XV. HAMSTERS*

A. INTRODUCTION

1. Origin

Hamsters are rodents of the family Cricetidae, which in nature are widely distributed across North Africa, parts of Europe, the Middle East and Siberia eastwards into China. At least 54 species and varieties have been characterized in five different genera. Three of these species, from three different genera, have become both widely used in research and popular as pets.

The Syrian or golden hamster (*Mesocricetus auratus*) has been by far the most extensively used species in the laboratory, although studies on the Chinese hamster (*Cricetulus griseus*) are also becoming fairly widespread. A comprehensive reference book on the biology and use of the Syrian (golden) hamster in biomedical research is available (Hoffman, Robinson and Magalhaes, 1968).

The terms "Syrian hamster" and "golden hamster" are synonymous in the literature, although the wild hamster of this species has a solid, reddish brown, short haired coat. Several mutations have occurred during domestication that, through selection, have resulted in a variety of different hair colours, lengths, and patterns. The term "Syrian hamster" will be used throughout this chapter and, unless otherwise specified, all comments and statements in the subsequent text refer to the Syrian hamster, although in most cases the information will also be applicable to other hamster species used in the laboratory.

Probably all domesticated hamsters trace back to a single male and its two female sibs, captured in 1930 in Syria for research purposes. Early descendants of these animals were introduced into Great Britain in 1931, but did not reach North America until during World War II (Hoffman, Robinson and Magalhaes, 1968; Alder, 1948). Chinese hamsters have proved to be more difficult to breed and establish in captivity, even though research reports based on their use considerably pre-date those on Syrian hamsters (Festing, 1976).

2. Biological Characteristics

Hamsters are stocky, short tailed little animals weighing an average of 97.2 + 11.7 g, with the female being some what larger, stronger, and more aggressive than the male. The Chinese hamsters average body weight is 42.5 + 3.2 g (Juszkiewicz and Stefaniak, 1969). A table compiled by Festing lists some interesting comparative data on the relative weights (size) of various organs between the two species (Festing, 1976).

Well developed cheek pouches, an aglandular diverticulum anterior to the cardiac region of the stomach, and adrenal glands which are larger in the male than in the female, characterize these rodents anatomically. Physiologically, the forestomach-like diverticulum provides for pregastric

fermentation, having flora and a capacity for nitrogen utilization somewhat comparable to that of ruminants. Hamster urine has a pH of 8.0 and is rich in a crystalluria which makes it turbid and milky (Stoliker, 1981).

3. Behavioral Characteristics

Hamsters are burrowers that, given the chance, will indulge in very extensive food hoarding. These habits have resulted in their being treated as gopher-like pests in many of the countries in which they are indigenous.

Another behavioral trait that is peculiar to the hamster, amongst laboratory animals, is its ability to occasionally go into short periods of hibernation. In hibernation, the hamster will curl up and enter a profound sleep during which the body temperature drops from its normal 37-38^{o}C (98.6-100.4^{o}F) to a degree or two above that of the ambient temperature. Respiration will fall to about one per minute from the normal 35-135/min, and heartbeats drop to 4-15/min from a normal 250-500/min (Festing, 1976; Stoliker, 1981; Harkness and Wagner, 1983).

4. Research Uses

Three strains of hamsters are used in the laboratory: the Syrian or golden hamster, which is the most popular and commonly used strain, the European or black hamster (*Cricetus cricetus*) and, in increasing proportions more recently, the Chinese hamster.

The hamster has unique characteristics which make it a valuable and well suited laboratory animal for biomedical research. The eversible cheek pouch is particularly suited for studies on the micro circulation and also for the transplantation of neonatal, adult, and neoplastic tissues. Its value as a transplantation site is greatly enhanced by the fact that the cheek pouch is both accessible for direct observation and is a particularly privileged site in an animal that normally exhibits an exceptional degree of immunological tolerance (Harkness and Wagner, 1983; Streilein *et al.* 1981). The teeth of this species have been widely utilized in the study of dental caries and periodontal diseases. The Syrian hamster has provided useful models in many other areas of biomedicine, particularly those concerned with the biochemical aspects of disease and in virology.

Certain strains of Chinese hamsters are genetically susceptible to diabetes mellitus and are frequently used in studies on that disease (Butler, 1967). This species has also been found of considerable use in a variety of pathology and parasitology investigations.

The Chinese hamster has only 22 chromosomes, as opposed to 44 in the Syrian hamster. A consequence of this low number of chromosomes has been an increasing interest in their use for cytological studies, notably those involving tissue culture and the evaluation of the effects of radiation and toxic substances (Festing, 1976).

The Syrian hamster is considered by some investigators to be well suited for teratology studies due to its short gestation period of 15-18 days, as opposed to the 21 or more days of other hamster species and common laboratory rodents (Ferm, 1967).

B. HOUSING

1. Environmental Requirements

Hamsters can, like most desert animals, adapt without discomfort to considerable fluctuations in temperature. However, as low temperatures are one of several factors that encourage hibernation, it is advisable to maintain hamster holding rooms at at least 20°C (68°F) and breeding rooms somewhat higher. Relative humidity should be between 45 and 70%. Short periods of daylight also encourage hibernation; thus the light-dark cycle should be at least 14:10 hours.

Several other environmental conditions are known to be associated with the onset of hibernation. These would include very deep litter that is infrequently changed, the opportunity to store a supply of food in a cache, and being left relatively undisturbed. As none of these conditions should normally occur in a properly run experimental animal facility, hibernation should not usually occur or prove a problem in laboratory hamsters. It should be noted that the hamster is a good, but seemingly under-utilized model for hibernation studies.

Hamsters are extremely active, mostly during the dark period. This seems to be particularly true of pregnant females, which have been shown to average about 8 km/day on an exercise wheel (Richards, 1966). In light of this sort of evidence, it has been suggested that there is a need for further ethology studies on the effects of restricted cage housing on hamster activity and on the effects of cage imposed limited exercise on various physiological parameters in this species.

2. Caging

Hamsters are experts at escape and, if given half a chance, will chew and wiggle their way out of cages of wood, aluminum, and certain soft plastics. Because of this, these materials should not be used for the construction of hamster cages.

Cage sizes should be such as to meet the needs of the breeder or investigator; however, a minimum of 650 sq cm (100 sq in) per single cage, and 100 sq cm (15 sq in) per animal in a group cage should be provided. The cage should also provide at least 18 cm (7.0 in) of height. Cages should have hinged, latchable lids and removable bottom trays.

Hamsters may be maintained in suspended wire cages containing a raised or perforated floor. However, this type is not suitable for the birthing and raising of young. In fact, hamsters, as burrowing animals, will always be more contented and probably do better with bedding on a solid floor.

Hamsters are solitary animals under natural conditions, and are usually best kept separate from each other in captivity. In a breeding colony, the female should be provided with an opaque cage, with sufficient food and bedding to allow her to litter and remain undisturbed for a period of at least one week postpartum.

Bedding should be of an appropriate absorbent material and should be non-edible. The most commonly used types of bedding are white pine wood shavings, shredded newspaper, or flax fibres. Chopped corn cobs are also satisfactory. Under most conditions, the bedding should be replaced at least once each week. The cages should be checked regularly for evidence of damage due to gnawing.

While specially designed hamster cages are available commercially, in practice it will be found that standard rat cages and mouse cages are well suited to Syrian and Chinese hamsters respectively, as long as they are made of hard plastic or metal.

C. **BREEDING**

1. **Mating Systems: Estrous Cycle**

Although females reach sexual maturity at the age of about one month, it is inadvisable to mate them until they are at least six weeks of age (11 weeks for the Chinese hamster). Hand matings are preferable to harem matings because of the tendency of this species to fight when group housed and, particularly, for the females to pick on the males. Monogamous pairs, if put together at weaning and left together for life, have proven to be a useful and safe breeding system for inbred strains (Festing, 1976).

When harem mating is practised, the female should be removed prior to parturition. The harem must be observed carefully when she is returned to it, as this is when fighting most often occurs.

Hand mating requires the accurate detection of estrus so that the female can be placed in the male's cage for mating. The estrous cycle normally lasts four days, with estrus usually occurring about an hour after dusk. Ovulation occurs from eight to ten hours later and is followed by a metestrous vaginal discharge of a viscous, creamy substance; the next estrus should come three days after this is observed.

A female placed in the male's cage for mating must be observed closely, for an antagonistic female may destroy the male. Usually coitus will take place almost immediately if the female is in estrus. The female should not be left in the cage with the male. A reversed light cycle in the breeding colony will permit the adaption of the hand mating system to the regular work day and facilitate monitoring.

2. **Reproduction**

Implantation takes place on the sixth day after breeding. Gestation averages 16 days in Syrian hamsters, 21 days in Chinese hamsters.

Hamsters do not have a *post-partum* estrus; however, a large percentage of females with litters will come into estrus on the second or third day after weaning.

Cannibalism occurs quite often, particularly with first litters. Hamsters, particularly those with pups, are quite sensitive to their environment and are easily disturbed by non-routine noises and activities.

Females should be housed in cages with a solid floor, as those raised on perforated floors invariably devour their young.

Young animals are weaned at about 21 days. They should then be separated on a sex basis and housed separately. The sexes can be differentiated on the ano-genital distance which, in the male, is much greater than in the female. Young animals can be maintained together until maturity, but should be carefully observed to determine if any individuals have a tendency to aggressive behavior. It may be necessary to remove such an animal to another cage.

D. **DIET**

1. **Nutrient Requirements**

Detailed information on the nutritional requirements for these omnivorous rodents have not been properly determined, although commercial rations developed for other rodent species have commonly been used and appear to have been quite satisfactory.

A minimum of 16% protein may be adequate in maintenance rations for mature animals; however, a level of 24% protein or more is required to ensure proper growth and for pregnancy (Stoliker, 1981; Harkness and Wagner, 1983).

Basic rations may be supplemented with fresh fruits and vegetables. However, care must be exercised in the amount of fresh foods offered, as the animals prefer these to manufactured pellets, with the risk of a resultant imbalance in nutrient intake.

It has been reported that some fruits, particularly apples, play an important part in the hamster diet, and that the removal of these items from their diet will often result in a decrease in the implantation rate and an increase in cannibalism (Poiley, 1950).

2. **Feeding**

Fresh fruits and vegetables should be washed in a 400 ppm chlorine solution as a precaution against diseases such as tularemia (Stoliker, 1981).

Fresh pellets should be provided at least once each week and all unused portions of food should be discarded from the feed hoppers.

Fresh, potable, drinking water should be available at all times.

Food consumption of standard laboratory feeds will be from 7-15 g/day and water consumption will be up to 20 ml/day for animals on dry feeds.

E. HANDLING AND RESTRAINT

Hamsters are solitary animals, with a tendency at certain times to be rather aggressive towards each other. However, they probably do not deserve their reputations for ill temper and biting; in fact, they tend to be naturally inquisitive and friendly.

When manipulations and treatments are necessary that do not involve pain, the animal can usually be picked up and restrained manually and without any difficulty.

Hamsters may be picked up in the cupped hands if they are docile and used to being handled, or by grasping as much of the loose skin as possible over the neck and shoulder region, if not used to being handled. Various other hand holds have been recommended, described, and illustrated by numerous authors (Hoffman, Robinson and Magalhaes, 1968; Stoliker, 1981; Harkness and Wagner, 1983).

It should not be necessary to use gloves when handling these animals. It is difficult to handle an animal gently and avoid hurting it when wearing gloves. Once an animal associates a gloved hand with being hurt, it will automatically attempt to bite. The warmth of a bare hand tends to calm and relax the animal.

All movements when approaching the animal should be deliberate and not sudden. Hamsters are sound sleepers and can occasionally even be picked up without awakening, however, this is not advisable, as sudden awakening during the process will startle the animal and lead to its biting.

Recommendations for chemical restraint, immobilizing agents, and anesthetics for hamsters may be found in the appropriate appendix of Volume 1 of this Guide. The anesthetic agents and methods discussed in the chapter on Gerbils, are also applicable to the hamster.

F. SPECIMEN COLLECTION

Urine and feces can best be collected from small animals of this sort by using a metabolism cage. The commercially obtainable plastic metabolism cages for rats are eminently suitable for this purpose.

For small samples of blood up to 0.5 ml, bleeding from the orbital sinus by the same procedure routinely used for mice and rats is the method of choice. A heparinized capillary pipette, with a polished tip should be used to avoid scratching the cornea. Restraint should be by anesthesia and by holding the loose skin at the back of the neck (see above). In either case, the hamster will have to be grasped in the same way, at the base of the neck and then the skin adjacent to the eye must be tightened by traction with the free index finger; this will keep the eye open and make it bulge slightly. The vessels of the opthalmic venous plexus in the angle of the eye can now be punctured with the tip of the pipette.

Withdrawing the pipette a fraction will allow the eye cavity to fill with blood and the pipette to fill by capillary action. Ocular pressure will return to normal on withdrawal of the pipette and the release of tension over the eye will stop further bleeding.

Large amounts of blood, up to 2 ml/150 g, can safely be withdrawn by cardiac puncture under general anesthesia.

G. **HEALTH CARE**

1. **Infectious Diseases**

A survey of hamster diseases (Renshaw, Van Hoosier and Amend, 1975) has shown that the most common and frequently recognized disease is the one commonly referred to as "wet tail". This is an enteric disease that is also known as proliferative ileitis, or transmissible ileal hyperplasia. It is characterized by severe diarrhea and has a very high mortality rate. Lethargy, irritability, anorexia, emaciation and finally death, is the usual course. Death usually occurs in from 48 hours to one week after the initial onset of the signs (Renshaw, Van Hoosier and Amend, 1975).

Although the cause is still not determined with certainty, some workers (Fisk, Wagner and Owens, 1978) suggest that *Escherichia coli* may be responsible for this condition. E. coli is almost certainly involved in the enteritis component of the disease, while a *Campylobacter*-like intracellular bacteria may be involved in producing the hyperplastic lesions (Harkness and Wagner, 1983). The onset of "wet tail" may be predisposed by the stresses of confinement and of weaning and the infection is probably latent in many colonies. It has been noticed that nursing mothers usually show no evidence of the disease and the mortality is highest amongst nursing or newly-weaned animals three to eight weeks of age.

Treatment of outbreaks of "wet tail" is usually not successful and should only be attempted as a last resort, or where the animals are of particular value. In such cases, tetracycline in the drinking water at 400 mg/L, for 10 days, may help. Prevention will prove to be much more rewarding than treatment. Maintenance of a high level of hygiene in the colony, the avoidance of stress, particularly to weanlings, and the constant genetic selection for resistance should be routinely practised in all colonies. In situations where there has been an outbreak, or where animals of an unknown (suspect) background must be introduced, it is advisable to make use of cage filter covers. In such situations, preventive treatments have also been suggested, using either

tetracycline (as above) or dimetridazole at 500 mg/L for 10 days (Tafts, 1976).

Pneumonia is seen periodically in hamster colonies and is considered to be second in importance to "wet tail" (Renshaw, Van Hoosier and Amend, 1975).

An epizootic disease with an acute course and death, caused by *Salmonella enteritidis* or *S. typhimurium* is occasionally observed in hamsters. Enteric signs do not dominate the clinical picture in this condition, however, and the outstanding lesion is a septic, partially occluding, *phlebothrombosis in the lungs*. Necrotizing foci are frequently seen in the liver and spleen.

Tyzzer's disease has been reported in a colony of Syrian hamsters (Zook, Huang and Rhorer, 1977).

Viruses reported to infect hamsters include:

a. The lymphocytic choriomeningitis virus which may give rise to clinical disease in humans.

b. The Sendai virus which may produce a pneumonia in suckling hamsters.

c. Pneumonia virus of mice.

d. Simian virus-5.

e. Reovirus type 3.

f. Polyoma virus.

Despite the above imposing array of pathogens, the hamster is itself a hardy and usually healthy animal. However, because of the numerous viral and bacterial pathogens that it may harbour, often without evidence of clinical disease, it is particularly important that hamsters be housed in rooms separate from other laboratory rodents.

2. **Parasitic Diseases**

Helminth infections include *Hymenolepis nana* (a dwarf tapeworm), *H. diminuta* and the nematode pinworm parasites *Syphacia obvelata* and *Aspiculuris tetraptera*. Controlling helminth infestations is largely a matter of eliminating their intermediate hosts: insects, arthropods and, indirectly, wild rodents in the case of Hymenolepis spp. Standards of hygiene must be implemented that will eliminate direct transmission; all animals at risk should be treated with an appropriate anthelminthic in the feed (Harkness and Wagner, 1983). Treatment of pinworms is relatively ineffective, as is control (Harkness and Wagner, 1983), although numerous drugs and systems have been recommended with some claims of success (Owen and Turnton, 1979; Taffs, 1976).

Arthropod infestations resulting in an alopecia and dermatitis often extending over the entire back may be due to *Demodex criceti* or *Demodex aurati*. Mite infestations are commonest in older animals and have been associated (possibly fortuitously) with chronic, renal disease in hamsters. It is difficult to completely rid a colony of demodex mites; however, 24-72 hour exposure to dichlorvos (vapona strip), repeated at 10 day intervals, three or four times, will usually provide effective control. It should be noted that cholinesterase is inhibited by dichlorvos.

Protozoa infections of the intestinal tract due to *Trichomonas* sp., *Giardia* sp. and *Hexamita* sp. have been observed, although clinical signs of disease are rare and usually restricted to weanlings.

3. Miscellaneous Health Problems

Spontaneous hemorrhagic necrosis is a fatal disease affecting fetal hamsters and causing necrosis of the brain stem, cerebrum and spinal cord, with grossly detectable intracranial hemorrhages. Affected young that are born at term will usually be cannibalized. The disease has interfered with the value of certain hamsters for teratology testing and with commercial production. Studies have indicated this to be a metabolic disease which can be reversed and possibly totally prevented by Vitamin E supplementation during pregnancy and lactation (Keeler and Young, 1979).

The incidence of spontaneous neoplasia is relatively high in certain strains of Syrian hamsters, particularly in animals over two years of age. Hamsters are particularly susceptible to induced tumors and their evertible cheek pouches are a favourite site for both induction and transplantation studies.

Hereditary cardiomyopathy, transmitted by an autosomal recessive gene, is occasionally observed in inbred hamsters. Myopathy and death from cardiac necrosis occurs in a high percentage of animals so affected, at about 120 days.

4. Antibiotic Sensitivity

Gastrogenic diarrhea results from use of antibiotics, such as penicillin, that act against Gram positive intestinal bacteria (Stoliker, 1981). Antibiotic toxicity is of very real concern in this species, with penicillin, lincomycin and erythromycin being regarded as toxic to varying degrees and contraindicated in the treatment of infectious (bacterial) diseases in the hamster. Tetracycline has also been reported as causing a fatal enterotoxemia at 50 mg/kg s.c., unless sulfaguanidine was administered simultaneously (Harkness and Wagner, 1983).

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