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**OVERVIEW**

**Palmer et al. Using White-tailed Deer (*Odocoileus virginianus*) in Infectious Disease Research, pp. 350-360**

Domain 4: Animal care

Tertiary Species: Other Livestock

SUMMARY:Wild cervids, especially white-tailed deer (WTD), elk, and red deer, can be used to monitor infectious diseases as either hosts (*Brucella*, *M. bovis*, hep E) or sentinels (Enterohemorrhagic *E. coli*, *Yersinia*, *Listeria*). They can also be used to monitor the wildlife-livestock-human interface with pathogens like brucellosis and tuberculosis. Studies involving highly infective agricultural agents and large animals require higher-than-normal BSL3 practices (BSL3Ag). The article first summarizes studies using cervids at different BSL levels from 1940-2004. Then the authors then describe the breeding herd maintained at the USDA National Animal Disease Center in Ames, Iowa for use in BSL3 studies. Particular husbandry details about WTD include their flighty, alert nature around humans which makes moving animals from room to room easy but requires adequately constructed, fenced enclosures (suggested 3m tall). Barbering is common in WTD once they enter captivity, so enrichment should be supplemented. WTD are particularly sensitive to dietary changes. Hand-raising of fawns greatly facilitates easier biocontainment management and should begin within 24 hours of birth. However, hand-raised breeding bucks create a significant risk of injury as an aggressive buck acclimated to humans may charge caretakers. Farmed deer are considered a minor species by the FDA, thus the only approved drugs for use in WTD are xylazine and yohimbine. At the NADC breeding herd, breeding starts November, finishes January, and gestation is 195-205d. Fawning starts in June and ends by August. Drop-floor chutes are preferred over tilt tables (see image). Antlers are removed in the hard-antler stage when velvet has been rubbed off, and care is taken to remove them above the pedicle. Anesthesia is not required for hard-antler removal. The timing of male fawn castration is important as antler development is under hormonal control. If a fawn is castrated prior to pedicle formation, no antler develops. If castration occurs when the pedicle has formed, castration results in a small velvet antler that is never cast. The authors conclude that hand-raising WTD improves animal well-being, decreases animal stress, and avoids painful injuries during controlled studies inside the confines of a BSL3 facility.

QUESTION

1. What are the scientific names for the WTD, elk, and red deer?

ANSWER

1. *Odocoileus virginianus* = WTD

*Cervus canadensis* = elk

*Cervis elaphus* = red deer

**ORIGINAL RESEARCH**

***Biology***

**Ueda et al. Echocardiographic Parameters of Clinically Normal Geriatric Rhesus Macaques (*Macaca mulatta*), pp. 361-368**

Domain 1: Management of Spontaneous and Experimentally Induced Diseases and Conditions; K1. diagnostic procedures

Primary Species: Macaques (*Macaca* spp)

SUMMARY: In the present study, authors report complete echocardiographic parameters for a population of geriatric rhesus macaques and established their reference intervals. Valve regurgitations, especially aortic and tricuspid, and diastolic dysfunction of the left ventricle were highly prevalent in the study population, even though the macaques were clinically healthy. These findings closely mimic those found in the aging human population. For future studies of adult-onset disease, particularly cardiac abnormalities, these reference intervals are especially useful. The proposed reference intervals make it possible to use geriatric rhesus macaques as well-phenotyped control animals in translational research.

Aim: The goal of this study was to generate reference intervals for echocardiographic variables in a population of clinically normal geriatric (Age >18 yrs.) rhesus macaques (*Macaca mulatta)*.

Study Design: To do this, we studied 51 animals (age, 18–29 y; weight, 5.24–17.04 kg). The normal values for cardiac indices, including geometry and systolic and diastolic function, were determined by 2D, M-mode, spectral Doppler, and tissue Doppler echocardiography under ketamine hydrochloride sedation. Statistical correlations be- tween the echocardiographic parameters and age, body weight, sex, and heart rate were investigated. All echocardiographic indices were acquired, and their reference intervals were established.

Findings/Results: Multiple weak to strong correlations emerged between variables and echocardiographic parameters, but no moderate or strong correlations between body weight or sex and these parameters were noted. Of the 51 geriatric rhesus macaques evaluated, 36 (71%) fulfilled the criteria for diastolic dysfunction. Valve regurgitation, especially tricuspid regurgitation (43%), and aortic regurgitation (51%) also were common in geriatric rhesus macaques. Although these findings merit follow-up, they are unlikely to have clinical significance given their prevalence in these apparently healthy animals.

QUESTIONS

1.  What parameters were highly prevalent via echocardiographic observations in this study for clinically healthy animals?

a. Diastolic dysfunction of the left ventricle

b. Aortic Valve Regurgitations

c. Tricuspid Valve Regurgitations

d. All of the above

2.  What metabolic disease is associated with left ventricular diastolic dysfunction in Rhesus Macaques.

a. Hypoglycemia

b. Type 2 Diabetes Mellitus

c. Vitamin E deficiency

d. Hypovitaminosis A

e. Nutritional Hyperparathyroidism

3.  In the present study, several moderate to strong associations were found between echocardiographic parameters and variables (Age, Body Weight (BW), Body Surface A, Sex, and HR). All of these correlations were noted with -------- and therefore these parameters need to be interpreted cautiously when ---------- is significantly low or high. (fill in the blanks)

a. Age

b. BW

c. HR

d. BSA

e. Sex

ANSWERS

1.  d

2.  b

3.  c

***Husbandry***

**Braden et al. Effects of Breeding Configuration on Maternal and Weanling Behavior in Laboratory Mice, pp. 369-376**

Domain 4: Animal Care

Primary Species: Mouse (*Mus musculus*)

SUMMARY

* Study to determine if effects of pair, trio, and harem breeding configurations on maternal and weanling behavior of C57BL/6J and 129S6/SvEvTac. Nest scores, performance in pup retrieval test, open-field test (OFT), elevated plus maze, and tail suspension were all used to study the behavior of these animals
* Harem breeding configuration enhanced B6 maternal behaviors demonstrated by significantly shorter pup retrieval times. When compared to pair housed B6 mice, Trio and harem raised B6 weanlings showed increased exploratory behaviors by showing greater time spent in the center of the OFT.
* Breeding configuration did not alter pup retrieval times for 129 mice. On the day of weaning and compared to pair housed 129 mice, trio and harem raised 129 mice showed increased anxiety behavior by spending more time in the periphery of the OFT.
* B6 and 129 weanling mice had significantly higher weaning weights than weanlings raised in a pair-breeding configuration. This showed a potential benefit for pups raised by more than one mother and had communal nesting.
* Pup mortality was higher in trio-bred animals. Nest scores were decreased for trio-raised mice compared with pair and singly housed animals likely due to a mass effect from increased housing density in trio and harem cages.
* Histopathology of the nasal cavity was unremarkable for weanling harem bred mice with mean levels of 83-ppm ammonia. OSHA permissible exposure limit in 8hrs is 50ppm and NIOSH exposure limit in 10hrs is 25ppm. In B6 mice, harem bred cages produced the highest concentration of ammonia. In 129 mice, all breeding configurations produced relatively high levels of ammonia.

Conclusions

* Should handle cages and bedding under a ventilated hood due to potential for higher level of ammonia.
* In B6 mice: fewer pups were produced per dam when housed in harem breeding configuration than when pair-bred. Harem breeding presented no significant welfare benefits over trio breeding and is more likely to result in ammonia levels that significantly exceed those recommended by OSHA and NIOSH. Harem breeding did not result in increased breeding efficiency in B6 mice.
* Pair and trio breeding in a standard 67-in2shoebox cage are appropriate and beneficial breeding strategies for C57BL/6 and 129S6/SvEvTac mice.

QUESTIONS

1. What is the recommended breeding configuration for B6 and 129 mice?

2. Why did harem-breeding configurations have higher weaning weights?

ANSWERS

1. Pair and Trio breeding

2. Increase of communal nesting and pups are raised by more than one mother.

**Lombaert et al. Behavioral Characteristics of Adult Zebrafish (*Danio rerio*) after MS222 Anesthesia for Fin Exclusion, pp. 377-381**

Domain 2: Management of Pain and Distress

Secondary Species: Zebrafish (*Danio rerio*)

SUMMARY: Fin-clipping is a common procedure to harvest tissue for genotyping in zebrafish. Zebrafish are anesthetized by MS222 before fin-clipping. In rodent studies, analogous surgical procedures have been shown to impact behavior and cognition studies. Zebrafish are commonly used in studies on learning, memory, fear, social behavior, anxiety, and addition, so examining how fin-clipping affects anxiety and feeding behavior in zebrafish is important. In this paper, zebrafish tested with the novel tank diving assay, feeding latency assay, and whole-body cortisol analysis after fin-clipping, and compared to a sham group. The fin-clipped group had increased anxiety and increased feeding latency 1 hr after the procedure compared to the sham group, but there was no significant difference between the two groups after 6h and 24 hrs. Cortisol levels were not significantly different between fin-clipped and control groups.

QUESTIONS

1. Exposure of zebrafish to ENU most commonly induces which type of tumor?
	1. Cavernous hemangioma
	2. Epidermal papilloma
	3. Peripheral nerve sheath tumor
2. Which of the following genetic modifications/cancer combinations are **NOT** true?
	1. C-myc oncogene – T-cell acute lymphoblastic leukemia
	2. AML1- ETO translocation/fusion– acute myelogenous leukemia
	3. BRAF oncogene – chronic lymphocytic leukemia
3. True or False: zebrafish have been shown to be able to regenerate all the following organs: retina, spinal cord, fin, heart, hair cells.
4. True or False: The frequency and intensity of territorial behaviors is inversely correlated with density

ANSWERS

1. b
2. c: BRAF – malignant melanoma
3. True
4. True – “Aggression is highest at low densities. As tank densities increase and it becomes progressively more difficult for dominance hierarchies to be maintained, the frequency and intensity of aggression and territoriality decreases.” - Laboratory Animal Medicine, Chapter 20

**Fish et al. Effect of Wearing a Telemetry Jacket on Behavioral and Physiologic Parameters of Dogs in the Open-Field Test, pp. 382-389**

Domain 3: Research: T3 Design and conduct research

Species Primary: Dog (*Canis familiaris*)

SUMMARY:Safety studies in dogs are often required to rely on non-invasive telemetry to monitor electrocardiology, respiration, temperature and locomotor activity. Non-invasive jacketed systems avoid surgical implantation and eliminates anesthesia and restraint-induced stress. Invasive and non-invasive methods have a good correlation for several endpoints. This study reviewed the previously unevaluated effect of telemetry vest wearing on physiological and behavioral outcome measures. 16 male and female Labrador retrievers were housed and maintained in an AAALAC accredited facility and all procedures were reviewed and approved by the institutional IACUC. Dogs were randomized into two groups (vest and no-vest wearing) of 8. Dogs were assigned an anxiety score in an open-field test (OFT). The anxiety score was a subjective evaluation of the dogs based on negative (ex. freezing and hiding) and positive (ex. panting, shaking and elimination) anxieties. An average of the negative and positive anxiety scores created a mean anxiety score (MAS). Anxiety was induced by an audio recording of a thunderstorm.  Manual temperature did not differ between groups, however there was an 8% decrease in heart rate in vest-wearing dogs compared to non-vest wearing dogs after the OFT. There was continuous recording of the ECG, respiration and skin temperature throughout the OFT through the jacket telemetry. There was no difference in total distance traveled in the OFT.  Telemetry data did not differ between the two groups. This research is consistent with previous studies that found anxiety reduction in dogs wearing a commercial available wrap (ThunderShirt). Limitations of this study included, research staff not being blinded to the presence or absence of a vest, the chosen randomization strategy created an unbalance by the sex of the dogs not being even between the groups, dogs were not acclimated to the vests, and the breed chosen in this study is rarely used in safety studies.

QUESTIONS

1. What were the two significant findings in this study?
2. What are some of the limitations of this study?
3. T/F:  Invasive (surgical implants) telemetry routinely provides superior data to non-invasive (jacketed) telemetry.

ANSWERS

1. There was an 8% decrease in heart rate in vest-wearing dogs compared to non-vest wearing dogs after the OFT and 2. The overall MAS was reduced by 34% in vest-wearing dogs compared to non-vest wearing dogs.
2. Limitations of this study included, research staff not being blinded to the presence or absence of a vest, the chosen randomization strategy created an unbalance by the sex of the dogs not being even between the groups, dogs were not acclimated to the vests, and the breed chosen in this study is rarely used in safety studies.
3. F

***Management***

**Zhang et al. Genetic Characterization of a Captive Colony of Pigtailed Macaques (*Macaca nemestrina*), pp. 390-395**

Domain 3: T3, K4

Primary Species: Macaques (*Macaca spp)*

SUMMARY: Pigtail macaques have been commonly used as models for studies of infectious diseases, immunology, neurosciences, pathology and behavior. Pigtailed macaques can be further divided into two species, *Macaca fasicularis* and *Macaca leonine.*In this study, genotyping was used to characterize the genetic makeup of the facility colony.  DNA samples were collected from 162 pigtailed macaques and 56 single-nucleotide polymorphisms (SNP) was used to genotype the colony. A total of 80 of the 162 pigtailed macaques evaluated yielded SNP genotype data that were at least 90% complete, representing 34 founder macaques, 22 animals from the 2003-2008 birth cohort, and 24 progeny in the 2009-2013 cohort. The 2 birth cohorts in the studied colony maintained approximately the same level of heterozygosity as in the founder population. The results demonstrated that the colony has maintained a high level of genetic diversity.

QUESTIONS

1. Pigtailed macaques have been widely used as models for which disciplines?

2. What is the genus and species of the northern pigtailed macaque?

3. What is one of the reasons why single-nucleotide polymorphisms (SNP) are used in population genetics with increasing frequency in mammalian genomes?

ANSWERS

1. Infectious diseases, immunology, neuroscience, pathology and behavior.

2. *Macaca leonine*

*3.*SNP are more abundant than short tandem repeats in the mammalian genome.

**Kanthaswamy et al. Population Genetic Structure of the Cayo Santiago Colony of Rhesus Macaques (*Macaca mulatta*), pp. 396-401**

Domains 3: Research, K4. Genetics and Nomenclature

Primary Species: Macaques (*Macaca* spp)

SUMMARY: The authors of this study characterized the genetic diversity of rhesus macaques on the island of Cayo Santiago (Puerto Rico) by using pedigree and molecular analysis approaches.  The purpose of this study was to determine the genetic relationship of the seven distinct social groups in an effort to determine genetic diversity of the groups.  The authors imply that this information may help to determine which groups to depopulate due to unsustainably large number of non-human primates in this geographic area.  The authors obtained the genetic material via annual trapping and blood collection for Short Tandem Repeat (STR) analysis.

The used 7 social groups of mixed females and males and a group of extra 5 males. The authors determined the degree of genetic variation and coefficients of inbreeding (F) and kinship by looking at pedigree and STR from 4738 NHPs.  The pedigree analysis used information on each animal’s parentage, sex, date of birth, and date of death or removal from the island were used to generate estimates of kinship (k), kinship value (kv), gene value (GV; 1-kv), genome uniqueness (GU), founder equivalents (fe), and founder genome equivalents (fg).

The authors found that the social groups did not differ genetically from each other due to male-mediated gene flows (moving in and out of groups) and showed sufficient genetic variation.  They found that genome uniqueness, founder equivalents, and founder genome equivalents show highly effective founders, and this has a positive effect on the colony’s genetic structure.  The authors further speculate culling one particular social group for research purposes but furthermore add that this particular group also exhibits relatively high kinship, kinship value, and fixation index and intermediate levels of genetic uniqueness and genetic diversity.

QUESTIONS

1. In this article the authors used which of the following to characterize genetic diversity and pedigree relationships?

a. Coefficients of inbreeding (F)

b. Short Tandem repeat (STR) analysis

c. Kinship (k)

d. Gene Value (GV)

e. All of the above

f. None of the above

2. The authors found that:

a. All the groups were vary genetically distinct from other each

b. The female only group was not genetically diverse

c. There was not movement in or out of social groups

d. The founder effects were negatively impacting the colony’s genetic structure

e. All of the above

f. None of the above

3. True/False. The authors believe that genetic analysis and pedigree analysis may be beneficial for determining future colony management.

ANSWERS

1. e. All of the above

2. f. None of the above

3. True

***Animal Health Surveillance***

**Compton et al. Murine Astrovirus Infection and Transmission, pp. 402-411**

Domain 3: Research

Primary Species: Mouse (*Mus musculus*)

SUMMARY: Murine astrovirus (MuAstV) has recently been detected but its effect on murine-based research and biosecurity is largely unknown. The goal of this study was to mimic the natural infection of neonates in endemically infected population. MuSatV was inoculated at 2 critical ages in CD1 mice: in 3-d-old mice when well-characterized murine viruses (mouse hepatitis and murine rotavirus) produce their highest viral titers and the greatest pathology, and in 13-d-old mice, when coprophagy begins. The ability of soiled-bedding sentinels and environmental monitoring to detect MuAstV was assessed. 8 dams and their PND 3 (Post Natal Day) litters as well as 8 dams and their PND 13 pups were inoculated orally. None of the pups showed clinical signs and the average weight of mice in all groups-regardless of sex, date of birth, or infection status-fell within the normal weight range for CD1 mice; consequently, these observed differences are clinically irrelevant. To determine the duration of fecal shedding of MuAstV from mice infected as neonates, feces were collected from weanlings at PND 21 through 63. The data shows that MuAstV caused a subclinical infection, primarily in the intestine, with varying levels of MuAstV RNA detectable in the intestines of all pups and trace levels of MuAstV RNA detectable in the spleen, liver and kidney of some pups. MuAstV was detected in feces from 15 of the 16 dams through PND 21 and 9 dams were still shedding MuAstV at PND42.

87% of the sentinels exposed to soiled bedding from cages housing dams with litters, dams alone, or weanlings became infected with MuAstV, confirming that MuAstV in feces, detected by RT-PCR analysis between PND 7 and 42, was infectious and present in sufficient amounts to cause infection of sentinel mice for at least 6 weeks. In addition, 75% of the sentinels exposed to soiled bedding that had been aged 1,2 or 3 weeks became infected, indicating that feces present in cages at the routine cage-change interval of 14 d likely still contains infectious MuAstV. Using swabs and RT-PCR analysis, monitoring of cage surfaces at 7 to 8 d after addition of MuAstV-infected mice to the cage was effective. Environmental air monitoring of the IVC exhaust manifolds for Mu AstV RNA by using swabs was variably effective depending on the location of the exhaust manifolds swabbed.

In conclusion, MuAstV causes a subclinical chronic infection, lasting at least 3 weeks, primarily in the intestines of CD1 mice regardless of the age at infection. Soil-bedding sentinels and TR-PCR analysis of feces, cage swab material, and exhaust air debris are all effective for detecting MuAstV.

QUESTIONS (True or False)

1. This study shows that oral inoculation of mice on PND3 with MuAstV resulted in only low-level intestinal infection, which peaked at PND15, and did not really disseminate to other tissues.

2. The data in this study suggests that oral inoculation of mice on PND 13 with MuAstV resulted in robust infection in the intestines, with dissemination to other tissues, but infection was cleared from the other tissues by 12 DPI.

3. The use of soiled bedding sentinels is not an effective method for monitoring MuAstV in a colony of laboratory mice.

ANSWERS

1. True

2. True

3. False

**Crim et al. Comparison of Antemortem and Environmental Samples for Zebrafish Health Monitoring and Quarantine, pp. 412-424**

Secondary Species: Zebrafish (*Danio rerio*)

SUMMARY: Health monitoring of zebrafish has up until now primarily involved histopathology of adult zebrafish. However, PCR based diagnostics have recently become available for zebrafish allowing for analysis of different samples such as feces, embryos and detritus. Prior to PCR based assays, testing of imported embryos have been difficult, and zebrafish have sometimes been kept in quarantine for several generations. The present study compared the utility of several antemortem and environmental sample types for pathogen detection by PCR. In addition, a comparison was made between disinfected and untreated embryos.

In the study that compared different sample types, the Zebrafish populations were enzootically infected with five pathogens:

* *Mycobacterium chelonae*
* *Mycobacterium fortuitum*
* *Mycobacterium peregrinum*
* *Pseudocapillaria tomentosa*
* *Pseudoloma neutrophilia*

In the study that compared disinfected with untreated embryos, embryos came from colonies historically positive for multiple pathogens including:

* *Mycobacterium chelonae*
* *Mycobacterium fortuitum*
* *Mycobacterium haemophilium*
* *Mycobacterium marinum*
* *Pleistophore hyphessobryconis*
* *Pseudocapillaria tomentosa*
* *Pseudoloma neutrophilia*

Environmental samples included water samples concentrated by filtration and detritus collected from the tank floor. Feces and embryos were collected and whole fish were sent for analysis.

Environmental samples detected mycobacterium more efficiently than testing zebrafish directly. There was no difference in detecting *Pseudocapillaria tomentosa*and*Pseudoloma neutrophilia*between environmental samples and whole zebrafish. *Mycobacterium spp*. and *P. tomentosa* were frequently detected in pooled fecal samples, whereas detection of *P. neurophilia* was inconsistent. Embryos proved insensitive as a diagnostic sample for all pathogens tested. The study provide evidence for the utility of multiple sample types to detect various pathogens in the zebrafish. Water concentrated by filtration and detritus provided excellent detection of mycobacterium spp. *P. tomentosa*was easily detected in detritus and fecal samples. Feces are a better antemortem sample type than embryos for detection of multiple pathogens.

QUESTIONS

1.   What is the most commonly detected pathogen of zebrafish?

2.  T/F: Multiple pathogens can easily be detected by PCR in zebrafish embryos.

ANSWERS

1. *Psedoloma neurophilia*

2.  False

***Anesthesia***

**Oliver et al. Evaluation of Pain Assessment Techniques and Analgesia Efficacy in a Female Guinea Pig (*Cavia porcellus*) Model of Surgical Pain, pp. 425-435**

Secondary Species: Guinea Pig (*Cavia porcellus*)

SUMMARY: This article evaluates the clinical efficacy of carprofen and an extended-release buprenorphine (BE), used alone and as multimodal combination, to relieve post-surgical pain for surgical procedures that produce more than slight or momentary pain. Therefore, nonevoked and evoked pain measurements were taken for 96 hours in addition to clinical assessments in female guinea pigs that underwent hysterectomy surgeries. Of the three analgesia regimens, carprofen alone, buprenorphine (BE) alone, and multimodal combination of buprenorphine and carprofen, the latter provided the most effective pain control in guinea pigs across multiple assessments of pain and nociception resulting in the shortest duration of ineffective pain coverage post hysterectomy. Furthermore, these results indicated that buprenorphine should be administered 8-12 hours prior to surgery. Thus, weight loss and sedation of BE treated animals remained a negative side effect in this study.

Guinea pigs are the most common laboratory species covered under the Animal Welfare Act. They are commonly used for research with potential to experience pain. In most of these cases opioids and NSAIDs are used to control pain. Doses are mostly determined by allometric scaling without analgesic efficacy studies for this species. 24 intact female guinea pigs were chosen for this study. Each guinea pig was assigned randomly into one out of three analgesic treatment groups: ER, carprofen and multimodal group with each animal serving as its own control. All guinea pigs on the study underwent baseline, anesthesia-analgesia, and surgery conditions which consisted in hysterectomy procedure. Animals in all three treatment groups were assessed for pain as followed: nonevoked and evoked pain assessment through video assessment, electronic von Frey measurements, cage side ethogram assessment, time-to consumption score in addition to pharmacokinetic evaluation. For the video assessment guinea pigs underwent video recordings at different time points to evaluate clinical behavior in absence of a human observer. For the cage side assessments, the guinea pigs were observed in their home cages at each time point for clinical signs indicating painful behavior. The time-to-consumption used an elevated platform which the animal needed to climb onto to access hay. Time to consume food and behavior were scored. Blood samples were collected at different time points for pharmacokinetic evaluations of therapeutic thresholds. The results of this study revealed that multimodal analgesia provided the best analgesic efficacy to guinea pigs across all tests including standard clinical assessment of body weight loss, 3 nonevoked assessments (cage side ethogram, video ethogram, and time-to-consumption test), and an established evoked (electronic von Frey) measure of pain under baseline, anesthesia-analgesia, and surgery conditions. Carprofen alone provided insufficient postsurgical analgesia.

In order to assure that ER reaches the therapeutic threshold before a painful surgical procedure takes place the study indicated that dosing animals with ER should start 8-12 hours prior to surgeries. Despite the analgesic efficacy of ER, there were side-effects observed including significant weight loss exceeding 10% and behavioral sedation, which needed further evaluation for using lower dosage.

In addition, the study demonstrated that nonevoked measures provide a more accurate and better clinical pain assessment than evoked measurements, thus used in combination provided accurate and thorough pain assessment.

QUESTIONS

1.  True or False: The results of this study revealed that multimodal analgesia did not provide the best analgesic efficacy to guinea pigs across all tests.

2. True or False: Carprofen alone provided insufficient postsurgical analgesia

3.  What were the side effect of buprenorphine when used alone:

a.  More than 10% of weight loss

b.   Sedation

c.  Hyperactive behavior

d. a + b

e. a + c

ANSWERS

1.  False

2.  True

3.  d

**Williams et al. Oral Transmucosal Detomidine Gel in New Zealand White Rabbits (*Oryctolagus cuniculus*), pp. 436-442**

Primary Species: Rabbit (*Oryctolagus cuniculus*)

**SUMMARY:** In this study 8 adult male New Zealand white rabbits each received 0.6, 1.2, or 1.8 mg/kg oral transmucosal detomidine gel-OTM (which is an FDA drug approved for use in horses for sedation/restraint). Physiologic parameters and sedation scores (SS) were assessed at 10-min intervals from before administration until 100 min afterwards. Histopathology of cardiac tissue was scored through 12 d after dosing. Overall results showed that gel administration increased the SS in all rabbits, but none of the animals developed clinically effective sedation (SS of 10 or greater, based on 5 reflex responses on a 3- or 4-point scale). The 5 reflex responses evaluated consecutively included: otic reflex, lip pinch, jaw resistance, pedal reflex, and positioning in lateral recumbency. The SS did not differ among dosage groups, and the time-dose interaction was not statistically significant. Heart rate decreased rapidly in all rabbits, with no difference among dosage groups, and there was no effect of time or dosage on peripheral capillary oxygen saturation. Minimal to mild degenerative changes were seen in the myocardium of all treated rabbits, but myocyte necrosis, inflammation, fibrosis, and mural thrombi-reported previously in rabbits that had received parenteral detomidine-did not occur. Authors concluded that OTM detomidine gel was safely and easily administered to rabbits, but the duration and level of sedation were unpredictable.

**Takeaway message: The use of OTM detomidine as a sole agent to facilitate handling and restraint of rabbits does not offer advantages over existing parenteral regiments.**



**QUESTIONS**

1.  Which of the following is a reported adverse effect with the use of alpha2-adrenergic receptor agonists in veterinary medicine?

a.  Bradyarrhythmia

b.  Sinus bradycardia

c.  Second-degree AV block

d.  Hypotension

e.   All of the above

2. T/F. alpha2-adrenergic receptors have been shown to cause myocardial necrosis in rabbits.

**ANSWERS**

1.  e

2.  T. This is attributed to direct impairment of coronary blood flow through effects on alpha2-adrenergic receptors in cardiac vessels, which override the normal metabolic signals for vasodilation. Subsequent anorexia has also been reported with use of high detomidine doses in rabbits (150mg/kg).

**Salyards et al. Pharmacokinetics of a Novel, Transdermal Fentanyl Solution in Rhesus Macaques (*Macaca mulatta*), pp. 443-451**

Domain 2: Management of Pain and Distress

Primary Species: Macaques (*Macaca* spp)

SUMMARY: Pain management in NHPs is important for ensuring animal welfare. Transdermal drug delivery is noninvasive, inexpensive, and improves patient compliance. Transdermal fentanyl patches are commonly used in human and veterinary medicine. The objective of this study was to establish to pharmacokinetic profile of 2 topical doses of transdermal fentanyl (Recuvyra) and compare the results to those previously published in beagles. Six healthy adult rhesus macaques were used in this study, and transdermal fentanyl solution (TFS) was applied at two different doses. All macaques remained healthy throughout the study, and no adverse effects were noted. T ½ was significantly longer than in canines at both dose levels (1.3 mg/kg, 2.6 mg/kg). T-max and AUC differed significantly between macaques and canines at one dose level but not at both dose levels. Mean plasma concentrations exceeded the lower bound of minimal effective concentration (MEC) after 2 h (both doses), and remained above the lower bound for 7 days (1.3 mg/kg dose) and 10d (2.6 mg/kg dose), was above the average reported MEC from 8h – 4d (1.3 mg/kg dose) and 4h-6d (2.6 mg/kg), and above the upper bound of the MEC at 4h-4d (2.6 mg/kg dose) and never (1.3 mg/kg dose) respectively. Plasma concentrations were lower in male macaques compared to female macaques (possibly related to sex-specific difference in fat distribution). In summary, both doses of TFS in rhesus macaques have similar pharmacokinetic profiles, with significantly longer half-lives than in dogs, and remain above the minimal effective plasma concentration (0.2 ng/mL) for 7 and 10 d, respectively.

QUESTIONS

1.  What is the mechanism of action of fentanyl?

2.  Side effects of full μ opioids include profound respiratory depression, apnea, and cardiovascular depression.

a. What drugs are μ antagonists?

b. What other drugs may be helpful in reversing the side effects of opioids?

c.  What is another way to reduce the side effects of opioids?

ANSWERS

1. μ-receptor, some activity at δ- and κ- receptors

2.  Opioids:

a.  μ antagonists: buprenorphine (nonemergency), naloxone (emergency)

b. Reverse opioid-induced bradycardia: atropine, glycopyrrolate (does not cross BBB)

c.  Decrease dose, and administer with other classes of anesthetics (ex: propofol)

**Chinnadurai et al. Minimum Alveolar Concentration and Cardiopulmonary Effects of Isoflurane in Ring-tailed Lemurs (*Lemur catta*), pp. 452-456**

Domain 2, T3 - Management of Pain and Distress - Administration of Anesthesia

Tertiary Species: Other NHPs

SUMMARY: This group aimed to determine the minimum alveolar concentration (MAC) of isoflurane and the cardiopulmonary effects of increasing concentrations of isoflurane in ring-tailed lemurs. In the MAC-determination study, the vaporizer was set to achieve 1.5% end-tidal isoflurane concentration (FeIso) for each animal. Based upon response to a noxious stimulus (a clamp placed on the tail) the FeIso was increased or decreased by 10%, respectively. After a negative response was achieved and a single 10% decrease in FeIso resulted in a positive response, the MAC for that animal was determined as the mean of the FeIso for consecutive positive and negative trials. The mean of the individual MAC values was considered the isoflurane MAC of the group, and was calculated to be 1.96%.

After establishing the isoflurane MAC for ring-tailed lemurs, a separate group of animals were anesthetized and maintained at 0.5, 1.5, or 2 times the established MAC, with no external stimulation. 8/10 lemurs became hypotensive (mean arterial pressure <60mmHg), but there was no consistent relation between BP and isoflurane concentration. pH was significantly lower and PaCO2 significantly higher at 2 MAC compared with 1 MAC, indicating more profound respiratory acidosis due to hypoventilation at 2 MAC. Additionally, this group found that noninvasive blood pressure measurements were an acceptable substitute for invasive measurements of systolic arterial pressure and mean arterial pressure, as values between the measurement modalities were not significantly different.

The isoflurane MAC for ring-tailed lemurs (1.96%) is much higher than reported for most other mammals. Interestingly, ring-tailed lemurs also demonstrated an unexpectedly high sevoflurane MAC (3.48%) in a separate study. The group concluded that isoflurane anesthesia at less than 2 times the MAC value of 1.9% is unlikely to cause significant cardiovascular depression in ring-tailed lemurs.

QUESTIONS

1.  What does the MAC of an inhalant anesthetic agent indicate?

2. What suborder of primates do *Lemur catta* belong to?

ANSWERS

1.  The concentration of inhalant required to prevent movement in response to a noxious stimulus in 50% of subjects.

2.  Prosimian

***Experimental Use***

**DenHerder et al. Effects of Time and Storage Conditions on the Chemical and Microbiologic Stability of Diluted Buprenorphine for Injection, pp. 457-461**

Domain 2: Management of Pain and Distress; T1. Recognize pain and/or distress; T2. Minimize or eliminate pain and/or distress

Primary Species: Mouse (*Mus musculus*)

SUMMARY:The authors looked to test an important hypothesis asking the question of whether diluted buprenorphine, a common pain medication used for moderate to severe pain, remained stable and sterile in different storage conditions and predicted that aseptically prepared diluted buprenorphine would remain sterile and the concentration of buprenorphine (diluted 1:10) would fall below 90% over a 180-day period. Interestingly, the authors found that diluted buprenorphine, when stored in glass vials, either refrigerated or at room temperature, remained stable, but if stored in plastic syringes, the concentration would rapidly decline, by over 80% in just one day. In glass vials, diluted buprenorphine—whether stored at room temperature or refrigerated—retained more than 90% of its initial concentration. This finding greatly impacts animal studies where pain meds are expected to manage moderate to severe pain and may not be if stored in plastic syringes.

QUESTIONS

1.   What did the authors suspect as the cause of the decreased concentration of diluted buprenorphine when it was stored in plastic syringes?

2.  Describe adsorption.

3.   Why did the authors think this was an important study to run?

ANSWERS

1.  Degradation of the buprenorphine molecule could have resulted from a chemical reaction, such as oxidation, or an interaction with a leached substance from syringe components. Another possibility is that the buprenorphine molecule adsorbed to one or more of the syringe components, decreasing its concentration in the solution.

2.  Adsorption to surfaces usually occurs when functional groups within a molecule interact with binding sites on the surface of the container. Adsorption is the most frequently reported drug interactions with plastic materials.

3.   Veterinary buprenorphine is FDA approved for subcutaneous use in cats, so human single dose vials of Buprenex are commonly used in lab animal settings. Since this human version is intended for immediate use, there are no preservatives.

**CASE REPORTS**

**Okpe and Kovach. A Redesign Approach for Improving Animal Care Services for Researchers, pp, 462-471**

Domains 3 & 5

SUMMARY: Attempts to improve Animal Care and Use Program (ACUP) processes rarely focus on the customer service aspect. This study concentrated solely on streamlining the interactions between researchers and the Animal Care Operations (ACO), using Design For Six Sigma (DFSS) methodology. DFSS focuses on building in quality by identifying the needs of those involved, and incorporating features that address those needs into the design of a product or process, and follows the define (identify process to be redesigned), measure (collect information from customers, translate to need statements), analyze (prioritize previously identified needs), design (develop and implement idea regarding how to fulfill needs), and verify (validate redesigned process) (DMADV) framework. 13 need statements were identified regarding how researchers and the ACO interact, of which 7 were chosen as top priorities. These included 1) providing valuable information for researchers, 2) providing responses to inquiries in a timely manner, 3) support collaboration among the ACO, IACUC, and researchers, 4) facilitating researcher’s access to ACO’s facilities, 5) improving support for researcher’s needs, 6) improving IACUC’s communication with ACO, and 7) facilitates making information accessible to researchers, as needed. 5 mechanisms were identified to address these needs: 1) revising the Division of Research’s ACO website, 2) updating the frequently asked questions section of the Division of Research’s ACO SharePoint page, 3) creating an ‘on-boarding’ checklist for new researchers, 4) hiring additional veterinary staff, and 5) instituting a biannual ACO newsletter. Metrics used to assess the efficacy of these changes included: 1) Number of facility-related information updates sent to researchers, 2) Number of researcher requests for the same or a similar issue, 3) FAQ section of the Division of Research’s ACO SharePoint page provides needed information, 4) Number of channels used to provide information to researchers, 5) General information about the ACO is accessible through the Division of Research’s ACO website, 6) Time taken by the ACO staff to respond to/resolve issues with researchers, 7) Number of ACO requests for clarification from IACUC, and 8) Time needed for researchers to get access to facility. Verification 5 weeks after implementation of changes revealed improvement in metrics 1, 2, 4, 7, 6, and 8, while metrics 3 and 5 were enhanced. This study showed that the DFFS methodology-DMADV could potentially be a useful approach in improving the ACUP.

QUESTIONS

1. Which one of the following improvement approaches focuses on building in quality by identifying the needs of those involved, and incorporating those needs into the design of a process?

a. Total Quality Management

b. Six Sigma Methodology

c. Toyota Production System

d. Lean

e. Design for Six Sigma Methodology

2. Which one of the following was NOT identified as a top priority need for researchers regarding their interactions with the ACO?

a. Improves support for researchers' needs

b. Facilitates researcher's contributions in facility administration

c. Facilitates making information accessible to researchers, as needed

d. Provides responses to inquiries in a timely manner

e. All of the above were identified as top priorities

ANSWERS

1. e
2. b