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Anatomy and Physiology of Animal Model Rats in Biomedical Research

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ABSTRACT

A distinguishing feature of rodents, including rats, is the absence of canines and the presence of prominent incisors. Rats are monophydontic, meaning they grow one set of teeth in their lifetime. The enamel of the rodent incisor contains iron, which gives it its yellow-orange color. Rats are mammals and as such, possess many similarities with other mammals. Only the peculiarities of the rat's anatomy are addressed. Male rats reach puberty at 40 - 60 days of age. Descent of the testes usually occurs between days 30 - 60. Sperm counts vary by strain. The male rat has an os penis. Male rats have the following accessory sexual organs: ampulla, seminal vesicles, prostate, bulbourethral glands, coagulating glands, and preputial glands. The coagulating gland and prostatic and vesicular secretions are responsible for the copulation plug, a firm plug deposited in the vagina of the female after copulation. (This plug, when found outside the female rat, is capsuleshaped and approximately 5 mm long.) The male rat has no nipples. The adult male rat has a prominent scrotum and a longer anogenital distance than the female rat.

1. Introduction

The average life span of the domestic rat is 2.5 - 3.5 years. Exceptional members have been recorded at 5 years, but this is uncommon. An adult female rat reaches 250 - 300 g body weight at adulthood (higher during pregnancy) and an adult male rat reaches 400 - 500 g adult body weight. A distinguishing feature of rodents, including rats, is the absence of canines and the presence of prominent incisors. Rats are monophydontic, meaning they grow one set of teeth in their lifetime. The enamel of the rodent incisor contains iron, which gives it its yellow-orange color and its hardness Fig. 1. These incisors grow continuously and must be worn down through gnawing. The molars are also open-rooted, but they wear on each other, and are only rarely misaligned. The dental formula of the rat is 2(1/1 0/0 0/0 3/3) = 16 and the vertebral formula is C7 T13 L6 S4 Cd 27-30.

Rats are mammals and as such, possess many similarities with other mammals. Only the peculiarities of the rat's anatomy are addressed. For clinical pathology and other normative biological data, please see Table 1, Table 2, Table 3, Table 4, Table 5 and Table 6. A rat's esophagus is lined entirely with keratinized epithelium. The stomach of the rat contains both a non-glandular and glandular portion, which are separated by the limiting ridge. The esophagus enters the stomach through a fold in the limiting ridge and this anatomic feature prevents rats from vomiting. The small intestine of rats is unremarkable, but rats

possess a prominent cecum, which occupies much of their abdominal cavity. The rat has a four-lobed liver with no gall bladder. The pancreas is diffuse. The inguinal canals remain open throughout life. The rat's lungs are immature at birth and lack alveoli, alveolar ducts, and respiratory bronchioles. Remodeling occurs 4 - 7 days after birth and respiratory bronchioles are found 10 days after birth. The right lung of the rat has four lobes, while the left has one. The rat's pulmonary veins contain cardiac muscle fibers. Rats have several unique glandular structures. Steno's gland (lateral nasal gland) is located in the maxillary sinus and it both humidifies air and controls mucus viscosity. Paired Zymbal's glands (sebaceous glands) are found at the base of each ear. They are auditory sebaceous glands that open into the external ear canal. Rats also have Harderian glands (lacrimal glands), which secrete porphyrin, behind each eye. Secretions from these glands usually go unnoticed unless the rat is ill or stressed. Then, reddish-brown secretions may be seen rimming the eye or at the external nares. Front paws may also show staining as the animal grooms the irritating secretions away. These secretions resemble blood, but porphyrin fluoresces under ultraviolet light while blood does not.

Like other rodents, rats do not have many physiologic mechanisms to allow them to cope with heat. They cannot sweat and they cannot pant. Some heat is dissipated through vasodilation in the tail. Although increased salivation is seen as a response to overheating, rats will not drink more water in response to increased temperature. They will take saliva and spread it on their heads and bodies in attempts to cool themselves. Rats also thermoregulate through behavioral means such as burrowing and seeking shade.

Reproductive anatomy and physiology

A summary of rat reproductive norms may be found in Table 6. Male rats reach puberty at 40 - 60 days of age. Descent of the testes usually occurs between days 30 - 60. Sperm counts vary by strain [4]. The male rat has an os penis. Male rats have the following accessory sexual organs: ampulla, seminal vesicles, prostate, bulbourethral glands, coagulating glands, and preputial glands. The coagulating gland and prostatic and vesicular secretions are responsible for the copulation plug, a firm plug deposited in the vagina of the female after copulation. (This plug, when found outside the female rat, is capsuleshaped and approximately 5 mm long.) The male rat has no nipples. The adult male rat has a prominent scrotum and a longer anogenital distance than the female rat.

Young female rats are born with a vaginal closure membrane, called the vaginal plate. This spontaneously ruptures before puberty (usually at 33 - 42 days of age), but may persist, resulting in a vagina and uterus distended with mucus and other secretions. Female rats reach puberty at 40 - 60 days of age (approximately 6 - 8 weeks). The female rat is a polyestrus spontaneous ovulator who cycles every 4 - 5 days. The rat is in proestrus for approximately 12 hours, estrus for approximately 12 hours, metestrus for approximately 21 hours, and diestrus for the longest portion of the cycle, approximately 55 hours. Rat estrus cycles can be evaluated through the use of vaginal smears. Vaginal cytology is similar to that of other animals in that a vaginal smear containing mainly cornified epithelial cells is a good indication of estrus. Ovulation usually occurs in the middle of the dark portion of the light/dark cycle. Rats are sensitive to changes in the light cycle, with continuous light readily producing persistent estrus due to polycystic ovaries [5]. The gestation period of the rat is 21 - 23 days and there is a fertile postpartum estrus. The female rat has 6 pairs of mammary glands and gives birth to an average of 10 - 12 pups. Cannibalism is uncommon, but does occur. It is a natural way for a dam to rid the nest of weak or ill pups, or may be precipitated by stress, especially in a first-time mother. Rat pups weigh 5 - 6 grams at birth, and are born blind, deaf, and hairless. Their ears open at approximately 12 days and their eyes between days 10 - 12. Rat pups are dependent on the female for their nutritional needs until they are approximately 14 days old. Once they are mobile, they may explore food if it is present in the

bottom of their cage, but will still receive most of their calories from milk. During the early food exploration period, young rats may be observed engaged in coprophagy. This is a normal means of obtaining gut flora and exploring their environment. Most rats are weaned at 21 days of age. Weaning is usually performed by removing the animals from the home cage and separating the animals into single-sex groups. Animals from multiple litters may be mixed together at weaning. Animals may be housed at higher densities when smaller and separated as they become larger. Rats may be housed in single-sex groups, in monogamous breeding situations, or in polygamous breeding situations. Male rats tolerate the company of other males quite well and may be housed together in single-sex groups. If breeding rats, the monogamous configuration allows for absolute knowledge of both maternity and paternity. Housing a male with more than one female allows for sure knowledge of paternity, but maternity may be confusing. Female rats will gang-nurse litters, and male rats will participate in care of the young. Housing more than one male with a group of females will result in fighting between the males.

Figure 1. Normal Rat Dentition

Table 1. normal physiological data for the rat [8,9]. As with all "normal", these values and the values presented in the other tables in this work, may not represent the mean or range for certain populations or strains of animal. For this reason, the value should be interpreted as approximations

Life expectancy	2.5 – 3.5 years
Body weight – male	300 – 500 grams
Body weight – female	250 – 350 grams
Body temperature	36.0 – 37.5 °C (96.5 – 99.5 °F)
Daily food consumption (adult)	5 g/100 g BW
Daily water consumption (adult)	8 – 10 ml / 100g body weight
Daily urine production	5 – 6 ml/6ml body weight
Urine pH	7.3 – 8.5
Urine specific gravity	1.04 – 1.07
Daily fecal production	10 – 15 grams

Table 2. Normal respiratory parameters for the rat [8,9]

Respiratory rate	70 – 110 breaths/min
Tidal volume	0.5 – 2.0 ml
Minute ventilation	75 – 130 ml/min
Trachea diameter	1.6 – 7.7 mm
Alveolar surface area (400 gram rat)	7.5 m^3
Total lung capacity	11.3 +/- 1.4 ml
Vital capacity	8.4 +/- 1.7 ml
Functional residual capacity	3.9 +/- 0.8 ml
Residual volume	2.9 +/- 1.0 ml

Table 3. normal cardiovascular parameters for the rat [8,9]

Heart rate	250 – 500 beats/min
Mean systolic arterial blood pressure	116 mm Hg
Mean diastolic arterial blood pressure	90 mm Hg
Cardiac output	50 ml/min
Blood volume	6 ml/100 gram body weight
Sample volume	2 – 4 ml
Sample site	Lateral tail vein; saphenous vein
pO_2	93.0 mm Hg
pCO_2	39.9 mm Hg
Arterial blood pH	7.41
H^+	38.6 +/- 0.6nM
Base excess	+1.8 +/- 0.4

Table 4. normal serum biochemistry values for the rat [21]. For a more exhaustive list, including hormones, the reader is referred to Kohn and Clifford [9]

Glucose (mg/dl)	85 – 132
Urea nitrogen (mg/dl)	32 – 54
Cholesterol (mg/dl)	46 – 92
Total protein (g/dl)	6.3 – 8.6
Albumin (g/dl)	3.3 – 4.9
Globulin (g/dl)	2.4 – 3.9
Aspartate aminotransferase (U/L)	39 – 92
Alanine aminotransferase (U/L)	17 – 50
Alkaline phosphatase (U/L)	39 – 216
Sodium (mEq/L)	141 – 150
Potassium (mEq/L)	5.2 – 7.8
Chloride (mEq/L)	99 – 114
Phosphorus (mg/dl)	6.2 – 11.7

Calcium (mg/dl)	10.7 – 13.7
Magnesium (mg/dl)	2.6 – 3.11

Table 5. Normal hematology values for the rat [21]

Red blood cells (x 10 ul)	5.4 – 8.5
Hemoglobin (g/dl)	11.5 – 16.0
Hematocrit (%)	37 – 49
Platelets (x 10 ul)	450 – 885
White blood cells (x 10 ul)	4.0 – 10.2
Neutrophils (x 10 ul)	1.3 – 3.6
Lymphocytes (x 10 ul)	5.6 – 8.3
Total blood volume (ml/kg)	50 - 65

2. References

1. 1.Hedrich HJ. History, strains, and models In: GJ Krinkle, ed. The Laboratory Rat. 1st ed. Vol. 1. San Diego: Academic Press, 2000; 3-16.
2. Richter CP. The effects of domestication and selection on the behavior of the Norway rat. J Natl Cancer Inst 1954; 15:727-738.
3. Koolhass JM. The laboratory rat. In: T Poole, ed. The UFAW Handbook on the Care and Management of Laboratory Animals. 7th ed. Malden, Massachussets: Blackwell Science, Ltd., 1999; 313-330.
4. Wilkinson JM, Halley S, Towers PA. Comparison of male reproductive parameters in three rat strains: Dark Agouti, Sprague-Dawley and Wistar. Lab Anim 2000; 34:70-5.
5. Brown-Grant K, Davidson JM, Greig F. Induced ovulation in albino rats exposed to constant light. J Endocrinol 1973; 57:7-22.
6. Peace TA, Singer AW, Niemuth NA, et al. Effects of caging type and animal source on the development of foot lesions in Sprague Dawley rats (Rattus norvegicus). Contemp Top Lab Anim Sci 2001; 40:17-21.
7. Keenan, KP, Ballam GC,Haught DG, et al. Nutrition. In: Krinke GG, ed. The Laboratory Rat. 1st ed. Vol 1. San Diego: Academic Press, 2000; 57-75.
8. Sharp PE, La Regina MC. The Laboratory Rat. In: M.A. Suckow, ed. The Laboratory Animal Pocket Reference Series. Boca Raton: CRC Press, 1998; 214.
9. Kohn DF, Clifford CB. Biology and diseases of rats. In: JG Fox, LC Anderson, FM Lowe, et al., eds. Laboratory Animal Medicine, 2nd ed. New York: Academic Press, 2002; 121-167.
10. Hubert MF, Laroque P, Gillet JP, et al. The effects of diet, ad libitum feeding, and moderate and severe dietary restriction on body weight, survival, clinical pathology parameters, and cause of death in control Sprague-Dawley rats. Toxicol Sci 2000; 58:195-207.