Endocrine/Exocrine - Modification Procedures

At Charles River, we understand how important high-quality surgical models that meet exacting scientific and regulatory standards are vital to your research. As the premiere provider of surgically altered research models, we have the specialized skills and resources that allow us to tailor research models to your specific needs.

Most of the surgical procedures for endocrine/exocrine modification that we offer in Europe can be conducted on rats and mice. For each procedure, this paper describes preoperative and surgical procedures along with postoperative care. For more detailed information or questions about any of the services offered, please contact Charles River Technical Services at surgery@eu.crl.com

Preoperative Preparation

Unlike humans, rodents do not normally regurgitate. Hence, except for certain procedures such as the vagotomy, there is no need to fast animals to prevent the potential aspiration of stomach contents during anaesthesia and surgery. However, a period of withholding food lasting less than twelve hours does help to ensure consistent absorption of intraperitoneally administered injectable anaesthetics.

Since it does not affect anaesthetic absorption, water is never withheld. Plus, the state of hydration could have adverse effects on the level of anaesthesia and survival postoperatively.

Following anaesthesia of the animals, the operative site is prepared by shaving. The skin surrounding the incision site is then decontaminated by a local wash with a povidone iodine soap followed by the application of both a povidone iodine solution and 70% isopropyl alcohol.

Incision Closure

The method of wound closure is dependent upon the size and location of the incision. Extensive incisions are closed by tissue layers using an interrupted suture pattern. Skin is generally closed by wound clips, but can also be closed either with nonabsorbable or absorbable sutures.

General Postoperative Care

Unless otherwise specified in the procedure, the following postoperative care is practiced at Charles River:

- Room temperature is maintained between 22-26°C. Animals are provided with supplemental heat to maintain core temperature, taking care to monitor the temperature closely to ensure that burns do not occur. During the surgery and postoperatively, the animals are placed on a temperature-controlled heating pad.
- If post-operative signs of dehydration are observed, the animals are rehydrated by injection of warm sterile solution (NaCl or Ringer lactate).
- Animals are observed at least twice a day during the post-operative period.
- The skin incisions are monitored for any signs of dehiscence or infection.
- Unless otherwise specified in the procedure, animals are maintained on standard rodent diets postoperatively ad libitum. Filtrated water is given ad libitum. A minimum of 24 hours of postoperative recovery is recommended before shipping the animal.

Analgesia

Buprenorphine or carprofen is injected subcutaneously. Buprenorphine is the standard default analgesic. Carprofen is used for neurological procedures and substituted upon request. Others analgesics could be used on demand.

For more information, contact us surgery@eu.crl.com
Adrenalectomy, Adrenal Medullectomy

An adrenalectomy is the surgical removal of one or both adrenal glands. An adrenal medullectomy is the surgical removal of the adrenal medulla. The adrenal glands are small, round, orange/pink-colored endocrine organs located cranially to the kidney. Each adrenal gland is composed of an inner core-like medulla and an outer bark-like cortex. These glands produce steroid-based glucocorticoid and mineralocorticoid hormones, as well as epinephrine. An animal can survive normally without the adrenal medullae, but sodium levels must be monitored and supplemented either with dietary sodium or mineralocorticoids for the animal to survive when the adrenal cortex is also removed.

Preoperative Procedure
The animal is weighed and anesthetised with appropriate anaesthetic (please refer to our Surgical Capabilities Reference Paper, Vol. 13. No. 1, for more details on anaesthesia) and an injection of an analgesic is administered (buprenorphin). The hair on the back of the lumbar area is clipped. The animal is then placed in ventral recumbency and the surgical site prepared as described in the preoperative section of this paper.

Surgical Procedure
A 1 cm dorsal midline skin incision is made using a #11 blade on a #3 scalpel handle at the level of the 1st to 3rd lumbar vertebra. The muscle wall is entered with a pair of halsted mosquito forceps 1.5 cm lateral to the spine on each side. The left adrenal is located lateral and cranial to the spleen and is embedded in adipose tissue. The right adrenal gland is located cranial to the kidney. In young animals, very little fat is present to obscure the adrenal glands; thus, they are very easily seen. However, some careful dissection may be necessary in older animals, where the presence of fat commonly conceals the glands. Once identified, the adrenal glands, together with the surrounding fat pad, are exteriorised by grasping the periadrenal fat with a pair of straight mouse-toothed thumb forceps. The adrenal glands are then excised by blunt dissection using two pairs of mouse-toothed forceps. The gland itself must not be grasped because this can cause pieces of the adrenal to be broken off and to possibly re-implant itself in the abdominal cavity and regain function. Please note that use of this surgical approach will miss accessory adrenal gland nodules if they are present. The incidence of these nodules is minimal and strain dependent.

Postoperative Care
A post operative injection of buprenorphine is administered at Day 1. In addition to normal postoperative care described in the above section, adrenalectomised animals require additional care. For long-term survival, adrenalectomised animals must be given postoperative treatment to replace the loss of sodium that occurs as a result of this operation. This may sometimes include the administration of corticosteroids; however, most often adrenalectomised animals are given normal physiological saline (0.85-0.90% NaCl) to drink ad libitum in order to maintain sodium levels. Other sources of water should not be presented.

Saline supplementation is critical during transportation to ensure the survival of the animal. Charles River gives every adrenalectomised animal sterile saline, injected subcutaneously prior to shipment to the customer. Depending on animal size, rats are given 5-10 mL and mice are given 2-3 mL.

It is important to understand that certain inbred strains of rats and mice may not tolerate this surgical procedure as well as outbred or hybrid strains can tolerate it. One may see an increased incidence of perioperative mortality as well as less tolerance of shipping stress, which may result in morbidity and mortality during transit.
**Adrenal Medullectomy**

The adrenal medulla secretes two hormones, epinephrine and norepinephrine. Adrenal medullectomy removes the medulla from the cortex, leaving the capsule plus a layer of glomerulus cells. Enough cortical tissue remains or regenerates from these to meet the requirements for cortical hormones.

**Preoperative Procedures**
See the adrenalectomy preoperative procedures previously described.

**Surgical Procedure**
A 1 cm dorsal midline skin incision is made using a #11 blade on a #3 scalpel handle at the level of the 1st to 3rd lumbar vertebra. The muscle wall is entered with a pair of halsted mosquito forceps 1.5 cm lateral to the spine on each side. The adrenal glands are located as described above in the adrenalectomy procedure. The adrenal glands are exteriorised by grasping the periadrenal fat with a pair of straight, mouse-toothed thumb forceps. A small incision is made on the adrenal capsule with 3-1/2” straight, sharp castroviejo microdissecting spring scissors, and the medulla is gently squeezed out with a pair of straight, atraumatic thumb forceps. The medulla pops easily out of the capsule. The capsule and the remaining attached fat pad are returned into the abdominal cavity. The skin incision is then closed with wound clips.

**Postoperative Care**
In addition to the standard postoperative care previously described, normal drinking water should be administered following this surgical procedure.

**Hypophysectomy**

A hypophysectomy is the surgical removal of the pituitary gland. Often considered the “master gland” of the endocrine system, the pituitary gland (or hypophysis) is a small, pink, oval endocrine organ found at the base of the brain. It produces several hormones that directly or indirectly impact most basic body functions, including growth.

**Preoperative Procedures**
The animal is weighed and anesthetised with appropriate anaesthetic. A pre operative injection of buprenorphin is administered.

**Surgical Procedure**
A 14 G needle is inserted into the brain of the animal via the ear. The pituitary gland is removed by suction and its integrity is checked.

**Postoperative Care**
A post-operative injection of buprenorphine is administered at Day 1. In addition to normal postoperative care, the animal is given 5% glucose or sucrose to drink ad libitum. A minimum of 72 hours of recovery is recommended before shipping the animal. In order to identify animals with incomplete removal of the pituitary gland, it is recommended that a comparison be done of preoperative body weight and postoperative body weight 5-7 days after surgery. Animals with complete removal of the pituitary will have minimal change in these values. It is important to understand that certain inbred strains of rats and mice may not tolerate this surgical procedure as well as outbred or hybrid strains can tolerate it. One may see an increased incidence of perioperative mortality as well as less tolerance of shipping stress, which may result in morbidity and mortality during transit.
Thyroid-Parathyroidectomy

The adrenal medulla secretes two hormones, epinephrine and norepinephrine. Adrenal medullectomy removes the medulla from the cortex, leaving the capsule plus a layer of glomerulus cells. Enough cortical tissue remains or regenerates from these to meet the requirements for cortical hormones.

Preoperative Procedures
See the adrenalectomy preoperative procedures previously described.

Surgical Procedure
A 1.5 cm ventral midline skin incision is made along the length of the neck from its base just below the point of the mandible using a #11 blade on a #3 scalpel handle. The two halves of the sternohyoid muscle are separated and retracted laterally using stainless steel retractors. The paired thyroid glands are small pink organs, one on either side of the trachea, just below the larynx and extending caudally along the first four tracheal rings. They are connected across the ventral aspect of the trachea, by a thin band of tissue, the isthmus. The minute parathyroid glands are embedded in the anterior part of each thyroid gland. Using fine-angled microdissecting forceps, gently tear the isthmus connecting the two lobes of the thyroid glands. With the forceps and blunt dissection, remove both halves of the thyroid gland, taking special care on the right side to avoid damage of the recurrent laryngeal nerve, which may cross the dorsal surface of the gland.

Postoperative Care
A post-operative injection of buprenorphine is administered at Day 1. In addition to the postoperative care described earlier, calcium supplementation (calcium chloride or calcium gluconate) in the drinking water is recommended following this surgical procedure. This supplementation is generally given for 7-10 days to help maintain calcium homeostasis during the post-recovery period. The most common complication of a parathyroidectomy is damage of the recurrent laryngeal nerve. Damaging this nerve can result in paralysis of the larynx, causing respiratory impairment that can be fatal.

Thyroidectomy

The paired thyroid glands are small pink organs, one on either side of the trachea just below the larynx. Thyroid glands synthesise and secrete thyroid hormones T3 and T4. These hormones regulate the development of the skeletal and central nervous system. T3 and T4 also play a role in oxidative, carbohydrate, lipid, and nitrogen metabolism.

Preoperative Procedures
Animals are weighed and anesthetised with appropriate anaesthetic and an injection of an analgesic (buprenorphine) is administered. The hair on the ventral neck area is clipped. The animal is then placed in dorsal recumbency with the tail or head towards the surgeon and the area is sterilised as previously described.

Surgical Procedure
A 1.5 cm ventral midline skin incision is made along the length of the neck from its base just below the point of the mandible using a #10 blade on a #3 scalpel handle. The two halves of the sternohyoid muscle are separated and retracted laterally using stainless steel retractors. The parathyroid glands are removed from the surface of the thyroid using fine-angled microdissecting forceps. The glands are placed in a sterile petri dish with saline. The thyroid glands are then removed as described previously. The parathyroids are then placed on either side of the trachea positioned where the thyroid glands have been extracted. The sternohyoid muscles are placed over the parathyroids and the skin incision closed with 9 mm auto clips for rats and 7 mm auto clips for mice or neonatal rats.

Postoperative Care
In addition to the standard postoperative care described above, normal drinking water is recommended following this surgical procedure.
Thymectomy

The thymus gland is a bilobed, roughly heart-shaped structure located in the anterior portion of the chest cavity cranial to the heart and at the thoracic inlet. It participates in the functional development of the body's immune system.

Preoperative Procedure
Animals should be weighed and anesthetised and an injection of an analgesic (buprenorphin) is administered. The hair on the chest and ventral neck area is clipped. The animal is placed in dorsal recumbency with the head toward the surgeon and the area prepared for surgery.

Surgical Procedure
Each lobe of the thymus is more or less separate, but held closely together by a connective tissue covering. Occasionally, when trying to remove the gland, it may separate, making it necessary to remove both parts individually. In older animals, care must be taken when separating the connective tissue, as it may have become tough. A 2.5 cm midline incision is made in the skin from the base of the neck posteriorly over the thorax using a #11 blade on a #3 scalpel handle. The thorax is opened by transecting the first two ribs starting at the thoracic inlet to expose the thymus. The tissue is then retracted to completely expose the thymus. Care should be taken because of the close proximity to major blood vessels. The gland is removed using a cotton-tip applicator to gently tease/scrape the thymus from the incision. After the gland is removed, the chest is compressed using pressure between the thumb and forefinger to expel air from the thoracic cavity. During compression, the skin is closed with 9 mm auto clips for rats and 7 mm auto clips for mice or neonatal rats to seal the thoracic cavity. It is important to close the thorax quickly to prevent and/or alleviate respiratory distress caused by the pneumothorax associated with this procedure.

Postoperative Care
A post-operative injection of buprenorphine is administered at Day 1. Normal postoperative care is practiced.

The Customer's Role in Postoperative Management

Providing surgically modified animals to the customer is a team effort that requires communication and follow-up between Charles River and the customer.

Post-Shipment Animal Evaluation
Upon receipt of the animals at the customer's facility, the customer should thoroughly examine the animals for signs of any postoperative complications or clinical abnormalities. The animals should be given free access to food and water as soon as possible and placed in a temperature-controlled environment. They should be provided with a clean, bedded cage, which should be changed as frequently as required to ensure that the operative site does not become excessively moistened with contaminated fluids from soiled bedding.

Post-Shipment Nutrition
In the case of animals in which endocrine organs have been removed, some supplementation may be required in either the food or drinking water. Charles River will provide the receiving institutions with the necessary information on which supplemental materials are required. Any animal that appears to be dehydrated should first be given access to drinking water and observed for ingestion of water. Supplemental fluids can be given subcutaneously, but should be done on the basis of veterinary input.
Wound Care

In most cases, dressing of wounds and applications of local antiseptics or disinfectants is not required. Wounds are closed most commonly with auto clips. These should be removed 7-10 days following the surgery. By this time, there is generally enough tensile strength in the healing wound to ensure that all layers will remain closed. Special auto clip removal forceps are commercially available, although other surgical instruments can be used for this purpose.

Customer’s Responsibility

Any abnormal occurrences with respect to the health of the animals or the success of the surgery should be conveyed to Charles River. Please contact Charles River’s Technical Services Department at surgery@eu.crl.com

Ethics Committee

Charles River’s Ethics Committee governs the entire surgical process, including any postoperative holding in Charles River facilities prior to shipment. The investigators and animal care staff are responsible for the well-being of the animal subsequent to its arrival at their institution. Justification for use of surgically modified animals, review of experimental protocols, authorisation to order animals that are surgically modified from Charles River, and all aspects concerning the use of surgically modified animals after they arrive at the institution are the responsibility of the receiving institution of the Ethic's Committee.