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Surgery results in hormonal and metabolic changes in all species including rodents which have the potential to negatively impact animal welfare and the integrity of experimental data. The purpose of this *BRL Bulletin* is to provide investigators with guidance regarding the perioperative care of mice and rats to minimize these changes and to help maintain physiologic homeostasis. In particular, we will focus on the implementation of non-pharmaceutical measures that can be used in the immediate postoperative period to support mice and rats undergoing surgical procedures. For more information regarding requirements for performing survival surgery in rodents, investigators are referred to “UIC Guideline: Survival Surgery in Rodents and Lower Vertebrates” available on the ACC website at <https://research.uic.edu/sites/default/files/0321.pdf>.

Acclimation and Assessment of Health Status

Rodents should be allowed to acclimate for a minimum of 3-5 days after arrival before experimental procedures are performed to overcome the physiologic impact of the stress of transportation. In addition, animals should be examined prior to surgery to ensure that they are free of clinical signs of illness. Use of ill animals for experiments is not only questionable from an animal welfare standpoint, but will likely generate unusable experimental data. An animal that is suitable for a surgical procedure should meet the following criteria:

- Normal posture and movement. Eyes should be bright and hair coat smooth and shiny. Skin should be free of fight wounds or dermatitis.
- Normal respiratory and cardiovascular status (normal coloration of ears, eyes, nose and feet).

- Normal intake of food and water. For animals that are the same sex and age, body weights should be similar. If there are animals with significantly lower weight, the investigator should consider eliminating them from the study.

To Fast or Not to Fast

Due to the anatomical relationship of the rodent esophagus and stomach, mice and rats do not have the ability to vomit. As a result, it is generally not necessary to withhold food prior to surgery. In addition, due to their high metabolic rate, fasting of rodents can lead to hypoglycemia, which may lead to prolonged surgical recovery or death.

Anesthesia and Analgesia

It is essential that investigators ensure adequate anesthesia and analgesia for surgical procedures. Failure to do so can lead to increased pain, prolonged recovery, and compromise of experimental data. Investigators should check the depth of anesthesia prior to and at least every 15 minutes throughout the surgical procedure. This is most commonly done by pinching the toe and verifying that the animal does not respond. Other methods include observing that animals do not respond to surgical stimulation and the respiratory rate. Analgesics are required for rodent surgery unless scientifically justified in the approved ACC protocol. As a reminder, if investigators are using anesthetics such as isoflurane or pentobarbital, these agents do not provide analgesia and therefore administration of an analgesic must be performed prior to making an incision. Investigators should refer to “UIC Guideline: Rodent Surgical Classifications and Analgesic Guidelines” available on the ACC website at <https://research.uic.edu/sites/default/files/0340.pdf> for more information

regarding the use of anesthetic and analgesics in rodents.

Aseptic Surgical Technique

Due to the common misconception that rodents are resistant to infection, investigators often do not think it is important to follow aseptic surgical technique for mice and rats. To the contrary, we have observed clinically significant postoperative infections in both mice and rats. Because clinically apparent infections are observed, it is likely that subclinical infections occur as well in rodents. There are numerous reports in the literature that show experimentally related infections can affect research. Finally, rodents have been used to model human bacterial diseases, including surgery related infections. These observations and facts provide evidence that rodents are not more resistant to perioperative infections and it is essential to follow aseptic surgical techniques. Administration of antibiotics is generally not necessary to prevent surgical infections provided that aseptic technique is used. Requirements for aseptic technique are described in the "UIC Guideline: Survival Surgery in Rodents and Lower Vertebrates."

Surgery Should Be Gentle

Surgery should be performed atraumatically regardless of the species. Rough tissue handling results in increased pain, risk of infection (clinical and subclinical), and prolonged recovery time. Here are methods that investigators should consider to help decrease tissue trauma and improve postoperative outcomes:

- Know the relevant anatomy of the animal and surgical site.
- Observe surgeons experienced perform the surgical technique.
- Practice on cadaver animals or animals that will not be recovered from anesthesia.
- Do not attempt to obtain experimental data from practice or training animals.
- Make the smallest incision possible without compromising visibility.

- Avoid cutting across muscle bellies whenever possible.
- Perform dissection along tissue planes.
- Avoid directly grasping organs especially with traumatic forceps.
- Avoid placing skin sutures too tightly. Tight sutures can cause tissues to become inflamed, delay healing, and may cause the animal to chew at the incision.

Thermal Support

The use of anesthetics and sedatives suppresses temperature control centers in the brain resulting in hypothermia. Due to their high surface area to body volume ratio, mice and rats lose body heat rapidly. Perioperative hypothermia slows organ function, prolongs recovery, and in some cases can lead to death. Investigators should consider providing thermal support during rodent surgical procedures. For procedures that are non-invasive or minimally invasive and performed within a short duration of anesthesia, such as a skin biopsy using isoflurane anesthesia, the use of a supplemental heat source may not be necessary. The risk of hypothermia is of greatest concern when anesthesia is prolonged and for procedures that require exposure of the thoracic or abdominal cavities. For these types of surgical procedures, supplemental heat is recommended to avoid perioperative hypothermia. However, care must be taken when providing supplemental heat to prevent hyperthermia and burns. Here are some methods that can be used to safely prevent perioperative hypothermia in animals:

- Provide optimal ambient temperature. If possible, surgical procedures should be performed in a room that is not too cold. In addition, avoid performing surgery under drafty room supply vents. Note: Surgical procedures performed in biosafety cabinets will result in additional cooling effects due to the flow of air. Investigators performing surgical procedures in biosafety cabinets should take extra care to follow the

recommendations here to avoid excessive cooling of animals.

- Avoid direct contact of the rodent with cooling surfaces such as stainless steel. This can be accomplished by placing an insulating material such as bubble wrap between the animal and surface.
- Avoid drenching the animal with skin disinfectants. This is especially important with regard to alcohol which has a cooling effect as it evaporates from the skin.
- If supplemental fluids are provided, they should be warmed to the animal's body temperature before administration.

When supplemental heat is provided, the following guidelines should be followed:

- The temperature of the animal should be monitored throughout the surgical procedure. A digital rectal thermometer is sufficient for this purpose. Normal body temperature for mice and rats varies by strain, age, sex and environmental conditions. In general normal body temperature can be expected to be around 37°C (98.6°F).
- Homeothermic heating pads are superior to other heating devices as they monitor body temperature and maintain it within a set temperature range.
- If homeothermic pads are not used, circulating warm water blankets or isothermic pads are preferred. These devices can often be maintained at a particular temperature which helps maintain body temperature without the risk of causing hyperthermia or burns.
- Electric heating pads are not recommended for rodents as the temperature is variable across the surface of the pad, and there can be hot spots which may cause hyperthermia or burns. Temperature settings are typically not specific, but may only be set at high, medium, or low.
- The use of incandescent lamps should be used with caution as their temperature is difficult to control.

- If supplemental heat is continued in the postoperative recovery period, the investigator should continue to monitor the animal's body temperature. Once awake and active, animals should resume normal homeothermic regulation of body temperature. Heating devices should either be removed at this time, or placed under only a portion of the rodent cage so the animal has the ability to move away from the heat source. In general, incandescent heating lamps should not be used over rodent cages once animals have recovered from anesthesia as the span of light is broad relative to a rodent cage making a temperature gradient difficult to achieve.
- The tail is an important thermoregulatory organ in rodents. It should be in contact with the heating device and kept covered.

Fluid Support

Dehydration of rodents may occur during the operative period as a result of decreased intake, increased evaporative losses due to exposure of tissues, and possibly blood loss. During the postoperative period, dehydration may worsen if recovery is complicated and normal fluid intake does not resume following the immediate postoperative period. Clinical signs of dehydration in rodents include lethargy, sunken eyes, and dry feces. In addition, by gently picking up the skin on the back of an animal, the skin should return to its normal position within one second. In a dehydrated animal, it will take 2-3 seconds or longer for the skin to return to its normal position. Mild dehydration in rodents is difficult to detect, therefore, any clinical evidence of dehydration is significant and should be treated. The following recommendations should be followed for rodents undergoing surgical procedures:

- Preoperative administration of 0.9% saline or Lactated Ringers solution SC or IP at a volume of 0.5-1.0ml for mice and 5-10ml for rats can help to decrease intra- and postoperative mortality. If possible the fluids

should be warmed to the approximate body temperature of the animal.

- If animals appear to be dehydrated postoperatively, additional fluids can be administered 2-3 times per day at the above volume. If signs of dehydration do not resolve within 24 hours postoperatively, the veterinary staff should be contacted.
- For surgical procedures that decrease the ability of animals to reach food and water, investigators should consider ways to facilitate intake. One option is to place a petri dish on the floor of the rodent cage to provide food moistened with drinking water. In addition, a gel water/nutritional supplement such as ClearH₂O[®] Hydrogel[®] or Diet Gel[®] (<https://clearh2o.com/>) may be provided to rodents by the investigative staff.

Ocular Care

Anesthetic agents typically used for rodent surgery inhibit blinking. The lack of blinking results in drying of the cornea and increases the risk of postoperative corneal ulceration. The blink reflex does not resume until sometime during the postoperative recovery period. It is recommended that an ophthalmic lubricating ointment be applied to the eyes upon induction of general anesthesia and re-applied as necessary until spontaneous blinking is resumed. Petroleum-based products such as mineral oil or Vaseline[®] are not acceptable.

Housing Considerations

Mice and rats should be placed in a clean dry cage following surgery. In addition, mice should be provided with nesting material. Nest making activity may be decreased postoperatively and therefore they may not manipulate the Nestlet[®] square which is standardly provided to all mice. If this is observed, investigators can request Crink-l'Nest[™] for their mice postoperatively which provides mice with ready-made nesting material with no required manipulation by the mouse.

Social Housing

According to "UIC Policy: Social Housing of Animals Used in Research, Testing and Teaching," which is available on the ACC website at <https://research.uic.edu/sites/default/files/0341.pdf> and reviewed in the most recent *BRL Bulletin* (Vol 30 No. 3), mice and rats are social species and should be maintained in stable, socially compatible groupings whenever possible. While some investigators may find it necessary to singly house rodents postoperatively, social housing should be considered.

In summary, this *BRL Bulletin* provides investigators with information and methods to help in maintaining physiologic homeostasis of rodents perioperatively. This will improve animal welfare, surgical outcomes, and produce more reliable experimental data.

ANNOUNCEMENTS

USDA Annual Report — Investigators should expect to receive their annual animal usage report the week of October 5th. This form needs to be completed and returned as soon as possible in order to facilitate submission of UIC's Annual USDA Report, which is due December 1st. Please contact a member of the veterinary staff should you have any questions regarding how to complete the form.

Congratulations — If you see Dr. Cyndy Adams walking around the COMRB vivarium with a big smile on her face there is good reason. Cyndy was one of 33 veterinarians to pass the American College of Laboratory Animal Medicine specialty board examination in July of this year. Way to go Cyndy!!!

