed two statistically significant differences-namely, that CBF at 1.0 MAC desflurane was 17% higher than CBF at 1.0 MAC isoflurane (P =.0025) and that MAP at 1.0 MAC sevoflurane was 16% higher than MAP at 1.0 MAC isoflurane (P =.011). Consequently, in this study at normocapnia, these agents did not seem to differ much in their cerebral vasodilating effects at lower doses. At higher doses, however, desflurane, in contrast to sevoflurane, was found to induce more cerebral vasodilation than isoflurane.

Descriptors: anesthetics, inhalation pharmacology, cerebrovascular circulation drug effects, isoflurane analogs and derivatives, isoflurane pharmacology, methyl ethers pharmacology, pulmonary alveoli metabolism, anesthetics, inhalation administration and dosage, anesthetics, inhalation pharmacokinetics, anesthetics, intravenous pharmacology, blood gas analysis, dose response relationship, drug, hemodynamic processes drug effects, intracranial hypertension physiopathology, isoflurane administration and dosage, isoflurane pharmacokinetics, methyl ethers administration and dosage, methyl ethers pharmacokinetics, propofol pharmacology, swine, vascular resistance drug effects.

Holmstrom, A. and J. Akeson (2004). **Desflurane increases intracranial pressure more and sevoflurane less than isoflurane in pigs subjected to intracranial hypertension.** *Journal of Neurosurgical Anesthesiology* 16(2): 136-43. ISSN: 0898-4921.

Abstract: Desflurane and sevoflurane may have advantages over isoflurane in neuroanesthesia, but this is still under debate. A porcine model with experimental intracranial hypertension was used for paired comparison of desflurane, sevoflurane, and isoflurane with respect to the effects on cerebral blood flow (CBF), cerebrovascular resistance (CVR), and intracranial pressure (ICP). The agents, given in sequence to each of six pigs, were compared at 0.5 and 1.0 minimal alveolar concentrations (MAC) and three mean arterial blood pressure (MAP) levels (50, 70, and 90 mm Hg) at normocapnia and one MAP level (70 mm Hg) at hypocapnia. MAC for each agent had been previously determined in a standardized manner for comparison reliability. CBF was measured with Xe. MAP was lowered by inflation of a balloon catheter in the inferior caval vein and raised by inflation of a balloon catheter in the descending aorta. ICP was measured intraparenchymally. Two Fogarty catheters positioned extradurally were inflated to a baseline ICP of 20 to 22 mm Hg at 0.2 MAC

of each agent. CBF and ICP with the three agents at normocapnia and MAP 70 and 90 mm Hg at both 0.5 and 1.0 MAC were as follows (P < 0.05): desflurane > isoflurane > sevoflurane. None of the agents abolished CO2 reactivity. High-dose desflurane resulted in a higher CBF at hypocapnia than corresponding doses of sevoflurane or isoflurane, but there were no significant differences between the agents in ICP at hypocapnia. The present study showed that desflurane increased ICP more and sevoflurane less than isoflurane during normoventilation, but the differences disappeared with hyperventilation.

Descriptors: anesthetics, inhalation pharmacology, intracranial hypertension physiopathology, intracranial pressure drug effects, isoflurane analogs and derivatives, isoflurane pharmacology, methyl ethers pharmacology, anesthetics, inhalation administration and dosage, blood gas analysis, blood loss, surgical, cerebrovascular circulation drug effects, dose response relationship, drug, heart rate drug effects, hemoglobins metabolism, intracranial hypertension chemically induced, isoflurane administration and dosage, methyl ethers administration and dosage, pulmonary alveoli metabolism, swine, xenon radioisotopes diagnostic use.

Holmstrom, A. and J. Akeson (2003). **Sevoflurane increases intracranial pressure less and desflurane more than isoflurane at experimentally raised intracranial pressure in pigs**. *Anesthesiology Abstracts of Scientific Papers Annual Meeting*(2003): Abstract No. A-271.

Descriptors: neuroanesthesia, cerebral blood flow (CBF), cerebrovascular resistance, hypocapnia, intracranial pressure, minimal alveolar concentration, normocapnia, hypcapnia, comparison study, desflurane, sevoflurane, isoflurane.

Notes: Meeting Information: 2003 Annual Meeting of the American Society of Anesthesiologists, San Francisco, CA, USA; October 11-15, 2003.

Horn, N.A., K.E. Hecker, B. Bongers, H.J. Baumert, S.M. Reyle Hahn, and R. Rossaint (2001). **Coagulation assessment in healthy pigs undergoing single xenon anaesthesia and combinations with isoflurane and sevoflurane.** *Acta Anaesthesiologica Scandinavica* 45(5): 634-8. ISSN: 0001-5172.

Abstract: BACKGROUND: With the introduction of new anaesthetics into clinical practice possible side effects of these novel anaesthetics have to be evaluated. This study was performed to clarify whether xenon or combinations of xenon with isoflurane or sevoflurane modify blood coagulation. METHODS: The study was performed in 20 healthy pigs which first underwent xenon anaesthesia (65 Vol%) and were then randomly assigned to combinations of xenon and isoflurane or sevoflurane at varying concentrations. During anaesthesia the following parameters were controlled: aPTT, PT, fibrinogen concentrations and thrombelastographic measurements. RESULTS: Xenon monoanaesthesia did not alter significantly any coagulation parameter. When isoflurane was introduced the aPTT showed a significant increase while fibrinogen concentration decreased. The introduction of sevoflurane led also to a decrease in fibrinogen concentration, while the aPTT was unchanged. These decreases in fibrinogen concentration were not accompanied by reduced maximal clot strength or elevated fibrinolysis evaluated by thrombelastography. Although the above-described changes were statistically significant, none of the parameters throughout the experiment exceeded the limits of normal values. CONCLUSION: In our study, xenon monoanaesthesia and combinations of xenon with isoflurane and sevoflurane did not lead to pathologic alterations in the measured coagulation parameters.

Descriptors: anesthesia, inhalation, anesthetics, inhalation, blood coagulation drug effects,

isoflurane, methyl ethers, xenon, blood pressure drug effects, platelet function tests, swine, thrombelastography.

Hurnik, D. (2006). **The Canadian Quality Assurance drug use policy does not specifically ban the use of general anesthesia in swine.** *Canadian Veterinary Journal, The; Revue Veterinaire Canadienne, La* 47(1): 7; Author Reply 8. ISSN: 0008-5286.
NAL Call Number: 41.8 R3224
Descriptors: anesthesia, general veterinary, pain veterinary, veterinary medicine ethics, anesthesia, general ethics, animal welfare, pain prevention and control, quality control, swine.
Notes: Comment On: Can Vet J. 2005 Jul;46(7):579.

Ivany, J.M. and W.W. Muir (2004). **Farm animal anesthesia**. In: S.L. Fubini and N.G. Ducharme (Editors), *Farm Animal Surgery,* Saunders, An Imprint of Elsevier: St. Louis, USA, p. 97-112. ISBN: 0721690629.
Descriptors: acepromazine, anesthesia, anesthetics, antagonists, calves, conduction anesthesia, detomidine, diazepam, domestic animals, drug delivery systems , eyes, feet, guaifenesin, horns, inhaled anesthetics, injection, ketamine, livestock , medetomidine, neuroleptics, pentobarbital, pharmacodynamics, preanesthetic medication, propofol, regulations, safety, surgery, surgical operations, thiopental, udders, xylazine, yohimbine, cattle, goats, pigs, sheep.

Jaggin, N., I. Kohler, J. Blum, and U. Schatzmann (2001). **Castration of newborn piglets under inhalation anesthesia with halothane [Die Kastration von neugeborenen Ferkeln unter Halothananasthesie.]**. *Praktische Tierarzt* 82(12): 1054-1054...1061. ISSN: 0032-681X.
NAL Call Number: 41.8 P882
Descriptors: age differences, anesthesia, blood plasma, castration, halothane, beta -endorphin, piglets, surgery, pigs.
Language of Text: German, Summary in English.

Jaynski, M., W. Brzeski, M. Chyczewski, M. Lew, and A. Rychlik (2004). **Propofol general anaesthesia in laparoscopic hernia treatment in pigs [Znieczulenie ogolne propofolem w leczeniu przepuklin swin metoda laparoskopowa.]**. *Medycyna Weterynaryjna* 60(2): 196-198. ISSN: 0025-8628.
NAL Call Number: 41.8 M463
Descriptors: anesthesia, anesthetics, atropine, azaperone, hernia, laparoscopy, pharmacodynamics, pharmacokinetics, pharmacology, piglets, propofol, surgery, surgical operations, pigs.
Language of Text: Polish, Summary in English.

Jennings, P., C. Koppelstaetter, W. Pfaller, J.P. Morin, T. Hartung, and M.P. Ryan (2004). **Assessment of a new cell culture perfusion apparatus for in vitro chronic toxicity testing. Part 2: toxicological evaluation.** *ALTEX Alternativen Zu Tierexperimenten* 21(2): 61-6. ISSN: 0946-7785.
Abstract: The goal of replacement, refinement and reduction of animal testing is critically dependent on the development and assessment of novel in vitro methodologies and the further development of existing methodologies. Here, we evaluated the use of a modified perfusion cell culture apparatus for application to chronic in vitro nephrotoxicity testing using DMSO, SDS, paracetamol and cyclosporine A as test compounds. Renal epithelial monolayers were cultured on microporous growth supports and exposed to test compounds

under static or perfusion conditions. Alamar Blue reduction, gamma-glutamyl transpeptidase activity (GGT), lactate dehydrogenase activity (LDH) and remnant protein were used to assay cell toxicity. There was no significant difference in IC(50) values between static and perfusion cultures up to 72 hours exposure. However, the perfusion system allowed continuous real-time monitoring of plasma membrane damage, which gives important information of time, duration and scale of toxicity. The complexity of the system restrains its use to low-throughput analysis. However, the real and theoretical advantages of this and similar systems merit further investigations.

Descriptors: acetaminophen toxicity, analgesics, non narcotic toxicity, animal testing alternatives, cell culture techniques methods, oxazines, toxicity tests, chronic methods, xanthenes, cell culture techniques instrumentation, coloring agents diagnostic use, cyclosporine toxicity, dimethyl sulfoxide toxicity, dose response relationship, drug, immunosuppressive agents toxicity, inhibitory concentration 50, kidney diseases chemically induced, l lactate dehydrogenase metabolism, llc pk1 cells, perfusion, sodium dodecyl sulfate toxicity, surface active agents toxicity, swine, time factors, toxicity tests, chronic instrumentation, gamma glutamyltransferase metabolism.

Johansson, J.S., G.A. Manderson, R. Ramoni, S. Grolli, and R.G. Eckenhoff (2005). **Binding of the volatile general anesthetics halothane and isoflurane to a mammalian beta-barrel protein.** *FEBS Journal, The* 272(2): 573-81. ISSN: 1742-464X.

NAL Call Number: QP501 .E8

Abstract: A molecular understanding of volatile anesthetic mechanisms of action will require structural descriptions of anesthetic-protein complexes. Porcine odorant binding protein is a 157 residue member of the lipocalin family that features a large beta-barrel internal cavity (515 +/- 30 angstroms(3)) lined predominantly by aromatic and aliphatic residues. Halothane binding to the beta-barrel cavity was determined using fluorescence quenching of Trp16, and a competitive binding assay with 1-aminoanthracene. In addition, the binding of halothane and isoflurane were characterized thermodynamically using isothermal titration calorimetry. Hydrogen exchange was used to evaluate the effects of bound halothane and isoflurane on global protein dynamics. Halothane bound to the cavity in the beta-barrel of porcine odorant binding protein with dissociation constants of 0.46 +/- 0.10 mM and 0.43 +/- 0.12 mM determined using fluorescence quenching and competitive binding with 1-aminoanthracene, respectively. Isothermal titration calorimetry revealed that halothane and isoflurane bound with K(d) values of 80 +/- 10 microM and 100 +/- 10 microM, respectively. Halothane and isoflurane binding resulted in an overall stabilization of the folded conformation of the protein by -0.9 +/- 0.1 kcal.mol(-1). In addition to indicating specific binding to the native protein conformation, such stabilization may represent a fundamental mechanism whereby anesthetics reversibly alter protein function. Because porcine odorant binding protein has been successfully analyzed by X-ray diffraction to 2.25 angstroms resolution [1], this represents an attractive system for atomic-level structural studies in the presence of bound anesthetic. Such studies will provide much needed insight into how volatile anesthetics interact with biological macromolecules.

Descriptors: anesthetics, inhalation metabolism, halothane metabolism, isoflurane metabolism, receptors, odorant chemistry, calorimetry, protein binding, protein folding, receptors, odorant metabolism, swine, x ray diffraction.

Johnson, K.B., T.D. Egan, S.E. Kern, S.W. McJames, M.L. Cluff, and N.L. Pace (2004). **Influence of hemorrhagic shock followed by crystalloid resuscitation on propofol: a pharmacokinetic and pharmacodynamic analysis.** *Anesthesiology* 101(3): 647-59. ISSN: 0003-3022.

Abstract: BACKGROUND: Previous work has demonstrated that ongoing hemorrhagic shock dramatically alters the distribution, clearance, and potency of propofol. Whether volume resuscitation after hemorrhagic shock restores drug behavior to baseline pharmacokinetics and pharmacodynamics remains unclear. This is particularly relevant because patients suffering from hemorrhagic shock are typically resuscitated before surgery. To investigate this, the authors studied the influence of an isobaric bleed followed by crystalloid resuscitation on the pharmacokinetics and pharmacodynamics of propofol in a swine model. The hypothesis was that hemorrhagic shock followed by resuscitation would not significantly alter the pharmacokinetics but would influence the pharmacodynamics of propofol. METHODS: After approval from the Animal Care Committee, 16 swine were randomly assigned to control and shock-resuscitation groups. Swine randomized to the shock-resuscitation group were bled to a mean arterial blood pressure of 40 mm Hg over a 20-min period and held there by further blood removal until 42 ml/kg of blood had been removed. Subsequently, animals were resuscitated with lactated Ringer's solution to maintain a mean arterial blood pressure of 70 mm Hg for 60 min. After resuscitation, propofol (750 microg x kg(-1) x min(-1)) was infused for 10 min. The control group underwent a sham hemorrhage and resuscitation and received propofol at the same dose and approximate time as the shock-resuscitation group. Arterial samples (20 from each animal) were collected at frequent intervals until 180 min after the infusion began and were analyzed to determine drug concentrations. Pharmacokinetic parameters for each group were estimated using a three-compartment model. The electroencephalogram Bispectral Index Scale was used as a measure of drug effect. Pharmacodynamics were characterized using a sigmoid inhibitory maximal effect model. RESULTS: The raw data demonstrated minimal differences in the mean plasma propofol concentrations between groups. The compartment analysis revealed some subtle differences between groups in the central and slow equilibrating volumes, but the differences were not significant. Hemorrhagic shock followed by resuscitation shifted the concentration effect relationship to the left, demonstrating a 1.5-fold decrease in the effect-site concentration required to achieve 50% of the maximal effect in the Bispectral Index Scale. CONCLUSIONS: Hemorrhagic shock followed by resuscitation with lactated Ringer's solution did not alter the pharmacokinetics but did increase the potency of propofol. These results demonstrate that alterations in propofol pharmacokinetics observed in moderate to severe blood loss can be reversed with resuscitation. These results suggest that a modest reduction in propofol is prudent to achieve a desired drug effect after resuscitation from severe hemorrhagic shock.

Descriptors: anesthetics, intravenous pharmacokinetics, anesthetics, intravenous pharmacology, cardiopulmonary resuscitation, propofol pharmacokinetics, propofol pharmacology, shock, hemorrhagic metabolism, algorithms, anesthesia, cardiac output drug effects, cardiac output physiology, computer simulation, electroencephalography drug effects, hemodynamic processes drug effects, hemodynamic processes physiology, nonlinear dynamics, respiration, artificial, swine.

Notes: Comment In: Anesthesiology. 2004 Sep;101(3):567-8.

Johnson, K.B., T.D. Egan, S.E. Kern, J.L. White, S.W. McJames, N. Syroid, D. Whiddon, and T. Church (2003). **The influence of hemorrhagic shock on propofol: a pharmacokinetic and pharmacodynamic analysis.** *Anesthesiology* 99(2): 409-20. ISSN: 0003-3022.

Abstract: BACKGROUND: Propofol is a common sedative hypnotic for the induction and maintenance of anesthesia. Clinicians typically moderate the dose of propofol or choose a different sedative hypnotic in the setting of severe intravascular volume depletion. Previous work has established that hemorrhagic shock influences both the pharmacokinetics and pharmacodynamics of propofol in the rat. To investigate this further, the authors studied the influence of hemorrhagic shock on the pharmacology of propofol in a swine isobaric hemorrhage model. METHODS: After approval from the Animal Care Committee, 16 swine were randomly assigned to control and shock groups. The shock group was bled to a mean arterial blood pressure of 50 mmHg over a 20-min period and held there by further blood removal until 30 ml/kg of blood was removed. Propofol 200 microg. kg(-1). min(-1) was infused for 10 min to both groups. Arterial samples (15 from each animal) were collected at frequent intervals until 180 min after the infusion began and analyzed to determine drug concentration. Pharmacokinetic parameters for each group were estimated using a three-compartment model. The electroencephalogram Bispectral Index Scale was used as a measure of drug effect. The pharmacodynamics were characterized using a sigmoid inhibitory maximal effect model. RESULTS: The raw data demonstrated higher plasma propofol levels in the shock group. The pharmacokinetic analysis revealed slower intercompartmental clearances in the shock group. Hemorrhagic shock shifted the concentration effect relationship to the left, demonstrating a 2.7-fold decrease in the effect site concentration required to achieve 50% of the maximal effect in the Bispectral Index Scale. CONCLUSIONS: Hemorrhagic shock altered the pharmacokinetics and pharmacodynamics of propofol. Changes in intercompartmental clearances and an increase in the potency of propofol suggest that less propofol would be required to achieve a desired drug effect during hemorrhagic shock.

Descriptors: anesthetics, intravenous pharmacology, propofol pharmacology, shock, hemorrhagic physiopathology, algorithms, analysis of variance, anesthesia, anesthetics, inhalation pharmacology, anesthetics, intravenous pharmacokinetics, blood glucose metabolism, blood pressure drug effects, computer simulation, heart rate drug effects, isoflurane pharmacology, lactic acid blood, nonlinear dynamics, pilot projects, propofol pharmacokinetics, swine.

Johnson, K.B., S.E. Kern, E.A. Hamber, S.W. McJames, K.M. Kohnstamm, and T.D. Egan (2001). **Influence of hemorrhagic shock on remifentanil: a pharmacokinetic and pharmacodynamic analysis.** *Anesthesiology* 94(2): 322-32. ISSN: 0003-3022.

Abstract: BACKGROUND: Hemorrhagic shock is known to alter significantly the pharmacokinetics of fentanyl, an opioid that requires delivery to the liver for metabolism. The authors hypothesized that the pharmacokinetics and pharmacodynamics of remifentanil, an esterase metabolized opioid that does not require delivery to a metabolic organ, would be altered less by hemorrhagic shock that those of fentanyl. METHODS: Sixteen pigs were assigned randomly to control and shock groups. The shock group was bled using an isobaric hemorrhage model. Remifentanil 10 microg x kg(-1) x min(-1) was infused for 10 min to both groups. Arterial samples were collected for remifentanil concentration assay. Pharmacokinetic parameters were estimated using a three-compartment model. The electroencephalogram spectral edge was used as a measure of drug effect. The pharmacodynamics were characterized using a sigmoid inhibitory maximal effect model. RESULTS: Remifentanil blood levels were higher in the shocked group. The central clearance was slower and the central compartment was smaller in shocked animals. No difference between groups was observed in the magnitude or time course of the remifentanil-induced decrease in spectral edge. CONCLUSIONS: Hemorrhagic shock altered the pharmacokinetics of remifentanil,

suggesting that less remifentanil would be required to maintain a target plasma concentration. However, because of its rapid metabolism, the impact of hemorrhagic shock on the concentration decline of remifentanil after termination of the infusion was minimal. Hemorrhagic shock did not alter the pharmacodynamics of remifentanil.
Descriptors: analgesics, opioid pharmacokinetics, piperidines pharmacokinetics, shock, hemorrhagic metabolism, computer simulation, dose response relationship, drug, piperidines pharmacology, swine.

Johnson, K.B., T.D. Egan, J. Layman, S.E. Kern, J.L. White, and S.W. Mcjames (2003). **The influence of hemorrhagic shock on etomidate: a pharmacokinetic and pharmacodynamic analysis.** *Anesthesia and Analgesia* 96(5): 1360-1368. ISSN: 0003-2999.
Descriptors: blood and lymphatics: transport and circulation, cardiovascular system: transport and circulation, metabolism, pharmacology, sedative hypnotics, opioids, etomidate, hemorrhagic shock, vascular disease, bispectral index scale.

Kaiser, G.M., F. Breuckmann, S. Aker, H. Eggebrecht, H. Kuehl, R. Erbel, N.R. Fruhauf, C.E. Broelsch, and H.H. Quick (2007). **Anesthesia for cardiovascular interventions and magnetic resonance imaging in pigs.** *Journal of the American Association for Laboratory Animal Science JAALAS* 46(2): 30-3. ISSN: 1559-6109.
NAL Call Number: SF405.3 .A23
Abstract: Large animal models are still required for many experimental purposes. The aim of the current study was to define a viable narcotic procedure for experimental cardiovascular interventions and imaging in pigs. A total of 32 domestic pigs were used. Animals received propofol, midazolam, and fentanyl as continuous intravenous infusion anesthesia for complex vascular interventions, angiographic X-ray imaging, and magnetic resonance imaging (MRI). Anesthesia was maintained for 6 to 10 h. The initial hourly doses were 2.29 mg/kg of propofol, 1.14 mg/kg of midazolam, and 0.009 mg/kg of fentanyl, with controlled ventilation. Anesthesia, interventions, imaging, periods of apnea of as long as 2 min, and transportation were well-tolerated. Stress-induced arrhythmias were not noted, and artifact-free imaging was achieved. The combination of propofol, midazolam, and fentanyl is well-suited for experimental angiographic interventional studies, experimental cardiovascular MRI, and MR-guided interventions in pigs.
Descriptors: anesthesia methods, cardiovascular surgical procedures, laboratory animal science methods, magnetic resonance imaging instrumentation, sus scrofa surgery, anesthesiology instrumentation.

Kaiser, G.M., N.R. Fruhauf, H. Zhang, S. Westermann, I. Bolle, K.J. Oldhafer, and C.E. Broelsch (2003). **Intravenous infusion anesthesia with Propofol-Midazolam-fentanyl for experimental surgery in swine.** *Journal of Investigative Surgery the Official Journal of the Academy of Surgical Research* 16(6): 353-7. ISSN: 0894-1939.
Abstract: There is a need for prolonged anesthesia procedures in experimental surgery. Animals in this study received fentanyl, Midazolam, and Propofol administered by continuous intravenous infusion for anesthesia along with controlled ventilation. Time of anesthesia was 413 +/- 95 min. Animals could be extubated 20 +/- 12 min after operation. Animals recovered completely from anesthesia by day 1 after surgery with almost normal physical activity. This study clearly shows that intravenous infusion anesthesia is safe and easy to handle in prolonged anesthesia for experimental surgery in swine. This anesthetic protocol

can also be used for intraoperative transportation.
Descriptors: anesthesia, intravenous methods, anesthetics, intravenous pharmacology, fentanyl pharmacology, midazolam pharmacology, propofol pharmacology, sus scrofa, abdomen surgery, anesthesia, intravenous mortality, infusions, intravenous, species specificity.

Kaiser, G.M., M.M. Heuer, N.R. Fruhauf, C.A. Kuhne, and C.E. Broelsch (2006). **General handling and anesthesia for experimental surgery in pigs.** *Journal of Surgical Research, The* 130(1): 73-9. ISSN: 0022-4804.
NAL Call Number: RD1
Abstract: The pig is a common large animal for experimental settings in many fields of surgery. In experimental surgery, there is a need for different narcotic procedures depending on the complexity of the surgical investigation. Narcotic procedures have to be safe, easy to handle, and should not influence the experimental results. We hereby present important aspects of handling and narcotic procedures for pigs. The aim of this publication is to supply an introduction for young surgical investigators who are planning or already have started investigations using pigs as an experimental animal. This publication is based on our institutional experience of narcotic and surgical procedures in more than 400 cases.
Descriptors: anesthesia veterinary, models, animal, surgical procedures, operative veterinary, swine, handling psychology.

Kazama, T., T. Kurita, K. Morita, J. Nakata, and S. Sato (2002). **Influence of hemorrhage on propofol pseudo-steady state concentration.** *Anesthesiology* 97(5): 1156-61. ISSN: 0003-3022.
Abstract: BACKGROUND: A small induction dose has been recommended in cases of hemorrhagic shock. However, the influence of hemorrhage on the amplitude of plasma propofol concentration has not yet been fully investigated during continuous propofol infusion. The authors hypothesized that the effect of hemorrhage on plasma propofol concentration is variously influenced by the different stages of shock. METHODS: After 120 min of steady state infusion of propofol at a rate of 2 mg x kg(-1) x h(-1), nine instrumented immature swine were studied using a stepwise increasing hemorrhagic model (200 ml of blood every 30 min until 1 h, then additional stepwise bleeding of 100 ml every 30 min thereafter, to the point of circulatory collapse). Hemodynamic parameters and plasma propofol concentration were recorded at every step. RESULTS: Before total circulatory collapse, it was possible to drain 976 +/- 166 ml (mean +/- SD) of blood. Hemorrhage of less than 600 ml (19 ml/kg) was not accompanied by a significant change in plasma propofol concentration. At individual peak systemic vascular resistance, when cardiac output and mean arterial pressure decreased by 31% and 14%, respectively, plasma propofol concentration increased by 19% of its prehemorrhagic value. At maximum heart rate, when cardiac output and mean arterial pressure decreased by 46% and 28%, respectively, plasma propofol concentration increased by 38%. In uncompensated shock, it increased to 3.75 times its prehemorrhagic value. CONCLUSIONS: During continuous propofol infusion, plasma propofol concentration increased by less than 20% during compensated shock. However, it increased 3.75 times its prehemorrhagic concentration during uncompensated shock.
Descriptors: anesthetics, intravenous pharmacokinetics, hemorrhage metabolism, propofol pharmacokinetics, cardiac output drug effects, hemodynamic processes drug effects, metabolic clearance rate, propofol pharmacology, shock, hemorrhagic metabolism, swine.
Notes: Comment In: Anesthesiology. 2002 Nov;97(5):6A.

Keates, H. (2003). **Induction of anaesthesia in pigs using a new alphaxalone formulation.** *Veterinary Record, The* 153(20): 627-8. ISSN: 0042-4900.
NAL Call Number: 41.8 V641
Descriptors: anesthesia veterinary, anesthetics pharmacology, pregnanediones pharmacology, swine physiology, anesthetics administration and dosage, azaperone administration and dosage, azaperone pharmacology, embryo implantation, heart rate drug effects, injections, intravenous veterinary, pregnanediones administration and dosage.

Keita, A., E. Pagot, A. Prunier, and C. Guidarini (2010). **Pre-emptive meloxicam for postoperative analgesia in piglets undergoing surgical castration**. *Veterinary Anaesthesia and Analgesia* 37(4): 367-74. ISSN: 1467-2995 (Electronic). 1467-2987 (Linking).
DOI: 10.1111/j.1467-2995.2010.00546.x
NAL Call Number: SF914 .V47
Abstract: OBJECTIVE: To investigate the effect of preoperative meloxicam administration on postoperative stress and pain induced by surgical castration in piglets. STUDY DESIGN: Prospective, blinded, randomized clinical trial. ANIMALS: One hundred and eighty male piglets of <1 week of age. METHODS: Castration was performed on 150 piglets which had received either an intramuscular injection of 0.4 mg kg(-1) meloxicam or a placebo 10-30 minutes before the procedure. Blood cortisol and ACTH concentrations were determined at 30 minutes post-castration and haptoglobin was measured at 24 hours post-castration. Presence or absence of foreleg movements, hind leg movements, urine or faeces emission, tremors or other body movements were recorded during the castration procedure. Scores for presence or absence of prostration, tremors, tail movements and isolation were recorded at 30 minutes, and at 1, 2, 4 and 24 hours post-castration and combined in a global behaviour score (GBS). Blood samples were taken from a further 30 piglets which did not undergo castration. RESULTS: Mean blood cortisol and ACTH concentrations at 30 minutes post-castration were both significantly lower in the meloxicam group than in the placebo group ($p < or = 0.01$). The mean haptoglobin concentration at 24 hours was not significantly reduced ($p = 0.178$). The distribution of the GBS during castration was similar in both groups. There were significant differences in the GBS after castration at both 2 and 4 hours post-castration with a greater proportion of piglets in the meloxicam group showing no behavioural alterations (82.7%versus 68.0% at both time points). The score distribution was similar in both groups at 30 minutes, 1 and 24 hours after castration. CONCLUSION AND CLINICAL RELEVANCE: This study suggests that pre-emptive administration of meloxicam is able to produce some postoperative analgesia after surgical castration of young piglets.
Descriptors: analgesia, behavior, castration, meloxicam, pain, piglets.

Kerbaul, F., M. Bellezza, C. Mekkaoui, H. Feier, C. Guidon, J. Gouvernet, P.H. Rolland, F. Gouin, T. Mesana, and F. Collart (2006). **Sevoflurane alters right ventricular performance but not pulmonary vascular resistance in acutely instrumented anesthetized pigs.** *Journal of Cardiothoracic and Vascular Anesthesia* 20(2): 209-16. ISSN: 1053-0770.
NAL Call Number: RD87.3.H43
Abstract: OBJECTIVE: Although the effects of halogenated agents on both normal and diseased left ventricles have been widely studied, the influence of these anesthetic agents on right ventricular (RV) performance remains less well characterized. This study was undertaken to examine the effects of 2 different concentrations of sevoflurane on RV function, and coronary and pulmonary hemodynamics in acutely instrumented anesthetized

pigs. DESIGN: Prospective experimental study. SETTING: Laboratory of experimental research in a university teaching hospital. SUBJECTS: Anesthetized pigs. INTERVENTIONS: Regional RV function in 10 pigs was determined from pressure segment length loop analysis, global RV function from stroke work versus end-diastolic pressure relation, right coronary blood flow, and pulmonary vascular resistance (PVR), without and then with 2.6% (minimum alveolar concentration [MAC]) and 3.9 % (1.5 MAC) end-tidal sevoflurane concentrations. MAIN RESULTS: Sevoflurane preserved inflow systolic shortening and RV regional external work, but significantly depressed outflow systolic shortening ($p < 0.05$). Global RV stroke work was depressed to 72% +/- 12% and 61% +/- 10% of baseline value, respectively, with 1 and 1.5 MAC of sevoflurane ($p < 0.05$), but without alteration of PVR. Right coronary blood flow decreased dose dependently. CONCLUSIONS: Sevoflurane causes significant depression of global RV function associated with a qualitatively different effect on inflow and outflow tracts, without any modification of PVR.
Descriptors: anesthesia, inhalation, anesthetics, inhalation administration and dosage, methyl ethers administration and dosage, pulmonary artery physiology, vascular resistance drug effects, ventricular function, right drug effects, blood pressure physiology, disease models, animal, dose response relationship, drug, follow up studies, prospective studies, swine.

Kerbaul, F., C. Guidon, J. Stephanazzi, M. Bellezza, P. Le Dantec, T. Longeon, and M. Aubert (2001). **Sub-MAC concentrations of desflurane do not inhibit hypoxic pulmonary vasoconstriction in anesthetized piglets.** *Canadian Journal of Anaesthesia; Journal Canadien D'Anesthesie* 48(8): 760-7. ISSN: 0832-610X.
NAL Call Number: RD78.68.C4
Abstract: PURPOSE: In vitro, halogenated agents reduce the pulmonary vasoconstrictor response to alveolar hypoxia in isolated perfused lungs. However, studies in intact animals have been less convincing. The aim of the present study was to assess the effect of sub-MAC concentrations of desflurane on hypoxic pulmonary vasoconstriction (HPV) in anesthetized piglets using the pressure/cardiac output relationship (P/Q). METHODS: Eleven large white piglets were anesthetized and ventilated mechanically, alternatively in hyperoxia (FIO2=0.4) and in hypoxia (FIO2=0.12). Multipoint plots of pulmonary arterial pressure (PAP), or differences between PAP and left atrial pressure (LAP) against Q were generated by gradual inflation of a balloon advanced into the inferior vena cava. P/Q relationships were established in hyperoxia and in hypoxia at baseline, and then with gradual concentrations of desflurane. RESULTS: In hypoxia, pressure gradients (PAP-LAP) increased significantly at every level of Q, demonstrating active pulmonary vasoconstriction. Desflurane did not affect these P/Q relationships either in hyperoxia, or in hypoxia, when compared with baseline. CONCLUSION: Desflurane at a clinically relevant dose has no significant effect on HPV in anesthetized piglets.
Descriptors: anesthetics, inhalation pharmacology, anoxia physiopathology, isoflurane pharmacology, pulmonary artery drug effects, vasoconstriction drug effects , anesthesia, cardiac output drug effects, isoflurane analogs and derivatives, pulmonary artery physiology, swine, sympathetic nervous system drug effects.

Kharasch, E.D., K.M. Powers, and A.A. Artru (2002). **Comparison of Amsorb, sodalime, and Baralyme degradation of volatile anesthetics and formation of carbon monoxide and compound a in swine in vivo.** *Anesthesiology* 96(1): 173-82. ISSN: 0003-3022.

Abstract: BACKGROUND: Consequences of volatile anesthetic degradation by carbon dioxide absorbents that contain strong base include formation of compound A from sevoflurane, formation of carbon monoxide (CO) and CO toxicity from desflurane, enflurane and isoflurane, delayed inhalation induction, and increased anesthetic costs. Amsorb (Armstrong Ltd., Coleraine, Northern Ireland) is a new absorbent that does not contain strong base and does not form CO or compound A in vitro. This investigation compared Amsorb, Baralyme (Chemetron Medical Division, Allied Healthcare Products, St. Louis, MO), and sodalime effects on CO (from desflurane and isoflurane) and compound A formation, carboxyhemoglobin (COHb) concentrations, and anesthetic degradation in a clinically relevant porcine in vivo model. METHODS: Pigs were anesthetized with desflurane, isoflurane, or sevoflurane, using fresh or partially dehydrated Amsorb, Baralyme, and new and old formulations of sodalime. Anesthetic concentrations in the fresh (preabsorber), inspired (postabsorber), and end-tidal gas were measured, as were inspired CO and compound A concentrations and blood oxyhemoglobin and COHb concentrations. RESULTS: For desflurane and isoflurane, the order of inspired CO and COHb formation was dehydrated Baralyme >> soda-lime > Amsorb. For desflurane and Baralyme, peak CO was 9,700 +/- 5,100 parts per million (ppm), and the increase in COHb was 37 +/- 14%. CO and COHb increases were undetectable with Amsorb. Oxyhemoglobin desaturation occurred with desflurane and Baralyme but not Amsorb or sodalime. The gap between inspired and end-tidal desflurane and isoflurane did not differ between the various dehydrated absorbents. Neither fresh nor dehydrated Amsorb caused compound A formation from sevoflurane. In contrast, Baralyme and sodalime caused 20-40 ppm compound A. The gap between inspired and end-tidal sevoflurane did not differ between fresh absorbents, but was Amsorb < sodalime < Baralyme with dehydrated absorbents. CONCLUSION: Amsorb caused minimal if any CO formation, minimal compound A formation regardless of absorbent hydration, and the least amount of sevoflurane degradation. An absorbent like Amsorb, which does not contain strong base or cause anesthetic degradation and formation of toxic products, may have benefit with respect to patient safety, inhalation induction, and anesthetic consumption (cost).
Descriptors: anesthetics, inhalation metabolism, barium compounds pharmacology, calcium chloride pharmacology, calcium compounds pharmacology, calcium hydroxide pharmacology, carbon monoxide metabolism, ethers metabolism, hydrocarbons, fluorinated metabolism, oxides pharmacology, potassium compounds pharmacology, sodium hydroxide pharmacology, absorption, carboxyhemoglobin analysis, isoflurane analogs and derivatives, isoflurane metabolism, methyl ethers metabolism, swine.
Notes: Comment In: Anesthesiology. 2002 Oct;97(4):1038; author reply 1038 .

Kimme, P., T. Ledin, and F. Sjoberg (2007). **Dose effect of sevoflurane and isoflurane anesthetics on cortical blood flow during controlled hypotension in the pig.** *Acta Anaesthesiologica Scandinavica* 51(5): 607-13. ISSN: 0001-5172.
Abstract: BACKGROUND: The ability of the brain to preserve adequate cerebral blood flow (CBF) during alterations in systemic perfusion pressure is of fundamental importance. At increasing concentrations, isoflurane and sevoflurane have been known to alter CBF, which may be disadvantageous for patients with increased intracranial pressure. The aim was to examine the effects of isoflurane and sevoflurane at increasing minimum alveolar concentrations (MAC) on CBF, during controlled hypotension. METHODS: We studied eight pigs during variations in perfusion pressure induced by caval block (100, 60, 50, and 40 mmHg) under normocapnia. CBF was measured locally in a defined area (4 x 5 measurement points

covering 1 cm(2)) of the motor cortex using laser Doppler perfusion imaging. Physiological variables, assessed by analysis of arterial O(2) and CO(2), hemoglobin and hematocrit, were controlled. CBF was measured during propofol (10 mg x kg(-1)x h(-1)) and fentanyl (0.002 mg x kg(-1)x h(-1)) anesthesia, and then during anesthesia with either isoflurane or sevoflurane (given in random order) at increasing MAC (0.3-1.2). After a washout period, the measurements were repeated with the other gas. RESULTS: CBF was significantly higher in the cortex during normotensive (control) settings, MAP approximately 100 mmHg, compared with during hypotension (MAP 40-60 mmHg). Neither different anesthetic nor MAC or local measurement sites were found to influence CBF at any perfusion pressure. CONCLUSION: In this experimental model, the effect of hypotension on CBF was not altered by the anesthetics used [isoflurane, sevoflurane (MAC 0.3-1.2) or propofol (10 mg x kg(-1) x h(-1))]. In this aspect (cortical tissue perspective), these volatile agents appear as suitable as propofol for neurosurgical anesthesia for patients at risk.

Descriptors: anesthesia, general, anesthetics, inhalation pharmacology, cerebrovascular circulation drug effects, isoflurane pharmacology, methyl ethers pharmacology, analysis of variance, brain radionuclide imaging, dose response relationship, drug, hypotension, controlled methods, intracranial pressure drug effects, laser doppler flowmetry instrumentation, swine.

Klc, N. and W. Erhardt (2004). **Infusion of pentobarbital and fentanyl combination for long-term anaesthesia in pigs**. *Turk Veterinerlik Ve Hayvanclk Dergisi* 28(3): 603-607. ISSN: 1300-0128.

NAL Call Number: SF1 .D57

Descriptors: anesthesia, anesthetics, blood gases, blood pressure, body temperature, drug combinations, fentanyl, haemoglobin, heart rate, pentobarbital, pharmacodynamics.

Klein, C. and P. Reinhold (2001). **Analysis of respiratory mechanics by impulse oscillometry in non-sedated and diazepam-sedated swine.** *Research in Veterinary Science* 70(3): 181-189. ISSN: 0034-5288 .

NAL Call Number: 41.8 R312

Abstract: Analysis of respiratory mechanics using impulse oscillometry is applicable to sedated, or non-sedated (trained) pigs when they are fixed in a sling. In this study, the influence of the following sources of variability on measurement results was examined: (i) sedation with diazepam; (ii) body weight of animals (ranging in age: 40 to 102 days); and (iii) time of the measurement (circadian influences). The following parameters were examined: respiratory rate (RR), tidal volume (V(t)), spectral resistance, reactance and coherence, each at 5, 10, 15 and 20 Hz (R5,...R20, X5,...X20, CO5...CO20, respectively), distal respiratory resistance (R(dist)), and proximal airway resistance (R(prox)). After sedation (using 1.5 mg diazepam per kg body weight), RR and V(t) decreased significantly. There was a significant improvement of CO5, CO10 and CO15. Increase in body weight was strongly correlated to V(t), furthermore to spectral resistance parameters. Impulse oscillometry system (IOS) parameters showed only slight non-significant alterations in dependency on the time of day. In consequence, different sources of variability must be taken into account when performing IOS measurements in swine.

Descriptors: swine, diagnostic techniques, measurement, diazepam, anesthesia, body weight, circadian rhythm, variation, respiration.

Kleinsasser, A., K.H. Lindner, C. Hoermann, A. Schaefer, C. Keller, and A. Loeckinger (2001). **Isoflurane and sevoflurane anesthesia in pigs with a preexistent gas exchange defect.** *Anesthesiology* 95(6): 1422-6. ISSN: 0003-3022.

Abstract: BACKGROUND: Decreased arterial partial pressure of oxygen (PaO2) during volatile anesthesia is well-known. Halothane has been examined with the multiple inert gas elimination technique and has been shown to alter the distribution of pulmonary blood flow and thus PaO2. The effects of isoflurane and sevoflurane on pulmonary gas exchange remain unknown. The authors hypothesized that sevoflurane with a relatively high minimum alveolar concentration (MAC) would result in significantly more gas exchange disturbances in comparison with isoflurane or control. METHODS: This study was performed in a porcine model with an air pneumoperitoneum that generates a reproducible gas exchange defect. After a baseline measurement of pulmonary gas exchange (multiple inert gas elimination technique) during propofol anesthesia, 21 pigs were randomly assigned to three groups of seven animals each. One group received isoflurane anesthesia, one group received sevoflurane anesthesia, and one group was continued on propofol anesthesia (control). After 30 min of volatile anesthesia at 1 MAC or propofol anesthesia, a second measurement (multiple inert gas elimination technique) was performed. RESULTS: At the second measurement, inert gas shunt was 15 +/- 3% (mean +/- SD) during sevoflurane anesthesia versus 9 +/- 1% during propofol anesthesia (P = 0.02). Blood flow to normal ventilation/perfusion (V(A)/Q) lung areas was 83 +/- 5% during sevoflurane anesthesia versus 89 +/- 1% during propofol anesthesia (P = 0.04). This resulted in a PaO2 of 88 +/- 11 mmHg during sevoflurane anesthesia versus 102 +/- 15 mmHg during propofol anesthesia (P = 0.04). Inert gas and blood gas variables during isoflurane anesthesia did not differ significantly from those obtained during propofol anesthesia. CONCLUSIONS: In pigs with an already existent gas exchange defect, sevoflurane anesthesia but not isoflurane anesthesia causes significantly more gas exchange disturbances than propofol anesthesia does.

Descriptors: anesthetics, inhalation pharmacology, isoflurane pharmacology, methyl ethers pharmacology, pneumoperitoneum physiopathology, pulmonary gas exchange drug effects, acid base equilibrium drug effects, anesthesia, anesthetics, intravenous pharmacology, blood gas analysis, noble gases diagnostic use, propofol pharmacology, swine.

Klockgether Radke, A.P., S. Huneck, S. Meyberg, P. Neumann, and G. Hellige (2005). **Ketamine enantiomers differentially relax isolated coronary artery rings.** *European Journal of Anaesthesiology* 22(3): 215-21. ISSN: 0265-0215.

Abstract: BACKGROUND AND OBJECTIVE: It has been shown that racemic ketamine increases coronary blood flow and that this effect is at least in part due to a direct vasorelaxing effect of this substance. This study was designed to determine whether ketamine might stereoselectively relax isolated porcine coronary arteries. METHODS: Using the model of isolated vessels we studied the effects of S(+) ketamine, R(-) ketamine, and racemic ketamine (5-500 microg mL(-1)) on artery strips pre-contracted by either potassium chloride (KCl) or prostaglandin F2alpha (PGF2alpha). To elucidate possible mechanisms of action these experiments were repeated in the presence of one of the following compounds: N(omega)-nitro-L-arginine (L-NNA), indomethacin, glibenclamide, and tetraethylammonium (TEA) chloride, an inhibitor of the BK(Ca) K+ channel. RESULTS: Both isoforms and racemic ketamine relaxed isolated coronary arteries in a concentration-dependent manner in concentrations beyond those used in clinical practice. S(+) ketamine exerted the strongest vasorelaxing effect, followed by racemic ketamine and R(-) ketamine. Pretreatment with

L-NNA, indomethacin, or glibenclamide did not alter the vasodilating properties of ketamine, whereas TEA chloride significantly attenuated the vasorelaxing effects of all the three forms of ketamine. CONCLUSIONS: Ketamine dilates coronary arteries in vitro when administered in high concentrations. There is a stereoselective difference with a stronger vasorelaxing effect of S(+) ketamine compared to racemic and R(-) ketamine. The impact of TEA chloride suggests that the activation of the BK(Ca) channel may contribute to the vasodilating effect of ketamine.

Descriptors: anesthetics, dissociative pharmacology, coronary vessels drug effects, ketamine pharmacology, vasodilator agents pharmacology, anesthetics, dissociative administration and dosage, anti arrhythmia agents pharmacology, cardiovascular agents pharmacology, dinoprost pharmacology, dose response relationship, drug, enzyme inhibitors pharmacology, glyburide pharmacology, indomethacin pharmacology, ketamine administration and dosage, nitroarginine pharmacology, potassium channel blockers pharmacology, potassium chloride pharmacology, stereoisomerism, swine, tetraethylammonium pharmacology, vasoconstrictor agents pharmacology, vasodilator agents administration and dosage.

Klockgether Radke, A.P., H. Schulze, P. Neumann, and G. Hellige (2004). **Activation of the K+ channel BK(Ca) is involved in the relaxing effect of propofol on coronary arteries.** *European Journal of Anaesthesiology* 21(3): 226-30. ISSN: 0265-0215.

Abstract: BACKGROUND AND OBJECTIVE: Propofol may cause undesirable hypotension due to vasodilation. The underlying mechanisms are not completely understood. We investigated the mechanisms by which propofol relaxes vascular segments. METHODS: We studied the effect of propofol on isolated porcine coronary artery rings precontracted with potassium chloride or prostaglandin F2alpha. RESULTS: Propofol, in a concentration-dependent manner, relaxed all segments at concentrations of 5 microg mL(-1) and above. This relaxation was unaltered in the presence of N(omega)-nitro-L-arginine, indomethacin, diltiazem and glibenclamide. Tetraethylammonium chloride, an inhibitor of the BK(Ca) K+ channel (a high conductance Ca2+-sensitive K+ channel), dose-dependently attenuated the vasodilating effect of propofol ($P < 0.001$). CONCLUSIONS: Our results suggests that the activation of the BK(Ca) channel may contribute to the vasodilating effect of propofol, hereby causing hyperpolarization of the smooth muscle membrane and reduction of smooth muscle tone.

Descriptors: anesthetics, intravenous pharmacology, coronary vessels drug effects , potassium channels drug effects, propofol pharmacology, vasodilator agents pharmacology, anesthetics, intravenous administration and dosage, anesthetics, intravenous antagonists and inhibitors, calcium channel blockers pharmacology, cyclooxygenase inhibitors pharmacology, diltiazem pharmacology, dinoprost pharmacology, dose response relationship, drug, enzyme inhibitors pharmacology, glyburide pharmacology, indomethacin pharmacology, muscle, smooth, vascular drug effects, nitroarginine pharmacology, potassium channel blockers pharmacology, potassium chloride pharmacology, propofol administration and dosage, propofol antagonists and inhibitors, swine, tetraethylammonium pharmacology, vasoconstrictor agents pharmacology, vasodilator agents administration and dosage, vasodilator agents antagonists and inhibitors.

Kmiec, M. (2005). ***Castration of piglets without or with general anesthesia (Azaperone-Ketamine): practicability, animal welfare, economy [Die Kastration von Saugferkeln ohne und mit Allgemeinanasthesie (Azaperon-Ketamin): Praktikabilitat, Wohlbefinden und***

Wirtschaftlichkeit.]. Dissertation, Freie Univ.: Berlin, Germany. 121 p.
Online: http://library.vetmed.fu-berlin.de/diss-abstracts/18.html
Descriptors: anesthesia , anesthetics, animal welfare, azaperone, castration, ketamine, pain, piglets, surgery, pigs.
Language of Text: German, Summary in English.

Kobr, J., V. Kuntscher, V. Treska, J. Molacek, V. Vobruba, and J. Fremuth (2010). **Ventilation and haemodynamic indicators in spontaneously breathing pigs under general anaesthesia**. *Acta Veterinaria Brno* 79(1): 61-65. ISSN: 0001-7213.
DOI: 10.2754/avb201079010061
NAL Call Number: SF604.B7
Descriptors: anesthesia, anesthetics, blood gases, cardiac output, fentanyl, azaperone, hemodynamics, pharmacodynamics, piglets, respiration rate, Czech Black Pied piglets.
Language of Text: Czech.

Konwar, B. and B. Saikia (2006). **Ketamine and its combination with diazepam for balanced anaesthesia in swine**. *Indian Veterinary Journal* 83(5): 507-508. ISSN: 0019-6479.
NAL Call Number: SF604.I45
Descriptors: pharmacology, ketamine, diazepam, methods and techniques, anesthesia, clinical techniques, drug combination, heart rate, temperature range .

Krismer, A.C., Q.H. Hogan, V. Wenzel, K.H. Lindner, U. Achleitner, S. Oroszy, B. Rainer, A. Wihaidi, V.D. Mayr, P. Spencker, and A. Amann (2001). **The efficacy of epinephrine or vasopressin for resuscitation during epidural anesthesia.** *Anesthesia and Analgesia* 93(3): 734-42. ISSN: 0003-2999.
Abstract: Cardiopulmonary resuscitation (CPR) during epidural anesthesia is considered difficult because of diminished coronary perfusion pressure. The efficacy of epinephrine and vasopressin in this setting is unknown. Therefore, we designed this study to assess the effects of epinephrine versus vasopressin on coronary perfusion pressure in a porcine model with and without epidural anesthesia and subsequent cardiac arrest. Thirty minutes before induction of cardiac arrest, 16 pigs received epidural anesthesia with bupivacaine while another 12 pigs received only saline administration epidurally. After 1 min of untreated ventricular fibrillation, followed by 3 min of basic life-support CPR, Epidural Animals and Control Animals randomly received every 5 min either epinephrine (45, 45, and 200 microg/kg) or vasopressin (0.4, 0.4, and 0.8 U/kg). During basic life-support CPR, mean +/- SEM coronary perfusion pressure was significantly lower after epidural bupivacaine than after epidural saline (13 +/- 1 vs 24 +/- 2 mm Hg, $P < 0.05$). Ninety seconds after the first drug administration, epinephrine increased coronary perfusion pressure significantly less than vasopressin in control animals without epidural block (42 +/- 2 vs 57 +/- 5 mm Hg, $P < 0.05$), but comparably to vasopressin after epidural block (45 +/- 4 vs 48 +/- 6 mm Hg). Defibrillation was attempted after 18 min of CPR. After return of spontaneous circulation, bradycardia required treatment in animals receiving vasopressin, especially with epidural anesthesia. Systemic acidosis was increased in animals receiving epinephrine than vasopressin, regardless of presence or absence of epidural anesthesia. We conclude that vasopressin may be a more desirable vasopressor for resuscitation during epidural block because the response to a single dose is longer lasting, and acidosis after multiple doses is less severe compared with epinephrine.

Descriptors: anesthesia, epidural, cardiopulmonary resuscitation, epinephrine pharmacology, vasoconstrictor agents pharmacology, vasopressins pharmacology, blood gas analysis, blood pressure drug effects, coronary circulation drug effects, electrocardiography drug effects, heart arrest, induced, hemodynamic processes drug effects, swine, ventricular fibrillation prevention and control.

Krismer, A.C., K.H. Lindner, V. Wenzel, V.D. Mayr, W.G. Voelckel, K.G. Lurie, and H.U. Strohmenger (2001). **The effects of endogenous and exogenous vasopressin during experimental cardiopulmonary resuscitation**. *Anesthesia and Analgesia* 92(6): 1499-1504. ISSN: 0003-2999.

Descriptors: vasopressin, epinephrine, biochemistry and molecular biophysics, pharmacology, cardiovascular system: transport and circulation, cardiopulmonary resuscitation, open chest model, therapeutic method, blood pressure.

Kumar, A., H.J. Mann, and R.P. Remmel (2006). **Pharmacokinetics of tiletamine and zolazepam (Telazol) in anesthetized pigs.** *Journal of Veterinary Pharmacology and Therapeutics* 29(6): 587-9. ISSN: 0140-7783.

NAL Call Number: SF915.J63

Descriptors: anesthetics, dissociative pharmacokinetics, anti anxiety agents pharmacokinetics, swine metabolism, tiletamine pharmacokinetics, zolazepam pharmacokinetics, anesthesia, general veterinary, anesthetics, dissociative administration and dosage, anesthetics, dissociative blood, anti anxiety agents administration and dosage, anti anxiety agents blood, area under curve, drug therapy, combination, infusions, intravenous veterinary, injections, intramuscular veterinary, swine physiology, tiletamine administration and dosage, tiletamine blood, zolazepam administration and dosage, zolazepam blood.

Kumar, V., P.N. Sahay, and L.L. Dass (2005). **Comparative evaluation of xylocaine, xylazine and bupivacaine for lumbosacral analgesia in pigs**. *Indian Veterinary Journal* 82(10): 1062-1065. ISSN: 0019-6479.

NAL Call Number: SF604.I45

Descriptors: pharmacology, veterinary medicine: medical sciences, anesthesiology : medical sciences, epidural anesthesia, clinical techniques.

Kurita, T., K. Morita, K. Fukuda, K. Takata, M. Uraoka, Y. Sanjo, and S. Sato (2006). **Landiolol, an ultra-short-acting beta 1-adrenoceptor antagonist, does not alter the electroencephalographic effect of isoflurane in swine model.** *British Journal of Anaesthesia* 96(5): 602-7. ISSN: 0007-0912.

Abstract: BACKGROUND: beta-Adrenergic blocking agents may interact with anaesthetics, and several studies suggest that beta-blockers attenuate electroencephalographic responses during general anaesthesia. We have investigated the influence of landiolol, an ultra-short-acting beta 1-adrenoceptor antagonist, on the electroencephalographic effect of isoflurane in pigs. METHODS: Ten swine were anaesthetized through inhalation of 2% isoflurane. The inhalational concentration was then decreased to 0.5% and maintained for 25 min, before being returned to 2% and maintained for a further 25 min (control period). After control measurements, infusion of landiolol (at 0.125 mg kg(-1) min(-1) for 1 min, and then at 0.04 mg kg(-1) min(-1)) was started. After a 20 min stabilization period, the inhalational concentration was varied as in the control period (40 gamma landiolol). Finally, infusion of landiolol was increased from 0.04 to 0.2 mg kg(-1) min(-1), and after a 20 min

stabilization period, the inhalational concentration was again varied as in the control period (200 gamma landiolol). End-tidal isoflurane concentrations and spectral edge frequencies were recorded throughout the study. Analysis of the pharmacodynamics was performed using a sigmoidal inhibitory maximal effect model for spectral edge frequency vs effect-site concentration. RESULTS: There were no significant differences in the effect of isoflurane among the conditions used. Landiolol did not shift the concentration-effect relationship [the effect-site concentration that produced 50% of the maximal effect was 1.35 (0.17)% under control conditions, 1.30 (0.12)% at 40 gamma landiolol, and 1.38 (0.30)% at 200 gamma landiolol]. CONCLUSION: Landiolol does not alter the electroencephalographic effect of isoflurane.

Descriptors: adrenergic beta antagonists pharmacology, anesthetics, inhalation pharmacology, electroencephalography drug effects, isoflurane pharmacology, morpholines pharmacology, urea analogs and derivatives, dose response relationship, drug, drug interactions, hemodynamic processes drug effects, models, animal, receptors, adrenergic, beta 1 antagonists and inhibitors, swine, urea pharmacology.

Kurita, T., K. Morita, K. Fukuda, M. Uraoka, K. Takata, Y. Sanjo, and S. Sato (2005). **Influence of hypovolemia on the electroencephalographic effect of isoflurane in a swine model.** *Anesthesiology* 102(5): 948-53. ISSN: 0003-3022.

Abstract: BACKGROUND: Hypovolemia alters the effect of several intravenous anesthetics by influencing pharmacokinetics and end-organ sensitivity. The authors investigated the influence of hypovolemia on the effect of an inhalation anesthetic, isoflurane, in a swine hemorrhage model. METHODS: Eleven swine were studied. After animal preparation with inhalation of 2% isoflurane anesthesia, the inhalation concentration was decreased to 0.5% and maintained at this level for 25 min before being returned to 2% (control). After 25 min, hypovolemia was induced by removing 14 ml/kg of the initial blood volume via an arterial catheter. After a 25-min stabilization period, the inhalation concentration was decreased to 0.5%, maintained at this level for 25 min, and then returned to 2% (20% bleeding). After another 25 min, a further 7 ml/kg blood was collected, and the inhalation concentration was altered as before (30% bleeding). End-tidal isoflurane concentrations and an electroencephalogram were recorded throughout the study. Spectral edge frequency was used as a measure of the isoflurane effect, and pharmacodynamics were characterized using a sigmoidal inhibitory maximal effect model for the spectral edge frequency versus end-tidal concentration. RESULTS: There was no significant difference in the effect of isoflurane among the conditions used. Hypovolemia did not shift the concentration-effect relation (the effect site concentration that produced 50% of the maximal effect was 1.2 +/- 0.2% under control conditions, 1.2 +/- 0.2% with 20% bleeding, and 1.1 +/- 0.2% with 30% bleeding). CONCLUSIONS: Hypovolemia does not alter the electroencephalographic effect of isoflurane, in contrast to several intravenous anesthetics.

Descriptors: anesthetics, inhalation pharmacology, electroencephalography drug effects, hypovolemia physiopathology, isoflurane pharmacology, anesthetics, inhalation pharmacokinetics, blood gas analysis, dose response relationship, drug, hematocrit, hemodynamic processes drug effects, hemorrhage physiopathology, isoflurane pharmacokinetics, lactic acid blood, swine.

Kurita, T., K. Morita, K. Fukuda, M. Uraoka, K. Takata, Y. Sanjo, and S. Sato (2005). **Influence of hemorrhagic shock and subsequent fluid resuscitation on the electroencephalographic effect of isoflurane in a swine model.** *Anesthesiology* 103(6): 1189-94. ISSN: 0003-3022.

Abstract: BACKGROUND: The authors have previously reported that hemorrhage does not alter the electroencephalographic effect of isoflurane under conditions of compensated hemorrhagic shock. Here, they have investigated the influence of decompensated hemorrhagic shock and subsequent fluid resuscitation on the electroencephalographic effect of isoflurane. METHODS: Twelve swine were anesthetized through inhalation of 2% isoflurane. The inhalational concentration was then decreased to 0.5% and maintained for 25 min, before being returned to 2% and maintained for 25 min (control period). Hemorrhagic shock was then induced by removing 28 ml/kg blood over 30 min. After a 30-min stabilization period, the inhalational concentration was varied as in the control period. Finally, fluid infusion was performed over 30 min using a volume of hydroxyethyl starch equivalent to the blood withdrawn. After a 30-min stabilization period, the inhalational concentration was again varied as in the control period. End-tidal isoflurane concentrations and spectral edge frequency were recorded throughout the study. The pharmacodynamics were characterized using a sigmoidal inhibitory maximal effect model for spectral edge frequency versus effect site concentration. RESULTS: Decompensated hemorrhagic shock slightly but significantly shifted the concentration-effect relation to the left, demonstrating a 1.12-fold decrease in the effect site concentration required to achieve 50% of the maximal effect in the spectral edge frequency. Fluid resuscitation reversed the onset of isoflurane, which was delayed by hemorrhage, but did not reverse the increase in end-organ sensitivity. CONCLUSIONS: Although decompensated hemorrhagic shock altered the electroencephalographic effect of isoflurane regardless of fluid resuscitation, the change seemed to be minimal, in contrast to several intravenous anesthetics.

Descriptors: anesthetics, inhalation pharmacology, electroencephalography drug effects, isoflurane pharmacology, resuscitation, shock, hemorrhagic physiopathology, anesthetics, inhalation pharmacokinetics, blood gas analysis, fluid therapy, hemodynamic processes drug effects, hetastarch therapeutic use, isoflurane pharmacokinetics, plasma substitutes therapeutic use, shock, hemorrhagic drug therapy, swine.

Kurita, T., K. Morita, T. Kazama, and S. Sato (2002). **Influence of cardiac output on plasma propofol concentrations during constant infusion in swine.** *Anesthesiology* 96(6): 1498-503. ISSN: 0003-3022.

Abstract: BACKGROUND: As propofol is a high-clearance drug, plasma propofol concentrations can be influenced by cardiac output (CO), which can easily change in response to several factors. If propofol is metabolized in the lungs, the difference between pulmonary and arterial propofol concentrations might also be affected by CO. The objective of the current study was to assess how much plasma propofol concentrations are affected by CO and to determine how much the lungs take part in propofol elimination and in concentration changes affected by CO in anesthetized swine. METHODS: Thirteen swine were studied. Propofol was administered via a peripheral vein at a rate of 6 mg x kg(-1) x h(- 1), and blood samples were simultaneously collected from pulmonary and femoral arteries at 0, 2, 3.5, 5, 7, 10, 20, and 30 min and at 20-min intervals up to 270 min. After 90 min of sampling (baseline 1), CO increased in response to a continuous infusion of dobutamine (20 microg x kg(-1) x min(- 1); high-CO state); the infusion was then stopped, and CO was allowed to return to baseline (baseline 2). Finally, CO decreased with the administration of proprano-

lol (2.0-4.0 mg administered intravenously; low-CO state). Each hemodynamic status was maintained for 1 h. RESULTS: As CO increased 36% from baseline 1, plasma propofol concentrations decreased by 18% from baseline 1, and as CO decreased 42% from baseline 1, plasma propofol concentrations increased by 70% from baseline 1. Plasma propofol concentrations can be expressed by the following equation: plasma propofol concentration (micrograms per milliliter) = 6.51/CO (l/min) + 1.11 ($r = 0.78$, $P < 0.0001$). No significant differences were observed between plasma propofol concentrations in pulmonary and femoral arteries in any state, and CO caused no apparent differences between pulmonary and arterial propofol concentrations. CONCLUSIONS: An inverse relation was observed between CO and propofol concentrations. The lungs appear to have a minor effect on plasma propofol concentrations during constant infusion in anesthetized swine.

Descriptors: anesthetics, intravenous blood, cardiac output, propofol blood, femoral artery metabolism, infusions, intravenous, propofol administration and dosage, pulmonary artery metabolism, swine.

Kurita, T., K. Morita, T. Kazama, and S. Sato (2003). **Comparison of isoflurane and propofol-fentanyl anaesthesia in a swine model of asphyxia.** *British Journal of Anaesthesia* 91(6): 871-7. ISSN: 0007-0912.

Abstract: BACKGROUND: There have been few studies comparing the response to asphyxia and the effectiveness of typical cardiopulmonary resuscitation (CPR) using exogenous epinephrine administration and manual closed-chest compression between total intravenous anaesthesia (TIVA) and inhalational anaesthesia. METHODS: Twenty pigs were randomly assigned to two study groups anaesthetized using either 2% end-tidal isoflurane (n=10) or propofol (12 mg x kg(-1) h(-1))-fentanyl (50 microg x kg(-1)) (n=10). Asphyxia was induced by clamping the tracheal tube until the mean arterial pressure (MAP) decreased to 40% of the baseline value (40% MAP time). The tracheal tube was declamped at that point, and CPR was performed. Haemodynamic parameters and blood samples were obtained before the induction of asphyxia, at 1-min intervals during asphyxia, and 1, 2, 3, 5, 10, 30 and 60 min after asphyxia. RESULTS: TIVA maintained the MAP against hypoxia-hypercapnia stress significantly longer than isoflurane anaesthesia (mean (SD) 40% MAP time 498 (95) and 378 (104) s respectively). In all animals in the isoflurane group, spontaneous circulation returned within 1 min of the start of CPR. In six of the TIVA animals, spontaneous circulation returned for 220 (121) s; spontaneous circulation did not return within 5 min in the remaining four animals. CONCLUSIONS: Although TIVA is less prone than isoflurane anaesthesia to primary cardiovascular depression leading to asphyxia, TIVA is associated with reduced effectiveness of CPR in which resuscitation because of asphyxic haemodynamic depression occurs.

Descriptors: anesthetics, inhalation pharmacology, anesthetics, intravenous pharmacology, asphyxia physiopathology, isoflurane pharmacology, anesthetics, combined pharmacology, anesthetics, intravenous blood, asphyxia therapy, blood pressure drug effects, cardiopulmonary resuscitation, disease models, animal, epinephrine blood, epinephrine therapeutic use, fentanyl pharmacology, norepinephrine blood, propofol blood, propofol pharmacology, swine.

Kurita, T., K. Takata, M. Uraoka, K. Morita, and S. Sato (2007). **Landiolol, an ultra short-acting beta1-adrenoceptor antagonist, does not alter the minimum alveolar anesthetic concentration of isoflurane in a swine model.** *Anesthesia and Analgesia* 105(3): 656-60.

Abstract: BACKGROUND: We previously reported that landiolol, an ultra-short-acting beta1-adrenoceptor antagonist, does not alter the electroencephalographic effect of isoflurane. Here, we investigated the influence of landiolol on the minimum alveolar anesthetic concentration (MAC) of isoflurane required to prevent movement in response to a noxious stimulus in 50% of subjects. METHODS: Ten swine (29.0 +/- 3.4 kg) were anesthetized by inhalation of isoflurane. MAC was determined using the dewclaw clamp technique, in which movement in response to clamping is recorded. After determination of MAC in the baseline period, an infusion of landiolol (0.125 mg x kg(-1) x min(-1) for 1 min, then 0.04 mg x kg(-1) x min(-1)) was started. After a 20-min stabilization period, MAC was again assessed (0.04 mg x kg(-1) x min(-1) landiolol). The infusion of landiolol was then increased from 0.04 to 0.2 mg x kg(-1) x min(-1), and after a 20-min stabilization period, MAC was again assessed (0.2 mg x kg(-1) x min(-1) landiolol). Finally, the infusion of landiolol was stopped, and after a 20-min stabilization period, MAC was assessed for a fourth time (Baseline 2). RESULTS: Landiolol clearly attenuated the increases in heart rate and mean arterial blood pressure that occurred in response to the dewclaw clamp, but did not alter the MAC of isoflurane. CONCLUSIONS: Landiolol does not alter the antinociceptive effect of isoflurane. This result, combined with that from our previous work, also suggests that landiolol does not influence the anesthetic potency of inhaled anesthetics.

Descriptors: adrenergic beta antagonists pharmacology, anesthetics, inhalation metabolism, isoflurane metabolism, morpholines pharmacology, pulmonary alveoli drug effects, receptors, adrenergic, beta 1 antagonists and inhibitors, urea analogs and derivatives, administration, inhalation, anesthetics, inhalation administration and dosage, blood pressure drug effects, cardiac output drug effects, consciousness drug effects, dose response relationship, drug, heart rate drug effects, isoflurane administration and dosage, models, animal, pain measurement, pain threshold drug effects, pulmonary alveoli metabolism, receptors, adrenergic, beta 1 metabolism, swine, urea pharmacology.

Kurth, C.D., M. Priestley, H.M. Watzman, J. McCann, and J. Golden (2001). **Desflurane confers neurologic protection for deep hypothermic circulatory arrest in newborn pigs.** *Anesthesiology* 95(4): 959-64. ISSN: 0003-3022.

Abstract: BACKGROUND: Cardiopulmonary bypass (CPB) and deep hypothermic circulatory arrest (DHCA), as used for infant heart surgery, carry a risk of ischemic neurologic injury. Volatile anesthetics have neuroprotective properties against both global and focal ischemia at normothermia. The authors examined the hemodynamic and neuroprotective effects of desflurane in a piglet CPB-DHCA model. METHODS: Twenty piglets aged 5-10 days received a desflurane- (6-9% expired) or fentanyl-based anesthetic before and during CPB (before and after DHCA). DHCA lasted 90 min at 19 degrees C brain. Cardiovascular variables (heart rate, arterial pressure, blood gases, glucose, brain temperature) were monitored. On postoperative day 2, neurologic and histologic outcomes were determined. RESULTS: Cardiovascular variables before, during, and after CPB were physiologically similar between groups. The desflurane group had better neurologic performance (P = 0.023) and greater postoperative weight gain (P = 0.04) than the fentanyl group. In neocortex, the desflurane group had less tissue damage (P = 0.0015) and fewer dead neurons (P = 0.0015) than the fentanyl group. Hippocampal tissue damage was less in the desflurane group (P = 0.05), but overall, neuronal cell counts in the CA1 sector of the right hippocampus were similar to those in the fentanyl group. CONCLUSIONS: Desflurane-based anesthesia yields hemodynamics during CPB with DHCA that are similar to those with fentanyl-based anesthesia.

However, desflurane-based anesthesia improves neurologic and histologic outcomes of CPB-DHCA in comparison with outcomes with fentanyl-based anesthesia.
Descriptors: anesthetics, inhalation pharmacology, heart arrest prevention and control, hypothermia complications, isoflurane pharmacology, neuroprotective agents, animals, newborn, behavior, animal drug effects, brain pathology, cardiopulmonary bypass, heart arrest etiology, hemodynamic processes drug effects, isoflurane analogs and derivatives, swine, time factors.

Lahrmann, K.H. (2005). **Castration of piglets without or with general anaesthesia (azaperone-ketamine): practicability, animal welfare, economy [Castracion de lechones con anestesia general: factibilidad, bienestar animal y economia**. *SUIS*(18): 22-29.
Descriptors: anesthesia, azaperone-ketamine protocol., animal welfare, castration, European Union, pigs.
Language of Text: Spanish, Summary in English.

Lahrmann, K.H. (2006). **Clinical and experimental studies on general anesthesia with ketamine/azaperone in the pig [Klinisch-experimentelle Untersuchungen zur Ketamin/Azaperon-Allgemeinanasthesie bei Schweinen.}**. *Praktische Tierarzt* 87(9): 713-725. ISSN: 0032-681X.
NAL Call Number: 41.8 P882
Descriptors: adverse effects, anesthesia, anesthetics, analgesia, azaperone, diagnosis, dosage effects, drug therapy, hypothermia, ketamine, piglets, potency, surgery.
Language of Text: German, Summary in English.

Lahrmann, K.H., M. Kmiec, and R. Stecher (2006). **Piglet castration with ketamine/azaperone-anaesthesia: concurring with animal welfare, practical, but economic? [Die Saugferkelkastration mit der Ketamin/Azaperon-Allgemein-anasthesie: tierschutzkonform, praktikabel, aberwirtschaftlich?]**. *Praktische Tierarzt* 87(10): 802-809. ISSN: 0032-681X.
NAL Call Number: 41.8 P882
Descriptors: anesthesia, anesthetics, animal health, animal welfare, azaperone, castration, economic analysis, growth, hypothermia, ketamine, pain, piglets, surgery, survival.
Language of Text: German, Summary in English.

Lang, S.A., B. Tsui, and T. Grau (2003). **New avenues of epidural research.** *Anesthesia and Analgesia* 97(1): 292-3. ISSN: 0003-2999.
Descriptors: anesthesia, epidural adverse effects, epidural space physiology, anesthesia, epidural methods, electric stimulation, epidural space ultrasonography, spinal nerve roots physiology, swine.
Notes: Comment On: Anesth Analg. 2003 Jan;96(1):3-6.

Larsen, J.R., S.R. Aagaard, J.M. Hasenkam, and E. Sloth (2007). **Pre-occlusion ischaemia, not sevoflurane, successfully preconditions the myocardium against further damage in porcine in vivo hearts.** *Acta Anaesthesiologica Scandinavica* 51(4): 402-9. ISSN: 0001-5172.
Abstract: BACKGROUND: Sevoflurane is proposed to possess important tissue protective effects based on experimental ischaemia-reperfusion studies from models with collateral coronary flow, unlike that of the normal human or the porcine heart. The objective was to evaluate the infarct-reducing capability of pre-ischaemic sevoflurane inhalation on myocar-

dial infarct size in a porcine model. METHODS AND MATERIALS: The study comprised 33 pigs under pentobarbital anaesthesia. Animals were divided into three groups: control (CON), sevoflurane intervention (SEVO) and ischaemic preconditioning (IP). The distal left anterior descending coronary artery was occluded for 40 min with a percutaneous coronary intervention catheter. Before occlusion, group IP underwent two 5-min ischaemia cycles, whereas SEVO received two 5-min sevoflurane 4%v/v inhalation cycles. Animals were reperfused for 150 min. We then measured risk area (AAR) and infarct size (IS) after tetrazolium staining. The [IS/AAR-ratio] was calculated. Haemodynamics and transthoracic tissue-Doppler echocardiography were monitored. RESULTS: Control animals developed a myocardial infarction in 46.4 (+/- 6.2)% (mean +/- SEM) of the AAR. Both SEVO and IP groups had infarction mitigated, to 34.4 (5.7)% and 23.1 (5.3)%, respectively; however, only in the IP group was this significant. No significant differences between groups with respect to AAR, haemodynamics or echocardiographic variables were found. CONCLUSION: Pre-ischaemic sevoflurane was found to reduce the extent of myocardial necrosis, but the change was not significant, whereas IP reduced IS by 50% (P= 0.038). Cardioprotection is species related and no previous results from porcine models have found sevoflurane to reduce IS. Anaesthetic washout, insufficient exposure or collateral coronary blood supply, dissimilar to human, may account for positive results in rodent models.

Descriptors: anesthetics, inhalation pharmacology, ischemic preconditioning methods, methyl ethers pharmacology, myocardial infarction prevention and control, blood pressure drug effects, cardiotonic agents administration and dosage, coronary circulation drug effects, disease models, animal, heart rate drug effects, necrosis prevention and control, severity of illness index, swine, time factors, treatment outcome.

Lee, H.T., M. Kim, M. Jan, and C.W. Emala (2006). **Anti-inflammatory and antinecrotic effects of the volatile anesthetic sevoflurane in kidney proximal tubule cells.** *American Journal of Physiology. Renal Physiology* 291(1): F67-78. ISSN: 0363-6127.

Abstract: Renal ischemia-reperfusion (IR) injury is a major clinical problem without effective therapy. We recently reported that volatile anesthetics protect against renal IR injury, in part, via their anti-inflammatory properties. In this study, we demonstrate the anti-inflammatory and antinecrotic effects of sevoflurane in cultured kidney proximal tubule cells and probed the mechanisms of sevoflurane-induced renal cellular protection. To mimic inflammation, human kidney proximal tubule (HK-2) cells were treated with tumor necrosis factor-alpha (TNF-alpha; 25 ng/ml) in the presence or absence of sevoflurane. In addition, we studied the effects of sevoflurane pretreatment on hydrogen peroxide (H2O2)-induced necrotic cell death in HK-2 or porcine proximal tubule (LLC-PK1) cells. We demonstrate that sevoflurane suppressed proinflammatory effects of TNF-alpha evidenced by attenuated upregulation of proinflammatory cytokine mRNA (TNF-alpha, MCP-1) and ICAM-1 protein and reduced nuclear translocation of the proinflammatory transcription factors NF-kappaB and AP-1. Sevoflurane reduced necrotic cell death induced with H2O2 in HK-2 cells as well as in LLC-PK1 cells. Sevoflurane treatment resulted in phosphorylation of prosurvival kinases, ERK and Akt, and increased de novo HSP-70 protein synthesis without affecting the synthesis of HSP-27 or HSP-32. We conclude that sevoflurane has direct anti-inflammatory and antinecrotic effects in vitro in a renal cell type particularly sensitive to injury following IR injury. These mechanisms may, in part, account for volatile anesthetics' protective effects against renal IR injury.

Descriptors: anesthetics, inhalation pharmacology, inflammation physiopathology, kidney

cortex necrosis physiopathology, kidney tubules, proximal drug effects, methyl ethers pharmacology, cell line, cell survival drug effects, cell survival physiology, enzyme activation drug effects, enzyme activation physiology, epithelial cells chemistry, epithelial cells drug effects, epithelial cells physiology, extracellular signal regulated map kinases metabolism, gene expression regulation drug effects, gene expression regulation physiology, hsp70 heat shock proteins metabolism, hydrogen peroxide pharmacology, intercellular adhesion molecule 1 analysis, intercellular adhesion molecule 1 genetics, intercellular adhesion molecule 1 physiology, kidney tubules, proximal chemistry, kidney tubules, proximal physiopathology, nf kappa b metabolism, protein serine threonine kinases metabolism, proto oncogene proteins c akt metabolism, rna, messenger analysis, signal transduction drug effects, signal transduction physiology, swine, transcription factor ap 1 metabolism, tumor necrosis factor alpha pharmacology, tumor necrosis factor alpha physiology.

Lee, P.J., N. Ahmad, R. Langer, S. Mitragotri, and V. Prasad Shastri (2006). **Evaluation of chemical enhancers in the transdermal delivery of lidocaine.** *International Journal of Pharmaceutics* 308(1-2): 33-9. ISSN: 0378-5173.

NAL Call Number: RS122.A1I5

Abstract: The effect of various classes of chemical enhancers was investigated for the transdermal delivery of the anesthetic lidocaine across pig and human skin in vitro. The lipid disrupting agents (LDA) oleic acid, oleyl alcohol, butenediol, and decanoic acid by themselves or in combination with isopropyl myristate (IPM) showed no significant flux enhancement. However, the binary system of IPM/n-methyl pyrrolidone (IPM/NMP) improved drug transport. At 2% lidocaine dose, this synergistic enhancement peaked at 25:75 (v/v) IPM:NMP with a steady state flux of 57.6 +/- 8.4 microg cm(-2) h(-1) through human skin. This observed flux corresponds to a four-fold enhancement over a 100% NMP solution and over 25-fold increase over 100% IPM at the same drug concentration ($p < 0.001$). NMP was also found to co-transport through human skin with lidocaine free base and improve enhancement due to LDA. These findings allow a more rational approach for designing oil-based formulations for the transdermal delivery of lidocaine free base and similar drugs.

Descriptors: anesthetics, local administration and dosage, drug delivery systems, lidocaine administration and dosage, pharmaceutic aids pharmacology, skin absorption drug effects, administration, cutaneous, anesthetics, local chemistry , anesthetics, local metabolism, drug combinations, hydrophobicity, lidocaine chemistry, lidocaine metabolism, myristates administration and dosage, myristates pharmacology, pharmaceutic aids administration and dosage, pyrrolidinones administration and dosage, pyrrolidinones pharmacology, solubility, swine.

Lee, Y.S., J. Wan, B.J. Kim, M.A. Bae, and B.J. Song (2006). **Ubiquitin-dependent degradation of p53 protein despite phosphorylation at its N terminus by acetaminophen.** *Journal of Pharmacology and Experimental Therapeutics, The* 317(1): 202-8. ISSN: 0022-3565.

NAL Call Number: 396.8 J82

Abstract: We previously reported that acetaminophen (APAP, 4-hydroxyacetanilide) caused apoptosis of C6 glioma cells. Therefore, we hypothesized that the level of p53, which usually stimulates apoptosis, might be increased after APAP exposure. However, APAP exposure for 24 h markedly decreased the p53 content and its downstream target p21 in a concentration-dependent manner. Reduction of p53 was not accompanied by a decrease in p53 mRNA in C6 glioma cells, suggesting that p53 was mainly affected at the protein level. Unexpectedly,

APAP stimulated phosphorylation of p53 at Ser15, Ser20, and Ser37, which usually elevates p53 content. However, phosphorylation of these residues did not prevent APAP-induced decrease in p53. The p53 reduction was independent from the level of phospho-Akt, which is known to promote p53 degradation. Immunoblot analysis of the immunoprecipitated p53 revealed that increased amounts of murine double minute 2 (mdm2) and ubiquitin were bound to p53 during its degradation. Lactacystin and N-benzoyloxycarbonyl (Z)-Leu-Leu-leucinal (MG132), inhibitors of proteasomal proteolysis, prevented the decrease, supporting the proteasomal degradation of p53 upon APAP exposure. Pretreatment with chlormethiazole, an inhibitor of ethanol-inducible CYP2E1, significantly lowered the CYP2E1 enzyme activity and the rate of APAP-induced cell death while it prevented the reduction of p53 and p21 in C6 glioma cells. A nontoxic analog of APAP, 3-hydroxyacetanilde, did not reduce p53 and p21 contents in C6 glioma cells and LLC-PK1 porcine kidney cells. Taken together, our results show that APAP or its reactive metabolite(s) can directly reduce the p53 content through mdm2-mediated ubiquitin conjugation, despite phosphorylation of p53 at its N terminus.

Descriptors: acetaminophen pharmacology, analgesics, non narcotic pharmacology, tumor suppressor protein p53 metabolism, ubiquitin physiology, cell death drug effects, cell line, tumor, cyclin dependent kinase inhibitor p21 metabolism, cytochrome p 450 cyp2e1 metabolism, down regulation, llc pk1 cells, phosphorylation, rats, swine.

Lefrant, J.Y., J.E. de La Coussaye, J. Ripart, L. Muller, L. Lalourcey, P.A. Peray, X. Mazoit, A. Sassine, and J.J. Eledjam (2001). **The comparative electrophysiologic and hemodynamic effects of a large dose of ropivacaine and bupivacaine in anesthetized and ventilated piglets.** *Anesthesia and Analgesia* 93(6): 1598-605, Table of Contents. ISSN: 0003-2999.

Abstract: Ropivacaine is less potent and less toxic than bupivacaine. We administered these two local anesthetics in a cardiac electrophysiologic model of sodium thiopental-anesthetized and ventilated piglets. After assessing the stability of the model, bupivacaine (4 mg/kg) and ropivacaine (6 mg/kg) were given IV in two groups (n = 7) of piglets. No alteration in biological variables was reported throughout the study. Bupivacaine and ropivacaine similarly decreased mean aortic pressure from 99 +/- 22 to 49 +/- 31 mm Hg and from 87 +/- 17 to 58 +/- 28 mm Hg, respectively, and decreased the peak of the first derivative of left ventricular pressure from 1979 +/- 95 to 689 +/- 482 mm Hg/s and from 1963 +/- 92 to 744 +/- 403 mm Hg/s, respectively. Left ventricular end-diastolic pressure was similarly increased from 6 +/- 5 to 9 +/- 5 mm Hg and from 6 +/- 4 to 12 +/- 4 mm Hg, respectively. Bupivacaine and ropivacaine similarly lengthened the cardiac cycle length (R-R; from 479 +/- 139 to 706 +/- 228 ms and from 451 +/- 87 to 666 +/- 194 ms, respectively), atria His (from 71 +/- 15 to 113 +/- 53 ms and from 64 +/- 6 to 86 +/- 10 ms, respectively), and QTc (QTc = QT x R-R(-0.5), Bazett formula; from 380 +/- 71 to 502 +/- 86 ms and from 361 +/- 33 to 440 +/- 56 ms, respectively) intervals. Bupivacaine altered to a greater extent the PQ (the onset of the P wave to the Q wave of the QRS complex) (from 97 +/- 20 to 211 +/- 60 ms versus from 91 +/- 8 to 145 +/- 38 ms, $P < 0.05$), QRS (from 58 +/- 3 to 149 +/- 34 ms versus from 60 +/- 5 to 101 +/- 17 ms, $P < 0.05$), and His ventricle interval (from 25 +/- 4 to 105 +/- 30 ms vs from 25 +/- 4 to 60 +/- 30 ms, $P < 0.05$) than ropivacaine. A 6 mg/kg ropivacaine dose induced similar hemodynamic alterations as 4 mg/kg bupivacaine. However, bupivacaine altered the variables of ventricular conduction (QRS and His ventricle) to a greater extent. IMPLICATIONS: A 6 mg/kg ropivacaine dose induced similar hemodynamic alterations as 4 mg/kg bupivacaine. However, bupivacaine altered the variables of ventricular conduction

(QRS and His ventricle) to a greater extent.
Descriptors: amides administration and dosage, anesthesia, anesthetics, local administration and dosage, bupivacaine administration and dosage, electrocardiography drug effects, hemodynamic processes drug effects, respiration, artificial, amides toxicity, anesthetics, local toxicity, bupivacaine toxicity, heart drug effects, heart conduction system drug effects, injections, intravenous, myocardial contraction drug effects, swine, ventricular pressure drug effects.

Lefrant, J.Y., L. Muller, J.E. de La Coussaye, L. Lalourcey, J. Ripart, P.A. Peray, X. Mazoit, M. Dauzat, A. Sassine, and J.J. Eledjam (2003). **Hemodynamic and cardiac electrophysiologic effects of lidocaine-bupivacaine mixture in anesthetized and ventilated piglets.** *Anesthesiology* 98(1): 96-103. ISSN: 0003-3022.
Abstract: BACKGROUND: The sensory blockade induced by a lidocaine-bupivacaine mixture combines the faster onset of lidocaine and the longer duration of bupivacaine. The current study compared the effects of large doses lidocaine (16 mg/kg), bupivacaine (4 mg/kg), and a mixture of 16 mg/kg lidocaine-4 mg/kg bupivacaine on hemodynamic and cardiac electrophysiologic parameters in anesthetized and ventilated piglets. METHODS: After carotid artery cannulation, a double micromanometer measured mean aortic pressure, left ventricular end diastolic pressure, and the first derivative of left ventricular pressure. Electrocardiogram recording and a bipolar electrode catheter measured RR, PQ, QRS, QT C, JT C, AH, and HV intervals. Lidocaine, bupivacaine, or the mixture was administered intravenously over 30 s, and studied parameters were measured throughout 30 min. RESULTS: Mean aortic pressure decreased in all groups ($P < 0.05$). The first derivative of left ventricular pressure was decreased in all groups ($P < 0.001$) but to a greater extent with the mixture compared with lidocaine ($P < 0.04$). RR, QT C, and JT C intervals were similarly increased in all groups ($P < 0.05$). In all groups, PQ, AH, HV, and QRS intervals were widened ($P < 0.001$). The lengthening of PQ was greater with bupivacaine ($P < 0.02$). The lengthening of AH was greater and delayed with bupivacaine compared with lidocaine ($P < 0.03$). The lengthening of HV and the widening of QRS were greater and delayed with bupivacaine ($P < 0.01$). The widening of QRS was greater with the mixture than with lidocaine ($P < 0.01$). CONCLUSIONS: The alterations of ventricular conduction parameters are greater with 4 mg/kg bupivacaine than with a mixture of 16 mg/kg lidocaine-4 mg/kg bupivacaine, whereas the hemodynamic parameters are similarly altered.
Descriptors: anesthetics, local pharmacology, bupivacaine pharmacology, heart drug effects, hemodynamic processes drug effects, lidocaine pharmacology, anesthesia, body weight physiology, bupivacaine administration and dosage, drug combinations, electrocardiography drug effects, electrophysiology, heart rate drug effects, infusions, intravenous, lidocaine administration and dosage, respiration, artificial, swine.

Lichtor, J.L. (2005). **Depth of anesthesia monitors and shock.** *Anesthesiology* 102(5): 1068; Author Reply 1069-70. ISSN: 0003-3022.
Descriptors: anesthesia, anesthetics, intravenous adverse effects, electroencephalography drug effects, propofol adverse effects, shock, hemorrhagic physiopathology, anesthetics, intravenous pharmacokinetics, monitoring, intraoperative, propofol pharmacokinetics, shock, hemorrhagic metabolism, swine.
Notes: Comment On: Anesthesiology. 2004 Sep;101(3):567-8.

Lim, K.H., A.P. Halestrap, G.D. Angelini, and M.S. Suleiman (2005). **Propofol is cardioprotective in a clinically relevant model of normothermic blood cardioplegic arrest and cardiopulmonary bypass.** *Experimental Biology and Medicine Maywood, N.J* 230(6): 413-20. ISSN: 1535-3702.

NAL Call Number: QP1 .S8

Abstract: The general anesthetic propofol has been shown to be cardioprotective. However, its benefits when used in cardioplegia during cardiac surgery have not been demonstrated. In this study, we investigated the effects of propofol on metabolic stress, cardiac function, and injury in a clinically relevant model of normothermic cardioplegic arrest and cardiopulmonary bypass. Twenty anesthetized pigs, randomized to propofol treatment (n = 8) and control (n = 12) groups, were surgically prepared for cardiopulmonary bypass (CPB) and cardioplegic arrest. Doses of warm blood cardioplegia were delivered at 15-min intervals during a 60-min aortic cross-clamped period. Propofol was continuously infused for the duration of CPB and was therefore present in blood cardioplegia. Myocardial biopsies were collected before, at the end of cardioplegic arrest, and 20 mins after the release of the aortic cross-clamp. Hemodynamic parameters were monitored and blood samples collected for cardiac troponin I measurements. Propofol infusion during CPB and before ischemia did not alter cardiac function or myocardial metabolism. Propofol treatment attenuated the changes in myocardial tissue levels of adenine nucleotides, lactate, and amino acids during ischemia and reduced cardiac troponin I release on reperfusion. Propofol treatment reduced measurable hemodynamic dysfunction after cardioplegic arrest when compared to untreated controls. In conclusion, propofol protects the heart from ischemia-reperfusion injury in a clinically relevant experimental model. Propofol may therefore be a useful adjunct to cardioplegic solutions as well as being an appropriate anesthetic for cardiac surgery.

Descriptors: anesthetics, intravenous pharmacology, cardiopulmonary bypass methods, cardiotonic agents pharmacology, heart drug effects, heart arrest, induced methods, propofol pharmacology, body temperature, cardioplegic solutions administration and dosage, cardiotonic agents administration and dosage, heart physiopathology, infusions, intravenous, models, animal, myocardial ischemia prevention and control, propofol administration and dosage, reperfusion injury prevention and control, swine, temperature, time factors.

Linkenhoker, J.R., T.H. Burkholder, C.G.G. Linton, A. Walden, K.A. Abusakran Monday, A.P. Rosero, and C.J. Foltz (2010). **Effective and safe anesthesia for Yorkshire and Yucatan swine with and without cardiovascular injury and intervention**. *Journal of the American Association for Laboratory Animal Science* 49(3): 344-351. ISSN: 1559-6109.

Online: http://www.ncbi.nlm.nih.gov/sites/ppmc/articles/PMC2877308/

NAL Call Number: SF405.3 .A23

Abstract: The goal of this study was to identify an injectable anesthetic protocol that provides sedation sufficient for peripheral vascular catheterization, intubation, and transport while minimizing cardiovascular changes in Yorkshire and Yucatan pigs with and without cardiovascular injury and intervention (CI). Phase 1 examined the safety and efficacy of acepromazine-ketamine, diazepam -ketamine, midazolam-ketamine, and medetomidine-ketamine in 5 healthy Yorkshire pigs. For each drug combination, we obtained multiple measurements of heart rate, blood pressure, respiratory rate, temperature, sedation score, ability to catheterize and intubate, and recovery score. Phase 2 evaluated and refined the dose of the most effective Phase 1 anesthetic combination (midazolam-ketamine) in healthy and CI Yorkshire pigs (n=53 trials). Phase 3 mirrored Phase 2 but tested midazolam-ketamine in

healthy and CI Yucatan pigs (n=34 trials). Midazolam (0.5 mg/kg)-ketamine (25 to 27 mg/kg) was the most effective anesthetic combination in healthy Yorkshire pigs, but this dose was less effective in healthy Yucatan pigs and CI Yorkshire and Yucatan pigs. Midazolam -ketamine resulted in tachycardia and apnea more frequently in CI pigs than healthy pigs. This combination also caused vomiting in one CI Yucatan pig. Overall, midazolam-ketamine provided safe and effective sedation for catheterization and intubation of both healthy and CI pigs. This study suggests Yucatan pigs may require a higher dose midazolam-ketamine to achieve the same level of sedation as that in Yorkshire pigs. Although anesthetic complication rates were higher in CI pigs, our results indicate that midazolam-ketamine can be safely used for sedation of both pig breeds with and without CI.
Descriptors: acepromazine, adverse effects, anesthesia, anesthetics, catheterization, diazepam, drug combinations, injectable anesthetics, ketamine, laboratory animals, medetomidine, potency, safety, surgery, surgical operations, pigs.

Liu, D., Y. Shao, X. Luan, M. Zhang, C. Shui, and Q. Wu (2009). **Comparison of ketamine-pentobarbital anesthesia and fentanyl-pentobarbital anesthesia for open-heart surgery in minipigs.** *Lab Animal* 38(7): 234-240. ISSN: 0093-7355.
DOI: 10.1038/laban0709-234
NAL Call Number: QL55.A1L33
Descriptors: laboratory animals, miniature swine, surgery, anesthesia, ketamine, pentobarbital, fentanyl, anesthetics, pharmacokinetics, dosage, intravenous injection, adverse effects, heart rate, blood pressure, mortality, postoperative care, drug therapy, cardiovascular agents, animal models, open-heart-surgery, arterial-bypass, Internet-resource.

Loeckinger, A., A. Kleinsasser, C. Keller, A. Schaefer, C. Kolbitsch, K.H. Lindner, and A. Benzer (2002). **Administration of oxygen before tracheal extubation worsens gas exchange after general anesthesia in a pig model.** *Anesthesia and Analgesia* 95(6): 1772-6, Table of Contents. ISSN: 0003-2999.
Abstract: Administration of 100% oxygen before tracheal extubation is common clinical practice. We determined the effect of this technique on postoperative gas exchange in a porcine model using the multiple inert gas elimination technique. After general anesthesia with mechanical ventilation for a period of 30 min (inspiratory fraction of oxygen of 0.3), anesthesia was discontinued, and the pigs were randomized to an inspiratory fraction of oxygen of 0.3 or 1.0 until they could be safely extubated. Thirty minutes after extubation while breathing air, blood flow to poorly ventilated units had significantly increased in pigs that had been administered 100% oxygen as compared with those receiving 30% oxygen (17% +/- 15% versus 7% +/- 5%; P = 0.009). We conclude that exposure to 100% oxygen before extubation may cause an undesirable alteration in gas exchange. IMPLICATIONS: Blood flow to lung units with a low V(A)/Q ratio was significantly larger in pigs that had been exposed to 100% oxygen before extubation as compared with those exposed to 30% oxygen before extubation.
Descriptors: anesthesia, general, intubation, intratracheal, oxygen toxicity, pulmonary gas exchange, models, animal, swine, ventilation perfusion ratio.
Notes: Comment In: Anesth Analg. 2002 Dec;95(6):1472-3.

Loepke, A.W., M.A. Priestley, S.E. Schultz, J. McCann, J. Golden, and C.D. Kurth (2002). **Desflurane improves neurologic outcome after low-flow cardiopulmonary bypass in newborn pigs.** *Anesthesiology* 97(6): 1521-7. ISSN: 0003-3022.

Abstract: BACKGROUND: Despite improvements in neonatal heart surgery, neurologic complications continue to occur from low-flow cardiopulmonary bypass (LF-CPB) and deep hypothermic circulatory arrest (DHCA). Desflurane confers neuroprotection against ischemia at normothermia and for DHCA. This study compared neurologic outcome of a desflurane-based with a fentanyl-based anesthetic for LF-CPB. METHODS: Thirty piglets aged 1 week received either fentanyl-droperidol (F/D), desflurane 4.5% (Des4.5), or desflurane 9% (Des9) during surgical preparation and CPB. Arterial blood gases, glucose, heart rate, arterial pressure, brain temperature, and cerebral blood flow (laser Doppler flowmetry) were recorded. After CPB cooling (22 degrees C brain) using pH-stat strategy, LF-CPB was performed for 150 min followed by CPB rewarming, separation from CPB, and extubation. On postoperative day 2, functional and histologic outcomes were assessed. RESULTS: Cardiovascular variables were physiologically similar between groups before, during, and after LF-CPB. Cerebral blood flow during LF-CPB (13% of pre-CPB value) did not differ significantly between the groups. Functional disability was worse in F/D than in Des9 (P = 0.04) but not Des4.5 (P = 0.1). In neocortex, histopathologic damage was greater in F/D than in Des4.5 (P = 0.03) and Des9 (P = 0.009). In hippocampus, damage was worse in F/D than in Des9 (P = 0.01) but not Des4.5 (P = 0.08). The incidences of ventricular fibrillation during LF-CPB were 90, 60, and 10% for F/D, Des4.5 (P = 0.06), and Des9 (P = 0.0002), respectively. CONCLUSIONS: Desflurane improved neurologic outcome following LF-CPB compared with F/D in piglets, indicated by less functional disability and less histologic damage, especially with Des9. Desflurane may have produced cardiac protection, suggested by a lower incidence of ventricular fibrillation.

Descriptors: anesthetics, inhalation therapeutic use, cardiopulmonary bypass, hemodynamic processes drug effects, isoflurane analogs and derivatives, isoflurane therapeutic use, neuroprotective agents therapeutic use, postoperative complications prevention and control, ventricular fibrillation prevention and control, anesthetics, inhalation administration and dosage, animals, newborn, disease models, animal, dose response relationship, drug, isoflurane administration and dosage, neuroprotective agents administration and dosage, swine, ventricular fibrillation etiology.

Lowe, J.F. (2004). **Biopsy of tonsils ante-mortem without anaesthesia [Biopsia de amigdalas ante-mortem sin anestesia.]**. *SUIS*(5): 32-34.

Descriptors: biopsy, diagnosis, techniques, nonanesthetic method, tonsils, pigs.

Language of Text: Spanish.

Lykkegaard, K., B. Lauritzen, L. Tessem, P. Weikop, and O. Svendsen (2005). **Local anaesthetics attenuates spinal nociception and HPA-axis activation during experimental laparotomy in pigs.** *Research in Veterinary Science* 79(3): 245-51. ISSN: 0034-5288.

NAL Call Number: 41.8 R312

Abstract: The effect of local anaesthetics on spinal nociception and activation of the hypothalamic-pituitary-adrenal axis (HPA-axis) was examined in a porcine model of abdominal surgery. A standardised laparotomy without visceral involvement was performed on 24 pigs. One group received a unilateral infiltration of mixed lidocaine and bupivacaine in skin, muscle and peritoneum of the surgical area prior to surgery (n=12), while local anaesthetics

were replaced by isotonic saline in a second group (n=12). A sham group was subjected to anaesthesia (n=8), but did not undergo surgery. Two hours after surgery, half of the pigs from each group were perfused with formalin and the spinal cord was taken out for stereological quantification of the total number of Fos-like-immunoreactive (Fos-LI) neurones in the dorsal horn. Surgery with saline gave rise to a significant increase in the number of Fos-LI neurones ipsilaterally (107,001+/-16,548; p<0.001) as well as contralaterally (12,766+/-3,842; p<0.01) compared to the sham group. In animals undergoing surgery with LA, the number of Fos-LI neurones ipsilaterally was not significantly different from the sham group (p=0.78), and was reduced significantly both ipsilaterally (6960+/-1662; p<0.001) and contralaterally (3974+/-1131; p<0.05) compared to the saline group. In the other half of each group, blood samples, for determination of ACTH, cortisol, C-reactive protein and interleukin-6 concentrations, were drawn prior to and at predetermined time-points during and after surgery. Surgery with saline gave rise to dramatic increases in plasma ACTH and cortisol (p<0.01 and p<0.001, respectively) within 15 min of incision. In contrast, no changes from the initial concentrations of ACTH and cortisol were observed in pigs receiving local anaesthetics. No changes in plasma concentrations of C-reactive protein or interleukin-6 were observed in either of the groups. These results indicate that spinal nociception and HPA-axis activation caused by laparotomy in pigs can be attenuated by use of infiltration and incisional local anaesthetics prior to surgery. The present model provides a valuable tool in the evaluation of analgesic treatment during surgery, offering objective measures of both nociception and stress.

Descriptors: anesthesia, local veterinary, anesthetics, local therapeutic use, hypothalamo hypophyseal system drug effects, laparotomy veterinary, pain drug therapy, pain physiopathology, pituitary adrenal system drug effects, adrenocorticotropic hormone blood, bupivacaine therapeutic use, c reactive protein metabolism, disease models, animal, hydrocortisone blood, interleukin 6 blood, lidocaine therapeutic use, pain veterinary, swine physiology, swine diseases drug therapy, swine diseases physiopathology.

Makiranta, M.J., J.P. Jauhiainen, J.T. Oikarinen , K. Suominen, O. Tervonen, S. Alahuhta, and V. Jantti (2002). **Functional magnetic resonance imaging of swine brain during change in thiopental anesthesia into EEG burst-suppression level--a preliminary study.** *Magma New York, N.Y.* 15(1-3): 27-35. ISSN: 0968-5243.

NAL Call Number: RC78.7.N83

Abstract: Deepening anesthesia produces well known changes in electroencephalogram (EEG) and evoked potentials, differing in pathological and normal brain. Yet, it is not known how the T2*-weighted signal changes in the healthy brain during deepening anesthesia. We studied the effect of thiopental bolus on functional magnetic resonance imaging (fMRI) in the healthy brain using porcine model. In five pigs (2-3 months, 20-25 kg), the control bolus prior to fMRI resulted in a change into burst-suppression. After the recovery of continuous EEG, fMRI (4 min) was performed with a single bolus of thiopental (11.4-17.1 mg/kg) administered 1 min after the onset of imaging. This was repeated in four of five pigs. Positive (6-8%) or negative (-3 to -8%) signal intensity changes correlated to the thiopental bolus injection were seen in the group average fMRI response. Positive response was 1.6% and negative response 2.3% of the total brain region of interest (ROI) voxels. Responding voxels were distributed more prominently in the thalamic ROI (4.5%) than in the cortical ROI (2.2%). The group average of unthresholded voxel time courses showed that the net effect of thiopental bolus was a small (0.5%) but a clear positive change in the thalamic region,

while variance changed in the global level. In conclusion, this study is the first to show that significant signal intensity changes occur in fMRI response during the sudden deepening of thiopental anesthesia. However, these responses are neither anatomically constant nor global in the healthy swine brain. Copyright 2002 Elsevier Science B.V.

Descriptors: anesthesia, intravenous, brain drug effects, electroencephalography drug effects, magnetic resonance imaging methods, thiopental administration and dosage, anesthesia recovery period, blood pressure drug effects, brain physiology, brain mapping methods, cerebral cortex drug effects, cerebral cortex physiology, electroencephalography methods, feasibility studies, infusions, intravenous, reference values, reproducibility of results, sensitivity and specificity, statistics, swine, thalamus drug effects, thalamus physiology.

Malavasi, L.M., H. Augustsson, M. Jensen Waern, and G. Nyman (2005). **The effect of transdermal delivery of fentanyl on activity in growing pigs.** *Acta Veterinaria Scandinavica* 46(3): 149-57. ISSN: 0044-605X.

NAL Call Number: 41.8 AC87

Abstract: Recently, decreased activity levels have been observed in pigs treated postoperatively with transdermal delivery of fentanyl (TD-fentanyl) after isoflurane anaesthesia. Whether the change in behaviour is related to opioid-induced sedation or to insufficient pain relief remains to be investigated. This study was therefore undertaken to evaluate the effect of TD-fentanyl 50 microg h(-1) on the activity level with and without isoflurane anaesthesia. Eight pigs (25.4 +/- 5.2 kg) were submitted to a cross-over study and given two treatments; 1) fentanyl patch applied after 30 minutes of anaesthesia (treatment A/F) and 2) fentanyl patch without anaesthesia (treatment F). The pigs' behaviour was observed from a video recording instantaneously every 10 minutes for 24 h before treatments and up to 72 h after the patch attachment. Venous blood samples were taken 1, 6, 12, 24, 48 and 72 h after the patch application. The behaviour recordings showed that TD-fentanyl did not produce sedation in any pig. No differences were found between the two treatments in activity level, weight gain or serum fentanyl concentration. This concentration measured after 24 h was 0.27 +/- 0.11 ng ml(-1) and 0.47 +/- 0.40 ng ml(-1) in the A/F and F group, respectively. In conclusion, transdermal delivery of 50 microg h(-1) fentanyl did not cause inactivity in growing pigs. However, the large variations in serum fentanyl concentration indicate that drug absorption from transdermal patches is unpredictable and sometimes deficient.

Descriptors: analgesics, opioid administration and dosage, behavior, animal drug effects, fentanyl administration and dosage, swine growth and development, administration, cutaneous, analgesics, opioid blood, analgesics, opioid metabolism, anesthetics, inhalation pharmacology, chromatography, gas veterinary, cross over studies, fentanyl blood, fentanyl metabolism, isoflurane pharmacology, longitudinal studies, video recording.

Malavasi, L.M., M. Jensen Waern, M. Jacobson, A. Ryden, P. eOhagen, and G. Nyman (2006). **Effects of extradural morphine on end-tidal isoflurane concentration and physiological variables in pigs undergoing abdominal surgery: a clinical study.** *Veterinary Anaesthesia and Analgesia* 33(5): 307-312. ISSN: 1467-2987.

DOI: 10.1111/j.1467-2995.2005.00260.x

NAL Call Number: SF914 .V47

Abstract: To evaluate the effects of preoperative extradural morphine on the end-tidal isoflurane (F [smallcapital e]'ISO) concentration and on physiological variables in pigs undergoing abdominal surgery. Prospective, randomized, blinded study. Fourteen healthy

pigs (20 * left-pointing-double-angle * 4 kg) undergoing intestinal cannulation. Anaesthesia was induced with a combination of medetomidine (50 (So(Bg kg superscript -1(B) and tiletamine-zolazepam (2.5 mg kg superscript -1(B) injected intramuscularly, and was maintained with isoflurane in air and oxygen (F [smallcapital i]O subscript 2(B = 50% O subscript 2(B). In the first group, morphine (0.1 mg kg superscript -1(B) was administered extradurally before surgery. The second group received an equivalent volume of extradural saline as control. During the experiment, heart and respiratory rates, mean arterial blood pressure, tidal volume and minute ventilation were recorded every 10 minutes. The concentration of F [smallcapital e]'ISO was adjusted, according to the depth of anaesthesia, by an experienced animal nurse. Within treatment groups, time-related changes in F [smallcapital e]'ISO and physiological variables were analysed using a repeated measurement [smallcapital anova]. Differences in data between treatment groups were analysed at specific time points using a Mann-Whitney U-test. Results are presented as mean * left-pointing-double-angle * SD; $p < 0.05$ was considered as significant. After the onset of action of the morphine, the F [smallcapital e]'ISO required to maintain anaesthesia was significantly lower in the extradural morphine group compared with control. During the expected maximal effect of the drug, F [smallcapital e]'ISO was significantly lower in the morphine group (0.6 * left-pointing-double-angle * 0.2%) than in the control group (0.9 * left-pointing-double-angle * 0.2%). The decrease in F [smallcapital e]'ISO indicated that the onset of action of morphine was approximately 30 minutes after injection. No significant differences in other clinical variables were found between the groups. Pigs that received extradural morphine before abdominal surgery achieved surgical anaesthetic depth at a lower F [smallcapital e]'ISO concentration. Extradural morphine allows abdominal surgery to be performed at a lower F [smallcapital e]'ISO concentrations.

Descriptors: analgesia, swine, cardiovascular and respiratory effects, end tidal isoflurane, extradural morphine.

Malavasi, L., G. Nyman, H. Augustsson, M. Jacobson, and M. Jensen Waern (2006). **Effects of epidural morphine and transdermal fentanyl analgesia on physiology and behaviour after abdominal surgery in pigs.** *Laboratory Animals* 40(1): 16-27. ISSN: 0023-6772.

NAL Call Number: QL55.A1L3

Abstract: The objective of this work was to evaluate the physiological and behavioural effects of opioid analgesic treatment in pigs subjected to abdominal surgery. Ten Swedish Landrace x Yorkshire pigs (20 * left-pointing-double-angle * 4 kg b.w.) were submitted for intestinal cannulation. The pigs were allocated into two groups during one preoperative, one surgical and two postoperative days. All pigs were anaesthetized with medetomidine, tiletamine and zolazepam. One group was treated with epidural morphine (0.1 mg/kg) preoperatively, and transdermal fentanyl patches (50 [mu]g/kg/h) were applied behind the ear immediately after surgery. The other group received epidural saline (equivalent volume) and placebo patches. All pigs were regularly weighed and clinically examined and repeated blood samples were analysed for serum concentrations of cortisol, [beta]-endorphin and fentanyl. Pre- and postoperative behaviours were evaluated by a swine specialist blinded to the treatment, three times a day, and were also videotape recorded for a total of 84 h per pig. No differences in behaviour were noted by the observer. During the first postoperative 12 h, treated pigs did not differ in activity compared with preoperative recordings, while untreated pigs were found to be less active. The treated group started to show interest in eating immediately after anaesthesia recovery, whereas the placebo group did not. During the 12-60 h postoperative period,

the treated group had lower activity levels compared with the preoperative levels, which were similar to those in the placebo group. Treated pigs gained 0.5 * left-pointing-double-angle * 0.2 kg during the subsequent two postoperative days, whereas the untreated pigs lost weight throughout the experiment. Cortisol concentration differed immediately after the surgery: Group P had 325 * left-pointing-double-angle * 120 nmol/L and Group M 159 * left-pointing-double-angle * 49 nmol/L. [beta]-endorphin concentration did not differ between groups. The highest serum fentanyl concentration (0.37 * left-pointing-double-angle * 0.3 ng/mL) was measured 24 h postoperatively. Preoperative epidural morphine in combination with postoperative transdermal fentanyl resulted in earlier return to normal activity levels and an immediate weight gain after surgery.

Descriptors: swine, laboratory animals, pain, postoperative care, analgesia, feeding behavior, physical activity, liveweight gain, cortisol, endorphins, animal use refinement.

Maneuf, Y.P., Z.D. Luo, and K. Lee (2006). **alpha2delta and the mechanism of action of gabapentin in the treatment of pain.** *Seminars in Cell and Developmental Biology* 17(5): 565-70. ISSN: 1084-9521.

NAL Call Number: QH573

Abstract: Gabapentin is a drug that has been widely used in the treatment of chronic pain states. Despite its widespread usage, it is only recently that light has been shed on the mechanism of action of this agent. In the current review, the authors document the pharmacological, biochemical and molecular information that has led to the identification of the alpha2delta1 auxilliary subunit of voltage gated calcium channels as the target for this drug's actions.

Descriptors: amines pharmacology, analgesics pharmacology, calcium channels metabolism, cyclohexanecarboxylic acids pharmacology, gaba modulators pharmacology, pain drug therapy, gamma aminobutyric acid pharmacology, brain metabolism, brain radiography, calcium channels genetics, mice, pain physiopathology, rats, swine.

Markstrom, A., A. Hedlund, U. Sjostrand, A. Nordgren, and M. Lichtwarck Aschoff (2001). **Effects of sustained pressure application on compliance and blood gases in healthy porcine lungs.** *Acta Anaesthesiologica Scandinavica* 45(10): 1235-40. ISSN: 0001-5172.

Abstract: BACKGROUND: Short periods of sustained increase in airway pressures (Press(up)) are believed to re-open lung areas that collapsed upon induction of anaesthesia. Recruitment of alveolar surface is usually assessed in terms of changes in the pressure-volume (PV) curve. The purpose of this study was to analyse PV-curves before and after a Press(up) and to ascertain whether such changes are compatible with the concept of recruitment of lung volume. METHODS: During ketamine anaesthesia, 12 healthy piglets were subjected to a Press(up) with end-expiratory pressure (PEEP) of 12 cmH2O and end-inspiratory pressure of 40 cmH2O. Before and after Press(up), PV-curves were obtained from a slow insufflation of 630 ml at zero PEEP (ZEEP). RESULTS: Compliance was non-linear both before and after Press(up) increasing up to 300 ml and sharply decreasing thereafter. After Press(up), the entire compliance curve was shifted to a higher absolute level. Up to 100 ml and a pressure level corresponding to the lower inflection point on the PV-curve (LIP), compliance was higher before Press(up). No effects on blood gases could be observed. CONCLUSION: If the similar shape of the compliance curve corresponds to a similar chain of re-opening and overdistension events, this would imply that all volume gained by Press(up) is lost within 10 min, without explaining the higher absolute compliance following Press(up).

We speculate that a) re-opening of rapidly collapsing small airways determines the initial compliance increase; b) the lower compliance after Press(up) until LIP indicates reduced intratidal re-opening of lung regions; and c) changes in bronchomotor tone induced by Press(up) raise the absolute compliance, with a similar scenario of alveolar and small airway recruitment now taking place but at different degrees of airway stiffness.
Descriptors: anesthesia, lung physiology, positive pressure respiration, pulmonary gas exchange, airway resistance, anesthetics, dissociative, hemodynamic processes, lung compliance, pressure, prone position, respiratory mechanics, swine, tidal volume.

Martin Cancho, M.F., M.S. Carrasco Jimenez, J.R. Lima, L.J. Ezquerra, V. Crisostomo, and J. Uson Gargallo (2004). **Assessment of the relationship of bispectral index values, hemodynamic changes, and recovery times associated with sevoflurane or propofol anesthesia in pigs.** *American Journal of Veterinary Research* 65(4): 409-16. ISSN: 0002-9645.
NAL Call Number: 41.8 Am3A
Abstract: OBJECTIVE: To evaluate bispectral index (BIS) values in pigs during anesthesia maintained with sevoflurane-fentanyl or propofol-fentanyl as a predictor of changes in hemodynamic parameters and duration of recovery from anesthesia. ANIMALS: 12 pigs. PROCEDURE: Pigs were randomly allocated to undergo 1 of 2 anesthetic regimens. Anesthesia was induced with propofol (2 mg/kg, i.v.); 6 pigs were administered sevoflurane via inhalation (1 minimum alveolar concentration [MAC] at a fresh gas flow rate of 3 L/min; group I), and 6 were administered propofol (11 mg/kg/h, i.v.; group II). All pigs received fentanyl (2.5 mg/kg, i.v., q 30 min). After abdominal surgery, pigs were allowed to recover from anesthesia. Cardiovascular variables and BIS values were recorded at intervals throughout the procedure; duration of recovery from anesthesia was noted. RESULTS: No correlation was established between arterial blood pressure and BIS and between heart rate and BIS. Mean BIS at discontinuation of administration of the anesthetic agent was greater in group-II pigs (65.2 +/- 10.6 minutes) than in group-I pigs (55.8 +/- 2.9 minutes). However, recovery from anesthesia was significantly longer in group II (59.80 +/- 2.52 minutes) than in group I (9.80 +/- 2.35 minutes). CONCLUSIONS AND CLINICAL RELEVANCE: In swine anesthetized with sevoflurane or propofol and undergoing abdominal surgery, the BIS value derived from an electroencephalogram at the end of anesthesia was not useful for predicting the speed of recovery from anesthesia. Moreover, BIS was not useful as a predictor of clinically important changes in arterial blood pressure and heart rate in those anesthetized pigs.
Descriptors: anesthesia, intravenous veterinary, anesthetics, combined pharmacology, electroencephalography veterinary, fentanyl pharmacology, methyl ethers pharmacology, propofol pharmacology, sus scrofa surgery, analysis of variance, anesthesia recovery period, blood pressure drug effects, electroencephalography drug effects, heart rate drug effects.

Martin Cancho, M.F., M.S. Carrasco Jimenez, J.R. Lima, L. Luis, V. Crisostomo, and J. Uson Gargallo (2006). **The measurement of neurovegetative activity during anesthesia and surgery in swine: an evaluation of different techniques.** *Anesthesia and Analgesia* 102(5): 1333-40.
Abstract: In this study we evaluated, in 10 sevoflurane-anesthetized pigs undergoing abdominal surgery, different techniques for measuring autonomic nervous system (ANS) activity: ANSiscope index, spectral analysis of heart-rate variability, hemodynamic variables, and plasma catecholamines and cortisol levels. Animals underwent a 120-min anesthesia during which unilateral ovariectomy was performed. Cardiovascular and respiratory responses were monitored. ANSiscope indices (ANSindex sympathetic, ANSindex parasympathetic and

balANSindex) were used to monitor ANS activity. Spectral analysis was performed using an autoregressive model with a parametric method. The low frequency (LF) and high frequency (HF) components were used to interpret the power spectral density of short-term electrocardiograms (ECGs). The relationship LF/(LF+HF) reflects sympathetic activity, HF/(LF+HF) indicates parasympathetic activity, and the LF/HF ratio gives the predominance of the system. Plasma concentrations of adrenaline, noradrenaline, and cortisol were determined at different times. Correlation ($P < 0.01$) was found between the balANSindex and adrenaline levels and between LF/HF ratio and plasma adrenaline concentrations. Moreover, a significant ($P < 0.01$) correlation was found between the balANSindex and LF/HF ratio. However, no correlation was seen between the registered ANSiscope indices and hemodynamic variables. The correlation seen in this study suggests that the balANSindex could be a useful tool to monitor ANS activity during anesthesia and surgery.
Descriptors: anesthesia, general methods, hemodynamic processes physiology, ovariectomy, autonomic nervous system drug effects, autonomic nervous system physiology, blood pressure drug effects, blood pressure physiology, heart rate drug effects, heart rate physiology, hemodynamic processes drug effects, hydrocortisone blood, methyl ethers administration and dosage, swine.

Martin Cancho, M., J. Lima, L. Luis, V. Crisostomo, M. Lopez, L. Ezquerra, M. Carrasco Jimenez, and J. Uson Gargallo (2006). **Bispectral index, spectral edge frequency 95% and median frequency recorded at varying desflurane concentrations in pigs.** *Research in Veterinary Science* 81(3): 373-381. ISSN: 0034-5288.
DOI: 10.1016/j.rvsc.2006.01.003
NAL Call Number: 41.8 R312
Abstract: The objective of this study is to evaluate the usefulness of bispectral index (BIS), spectral edge frequency 95% (SEF) and median frequency (MED) in relation to a simple descriptive scale (SDS) as indicators of anaesthetic depth at different desflurane concentrations in swine. Sixteen pigs were randomly allocated to four groups. Electroencephalograms (EEG) were recorded during desflurane anaesthesia, and BIS, SEF and MED were calculated from the EEG. The agent was administered in pure oxygen at 1, 1.25, 1.5 and 1.7 MAC in randomized order. Anaesthetic depth was evaluated on a SDS. BIS decreased significantly ($P < 0.001$) at the different anaesthetic dosages used. SEF decreased significantly ($P < 0.001$) from basal to 1 MAC of desflurane. MED decreased significantly ($P < 0.001$) from basal to 1 MAC and from 1 to 1.75 MAC. Good correlation was seen between SDS scores and BIS values and between SDS scores and MED values. BIS appeared to be useful to predict changes in anaesthetic depth at clinically used dosages of inhalant anaesthesia.
Descriptors: veterinary medicine, electroencephalography, prediction, anesthetics, animal models, desflurane.

Martoft, L., E. Jensen, B. Rodriguez, P. Jorgensen, A. Forslid, and H. Pedersen (2001). **Middle-latency auditory evoked potentials during induction of thiopentone anaesthesia in pigs.** *Laboratory Animals* 35(4): 353-363. ISSN: 0023-6772.
NAL Call Number: QL55.A1L3
Abstract: A method is described for measuring middle-latency auditory evoked potentials (MLAEP) in consciously awake, non-sedated pigs during the induction of thiopentone anaesthesia (0.6 ml/kg, 2.5% thiopentone solution). It was done by using autoregressive modelling with an exogenous input (ARX). The ability to perceive pain during the induc-

tion was compared with (1) the changes in latencies and amplitudes of the MLAEP, (2) the change in a depth of anaesthesia index based on the ARX-model and (3) the change in the 95% spectral edge frequency. The pre-induction MLAEP was easily recordable and looked much like the one in man, dogs and rats. The temporal resolution in the ARX method was sufficiently high to describe the fast changes occurring during induction of thiopentone anaesthesia. As previously reported from studies in man, dogs and rats, induction of thiopentone anaesthesia resulted in significantly increased latencies and decreased amplitudes of the MLAEP trace as well as in a significantly reduced depth of anaesthesia index and spectral edge frequency. None of the changes, however, related well to the ability to react to a painful stimulus. Whether an ARX-based depth of anaesthesia index designed especially for pigs might be better than the present index (designed for man) for assessing depth of anaesthesia must await the results of further studies.
Descriptors: swine, anesthesia, hearing, thiopental, heart rate, electroencephalography, depth of anesthesia, laboratory mammals.

Martoft, L., L. Lomholt, C. Kolthoff, B. Rodriguez, E. Jensen, P. Jorgensen, H. Pedersen, and A. Forslid (2002). **Effects of CO2 anaesthesia on central nervous system activity in swine.** *Laboratory Animals* 36(2): 115-126. ISSN: 0023-6772.
NAL Call Number: QL55.A1L3
Abstract: The objective of the study was to examine the changes in central nervous system (CNS) activity and physical behaviour during induction and awakening from CO2 anaesthesia. Two studies, each using pigs immersed into 90% CO2 gas for a period of 60 s were performed. In study 1, we monitored middle latency auditory evoked potentials (changes in latencies, amplitudes and a depth of anaesthesia index), electroencephalographic parameters (delta, theta, alpha and beta electroencephalographic power and 95% spectral edge frequency) and heart rate; and in study 2, we monitored body movements and arterial and venous partial pressure of CO2 and O2. No behavioural signs of distress were observed during the early part of the induction. The swine exhibited muscular activity from 13-30 s after induction-start as well as during awakening from anaesthesia, possibly because of a transitory weaker suppression of the brain stem than of the cortex. The CNS and blood gas parameters started to change from the very start of induction. The CNS suppression lasted only approximately one minute after the end of the induction period. The two studies indicated a good temporal relationship between changes in amplitude, depth of anaesthesia index, spectral edge frequency, and arterial P(CO2) during the induction period.
Descriptors: swine, anesthesia, carbon dioxide, consciousness, blood sampling, oxygen, heart rate, animal welfare, animal stress, depth of anesthesia, distress.

Martoft, L., H. Stodkilde Jorgensen, A. Forslid, H.D. Pedersen, and P.F. Jorgensen (2003). **Co2 induced acute respiratory acidosis and brain tissue intracellular ph: a 31p nmr study in swine.** *Laboratory Animals (London)* 37(3): 241-248. ISSN: 0023-6772.
NAL Call Number: QL55.A1L3
Descriptors: High concentration carbon dioxide (CO2), pre-slaughter anesthesia, short-lasting surgical anesthesia, euthanasia, blood and lymphatics: transport and circulation, metabolism, methods and techniques, nervous system: neural coordination, carbon dioxide induced acute respiratory acidosis, metabolic disease, toxicity, carbon dioxide anesthesia, clinical techniques, laboratory techniques, phosphorus 31 nmr spectroscopy, laboratory

techniques, spectrum analysis techniques, animal welfare, arterial ph, carbon dioxide partial pressure, intracellular ph.

Marx, T. (2002). **Is xenon uptake in animals higher than reported previously?** *British Journal of Anaesthesia* 88(3): 452; Author Reply 453. ISSN: 0007-0912.
Descriptors: anesthetics, inhalation pharmacokinetics, xenon pharmacokinetics, research methods, swine.
Notes: Comment On: Br J Anaesth. 2001 Sep;87(3):497-8.

Mauch, C. and G. Bilkei (2004). **Castration of suckling piglets under general anaesthesia [Saugferkelkastration unter Anasthesie.]**. *Wiener Tierarztliche Monatsschrift* 91(4): 93-98. ISSN: 0043-535X.
NAL Call Number: 41.8 T345
Descriptors: acepromazine, anesthesia, azaperone, castration, healing, ketamine, neuroleptics, piglets, pigs.
Language of Text: German, Summary in English.

Mayr, V.D., C. Raedler, V. Wenzel, K.H. Lindner, and H.U. Strohmenger (2004). **A comparison of epinephrine and vasopressin in a porcine model of cardiac arrest after rapid intravenous injection of bupivacaine.** *Anesthesia and Analgesia* 98(5): 1426-31, Table of Contents. ISSN: 0003-2999.
Abstract: In a porcine model, we compared the efficacy of epinephrine, vasopressin, or the combination of epinephrine and vasopressin with that of saline placebo on the survival rate after bupivacaine-induced cardiac arrest. After the administration of 5 mg/kg of a 0.5% bupivacaine solution i.v., ventilation was interrupted for 3 +/- 1 min (mean +/- SD) until asystole occurred. Cardiopulmonary resuscitation (CPR) was initiated after 1 min of cardiac arrest. After 2 min of CPR, 28 animals received, every 5 min, epinephrine; vasopressin; epinephrine combined with vasopressin; or placebo i.v.. Three minutes after each drug administration, up to 3 countershocks (3, 4, and 6 J/kg) were administered; all subsequent shocks were 6 J/kg. Blood was drawn throughout the experiment for the determination of plasma bupivacaine concentration. In the vasopressin/epinephrine combination group, all pigs survived ($P < 0.01$ versus placebo); in the vasopressin group 5 of 7, in the epinephrine group 4 of 7, and in the placebo group none of 7 swine survived. The plasma concentration of total bupivacaine showed no significant difference among groups. In this model of bupivacaine-induced cardiac arrest, CPR with a combination of vasopressin and epinephrine resulted in significantly better survival rates than in the placebo group. IMPLICATIONS: Although cardiovascular collapse occurs mostly immediately after rapid injection of a local anesthetic in the presence of anesthesiologists, resuscitation may be difficult, and the outcome is usually poor. In this model of bupivacaine-induced cardiac arrest, cardiopulmonary resuscitation with a combination of vasopressin and epinephrine resulted in significantly better survival rates than in the placebo group.
Descriptors: anesthetics, local, bupivacaine, epinephrine therapeutic use, heart arrest chemically induced, heart arrest drug therapy, vasoconstrictor agents therapeutic use, vasopressins therapeutic use, cardiac output drug effects, drug combinations, epilepsy, tonic clonic chemically induced, epilepsy, tonic clonic physiopathology, heart arrest physiopathology, hemodynamic processes drug effects, injections, intravenous, survival, swine, vascular resis-

tance drug effects.
Notes: Comment In: Anesth Analg. 2004 Dec;99(6):1875-6; author reply 1876.

Melzer, W. and B. Dietze (2001). **Malignant hyperthermia and excitation-contraction coupling**. *Acta Physiologica Scandinavica* 171(3): 367-378. ISSN: 0001-6772.
NAL Call Number: QP1 .A2
Descriptors: metabolism, muscular system: movement and support, excitation contraction coupling, malignant hyperthermia, genetically pre-disposed individualss, voltage clamp conditions.

Merritt Charles, L., D. Chen, C. Legall, N. Mootoo, S.H. Brann, L. Perrault, D. Williams, C.N. Thomas, and C. Ezeokoli (2003). **Provision of anaesthesia for porcine cardiac transplantation at the veterinary school in Trinidad and Tobago.** *West Indian Medical Journal, The* 52(2): 95-8. ISSN: 0043-3144.
Abstract: A successful heterotopic cardiac transplantation was performed between sibling female Yorkshire Juvenile swine. Adequate pre-medication with azaperone and a smooth induction were ensured for both pigs, which were anaesthetized simultaneously with sodium thiopentone followed by endotracheal intubation and intermittent positive pressure ventilation. Inhalation anaesthetic agents were used for maintenance, neuromuscular blockade was achieved with cisatracurium and both fentanyl and tramadol were used to provide analgesia. Invasive monitoring was used in both the donor and recipient. Central venous pressure (CVP) was maintained at > 10 cm H2O and mean arterial pressure (MAP) > 60 mmHg. Heparin was injected during the surgical dissection of the heart in the donor to prevent coronary thrombosis and prior to aortic side clamping for end-to-side anastomosis of the donor heart in the recipient abdomen. After transplantation, the cardiovascular parameters of the recipient showed a MAP of 85-105 mmHg and a CVP of 8-10 cm H2O while echocardiography of the transplanted heart confirmed an ejection fraction (EF) of 80%. A functional anaesthetic team was assembled and trained to provide anaesthesia for porcine cardiac transplantation. The transplanted heart suffered pump failure after 69 days and was excised for performance of tissue analysis.
Descriptors: anesthesia, general veterinary, heart transplantation methods, heart transplantation veterinary, swine surgery, transplantation, heterotopic veterinary, anesthesia, intravenous, anesthetics administration and dosage, graft rejection, graft survival, intubation, intratracheal veterinary, monitoring, intraoperative methods, monitoring, intraoperative veterinary, risk assessment, schools, veterinary, sensitivity and specificity, transplantation, heterotopic methods, trinidad and tobago.

Mets, B. and E.A. Walker (2006). **Local anesthetic effect on liver function.** *Anesthesia and Analgesia* 103(4): 1045-6.
Descriptors: anesthetics, local pharmacology, lidocaine pharmacology, liver drug effects, amides pharmacology, bupivacaine pharmacology, liver metabolism, models, animal, perfusion, rats, swine.
Notes: Comment On: Anesth Analg. 2006 Feb;102(2):473-7.

Mills, P.C. and S.E. Cross (2006). **Transdermal drug delivery: basic principles for the veterinarian**. *Veterinary Journal* 172(2): 218-233. ISSN: 1090-0233.
NAL Call Number: SF601.V484
Descriptors: pharmacology, veterinary medicine: medical sciences, integumentary system:

chemical coordination and homeostasis, electroporation, laboratory techniques, genetic techniques, iontophoresis, clinical techniques, drug patch, drug delivery device, particle mediated epidermal delivery, clinical techniques, blood flow.

Morrison, S.G., J.J. Dominguez, P. Frascarolo, and S. Reiz (2000). **A comparison of the electrocardiographic cardiotoxic effects of racemic bupivacaine, levobupivacaine, and ropivacaine in anesthetized swine**. *Anesthesia and Analgesia* 90(6): 1308-1314. ISSN: 0003-2999.
Descriptors: pharmacology, lethal dose, local anesthetics, levobupivacaine, racemic bupivacaine, ropivacaine, after intracoronary injection, QRS interval, precordial electrocardiograph.

Mutschler, D.K., U. Gustafsson, S. Basu, A.O. Larsson, and M.B. Eriksson (2006). **Ropivacaine may have advantages compared to bupivacaine in porcine endotoxemic shock.** *Upsala Journal of Medical Sciences* 111(2): 189-99. ISSN: 0300-9734.
Abstract: Patients that undergo major abdominal surgery often receive epidural postoperative analgesia. Septic complications are frequently seen in this cohort. In a porcine model of endotoxemic shock, resembling human gram-negative septic shock, we evaluated the effects of two widely used local anaesthetics, bupivacaine and ropivacaine given intravenously. In the endotoxin-ropivacaine group mixed venous saturation and platelet count were higher as compared to endotoxemic controls. Mean arterial blood pressure and platelet count were higher in ropivacaine-endotoxin pigs than in bupivacaine-endotoxin ones. Bupivacaine augmented endotoxin-mediated decrease in left ventricular stroke work index. Ropivacaine displays pathophysiological advantages compared to bupivacaine in septic shock, which may be explained by improved tissue perfusion by ropivacaine.
Descriptors: amides therapeutic use, anesthetics, local therapeutic use, endotoxemia drug therapy, protective agents therapeutic use, shock, septic drug therapy, amides pharmacology, anesthetics, local pharmacology, blood platelets drug effects, blood pressure drug effects, bupivacaine pharmacology, bupivacaine therapeutic use, disease models, animal, lipid peroxidation drug effects, platelet count, protective agents pharmacology, stroke volume drug effects, sus scrofa, ventricular function, left drug effects.

Nakayama, T., M. Hayashi, D.O. Warner, and K.A. Jones (2005). **Anesthetics inhibit membrane receptor coupling to the Gq/11 heterotrimeric G protein in airway smooth muscle.** *Anesthesiology* 103(2): 296-305 . ISSN: 0003-3022.
Abstract: BACKGROUND: Some anesthetics relax airway smooth muscle in part by inhibiting acetylcholine-induced increases in Ca2+ sensitivity, an effect associated with inhibition of guanosine nucleotide exchange at the alpha subunit of the Gq/11 (Galphaq/11) heterotrimeric G protein. This study tested the hypothesis that these anesthetic effects are not unique to the muscarinic receptor but are a general property of the heptahelical receptors that increase Ca2+ sensitivity in airway smooth muscle. METHODS: Anesthetic effects on agonist-induced increases in Ca2+ sensitivity were measured in porcine airway smooth muscle strips permeabilized with S. aureus alpha-toxin. Anesthetic effects on basal (without agonist stimulation) and agonist-promoted Galphaq/11 guanosine nucleotide exchange were determined in crude membranes prepared from porcine airway smooth muscle. The nonhydrolyzable, radioactive form of guanosine 5'-triphosphate was used as the reporter for nucleotide exchange at Galphaq/11. RESULTS: Acetylcholine, endothelin-1, and histamine caused a concentration-dependent increase in Ca2+ sensitivity. Halothane (0.67 +/- 0.07 mM) and hexanol (10 mM) significantly inhibited the increase in Ca2+ sensitivity induced

by each agonist. Each agonist also caused a time- and concentration-dependent increase in Galphaq/11 nucleotide exchange. Neither anesthetic had an effect on basal Galphaq/11 nucleotide exchange, whereas halothane and hexanol significantly inhibited the increase in Galphaq/11 nucleotide exchange promoted by each agonist. CONCLUSION: These data suggest that inhibition of agonist-promoted guanosine nucleotide exchange at Galphaq/11 by some anesthetics may be a general property of heptahelical receptors involved cellular processes mediated by Galphaq/11, including muscarinic, endothelin-1, and histamine receptor activation of Ca2+ sensitivity.

Descriptors: anesthetics pharmacology, gtp binding protein alpha subunits, gq g11 metabolism, trachea drug effects, acetylcholine pharmacology, calcium metabolism, cell membrane metabolism, dose response relationship, drug, endothelin 1 pharmacology, guanosine 5' o 3 thiotriphosphate metabolism, guanosine diphosphate metabolism, histamine pharmacology, swine, trachea metabolism.

Nalos, M., U. Wachter, A. Pittner, M. Georgieff, P. Radermacher, and G. Froeba (2001). **Arterial and mixed venous xenon blood concentrations in pigs during wash-in of inhalational anaesthesia.** *British Journal of Anaesthesia* 87(3): 497-8. ISSN: 0007-0912.

Abstract: There are no data available on the kinetics of blood concentrations of xenon during the wash-in phase of an inhalation anaesthesia aiming at 1 MAC end-expiratory concentration. Therefore, we anaesthetized eight pigs with continuous propofol and fentanyl and measured arterial, mixed venous and end-expiratory xenon concentrations by gas chromatography-mass spectrometry 1, 2, 3, 4, 5, 7, 10, 15, 20, 30, 60 and 120 min after starting the anaesthetic gas mixture [67% xenon/33% oxygen; 3 litre x min(-1) during the first 10 min, thereafter minimal flow with 0.48 (SD 0.03) litre x min(-1)]. End-expiratory xenon concentrations plateaued (defined as <5% change from the preceding value) at 64 (6) vol% after 7 min, and arterial and mixed venous xenon concentrations after 5 and 15 min respectively. The highest arterio-venous concentration difference occurred after 3 min. Using the Fick principle, we calculated a mean xenon uptake of 3708 (829) and 9977 (3607) ml after 30 and 120 min respectively.

Descriptors: anesthetics, inhalation blood, xenon blood, anesthesia, inhalation methods, anesthetics, inhalation pharmacokinetics, swine, xenon pharmacokinetics.

Notes: Comment In: Br J Anaesth. 2002 Mar;88(3):452; author reply 453.

Oelschlager, H., P. Glassl, A. Seeling, J. Wange, M. Listing, and B. Jung (2001). **Synthese und pharmakologische Wirkung chiraler Fomocaine ((4-[2-Methyl-3-(morpholin-4-yl) propyl]benzyl)-phenyl-ether und (4-[1-Methyl-3-(morpholin-4-yl)propyl]benzyl)-phenyl-ether). 13. Mitteilung zur Synthese neuer Verbindungen mit lokalanasthetischer Wirkung. [Synthesis and pharmacologic action of chiral fomocaine ((4-[2-methyl-3-(morpholin-4-yl)propyl)benzyl)-phenyl-ether and (4-(1-methyl-3-(morpholin-4-yl) propyl]benzyl)-phenyl-ether). 13. Synthesis of new compounds with local anesthetic action]**. *Pharmazie, Die* 56(8): 620-5. ISSN: 0031-7144.

Abstract: The syntheses of two chiral fomocaines namely rac ((4-[2-methyl-3-(morpholin-4-yl)propyl]-benzyl)-phenyl-ether (O/G 3) and rac (4-[1-methyl-3-(morpholin-4-yl)propyl] benzyl)-phenyl-ether) (O/G 5) are reported. These compounds are part of a new research program concerning the relation between chirality and local anaesthetic activity in the group of fomocaines. The yield over five steps is in the range of 9% (O/G 3) up to 19.2% (O/G 5). The racemates were resoluted via the diastereomeric salts formed with (+)- or (-)-campher-

sulfonic acid. The chromatographic resolution in analytical scale is successful using a Daicel OD-column. The enantiomers are stable. The surface anaesthesia of the racemates as well as of the enantiomeres is weaker in comparison with fomocaine. The rate of tissue irritation is higher. The LD50 (mouse i.v.) is in the range between 290-390 mg/kg, while fomocaine shows a LD50 value of 175 mg/kg.

Descriptors: anesthetics, local chemical synthesis, ethers chemical synthesis, morpholines chemical synthesis, phenyl ethers chemical synthesis, anesthetics, local pharmacology, anesthetics, local toxicity, biopharmaceutics, chromatography, high pressure liquid, chromatography, thin layer, ethers pharmacology, indicators and reagents, lethal dose 50, mass spectrometry, microsomes, liver drug effects, morpholines pharmacology, phenyl ethers pharmacology, phenyl ethers toxicity, spectrophotometry, infrared, stereoisomerism, swine.

Language of Text: German.

Pabelick, C.M., B. Ay, Y.S. Prakash, and G.C. Sieck (2004). **Effects of volatile anesthetics on store-operated Ca(2+) influx in airway smooth muscle.** *Anesthesiology* 101(2): 373-80. ISSN: 0003-3022.

Abstract: BACKGROUND: In airway smooth muscle (ASM), volatile anesthetics deplete sarcoplasmic reticulum (SR) Ca(2+) stores by increasing Ca(2+) "leak." Accordingly, SR replenishment becomes dependent on Ca(2+) influx. Depletion of SR Ca(2+) stores triggers Ca(2+) influx via specific plasma membrane channels, store-operated Ca(2+) channels (SOCC). We hypothesized that anesthetics inhibit SOCC triggered by increased SR Ca(2+) "leak," preventing SR replenishment and enhancing ASM relaxation. METHODS: In porcine ASM cells, SR Ca was depleted by cyclopiazonic acid or caffeine in 0 extracellular Ca(2+), nifedipine and KCl (preventing Ca(2+) influx through L-type and SOCC channels). Extracellular Ca(2+) was rapidly introduced to selectively activate SOCC. After SOCC activation, SR was replenished and the protocol repeated in the presence of 1 or 2 minimum alveolar concentration halothane, isoflurane, or sevoflurane. In other cells, characteristics of SOCC and interactions between acetylcholine (Ach) and volatile anesthetics were examined. RESULTS: Cyclopiazonic acid produced slow SR leak, whereas the caffeine response was transient in ASM cells. Reintroduction of extracellular Ca(2+) rapidly increased [Ca(2+)] i. This influx was insensitive to nifedipine, SKF-96365, and KBR-7943, inhibited by Ni and blockade of inositol 1,4,5-triphosphate-induced SR Ca(2+) release, and enhanced by ACh. Preexposure to 1 or 2 minimum alveolar concentration halothane completely inhibited Ca(2+) influx when extracellular Ca(2+) was reintroduced, whereas isoflurane and sevoflurane produced less inhibition. Only halothane and isoflurane inhibited ACh-induced augmentation of Ca(2+) influx. CONCLUSION: Volatile anesthetics inhibit a Ni/La-sensitive store-operated Ca(2+) influx mechanism in porcine ASM cells, which likely helps maintain anesthetic-induced bronchodilation.

Descriptors: anesthetics, inhalation pharmacology, calcium metabolism, muscle, smooth metabolism, respiratory muscles metabolism, acetylcholine pharmacology, caffeine pharmacology, calcium channels drug effects, calcium channels metabolism, microscopy, confocal, muscle, smooth drug effects, phosphodiesterase inhibitors pharmacology, respiratory muscles drug effects, sarcoplasmic reticulum drug effects, sarcoplasmic reticulum metabolism, swine, vasodilator agents pharmacology.

Pabelick, C.M., Y.S. Prakash, M.S. Kannan, D.O. Warner, and G.C. Sieck (2001). **Effects of halothane on sarcoplasmic reticulum calcium release channels in porcine airway smooth muscle cells.** *Anesthesiology* 95(1): 207-15. ISSN: 0003-3022.

Abstract: BACKGROUND: Volatile anesthetics relax airway smooth muscle (ASM) by altering intracellular Ca2+ concentration ([Ca2+]i). The authors hypothesized that relaxation is produced by decreasing sarcoplasmic reticulum Ca2+ content via increased Ca2+ "leak" through both inositol trisphosphate (IP3) and ryanodine receptor channels. METHODS: Enzymatically dissociated porcine ASM cells were exposed to acetylcholine in the presence or absence of 2 minimum alveolar concentration (MAC) halothane, and IP3 levels were measured using radioimmunoreceptor assay. Other cells were loaded with the Ca2+ indicator fluo-3 and imaged using real-time confocal microscopy. RESULTS: Halothane increased IP3 concentrations in the presence and absence of acetylcholine. Inhibition of phospholipase C blunted the IP3 response to halothane. Exposure to 2 MAC halothane induced a transient [Ca2+]i response, suggesting depletion of sarcoplasmic reticulum Ca2+. Exposure to 20 microM Xestospongin D, a cell-permeant IP3 receptor antagonist, resulted in a 45+/-13% decrease in the [Ca2+]i response to halothane compared with halothane exposure alone. In permeabilized cells, Xestospongin D or 0.5 mg/ml heparin decreased the [Ca2+]i response to halothane by 65+/-13% and 68+/-22%, respectively, compared with halothane alone. In both intact and permeabilized cells, 20 microM ryanodine blunted the [Ca2+]i response to halothane by 32+/-13% and 39+/-21%, respectively, compared with halothane alone. Simultaneous exposure to Xestospongin D and ryanodine completely inhibited the [Ca2+] i response to halothane. CONCLUSIONS: The authors conclude that halothane reduces sarcoplasmic reticulum Ca2+ content in ASM cells via increased Ca2+ leak through both IP3 receptor and ryanodine receptor channels. Effects on IP3 receptor channels are both direct and indirect via elevation of IP3 levels.

Descriptors: anesthetics, inhalation pharmacology, calcium channels metabolism, halothane pharmacology, muscle, smooth metabolism, sarcoplasmic reticulum metabolism, calcium channels drug effects, calibration, escin pharmacology, inositol 1,4,5 trisphosphate metabolism, microscopy, confocal, muscle, smooth cytology, muscle, smooth drug effects, receptors, cytoplasmic and nuclear drug effects, receptors, cytoplasmic and nuclear metabolism, ryanodine receptor calcium release channel drug effects, ryanodine receptor calcium release channel metabolism, sarcoplasmic reticulum drug effects, swine.

Perk, E.C., O. Duzgun, O. Guzel, and Z. Mutlu (2004). **Inhalation anaesthesia in swine [Domuzlarda inhalasyon anestezisi.]**. *Veteriner Fakultesi Dergisi Istanbul* 30 (1): 47-59. ISSN: 0378-2352.

Descriptors: anesthesia, anesthetics, atropine, halothane, inhaled anesthetics, isoflurane, ketamine, pharmacodynamics, pharmacokinetics, preanesthetic medication, thiopental, xylazine, surgery.

Language of Text: Turkish, Summary in English.

Pittner, A., M. Nalos, M. Theisen, F. Ploner, U.B. Bruckner, M. Georgieff, P. Radermacher, and G. Froba (2002). **Inhaling nitrous oxide or xenon does not influence bowel wall energy balance during porcine bowel obstruction.** *Anesthesia and Analgesia* 94(6): 1510-6, Table of Contents. ISSN: 0003-2999.

Abstract: Xenon (Xe) is less soluble than nitrous oxide (N(2)O) and hence may be more suitable during bowel obstruction. Therefore, we compared the intestinal mechanical and

biochemical effects of these two gases with those of total IV anesthesia in a porcine model of small-bowel obstruction. Intestinal obstruction was induced in 33 anesthetized pigs, in 18 of which segmental ileal perfusion was reduced by partial arterial occlusion. Pigs received total IV anesthesia, Xe, or N(2)O (in 30% oxygen) for 4 h, and we determined the intraluminal pressure and volume, the arterial-ileal PCO(2) gap, and the lactate and pyruvate levels in the segmental mesenteric vein. Under both experimental conditions, Xe or N(2)O ventilation caused the volume to significantly increase with a concomitant significant increase in the intraluminal pressure during N(2)O ventilation. Regardless of the anesthesia technique, none of the biochemical variables was influenced in the animals with maintained ileal blood supply. In contrast, reducing the segmental perfusion induced pronounced alterations of all variables of bowel wall energy metabolism. The type of anesthesia, however, had no further statistically significant effect. Short-term inhalation of Xe or N(2)O seems to have no deleterious effects on the metabolic balance of the gut wall during intestinal obstruction. IMPLICATIONS: In anesthetized pigs, short-term inhalation of xenon or nitrous oxide over 4 h when compared with total IV anesthesia had no additional deleterious effects on the metabolic balance of the gut wall during intestinal obstruction, no matter whether the arterial blood flow was reduced or not.

Descriptors: anesthetics, inhalation pharmacology, energy metabolism drug effects, intestinal obstruction metabolism, intestines physiology, nitrous oxide pharmacology, xenon pharmacology, blood gas analysis, blood pressure drug effects, central venous pressure drug effects, gastrointestinal motility drug effects, intestinal obstruction physiopathology, intestines blood supply, pulmonary gas exchange drug effects, regional blood flow drug effects, swine.

Polydoro, A.S., C. White, C. Hennemann, J.A. Ferreira, C.M. Gomes, G. Costi, and M. Feser (2001). **Dissociative anaesthesia in pigs with xylazine and tiletamine/zolazepam [Anestesia dissociativa em suinos com a associacao xilazina e tiletamina/zolazepam.]**. *A Hora Veterinaria*(122): 9-13. ISSN: 0101-9163.

Descriptors: anesthesia, hemodynamics, pharmacodynamics, respiration, xylazine, restraint, cardiopulmonary parameters.

Language of Text: Portuguese, Summary in English.

Prakash, Y.S., A. Iyanoye, B. Ay, G.C. Sieck, and C.M. Pabelick (2006). **Store-operated Ca2+ influx in airway smooth muscle: Interactions between volatile anesthetic and cyclic nucleotide effects.** *Anesthesiology* 105(5): 976-83. ISSN: 0003-3022.

Abstract: BACKGROUND: Volatile anesthetics produce bronchodilation in part by depleting sarcoplasmic reticulum Ca stores in airway smooth muscle (ASM). Other bronchodilatory drugs are known to act via cyclic nucleotides (cyclic adenosine 3',5'-cyclic monophosphate, cyclic guanosine 3',5'-cyclic monophosphate). Intracellular Ca regulation in ASM involves plasma membrane Ca influx, including that triggered by sarcoplasmic reticulum Ca depletion (store-operated Ca entry [SOCE]). The authors hypothesized that anesthetics and bronchodilatory agents interact in inhibiting SOCE, thus enhancing ASM relaxation. METHODS: In enzymatically dissociated porcine ASM cells imaged using fluorescence microscopy, sarcoplasmic reticulum Ca was depleted by 1 microm cyclopiazonic acid in 0 extracellular Ca, nifedipine, and potassium chloride (preventing Ca influx through L-type channels and SOCE). Extracellular Ca was rapidly reintroduced to selectively activate SOCE in the presence or absence of 1 minimum alveolar concentration (MAC) halothane,

isoflurane, or sevoflurane. Anesthetic interference with SOCE regulation by cyclic nucleotides was examined by activating SOCE in the presence of (1) 1 microm acetylcholine, (2) 100 microm dibutryl cyclic adenosine 3',5'-cyclic monophosphate, or (3) 100 microm 8-bromo-cyclic guanosine 3',5'-cyclic monophosphate. RESULTS: SOCE was enhanced by acetylcholine, whereas volatile anesthetics and both cyclic nucleotides partially inhibited Ca influx. Preexposure to 1 or 2 MAC anesthetic (halothane > isoflurane > sevoflurane) inhibited SOCE. Only halothane and isoflurane inhibited acetylcholine-induced augmentation of Ca influx, and significantly potentiated cyclic nucleotide inhibition such that no influx was observed in the presence of anesthetics and cyclic nucleotides. CONCLUSIONS: These data indicate that volatile anesthetics prevent sarcoplasmic reticulum refilling by inhibiting SOCE and enhancing cyclic nucleotide blunting of Ca influx in ASM. Such interactions likely result in substantial airway relaxation in the presence of both anesthetics and bronchodilatory agents such as beta agonists or nitric oxide.
Descriptors: anesthetics, inhalation pharmacology, calcium signaling drug effects, muscle, smooth metabolism, respiratory system metabolism, acetylcholine pharmacology, bucladesine pharmacology, cyclic gmp analogs and derivatives, cyclic gmp pharmacology, halothane pharmacology, isoflurane pharmacology, methyl ethers pharmacology, muscle, smooth cytology, muscle, smooth drug effects, myocytes, smooth muscle drug effects, myocytes, smooth muscle metabolism, respiratory system cytology, respiratory system drug effects, swine.

Prunier, A., G. Bataille, M.C. Meunier Salaun, A. Bregeon, and Y. Rugraff (2001). **Influence of tail docking, with or without a cold analgesic spray, on the behaviour, performance and physiology of piglets [Consequences comportementales, zootechniques et physiologiques de la caudectomie realisee avec ou sans "insensibilisation" locale chez le porcelet.]**. *Journees De La Recherche Porcine En France* 33: 313-318. ISSN: 0767-9874.
NAL Call Number: SF391.I53
Descriptors: analgesics, animal behavior, animal welfare, corticotropin, docking, glucose, growth, hydrocortisone, lactic acid, pain, physical activity, piglets, tail docking.
Language of Text: French, Summary in English.
Notes: Meeting Information: 33emes Journees de la Recherche Porcine en France, 30-31 janvier et 1er fevrier 2001, Paris, France.

Prunier, A., M. Bonneau, E.v. Borell, S. Cinotti, M. Gunn, B. Fredriksen, M. Giersing, D. Morton, F. Tuyttens, and A. Velarde (2006). **A review of the welfare consequences of surgical castration in piglets and the evaluation of non-surgical methods.** *Animal Welfare* 15(3): 277-289. ISSN: 0962-7286.
NAL Call Number: HV4701.A557
Descriptors: piglets, castration, local anesthetics, immunization, gonadotropin releasing hormone, vaccine development, animal welfare, males, literature reviews, food animals, boar taint.

Prunier, A., A. Mounier, and M. Hay (2005). **Effects of castration, tooth resection, or tail dockings on plasma metabolites and stress hormones in young pigs.** *Journal of Animal Science* 83(1): 216-222. ISSN: 0021-8812.
NAL Call Number: 49 J82
Descriptors: swine, young animals, castration, tail docking, veterinary dentistry, metabo-

lites, pain, blood glucose, lactic acid, catecholamines, males, anesthesia, animal handling, females, corticotropin, hormone secretion, cortisol, animal welfare.

Puglisi, F., A. Crovace, F. Staffieri, P. Capuano, G. Carravetta, M. De Fazio, G. Lograno, L. Lacitignola, V.L. Troilo, G. Martines, C. Chiumarulo, and V. Memeo (2007). **Comparison of hemodynamic and respiratory effects of propofol and sevoflurane during carbon dioxide pneumoperitoneum in a swine model.** *Chirurgia Italiana* 59(1): 105-11. ISSN: 0009-4773.

Abstract: The aim of this study was to compare intraoperative hemodynamic and respiratory parameters using propofol and sevoflurane during laparoscopic surgery in a porcine model. After induction of general anaesthesia in 16 pigs with fentanyl (0.005 mg kg(-1)) followed by propofol (6 mg Kg(-1)), it was maintained with fentanyl (0.01 mg kg(-1)h(-1)) and sevoflurane in O2 in group 1 (G1, n = 8) and fentanyl and propofol (12 mg kg(-1)h(-1)) in group 2 (G2, n = 8). The parameters monitored were heart rate, airway pressure (PAW), arterial and venous blood pressures and arterial blood gas analysis. The carbon dioxide pneumoperitoneum was maintained at 12 mmHg for 2 hours. Data were expressed as mean +/- standard deviation and were analysed using the Wilcoxon test ($p < 0.05$). G1 showed significantly higher PAW values than G2 at T60, T90 and T120. The heart rate values were significantly higher in G1 at T90 and T120. Middle arterial pressure was significantly lower in G1 than G2 at T30 and T60. The base deficit was significantly greater in G1 at T60, T90, T120 and Tpost. In this study propofol assured better hemodynamic and respiratory conditions than sevoflurane during laparoscopy in a porcine model.

Descriptors: anesthetics, combined pharmacology, blood pressure drug effects, heart rate drug effects, methyl ethers pharmacology, pneumoperitoneum, artificial, propofol pharmacology, pulmonary gas exchange drug effects, anesthetics, combined administration and dosage, anesthetics, inhalation administration and dosage, anesthetics, inhalation pharmacology, anesthetics, intravenous administration and dosage, anesthetics, intravenous pharmacology, blood gas analysis methods, carbon dioxide, disease models, animal, laparoscopy methods, methyl ethers administration and dosage, propofol administration and dosage, statistics, nonparametric, swine.

Rai, A., S. Bhalla, S.S. Rebello, H. Kastrissios, and A. Gulati (2005). **Disposition of morphine in plasma and cerebrospinal fluid varies during neonatal development in pigs.** *Journal of Pharmacy and Pharmacology, The* 57(8): 981-6. ISSN: 0022-3573.

NAL Call Number: RS11.J6

Abstract: The pharmacological effects of morphine are mediated via the central nervous system (CNS) but its clearance from the CNS in neonates has not been investigated. We have proposed that neonatal development of the blood-brain barrier affected CNS clearance mechanisms and CNS exposure to morphine. Male piglets (n = 5) aged one, three and six weeks were given morphine sulfate (0.5 mg kg(-1), i.v.). Serial blood and cerebrospinal fluid (CSF) samples were withdrawn over 360 min after morphine administration. Morphine concentration was measured by radioimmunoassay. A three-compartment model was fitted to individual data. Estimated parameters were reported as median and range. The peak morphine concentrations in plasma were not significantly different in the one-, three- or six-week-old piglets. Plasma clearance at one week (4.5, 3.8-8.6 mL min(-1) kg(-1)) was significantly lower than at three weeks (30.0, 19.1- 39.0 mL min(-1) kg(-1)) and six weeks (37.0, 29.7-82.8 mL min(-1) kg(-1)). The peak morphine concentration in CSF at one week

(59.84, 31-67 ng mL(-1)) was higher than at three weeks (18.8, 17.7-25 ng mL(-1)) and six weeks (24.51, 16.5-84 ng mL(-1)), while CSF clearance was lower at one week (1.0, 0.18-9 mL min(-1) kg(-1)) compared with three weeks (6.2, 2.3-9.3 mL min(-1) kg(-1)) and six weeks (3.95, 1.3-85.7 mL min(-1) kg(-1)). Apparent plasma:CSF transfer ratio at one week was greater than at three and six weeks. The reduced plasma and CSF morphine clearance in early infancy resulted in elevated systemic and central morphine exposure in neonatal pigs.
Descriptors: aging physiology , analgesics, opioid pharmacokinetics, growth and development physiology, morphine pharmacokinetics, neonatology, analgesics, opioid blood, analgesics, opioid cerebrospinal fluid, analgesics, opioid toxicity, animals, newborn, morphine blood, morphine cerebrospinal fluid, morphine toxicity, swine.

Ranheim, B., H. Haga, and K. Ingebrigtsen (2005). **Distribution of radioactive lidocaine injected into the testes in piglets.** *Journal of Veterinary Pharmacology and Therapeutics* 28(5): 481-483. ISSN: 0140-7783.
NAL Call Number: SF915.J63
Descriptors: piglets, lidocaine, radiolabeling, swine breeds, testes, injection site, anesthesia, castration, males, Yorkshire (swine breed), animal age, body weight, epinephrine, drug evaluation, Norwegian-Landrace-(swine-breed).

Reinelt, H., T. Marx, J. Kotzerke, P. Topalidis, S. Luederwald, S. Armbruster, U. Schirmer, and M. Schmidt (2002). **Hepatic function during xenon anesthesia in pigs.** *Acta Anaesthesiologica Scandinavica* 46(6): 713-6. ISSN: 0001-5172.
Abstract: BACKGROUND: Inhalation anesthetics decrease liver perfusion and oxygen consumption by changing the distribution pattern of perfusion between the hepatic artery and the portal vein and by direct effects on liver cells. The effects of xenon on liver perfusion and function have been not investigated until now. METHODS: Fourteen pigs were randomly assigned to two groups to receive either 73-78% xenon or 75% nitrogen in oxygen with additional supplementation of pentobarbital and buprenorphine. Microspheres were used to determine the arterial perfusion of the liver and splanchnic organs. Oxygen contents were measured by catheterization of the portal and a liver vein. Lactate and glucose plasma concentrations were measured in hepatic, mixed venous and arterial blood. Alanine aminotransferase (ALT) and lactate dehydrogenase (LOH) plasma concentrations were measured in arterial blood. Urea production rates were calculated to assess hepatic metabolic function. RESULTS: Significant higher oxygen contents were found in the liver venous blood during xenon anesthesia. No differences were found in any other investigated parameters. CONCLUSION: Higher oxygen content in liver venous blood observed during xenon anesthesia was not induced by changes in hepatic perfusion distribution or by an impairment of liver metabolic capacity. However, it can be explained by similar results known from inhalation anesthesia. Additionally, the effect can be caused by the reduction of plasma catecholamine concentrations during xenon anesthesia.
Descriptors: adjuvants, anesthesia pharmacology, anesthetics, inhalation pharmacology, anesthetics, intravenous pharmacology, buprenorphine pharmacology, liver drug effects, liver physiology, liver circulation drug effects, pentobarbital pharmacology, xenon pharmacology, analgesics, opioid pharmacology, liver circulation physiology, oxygen consumption drug effects, swine.

Reinelt, H., T. Marx, U. Schirmer, S. Luederwald, P. Topalidis, and M. Schmidt (2002). **Diffusion of xenon and nitrous oxide into the bowel during mechanical ileus.** *Anesthesiology* 96(2): 512-3. ISSN: 0003-3022.

Descriptors: anesthetics, inhalation pharmacokinetics, digestive system metabolism, intestinal obstruction physiopathology, nitrous oxide pharmacokinetics, xenon pharmacokinetics, blood pressure drug effects, cardiac output drug effects, disease models, animal, perfusion, pressure, swine.

Reinelt, H., T. Marx, U. Schirmer, and M. Schmidt (2001). **Xenon expenditure and nitrogen accumulation in closed-circuit anaesthesia.** *Anaesthesia* 56(4): 309-11. ISSN: 0003-2409.

Abstract: The high price of xenon has prevented its use in routine, clinic anaesthetic practice. Xenon therefore has to be delivered by closed-circuit anaesthesia. The accumulation of nitrogen is a significant problem within the closed circuit and necessitates flushing, which in turn increases gas expenditure and costs. In previous investigations, nitrogen concentrations between 12% and 16% have been reported in closed-circuit anaesthesia. In order to avoid such nitrogen accumulation, we denitrogenised seven pigs using a non-rebreathing system and connected the animals to a system primed with a xenon/oxygen mixture. In comparison, seven pigs were anaesthetised with xenon using a standard low-flow anaesthetic procedure. Anaesthesia time was 2 h. Nitrogen concentrations in the closed system ranged from 0.08 to 7.04% and were not significantly different from those observed during low-flow anaesthesia. Closed-circuit anaesthesia reduced the xenon expenditure 10-fold compared with low-flow anaesthesia.

Descriptors: anesthesia, closed circuit, anesthetics, inhalation administration and dosage, nitrogen analysis, xenon administration and dosage, anesthetics, inhalation economics, drug administration schedule, drug costs, nitrogen metabolism, swine, xenon economics.

Reinelt, H., U. Schirmer, T. Marx, P. Topalidis, and M. Schmidt (2001). **Diffusion of xenon and nitrous oxide into the bowel.** *Anesthesiology* 94(3): 475-7; Discussion 6a. ISSN: 0003-3022.

Abstract: BACKGROUND: Nitrous oxide diffuses easily from blood into air filled spaces. Xenon is also a relatively insoluble gas, like nitrous oxide. Therefore, the authors measured xenon diffusion into obstructed bowel segments during xenon anesthesia and compared this with nitrous oxide and nitrogen diffusion. METHODS: Twenty-one pentobarbital-anesthetized pigs were randomly assigned to three groups to receive either xenon-oxygen, nitrous oxide-oxygen, or nitrogen-oxygen (75%-25%), respectively. In each animal four bowel segments of 15-cm length were isolated. A pressure-measuring catheter was inserted into the lumen, and 30 ml of room air was injected into the segments. Anesthesia with the selected gas mixture was performed for 4 h. Pressure in the segments was measured continuously. The volume of gaseous bowel content was measured on completion of the study. RESULTS: The median volume of bowel gas in animals breathing nitrous oxide was 88.0 ml as compared with 39.0 ml with xenon anesthesia and 21.5 ml in the nitrogen-oxygen group. After 4 h of anesthesia, the intraluminal pressures in the nitrous oxide group were found to be significantly greater than in the control group and in the xenon group. CONCLUSIONS: The amount of diffused gas was significantly lower during xenon anesthesia than with nitrous oxide anesthesia but greater than with controls. Blood solubility can therefore be regarded as an important factor influencing gas diffusion into air filled cavities.

Descriptors: anesthesia, inhalation, anesthetics, inhalation pharmacokinetics, colon, nitrous oxide pharmacokinetics, xenon pharmacokinetics, diffusion, swine.

Rex, S., C. Missant, P. Segers, and P.F. Wouters (2007). **Thoracic epidural anesthesia impairs the hemodynamic response to acute pulmonary hypertension by deteriorating right ventricular-pulmonary arterial coupling.** *Critical Care Medicine* 35(1): 222-9. ISSN: 0090-3493.
Abstract: OBJECTIVE: Thoracic epidural anesthesia is increasingly used in critically ill patients. This analgesic technique was shown to decrease left ventricular contractility, but effects on right ventricular function have not been reported. A deterioration of right ventricular performance may be clinically relevant for patients with acute pulmonary hypertension, in which right ventricular function is an important determinant of outcome. In the present study, we tested the hypothesis that thoracic epidural anesthesia decreases right ventricular contractility and limits its capacity to tolerate pulmonary hypertension. DESIGN: Prospective, placebo-controlled study using an established model of acute pulmonary hypertension. SETTING: University hospital laboratory. SUBJECTS: A total of 14 pigs (mean weight, 35 +/- 2 kg). INTERVENTIONS: After instrumentation with an epidural catheter, biventricular conductance catheters, a pulmonary flow probe, and a high-fidelity pulmonary pressure catheter, seven pigs received thoracic epidural anesthesia and seven pigs served as control. Hemodynamic measurements were performed in baseline conditions and after induction of pulmonary hypertension via hypoxic pulmonary vasoconstriction (Fio2 of 0.15). MEASUREMENTS AND MAIN RESULTS: Ventricular contractility was assessed using load- and heart rate-independent variables. Right ventricular afterload was characterized with instantaneous pressure-flow measurements. In baseline conditions, thoracic epidural anesthesia decreased left but not right ventricular contractility. In untreated animals, pulmonary hypertension was associated with an increase in right ventricular contractility and cardiac output. Pretreatment with thoracic epidural anesthesia completely abolished the positive inotropic response to acute pulmonary hypertension. As a result, ventriculo-vascular coupling between the right ventricle and pulmonary-arterial system deteriorated, and cardiac output was significantly lower in animals with thoracic epidural anesthesia than in untreated controls during hypoxia-induced pulmonary hypertension. CONCLUSIONS: Thoracic epidural anesthesia inhibits the native positive inotropic response of the right ventricle to increased afterload and deteriorates the hemodynamic effects of acute pulmonary hypertension.
Descriptors: anesthesia, epidural adverse effects, disease models, animal, thoracic vertebrae, ventricular dysfunction, right etiology, ventricular dysfunction, right physiopathology, acute disease, anesthesia, epidural methods, anoxia complications, blood pressure, cardiac output, critical care, heart rate, homeostasis, hypertension, pulmonary complications, hypertension, pulmonary physiopathology, myocardial contraction, prospective studies, pulmonary circulation, pulmonary wedge pressure, random allocation, stroke volume, swine, vascular resistance, ventricular dysfunction, left etiology.
Notes: Comment In: Crit Care Med. 2007 Jan;35(1):321-2.

Reyes, L., K.D. Tinworth, K.M. Li, D.F. Yau, and K.A. Waters (2002). **Observer-blinded comparison of two nonopioid analgesics for postoperative pain in piglets.** *Pharmacology, Biochemistry, and Behavior* 73(3): 521-8. ISSN: 0091-3057.
Abstract: Piglets are popular for studies of respiratory and cardiovascular function, but opioid analgesics are contraindicated in these studies because of central nervous system depression. We evaluated two nonopioid analgesics for postoperative pain relief following

implantation of a central arterial catheter via an inguinal incision. Animals were randomly assigned to paracetamol-treated (n=8, rectal suppositories, 100 mg/kg) meloxicam-treated (n=8, 1 mg/kg meloxicam via the catheter) or untreated control group (n=8, placebo suppositories and normal saline). Additional controls received paracetamol or meloxicam, without pain (n=6 for both groups). Behavioral and physiological assessments, and blood sampling were undertaken at nine timed intervals until 24 h after surgery. Multifactorial numerical rating scale (NRS), behavioral and physiological pain scores (PPS) decreased over time for all groups (P<.001). On NRS and behavioral criteria, meloxicam was significantly better than paracetamol (P<.001), and both were better than control (p<.001 for each). Physiological parameters discriminated between the control and analgesia-treated groups, but not between paracetamol and meloxicam. Preliminary pharmacokinetics, determined by isocratic high-performance liquid chromatography (HPLC), revealed no difference in the half-life of paracetamol (2.5+/-0.3 h) vs. meloxicam (3.4+/-0.4 h). Paracetamol and meloxicam provided effective postoperative analgesia in piglets, with meloxicam superior to paracetamol on behavioral criteria.

Descriptors: acetaminophen therapeutic use, analgesics, non narcotic pharmacology, pain measurement drug effects, pain, postoperative drug therapy, thiazines therapeutic use, thiazoles therapeutic use, acetaminophen adverse effects, acetaminophen pharmacokinetics, analgesics, non narcotic adverse effects, analgesics, non narcotic pharmacokinetics, behavior, animal drug effects, blood pressure drug effects, body temperature drug effects, half life, heart rate drug effects, kidney drug effects, liver drug effects, models, biological, respiratory mechanics drug effects, swine, thiazines adverse effects, thiazines pharmacokinetics, thiazoles adverse effects, thiazoles pharmacokinetics.

Rice, M.T. (2006). **Errors in the April 2005 ethical question.** *Canadian Veterinary Journal, The; Revue Veterinaire Canadienne, La* 47(1): 7. ISSN: 0008-5286.

NAL Call Number: 41.8 R3224

Descriptors: anesthesia, general veterinary, pain veterinary, veterinary medicine ethics, anesthesia, general ethics, animal welfare, pain prevention and control, quality control, swine.

Notes: Comment On: Can Vet J. 2005 Jul;46(7):579.

Risk, D., D. Verpy, J.D. Conley, T. Jacobson, and T.W. Sawyer (2001). **Volatile anesthetics give a false-positive reading in chemical agent monitors in the "H" mode.** *Military Medicine* 166(8): 708-10. ISSN: 0026-4075.

Abstract: Chemical agent monitors (CAMs) are routinely used by the armed forces and emergency response teams of many countries for the detection of the vesicant sulfur mustard (HD) and the G series of organophosphate nerve agents. Ambient operating room isoflurane levels were found to produce strong positive signals in the "H" mode when the CAM was used to monitor the efficacy of decontamination procedures during routine surgical procedures on HD-poisoned animals requiring up to 8 hours of general anesthesia. Subsequent testing showed that isoflurane, as well as desflurane, sevoflurane, halothane and methoxyflurane, produce two ionization peaks in the CAM response. One of these peaks is interpreted by the CAM processing software as HD, resulting in a CAM "H" mode bar response. No interference was encountered with isoflurane, desflurane, and sevoflurane when the CAM was set to the "G" mode, although extremely high (nonclinical) concentrations of halothane and methoxyflurane yielded a weakly positive bar response. These findings have potentially serious ramifications for the medical management of patients resulting from terrorist, mili-

tary, or chemical agent decommissioning activity when concomitant chemical injuries are also possible.
Descriptors: anesthetics analysis, chemical warfare agents analysis, environmental monitoring instrumentation, operating rooms, environmental monitoring methods, false positive reactions, swine.

Rocco, A.G. and J.H. Philip (2006). **Hydrodynamics of the spinal epidural space.** *Regional Anesthesia and Pain Medicine* 31(6): 588; Author Reply 589. ISSN: 1098-7339.
NAL Call Number: RB127
Descriptors: anesthesia, epidural, cerebrospinal fluid pressure drug effects, epidural space physiology, epidural space drug effects, infusion pumps, injections, epidural, research design, sodium chloride administration and dosage, swine, transducers, pressure.
Notes: Comment On: Reg Anesth Pain Med. 2006 Mar-Apr;31(2):100-4.

Rodriguez Lopez, J.M., P. Sanchez Conde, F.S. Lozano, J.L. Nicolas, F.J. Garcia Criado, C. Cascajo, and C. Muriel (2006). **Laboratory investigation: effects of propofol on the systemic inflammatory response during aortic surgery.** *Canadian Journal of Anaesthesia; Journal Canadien D'Anesthesie* 53(7): 701-10. ISSN: 0832-610X.
NAL Call Number: RD78.68.C4
Abstract: PURPOSE: A laboratory investigation was undertaken to assess the effects of propofol on renal function, through modulation of the systemic inflammatory response, in an in vivo experimental model of aortic surgery in comparison with sevoflurane. METHODS: Twenty young male piglets were anesthetized with either propofol 4 mg.kg(-1).hr(-1) (n = 10) or sevoflurane 1.5% end-tidal concentration (n = 10). Animals were subjected to aorta-aortic bypass with suprarenal aortic clamping for 30 min. At specific intervals (basal -before the start of surgery; reperfusion 15 min after unclamping the aorta; at 24, 48 and 72 hr after surgery, and on the seventh day after surgery) the levels of the following were determined: plasma creatinine, renal myeloperoxidase, tumour necrosis factor-alpha, interleukin 1-ss, and interferon-gamma; kidney superoxide anion and its detoxifying enzyme superoxidase dismutase, kidney malondialdehyde and the activity of inducible nitric oxide synthase. Seven days after surgery, the animals were anesthetized using the described techniques, and after blood withdrawal and kidney sampling they were sacrificed. RESULTS: In comparison with sevoflurane, propofol was associated with a lower concentration of plasma creatinine ($P < 0.05$) together with lower concentrations of myeloperoxidase, tumour necrosis factor-alpha, interleukin 1-ss, interferon-gamma, superoxide anion and superoxidase dismutase, malondialdehyde and inducible nitric oxide synthase ($P < 0.05$). CONCLUSION: In an experimental model of aortic reconstructive surgery, and compared with sevoflurane, propofol anesthesia is associated with less neutrophil infiltration, lower plasma proinflammatory cytokine levels, lower production of oxygen free radicals, less lipid peroxidation, and reduced inducible nitric oxide synthase activity. These observations suggest a possible renal protective effect of propofol in this surgical setting.
Descriptors: anesthetics, intravenous pharmacology, aorta surgery, propofol pharmacology, systemic inflammatory response syndrome metabolism, systemic inflammatory response syndrome prevention and control, anesthetics, inhalation administration and dosage, creatinine blood, disease models, animal, enzyme linked immunosorbent assay methods, interferon type ii blood, interferon type ii drug effects, interleukin 1beta blood, interleukin 1beta drug effects, malondialdehyde metabolism, methyl ethers administration and dosage, nitric oxide

synthase drug effects, nitric oxide synthase metabolism, peroxidase drug effects, peroxidase metabolism, superoxide dismutase drug effects, superoxide dismutase metabolism, superoxides metabolism, swine, systemic inflammatory response syndrome blood, time factors , tumor necrosis factor alpha blood, tumor necrosis factor alpha drug effects.

Rodriguez, N.A., D.M. Cooper, and J.M. Risdahl (2001). **Antinociceptive activity of and clinical experience with buprenorphine in swine.** *Contemporary Topics in Laboratory Animal Science American Association for Laboratory Animal Science* 40(3): 17-20. ISSN: 1060-0558.
NAL Call Number: SF405.3 .A23
Abstract: We performed antinociceptive testing on swine receiving buprenorphine. Intravenous access was achieved, and animals were allowed to recover for 24 h. Baseline skin-twitch latency to a focused light source was determined for each animal. Animals received intravenous (i.v.) buprenorphine at 0.08 (n =1), 0.16 (n = 1), 0.005 (n = 5), 0.01 (n = 5), or 0.02 mg/kg (n = 6). Skin-twitch latency was determined 15, 30, 60, 120, 180, 240, 300, 360, 420, 480, 540, and 600 min after buprenorphine administration. Analgesic activity as measured by a significant increase in latency time over baseline values occurred at all time points except 480 min in animals that received 0.02 mg/kg buprenorphine i.v. Analgesic activity to 420 min was demonstrated in animals that received 0.01 mg/kg buprenorphine i.v. Analgesic activity was not demonstrated at any time point in animals that received 0.005 mg/kg buprenorphine i.v. A retrospective analysis of postoperative care records was performed to determine whether 0.01 mg/kg buprenorphine i.v. or intramuscularly (i.m.) postoperatively to swine provided clinically relevant analgesia. Records of swine receiving buprenorphine from 1997 to 2000 were reviewed for indications of treatment failure, such as pain or a change in analgesic regimen from that used routinely. Treatment failure occurred in 18 of 416 (4.3%) cases treated with buprenorphine. This failure occurred in 17% of cases with problems categorized as inflammatory in nature and in 15.5% of those with systemic problems or organ failure. We concluded that antinociceptive testing predicted that buprenorphine administered at 0.01 mg/kg i.v. in swine likely would provide analgesic efficacy for 6 h and when administered at 0.02 mg/kg i.v. likely would provide 10 h analgesia. Clinical signs of pain in animals recovering from surgery were not observed in the majority of cases when buprenorphine was administered twice or thrice daily at 0.01 mg/kg i.m. or i.v. However, buprenorphine was less effective at treating signs of pain associated with inflammation, organ failure, or systemic disease than at ameliorating pain associated with surgical incisions and orthopedic, dental, and ophthalmic procedures.
Descriptors: analgesics, opioid pharmacology, buprenorphine pharmacology, pain measurement veterinary, swine physiology, analgesics, opioid administration and dosage, buprenorphine administration and dosage, injections, intravenous veterinary, nociceptors drug effects, pain measurement drug effects, retrospective studies, swine surgery, time factors.

Rollin, B.E. (2002). **An ethicist's commentary on the case of the client requesting anesthesia medication.** *Canadian Veterinary Journal, The; Revue Veterinaire Canadienne, La* 43(11): 827. ISSN: 0008-5286.
NAL Call Number: 41.8 R3224
Descriptors: anesthesia veterinary, cesarean section veterinary, surgery, veterinary ethics, swine surgery, veterinarians ethics, anesthesia ethics, animal welfare, cesarean section ethics, ethics, professional, surgery, veterinary economics, veterinarians psychology.

Rud, H., O. Andresen, B. Ranheim, and H.A. Haga (2002). **Boar taint and castration of pigs - do suitable alternatives to local anaesthesia exist? [Kjonnslukt og kastrering av gris finnes det gode alternativer til lokalbedovelse?]**. *Norsk Veterinaertidsskrift* 114(4): 383-387. ISSN: 0332-5741.
Descriptors: anesthesia, boars, castration, piglets, pigs.
Language of Text: Norwegian, Summary in English.

Saers, A.S., M. Ritzmann, and K. Heinritzi (2005). **Evaluation and dosage determination of the anaesthetic thiopental for the anaesthesia of pigs after induction with neuroleptanalgesia [Anwendbarkeit und Dosisfindung des Anasthetikums Thiopental fur die Narkose des Schweins nach vorhergehender Neuroleptanalgesie.]**. *Tierarztliche Praxis Ausgabe G, Grosstiere/Nutztiere* 33(6): 432-437. ISSN: 1434-1220.
NAL Call Number: SF603.V43
Descriptors: anesthesia, anesthetics, analgesics, atropine, azaperone, body temperature, dosage, heart rate, ketamine, miniature pigs, neuroleptics, pharmacodynamics, piglets, respiration rate, thiopental, pigs.
Language of Text: German, Summary in English.

Sakihara, C., W.J. Perkins, D.O. Warner, and K.A. Jones (2004). **Anesthetics inhibit acetylcholine-promoted guanine nucleotide exchange of heterotrimeric G proteins of airway smooth muscle.** *Anesthesiology* 101(1): 120-6. ISSN: 0003-3022.
Abstract: BACKGROUND: Anesthetics inhibit airway smooth muscle contraction in part by a direct effect on the smooth muscle cell. This study tested the hypothesis that the anesthetics halothane and hexanol, which both relax airway smooth muscle in vitro, inhibit acetylcholine-promoted nucleotide exchange at the alpha subunit of the Gq/11 heterotrimeric G protein (Galphaq/11; i.e., they inhibit muscarinic receptor-Galphaq/11 coupling). METHODS: The effect of halothane (0.38 +/- 0.02 mm) and hexanol (10 mm) on basal and acetylcholine-stimulated Galphaq/11 guanosine nucleotide exchange was determined in membranes prepared from porcine tracheal smooth muscle. The nonhydrolyzable, radioactive form of guanosine-5'-triphosphate, [S]GTPgammaS, was used as the reporter for Galphaq/11 subunit dissociation from the membrane to soluble fraction, which was immunoprecipitated with rabbit polyclonal anti-Galphaq/11 antiserum. RESULTS: Acetylcholine caused a significant time- and concentration-dependent increase in the magnitude of Galphaq/11 nucleotide exchange compared with basal values (i.e., without acetylcholine), reaching a maximal difference at 100 microm (35.9 +/-2.9 vs. 9.8 +/-1.2 fmol/mg protein, respectively). Whereas neither anesthetic had an effect on basal Galphaq/11 nucleotide exchange, both halothane and hexanol significantly inhibited the increase in Galphaq/11 nucleotide exchange produced by 30 microm acetylcholine (by 59% and 68%, respectively). CONCLUSIONS: Halothane and hexanol interact with the receptor-heterotrimeric G-protein complex in a manner that prevents acetylcholine-promoted exchange of guanosine-5(')-triphosphate for guanosine-5'-diphosphate at Galphaq/11. These data are consistent with the ability of anesthetics to interfere with cellular processes mediated by heterotrimeric G proteins in many cells, including effects on muscarinic receptor-G-protein regulation of airway smooth muscle contraction.
Descriptors: acetylcholine antagonists and inhibitors, acetylcholine pharmacology, anesthetics pharmacology, gtp binding proteins metabolism, guanine nucleotides metabolism, muscle, smooth metabolism, anesthetics, inhalation pharmacology, gtp binding protein alpha

subunits, gs metabolism, guanosine 5' o 3 thiotriphosphate pharmacology, guanosine diphosphate metabolism, guanosine triphosphate metabolism, halothane pharmacology, hexanols pharmacology, membranes drug effects, membranes metabolism, muscle contraction physiology, muscle relaxation drug effects, muscle, smooth drug effects, precipitin tests, swine, trachea drug effects, trachea metabolism.

Sanchini, L., S. Pinna, and A. Venturini (2002). **Prolonged anaesthesia in minipigs [L'anestesia di lunga durata nel minipig.]** . *Obiettivi e Documenti Veterinari* 23(3): 67-71. ISSN: 0392-1913.
Descriptors: anesthesia, injectable anesthetics, laboratory animals, miniature pigs, pigs.
Language of Text: Italian, Summary in English.

Schmidt, A., I. Oye, and J. Akeson (2005). **Cerebral physiological responses to bolus injection of racemic, S(+)- or R(-)-ketamine in the pig.** *Acta Anaesthesiologica Scandinavica* 49(10): 1436-42. ISSN: 0001-5172.
Abstract: BACKGROUND: Little is known about the influence of ketamine and its enantiomers on cerebral haemodynamics, and there are no direct comparison reports. This study was designed to evaluate cerebrovascular responses to bolus injections of racemic, S(+)- and R(-)-ketamine in an established experimental model. METHODS: Anaesthesia was induced with propofol in 14 pigs and maintained with fentanyl and vecuronium. The intra-arterial xenon clearance technique was used to calculate the cerebral blood flow (CBF). Eight pigs (part I) were given three consecutive 60-s intravenous (i.v.) bolus injections of 10 mg/kg of racemic ketamine (Ketalar, Pfizer), and cerebral and systemic physiological responses were studied for 30 min after each injection. Following the determination of equipotent doses of the racemate and its enantiomers by recumbency tests, bolus injections of racemic ketamine (10 mg/kg), S-ketamine (5 mg/kg) and R-ketamine (20 mg/kg) were given in randomized sequence to another six pigs (part II) and evaluated at 1, 5, 10, 15, 25 and 40 min. RESULTS: No statistically significant acute tolerance in the CBF response to racemic ketamine was found in part I of the study. In part II, the decreases in the mean arterial pressure (MAP) and CBF by S-ketamine were significantly smaller than those by racemic and R-ketamine (both $P < 0.001$). No study drug had any significant effect on the cerebral arteriovenous oxygen content difference (C(av)O(2)) over time, but S-ketamine was associated with lower C(av)O(2) than racemic ketamine ($P = 0.008$) and R-ketamine ($P = 0.016$). CONCLUSIONS: Bolus injection of S-ketamine was associated with less cerebral and systemic haemodynamic depression than racemic or R-ketamine in equipotent doses in this experimental model. These findings indicate possible advantages of S-ketamine over racemic ketamine.
Descriptors: anesthetics, dissociative pharmacology, cerebrovascular circulation drug effects, ketamine pharmacology, anesthetics, dissociative administration and dosage, anesthetics, dissociative chemistry, biotransformation, blood pressure drug effects, hemodynamic processes drug effects, injections, intravenous, ketamine administration and dosage, ketamine chemistry, oxygen blood, stereoisomerism, swine, vascular resistance drug effects.

Schmidt, A., E. Ryding, and J. Akeson (2003). **Racemic ketamine does not abolish cerebrovascular autoregulation in the pig.** *Acta Anaesthesiologica Scandinavica* 47(5): 569-75. ISSN: 0001-5172.
Abstract: BACKGROUND: Little is known about the influence of racemic ketamine on

autoregulation of cerebral blood flow (CBF), and available reports regarding its influence on cerebral hemodynamics are contradictory. This study was designed to evaluate cerebrovascular responses to changes in the mean arterial pressure (MAP) during ketamine anesthesia. METHODS: In eight normoventilated pigs anesthesia was induced with propofol and maintained by i.v. infusion of ketamine (15.0 mg kg(-1) x h(-1)) during measurements. The intra-arterial xenon clearance technique was used to calculate CBF. Balloon-tipped catheters were introduced in the inferior caval vein and mid-aorta, and increases or decreases by up to 40% in mean arterial pressure (MAP) in random order were achieved by titrated inflation of these balloon catheters. Cerebral blood flow was determined at each MAP level. Regression coefficients of linear pressure-flow curves were calculated in all animals. RESULTS: From the mean baseline level (101 mmHg) MAP was reduced by 20% and 40%, and increased by 26% and 43%. The maximal mean increase and decrease in MAP induced a 12% increase and a 15% decrease, respectively, of CBF from the mean baseline level (52.6 ml.100 g(-1) x min1). The 95% confidence interval (-0.02; 0.38) of the mean regression coefficient of individual pressure-flow curves does not include the regression coefficient (0.64) of a linear correlation between MAP and CBF including origo (correlation coefficient 0.99), which indicates complete lack of cerebrovascular autoregulation. CONCLUSIONS: We conclude that autoregulation of CBF is not abolished during continuous ketamine infusion in normoventilated pigs and that previous divergent conclusions are unlikely to be associated with severe impairment of cerebrovascular autoregulation.

Descriptors: anesthetics, dissociative pharmacology, cerebrovascular circulation drug effects, homeostasis drug effects, ketamine pharmacology, analgesics, opioid pharmacology, anesthesia, anesthetics, dissociative administration and dosage, anesthetics, dissociative pharmacokinetics, anesthetics, intravenous pharmacology, blood pressure drug effects, dose response relationship, drug, fentanyl pharmacology, hemodynamic processes drug effects, infusions, intravenous, ketamine administration and dosage, ketamine pharmacokinetics, propofol pharmacology, respiration, artificial, stereoisomerism, swine.

Schmidt, M., T. Marx, S. Armbruster, H. Reinelt, and U. Schirmer (2005). **Effect of Xenon on elevated intracranial pressure as compared with nitrous oxide and total intravenous anesthesia in pigs.** *Acta Anaesthesiologica Scandinavica* 49(4): 494-501. ISSN: 0001-5172.

Abstract: BACKGROUND: Xenon in low concentrations has been investigated in neuroradiology to measure cerebral blood flow (CBF). Several reports have suggested that inhalation of Xenon might increase intracranial pressure (ICP) by increasing the cerebral blood flow and blood volume, raising concerns about using Xenon as an anesthetic in higher concentrations for head-injured patients. A porcine study is presented in which the effects of inhaled 75% Xenon on elevated ICP, cerebral perfusion pressure and the efficacy of hyperventilation for ICP treatment were compared with nitrous oxide anesthesia and total intravenous anesthesia (TIVA). METHODS: Twenty-one pentobarbital-anesthetized pigs (age: 12-16 weeks) were randomly assigned to three groups to receive either 4 h of Xenon-oxygen ventilation, nitrous oxide-oxygen ventilation or air-oxygen (75%/25%) ventilation, respectively. After instrumentation for parenchymal ICP measurement and ICP manipulation, an epidurally placed 6-F balloon catheter was inflated until a target ICP of 20 mmHg was achieved. After 4 h of anesthesia hyper- and hypoventilation maneuvers were performed and consecutive ICP and CBF changes were investigated. RESULTS: Intracranial pressure and CBF increased significantly in the nitrous oxide group as compared with the controls. There was no increase of ICP or CBF in the Xenon or control group. Intracranial pressure changed in all three groups

corresponding to hyper- and hypoventilation. CONCLUSIONS: During Xenon anesthesia, elevated ICP is not increased further and is partially reversible by hyperventilation. Our study suggests that inhalation of 75% Xenon seems not to be contraindicated in patients with elevated ICP.

Descriptors: anesthesia, intravenous, anesthetics, inhalation pharmacology, anesthetics, intravenous pharmacology, intracranial pressure drug effects, nitrous oxide pharmacology, xenon pharmacology, cardiac output drug effects, electroencephalography drug effects, hypnotics and sedatives pharmacology, pentobarbital pharmacology, s100 proteins metabolism, swine.

Schmidt, M., T. Marx, E. Gloggl, H. Reinelt, and U. Schirmer (2005). **Xenon attenuates cerebral damage after ischemia in pigs.** *Anesthesiology* 102(5): 929-36. ISSN: 0003-3022.

Abstract: BACKGROUND: Cerebral blood flow may be compromised in a variety of anesthetic procedures, and ischemic cerebral complications represent the leading cause of morbidity after cardiac operations. With the growing importance of neuroprotective strategies, the current study was designed to determine whether xenon would attenuate cardiac arrest-induced brain injury in pigs. METHODS: Twenty-four pigs (aged 12-16 weeks) were investigated in a randomized design. General hemodynamics, intracranial pressure, brain tissue oxygenation, and cerebral microdialysis parameters were investigated. The animals were assigned to two groups to receive anesthesia with either xenon (75%) in oxygen (25%) or total intravenous anesthesia combined with air in oxygen (25%) ventilation 15 min before cardiac arrest. After induction (t0) of cardiac arrest of 4 min, cardiopulmonary resuscitation was performed for 1 min, and the induced ventricular fibrillation was terminated by electrical defibrillation. The investigation time was 240 min. RESULTS: Approximately 60 s after cardiac arrest, brain tissue oxygenation decreased to a critical level of less than 5 mmHg, paralleled by a decrease in electroencephalographic activity. Glycerol as a damage marker increased significantly (> 200 m; $P < 0.05$), with a peak 90 min after cardiac arrest in both groups. Glycerol concentrations during reperfusion were significantly lower and normalized faster in the xenon group as compared with the total intravenous anesthesia group. CONCLUSION: Although the primary ischemic lesion in this model was similar in both groups, the cerebral microdialysis data show that xenon induces a differential neurochemical benefit in cerebral cell damage and metabolism as compared with total intravenous anesthesia in vivo during cerebral reperfusion after cardiac arrest in a pig model.

Descriptors: anesthetics, inhalation pharmacology, ischemic attack, transient prevention and control, neuroprotective agents, xenon pharmacology, anesthesia, intravenous, blood gas analysis, body temperature, brain pathology, brain chemistry drug effects, electroencephalography drug effects, glutamic acid metabolism, glycerol metabolism, heart arrest physiopathology, hemodynamic processes drug effects, intracranial pressure drug effects, ischemic attack, transient etiology, ischemic attack, transient pathology, lactic acid blood, microdialysis, oxygen consumption drug effects, pyruvic acid metabolism, swine.

Notes: Comment In: Anesthesiology. 2006 Jan;104(1):211; author reply 211-2.

Schmidt, M., T. Marx, J. Kotzerke, S. Luderwald, S. Armbruster, P. Topalidis, U. Schirmer, and H. Reinelt (2001). **Cerebral and regional organ perfusion in pigs during xenon anaesthesia.** *Anaesthesia* 56 (12): 1154-9. ISSN: 0003-2409.

Abstract: Little is known about the haemodynamic effects of inhaled xenon on regional organ perfusion. The aim of this study was to investigate the effect of 79% xenon ventila-

tion on organ perfusion in pigs. We investigated 10 pigs, which were randomly allocated to receive either xenon 79% or total intravenous anaesthesia (TIVA)/oxygen anaesthesia. Microspheres were used to determine organ perfusion. The following regions of interest were investigated: cerebral cortex, medulla oblongata, brainstem, cerebellum, liver, kidney, small intestine, colon, muscle, skin and heart. The results demonstrated a significant increase in regional perfusion in the brainstem (+63%), cerebral cortex (+38%), medulla oblongata (+35%) and cerebellum (+34%). All other organs showed no significant change in regional perfusion. We conclude that xenon should be used with caution in clinical situations associated with pathological increases in intracranial pressure, e.g. neurosurgical procedures, head injury, cerebral mass lesions or stroke.
Descriptors: anesthetics, inhalation pharmacology, cerebrovascular circulation drug effects, hemodynamic processes drug effects, xenon pharmacology, anesthetics, combined pharmacology, anesthetics, intravenous pharmacology, buprenorphine pharmacology, microspheres, pentobarbital pharmacology, regional blood flow drug effects, swine.

Schmidt, M., T. Marx, C. Papp Jambor, U. Schirmer, and H. Reinelt (2002). **Effect of xenon on cerebral autoregulation in pigs.** *Anaesthesia* 57(10): 960-6. ISSN: 0003-2409.
Abstract: There are little data on the effect of anaesthetic concentrations of xenon on cerebral pressure autoregulation. In this study, we have investigated the effect of 79% xenon inhalation on cerebral pressure autoregulation and CO2 response in pigs. Ten pigs were randomly allocated to receive xenon 79% or halothane anaesthesia, respectively, in a crossover designed study. Halothane was used to validate the experimental set-up. Transcranial Doppler was performed to determine the mean flow velocities in the middle cerebral artery (vMCA) during defined cerebral perfusion pressures and during normo-, hyper- and hypoventilation. The results showed that the inhalation of 79% xenon preserved cerebral autoregulation during conditions of normo-, hyper- and hypoventilation and at different cerebral perfusion pressures in pigs. These results suggest that with the inhalation of xenon, in the highest concentration suitable for a safe clinical use, cerebral autoregulation is preserved.
Descriptors: anesthetics, inhalation pharmacology, homeostasis drug effects, intracranial pressure drug effects, xenon pharmacology, blood pressure drug effects, carbon dioxide blood, cerebrovascular circulation drug effects, cross over studies, halothane pharmacology, hydrogen ion concentration drug effects, partial pressure, swine, ultrasonography, doppler, transcranial.

Schnoor, J., J.K. Unger, B. Kochs, J. Silny, and R. Rossaint (2005). **Effects of a single dose of ketamine on duodenal motility activity in pigs.** *Canadian Veterinary Journal, The; Revue Veterinaire Canadienne, La* 46(2): 147-52. ISSN: 0008-5286.
NAL Call Number: 41.8 R3224
Abstract: In order to investigate the effects of a single dose of ketamine on duodenal motility, the present study focused on the electric impedance technique. Five pigs (32 to 40 kg, CVC group) were instrumented with a central venous catheter 1 d before measurements. The next day, general anesthesia was started and maintained via central venous catheter by propofol and fentanyl. In contrast, the pigs of the KETA group (n = 5) received ketamine intramuscularly prior to the induction of anesthesia by the injection of propofol-fentanyl via an ear vein. An intraluminal impedance catheter was manually introduced into the proximal duodenum. Measurements were recorded for 4 h. The KETA group showed a median duration of phase II that was shortened by 35%, while phase I was prolonged by 73% ($P < 0.05$).

In conclusion, when gastrointestinal motility has to be investigated, the effects of a single dose of ketamine, even for premedication, should be taken into consideration.
Descriptors: anesthetics, dissociative pharmacology, duodenum drug effects, gastrointestinal motility drug effects, ketamine pharmacology, swine physiology, duodenum physiology, electric impedance, gastrointestinal motility physiology, injections, intramuscular veterinary, random allocation.

Schoffmann, G., P. Winter, R. Palme, A. Pollak, G. Trittenwein, and J. Golej (2009). **Haemodynamic changes and stress responses of piglets to surgery during total intravenous anaesthesia with propofol and fentanyl.** *Laboratory Animals* 43(3): 243-248. ISSN: 0023-6772.
NAL Call Number: QL55.A1L3
Abstract: The purpose of the study was to assess the haemodynamic (blood pressure and heart rate) changes and stress responses (serum cortisol and serum amyloid A [SAA] concentrations) to surgery in piglets during total intravenous anaesthesia (TIVA) with propofol and fentanyl. After preanaesthetic medication with intramuscular midazolam (0.5 mg/kg body mass), ketamine (10 mg/kg) and butorphanol (0.5 mg/kg) anaesthesia was induced in five piglets, with intravenous propofol (1 mg/kg) followed by tracheal intubation and mechanical lung ventilation. Soft tissue surgery was performed in the jugular and inguinal regions during TIVA with propofol (8 mg/kg/h) and fentanyl (35 og/kg/h). Anaesthesia was maintained for 300 min after surgery as the piglets were the control group of a project involving extracorporeal membrane oxygenation. Mean plasma cortisol concentration decreased significantly ($P < 0.05$) from 59 pl 39.9 nmol/L (mean pl 1 SD) before surgery to 7.5 pl 2.5 nmol/L 300 min after end of surgical procedure. The mean SAA concentrations increased over the same period from 1.6 pl 2.3 og/mL to 4.2 pl 5.6 og/mL without statistical significance. The baseline (presurgery) mean arterial pressure (MAP) was 72 pl 9 mmHg compared with 72 pl 11 mmHg 300 min after end of surgery. Neither heart rate nor lactate concentrations changed significantly over the same time points: heart rate was 104 pl 11 and 103 pl 15 beats/min whereas mean lactate concentrations were reduced from 1.14 pl 0.45 mmol/L to 0.90 pl 0.22 mmol/L. Haemodynamic stability, a decrease in serum cortisol and a non-statistically significant rise in mean SAA concentrations suggest that the anaesthetic described suppresses the stress response of piglets to surgery without adverse cardiovascular effects. Therefore, it may prove useful in cardiovascular research.
Descriptors: piglets, laboratory animals, surgery, anesthesia, general anesthetics, fentanyl, drug evaluation, combination drug therapy, intravenous injection, risk assessment, adverse effects, cardiovascular system, blood pressure, heart rate, animal stress, stress tolerance, biomarkers, cortisol, lactates, propofol-, serum-amyloid-A.

Schonreiter, S., V. Lohmuller, H. Huber, A.J. Zanella, J. Unshelm, and W. Erhardt (2000). **Effects of CO2/O2-anaesthesia on behaviour, beta -endorphin- and cortisol concentrations of male piglets after castration. [Auswirkungen der CO2/O2-Narkose auf das Verhalten sowie die beta -Endorphin- und Cortisolkonzentrationen mannlicher Saugferkel nach der Kastration.]**. *KTBL Schrift*(391): 137-145.
Descriptors: anesthesia, animal behavior, animal welfare, carbon dioxide, castration, endorphins, hydrocortisone, oxygen, stress, surgery.
Language of Text: German, Summary in English.
Notes: Meeting Information: Aktuelle Arbeiten zur artgemassen Tierhaltung 1999. Vortrage

anlasslich der 31. Internationalen Arbeitstagung Angewandte Ethologie bei Nutztieren der Deutschen Veterinarmedizinischen Gesellschaft e. V. Fachgruppe Verhaltensforschung vom 18. bis 20. November 1999 in Freiburg/Breisgau.

Schulz, C., M. Ritzmann, A. Palzer, K. Heinritzi, and S. Zols (2007). **Effect of isoflurane-anesthesia on postoperative pain due to castration of piglets [Auswirkung einer Isofluran-Inhalations-narkose auf den postoperativen Kastrationsschmerz von Ferkeln.]**. *Berliner Und Munchener Tierarztliche Wochenschrift* 120(5/6): 177-182. ISSN: 0005-9366.
NAL Call Number: 41.8 B45
Descriptors: anesthesia, castration, hydrocortisone, isoflurane, non steroidal antiinflammatory agents, cortisol peak, pain, piglets, postoperative care, postoperative complications.
Language of Text: German, Summary in English.

Schulz, C., M. Ritzmann, A. Palzer, K. Heinritzi, and S. Zols (2007). **Auswirkung einer Isofluran-inhalations- narkose auf den postoperativen Kastrationsschmerz von Ferkeln. [Effect of isoflurane inhalation anesthesia on postoperative pain due to castration of piglets]**. *Berliner Und Munchener Tierarztliche Wochenschrift* 120(5-6): 177-82. ISSN: 0005-9366.
NAL Call Number: 41.8 B45
Abstract: Since April 2006 piglets in Germany can only be castrated without anesthesia in the first 7 days of life. However, a castration is a painful experience even for an animal of this young age. Whether the castration under isoflurane-anesthesia is a reasonable alternative to castration without anesthesia was tested in the following investigation at 206 4 to 6 day old piglets.The serum-cortisol-concentration was chosen as the parameter for the pain caused by castration. A part of the animals was castrated without anesthesia (group II, n = 42) or with anesthesia (group IV, n = 41). Additionally Meloxicam, a non-steroidal anti-inflammatory drug, was applicated to piglets castrated with anesthesia (group V, n = 41). For control another part of the animals were only handled without (group I, n = 41) or with anesthesia (group III, n = 41), but they were not castrated. Cortisol-concentration prior to castration was compared to the concentration 0.5, 1,4 and 24 hours after castration. In addition cortisol was compared between groups at all points of time. Cortisol did rise significantly in castrated animals with animals with or without anesthesia than in animals of the non-castrated control groups. Cortisol after castration was significantly lower in piglets with an application of Meloxicam prior to castration. The pain caused by castration is an explanation for the differences in cortisol-concentration between castrated and not-castrated animals. Regarding those results, we assume that castration with isoflurane-anesthesia does not fulfil the demand for reducing pain after castration compared to castrating piglets without anesthesia.
Descriptors: anesthesia, inhalation veterinary, anesthetics, inhalation administration and dosage, isoflurane administration and dosage, orchiectomy veterinary, pain, postoperative veterinary, swine surgery, animals, newborn surgery, anti inflammatory agents, non steroidal administration and dosage, handling psychology, hydrocortisone blood, orchiectomy adverse effects, orchiectomy methods, pain, postoperative drug therapy, pain, postoperative prevention and control, thiazines administration and dosage, thiazoles administration and dosage, time factors, treatment outcome.
Language of Text: German.

Schuster, F., H. Scholl, M. Hager, R. Muller, N. Roewer, and M. Anetseder (2006). **The dose-response relationship and regional distribution of lactate after intramuscular injection of halothane and caffeine in malignant hyperthermia-susceptible pigs.** *Anesthesia and Analgesia* 102(2): 468-72.

Abstract: We hypothesized that IM halothane and caffeine injection increases local lactate concentration dose-dependently in malignant hyperthermia-susceptible (MHS) and nonsusceptible (MHN) pigs and that the hypermetabolic reaction measured by regional distribution of lactate and carbon dioxide is limited to a small muscle volume. Microdialysis probes were placed in the hindlimbs of 7 MHS and 7 MHN pigs and perfused with Ringer's solution. After equilibration, boluses of increasing halothane and caffeine concentrations were injected. For the second hypothesis regarding regional distribution, microdialysis probes were positioned in 7 MHS and 6 MHN pigs at the injection site for halothane and caffeine and at a distance of 10 mm and 25 mm. Lactate was measured in the dialysate by spectrophotometry. In addition, PCO2 was measured in the halothane experiments. Halothane and caffeine increased IM lactate dose-dependently in MHS pigs significantly more than in MHN pigs. Lactate and PCO2 were increased only at the injection site but not at 10 mm and 25 mm distance. MH susceptibility leads to a leftward shift of the dose-response curve for IM lactate after local injection of halothane and caffeine. The increase of lactate and carbon dioxide levels after local MH trigger injection is limited to a small area around the probe.

Descriptors: anesthetics, inhalation pharmacology, caffeine pharmacology, halothane pharmacology, lactic acid metabolism, malignant hyperthermia metabolism, anesthetics, inhalation administration and dosage, caffeine administration and dosage, carbon dioxide blood, disease susceptibility, dose response relationship, drug, halothane administration and dosage, injections, intramuscular, malignant hyperthermia diagnosis, microdialysis, swine.

Schwarzkopf, K., T. Schreiber, R. Bauer, H. Schubert, N.P. Preussler, E. Gaser, U. Klein, and W. Karzai (2001). **The effects of increasing concentrations of isoflurane and desflurane on pulmonary perfusion and systemic oxygenation during one-lung ventilation in pigs.** *Anesthesia and Analgesia* 93(6): 1434-8, Table of Contents. ISSN: 0003-2999.

Abstract: During one-lung ventilation (OLV), hypoxic pulmonary vasoconstriction (HPV) reduces venous admixture and attenuates the decrease in arterial oxygen tension by diverting blood from the nonventilated lung to the ventilated lung. In vitro, desflurane and isoflurane depress HPV in a dose-dependent manner. Accordingly, we studied the effects of increasing concentrations of desflurane and isoflurane on pulmonary perfusion, shunt fraction, and PaO(2) during OLV in vivo. Fourteen pigs (30-42 kg) were anesthetized, tracheally intubated, and mechanically ventilated. After placement of femoral arterial and thermodilution pulmonary artery catheters, a left-sided double-lumen tube (DLT) was placed via tracheotomy. After DLT placement, FIO(2) was adjusted at 0.8 and anesthesia was continued in random order with 3 concentrations (0.5, 1.0, and 1.5 minimal alveolar concentrations) of either desflurane or isoflurane. Differential lung perfusion was measured with colored microspheres. All measurements were made after stabilization at each concentration. Whereas mixed venous PO(2), mean arterial pressure, cardiac output, nonventilated lung perfusion, and shunt fraction decreased in a dose-dependent manner, PaO(2) remained unchanged with increasing concentrations of desflurane and isoflurane during OLV. In conclusion, increasing concentration of desflurane and isoflurane did not impair oxygenation during OLV in pigs. IMPLICATIONS: In an animal model of one-lung ventilation, increasing concentrations of desflurane and isoflurane dose-dependently decreased shunt fraction and perfusion of the

nonventilated lung and did not impair oxygenation. The decreases in shunt fraction are likely the result of anesthetic-induced marked decreases in cardiac output and mixed venous saturation.

Descriptors: anesthetics, inhalation pharmacology, isoflurane pharmacology, pulmonary circulation drug effects, respiration, artificial methods, anesthetics, inhalation administration and dosage, blood pressure drug effects, dose response relationship, drug, isoflurane administration and dosage, isoflurane analogs and derivatives, oxygen blood, respiratory mechanics drug effects, swine, vasoconstriction drug effects.

Schwarzkopf, K., T. Schreiber, N.P. Preussler, E. Gaser, L. Huter, R. Bauer, H. Schubert, and W. Karzai (2003). **Lung perfusion, shunt fraction, and oxygenation during one-lung ventilation in pigs: the effects of desflurane, isoflurane, and propofol.** *Journal of Cardiothoracic and Vascular Anesthesia* 17(1): 73-5. ISSN: 1053-0770.

NAL Call Number: RD87.3.H43

Abstract: OBJECTIVE: To study how desflurane, isoflurane, and propofol affect pulmonary perfusion, shunt fraction, and systemic oxygenation during one-lung ventilation (OLV) in vivo. DESIGN: Prospective animal study with a crossover design. SETTING: Animal laboratory of a university hospital. PARTICIPANTS: Twelve female pigs. INTERVENTIONS: The pigs were anesthetized, tracheally intubated, and mechanically ventilated. After placement of femoral arterial and thermodilution pulmonary artery catheters, a left-sided, double-lumen tube (DLT) was placed via tracheotomy. After DLT placement, F(I)O(2) was adjusted at 0.8, and anesthesia was continued in random order with 1 minimal alveolar concentration of desflurane, 1 minimal alveolar concentration of isoflurane, or propofol. MEASUREMENTS AND MAIN RESULTS: Measurements of respiratory and hemodynamic parameters were made after stabilization at each anesthetic. During OLV, perfusion of the nonventilated lung and shunt fraction were comparable during all 3 anesthetics. PaO(2) was lower during desflurane and isoflurane anesthesia as compared with propofol anesthesia. Mixed venous PO(2) and cardiac output were lower with desflurane and isoflurane as compared with propofol. CONCLUSIONS: In a clinically relevant model of OLV cardiac output, PaO(2) and mixed venous PO(2) decreased during desflurane and isoflurane as compared with propofol, whereas perfusion of the nonventilated lung and shunt fraction remained comparable.

Descriptors: anesthetics, inhalation pharmacology, anesthetics, intravenous pharmacology, isoflurane analogs and derivatives, isoflurane pharmacology, oxygen blood, propofol pharmacology, pulmonary circulation drug effects, pulmonary circulation physiology, respiration, artificial statistics and numerical data, cross over studies, intubation, intratracheal, prospective studies, swine.

Schwarzkopf, K., T. Schreiber, E. Gaser, N.P. Preussler, L. Hueter, H. Schubert, H. Rek, and W. Karzai (2005). **The effects of xenon or nitrous oxide supplementation on systemic oxygenation and pulmonary perfusion during one-lung ventilation in pigs**. *Anesthesia and Analgesia* 100(2): 335-339. ISSN: 0003-2999.

DOI: 10.1213/01.ANE.0000142118.84049.80

Abstract: During experimental one-lung ventilation (OLV), the type of anesthesia may alter systemic hemodynamics, lung perfusion, and oxygenation. We studied whether xenon (Xe) or nitrous oxide (N2O) added to propofol anesthesia would affect oxygenation, lung perfusion, and systemic and pulmonary hemodynamics during OLV in a pig model. Nine

pigs were anesthetized, tracheally intubated, and mechanically ventilated. After placement of arterial and pulmonary artery catheters, a left-sided double-lumen tube was placed via tracheotomy. W anesthesia with propofol was supplemented in random order with N2O/O2 60:40 or Xe/O2 60:40 or N2/O2 60:40. All measurements were made after stabilization at each concentration. Differential lung perfusion was measured with colored microspheres. Oxygenation (Pao2: 90 +/- 17, 95 +/- 20, and 94 +/- 20 mm Hg for N2/O2, N2O/O2, and Xe/O2) and left lung perfusion (16% +/- 5%, 14% +/- 6%, and 18.8% for N2/O2, N2O/O2, and Xe/O2) during OLV did not differ among the 3 groups. However, mean arterial blood pressure (78 +/- 25, 62 +/- 23, and 66 +/- 23 mm Hg for N2/O2, N2O/O2, and Xe/O2) and mixed venous saturation (55% +/- 12%, 48% +/- 12%, and 50% +/- 12% for N2/O2, N2O/O2, and Xe/O2) were reduced during N2O/O2 as compared with the control group (N2/O2), Supplementation of IV anesthesia with Xe or N2O does not impair oxygenation nor alter lung perfusion during experimental OLV.
Descriptors: anesthesiology, cardiovascular system, anesthesia, lung perfusion , mechanical ventilation, one lung ventilation, oxygenation, tracheal intubation, tracheotomy, pulmonary hemodynamics, rnean arterial blood pressure, systemic hemodynamics .

Scolletta, S., S.M. Romano, B. Biagioli, G. Capannini, and P. Giomarelli (2005). **Pressure recording analytical method (pram) for measurement of cardiac output during various haemodynamic states**. *British Journal of Anaesthesia* 95(2): 159-165. ISSN: 0007-0912.
Descriptors: pharmacology, cardiovascular system: transport and circulation, methods and techniques, bland altman analysis, mathematical and computer techniques, pulmonary artery catheter, medical equipment, thermodilution, clinical techniques, diagnostic techniques, pressure recording analytical method, pram, clinical techniques, diagnostic techniques, beat by beat stroke volume monitoring, clinical techniques, diagnostic techniques, electromagnetic flowmetry, em co, clinical techniques, diagnostic techniques, femoral artery catheter, medical equipment, cardiac output, method accuracy, hemodynamic state, hypodynamic state.

Sen, S., L.M. Ytrebo, C. Rose, O.M. Fuskevaag, N.A. Davies, G.I. Nedredal, R. Williams, A. Revhaug, and R. Jalan (2004). **Albumin dialysis: a new therapeutic strategy for intoxication from protein-bound drugs.** *Intensive Care Medicine* 30(3): 496-501. ISSN: 0342-4642.
NAL Call Number: RC86
Abstract: OBJECTIVE: Although water-soluble drugs can be removed by haemofiltration/haemodialysis, morbidity and mortality from intoxication with protein-bound drugs remains high. The present study investigates whether albumin dialysis in the form of the Molecular Adsorbents Recirculating System (MARS) is effective in removal of protein-bound drugs. DESIGN: Prospective animal study. SETTING: Surgical research laboratory in a university hospital. SUBJECTS: Seven female Norwegian Landrace pigs. INTERVENTION: We studied whether midazolam (97% albumin-bound) and fentanyl (85% alpha-1-acid glycoprotein-bound), administered as anaesthetics to pigs with induced acute liver failure, could be removed by MARS dialysis lasting for 4 h. MEASUREMENTS: After 4 h of dialysis, total and free anaesthetic concentrations were measured in the blood and dialysate from different segments of the MARS circuit. MAIN RESULTS: Midazolam: total plasma concentrations fell by 47.1+/-2.1% (in 4 h) across the MARS filter ($p<0.01$). The charcoal component of the system reduced the total dialysate drug concentration by 16.4+/-2.2% ($p<0.05$). Free midazolam removal followed a similar pattern. Fentanyl: total plasma concentrations fell by

56.1+/-2.4% (in 4 h) across the MARS filter (p<0.01). Clearance of fentanyl from the dialysate by the charcoal was 70+/-0.7% at 4 h (p<0.001). CONCLUSIONS: The results of the study show that MARS can remove both albumin and other protein-bound drugs efficiently from the plasma, and it may have a place for the treatment of patients suffering from intoxication with this class of compounds.
Descriptors: anesthetics, intravenous blood, fentanyl blood, liver failure, acute therapy, midazolam blood, sorption detoxification methods, anesthetics, intravenous chemistry, fentanyl chemistry, linear models, midazolam chemistry, orosomucoid, protein binding, serum albumin, swine.
Notes: Comment In: Clin Toxicol (Phila). 2006;44(2):195-6.

Shafer, S.L. (2004). **Shock values.** *Anesthesiology* 101(3): 567-8. ISSN: 0003-3022.
Descriptors: anesthetics, intravenous adverse effects, cardiopulmonary resuscitation, propofol adverse effects, anesthetics, intravenous pharmacokinetics, propofol pharmacokinetics, shock, hemorrhagic physiopathology, shock, hemorrhagic therapy, swine.
Notes: Comment On: Anesthesiology. 2004 Sep;101(3):647-59.

Shahani, S.K., R. Lingamaneni, and H.C.J. Hemmings (2002). **General anesthetic actions on norepinephrine, dopamine, and gamma-aminobutyric acid transporters in stably transfected cells.** *Anesthesia and Analgesia* 95(4): 893-9, Table of Contents. ISSN: 0003-2999.
Abstract: The effects of general anesthetics on neurotransmitter uptake by plasma membrane transporters are controversial. We analyzed the effects of representative volatile and IV general anesthetics on recombinant transporters for norepinephrine (human NET), dopamine (rat DAT), or gamma-aminobutyric acid (rat GAT-1) stably expressed in a porcine kidney cell line (LLC-PK(1)). This approach avoids complicating factors associated with neuronal preparations, such as the involvement of multiple transporters and the indirect effects of membrane potential. At clinical concentrations, human NET was inhibited only by halothane (50% inhibitory concentration [IC(50)] = 0.54 mM), rat DAT was sensitive to both halothane and isoflurane (IC(50) = 0.60 and 0.64 mM, respectively), and rat GAT-1 was insensitive to both volatile anesthetics. Human NET was inhibited in a dose-dependent fashion by propofol (IC(50) = 41 micro M), ketamine (IC(50) = 150 micro M), and etomidate (IC(50) > 200 micro M), but not by pentobarbital. Only propofol inhibited NET at a clinically relevant concentration (5 micro M). Rat DAT was inhibited in a dose-dependent fashion by propofol (IC(50) = 120 micro M), etomidate (IC(50) = 100 micro M), and ketamine (IC(50) = 210 micro M), but not by pentobarbital. None of these anesthetics was predicted to inhibit DAT at concentrations that produce anesthesia. Propofol inhibited rat GAT-1, but only at the largest concentration tested. General anesthetics have drug- and subtype-selective actions on neurotransmitter transporters. We conclude that effects on catecholamine, but not gamma-aminobutyric acid, transporters may contribute to secondary synaptic actions of certain anesthetics but are unlikely to be essential to their anesthetic properties. IMPLICATIONS: Previous studies have implicated neurotransmitter transporters as targets for general anesthetic effects on synaptic transmission. Recombinant transporters for norepinephrine and dopamine were sensitive to certain volatile and IV anesthetics, whereas gamma-aminobutyric acid transporters were insensitive. These anesthetic- and neurotransmitter-specific effects may underlie some of the secondary effects of general anesthetics.
Descriptors: anesthetics, general pharmacology, carrier proteins antagonists and inhibitors, membrane glycoproteins, membrane proteins antagonists and inhibitors, membrane

transport modulators, membrane transport proteins antagonists and inhibitors, nerve tissue proteins, organic anion transporters, symporters antagonists and inhibitors, dopamine plasma membrane transport proteins, dose response relationship, drug, gaba plasma membrane transport proteins, llc pk1 cells, norepinephrine plasma membrane transport proteins, rats, swine, transfection.

Shepherd, P.A., P.D. Eleazer, S.J. Clark, and J.P. Scheetz (2001). **Measurement of intraosseous pressures generated by the Wand, high-pressure periodontal ligament syringe, and the Stabident system.** *Journal of Endodontics* 27(6): 381-4. ISSN: 0099-2399.
NAL Call Number: RK351
Abstract: Intraosseous pressure generated by the use of three anesthetic systems-the Wand; a hand-operated high-pressure periodontal ligament (PDL) syringe; and the Stabident system-were studied in fresh mandibles of 14 large swine. The mandibles were drilled and tapped in one area of both the right and left posterior molar regions. Pressure gauges were attached via threaded fittings. Pressures during injection were recorded for the Wand first, then the PDL syringe, and finally Stabident. Results showed averages of 8.3 mm Hg generated by the Wand, 16.3 mm Hg with the high-pressure PDL syringe, and 43.7 mm Hg from the Stabident system. Results were corroborated with data from three human cadaver mandibles.
Descriptors: anesthesia, dental instrumentation, mandible physiology, syringes, analysis of variance, cadaver, equipment design, injections instrumentation, manometry instrumentation, periodontal ligament, pressure, rheology, statistics, swine.

Sidi, A., J.D. Muehlschlegel, D.S. Kirby, and E.B. Lobato (2006). **Treatment of ischaemic left ventricular dysfunction with milrinone or dobutamine administered during coronary artery stenosis in the presence of beta blockade in pigs**. *British Journal of Anaesthesia* 97(6): 799-807. ISSN: 0007-0912.
Descriptors: pharmacology, milrinone, dobutamine, cardiovascular system: transport and circulation, veterinary medicine: medical sciences, ischemic left ventricular dysfunction, vascular disease, drug therapy, surgery, etiology , coronary artery stenosis, heart disease, vascular disease, drug therapy, etiology, coronary occlusion.

Sigg, D.C. and P.A. Iaizzo (2006). **In vivo versus in vitro comparison of swine cardiac performance: induction of cardiodepression with halothane.** *European Journal of Pharmacology* 543(1-3): 97-107. ISSN: 0014-2999.
NAL Call Number: RS1
Abstract: An in situ versus in vitro comparison of relative dose-dependent effects of halothane on cardiac performance was investigated, including ventricular systolic/diastolic function. Such comparative studies may be of interest to individuals working on heart failure models, cardiac device testing, or xenotransplantation. Normal swine (n=9) received halothane at levels of 0.25, 0.5 and 1 MAC (minimum alveolar concentration) for 30 min each. Parameters assessed included: 1) heart rate; 2) arterial blood pressure; 3) pulmonary artery, central venous, left and right ventricular pressures; 4) cardiac output; 5) end-expiratory CO(2) and halothane levels; 6) cardiac temperature; and 7) arterial blood gases. Hearts were removed using standard cardioplegic procedures and reperfused in four-chamber working mode (n=8); again the effects of increasing halothane concentrations on cardiac performance were analyzed. When comparing biventricular depressive effects (negative inotropic, negative lusitropic) of halothane in vivo and in vitro, there were distinct quantitative differences.

The negative lusitropic effects were less pronounced in vitro; this was especially true for the right ventricle. Yet, in vitro, halothane at all doses induced more pronounced decreases in left heart output compared to the right. The large mammalian isolated four-chamber working heart model allows for novel assessment of pharmacodynamics and/or evaluation of cardiac devices under a range of hemodynamic performances. Halothane, a cardiodepressive agent, induced direct myocardial depressive effects in vitro similar to those recorded in vivo; hence additional systemic effects are considered to play a minor role in ultimate performances, e.g., compensatory responses due to autonomic controls.

Descriptors: anesthetics, inhalation pharmacology, halothane pharmacology, heart drug effects, myocardial contraction drug effects, blood gas analysis, blood pressure drug effects, body temperature drug effects, cardiac output drug effects, central venous pressure drug effects, depression, chemical, dose response relationship, drug, heart physiology, heart rate drug effects, models, animal, pulmonary gas exchange drug effects, swine, ventricular function, left drug effects, ventricular function, right drug effects, ventricular pressure drug effects.

Singer, D.D., A.J. Singer, S.A. McClain, and G. Tortora (2005). **Histologic effects of laser-assisted topical anesthesia in a porcine model.** *Academic Emergency Medicine Official Journal of the Society for Academic Emergency Medicine* 12(12): 1148-52.

Abstract: OBJECTIVES: A handheld laser device that removes the stratum corneum, the major barrier to transdermal absorption, has recently been approved to assist with topical anesthesia before painful procedures such as intravenous cannulation. The authors assessed the cutaneous histomorphologic effects of the laser device and the ability of the laser-treated skin to resist infection in a porcine model. METHODS: This was a blinded, randomized animal experiment using isoflurane-anesthetized young domestic pigs. The ventral surface of the animals was irradiated multiple times with a lightweight, portable erbium yttrium-aluminum-garnet unit or a sham laser. One third of the wounds were inoculated with a Staphylococcus aureus suspension. The treated areas were then covered with a dry dressing, and full-thickness biopsy specimens of the treated areas were obtained immediately after treatment and at three, seven, ten, and 14 days for blinded histopathologic evaluation using hematoxylin and eosin staining and electron microscopy. Quantitative bacterial counts were obtained at three days in wounds exposed to bacteria. Main outcomes were quantitative bacterial counts, presence of cellular necrosis, epidermal integrity, and dermal scarring. Data analysis was conducted with descriptive statistics. RESULTS: Laser irradiation resulted in immediate disruption of the cornified layer of the skin and necrosis of the stratum spinosum in all treated areas. There were also focal areas of vacuolar alteration of the basal one third of the epidermis. There was no evidence of any damage to the basement membrane or the underlying dermis. At three days, the epidermis had healed and there was evidence of epidermal hyperplasia and hyperkeratosis that was completely resolved by 14 days. There were no infections and no scarring. Sham laser had no histomorphologic effects on the skin. There was no bacterial growth from all sham laser-treated wounds challenged with bacteria. Three of 20 (15%; 95% confidence interval = 0% to 31%) laser-irradiated wounds that were challenged with bacteria grew between 280,000 and 1,600,000 colony-forming units/g. CONCLUSIONS: Laser irradiation results in ablation of the stratum corneum and a superficial burn to the epidermis that heals by three to 14 days without any scarring or infection in pigs. Challenging laser-irradiated cutaneous wounds with a large bacterial inoculum resulted in bacterial growth in a minority of wounds.

Descriptors: anesthesia, local methods, laser therapy, low level methods, skin pathology, skin radiation effects, administration, topical, bacterial infections radiotherapy, disease models, animal, random allocation, reference values, sus scrofa, wound healing radiation effects.

Sintov, A.C. and R. Brandys Sitton (2006). **Facilitated skin penetration of lidocaine: combination of a short-term iontophoresis and microemulsion formulation.** *International Journal of Pharmaceutics* 316(1-2): 58-67. ISSN: 0378-5173.

NAL Call Number: RS122.A1I5

Abstract: The objective of this study was to demonstrate the potential of the application of a short-term iontophoresis on the topical delivery of lidocaine hydrochloride from a microemulsion-based system. Five- and 10-min durations of anodal iontophoresis applied onto porcine skin were examined in combination with a microemulsion containing 2.5% lidocaine hydrochloride. A similar combination (10-min iontophoresis with microemulsion in the anodal electrode) was also examined in vivo in a rat model. It was shown in vitro that by combining microemulsion application with a 10-min iontophoresis of 1.13 mA/cm2 electric current density, a significantly increased flux was obtained compared with a combination of aqueous drug solution with the same iontophoresis protocol. In vivo studies revealed that 57.71 +/- 18.65 and 18.43 +/- 9.17 microg cm(-2) were reached in the epidermis and dermis, respectively, at t = 30 min of microemulsion application, when iontophoresis was applied for 10 min. In contrast, the application of aqueous solution-iontophoresis resulted in a relatively lower drug accumulation (21.44 +/- 10.42 and 5.30 +/- 2.25 microg cm(-2) in the epidermis and dermis, respectively, at t = 30) with more rapid clearance of the drug from the skin. Ten-minute application of a low-current electric field on a new topical microemulsion appears to make significant changes in skin permeability. The potential advantages of this procedure include significantly increased flux, accumulation of a large skin drug depot, short lag times, reduced irritation (compared to long-term iontophoresis), simplicity and ease of compliance.

Descriptors: anesthetics, local administration and dosage, anesthetics, local chemistry, anesthetics, local pharmacokinetics, iontophoresis, lidocaine administration and dosage, lidocaine chemistry, lidocaine pharmacokinetics, skin metabolism, chromatography, high pressure liquid, drug carriers, drug compounding, emulsions, hydrogen ion concentration, rabbits, rats, rats, sprague dawley, skin absorption, skin physiology, swine, time factors.

Slater, J.M., T.A. Orszulak, and D.J. Cook (2001). **Independent control of brain and body temperature using an endoaortic baffle (cardeon cobratm) during cardiopulmonary bypass (cpb) in swine**. *Anesthesia and Analgesia* 92(4 Supplement): SCA61. ISSN: 0003-2999.

Descriptors: equipment, apparatus, devices and instrumentation, cardiovascular system: transport and circulation, cobra endoaortic baffle, equipment , cardiopulmonary bypass, experimental method, surgical method, body temperature, cerebral protection, hemodynamics, meeting abstract.

Notes: Meeting Information: 23rd Annual Meeting of the Society of Cardiovascular Anesthesiologists, Vancouver, BC, Canada; May 5-9, 2001.

Smith, A.C. and M. Swindle (2008). **Anesthesia and analgesia in swine.** In: R.E. Fish *Anesthesia and Analgesia in Laboratory Animals.,* 2nd edition, Academic: Amsterdam; Boston; London, p. 413-440. ISBN: 978-0-12-373898-1.

NAL Call Number: SF996.5 .A54 2008
Abstract: This chapter is an updated version of the book chapter on porcine anesthesia that was written for the first edition of this textbook. In the first edition, the submission on cardiopulmonary bypass (CPB) and malignant hyperthermia (MH) was written by William J. Ehler, DVM. He is not a coauthor on this version of the chapter; however, his original submission is retained mostly intact with updates from the literature.
Descriptors: surgery, anesthetic delivery, inhalation anesthesia, injectable anesthetics and tranquilizers, analgesia, postsurgical care, cardiopulmonary bypass .
Notes: Previous ed.: 1997.

Sondhi, S.M., N. Singh, A.M. Lahoti, K. Bajaj, A. Kumar, O. Lozach, and L. Meijer (2005). **Synthesis of acridinyl-thiazolino derivatives and their evaluation for anti-inflammatory, analgesic and kinase inhibition activities.** *Bioorganic and Medicinal Chemistry* 13(13): 4291-9. ISSN: 0968-0896.
NAL Call Number: QP550.B55
Abstract: Variety of N-(4-phenyl-3-(2',3',4'(un)substituted phenyl)thiazol-2(3H)-ylidene)-2,4(un)substituted acridin-9-amine (4a-o) and 1-[(2,4-(un)substituted acridin-9-yl)-3-(4-phenyl-3-(2',3',4'(un)substituted phenyl)thiazol-2(3H)-ylidene)]isothiourea (5a-h) derivatives have been synthesized by condensation of 4-phenyl-3-(2',3',4'(un) substituted phenyl)thiazol-2(3H)-imine (3a-g) with 9-chloro-2,4-(un)substituted acridine (1a-c) and 9-isothiocyanato-2,4-(un)substituted acridine (2a-d), respectively. All these compounds were characterized by correct 1H NMR, FT-IR, MS and elemental analyses. These compounds were screened for anti-inflammatory, analgesic and kinase (CDK1, CDK5 and GSK3) inhibition activities. Some compounds exhibited good anti-inflammatory (25-32%) and potent analgesic (50-75%) activities, at 50 mg/kg p.o. A compound, 4o (R1 = H, R2 = OCH3, R3 = CH3, R4 = CH3, R5 = H) exhibited moderate CDK1 (IC50 = 8.5 microM) inhibition activity.
Descriptors: acridines chemical synthesis, analgesics chemical synthesis, anti inflammatory agents, non steroidal chemical synthesis, enzyme inhibitors chemical synthesis, thiazoles chemical synthesis, acridines chemistry, acridines pharmacology , analgesics chemistry, analgesics pharmacology, anti inflammatory agents, non steroidal chemistry, anti inflammatory agents, non steroidal pharmacology, benzoquinones toxicity, brain metabolism, cdc2 protein kinase metabolism, carrageenan toxicity, cyclin dependent kinase 5, cyclin dependent kinases metabolism, edema chemically induced, edema prevention and control, enzyme inhibitors chemistry, enzyme inhibitors pharmacology, glycogen synthase kinase 3 metabolism, mice, pain measurement drug effects, rats, swine, thiazoles chemistry, thiazoles pharmacology.

Sugaya, I., T. Qu, K. Sugaya, and G.D. Pappas (2006). **Genetically engineered human mesenchymal stem cells produce met-enkephalin at augmented higher levels in vitro.** *Cell Transplantation* 15(3): 225-30. ISSN: 0963-6897.
NAL Call Number: RM287.C45
Abstract: We have reported that transplantation of adrenal medullary chromaffin cells that release endogenous opioid peptides into pain modulatory regions in the CNS produce significant antinociceptive effects in patients with terminal cancer pain. However, the usefulness of this procedure is minimal because the availability of human adrenal tissue is very limited. Alternative xenogeneic materials, such as porcine and bovine adrenal chromaffin cells present problems of immune rejection and possible pathogenic contamination. In an attempt to

develop opioid peptide-producing cells of autologous origin, we have transfected human mesenchymal stem cells (hMeSCs) with a mammalian expression vector containing a fusion gene of green fluorescent protein (GFP) and human preproenkephalin (hPPE), a precursor protein for enkephalin opioid peptides. Enkephalins are major neurotransmitters that play an important role in analgesia by activating peripheral opioid receptors. Following the establishment of stable transfection of hMeSCs, the expressions of hPPE and GFP were confirmed and the production of methionine enkephalin (Met-enkephalin) was significantly increased compared to control naive hMeSCs ($p < 0.05$). Our in vitro data demonstrated that genetically engineered hMeSCs with transfected hPPE gene can constitutively produce opioid peptide Met-enkephalin at an augmented high level. hMeSCs are relatively easy to isolate from a patient's bone marrow aspirates and expand in culture by repeated passages. Autologous hMeSCs would not require immunosuppression when transplanted back into the same patient. Through targeted gene manipulation such as hPPE gene transfection, this may offer a virtually unlimited safe cell supply for the treatment of opioid-sensitive pain in humans.
Descriptors: analgesics metabolism, enkephalin, methionine genetics, enkephalin, methionine metabolism, mesenchymal stem cell transplantation methods, mesenchymal stem cells metabolism, analgesics therapeutic use, analgesics, opioid therapeutic use, cell proliferation, cells, cultured, dna genetics, enkephalins genetics, gene expression regulation genetics, gene fusion, genetic engineering, genetic vectors, green fluorescent proteins genetics, mesenchymal stem cells cytology, pain drug therapy, protein precursors genetics, reverse transcriptase polymerase chain reaction, transfection.

Swindle, M.M. (2007). **Anesthesia, analgesia, and perioperative care.** In: M.M. Swindle *Swine in the Laboratory: Surgery, Anesthesia, Imaging, and Experimental Techniques,* 2nd edition, CRC Press: Boca Raton, p. 33-98. ISBN: <41 ISBN>.
Online: Table of contents only: http://www.loc.gov/catdir/toc/ecip077/2006102924.html
NAL Call Number: RD29.5.S94.S944 2007
Descriptors: anesthetic induction, endotracheal intubation, malignant hyperthermia, paralytic agents, postoperative monitoring, preanesthetic agents, injectable anesthetic agents, inhalant anesthetics, analgesics, general physiological effects of anesthetics, euthanasia.

Taguchi, K. (2006). **Indications for ketamine in the anaesthesia and surgery of farm animals**. *Journal of Veterinary Medicine, Japan* 59(8): 659-662. ISSN: 0447-0192 .
Descriptors: anesthesia, ketamine, surgery, cattle, pigs.
Language of Text: Japanese.

Takala, R.S., H.R. Soukka, O.A. Kirvela, H.P. Kujari, L.J. Pelliniemi, P.O. Kaapa, and R.E. Aantaa (2002). **Alveolar integrity and ultrastructure in pigs remain undamaged after exposure to sevoflurane.** *Acta Anaesthesiologica Scandinavica* 46(9): 1137-43. ISSN: 0001-5172.
Abstract: Previous studies have shown that both halothane and isoflurane have adverse but reversible effects on alveolar physiology. The present study was designed to test the hypothesis that also sevoflurane may affect alveolar integrity. Fifteen pigs were randomly selected to receive either thiopentone infusion (control group, n=8) or sevoflurane (n=7) at 4.0% inspiratory concentration (1.5 MAC) in air for 6 h. Tissue samples from the lungs were obtained at the end of the experiment. Both histopathological light microscopy and electron microscopy were used to assess the structural integrity of the alveoli. Pulmonary hemodynamics were comparable in both groups. Light microscopy showed no difference between the groups

in the amount of alveolar macrophages, red blood cells or edema. Electron microscopy showed minor changes such as moderate local swelling of alveolar epithelium in both study groups. Alveolar type II cells were ultrastructurally unaltered in both study groups. We conclude that long-term, high concentration exposure to sevoflurane has no detrimental effect on the alveolar integrity in pigs.

Descriptors: anesthetics, inhalation pharmacology, methyl ethers pharmacology, pulmonary alveoli drug effects, anesthesia, anesthetics, inhalation toxicity, anesthetics, intravenous pharmacology, epithelium ultrasonography, hemodynamic processes drug effects, methyl ethers toxicity, microscopy, electron, pulmonary alveoli pathology, pulmonary alveoli ultrastructure, swine, thiopental toxicity.

Takala, R.S., H.R. Soukka, M.S. Salo, O.A. Kirvela, P.O. Kaapa, A.A. Rajamaki, A. Riutta, and R.E. Aantaa (2004). **Pulmonary inflammatory mediators after sevoflurane and thiopentone anaesthesia in pigs.** *Acta Anaesthesiologica Scandinavica* 48(1): 40-5. ISSN: 0001-5172.

Abstract: BACKGROUND: Volatile anaesthetics have been shown to affect the release of pulmonary inflammatory mediators and exacerbate pulmonary injury after experimental aspiration. Thus, in theory, volatile anaesthetics may worsen inflammatory pulmonary injury and disease. We have previously described that no significant changes in alveolar ultrastructure are seen after sevoflurane anaesthesia. However, this does not exclude any possible physiological alterations. The aim of our study was to evaluate pulmonary inflammatory mediators in bronchoalveolar lavage (BAL) after sevoflurane and thiopentone anaesthesia in pigs with intact lungs. METHODS: Sixteen pigs were randomly selected to receive either a continuous thiopentone infusion (control group, n = 8) or sevoflurane (n = 8) at 4.0% inspiratory concentration (1.5 MAC) in air for 6 h. Bronchoalveolar lavage samples were collected at the end of the study to determine pulmonary inflammatory markers. RESULTS: Compared with thiopentone anaesthesia, significant increases in BAL leukotriene C4 (LTC4), NO3-, and NO2- levels were observed after sevoflurane anaesthesia. In addition, there was a significant decrease in total blood leukocyte count in sevoflurane-treated animals. CONCLUSION: We conclude that sevoflurane increases pulmonary LTC4, NO3-, and NO2- production in pigs, indicating an inflammatory response.

Descriptors: anesthesia, anesthetics, inhalation pharmacology, anesthetics, intravenous pharmacology, inflammation mediators metabolism, lung metabolism, methyl ethers pharmacology, thiopental pharmacology, bronchoalveolar lavage fluid chemistry, bronchoalveolar lavage fluid cytology, cytokines biosynthesis, eicosanoids biosynthesis, leukocyte count, leukotriene c4 biosynthesis, lung drug effects, nitric oxide biosynthesis, swine.

Tanaka, H., T. Igarashi, A.T. Lefor, and E. Kobayashi (2009). **The effects of fasting and general anesthesia on serum chemistries in KCG miniature pigs**. *Journal of the American Association for Laboratory Animal Science* 48(1): 33-38. ISSN: 1559-6109.

Online: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2694709

NAL Call Number: SF405.3 .A23

Abstract: Investigators are obligated to optimize the perioperative care of experimental animals, but little is known about the effects of anesthesia and surgery on serum chemistries in KCG pigs. The objective of this study was to examine the influence of fasting and surgery under general anesthesia on 27 serum chemistries in KCG miniature pigs to improve management. Crossbred KCG minipigs were used at a mean of 12.3 mo of age (range, 8.6 to 14.9) and 33.4 kg of body weight (range, 24.0 to 40.2). Serum chemistries were evaluated

at the start and end of a 24 h fasting period in fasted animals (n=6). No significant differences were observed between the starting and postfasting studies. Partial hemilaminectomy of the lumbar spine was carried out in 2 groups of animals. Those given sevoflurane anesthesia (n=7) had significant decreases in serum albumin, potassium, inorganic phosphorus, gamma -glutamyltransferase peptidase, cholinesterase, and glucose postoperatively compared with preoperative values. Animals given isoflurane (n=7) anesthesia had significantly decreased total protein, albumin, triglyceride, phospholipids, sodium, potassium, calcium, alanine aminotransferase, alkaline phoshatase and glucose after surgery compared with levels before surgery. In a separate experiment (n=7), serum glucose and insulin also decreased during the postoperative period after isoflurane anesthesia. These results demonstrate that select serum electrolytes, glucose, and insulin of KCG miniature pigs are altered after general anesthesia. Investigators must be aware of the effects of anesthetic agents on experimental animals to provide optimal care and for interpretation of experimental data.
Descriptors: alanine aminotransferase, albumins, anesthesia, blood chemistry, blood proteins, blood sugar, calcium, cholinesterase, crossbreds, enzyme activity, fasting, gamma glutamyltransferase, isoflurane, miniature pigs , peptidases, phospholipids, phosphorus, pig feeding, potassium, sodium, surgery, surgical operations, triacylglycerols, pigs.

Tiwari, S.K., R. Sharda, O.P. Mishra, S.P. Ingole, S.K. Chourasia, S. Jogi, and R. Dewangan (2006). **Clinico-physiological and haemato-biochemical response to xylazine-propofol anaesthesia in pigs**. *Indian Journal of Veterinary Surgery* 27(2): 119-120. ISSN: 0254-4105.
NAL Call Number: SF604.I45
Descriptors: anesthesia, anesthetics, blood chemistry, body temperature, haematology, heart rate, potency, propofol, reflexes, respiration rate, xylazine, pigs.

Tsibiribi, P., C. Bui Xuan, B. Bui Xuan, A. Tabib, J. Descotes, P. Chevalier, M.C. Gagnieu, M. Belkhiria, and Q. Timour (2006). **The effects of ropivacaine at clinically relevant doses on myocardial ischemia in pigs.** *Journal of Anesthesia* 20(4): 341-3. ISSN: 0913-8668.
Abstract: A major risk associated with bupivacaine during myocardial ischemia is ventricular fibrillation. We investigated the influence of ropivacaine on cardiac contractility and the propensity to ventricular fibrillation before and after myocardial ischemia in a placebo-controlled pig study. Anesthetized domestic pigs were administered 1 mg.kg(-1) of ropivacaine intravenously over 1 min and then 0.03 mg.kg(-1).min(-1) as a 30-min infusion, or saline. The following endpoints were measured before and after ropivacaine administration: (1) the ventricular fibrillation threshold (VFT) before and during myocardial ischemia induced by total transient ligation of the anterior interventricular artery and (2) electrophysiological (sinus heart rate, duration of QRS and QT intervals) and hemodynamic (blood pressure, the time derivative of left ventricular pressure [peak LV dP/dt]) parameters. Ropivacaine induced no changes in sinus heart rate, QRS, and or QT before or during ischemia. In contrast, there was a mild increase in the VFT before ischemia, which was drastically and significantly reduced during ischemia. The reduction of peak LV dP/dt during ischemia was further increased by ropivacaine. We also found that the effect of ropivacaine on the VFT was coronary blood flow-dependent, with a markedly decreased threshold in the presence of ischemia. Similar effects have been observed in humans with several other local anesthetics, as well as with class I antiarrhythmic drugs. The results of this study should be taken into account by anesthesiologists when administering ropivacaine to coronary patients.
Descriptors: amides pharmacology, anesthetics, local pharmacology, myocardial contrac-

tion drug effects, myocardial ischemia physiopathology, ventricular fibrillation chemically induced, monitoring, physiologic, swine, ventricular fibrillation physiopathology.

Tsui, B.C., D. Emery, R.R. Uwiera, and B. Finucane (2005). **The use of electrical stimulation to monitor epidural needle advancement in a porcine model.** *Anesthesia and Analgesia* 100(6): 1611-3. ISSN: 0003-2999.

Abstract: Muscle twitches elicited with electrical stimulation (ES) during epidural insertion may indicate epidural needle location. We examined the potential application of ES at 5 mA as a continuous method of monitoring the response to epidural needle advancement in a porcine model. Five 20-kg pigs were used in this study. A needle with a stimulating current of 5 mA was inserted at 20 separate levels in each pig. The needle was advanced until a muscle twitch was observed without loss-of-resistance (LOR). The needle position was then assessed using LOR. At the end of the experiment, an autopsy was performed to assess the spinal cord for injury. A total of 100 needle insertions were performed in the 5 pigs. The threshold current in the epidural space was 3.6 +/- 0.6 mA. In 59 of the needle insertions, LOR was not obtained at the depth at which a muscle twitch was initially observed. However, after advancing these 59 needles another 1-2 mm, LOR was obtained. In the other 41 insertions, LOR was observed without further advancement of the needle. Autopsies indicated there were no dural punctures or spinal cord damage in any of the pigs. These observations suggest that ES can be used to signal that the epidural needle is in or approaching the epidural space. However, the high false positive predictive value (59%) makes it impractical and unreliable to detect the precise entry of a needle into the epidural space in pigs.

Descriptors: anesthesia, epidural methods, electric stimulation, anesthesia, epidural instrumentation, dura mater anatomy and histology, false positive reactions, monitoring, intraoperative, needles, pilot projects, swine.

Tsyv'ian, P.B., I.D. Medvinskii, O.G. Artem'eva, and S.V. Kinzhalova (2001). **Anestetiki i razvivaiushcheesia serdtse. [Anesthetics and the developing heart]**. *Anesteziologiia i Reanimatologiia*(1): 72-5. ISSN: 0201-7563.

Abstract: Effects of various anesthetics on the myocardium of developing heart are reviewed. Anesthetics suppress myocardial contractility in a fetus and newborn more intensively than in an adult. This is due to immature cell mechanisms regulating cardiomyocyte contractile activity and specific effect of the autonomic nervous system on the heart. It is obvious that the problem of interactions between anesthetics and developing cardiovascular system remains important because of constant introduction of new drugs with new cell and organ effects into practical anesthesiology.

Descriptors: anesthetics pharmacology, fetal heart drug effects, heart drug effects, adult, age factors, anesthetics, inhalation pharmacology, anesthetics, local pharmacology, animals, newborn, baroreflex drug effects, cats, diastole drug effects, heart growth and development, infant, newborn, myocardial contraction drug effects, rabbits, swine, systole drug effects.

Language of Text: Russian.

Ugarte, C.E. and K. O'Flaherty (2005). **The use of a medetomidine, butorphanol and atropine combination to enable blood sampling in young pigs.** *New Zealand Veterinary Journal* 53(4): 249-52. ISSN: 0048-0169.

NAL Call Number: 41.8 N483

Abstract: AIM: To determine the suitability of a reversible, injectable anaesthetic com-

bination including medetomidine, butorphanol and atropine to produce the degree of immobilisation required to allow blood sampling in young pigs. METHODS: Twenty 6-week-old crossbred, intact male pigs were sedated with an intramuscular (I/M) injection of 80 microg/kg medetomidine, 200 microg/kg butorphanol and 25 microg/kg atropine. Heart and respiratory rates and rectal temperatures were monitored. Excessive salivation, gagging, laryngeal reflex, presence of pedal reflex and deep and surface analgesia were noted. Time of injection and the time when pigs reached mild and full sedation were also recorded. RESULTS: Mild sedation was produced in 90% of pigs after 5.6 (SEM 0.96) min (n = 18; median 5, range 2-16 min), and full sedation (lateral recumbency and loss of jaw tone) in 60% of pigs after 12.5 (SEM 2.14) min (n = 12; median 10, range 5-28 min). The depth and duration of sedation were very variable and most animals were easily aroused. Ninety percent of the animals required the administration of halothane by mask to allow blood sampling, but the amount of halothane required was small. Heart and respiratory rates decreased ($p < 0.001$) but remained within the normal range. Rectal temperature was above normal at the time of sedation and at the time of blood sampling when the ambient temperature was 29 degrees C but not when the ambient temperature was reduced to 25 degrees C. CONCLUSIONS: The combination of medetomidine, butorphanol and atropine at these doses produced sedation of variable depth and duration that was insufficient on its own to allow blood sampling in the majority of pigs. Hyperthermia can occur in temperature-controlled environments when using medetomidine, butorphanol and atropine in pigs. Reduction of stress and a quieter environment may improve the effects of the anaesthetic combination.
Descriptors: anesthesia veterinary, anesthetics, combined administration and dosage, blood specimen collection veterinary, swine physiology, animals, newborn, atropine administration and dosage, blood specimen collection methods, butorphanol administration and dosage, injections, intramuscular veterinary, medetomidine administration and dosage, swine blood.

Vagts, D.A., K. Hecker, T. Iber, J.P. Roesner, A. Spee, B. Otto, R. Rossaint, and G.F. Noldge Schomburg (2004). **Effects of xenon anaesthesia on intestinal oxygenation in acutely instrumented pigs.** *British Journal of Anaesthesia* 93(6): 833-41. ISSN: 0007-0912.
Abstract: BACKGROUND: Xenon is a narcotic gas that might be able to replace volatile anaesthetics or nitrous oxide due to its favourable pharmacological properties, such as providing haemodynamic stability. Intestinal oxygenation is affected by most volatile anaesthetics as a result of cardiodepressive effects. Reducing oxygenation of the gut might be a factor leading to perioperative organ dysfunction. This animal study was designed to assess the effects of xenon on intestinal oxygenation. METHODS: After ethical approval, 24 anaesthetized, acutely instrumented pigs were randomly assigned to three groups: nine animals received xenon anaesthesia with inspiratory concentrations of 0, 20, 50 and 65% in addition to their basic i.v. anaesthesia, nine animals served as a study control group, and five animals were used to assess model stability. Measurement of systemic and regional haemodynamic and oxygenation parameters was made 30 min after changing the xenon concentration. RESULTS: Xenon elicited dose-dependent systemic haemodynamic changes: heart rate and cardiac output decreased by 30%, while mean arterial pressure was stable. Superior mesenteric artery blood flow was lower in the xenon group. Vascular resistance of the superior mesenteric artery increased. The small intestinal oxygen supply decreased with increasing xenon concentration; the mucosal tissue oxygen partial pressure decreased but did not reach hypoxic (<5 mm Hg) values. Serosal tissue oxygen partial pressure was maintained. CONCLUSIONS: Xenon, in addition to basic i.v. anaesthesia, elicited a decrease in cardiac output

and maintained mean arterial pressure. Intestinal oxygenation was maintained, although regional macrohaemodynamic perfusion decreased. Xenon does not impair intestinal oxygenation under physiological conditions.

Descriptors: anesthetics, inhalation pharmacology, intestines blood supply, oxygen consumption drug effects, xenon pharmacology, anesthetics, combined pharmacology, anesthetics, intravenous pharmacology, dose response relationship, drug, epinephrine blood, hemodynamic processes drug effects, intestinal mucosa blood supply, mesenteric artery, superior drug effects, mesenteric artery, superior physiology, models, animal, norepinephrine blood, oxygen blood, partial pressure, regional blood flow drug effects, swine, vascular resistance drug effects.

Vagts, D.A., T. Iber, M. Puccini, B. Szabo, J. Haberstroh, F. Villinger, K. Geiger, and G.F. Noldge Schomburg (2003). **The effects of thoracic epidural anesthesia on hepatic perfusion and oxygenation in healthy pigs during general anesthesia and surgical stress.** *Anesthesia and Analgesia* 97(6): 1824-32. ISSN: 0003-2999.

Abstract: Perioperative liver injury due to decreased perfusion may be an underlying mechanism behind the development of systemic inflammatory response syndrome. We designed this animal study to assess whether thoracic epidural anesthesia (TEA) impairs liver oxygenation due to induced hypotension. After ethical approval, 19 anesthetized and acutely instrumented pigs were randomly assigned to 3 groups (control and TEA alone versus TEA plus volume loading). Bupivacaine 0.5% 0.75 mL per segment was injected into the epidural space, aiming for a T5 to T12 block. After baseline values were obtained, measurements were repeated 60 and 120 min after epidural injection. TEA was associated with decreased mean arterial blood pressure but no change in total hepatic blood flow. Oxygen delivery to the liver and oxygen uptake remained unchanged. Liver tissue oxygen partial pressure did not decrease. The plasma indocyanine green disappearance rate remained stable. Volume loading before TEA did not relevantly affect total hepatic blood flow; it even decreased oxygen supply to the liver by hemodilution. We conclude that, despite decreased mean arterial blood pressure, TEA did not affect liver oxygenation. There was no clinically relevant effect of volume loading on total hepatic perfusion.

Descriptors: anesthesia, epidural, anesthesia, general, liver metabolism, liver circulation physiology, oxygen consumption physiology, stress physiopathology, surgical procedures, operative adverse effects, cardiac output physiology, catheterization, epinephrine blood, hepatic artery physiology, lactic acid metabolism, laparotomy, nitroglycerin pharmacology, norepinephrine blood, portal vein physiology, pulmonary artery physiology, swine, vasodilator agents pharmacology.

Vagts, D.A., T. Iber, J.P. Roesner, C. Mutz, V. Kurzweg, C. Harkner, K. Bruderlein, and G.F. Noldge Schomburg (2005). **Effects of systemically applied clonidine on intestinal perfusion and oxygenation in healthy pigs during general anaesthesia and laparotomy.** *European Journal of Anaesthesiology* 22(11): 879-86. ISSN: 0265-0215.

Abstract: BACKGROUND AND OBJECTIVE: Clonidine, which is used for induction of sympatholysis and prevention or treatment of alcohol withdrawal in anaesthesia and intensive care medicine, may have deleterious effects on intestinal mucosal perfusion. This study was designed to investigate the effects of clonidine on intestinal perfusion and oxygenation. METHODS: Following ethical approval 17 anaesthetized, and acutely instrumented pigs were randomly assigned to two groups: eight animals received intravenous clonidine

(2 microg kg(-1) bolus and 2 microg kg(-1) h(-1)), nine animals served as a control group. Measurement points for systemic and regional haemodynamic and oxygenation parameters were 135 and 315 min after starting the clonidine application. RESULTS: Clonidine elicited systemic haemodynamic changes (median [25-75th interquartile range]): heart rate (106 [91, 126] to 84 [71, 90] beats min(-1)) cardiac output (147 [123, 193] to 90 [87, 107] mL min(-1) kg(-1)) and mean arterial pressure (77 [72, 93] to 69 [61, 78] mmHg) decreased. Despite systemic haemodynamic changes, the superior mesenteric artery blood flow did not change in the clonidine group. The vascular resistance of the superior mesenteric artery decreased. The small intestinal oxygen supply, the mucosal and the serosal tissue oxygen partial pressure did not change. CONCLUSIONS: Systemic sympatholysis induced by intravenously applied clonidine in addition to basic intravenous anaesthesia elicited a decrease in cardiac output and mean arterial pressure. However, regional macrohaemodynamic perfusion was maintained and intestinal oxygenation did not change. Clonidine does not impair intestinal mucosal and serosal oxygenation under physiological conditions.

Descriptors: anesthesia, general, clonidine adverse effects, intestine, small blood supply, intestine, small drug effects, intestine, small metabolism, laparotomy, oxygen metabolism, sympatholytics adverse effects, clonidine administration and dosage, hemodynamic processes drug effects, intestinal mucosa blood supply, intestinal mucosa drug effects, intestinal mucosa metabolism, splanchnic circulation drug effects, sus scrofa, sympatholytics administration and dosage.

Vagts, D.A., T. Iber, B. Szabo, J. Haberstroh, K. Reising, M. Puccini, K. Geiger, and G.F. Noldge Schomburg (2003). **Effects of epidural anaesthesia on intestinal oxygenation in pigs.** *British Journal of Anaesthesia* 90(2): 212-20. ISSN: 0007-0912.

Abstract: BACKGROUND: Perioperative intestinal hypoperfusion is a major contributing factor leading to organ dysfunction. It can be caused by stress as a result of surgical manipulation or hypoxia. Additionally, anaesthesia can affect intestinal oxygenation. This animal study was designed to assess the effects of reduced regional sympathetic nervous activity induced by thoracic epidural anaesthesia on intestinal oxygenation. METHODS: After ethical approval, 16 anaesthetized and acutely instrumented pigs were randomly assigned to two groups (epidural anaesthesia alone vs epidural anaesthesia plus volume loading). The epidural anaesthesia aimed for a T5-T12 block. Measurements were at baseline and after 1 and 2 h. RESULTS: Epidural anaesthesia was associated with a decrease in mean arterial blood pressure and pronounced mesenteric vasodilatation. Mesenteric blood flow did not change. Intestinal oxygen uptake, mucosal tissue oxygen partial pressure and tissue carbon dioxide partial pressure remained unchanged. CONCLUSIONS: Despite marked systemic hypotension, epidural anaesthesia did not affect intestinal oxygenation. There was no benefit obtained from volume loading.

Descriptors: anesthesia, epidural, intestines drug effects, oxygen physiology, carbon dioxide physiology, epinephrine blood, hemodynamic processes drug effects, hemodynamic processes physiology, hemoglobins analysis, intestinal mucosa drug effects, intestinal mucosa physiology, intestines physiology, jejunum drug effects, jejunum physiology, mesenteric arteries drug effects, mesenteric arteries physiology, norepinephrine blood, swine, sympathetic nervous system physiology.

Van Besouw, J. (2001). **Anestesia en el trasplante cardiaco. [Anesthesia for heart transplantation]**. *Revista Espanola De Anestesiologia y Reanimacion* 48(10): 473-5. ISSN: 0034-9356.

Abstract: This review covers the management of patients proposed for heart transplantation from the moment of preoperative assessment. Drug treatments that provide a bridge to transplantation are emphasized, with mention of traditional drugs such as dobutamine, more recent agents such as phosphodiesterase inhibitors, and finally new drugs such as levosimendan.Mechanical support devices and indications for their use leading to transplantation are discussed. Finally, the notion of xenotransplantation is mentioned as a possible solution to the imbalance between supply and demand for transplantable organs.

Descriptors: anesthesia, general methods, heart transplantation, cardiovascular agents pharmacology, cardiovascular agents therapeutic use, combined modality therapy, dobutamine pharmacology, dobutamine therapeutic use, forecasting, heart failure, congestive drug therapy, heart failure, congestive surgery, heart assist devices, hemodynamic processes drug effects, phosphodiesterase inhibitors pharmacology, phosphodiesterase inhibitors therapeutic use, preanesthetic medication, preoperative care, swine, tissue and organ procurement, transplantation, heterologous, transplantation, homologous.

Language of Text: Spanish.

Van Woerkom, R., K.D. Beharry, H.D. Modanlou, J. Parker, V. Rajan, Y. Akmal, and J.V. Aranda (2004). **Influence of morphine and naloxone on endothelin and its receptors in newborn piglet brain vascular endothelial cells: clinical implications in neonatal care.** *Pediatric Research* 55 (1): 147-51. ISSN: 0031-3998.

NAL Call Number: RJ1.P4

Abstract: The present study examines the hypothesis that morphine exposure alters newborn brain vascular endothelial cell production of endothelin (ET)-1, as well as the mRNA expression of its receptors. Newborn piglet vascular endothelial cells were treated with morphine (100 ng/mL media), naloxone (100 ng/mL media), or drug-free media (control) for 6, 24, 48, and 96 h. Media was analyzed for ET-1 and big ET-1 levels and the cells were assessed for ETA and ETB receptor mRNA expression. Morphine exposure progressively increased ET-1 production from 6 to 96 h with concurrent reductions in big ET-1 levels starting at 24 h to almost undetectable levels by 96 h. Whereas ETA receptor mRNA expression increased 2-fold at 6 h and 4-fold at 96 h, ETB receptor mRNA expression remained unchanged. Naloxone exposure caused significant decreases in ET-1 levels, whereas an opposite effect was noted in big ET-1 levels, which increased from 6 through 96 h. Naloxone caused a progressive decrease in ETA receptor mRNA expression at 6 h through 96 h and a 2-fold increase in ETB receptor mRNA expression at 48 and 96 h. Increased ET-1 and its receptors in response to morphine may suggest altered cerebrovascular perfusion and brain metabolism in the immature piglet brain.

Descriptors: analgesics, opioid pharmacology, endothelin 1 metabolism, morphine pharmacology, naloxone pharmacology, narcotic antagonists pharmacology, receptor, endothelin a genetics, receptor, endothelin b genetics, animals, newborn, brain blood supply, cells, cultured, endothelium, vascular cytology, endothelium, vascular drug effects, endothelium, vascular metabolism, gene expression drug effects, rna, messenger analysis, sus scrofa.

Vezina, D.P., C.A. Trepanier, M.R. Lessard, M. Gourdeau, C. Tremblay, and R. Guidoin (2004). **An in vivo evaluation of the mycobacterial filtration efficacy of three breathing filters used in anesthesia.** *Anesthesiology* 101(1): 104-9. ISSN: 0003-3022.

Abstract: BACKGROUND: The use of breathing filters (BFs) has been recommended to protect the anesthesia apparatus in proven or suspected cases of tuberculosis. Some investigators have also suggested the use of BF to alleviate the need to change anesthesia breathing circuits after each case. This study evaluated the filtration efficacy of three different BFs to prevent mycobacterial contamination of breathing circuits in a model that uses a test animal. METHODS: Ten Pall BB25A (pleated hydrophobic) (Pall Canada Ltd., Mississauga, Ontario, Canada), six DAR Barrierbac S (felted electrostatic; Mallinckrodt DAR, Mirandola, Italy), and six Baxter Airlife (felted electrostatic; Baxter Canada, Mississauga, Ontario, Canada) BFs were studied. For each BF tested, 20 ml of a high concentration suspension of Mycobacterium chelonae (range, 2.0 x 10 to 9.0 x 10 colony-forming units/ml) was nebulized during 2 h at the proximal end of the endotracheal tube of anesthetized pigs. At the end of the nebulization period, the BFs were sampled for culture. The titer reduction value (number of microorganisms challenging the BF divided by the number of microorganisms recovered downstream of the BF) and the removal efficiency (difference between the number of microorganisms challenging the BF and the number of microorganisms recovered downstream of the BF, divided by the number of microorganisms challenging the BF) were calculated. RESULTS: The median titer reduction values were 5.6 x 10, 6.0 x 10, and 8.0 x 10 ($P < 0.0005$), and the median removal efficiencies were greater than 99.999%, greater than 99.999%, and 100% (P = not significant) for the DAR Barrierbac S, the Baxter Airlife, and the Pall BB25A, respectively. CONCLUSIONS: Among the three BFs studied, only the Pall BB25A completely prevented the passage of M. chelonae, thus protecting the anesthesia breathing circuit from mycobacterial contamination.

Descriptors: anesthesiology instrumentation, mycobacterium ultrastructure, ultrafiltration instrumentation, canada, colony count, microbial, microscopy, electron, scanning, mycobacterium chelonae ultrastructure, mycobacterium tuberculosis ultrastructure.

Walker, B., N. Jaggin, M. Doherr, and U. Schatzmann (2004). **Inhalation anaesthesia for castration of newborn piglets: experiences with isoflurane and isoflurane/NO.** *Journal of Veterinary Medicine. A, Physiology, Pathology, Clinical Medicine* 51(3): 150-4. ISSN: 0931-184X.

NAL Call Number: 41.8 Z5

Abstract: The aim of this study was to evaluate the inhalation anaesthesia with isoflurane and isoflurane/N2O by mask induction for routine castration of piglets under 14 days of age. MATERIAL AND METHODS: Eighty-five male piglets aged between 4 and 12 days were used in a matched pair test. Two piglets of the same litter with the same weight were selected. One was castrated with, the other without anaesthesia. Induction was performed with either isoflurane (group ISO) or isoflurane/nitrous oxide (group ISO/N2O) in oxygen through a modified bain-breathing system. Induction time was 90 and 60 s for group ISO and group ISO/N2O, respectively. The disappearance of the palpebral reflex was recorded. The reaction of the piglets during castration was judged according to a scoring system separately for both testicles during skin incision and dissection of the spermatic cord. The scores were added and mean values were calculated. Total anaesthesia time, castration time and quality of recovery was recorded. Blood was collected from all piglets immediately after castration for measurement of ACTH and beta-endorphin values. Statistical analysis were performed by the Kruskal-Wallis test for nonparametric data and one-way anova (NCSS 2000, Kaysville, UT, USA). RESULTS: Induction of anaesthesia proved to be smooth in all cases. The palpebral reflex disappeared after 36.5 s in group ISO/N2O versus 51 s in group ISO. Mean castration scores were 0.6 in group ISO and 0 in group ISO/N2O, whereas 7.7 in piglets with

no anaesthesia. These scores were significantly different. Mean anaesthesia time was 128 s (30-390) for group ISO and 123 s (70-220) for group ISO/N2O. No deaths occurred. The differences in the levels of ACTH and beta-endorphins in the blood plasma in the different groups showed no statistical difference. DISCUSSION: This study demonstrates that isoflurane or isoflurane/N2O anaesthesia by mask induction proves to be a safe, short and reliable method in piglets undergoing castration. Reaction to the castration procedure were significantly reduced. Stress hormone values were not different between the groups because of a large individual difference.
Descriptors: anesthesia, inhalation veterinary, anesthetics, inhalation administration and dosage, isoflurane administration and dosage, nitrous oxide administration and dosage, orchiectomy veterinary, swine physiology, animals, newborn physiology, animals, newborn surgery, orchiectomy methods, swine surgery, treatment outcome.

Wallace, A.W. and W.L. Tom (2000). **Interaction of l-arginine and phosphodiesterase inhibitors in vasodilation of the porcine internal mammary artery**. *Anesthesia and Analgesia* 90(4): 840-846. ISSN: 0003-2999.
Descriptors: pharmacology, cardiovascular system: transport and circulation, zaprinast, sildenafil .

Weed, M.R. and R.D. Hienz (2006). **Effects of morphine on circadian rhythms of motor activity and body temperature in pig-tailed macaques.** *Pharmacology, Biochemistry, and Behavior* 84(3): 487-96. ISSN: 0091-3057.
NAL Call Number: QP901.P4
Abstract: Previous studies of the effects of opiates on motor activity and body temperature in nonhuman primates have been limited in scope and typically only conducted with restrained animals. The present study used radio-telemetry devices to continuously measure activity and temperature in unrestrained pig-tailed macaques for 24 h following morphine administration. Two dose-response functions (0.56 to 5.6 mg/kg, i.m.) were determined, one with morphine administered at 9 a.m. and one with morphine administrated at 3 p.m. Under both the 9 a.m. or 3 p.m. administration schedules, body temperature and activity were increased acutely. Activity was also reduced the following morning after morphine administered at either time. In other regards, morphine's effects on both temperature and activity differed between 9 a.m. and 3 p.m. injection, including periods of decreased activity immediately after the acute increases after 9 a.m. but not 3 p.m. administration. Surprisingly, motor activity also increased 9-12 h post-injection following morphine administered at 9 a.m., but not at 3 p.m. These results clearly show an interaction between timing of morphine administration and effects on temperature and activity. These results also underscore the fact that single injections of drugs may have multiple and delayed effects on circadian rhythms in macaques.
Descriptors: analgesics, opioid pharmacology, body temperature drug effects, circadian rhythm drug effects, morphine pharmacology, motor activity drug effects, data interpretation, statistical, macaca, monitoring, physiologic, software, temperature, time factors.

Wei, H., Y. Chen, L. Xu, and J. Zheng (2007). **Percutaneous penetration kinetics of lidocaine and prilocaine in two local anesthetic formulations assessed by in vivo microdialysis in pigs.** *Biological and Pharmaceutical Bulletin* 30(4): 830-4 . ISSN: 0918-6158.
NAL Call Number: QP501

Abstract: The aim of this study was to characterize and compare the percutaneous penetration kinetics of lidocaine (L) and prilocaine (P) in two local anesthetic formulations by in vivo microdialysis coupled with HPLC. The microdialysis system for studying lidocaine and prilocaine was calibrated by a no-net-flux method in vitro and retrodialysis method in vivo, respectively. A dosage of 0.2 g/cm2 of an in-house P-L formulation (2.5% lidocaine and 2.5% prilocaine, methylcellulose-based) and commercially available Eutectic Mixture of Local Anesthesia (EMLA, 2.5% lidocaine and 2.5% prilocaine, carbopol-based) was separately but symmetrically applied in the dorsal region of pigs. Saline (0.9%, w/v) was perfused into the linear microdialysis probe at a flow rate of 1.5 microl/min. Dialysate was collected upon topical application up to 6 h at 20-min intervals and assessed by HPLC. The results demonstrated the area under the concentration-time curve (AUC(0-6 h)) of lidocaine and prilocaine in EMLA was 71.95+/-23.36 microg h/ml and 38.01+/-14.8 microg h/ml, respectively, in comparison to 167.11+/-56.12 microg h/ml and 87.02+/-30.38 microg h/ml in the P-L formulation. The maximal concentrations (Cmax) of lidocaine and prilocaine in the dermis were 29.2+/-9.08 microg/ml and 16.54+/-5.31 microg/ml in EMLA and 80.93+/-17.98 microg/ml and 43.69+/-12.87 microg/ml in the P-L formulation, respectively. This study indicates a well-calibrated microdialysis system can provide vital real-time information on percutaneous drug delivery and specifically a methylcellulose-based P-L formulation can increase percutaneous absorption of both lidocaine and prilocaine in pigs compared to carbopol-based EMLA.
Descriptors: anesthesia , local, anesthetics, combined pharmacokinetics, anesthetics, local pharmacokinetics, skin absorption, anesthetics, combined pharmacology, anesthetics, local pharmacology, area under curve, calibration, chromatography, high pressure liquid, lidocaine, microdialysis, prilocaine, swine.

Wei, J., X. Shao, M. Gong, B. Zhu, Y. Cui, Y. Gao, and R. Wang (2005). **Structure-activity relationships of novel endomorphin-2 analogues with N-O turns induced by alpha-aminoxy acids.** *Bioorganic and Medicinal Chemistry Letters* 15(12): 2986-9. ISSN: 0960-894X.
NAL Call Number: QP501.B57
Abstract: Endomorphin-2 (H-Tyr-Pro-Phe-Phe-NH2, EM-2) is a putative endogenous mu-opioid receptor ligand. To study the structure-activity relationship against its receptor, we introduced N-O turns into EM-2 and got the analogues with potent affinities for mu-opioid receptor. Our results indicated that N-O turn structures at the Pro2-aminoxy-Phe3 position of EM-2 analogues played important roles for their affinities. These novel analogues with N-O turns provided a new approach to develop potent analgesics related to EM-2.
Descriptors: amino acids chemistry, analgesics, opioid pharmacology, oligopeptides pharmacology, receptors, opioid, delta agonists, receptors, opioid, mu agonists , amino acids, cyclic, analgesics, opioid chemical synthesis, analgesics, opioid chemistry, brain drug effects, brain metabolism, ileum drug effects, ileum metabolism, ligands, mice, molecular structure, oligopeptides chemical synthesis, oligopeptides chemistry, rats, rats, wistar, structure activity relationship, swine, vas deferens drug effects, vas deferens metabolism.

Weinberg, G., P. Hertz, and J. Newman (2004). **Lipid, not propofol, treats bupivacaine overdose.** *Anesthesia and Analgesia* 99(6): 1875-6; Author Reply 1876. ISSN: 0003-2999.
Descriptors: anesthetics, intravenous therapeutic use, anesthetics, local poisoning, bupivacaine poisoning, fat emulsions, intravenous therapeutic use, overdose drug therapy, propofol

therapeutic use, dogs, swine.
Notes: Comment On: Anesth Analg. 2004 May;98(5):1426-31, table of contents.

Weisshorn, R., F. Wappler, M. Fiege, M.U. Gerbershagen, and J.S. Am Esch (2002). **Effects of fulminant malignant hyperthermia to the oxygen saturation in skeletal muscle tissue.** *Anesthesiology Abstracts of Scientific Papers Annual Meeting*(2002): Abstract No. A-1002.
Descriptors: metabolism, muscular system: movement and support, pharmacology, malignant hyperthermia, metabolic disease, tracheostomy, experimental surgical techniques, laboratory techniques, blood pressure, body temperature, hypercarbia, hypermetabolism, hypoxia .
Notes: Meeting Information: 2002 Annual Meeting of the American Society of Anesthesiologists, Orlando, FL, USA; October 12-16, 2002.

Wenger, S., N. Jaggin, M. Doherr, and U. Schatzmann (2002). **Halothane anaesthesia for piglet castration: field study to evaluate costs and benefits [Die Halothananasthesie zur Kastration des Saugferkels Machbarkeitsstudie und Kosten-Nutzen-Analyse.]**. *Tierarztliche Praxis Ausgabe G, Grosstiere/Nutztiere* 30(3): 164-170. ISSN: 1434-1220.
NAL Call Number: SF603.V43
Descriptors: anesthesia, castration, costs, halothane, piglets, recovery .
Language of Text: German, Summary in English.

Wilkinson, A.C., M.L.3. Thomas, and B.C. Morse (2001). **Evaluation of a transdermal fentanyl system in yucatan miniature pigs.** *Contemporary Topics in Laboratory Animal Science American Association for Laboratory Animal Science* 40(3): 12-6. ISSN: 1060-0558.
NAL Call Number: SF405.3 .A23
Abstract: Of 18 pigs used on a coronary stent experimental protocol, 6 each received a transdermal fentanyl patch to document the patterns of transdermal fentanyl absorption in swine. This approach was taken to reduce animal use and potentially refine the surgical regimen. The objective of the fentanyl portion of the study was to demonstrate that transdermal fentanyl may be useful in the management of postoperative analgesia in swine. This study sought to document that demonstrable levels of fentanyl are achievable in swine plasma via a transdermal system and to compare the magnitude of these levels to data in other species. This study does not directly correlate plasma fentanyl levels with analgesic efficacy. Plasma fentanyl concentration peaked within 42 h in five pigs and within 48 h in the remaining pig. All pigs had similar absorption patterns; the only difference was in magnitude. One pig reached 0.99 ng/ml at 42 h; the next highest concentration was 0.77 ng/ml at 48 h in a different animal. The peak concentration in the others ranged from 0.38 to 0.71 ng/ml.
Descriptors: analgesics, opioid pharmacokinetics, fentanyl pharmacokinetics, swine, miniature metabolism, administration, cutaneous, analgesics, opioid administration and dosage, analgesics, opioid blood, fentanyl administration and dosage, fentanyl blood, skin absorption, swine, swine, miniature surgery .

Xu, D., S. Abbas, and V.W. Chan (2005). **Ultrasound phantom for hands-on practice.** *Regional Anesthesia and Pain Medicine* 30(6): 593-4. ISSN: 1098-7339.
Descriptors: anesthesiology education, nerve block methods, phantoms, imaging, ultrasonography, interventional instrumentation, clinical competence, equipment design, models, animal, swine, ultrasonography, interventional methods.

Yamakage, M., X. Chen, A. Kimura, S. Iwasaki, and A. Namiki (2002). **The repolarizing effects of volatile anesthetics on porcine tracheal and bronchial smooth muscle cells.** *Anesthesia and Analgesia* 94(1): 84-8, Table of Contents. ISSN: 0003-2999.

Abstract: This study was conducted to determine the effects of volatile anesthetics (potent bronchodilators) on membrane potentials in porcine tracheal and bronchial smooth muscle cells. We used a current-clamp technique to examine the effects of the volatile anesthetics isoflurane (1.5 minimum alveolar anesthetic concentration [MAC]) and sevoflurane (1.5 MAC) on membrane potentials of porcine tracheal and bronchial (third- to fifth-generation) smooth muscle cells depolarized by a muscarinic agonist, carbachol (1 microM). The effects of volatile anesthetics on muscarinic receptor binding affinity were also investigated by using a radiolabeled receptor assay technique. The volatile anesthetics isoflurane and sevoflurane induced significant repolarization of the depolarized cell membranes in the trachea (from -19.8 to -23.6 mV and to -24.8 mV, respectively) and bronchus (from -24.7 to -29.3 mV and -30.4 mV, respectively) without affecting carbachol binding affinity to the muscarinic receptor. The repolarizing effect was abolished by a Ca(2+)-activated Cl(-) channel blocker, niflumic acid. These results indicate that volatile anesthetic-induced repolarization of airway smooth muscle cell membranes might be caused by a change in Ca(2+)-activated Cl(-) channel activity and that the different repolarized effects of the volatile anesthetics could in part contribute to the different effects of volatile anesthetics on tracheal and bronchial smooth muscle contractions. IMPLICATIONS: By use of a current-clamp technique, the volatile anesthetics isoflurane and sevoflurane repolarized porcine airway smooth muscle cell membranes depolarized by a muscarinic agonist. This effect might be caused mainly by change in Ca(2+)-activated Cl(-) channel activity, not in K(+) channel activity.

Descriptors: anesthetics, inhalation pharmacology, bronchi physiology, isoflurane pharmacology, methyl ethers pharmacology, muscle, smooth physiology, trachea physiology, bronchi drug effects, calcium channel blockers pharmacology, carbachol pharmacology, chloride channels antagonists and inhibitors, electrophysiology, membrane potentials drug effects, muscarinic agonists pharmacology, muscle, smooth drug effects, niflumic acid pharmacology, patch clamp techniques, receptors, muscarinic drug effects, receptors, muscarinic metabolism, swine, trachea drug effects.

Yamakage, M., X. Chen, N. Tsujiguchi, Y. Kamada, and A. Namiki (2001). **Different inhibitory effects of volatile anesthetics on T- and L-type voltage-dependent Ca2+ channels in porcine tracheal and bronchial smooth muscles.** *Anesthesiology* 94(4): 683-93. ISSN: 0003-3022.

Abstract: BACKGROUND: The distal airway is more important in the regulation of airflow resistance than is the proximal airway, and volatile anesthetics have a greater inhibitory effect on distal airway muscle tone. The authors investigated the different reactivities of airway smooth muscles to volatile anesthetics by measuring porcine tracheal or bronchial (third to fifth generation) smooth muscle tension and intracellular concentration of free Ca2+ ([Ca2+] i) and by measuring inward Ca2+ currents (ICa) through voltage-dependent Ca2+ channels (VDCs). METHODS: Intracellular concentration of free Ca2+ was monitored by the 500-nm light emission ratio of Ca2+ indicator fura-2. Isometric tension was measured simultaneously. Whole-cell patch clamp recording techniques were used to investigate the effects of volatile anesthetics on ICa in dispersed smooth muscle cells. Isoflurane (0-1.5 minimum alveolar concentration) or sevoflurane (0-1.5 minimum alveolar concentration) was introduced into a bath solution. RESULTS: The volatile anesthetics tested had greater inhibitory

effects on carbachol-induced bronchial smooth muscle contraction than on tracheal smooth muscle contraction. These inhibitory effects by the anesthetics on muscle tension were parallel to the inhibitory effects on [Ca2+]i. Although tracheal smooth muscle cells had only L-type VDCs, some bronchial smooth muscle cells (approximately 30%) included T-type VDC. Each of the two anesthetics significantly inhibited the activities of both types of VDCs in a dose-dependent manner; however, the anesthetics had greater inhibitory effects on T-type VDC activity in bronchial smooth muscle. CONCLUSIONS: The existence of the T-type VDC in bronchial smooth muscle and the high sensitivity of this channel to volatile anesthetics seem to be, at least in part, responsible for the different reactivities to the anesthetics in tracheal and bronchial smooth muscles.

Descriptors: anesthetics, inhalation pharmacology, bronchi drug effects, calcium channel blockers pharmacology, calcium channels, l type drug effects, calcium channels, t type drug effects, muscle, smooth drug effects, trachea drug effects, muscle contraction drug effects, muscle, smooth physiology, nifedipine pharmacology, swine.

Yang, Q., A.P. Yim, A.A. Arifi, and G.W. He (2002). **Procaine in cardioplegia: the effect on EDHF-mediated function in porcine coronary arteries.** *Journal of Cardiac Surgery* 17(5): 470-5. ISSN: 0886-0440.

Abstract: OBJECTIVES: Hyperkalemia in cardioplegia impairs the endothelium-derived hyperpolarizing factor (EDHF)-mediated function. This study examined the effect of procaine in cardioplegia on the EDHF-mediated response in porcine coronary arteries. METHODS: An isometric force study was performed in a myograph. Two rings taken from the same artery (diameter 200-450 microm) were incubated with Krebs solution (group I) or 20 mM K+ (group II) with/without procaine (1 mM) at 37 degrees C for 1 hour. The EDHF-mediated relaxation was induced by bradykinin (BK, -10 approximately -6.5 log M) after U46619 (-8 log M, in group I) or K+-precontraction (in group II) in the presence of indomethacin (7 microM), NG-nitro-L-arginine (300 microM), and hemoglobin (20 microM). The membrane potential of a single smooth muscle cell was measured by a microelectrode after superfusion with Krebs solution with/without procaine for 1 hour. RESULTS: The EDHF-mediated relaxation was increased by the treatment with procaine with the EC50 shifted leftward (97.3 +/- 0.6% vs. 83.0 +/- 5.1% at -7 log M and 99.4 +/- 0.6% vs. 96.7 +/- 1.6% at -6.5 log M, $p < 0.05$; EC50: -8.57 +/- 0.24 vs. -7.92 +/- 0.23 log M, $p < 0.05$). Procaine decreased the BK-induced hyperpolarization from -72.3 +/- 0.7 mV to -68.8 +/- 0.8 mV (-6.5 log M, $p < 0.01$). The EDHF-mediated relaxation in arteries exposed to 20 mM K+ was not altered by procaine (49.9 +/- 7.4% vs. 55.8 +/- 7.6%, $p > 0.05$). CONCLUSIONS: In the coronary arteries, procaine has a depolarizing effect but it enhances EDHF-mediated relaxation. Addition of procaine in cardioplegia did not change the EDHF-mediated endothelial function.

Descriptors: anesthetics, local pharmacology, biological factors physiology, muscle, smooth, vascular drug effects, procaine pharmacology, algorithms, bicarbonates, calcium chloride, cardioplegic solutions, computer graphics, coronary vessels drug effects, coronary vessels physiology, heart arrest, induced, magnesium, membrane potentials drug effects, membrane potentials physiology, models, animal, muscle relaxation drug effects, muscle, smooth, vascular physiology, potassium chloride, sodium chloride, swine.

Yokoyama, T., K. Yamashita, T. Nishiyama, C. Yajima, M. Manabe, and K. Hanaoka (2005). **[A case of thoraco-amniotic shunt for congenital cystic adenomatoid malformation]**. *Masui; Japanese Journal of Anesthesiology, The* 54(3): 287-90. ISSN: 0021-4892.

Abstract: Congenital cystic adenomatoid malformation (CCAM) is a congenital pulmonary anomaly, which may lead to fetal hydrops, pulmonary hypoplasia, and fetal or neonatal death. Recently, diagnosis and surgery for fetus have been improved. We experienced a case of CCAM, classified in Stocker class I, with a single cyst of about 5 cm in diameter. A 32 year-old pregnant woman had a fetus diagnosed as CCAM at 25 th gestational week. The thoraco-amniotic shunt placement using a modified double pig tail catheter was performed at 27 th gestational week under general anesthesia with 1% isoflurane in oxygen 2 l x min(-1) and nitrous oxide 4 l x min(-1), and 100 microg of fentanyl. Fetal movement was suppressed during surgery. This fetal therapy was effective and the cyst disappeared after surgery. The baby was delivered with caesarian section under spinal anesthesia with 0.5% bupivacaine 2.5 ml. On the next day, right lung lobectomy was accomplished under general anesthesia with fentanyl 0.2 mg and pancuronium 6.0 mg. Anesthesia with isoflurane, nitrous oxide, and fentanyl was useful for the fetal surgery of thoraco-amniotic shunt placement. Consequently, caesarian section and lung lobectomy were completed successfully.

Descriptors: anesthesia, obstetrical, cesarean section, cystic adenomatoid malformation of lung, congenital surgery, fetal diseases surgery, adult, amniotic fluid, anesthesia, general, anesthesia, spinal, cystic adenomatoid malformation of lung, congenital ultrasonography, fetal diseases ultrasonography, ultrasonography, prenatal.

Language of Text: Japanese.

Zaballos, M., J. Almendral, M.J. Anadon, P. Gonzalez, and J. Navia (2004). **Comparative effects of thiopental and propofol on atrial vulnerability: electrophysiological study in a porcine model including acute alcoholic intoxication.** *British Journal of Anaesthesia* 93(3): 414-21. ISSN: 0007-0912.

Abstract: BACKGROUND: Atrial tachyarrhythmias (AT) frequently complicate the perioperative period. Alcohol intoxication is a recognized causative factor for dysrrhythmias. We studied the effects of propofol and thiopental on atrial electrophysiology and vulnerability to AT in a closed-chest porcine model in which AT are facilitated by ethanol. METHODS: Thirty-eight pigs were randomly assigned to thiopental (T-group, n=19) or propofol (P-group n=19). All animals were assigned to undergo a right atrial electrical stimulation protocol (RASP) at baseline. Thirty pigs were assigned to undergo additional RASP during ethanol infusion, while the remaining eight were assigned to undergo additional RASP during saline infusion (control group). We analysed effective refractory period (ERP), and intra-atrial conduction interval (ICI) (between atrial sites 4 cm apart), at several cycle lengths (CL). RESULTS: There were no significant differences at baseline. During ethanol infusion, propofol produced a greater rate-dependent decrease in excitability, manifested by a longer minimum paced CL with 1:1 atrial capture: 145 (11) vs 164 (27) ms in the T- and P-group, respectively (P=0.01). Propofol was associated with a greater rate-related slowing in conduction: difference between ICI at CL of 300 ms and ICI at minimum CL: 30 ms in P-group and 22 ms in T-group (P<0.03). In the P-group we observed a longer duration of induced arrhythmias (145 (131) vs 74 (91) s, P<0.03) and a higher proportion with atrial flutter (AFl) (76 vs 19%, P<0.001). CONCLUSIONS: Propofol in this model was more arrhythmogenic than thiopental, as manifested by a longer duration of induced arrhythmias, particularly AFI.

Descriptors: alcoholic intoxication complications, anesthetics, intravenous toxicity, arrhythmia chemically induced, propofol toxicity, thiopental toxicity, alcoholic intoxication physiopathology, arrhythmia etiology, atrial flutter chemically induced, atrial function, right drug effects, disease models, animal, electrophysiology, ethanol, random allocation, swine.

Zhou, J.X. and J. Liu (2002). **Tissue solubility of four volatile anesthetics in fresh and frozen tissue specimens from swine.** *American Journal of Veterinary Research* 63(1): 74-7. ISSN: 0002-9645.

NAL Call Number: 41.8 Am3A

Abstract: OBJECTIVE: To determine tissue solubilities of desflurane, sevoflurane, enflurane, and halothane in swine and to evaluate the effects of freezing specimens on tissue solubility, SAMPLE POPULATION: Arterial blood samples and specimens of brain, heart, liver, kidney, muscle, and subcutaneous fat from 5 healthy female adult Chinese Meishan pigs. PROCEDURE: Each tissue specimen was divided into 2 parts. One part was used to measure tissue-gas partition coefficients immediately after collection. The other part was frozen at -20 C for 6 days prior to determination of tissue-gas partition coefficients. Tissue-gas and blood-gas partition coefficients were measured by use of gas chromatography, and tissue-blood partition coefficients were calculated. Regression analysis was performed to determine whether fat-gas partition coefficients were correlated with lean tissue-gas partition coefficients. RESULTS: Tissue-gas and blood-gas partition coefficients of halothane were greater than those of enflurane followed by coefficients of sevoflurane and desflurane. However, the order of anesthetic agents with the greatest to smallest tissue-blood partition coefficients was sevoflurane, halothane, enflurane, and desflurane. Muscle-gas partition coefficients of sevoflurane and enflurane, liver-gas partition coefficients of desflurane and halothane, and the kidney-gas partition coefficient of enflurane were significantly greater in frozen specimens, compared with fresh specimens. Lean tissue-gas partition coefficients of all 4 volatile anesthetics correlated directly with fat-gas partition coefficients. CONCLUSIONS AND CLINICAL RELEVANCE: The fat content of lean tissue is an important factor in determining the tissue solubility of volatile anesthetics. Freezing specimens before determination of tissue-gas partition coefficients may result in a false increase in tissue solubility.

Descriptors: anesthetics, inhalation pharmacokinetics, swine metabolism, adipose tissue metabolism, brain metabolism, enflurane blood, enflurane pharmacokinetics, halothane blood, halothane pharmacokinetics, isoflurane analogs and derivatives, isoflurane blood, isoflurane pharmacokinetics, kidney metabolism, liver metabolism, methyl ethers blood, methyl ethers pharmacokinetics, muscle, skeletal metabolism, myocardium metabolism, tissue distribution.

Zink, W., J.R. Bohl, N. Hacke, B. Sinner, E. Martin, and B.M. Graf (2005). **The long term myotoxic effects of bupivacaine and ropivacaine after continuous peripheral nerve blocks.** *Anesthesia and Analgesia* 101(2): 548-54, Table of Contents. ISSN: 0003-2999.

Abstract: Compared with bupivacaine, acute myotoxicity of ropivacaine is less severe. Thus, in this study we compared the long term myotoxic effects of both drugs in a clinically relevant setting. Femoral nerve catheters were inserted in anesthetized pigs, and either 20 mL of bupivacaine (5 mg/mL) or ropivacaine (7.5 mg/mL) was injected. Subsequently, bupivacaine (2.5 mg/mL) and ropivacaine (3.75 mg/mL) were continuously infused (8 mL/h) over 6 h. Control animals were treated with corresponding volumes of normal saline. After 7 and 28 days, respectively, muscle samples were dissected at the former injection sites, and histological

patterns of muscle damage were blindly scored (0 = no damage to 3 = marked lesions/myonecrosis) and compared. No morphological tissue changes were detected in control animals. In the observed period, both local anesthetics induced morphologically identical patterns of calcific myonecrosis, formation of scar tissue, and a marked rate of fiber regeneration. However, bupivacaine's effects were constantly more pronounced than those of ropivacaine. These data show that both drugs induce irreversible skeletal muscle damage in a clinically relevant model, and confirm the exceeding rate of myotoxicity of bupivacaine. However, the clinical impact of these long term myotoxic effects still has to be assessed. IMPLICATIONS: In a period of 4 wk after peripheral nerve block, both long-acting local anesthetics, bupivacaine and ropivacaine, produced calcific myonecrosis suggestive of irreversible skeletal muscle damage. In comparison with ropivacaine, however, the extent of bupivacaine-induced muscle lesions was significantly larger.

Descriptors: amides toxicity, anesthetics, local toxicity, bupivacaine toxicity, muscular diseases chemically induced, nerve block, peripheral nerves, muscle cells drug effects, muscle cells pathology, muscle fibers pathology, muscle, skeletal pathology, muscular diseases pathology, necrosis, swine.

Zink, W., C. Seif, J.R. Bohl, N. Hacke, P.M. Braun, B. Sinner, E. Martin, R.H. Fink, and B.M. Graf (2003). **The acute myotoxic effects of bupivacaine and ropivacaine after continuous peripheral nerve blockades.** *Anesthesia and Analgesia* 97(4): 1173-9, Table of Contents. ISSN: 0003-2999.

Abstract: Bupivacaine causes muscle damage. However, the myotoxic potency of ropivacaine is still unexplored. Therefore, we performed this study to compare the effects of bupivacaine and ropivacaine on skeletal muscle tissue in equipotent concentrations. Femoral nerve catheters were inserted into anesthetized minipigs, and 20 mL of either bupivacaine (5 mg/mL) or ropivacaine (7.5 mg/mL) was injected. Subsequently, bupivacaine (2.5 mg/mL) and ropivacaine (3.75 mg/mL) were continuously infused over 6 h. Control animals were treated with corresponding volumes of normal saline. Finally, muscle samples were dissected at injection sites. After processing and staining, histological patterns of muscle damage were blindly examined, scored (0 = no damage to 3 = myonecrosis), and statistically analyzed. After normal saline, only interstitial edema was found. Bupivacaine treatment caused severe tissue damage (score, 2.3 +/- 0.7), whereas ropivacaine induced fiber injury of a significantly smaller extent (score, 1.3 +/- 0.8). Furthermore, bupivacaine, but not ropivacaine, induced apoptosis in muscle fibers. In summary, both drugs induce muscle damage with similar histological patterns. Compared with bupivacaine, which induces both necrosis and apoptosis, the tissue damage caused by ropivacaine is significantly less severe. We conclude that ropivacaine's myotoxic potential is more moderate in comparison with that of bupivacaine. IMPLICATIONS: After continuous peripheral nerve blockades, the long-acting local anesthetics bupivacaine and ropivacaine both induce fiber necrosis in porcine skeletal muscle tissue. In comparison with ropivacaine, bupivacaine causes tissue damage of a significantly larger extent and additionally induces apoptosis in skeletal muscle cells.

Descriptors: amides adverse effects, anesthetics, local adverse effects, bupivacaine adverse effects, muscular diseases chemically induced, nerve block, peripheral nerves, edema pathology, in situ nick end labeling, microscopy, electron, muscle fibers pathology, muscle fibers ultrastructure, muscle, skeletal pathology, muscle, skeletal ultrastructure, muscular diseases pathology, swine, swine, miniature, tissue fixation.

Zols, S., M. Ritzmann, and K. Heinritzi (2006). **Effect of analgesics on castration of male piglets [Einfluss von Schmerzmitteln bei der Kastration mannlicher Ferkel**. *Berliner Und Munchener Tierarztliche Wochenschrift* 119(5/6): 193-196. ISSN: 0005-9366.
NAL Call Number: 41.8 B45
Descriptors: piglets, anesthesia, analgesics, animal welfare, German law, castration, hydrocortisone, immobilization, non steroidal antiinflammatory agents, postoperative castration pain, preanesthetic medication, stress, stress response, surgery.
Language of Text: German, Summary in English.

Zols, S., M. Ritzmann, and K. Heinritzi (2006). **Effect of local anaesthesia in castration of piglets [Einsatz einer Lokalanasthesie bei der Kastration von Ferkeln**. *Tierarztliche Praxis Ausgabe G, Grosstiere/Nutztiere* 34(2): 103-106. ISSN: 1434-1220.
NAL Call Number: SF603.V43
Descriptors: piglets, analgesic properties, animal welfare, blood serum, castration, hydrocortisone, local anesthesia, male animals, pain, procaine.
Language of Text: German, Summary in English.

Zols, S., M. Ritzmann, and K. Heinritzi (2006). **Einfluss von Schmerzmitteln bei der Kastration mannlicher Ferkel. [Effect of analgesics on the castration of male piglets]**. *Berliner Und Munchener Tierarztliche Wochenschrift* 119(5-6): 193-6. ISSN: 0005-9366.
NAL Call Number: 41.8 B45
Abstract: According to the current German animal welfare law, male piglets may be surgical castrated without anaesthesia up to four weeks of life. This surgical procedure is painful during and also after the operation, for newborn animals as well as for adults. This study was aimed to investigate the impact of preoperative application of analgesics (Meloxicam) on the postoperative castration - pain of four to six days old male piglets. In this investigation all animals were randomly distributed in three groups:the first one was only immobilized but had no surgery, the second one was castrated without analgesics, and the third group was castrated after application of Meloxicam. Blood samples were taken immediately before immobilization, castration or application of the analgesic as well as one, four and 28 hours afterwards to determine Cortisol-concentration in the blood serum and, via this stress-marker, to indirectly evaluate the postoperative und possible intraoperative castration-pain. As a result all piglets castrated without preoperative application of Meloxicam showed significantly increased Cortisol-concentration one and four hours after castration. In contrast, piglets castrated with analgesics resulted in no significant increase during the entire experiment.
Descriptors: analgesics, non-narcotic administration and dosage, pain prevention and control, stress, swine surgery, thiazines administration and dosage, thiazoles administration and dosage, analysis of variance, animal husbandry methods, animal welfare, hydrocortisone, orchiectomy adverse effects, pain etiology, pain measurement, stress prevention and control, swine blood.
Language of Text: German.