Proceedings of the Society for Theriogenology 2013 Annual Conference

Aug. 7-10, 2013 – Louisville, KY, USA

www.therio.org/

Next SFT Meeting:

Aug. 6-9, 2014 – Portland, OR, USA

Reprinted in the IVIS website with the permission of the Society for Theriogenology
A brief overview of reproduction in common rodent pocket pets
Angela M. Craig
Department of Research Animal Resources, University of Minnesota, Minneapolis, MN

Abstract

The aim of this paper is to provide a brief overview of the reproductive characteristics of six common small rodent species typically seen in pocket pet practice and used as animal models in research studies. These species are the mouse, rat, gerbil, hamster, chinchilla, and guinea pig.

Keywords: Rodent, pocket pet, laboratory animal, reproduction

In private practice, knowledge of normal characteristics, similarities and differences among the species, and common reproductive problems can aid the practitioner in providing services requested by clients who present their rodent pets for annual examinations, sexing, litter prevention education, and interventions necessary during abnormal reproductive events. From a biomedical research perspective, understanding the reproductive processes in common animal models guides scientists and laboratory animal veterinarians as they develop studies and directs breeding colony management decisions.

Mouse (Mus musculus)

Mice may be less commonly presented in small animal practice than other pocket pets, but this species is the workhorse of biomedical research. The mouse is the most commonly used mammalian laboratory animal worldwide. Mice breed readily, are genetically well-characterized, and have a short generation time. Managing mouse breeding in laboratory animal facilities is a standard component of colony management.

Males can be differentiated from females by examining the anogenital distance. This distance from the anus to the genital opening is 1.5-2 times greater in the male than the female. Both sexes have an external urinary papilla, though it often appears larger in the male. With gentle digital pressure on either side of the papilla, the penis of the adult male can be everted. Males have an os penis. In the perineal region, the female has paired clitoral glands and the male has paired preputial glands. Both types of glands can develop secondary infections causing visible swelling. Females have five pairs of mammary glands. Males do not have visible nipples.

Female mice are continuously polyestrus and are spontaneous ovulators with a cycle of 4-5 days. They are most receptive to breeding during the dark phase of their light cycle. Males are vigorous breeders and can successfully impregnate small harems of females. Following mating, the male leaves a copulatory plug in the female’s vagina. The plug is a concretion of secretions from the seminal vesicles and coagulating gland. It is believed to help retain the ejaculate in the vagina and prevent breeding of the receptive female by another male. The plug remains in the vagina for up to 24 hours before falling out. To have the best chance of finding one in situ, the female should be checked in the early morning following overnight exposure to a male. The presence of the plug confirms that mating has occurred, but does not guarantee pregnancy.

Three pheromone-based effects are well-described in the mouse. They are the Whitten, Bruce, and Lee-Boot effects. When exposed to a male or his scent, 40-50% of female mice housed together will cycle into estrus synchronously within three days. This is the Whitten effect. A pregnant mouse exposed to a strange male mouse or his scent during the first one to four days of pregnancy will have failure of implantation. This is the Bruce effect. The Lee-Boot effect describes how females housed together in the absence of a male will have false pregnancy or stop cycling altogether. With mindfulness of these effects, breeding managers attempt to achieve optimum reproductive performance in their colonies. A typical breeding strategy in mouse colonies is to have one male service a harem of one to three females. In a laboratory setting, a reason for having one male housed continuously with a single female is that he can take advantage of the post-partum estrus which occurs 14-24 hours following parturition.
Mice have a bicornuate uterus and are capable of carrying litters of one to 12 young.\textsuperscript{5} Mouse gestation is 19-21 days.\textsuperscript{5} By late gestation females assume a pear-shaped appearance as the young distend the caudal abdomen. Females give birth to altricial young. Newborn pups are completely hairless and have sealed eyes and ears. Their skin is bright red at birth and develops into a light pink color over the next few days. Post-natal pup development is well described in the literature and they can easily be aged by their developmental state. Most are ready to wean at 21 days. In some laboratory strains, the pups mature more slowly and require later weaning at up to 28 days.\textsuperscript{1} Mice become sexually mature by seven to eight weeks.\textsuperscript{5}

Adult male mice can be aggressive to other males and can be suspicious fathers. Infanticide and cannibalism can occur if a male mouse is reintroduced to a female with a litter whether or not he fathered the pups. It is important not to disturb the early postpartum female and breeding colony staff will often wait at least three days after parturition before entering the cage.

Dystocia occurs regularly in large breeding colonies.\textsuperscript{5} The prevalence may be due to the high number of pregnant animals, and the wide variety of strains, many of which are selected for traits unrelated to reproductive success. Similar to other species, causes of dystocia are an overlarge pup, two pups descending at the same time, maternal anatomic abnormalities, and uterine inertia. Unfortunately, oxytocin administration is rarely successful in dystocic dams. Supportive care, including fluids, warmth, analgesia, nutritional supplementation, and lubrication of the vaginal canal, is believed to have a greater chance of bringing the female to successful parturition.\textsuperscript{7} In a laboratory setting, if the mother cannot be saved and the pups are valuable, cesarean section with euthanasia of the dam may be undertaken to prevent loss of the young. The living pups can be fostered onto a lactating, receptive mother.

Mammary neoplasia in mice is most commonly adenocarcinoma. By the time it is detected, metastasis to the lungs may already have occurred.\textsuperscript{8}

The prime breeding period for mice in laboratory conditions is seven to eight months long and it is common to replace breeders that are older than one year or have gone 60 days since their last pregnancy. Ovariohysterectomy and castration of mice are performed occasionally in pet practice, and these, in addition to ovariectomy, are well-described in the literature due to their importance for specific research studies in which reproductive hormones must be manipulated.

Rat (\textit{Rattus norvegicus})

As intelligent, social, and tractable animals, rats are popular pocket pets and common research models. Like mice, they have been used extensively in research and much is known about their reproductive physiology and behavior. As in mice, the anogenital distance is used to differentiate males from females. Adult male rats have pendulous testicles. They can draw them into the abdomen via the inguinal canal, which remains open throughout life. Males have an os penis. Females have six pairs of mammary glands.\textsuperscript{9} Males have no nipples.

Females are continually polyestrus, and are spontaneous ovulators with a four to five day cycle. The estrous cycle is light sensitive and if exposed to constant light, rats can develop persistent estrus and polycystic ovaries.\textsuperscript{10} Optimal lighting conditions to promote appropriate cycling are described in the literature. After breeding, the male leaves a copulatory plug in the vagina.

The Bruce effect does not occur in rats. The Whitten effect is not believed to occur. The Lee-Boot effect occurs, but is much less pronounced in rats when compared to mice.\textsuperscript{11} Rats have a 21-23 day gestation.\textsuperscript{3} They give birth to three to 18 pups.\textsuperscript{11} Rat pups are hairless and helpless at birth. Rat dams are nurturing mothers and male rats, if kept with the mother as a pair, will help care for the pups. Rat mothers will nurse each others’ pups and if kept in groups, mothers may share a nest.\textsuperscript{10,12} In contrast to mice, neither sex is particularly prone to infanticide or cannibalism of the young. Rat pups wean at 21 days.\textsuperscript{11} They are sexually mature by 40-60 days.\textsuperscript{11}

Mammary neoplasia is common in both sexes. In most cases it is benign fibroadenoma. Even when rats present with very large mammary masses, removal is relatively simple. Unfortunately, additional masses may occur along the mammary chain during the remainder of the animal’s life. Spay of
the female may be preventative. Both ovariohysterectomy and castration are well described in the literature.

**Mongolian gerbil (Meriones unguiculatus)**

Male gerbils are easy to sex even at a young age due to their darkly pigmented scrotum. The anogenital distance is also reliable. Both sexes have a ventral midline scent gland, but in adult males it is well-developed. Females have four pairs of teats.

Male gerbils become sexually mature by 70-84 days of age. Vaginal opening occurs at 40-60 days, but females may not achieve sexual maturity until 30 days later. Breeding pairs are monogamous, and if the male dies the female may not accept another partner. Females are continually polyestrus, and are spontaneous ovulators with a four to six day cycle. Mating generally occurs during the evening hours. Females have a postpartum estrus. If no young from a previous litter are being nursed, gestation is 24-26 days.

Like mice and rats, gerbil mothers should not be disturbed immediately following parturition. Litters contain three to eight young. Pups are dependent on the mother until weaning at 21-28 days. Bonded pairs will share care of the young.

Reproductive disorders are relatively uncommon in gerbils in comparison to other species. Cystic ovaries are common in old females. Cysts can form on one or both ovaries and reproduction is adversely affected. For animals that present with severe abdominal distension and dyspnea, ultrasound-guided cyst aspiration will reduce intrabdominal pressure temporarily, but only ovariohysterectomy is curative.

**Golden or Syrian hamster (Mesocricetus auratus)**

Hamsters, like the rodents already described, can be sexed by anogenital distance. Males have pendulous testicles in adulthood which gives them a rounded perineal silhouette when viewed from above. Females have an angular, tapering perineal silhouette. Both sexes have bilateral flank glands, but females do not have the androgen stimulation needed to make them apparent. When males are sexually stimulated, the glands become moist with secretions. Females have six to 17 teats.

Sexual maturity occurs by six to eight weeks of age. Females are continuously polyestrus, and are spontaneous ovulators with a four day cycle. They produce a creamy, white, strong-smelling vulvar discharge around day two of estrus. For practitioners unfamiliar with hamsters, this can be mistaken for pus, but pyometra is rare in this species. Vaginal cytology is not a reliable way to determine the stage of estrus because sloughed cells collect within the paired vaginal pouches.

Hamsters can be aggressive to one another. When mating is desired, the female should be added to the male’s enclosure or both should be placed in a neutral enclosure. Close observation is necessary and if the female attacks the male, they should be separated immediately to prevent life-threatening damage. They can be reintroduced later when she is at a more receptive phase of her cycle. When she is receptive, the female will exhibit lordosis and allow the male to breed her multiple times within a short period. After mating they should be separated.

The gestation period is 15-18 days. Females have an infertile postpartum estrus. Litter size ranges from four to 12 pups. The pups are altricial. New mothers, especially primiparous dams, are highly prone to litter desertion, infanticide, and cannibalism. Following parturition, they should be left undisturbed for one to two weeks to prevent these problems. Hamsters will not accept orphan young and may kill both their own young and the orphans if an attempt at fostering is made.

When disturbed, hamster dams may move their litter around the enclosure to new nesting sites, using their cheek pouches to carry the young. This can appear as cannibalism to the untrained eye. Clients may report mysteriously reappearing litters after they thought the mother had eaten the young. The young are weaned at 21-25 days. They should be separated from the mother shortly thereafter.

**Chinchilla (Chinchilla lanigera)**

Chinchillas can be sexed using anogenital distance. The external appearance of the genitalia can be deceiving. The female has a cone-like urinary papilla which can be mistaken for a penis and prepuce.
This papilla is also called the clitoris or urethral cone. To ensure correct sexing, gentle digital pressure can be used to attempt to evert a penis from the papilla. Females have three pairs of mammary glands. Vaginal closure membranes are present except during estrus and parturition. In males the inguinal canals are open throughout life. There is no true scrotum.

Chinchillas are sexually mature by eight months of age, but the onset of sexual maturity ranges from two to 14 months. Female chinchillas are seasonally polyestrus, and are spontaneous ovulators with an estrus cycle of 30-50 days. During estrus no swelling of the vulva is apparent, but the perineal skin tone flushes to a dark red. In captivity two litters may be born between November and May. Breeding strategies in chinchillas include pairing or polygamous groups with one male to a harem of six to 12 females. Females may not tolerate the presence of the male after parturition. Copulatory plugs are common after mating.

Chinchilla gestation is long at an average of 111 days, allowing for greater neonatal development and the birth of precocious young. Females give birth in the morning, eat their placenta, and nurse their young while standing erect. Litter size is one to five pups, with two being average. Pups can eat solid food within a week of birth, but they typically wean from dam’s milk at six to eight weeks of age.

A chinchilla that is in labor for more than four hours or is attempting to give birth after noon may be in dystocia. Other signs include restlessness, distressed vocalization, and continual cleaning of the genital area. Causes include uterine inertia, malpositioned fetuses, or oversized fetuses. Cesarean section should be performed to relieve the dystocia. It is generally well-tolerated if the dam is in good condition when presented.

Chinchillas may not produce milk for up to 12-72 hours after parturition. If necessary, oxytocin can be administered to promote milk-letdown. If unsuccessful, the young must be hand-raised.

In males, the primary reproductive concern is a fur ring on the penis. Males may present with paraphimosis, straining to urinate, and excessive cleaning of the penis. When examined, there will be a yarn-like ring of compacted fur around the penis. It should be well-lubricated and cut away. A hooked suture scissors works well to remove fur rings. Fur rings occur in both sexually active and inactive males, but the condition is much more common in breeding animals. The examination of the penis for a fur-ring should be part of every annual examination and owners can be taught to check for the condition so the ring can be removed before damage occurs.

**Guinea pig (Cavia porcellus)**

Male guinea pigs are called boars and the females are sows. Males have visible scrotal pouches and large testes that can be drawn up into the abdomen through the inguinal canal, which is open throughout life. Gentle abdominal pressure will help drop the testes into the scrotal pouches. The penis can be extruded with gentle digital pressure. The boar has an os penis. Internally, the seminiferous vesicles are extensive and can extend 10 cm cranially into the abdomen. Due to their size and texture, they could be misidentified as a uterus. Adult boars have a scent gland on their lower back. In aged boars it can be become large and encrusted with secretions.

Visually, females have a Y-shaped appearance to the genital area. Like the chinchilla, they have vaginal membranes which cover the opening except during breeding and parturition. Both sexes have a single pair of nipples on the caudal abdomen.

Females are sexually mature by two months of age and males are mature by three months, though they will begin mounting behavior as early as one month of age. Females are polyestrus, and are spontaneous ovulators with an estrous cycle of 15-17 days. An estrus sow will exhibit lordosis. Males leave a copulatory plug after mating.

Gestation is long, at 59-72 days, and this period allows for greater development of the young. Like chinchillas, guinea pigs eat their placenta. They have a postpartum estrus. There are generally two to five young per litter. They are precocious at birth, but cannot fend entirely for themselves. Sows can be passive caregivers, allowing nursing to take place, but not actively seeking out their young. They can eat solid food within a week of birth, but pups may nurse for up to three weeks. They are weaned by 14-21 days.
Dystocia is common in sows which are bred for the first time after six to seven months of age.\textsuperscript{30} Prior to parturition, the pubic symphysis separates with a gap of up to 25 mm or more. If this does not occur early in life, the pubis cannot open as far or is fused.\textsuperscript{30} Subsequently, the older primagravid sow cannot pass her young and develops dystocia. Other causes of dystocia include obesity, large fetal size, and pregnancy toxemia. Normal delivery of guinea pigs is rapid, with pups coming out within a few minutes of one another. Dystocia should be suspected in a sow that becomes depressed or develops bloody to dark brown vulvar discharge. A cesarean section is warranted, but if the sow presents severely debilitated from long hours of laboring the prognosis is guarded even with intervention.

Sows are also prone to pregnancy toxemia, vaginitis, and mastitis.\textsuperscript{34} Clinical signs and treatment strategies are described in the literature.\textsuperscript{34} Ovarian cysts are very common in middle-aged to old sows.\textsuperscript{35} Males experience a condition similar to vaginitis in the sow in which their genital area becomes impacted with bedding and fecal material.\textsuperscript{34} Boars may develop orchitis or epididymitis following sexual contact with a sow. These problems also occur through trauma or hematogenous spread of Bordetella or other common bacteria.\textsuperscript{34}

This paper is not exhaustive. Information about internal anatomy, copulatory and maternal behavior, medical and surgical treatments, and pathology are well-described in the literature. Excellent texts, written for both laboratory animal veterinarians and exotic animal practitioners, exist and serve as valuable resources. Many of these are referenced as part of this overview and numerous others, while not mentioned directly, have contributed greatly to the vast body of information on small rodent reproduction.

References