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Unusual Mammalian Models

Unusual Laboratory Rodent Species: Research Uses, Care, and Associated Biohazards

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INTRODUCTION

Although laboratory rats, mice, guinea pigs, and hamsters account for the majority of rodents used in biomedical research, wild rodent species are used infrequently to study various disease processes. Rodents are the largest mammalian order with more than one-third of the genera, and they account for over one-half of the total known species of living mammals (Clark 1984). Based on similarities in skull and mandibular structure and in the origins of portions of the masseter muscle complex, rodents have historically been ascribed to one of the following 3 groups: sciuromorph, myomorph, or hystricomorph. While there are a few breeding colonies of unusual rodents maintained by research institutions, these species cannot be considered domesticated.

Prior to using any of these species in a research project, there are several factors the scientist, animal care staff, veterinarians, and institutional animal care and use committee (IACUC) should consider. Many of these species represent a biohazard to the research and animal care staff. Wild rodents may serve as reservoirs for diseases with zoonotic potential such as plague, Lyme disease, hantavirus, or one of the many other hemorrhagic fevers. These species may also have special environmental or nutritional requirements that must be satisfied. A previously published report in *ILAR News* provides an excellent and still relevant annotated bibliography and review of uncommonly used laboratory mammals (Fine and others 1986).

This manuscript is intended to provide the reader with an understanding of the value of some of the more frequently used wild rodents in biomedical research, special husbandry considerations that are associated with their use, and potential hazards they may present to research and animal care personnel. It is not intended to be a complete review of all unusual rodent models. Particular attention will be given to voles *(Microtus* and *Clethrionomys),* deer mice *(Peromyscus spp.),* cotton rats *(Sigmodon hispidus),* ground squirrels *(Spermophilus spp.),* trumpet-tailed rats *(Octodon degus), the* multimammate rat *(Praomys [Mastomys] coucha),* and woodchucks *(Marmota spp.).* A more complete list of unusual rodents used in biomedical research may be found in Table 1.

USES IN RESEARCH

Because rodents exist in relatively high density, often live in close proximity to humans, and have similar nutritional requirements to humans, they are frequently used in field studies investigating environmental impact. The effect of chemical or physical insults to the environment on indigenous rodents can give insight into hazards that could threaten other mammalian species, including human beings. Many of these investigations are retrospective, indicating potential hazards after exposure. Population biology studies of voles, ground squirrels, and chipmunks have been done to investigate the immediate and long-term effects of pesticides and chemical spills on the environment. Knowledge of the effect of these chemicals on local rodent populations and measurements of tissue residues indicate the potential effect of toxins on the predatory species that rely on rodents as a source of food. Toxicologic investigations are also conducted in laboratory settings to study the potential effects of herbicides and insecticides used in agribusiness.

Many wild rodent species have been used as models of human disease in biomedical research laboratories because a disease process either occurs naturally or can be induced via surgical, nutritional, or environmental manipulation. Muroidea rodents also represent a group of animals with potential for use in comparative behavioral studies (Dewsbury 1974, 1984).

Voles

Of the 62 species *of Microtus,* only a few have been used to any significant extent in research. They are *M. pennsylvanicus* (meadow vole), *M. montanus* (mountain vole), M. *oeconomus* (tundra vole), and *M. ochrogaster* (prairie vole). *Clethrionomys rutilus* (red-backed vole) is another genus and species of vole used in research (Dieterich and

Preston 1977, 1979).

M. pennsylvanicus have been found to be a reliable bio-assay subject to test for the nutritive quality of food plants as well as the presence of toxins (Schillinger and Elliot 1966; Kendall and Scherwood 1975). Some meadow voles are predisposed to prolonged tonic-clonic seizures when stressed (Bronson and De La Rosa 1994). Seizures are induced by handling the animals or exposing them to a strange environment and are preceded by a period of slow head-shaking or a stilted gait. The genetic trait resulting in seizure activity can be used as a model for epileptiform seizures in humans. The fact that seizure activity has been exhibited in wild-caught voles lends this species to the study of naturally occurring variation in the genetic and neurological levels of control of seizure susceptibility in a mammalian species other than human beings (Bronson and De La Rosa 1994).

M. montanus has been proposed as a suitable model for the study of acute *Trypanosoma brucei* infection. However, since encephalitis with parasitemia of brain tissue is only occasionally observed, the mountain vole is not suitable for the study of chronic African sleeping sickness with cerebral involvement (Bafort and Schmidt 1984). *M. oeconomus* has been used to study the effects of cholesterol with atherogenic diets (Dieterich and Preston 1979). *Microtus* have also been used to study trypanosomiasis (Frommel and others 1991), and cells from *Microtus* have been used to culture *Trypanosoma brucei* (Himmi and others 1992; Alafiatayo and others 1994).

Deer Mice

Peromyscus maniculatus and *P. leucopus* are the most common species of deer mice used in research. Since *Peromyscus* raised in the laboratory live at least twice as long as laboratory mice, investigators have found this species to be useful for studying comparative aspects of the biology of aging (Harrison and others 1978; Hart and others 1979; Fry and others 1981; Martin and others 1983; Cutler 1985; Burger and Gochfeld 1992). Comparative studies investigating how wounds heal in aging murine species showed a more rapid rate of wound repair with increased age in *Peromyscus* when compared to C57BL/6J mice. This finding is contrary to the assumption that the rate of wound healing decreases with age in all mammalian species (Cohen and others 1987).

Peromyscus maniculatus is a useful model of both hereditary and senile cataracts (Tripathi and others 1991). Cataracts in deer mice occur as an autosomal recessive trait in 2 forms. Type I cataracts have an early onset developing by 90 days, while Type II have a later onset occurring 1 year after birth.

Convulsive mutants of several strains of deer mice have been described in which the tonic and clonic phases of the seizure, recovery, and post-convulsive behavior are almost identical to idiopathic epilepsy in human beings (Clark 1984). Deer mice have also proven to be a good animal model for human sleeping sickness caused by *Trypanosoma brucei,* with lesions characteristic of the disease in people (Moulton and Stephen 1978; Anosa and Kaneko 1984).

Ground Squirrels

Of the 28 species of ground squirrels in North America, *Spermophilus richardsonii* (Richardson ground squirrel), *Spermophilus beecheyi* (Beechey ground squirrel) and *Spermophilus tridecemlineatus* (the 13-lined ground squirrel) are the most commonly used in research. Cholesterol-fed Richardson ground squirrels have been used as a model to study aspects of cholelithiasis (Pemsingh and others 1988). The composition and configuration of the concretions formed closely resemble those of humans, and many of the pathologic events are similar to those of the human disease (MacPherson and others 1988).

Spontaneous diabetes mellitus has been reported in a laboratory-maintained colony of 13-lined ground squirrels that showed clinical signs of polyuria, glycosuria, ketonuria, polyphagia, and weight loss. Serum glucose values increased, while serum insulin levels concomitantly decreased (Clark 1984). It has also been reported that *S. tridecemlineatus* are resistant to marked hypercholesterolemia and atherosclerosis associated with a high cholesterol diets (Naito and Geffity 1979).

Beechey ground squirrels have been found to be susceptible to infection with ground squirrel hepatitis virus (GSHV), a virus with many of the characteristics of human hepatitis B virus and woodchuck hepatitis (Marion and others 1980).

It should be noted that with the exception of primates, ground squirrels and a few of their Sciuridae relatives are the only mammals known to have well-developed color vision (Jacobs and Yolton 1971; Gur and Purple 1978).

Cotton Rats

The cotton rat has been used for a number of different research purposes. Historically, *Sigmodon hispidus* has been used in studies of dental caries (Feller and others 1974), poliomyelitis (Perkins 1957), murine typhus (Worth and Rickard

1951), filariasis (Pringle and King 1968), and Venezuelan equine encephalitis (Howard 1974). It has also been used to study echinococcosis (Sakamoto and others 1965; Sousa and Thatcher 1969) and in behavioral studies (Powell 1973).

More recently, *S. hispidus* and *S. fulviventer* have been identified as the primary small mammal models for respiratory syncytial virus (RSV) (Prince and others 1978; Piedra and others 1989) and parainfluenza virus type 3 (PIV3) (Porter and others 1991). The cotton rat is the only known rodent model of human adenovirus type 5 (Ad-5) (Ginsberg and others 1989). *Sigmodon hispidus* develops pulmonary disease characterized by peribronchiolitis, while *S. fulviventer* develops an interstitial pneumonitis. This is of interest to scientists as these are the forms of pulmonary disease seen with human RSV and PIV3 infections. Wild cotton rats have also been reported to be an excellent toxicological model because they live in close proximity to people (Elangbam and others 1989).

Degus

The *Octodon degus,* more commonly known as the trumpet-tailed rat or degu, is a hystricomorph rodent in which congenital, hereditary cataracts occur naturally (Worgul and Rothstein 1975; Tripathi and others 1991). In mildly diabetic degus, cataracts form very rapidly with nuclear opacity developing in 10 to 12 days (Varma and others 1977). Spontaneous lesions from one colony, including cataracts, amyloidosis, and hyperplasia of the islets of Langerhans, were associated with diabetes mellitus (Murphy and others 1980). In addition to cataracts and diabetes, the degu has been used as a model to study the effects of chemotoxic agents on ocular tissue (Weinsieder 1975) and the role of the thymus in immune reactions (Boraker 1975).

Woodchucks

The captive and laboratory-reared woodchuck *(Marmota monax)* may develop many of the nutritional and medical problems that plague human beings in modern society (Young and Sims 1979). Obesity, cardiovascular disease, and neoplasia all occur in the laboratory marmot. Hibernators appear to have a sliding set point for body weight (Mrosovsky and Fisher 1970), which makes the woodchuck a useful model for studying neuroendocrine control of body weight. Likewise, weight gain in *M. monax* parallels the situation in adult human beings, with many of the same metabolic changes (Young and Sims 1979). A high incidence of arteriosclerosis, aortic rupture, and cerebrovascular disease has also been reported (Snyder and Ratcliffe 1969; Bond 1970).

Early reports of hepatocellular carcinoma in woodchucks have led to the discovery that this disease is associated with a hepa-DNA-virus (Robinson and others 1981). In addition to woodchuck hepatitis virus (WHV), this family of viruses includes Pekin duck hepatitis virus, ground squirrel hepatitis virus, and human hepatitis B virus (HBV). The close structural similarities and clinical pathology between WHV and HBV makes the woodchuck an excellent model for studying persistent hepatitis virus infections and their relation to the development of hepatocellular carcinoma. The woodchuck has been suggested as a model for the investigation of the interaction between schistosomiasis and viral hepatitis in the pathogenesis of chronic liver disease (Anderson and others 1991). Investigations have also been undertaken to study the inter-relationship between herpes virus of marmots and its possible role in the pathogenesis of WHV (Schechter and others 1988).

Mastomys

Praomys (Mastomys) coucha formerly *Mastomys natalensis* has made valuable contributions to biomedical investigations. The species has a high incidence of neoplastic disease and pre-neoplastic lesions (Hollander and Higginson 1971; Stewart and Snell 1975; Solleveld and others 1982). Captive mastomys have been found to develop spontaneous tumors of the glandular stomach (Oettle 1955) with the Y and Z strains developing carcinoids as well as antral adenocarcinomas that are anatomically and histologically analogous to those found in human beings (Randeria 1979). Mastomys are also afflicted with a high incidence of keratoacanthomas and squamous carcinomas associated with the papilloma-virus, *M. natalensis* papillomavirus (MnPV), which may be a useful model for tumorigenesis of cutaneous epithelia in human beings (Tan and others 1994).

While spontaneous thyroiditis in mastomys generally resembles lymphocytic thyroiditis in humans, there are some differences. Other spontaneous models of autoimmune thyroiditis include the obese strain of chickens, BUF rats, BB Wistar rats, marmosets, and beagle dogs. Each model has advantages for studying different aspects of the disease. Since it is not known which animal model best parallels the disease in people, investigations of the pathogenesis of autoimmune thyroiditis should not be confined to a single animal species (Solleveld and others 1985).

Both gastric and duodenal ulcer disease have been studied in the multimammate rat (Andre and Andre 1981; Andre and others 1985; Smedley and others 1990). Gastric ulcers induced by mucosal anaphylaxis in mastomys is similar to peptic ulceration in humans in that perforation and massive hemorrhage is a major complication. Ulceration in other experimental models more often tends to be superficial erosions (Andre and Andre 1981). This rodent has also been used

extensively in parasitology studies investigating schistosomiasis (Lurie and de Meillon 1956; Schuster-Nielsen and others 1973), Brug's filariasis (Petranyi and others 1975), and toxoplasmosis (Werner and Egger 1974).

SPECIAL HUSBANDRY CONSIDERATIONS

With the exception of woodchucks, the rodents discussed here can easily be housed in polycarbonate rodent caging on contact bedding. Woodchucks are best housed in pens with smooth walls to prevent climbing, but can be housed in stainless steel caging for dogs or cats. Solid floors will help to prevent excessive nail trauma. Although woodchucks can be robust in stature, with time they can work their way through any opening large enough to admit their head. All caging for woodchucks must be modified and maintained to prevent escape. Small rodents should be housed in contact bedding with either Nestlets® (Ancare Corp.) or unbleached cotton batting provided as nesting material.

As a general rule, the rodents covered in this manuscript drink from water bottles and adapt well to automatic watering systems. Commercially available laboratory rodent chow is an adequate diet for most wild rodents. Prairie voles, montane voles, and woodchucks require diets formulated for laboratory rabbits to meet their nutritional requirements.

A photoperiod of 12 hours of light and 12 hours of darkness is adequate for colony maintenance, however a lighting regime with 14 hours of light and 10 hours of darkness or 16 hours of light and 8 hours of darkness may promote breeding. Hibernating rodents may require lighting which matches the natural circannual cycle.

Voles

The prairie vole *(M. ochrogaster)* has a social structure in which monogamous relationships are established and both parents share responsibilities for raising offspring. Young remain as a part of a family group until they are ready to establish their own relationships, and sexual activity among family members is rare (Touchette 1994). His dedication to family has led some to describe the male prairie vole as the "model male" (Haller 1994). In contrast, the meadow vole *(M. pennsylvanicus)* is promiscuous and the sexes nest separately. Pine voles *(Microtus pinetorum)* display a cooperative system of breeding in social groups consisting of 2 to 9 animals in which only I female reproduces, but all members of the group contribute to the care of the young born in the nest (Solomon and Vandenbergh 1994). Presence of prairie vole fathers within the family group accelerates pup development, while meadow vole pups reared with fathers present develop less rapidly (McGuire and others 1992). Knowledge of these differences in behavior is important in establishing breeding strategies.

In general, voles are susceptible to pregnancy termination if exposed to males other than the stud male or urine from unknown males (Heske and Nelson 1984). A photoperiod of 14 hours of light and 10 hours of darkness is consistently cited in the literature as being appropriate for vole breeding colonies.

As previously mentioned, meadow voles may be prone to epileptiform seizures. When working with *M. pennsylvanicus,* seizure activity can occur in response to such mild disturbances as the vole being carried in its home cage from one room to another (Bronson and De La Rosa 1994). Seizures are not elicited by either auditory or olfactory stimulation as in some other rodent species.

Another husbandry consideration in this species is its high metabolic rate, and adaptation to herbivory. Meadow voles have evolved such that they subsist on a low calorie diet and must feed frequently. As such, this species of vole relies more heavily on the breakdown of carbohydrates during fasting. This carbohydrate catabolism results in profound hypoglycemia after only 6 hours of fasting (Nagy and Pistole 1988).

It has been reported that voles can detect the presence of various solutes added to drinking water (Laughlin and others 1975) which could complicate oral dosing in these animals.

Deer Mice

Deer mice adapt well to being housed in a vivarium and will live 6-8 years in a laboratory setting (Cohen 1987). Although they do well with a photoperiod of 12 hours of light and 12 hours of darkness, it should be kept in mind that alterations to the photoperiod may have an effect on their immune status. *P. maniculatus* housed using a photoperiod simulating short days have higher white blood cell and lymphocyte numbers than their cohorts housed in long-day conditions. Additionally, animals gestated in short-day conditions display a higher immune status throughout life (Blom and others 1994). It has also been reported that although deer mice develop a significant titer to MHV, they do not develop clinical manifestations of the disease, nor do they transmit the virus (Silverman and others 1982).

Ground Squirrels

Richardson ground squirrel, Beechey ground squirrel, and the 13-lined ground squirrel all hibernate in their natural habitat, however they may not do so when maintained in an environment that provides constant temperature, photoperiod, and food supply (Clark 1984). Under artificial conditions, they may go through periods of torpor and arousal with dormant periods lasting several days to weeks. The frequency of torpor varies between individuals and increases with age. Females enter torpor more frequently than do males (Davis and Swade 1983). Arousal periods in hibernating ground squirrels are dependent on ambient temperatures (Pengelley and Fischer 1968). Ground squirrels maintained in constant conditions display similar circannual cycles of food intake and body weight to their relatives in nature (Mrosovsky and Boshes 1986). During prehibernation fattening periods, the animals eat well and gain weight. They subsequently become anorexic and lose weight even when food is available ad libitum. Prolongation of clotting time has been observed in hibernating *Spermophilus franklinii* (Pivorun and Sinnamon 1981), *S. columbianus,* (Svihla and others 1951, 1952) and *S. tridecemlineatus* (Lechler and Penick 1963). If ground squirrels are allowed to remain in hibernation following blood collection, massive hemorrhage will result. Forced arousal will markedly decrease the likelihood of serious bleeding. Studies of other blood and circulatory changes in *S. tridecemlineatus* during hibernation showed a reduction in hematocrit and leukopenia and an increased mean corpuscular volume (Spurrier and Dawe 1972). These studies also exhibited an increased resistance of erythrocytes to hemolysis.

Cotton Rats

Both *S. hispidus* and *S. fulviventer* breed well in captivity. However, if young are allowed to remain with the parents, cannibalism may occur once they reach puberty. Overcrowding and unsupervised pairing may also result in increased mortality due to fighting (Williams 1980). If cotton rats are to be housed in groups, these must be established before the rats reach puberty, and the groups observed closely for aggressive individuals. If an aggressor is identified, it should be removed from the group, but observation of the group for other aggressive individuals must continue. Permanent breeding pairs should be established at 6 to 7 weeks of age.

Degus

In nature, degus are communal animals living in extended family groups. Females are induced ovulators. Captive degus reproduce year round, giving birth to an average litter of 5 precocial offspring. Since young are active, physically and behaviorally mature, and far advanced developmentally as compared with the more commonly used laboratory rodents, degus may be a superior animal for investigation of early experience and development (Reynolds and Wright 1979). This species is diurnal, and although they store food in burrows in a natural setting, they neither hibernate nor estivate. Degus adapt well to the laboratory environment, thrive on commercial rodent diet, and have been housed successfully in wire-bottomed caging as well as on contact bedding (Fine and others 1986). It should be noted that O. *degus* has an extremely high tolerance to the pharmacologic effects of morphine (Villanueva and others 1980; Pelissier and others 1989), and has a greater ability to metabolize drugs than do other rodent species (Gaule and others 1990)

Woodchucks

Woodchucks are solitary and generally agonistic (Fine and others 1986). Although young males and females can be housed together through their first winter, adult males must be housed singly until breeding season when they can be paired with a mate for breeding. Once the testes have ascended back into the abdomen, male woodchucks may be housed together. Adult females can be housed in small groups, however, these groups must be closely monitored to ensure that the dominant female does not monopolize the food. Pregnant females should be separated from the group, and housed singly until 5-10 days following weaning. In all group housing situations, cage complexities in which the animals can hide must be provided. The recommended diet for woodchucks is commercial rabbit diet processed into 9x16 mm blocks. This reduces spillage and forces the animal to gnaw, helping to prevent overgrowth of the incisors (Young and Sims 1979).

Woodchucks hibernate in a manner similar to ground squirrels. Although woodchucks normally fast throughout the winter period, individuals may awaken periodically and should be provided access to food and water. Those that do awaken have a lower metabolic rate and eat and drink less than normal. In a vivarium, induction of hibernation requires reduced temperature and withdrawal of food (Davis 1976; Young and Sims 1979). Forced hibernation has been reported to result in increased mortality and morbidity and decreased fertility (Concannon and others 1989). As such, woodchucks not involved in hibernation studies have been maintained in a euthermic environment with unrestricted access to food and water and a constant photoperiod. However, at least one study indicates that long-term exposure of marmots to 12L:12D photoperiods and interruption of the natural circannual cycles can result in alterations in the animal's metabolic or reproductive state (Concannon 1992).

Mastomys

Multimammate rats form monogamous pairs and reproduce well in captivity. Although they do not appear to be

aggressive in the wild, they may bite without provocation in the laboratory and require consistent handling to tame (Williams 1980). Their life span in captivity is between 2 and 3 years.

POTENTIAL ZOONOSES AND BIOHAZARDS

Virtually all of the wild rodent species used in research pose a potential risk to laboratory personnel in the form of zoonotic diseases. Even though animals from long standing laboratory or commercial colonies present less of a risk, individuals working with these species must be aware of the potential hazards they represent. Wild-caught rodents can pose a serious health threat. Lyme disease and hantavirus are currently the most publicized zoonoses found in wild rodents.

Hantaviruses are carried by a number of different rodent species and can exhibit a wide spectrum of pathogenicity for humans. Three major pathogenic forms of the disease exist. Hemorrhagic fever with renal syndrome (HFRS) is caused by serotypes Hantaan, Seoul, and Puumala. In 1993, hantavirus pulmonary syndrome, a deadly hantavirus-associated disease, was identified in the Four Comers region of Arizona, Colorado, New Mexico, and Utah and has been subsequently named Sin Nombre Virus (CDC 1994). In addition, a novel hantavirus, Tula virus, which is closely related to the Sin Nombre strain was discovered in European common voles *(Microtus arvalis* and *Microtus rossiaemeridionalis)* (Plyusnin and others 1994). Since May of 1993 hantavirus pulmonary syndrome in the United States has been identified in 17 different states (Khan and others 1995). Prior to the emergence of hantavirus pulmonary syndrome, the only 2 recognized hantaviruses in North America were Seoul virus and Prospect Hill virus. Both strains had been isolated from wild and laboratory rodents, but had not been shown to cause acute human infections in the United States (Schmaljohn and others 1995). *P. maniculatus, P. leucopus, M. pennsylvanicus, C. rutilus,* and *C. glareolus* are wild rodent species used in research that have been identified as reservoirs for at least I strain of hantavirus pathogenic to people (Yanagihara and others 1985, 1987; Nerurkar and others 1993; Telford and others 1995)

P. leucopus is the rodent species most commonly associated with *Borrelia burgdorferi,* the causative agent for Lyme disease. However, *P. maniculatus* and *M. pennsylvanicus* have also been implicated as potential rodent reservoirs (Anderson and others 1986; Burgess and others 1986). The bank vole, C. *glareolus,* has been shown to infect larval ticks with the causative agent of Lyme disease as well (Tallenklint and others 1993). Transmission of *Borrelia burgdo.rJbri* is accomplished via the tick vector, primarily by *lxodes dammini,* commonly called the deer tick. However, experimental inoculation of *Peromyscus* with *B. burgdorferi* resulted in subsequent transmission to naive deer mice indicating that transmission can occur by direct contact without an arthropod vector (Burgess 1986). *P. leucopus* and *M. pennsylvanicus* also serve as rodent reservoirs for *Babesia microti* the etiologic agent for human babesiosis. This is a rare, but potentially fatal disease affecting the red blood cells of human beings and causing malaria-like symptoms. As with Lyme disease, nymphal deer ticks serve as the vector (Anderson and others 1986).

A variety of wild rodents used in research can serve as vectors for viral hemorrhagic fevers, acute febrile viral illnesses caused by arenaviruses. The viral hemorrhagic fever syndromes share similar signs consisting of gradual onset with malaise, headache, retroorbital pain, and sustained fever. Generalized petechiae and ecchymoses may be evident. In severe cases, epistaxis, hematemesis, melena, and hematuria occur. Bradycardia and hypotensive shock may result in the death of the patient (Anderson and others 1986). Junin virus is the infectious agent for Argentine hemorrhagic fever, while Machupo virus is responsible for the Bolivian disease. The vesper mouse *(Calomys spp.)* is a South American rodent occasionally used in research, which serves as a reservoir for these viruses. Lassa virus is an arenavirus closely related to Junin and Machupo and is the causative agent for Lassa fever. The multimammate rat *(M. natalensis)* serves as a reservoir. Transmission occurs primarily through direct contact with excreta of infected rodents, however, airborne transmission may occur via contaminated dust or aerosols.

Rodents and lagomorphs have not been considered to be important reservoirs or vectors of rabies, nor have exposure to these species ever been shown to cause the disease in humans in the United States (Fishbein 1986). However, woodchucks have become involved in rabies epizootics in the mid-Atlantic region by virtue of their competition with raccoons for den sites. Rabies does occur in other rodent species, but is rare.

Although *Yersinia pestis* has been found in 230 species of wild rodents (Acha and Szyfres 1987), ground squirrels serve as the primary reservoir for plague (Anderson and others 1986). Susceptibility varies between different rodent species. Prairie dogs and Beechey ground squirrels are highly susceptible while certain species of *Microtus* and *Peromyscus* are resistant (Acha and Szyfres 1987). Sylvatic plague perpetuates itself in nature by a continuous cycling in which the etiologic agent is transmitted from rodent to rodent by the flea vector. Resistant animals serve to harbor the bacterium, while susceptible individuals die. Epizootics occur when there are large numbers of susceptible rodents, however, the infection continues in enzootic form within the surviving population. In human beings, the initial signs are that of lymphadenitis in those lymph nodes receiving drainage from the site of a bite from an infective flea. This is referred to as the bubonic form of plague. If untreated, spread of *Y. pestis* via the bloodstream can result in dissemination to other organ systems. Pneumonic plague is of particular concern since aerosolized sputum may serve to transmit the organism directly.

Francisella tularensis, the causative agent of tularemia was originally isolated from ground squirrels (McCoy and Chapin 1912), and has more recently been reported in prairie dogs (La Regina and others 1986). Human beings can be exposed to *F. tularensis* via open wounds while handling infected carcasses, through animal bites and scratches, or by blood sucking insects (La Regina and others 1986). The most common clinical manifestations, ulceroglandular tularemia, is characterized by fever, a skin pustule or ulceration at the site of inoculation, lymphadenitis, headache, and nausea. Less common forms of the disease include the pulmonary form, oropharyngeal form, and oculoglandular form (La Regina and others 1986).

Other potentially zoonotic bacterial, mycotic, viral, and parasitic agents may also be found in wild rodents, however, it is beyond the scope of this manuscript to detail these infections. Diligent monitoring of the health status of rodent colonies and the use of appropriate personal protective equipment such as latex gloves and surgical masks or respirators can help prevent the transmission of these agents to humans. Education of institutional or contract health and hygiene support personnel as to the potential health risks posed by different animal species is essential.

SUMMARY

Wild rodent species have proven to be valuable resources in biomedical and environmental research. Because they are mammals and because many of these species live in close proximity to people, wild rodents are of particular importance in studying toxicological insults to the environment. As in the case of cotton rats and human adenovirus (Ad-5), a wild rodent may be the only animal model for studying a disease process, however, in many cases wild rodents are but one of many potential animal models.

When using any of these rodents in the laboratory, the scientist and IACUC must carefully consider special husbandry needs and potential biohazards against the true value of the model. Care must be taken to ensure that a laboratory and vivarium environment is provided that meets the needs of the species. Although some wild rodents can be kept in an environment designed to house standard laboratory rodents, desert rodents cannot be adequately kept in an artificial environment where humidity levels are maintained above 50 percent. Every effort must be made to monitor the health status of the rodents for potential zoonoses, and to control or eliminate potential insect and arthropod vectors of disease.

With diligent preparation and prudent precautions, wild rodents can safely serve to enhance our scientific knowledge and assist in efforts to develop effective measures to treat and prevent many of the disease processes that plague humankind.

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TABLE 1 Unusual rodents used in biomedical research (bolded species are covered within this manuscript)

Suborder	**Genus and Species**	**Common Name(s)**
Myomorpha	***Peromyscus leucopus***	**white-footed deer mouse**
	Peromyscus maniculatus	**common deer mouse**
	Microtus pennsylvanicus	**meadow vole**
	Microtus montanus	**mountain vole**
	Microtus oeconomus	**tundra vole**
	Microtus ochrogaster	**prairie vole**
	Microtus pinetorum	**pine vole**
	Clethrionomys rutilus	**red-backed vole**
	Clethrionomys glareolus	**bank vole**
	Sigmodon hispidus; Sigmodon fulviventer	**cotton rat**
	Praomys (Mastomys) coucha--formerly Mastomys natalensis	**multimammate mouse; multimammate rat; mastomys**
	Calomys callosus	vesper mouse
	Dicrostonyx stevensonii	Collard lemming
	Psammomys obesus	Obese sand rat
	Oryzomys palustris; Oryzomys minutis	rice rat
	Mystromys albacaudatus	South African hamster; white-tailed rat
Sciuromorpha	***Marmota monax***	**woodchuck; ground hog; marmot; whistle pig**
	Spermophilus richardsonii	**Richardson ground squirrel**

	Spermophilus franklinii	**Franklin's ground squirrel**
	Spermophilus beecheyi	**Beechey ground squirrel**
	Spermophilus columbianus	ground squirrel
	Spermophilus tridecemlineatus	13-lined ground squirrel
	Sciurus niger	fox squirrel
	Sciuris carolinensis	gray squirrel
	Cynomys ludovicianus	black-tailed prairie dog
Histricomorpha	***Octodon degus***	**degu; trumpet-tailed rat**
	Chinchilla laniger	chinchilla

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