**Journal of the American Association for Laboratory Animal Science**

Volume 55, Number 1, January 2016

**OVERVIEW**

**Haughton et al. The Biology and Husbandry of the African Spiny Mouse (*Acomys cahirinus*) and the Research Uses of a Laboratory Colony, pp. 9-17**

Domain 3: Research, Domain 4: Animal Care

Species: Tertiary – Other Rodents

SUMMARY: African spiny mice (Acomys spp.) are unique precocial rodents that are found in Africa, the Middle East, and southern Asia. They exhibit several interesting life-history characteristics, including precocial development, communal breeding, and a suite of physiologic adaptations to desert life. Spiny mice are notable for large spiny hairs that form most of the dorsal pelage. They possess very weak skin (21 times weaker than laboratory mice) that tears easily in response to attack or handling. Given their predilection for rocky outcroppings and because they do not dig burrows, they are thought to rely on rock crevices and already established burrows for shelter.

Acomys species have a lifespan of 2 to 4 y and exhibit sexual dimorphism, with males being slightly larger than females. They are sexually mature at 2 to 3 mo. of age, which is coincident with the emergence of spiny hairs that have a light-golden color. Spiny mice exhibit seasonal breeding in the wild, though captive females cycle year round. The estrus cycle is approximately 11 d long. After ovulation, functionally active corpora lutea are spontaneously present in A. cahirinus and A. spinosissimus, unlike in most laboratory rodents. Males do not have preputial glands. Gestation in African spiny mice reportedly lasts 38 to 45 d, about twice as long as that in mice and rats. Litter size tends to be small, consisting of 1 to 4 pups (normally 2). Spiny mice complete the majority of neurogenesis prior to birth, making comprehensive behavioral assessments in neonatal spiny mice possible. Increased group size as measured by number of sexually mature females positively affects litter size and breeding efficiency. They are healthiest living in small groups consisting of 1 to 2 males, several females, and their progeny.

24 in. × 18 in. × 16 in. powder-coated galvanized steel cages with wire sides and lids and soft, dust-free bedding for cage bottoms is ideal. Spiny mice are desert adapted and prefer warm temperatures; they live and breed well in a temperature range between 21-26°C and humidity from 30% to 70%. Acomys species are omnivorous and are known to ingest insects, snails, and seeds and other plant material. They do well on a 3:1 mixture of low-protein mouse pellets (14.3% protein, 4% fat with 2.9 kcal/g) and black-oil sunflower seeds. Spiny mice acclimate to being handled by either gently scooping or cupping them in the hand or by grabbing the entire body from the dorsal side.

Reports of overt disease in captive spiny mice colonies are uncommon, and there are few reports of infectious agents in wild spiny mice. Spiny mice have served as a model to examine physiologic adaptations to desert life, diet-induced type 2 diabetes, diel rhythmicity, late-gestation development, female aggression, and parental behavior. Recently, spiny mice have emerged as a new animal model for evolution, development, and regeneration research. Given the precocial development of most organ systems in spiny mice, they are useful models to understand developmental defects that occur during late gestational development and for near-term birth asphyxia.

QUESTIONS

1. Acomys spp. males have all of the following accessory sex glands EXCEPT?

a. Prostate

b. Preputial glands

c. Seminal vesicles

d. Coagulating glands

e. Ampullary glands

2. Which male copulatory behavior(s) is/are rare among murids? (Pick all that apply)

a. Multiple intromissions

b. No thrusting

c. Single to few ejaculations

d. Short incipient lock

3. What temperature range is ideal for captive Acomys spp.?

a. 17-22°C

b. 19-24°C

c. 21-26°C

d. 23-28°C

ANSWERS

1. b

2. c, d

3. c

**ORIGINAL RESEARCH**

***Biology***

**Alstrup. Blood Lactate Concentrations in Gottingen Minipigs Compared with Domestic Pigs, pp. 18-20**

Domain 1: Management of Spontaneous and Experimentally Induced Diseases and Conditions

Task 2 - Control spontaneous or unintended disease or condition

Primary Species: Pig (Sus scrofa)

SUMMARY: Elevated plasma lactate in anesthetized patients can indicate poor surgical outcomes. Plasma lactate has been used to monitor anesthetized pigs, but there is minimal information regarding what parameters can impact plasma lactate in swine. A study was conducted to evaluate the plasma lactate in different breeds (domestic swine vs. Gottingen minipigs) and under different conditions (major vs. minor surgery, types of anesthesia and body weight).

Plasma lactate was significantly higher in in minipigs as compared to domestic swine. No other condition evaluated significantly altered lactate concentration.

QUESTION

1. What is the significance of elevated plasma lactate concentrations in surgery patients?

ANSWER

1. Increased plasma lactate is associated with poor post-surgical outcomes. It is used as an indicator of hypoxia and poor quality anesthesia.

***Husbandry***

**Allen et al. Rat Breeding Parameters According to Floor Space Available in Cage, pp. 21-24**

Domain 3: Research and Domain 4: Animal Care

Primary Species: Rat (Rattus norvegicus)

SUMMARY: The authors of this study sought to identify an optimal rodent bedding and cage-change interval to establish standard procedures for the individually ventilated cages (IVC) in their rodent vivarium.

Methods: Disposable cages were prefilled with either corncob or α-cellulose bedding and were used to house 2 adult Sprague–Dawley rats (experimental condition) or contained no animals (control). Rats approximately 450 g, 18 weeks of age were observed and intracage ammonia levels measured daily for 21 days.

Results: Intracage ammonia accumulation became significant by day 8 in experimental cages containing α-cellulose bedding, whereas experimental cages containing corncob bedding did not reach detectable levels of ammonia until day 14. In all 3 experimental cages containing α-cellulose, ammonia exceeded 100 ppm (our maximum acceptable limit) by day 11. Two experimental corncob cages required changing at days 16 and 17, whereas the remaining cage containing corncob bedding lasted the entire 21 days without reaching the 100-ppm ammonia threshold.

Conclusion: The authors concluded that corncob bedding provides nearly twice the service life of α-cellulose bedding in the IVC system.

QUESTION

1. Intracage ammonia concentrations should remain below 25 ppm. Currently, upper-level ammonia exposure guidelines are not available for rodents. In this study, the experimental endpoint was when ammonia levels exceeded the following concentration?

a.  25 ppm

b.   75 ppm

c. 100 ppm

d. 150 ppm

ANSWER

1. c. 100 ppm

**Koontz et al. Effect of 2 Bedding Materials on Ammonia Levels in Individually Ventilated Cages, pp. 25-28**

Domain 4

SUMMARY: This study tries to identify an optimal rodent bedding and cage-change interval to establish standard procedures for the individually ventilated cage. Disposable cages were prefilled with either corncob or α-cellulose bedding and were used to house 2 adult Sprague–Dawley rats (experimental condition) or contained no animals (control). Rats were observed and intracage ammonia levels measured daily for 21 d. Intracage ammonia accumulation became significant by day 8 in experimental cages containing α-cellulose bedding, whereas experimental cages containing corncob bedding did not reach detectable levels of ammonia until day 14. In all 3 experimental cages containing α-cellulose, ammonia exceeded 100 ppm (the maximum set acceptable limit) by day 11. Two experimental corncob cages required changing at days 16 and 17, whereas the remaining cage containing corncob bedding lasted the entire 21 d without reaching the 100-ppm ammonia threshold. There was no statistically significant difference in water consumption, and presumably urine production, between the α-cellulose and corncob groups in the study. A difference in growth rates between the groups might account for some of the difference observed in intracage ammonia levels. Total cage biomass did not differ between the 2 groups. The authors conclude that the data suggests that corncob bedding provides nearly twice the service life of α-cellulose bedding in the IVC system.

QUESTIONS (True or False)

1. In all 3 experimental cages containing corncob, ammonia exceeded 100 ppm (the maximum set acceptable limit) by day 11.

2. There was no statistically significant difference in water consumption, and presumably urine production, between the α-cellulose and corncob groups in the study.

3. α-Cellulose bedding provides nearly twice the service life of corncob bedding in the IVC system.

ANSWERS

1. False

2. True

3. False

**Dunbar et al. Validation of a Behavioral Ethogram for Assessing Postoperative Pain in Guinea Pigs, pp. 29-34**

Domain 3: Research, K3 – Animal models including normative biology relevant to the research

Primary Species:Guinea Pig (Cavia porcellus)

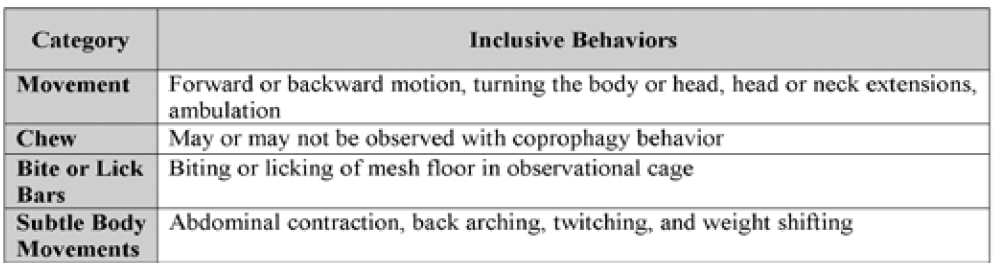
SUMMARY: Nearly 200,000 guinea pigs were used according to most recent published USDA report. Guinea pigs, like most rodents, exhibit a “conservation withdrawal” response and tend to hide overt signs of illness. Commonly used methods to assess reflexive (as opposed to spontaneous pain) pain in guinea pigs: Hargreaves apparatus (“plantar test”) measures thermal hypersensitivity; Randall and Selitto and von Frey measure mechanical hypersensitivity. Other measures to assess postoperative pain include facial grimace score and behavioral ethogram. “Proxy indicator” is an indirect measure that represents the animal’s normal spontaneous behavior when an observer is not present, and the absence of these behaviors may indicate an alteration in the animal’s wellbeing, such as the presence of pain or illness.

In this study, investigators seek to identify measures to assess postoperative pain. Gold standard nociception assay is electronic von Frey measurement. Other measures used includes “Time-to-consumption” (TTC), with investigators hypothesizing guinea pigs in postoperative pain will increase TTC; investigators also used novel behavioral ethogram.

10 singly-housed intact guinea pigs were acclimated to humans prior to surgery. Half animals were provided anesthesia and open castration while the other half provided anesthesia only. Animals were assessed at 2h, 8, 24h after manipulation. Assessment included electronic von Frey Assay (placement of probe at incision, with measurement of forces required to elicit a response from animal), then TTC score with hay and parsley. Video recordings were also taken and scored by an observer.

Mechanical hyperalgesia and subtle body-movement (abdominal contraction, back arching, twitching and weight shifting) was significantly increased at 2h and 8h post-surgery, but not 24h. No significant differences in movement, chewing, licking between conditions or over time. No significant differences in TTC between castration and anesthesia only.

Postoperative pain can be assessed by observing weight shifting as this increased significantly only during the postsurgical time points. Given findings in this manuscript, investigators state analgesic is recommended for procedures expected to result in similar pain.



QUESTIONS

1.   Facial grimace scores are NOT validated for which species?

a.  Mouse

b.  Rat

c.  Rabbit

d.   Guinea pig

2.  In a recent JAALAS article, postoperative pain in castrated guinea pigs have shown an increase in

a.   Turning body and head

b.  Coprophagy

c.  Time to eat treats

d.   Weight shifting

e.  Biting cage side

3. Which of following assays tests for thermal hypersensitivity

a.  Randall-Selitto test

b.   Von Frey assay

c. Hargreaves apparatus

d.  Acetic acid test

ANSWERS

1. d

2. d

3. c

**Bradbury and Clutton.**  **Review of Practices Reported for Preoperative Food and Water Restriction of Laboratory Pigs (*Sus scrofa*), pp. 35-40**

Domain 4: Animal Care; K1 - Species-specific husbandry; K13 - Watering and feeding

Primary Species: Pig (*Sus scrofa*)

SUMMARY: Preoperative food and water restriction (PFWR) recommendations for pigs are extremely varied and do not appear to be evidence based.  This report is based on a literature review of articles published between 2012 and 2014.  The literature search was conducted in the search engines MEDLINE, Web of Knowledge, and Google Scholar.  A total of 233 articles and published reports describing PFWR with survival surgery in pigs were examined for information regarding feed, water, and bedding withdrawal and the procedure performed.  Food withdrawal was described in 73 of the 233 publications.  Water restriction was described in 13 publications and bedding withdrawal was described in 5 publications.  The median duration of food restriction was 12 hours with a range of 4 to 48 hours.  The median duration of water restriction was 12 hours as well with a range of 2 to 12 hours.  The justification for the restriction was varied based on surgery and often a justification was not provided in the publication.  160 of the 233 (69%) of the publications did not describe the fasting practice which means the animals were not restricted or the practice was not documented.  Emesis is often cited as the primary reason for preoperative food restriction in pigs but there is little evidence that vomiting on induction or recovery is common occurrence.  Post-operative food consumption is often used as a measure of pain.  It was noted that preoperative fasting might increase an animal’s postoperative hunger, thus masking the signs of discomfort.  There were 7 papers that reported food and water restriction for 12 hours.  Combined restriction of food and water for 12 hours or more can cause a significant reduction in blood volume in pigs increasing the potential for adverse events.  The cost:benefit ratio of PFWR in laboratory pigs should be formally evaluated to provide some standardization to the practice.  In the absence of that, the authors recommend that the decision to restrict food and water should be based on the pig’s age, growth rate, breed, pregnancy status, disease status, and the procedure to be performed.

QUESTIONS

1. What are the common adverse effects associated with prolonged food and water restriction in pigs?

2. T/F.  The adverse effects of PFWR are likely to be greater in juvenile animals because food and water requirements per unit body mass are greater.

3. What duration of food restriction will cause a depletion of liver glycogen stores?

4. What adverse behavior is increased in animals that are initially reared with straw and then subsequently housed without straw?

ANSWERS

1. Aggression, decreased circulating blood volume, decreased pack cell volume, gastric ulceration, temperature changes, microbiologic changes in the GI, endocrine and biochemical changes

2. T

3. 12-18 hours

4. Tail biting

**Bliss-Moreau and Moadab. Variation in Behavioral Reactivity Is Associated with Cooperative Restraint Training Efficiency, pp. 41-49**

Domain 3: Research

Primary Species: Macaques (Macaca spp)

SUMMARY: 14 male rhesus macaques raised outside in field cages were relocated indoors to paired housing in preparation for a study requiring chair training to noninvasively record eye-tracking and psychophysiologic data. Half of the animals underwent brain lesioning, and the other half served as sham controls.

Prior to chair training, animals underwent basic behavior training such as targeting using positive reinforcement training (PRT) and a vocal cue bridging stimulus. Several observations were made during indoor acclimation of the animals’ social behavior and reactivity to humans. In addition, animals underwent human intruder testing prior to chair training.

Chair training consisted of a combination of PRT, negative reinforcement (NRT) and desensitization. During basic and chair training, behavior indices were scored and recorded for willingness to participate, attentiveness and reactivity.  Chair training session length and time needed to yoke animals were also recorded.

There were no differences in training times between lesioned and control groups.  The described cohort of animals was chair-trained more quickly than the cohort previously trained by these authors, which may be attributed to the animals’ experience with PRT during basic training or to the increased experience of the trainers. Most animals were chair trained using PRT; 5 animals required NRT.

Animals that exhibited submissive-affiliative reactivity to humans during previous observations and in response to human intruder testing had worse training performance, with increased reactivity to trainers and increased session times. Animals exhibiting the most submissive-affiliative reactivity required the most NRT for successful chair training.

This study suggests that temperament may predict which animals require the most experience in order to participate in being chaired. Using temperament to understand how animals will progress along learning trajectories can provide trainers with information to design training schedules and set learning expectations.  Future studies should investigate whether other temperamental variables recorded at different times in an animal’s experimental history influence this type of learning.

QUESTIONS

1. Cooperative training can be used to elicit a variety of voluntary behaviors on the part of laboratory animals and consists of:

a. Desensitization

b.  Positive reinforcement training

c. Negative reinforcement training

d. All of the above

2. A \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ is an event marker identifying a desired response prior to delivery of a treat during training.

a.  Target

b. Desensitizer

c.  Bridging stimulus

d. Hook

ANSWERS

1. d

2. c

***Management***

**Goodly et al. Developing a Comprehensive Animal Care and Occupational Health and Safety Program at a Land-Grant Institution, pp. 50-57**

Domain 5

SUMMARY: Federally funded programs as well as those that are AAALAC accredited are required to have occupational health and safety programs.  This can be particularly challenging in land-grant institutions due to decentralization, lack of medical hospital, and potentially limited availability of safety resources.  This article describes how one institution handles these challenges; their practices were recently updated due to AAALAC granting “Full Accreditation with Condition” in order to evaluate the occupational health and safety programs.

First they conducted an eternal review of their program, which identified lack of a senior leadership official in charge of occupational health and safety; therefore, next a leadership group was formed.  The leadership group worked with the legal department to address privacy concerns and ultimately approved the mandatory requirement for individuals to participate in the program, as long as the individual health surveillance portion of the program remained voluntary.  A Medical Reviewer (nurse or physician) reviews the health questionnaires and communicates with individuals to address concerns.

A senior level individual was placed in charge of the occupational health and safety program (in their case it made sense that this be the institutional veterinarian), and an occupational health and safety specialist position was created.  The next major program improvement was the development of a web-based program for enrollment and training.  Multiple flow charts and forms are provided in the figures to illustrate enrollment in the program, the overall structure, and examples of the information requested in the health screening process.

QUESTIONS

1.   What does OHSP stand for?

2.   What regulatory body required this institution to have an OHSP?

3.  What guidance document, particularly relevant to land-grant institutions, states that an occupational health and safety program must be established for persons working with agricultural animals?

ANSWERS

1. Occupational Health and Safety Program

2.  OLAW

3.   Guide for the care and use of agricultural animal in research and teaching

***Health Surveillance***

**Manuel et al. Surveillance of a Ventilated Rack System for *Corynebacterium bovis* by Sampling Exhaust-Air Manifolds, pp. 58-65**

Domain 1 Management of Spontaneous and Experimentally Induced Diseases and Conditions T4 TT1.12b diagnostic procedures

SUMMARY: *Corynebacterium bovis* is an opportunistic pathogen of immunodeficient mice causing hyperkeratotic dermatitis in athymic nude mice. This infection has proved difficult to eradicate in colonies due to diffuse environmental contamination of the organism via airborne deposition of bacterially populated skin flakes. Early detection is key to maintaining a *C. bovis* free colony, followed by restriction of animal movement and manipulation and localized decontamination and depopulation of infected cages. The authors of this paper tested the efficacy of rack sanitation methods for removing *C. bovis* DNA from the horizontal exhaust manifolds (HEM). The authors also tested 3 variables on how quickly *C. bovis* could be detected by qPCR analysis of the HEM: 1) stage of *C. bovis* infection, 2) cage density and 3) proximity of the positive cage to the HEM.

Results for the efficacy of rack sanitation showed that only after autoclaving were the racks from of *C. bovis* DNA. Pressurized water and processing through a rack-washer was not enough to remove *C. bovis* DNA from the HEM. The time required for acutely exposed mice to test positive for *C. bovis* by qPCR was 4d. All exposed mice were positive by day 5. The cage density did not significantly affect the amount of time required to detect *C. bovis* at the HEM of the rack. However, cage position in a row did significantly affect the amount of time before *C. bovis* was detected. The cage closest to the HEM had a significantly decreased time to detection compared with the cages furthest from the HEM. The stage of infection (early or established) also affected the time to detection via HEM qPCR. The established infection group was detected on day 1, whereas the early infection group required 7.3 days until detection. Based on these findings, the authors recommend performing rack sampling every 7 days for populations of mice at risk of infection with *C. bovis.*

QUESTIONS

1. True or False: Cage position on a rack does not affect time to detect of *C. bovis* DNA via qPCR of the horizontal exhaust manifold (HEM)

2. True or False: Cage density does not significantly affect the time to detection of *C. bovis* DNA via qPCR of the horizontal exhaust manifold (HEM)

3. What sanitation methods are required to remove *C. bovis* DNA from a contaminated IVC rack HEM?

a. Pressurized rinse with hot water

b. Pressurized rinsing and sanitation by rack-washer

c. Pressurized rinsing and sanitation via rack-washer, followed by autoclaving

d. Soaking with 1:25 dilution hyperchlorite solution followed by hot water rinse

ANSWERS

1. False. The cage closer to the HEM has a significantly faster time to detection compared with a cage further from the HEM.

2. True

3. c

***Anesthesia***

**Kendall et al.  Efficacy of Sustained-Release Buprenorphine in an Experimental Laparotomy Model in Female Mice, pp. 66-73**

Domain 2: Management of pain and distress

Primary Species: Mouse (*Mus musculus*)

SUMMARY: Buprenorphine HCl (Bup-HCl) is typically dosed every 8-12 hr in LAM species. According to the most recent pharmacokinetic studies, Bup-HCl may not retain therapeutic concentrations during the entire dosing interval. In CD-1 mice, sustained-release buprenorphine (Bup-SR) has been shown to exceed reported (unconfirmed) therapeutic plasma concentrations for 24-48 hr when dosed at 0.6 mg/kg. This study used a laparotomy model to determine the clinical efficacy of Bup-SR after surgery in mice (female CD1). Study groups included: 1) Bup-SR treatment, 2) Bup-HCl treatment, & 3) saline treatment. Baseline behavioral assessments were performed prior to surgery and analgesic treatment, and activity and behavior were assessed at 1, 3, 6, 12, 24, 48, and 72 hours after surgery. The Bup-SR mice were more active than the Bup-HCl mice at 1 and 3 h postop, and more active than the saline-treated group at 1, 3, and 6 h postop. The authors found that Bup-SR provided adequate analgesia (greater than that in Bup-HCl-or saline-treated mice) for the first 12 hr after surgery, while there was no difference in the analgesic response after the 12 hr time point.

Conclusion: Bup-SR is a suitable alternative to Bup-HCl for abdominal surgical procedures in mice, as it demonstrated superior clinical efficacy to Bup-HCl in the present study (based on results from postop pain ethogram).

QUESTIONS

1. According to the most recent literature, what plasma concentration does a cumulative dose of 0.1mg/kg of Bup-HCl provide in mice?

a. 0-0.5 ng/mL for 48 hr

b. 0.5-1.0 ng/mL for 48 hr

c. 1.5-2.0 ng/mL for 48 hr

d. >2.0 ng/mL for 48 hr

2. T/F: The therapeutic plasma concentration of Buprenorphine has been determined in mice.

3. Which behaviors were increased in the saline-treated and Bup-HCl group, but not in the Bup-SR group, after surgery?

a. General activity

b. Wheel-running

c. Orbital tightening

d. Wound licking

e. Rearing

f. Grooming

ANSWERS

1. b

2. F - it has been determined in humans and rats, but not mice.

c. c & d

**Taylor et al. Analgesic Activity of Tramadol and Buprenorphine after Voluntary Ingestion by Rats (*Rattus norvegicus*), pp. 74-82**

Domain 3

Primary Species: Rat (Rattus norvegicus)

SUMMARY: Effective pain management for rodents is crucial due to their widespread in biomedical research. It is necessary not only because of ethical and legal standards, but providing effective pain management can also reduce distress, decrease mortality, and eliminate many of the postsurgical physiologic consequences associated with pain that may confound the research. The goal of the current study was to evaluate the analgesic effects of a range of oral doses of tramadol or buprenorphine mixed with nut paste (Nutella) provided to male and female rats by voluntary ingestion. Rats were evaluated by using a recently described, nontraumatic, reversible, operant-based, thermal orofacial pain assessment device to determine dose–response curves.

Providing analgesics mixed in the food or water of rats and mice is one of the least stressful methods of administration. This method eliminates postoperative manual restraint and parenteral injections which have been shown to induce stress-like responses in mice and rats. Providing analgesics by this method has multiple drawbacks, however. First, the neophobic behavior of rats and mice may lead to significant underdosing when a period of habituation to the drug is not observed. Second, some drugs are unpalatable and so may not be consumed in sufficient quantities to provide analgesia. Third, animals undergoing surgery typically have reduced food and water intake during the immediate postoperative period, and this behavior may limit the dose administered. Fourth, overdosing may occur when analgesics are provided with a palatable vehicle, such as a cherry-flavored solution. Finally, when opioids are administered in the food or water, tolerance may develop, leading to a decrease in analgesic efficacy. Several recent studies using a sweet nut paste for the administration of buprenorphine have shown its promise as an effective vehicle for administration as it is usually consumed *en bloc*. Providing analgesics in this manner allows for a fixed dosage of the drug to be administered consistently, with the added assurance that the animals are consuming an effective dose and are not under- or overdosed.

Statistically significant analgesic doses of tramadol in nut paste included doses of 20, 30, and 40mg/kg for female rats but only 40mg/kg for male rats. For male rats receiving buprenorphine mixed in nut paste, a significant analgesic response was observed at 0.5 and 0.6 mg/kg. None of the doses tested produced a significant analgesic response in female rats. This study indicates that at the doses tested, tramadol and buprenorphine produced an analgesic response in male rats. In female rats, tramadol shows a higher analgesic effect than buprenorphine. The analgesic effects observed 60min after administration of the statistically significant oral doses of both drugs were similar to the analgesic effects of 0.03mg/kg subcutaneous buprenorphine 30min after administration. The method of voluntary ingestion could be effective, is easy to use, and would minimize stress to the rats during the immediate postoperative period.

QUESTIONS

1. What is the mechanism of action of buprenorphine?

a. Partial µ-opioid receptor agonist

b. Partial κ-opioid receptor agonist

c. Partial δ-opioid receptor antagonist

d. Partial γ-opioid receptor antagonist

2.   What is the mechanism of action of tramadol?

a. Opioid activity

b. Opioid and non-opioid activity

c. Dissociative analgesic activity

d. Non-steroidal anti-inflammatory action

3.  Historically, oral dosing of buprenorphine has been shown to be:

a. Effective for analgesia

b. Ineffective for analgesia   

c. Data is inconclusive for analgesia

d. Buprenorphine is not palatable when dosed orally

4. Which condition describes an animal’s fear of consuming something novel?

a. Autophagia

b. Neophobia

c. Thigmotaxis

d. Pica

ANSWERS

1. a

2. b

3. c

4. b

Domain 2: Management of Pain and Distress)

Primary Species: Rat (Rattus norvegicus)

SUMMARY: Male and female Sprague-Dawley rats were trained to via operant conditioning to press their hair shaved cheeks against thermodes (set at 45®C) in order to access a reward solution of sweetened condensed milk.

On test days, Capsaicin cream was applied to the shaved areas of the face (Capsaicin sensitizes this skin to heat).

Rats were offered a nut paste containing Tramadol (0, 10, 20, 30, and 40 mg/kg) or Buprenorphine (0, 0.3, 0.4, 0.5 and 0.6 mg/kg)

In male and female rats, the amount of facial contact events increased with Tramadol dosage, with the dose-dependent increase of contact events being more significant in the females.

Significant pain control for male rats was seen at doses of 40 mg/kg, while female pain control was seen at 20, 30, and 40 mg/kg.

Buprenorphine also caused a dose dependent increase of facial contact events, however 0.5 and 0.6mg/kg buprenorphine provided adequate analgesia for male rats, while none of the doses tested provided adequate analgesia for female rats.

QUESTIONS

1.  Tramadol is classified as a controlled substance in which of the following categories?

a.  Schedule I

b.  Schedule II

c.  Schedule III

d. Schedule IV

2.  Which of the following statements is correct in regards to Buprenorphine activity in Rats?

a.  A partial agonist with activity at the mu and kappa receptors with a common side effect of hepatocellular degeneration

b.  A mu antagonist with the side effect of Pica

c.  A partial mu agonist with kappa receptor activity, with the side effect of Pica

d.  A partial mu and kappa antagonist with the side effect of Pica

3. According to the Guide, what is the recommended height of primary enclosures housing rats?

a.  5 inches

b.  6 inches

c.  7 inches

d.  14 inches

ANSWERS

1. d. Tramadol is classified as a Schedule IV drug by the U.S. Drug Enforcement Agency - <http://www.deadiversion.usdoj.gov/drug_chem_info/tramadol.pdf>

2. c. Buprenorphine is usually described as a partial mu agonist, with significant activity at the kappa receptor (a partial agonist with mu and kappa receptor activity). Pica has been observed with bedding ingestion. (The Laboratory Rat 2nd Edition – Pg 650 – 651)

3.  c. 7 inches.  5 inches is for mice, 6 inches is for hamsters, and 7 inches is for rats and guinea pigs (per the Guide). 14 inches is what the AWA/R requires for rabbits, while the Guide recommends 16 inches for rabbits.

**Huss et al. The Physiologic Effects of Isoflurane, Sevoflurane and Hypothermia Used for Anesthesia in Neonatal Rats (*Rattus norvegicus*), pp. 83-88**

Domain 2: Management of pain and distress

Primary Species: Rat (Rattus norvegicus)

SUMMARY: This group looked to investigate the effectiveness of anesthetic regimens for neonatal rat pups. For this paper the three regimens used were: isoflurane, sevoflurane and hypothermia. The group anesthetized the neonates and then measured several physiologic parameters including heart rate, respiratory rate, and oxygen saturation. In addition, they measured loss and return of righting reflex, withdrawal reflex and maternal acceptance. The levels of corticosterone and glucose were sampled at 20 minutes post anesthetic induction and again at 24 hours.

The anesthesia of neonates is challenging due to a multitude of factors. These factors include narrow therapeutic windows, differences in physiology and pharmacology, immature organ structure and function. Injectable anesthetics such as ketamine or pentobarbital are not ideal options for neonates because they often lead to inadequate anesthetic depth, prolonged recovery or death. Inhalant anesthetics have the advantage of low blood gas solubility leading to both rapid induction and recovery, precise control of anesthetic depth and minimal hepatic metabolism. The disadvantages associated with inhalant anesthetics include complexity and expense of delivery systems, waste gases and personnel exposure.

With these advantages and disadvantages in mind the group divided 3-day old Sprague-Dawley rat pups into 3 groups. The isoflurane and sevoflurane groups went through chamber induction (maintenance via mask with supplemental heat provided) while the hypothermia group was placed on top of a latex sleeve, placed in an ice bath, and held in position until anesthesia was attained. The first measurement was recorded 1 minute after adequate anesthetic depth had been attained as determined by lack of withdrawal reflex. The measurements were then taken at 5, 10, and 15 minutes post induction. At the 15 minute mark after confirmation of a surgical plan of anesthesia (withdrawal) a 0.5cm skin incision was made over the right later thigh then closed with skin glue.

All of the dams accepted and cared for their returned pups. It was found that heart rate gradually declined over time as the anesthetic depth increased. Similarly, the respiratory rate decreased over time due to increased anesthetic depth in all groups; however the hypothermia group was found to be significantly lower at all-time points by comparison. The rate in this group lowered to the point that is was unable to be read by the monitoring equipment. Induction times were longer for hypothermia than for inhalation. Recovery time was 7 minutes longer for hypothermia than inhalant. Glucose levels fit the pattern most seen post procedurally, while corticosterone levels were found to be no different in the 20 minute versus 24 hour sampling groups. It was hypothesized that this is due to several factors including age, hypothermia, etc.

Based on these results it was determined that for short, minor surgical procedures all three methods of anesthesia are adequate for maintaining a surgical plane. Pups in the isoflurane and sevoflurane groups had more stable anesthetic parameter measurements throughout the procedure than the hypothermia group.

QUESTIONS

1. What is the site of release of glucocorticoids?

2. True or False – Hypothermia anesthesia has been associated with hyperglycemia.

ANSWERS

1.  Adrenal cortex

2.  True – Hypothermia simultaneously decreases insulin sensitivity and reduces insulin secretion by pancreatic islet cells

**Moheban et al. The Suitability of Propofol Compared with Urethane for Anesthesia during Urodynamic Studies in Rats, pp. 89-94**

Primary Species: Rat (Rattus norvegicus)

SUMMARY: Urethane anesthesia preserves many reflex functions and is often the preferred anesthetic for urodynamic studies in rats. Because of the toxicity profile of urethane, its use as an anesthetic typically is limited to acute and terminal investigations.

In this article, urodynamic studies were performed to compare the effects of urethane and propofol anesthesia on lower urinary tract function in rats. For this purpose, cystometrography and EUS EMG were investigated after a standard dose of urethane and after various doses of propofol.

No reflex micturition was noted after rats received 100%, 80%, or 60% of a previously reported anesthetic dose of propofol. At 40% of the standard propofol dose, a subset of rats showed reflex voiding, with bladder contractions and associated EUS EMG activity. In contrast, urethane anesthesia at a surgical plane allowed for reflex voiding with bladder contractions and EUS activation. Latency to leaking or voiding was longer in rats under propofol anesthesia than those under urethane anesthesia. In a subset of rats with reflex voiding under propofol anesthesia, voiding efficiency was decreased compared with that of rats anesthetized with urethane. Propofol anesthesia suppresses micturition reflexes in rats more efficiently than urethane.

Overall Conclusion: Propofol is a good suitable anesthetic for longitudinal studies in rat, but its use for urodynamic evaluations is limited in these animals due to its marked suppression of both bladder contractions and EUS EMG activation.

QUESTIONS

1. T\F:  Urethane is widely used as an anesthetic for animal studies because of its minimal effects on cardiovascular and respiratory systems and maintenance of spinal reflexes.

2.  Urethane potentiated\inhibit what?

a. Neuronal nicotinic acetylcholine

b. Gamma-aminobutyric acid (A)

c. Glycine receptors,

d. N-methyl-D-aspartate and

e. Alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptors

f. None of them

g. All of them

3.  T\F: Propofol activity is through GABA receptor?

4.  What is the most common side effect of propofol?

ANSWERS

1.   T

2.  Potentiated 1-3, inhibit 4-5.

3.  T

4.  Apnea





***Experimental Use***

**Ansari-Mood et al. 24–Hour Measurement of Intraocular Pressure in Guinea Pigs (*Cavia porcellus*), pp. 95-97**

Domain 1

Secondary Species: Guinea Pig (Cavia porcellus)

SUMMARY: Increased IOP is a major risk factor for the development of glaucoma. This study measured intraocular pressure (IOP) in intact, healthy guinea pigs (15 male, 15 female) every 2 h for a 24-h period. First, they measured IOP using a rebound tonometer (RBT). After the completion of the RBT, topical proparacaine ophthalmic solution was applied to both eyes before IOP was measured using an applanation tonometer (APT). For IOP assessment during the nocturnal phase, the measurements were performed under dim red light illumination to minimize the alteration of IOP by light perception. IOP was lower during the light period (0700 to 1900) than during the dark period (2000 to 0600). The lowest IOP measured by both RBT and APT (3.68 and 13.37 mm Hg, respectively) occurred at 0700. Maximal IOP occurred at 2300 for RBT (8.125 mm Hg) and at 2100 by APT (20.62 mm Hg). IOP in guinea pigs did not differ significantly between the left and right eyes or between RBT and APT. The results of the current study may be useful in the diagnosis and monitoring of glaucoma in guinea pigs. Although glaucoma is not a common condition in guinea pigs, it has been reported to occur.

QUESTIONS

1.  Which of the following oversees research using guinea pigs?

a. OLAW

b. AAALAC

c. USDA

d. NIH

e. All of the above

2.  A common disorder seen in guinea pigs is blepharitis with epithelial flaking, crusting, alopecia, swelling, and reddening of the lids. These signs, often called ‘dull eyes’ are seen usually with marginal hypovitaminosis \_\_\_\_\_\_.

a. A

b. C

c. E

d. K

ANSWERS

1. e

2. b

**CASE STUDY**

**Carter et al. An Incidence of Pseudopregnancy Associated with the Social Enrichment of Rabbits (*Oryctolagus cuniculi*), pp. 98-99**

Primary Species: Rabbit (Oryctolagus cuniculus)

Domain 1: Management of Spontaneous and Experimentally Induced Diseases and Conditions

SUMMARY

Background

* Pseudopregnancy
  + Incidence rate: As high as 23% in commercial breeding facility
  + Can result from:
    - Sterile mating
    - Injection of LH
    - Stimulation from mounting rabbits (female or male)
  + Caused by a persistent corpus luteum secreting progesterone. The corpus luteum should regress in a normal estrus cycle if animal is not pregnant.
  + Lasts 16-18 days
  + May see enlargement of uterus and mammary tissue
  + May see maternal behaviors such as hair pulling and nest building
  + May spontaneously resolve but often recurs
  + Complications:
* include endometritis, pyometra, hydrometra, and mastitis

Case Report

* A 2 year old New Zealand White rabbit showed signs of pseudopregnancy (hair pulling and nest building) after separation from an aggressive cage-mate. Histopathology confirmed diagnosis.

QUESTIONS

1. Which best defines a rabbit?

a. An induced ovulator with hemoendothelial placenta

b. A spontaneous ovulator with hemoendothelial placenta

* 1. A spontaneous ovulator with epithelialchorial placenta
  2. An induced ovulator with epithelialchorial placenta

1. What is the treatment of choice for pseudopregnancy in non-breeding rabbits?

ANSWERS

1. a

2. Ovariohysterectomy