Chapter 1

Introduction, General Husbandry, and Disease Prevention

INTRODUCTION

Populations of rabbits, rodents, and other small mammal pets are difficult to estimate; however, a 2017 study conducted by the American Veterinary Medical Association (AVMA) estimated that more than 13% of US families keep these species as companion animals, including approximately 3.2 million rabbits, 1.4 million guinea pigs, 1.1 million hamsters, and 470,000 gerbils. However, only about 1.8% of these owners obtain annual veterinary care for their small mammal companions.

Numbers of animals used in research are also difficult to determine because of the limitations of applicable surveys and estimates where fixed data do not exist. Based on United States Department of Agriculture Animal and Plant Health Inspection Service (USDA-APHIS) data, approximately 107,000 hamsters, 197,000 guinea pigs, and 144,000 rabbits were used in the United States in research, testing, and teaching in 2021, whereas many fewer numbers of gerbils and chinchillas were used. The numbers of rats and mice used are significantly more difficult to estimate because these data are not collected or reported by US federal agencies. Approximately 1.3 million mice were used in Canada in 2022, and this accounted for 38% of animals used in research (www.ccac.ca). Estimates of mice used in the United States in biomedical research range from 6 to 20 million mice per year. It is even more difficult to find accurate references for numbers of rats used annually in research, although estimates of up to four million have been suggested. Mice and rats are typically thought to account for up to 85% of all animals used in research in the United States, although significant numbers of fish, poultry, swine, and cattle are also used for food and fiber research. Availability of genetically characterized strains and stocks with increased relevance to the diseases being studied, sequencing of the mouse and rat genomes (completed in 2002 and 2004, respectively), development of new transgenic technologies, and ease and economy of housing large numbers of animals have significantly contributed to the popularity of rodents as models for many aspects of biomedical research.

Rabbits are the third most common farmed animal species in the world with almost one billion slaughtered annually, and global production increased by almost 10% between 2008 and 2018. In 2020, China accounted for ~38% of world production of rabbit meat with approximately 314 million rabbits produced annually, followed by Europe at 20% with 117 million rabbits (http://faostat.fao.org/en). Both the United States and Canada account for a negligible amount of world rabbit meat production. Production is by and large proportional to per capita consumption, as rabbit meat is rarely exported from North America; however, increasing amounts of rabbit meat are being incorporated into premium companion animal feeds, necessitating import of frozen rabbit meat from outside of North America. Specific legislation covering meat rabbit production and welfare is lacking in many countries, including the European Union and China, although a new rabbit code of practice was published in Canada in 2018.

With the exception of China, the number of rabbits used for fur, felt, and pelt production is much lower than the number raised for food consumption. Rabbit pelts harvested at slaughter for meat are typically of poor quality, as breed, age at harvest, time of year, and husbandry conditions differ significantly for optimal production of meat compared with pelts. Rex rabbits are the primary breed used for pelt harvest, whereas angora rabbit hair is brushed and shorn regularly for yarn production and weaving. China is the world's largest producer of rabbit pelts and angora fiber today, but the industry lacks national welfare oversight and standards, bringing into question the ethics of angora fur production.

Chinchillas have been used by humans as a source of pelts for clothing for centuries, a practice that drove them to near extinction in the wild in the early twentieth century. In 1983, it was estimated that the United States led production of chinchilla pelts, but by the late twentieth century, South American and eastern European suppliers significantly outpaced US and Canadian production. The industry is decreasing in size with a global estimated production of 80,000 pelts in 2023. Public perception about the use of animal pelts for fashion has led to

Harkness and Wagner's: Biology and Medicine of Rabbits and Rodents, Sixth Edition. Patricia V. Turner, Colette L. Wheler, Hugues Beaufrère, Niora Fabian, and John E. Harkness.

development of specific industry husbandry guidelines as well as US state bans, and other country bans on fur farming.

While veterinary care is relevant for all the aforementioned reasons, the subjects of this book—rabbits, guinea pigs, chinchillas, hamsters, gerbils, mice, and rats—are becoming increasingly popular as companion animals. As a result, veterinary practitioners should expect to see them as patients, regardless of whether they work in exotic specialty practices or more traditional veterinary animal clinics.

Certainly, the human–animal bond applies regardless of animal size, and companion rabbit or rodent owners are often frustrated in their attempts to find veterinarians who are knowledgeable about their small mammal companions. Problems of management and husbandry are often at the root of several disease conditions and can often be addressed by appropriate client education. Small mammal practice does require a modicum of special knowledge; however, careful extrapolation of experiences from other small animals (i.e., dogs and cats) to rabbits and rodents is often useful and appropriate. Common disease conditions not encountered in dogs and cats must be understood though, before attending to small mammal species, such as specific gastrointestinal conditions, antimicrobial sensitivities, dentistry issues, and various infectious diseases, including some that are zoonotic. Small animal clinicians can become competent with most small mammal problems through continuing professional development, and practitioners inclined to develop a client base in this area should not be deterred because of a perceived lack of specialized veterinary training.

Veterinary clinicians are likely to encounter rabbits and rodents in a wide spectrum of situations, presenting a significant challenge when compiling literature regarding management of health and diseases of these species. For example, rabbits and rodents are produced by commercial breeders for the purposes of research and testing. Most animals raised in this manner are reared in specific pathogen-free (SPF) barriers that preclude introduction of disease agents, and they are sold to research establishments that maintain highly controlled environments for housing these animals. Because of the sophisticated nature of some research, these animals are usually defined physiologically, genetically, and microbiologically. In contrast, rodents and rabbits in the retail pet trade have less certain genetic identification and health histories, and are often managed in ways that do not limit disease transmission among species and conspecifics, including mixing of species from different sources in large distribution centers. Commercial breeding operations for food and fiber production are intermediate between these two scenarios, emphasizing production as a goal, and employing management schemes that result in yet a third spectrum of disease issues. For example, in rabbits, the prevalence of certain diseases tends to be radically different between companion, laboratory, and meat animals. Therefore, medical challenges for private practitioners evaluating small mammal pets are substantially different from those seen by institutional laboratory animal veterinarians, and veterinarians treating animals in meat or fiber operations.

Early literature describing the attributes of these species originated from the laboratory animal and commercial breeder industry; however, more recent texts have been developed with the private practitioner in mind, adopting an individual animal approach versus a herd health approach to treatment. Although the biology, physiology, and disease susceptibility of animals reared and kept for research or as companion animals are similar, differences in purpose and management requirements should be kept in mind when reviewing the available literature on these animals. For example, housing requirements for mice held in a laboratory animal facility emphasize environmental and microbiological controls for the sake of experimental uniformity. These standards may exceed practical recommendations for owners rearing fancy mice for show or breeding rodent prey for reptile feeding. Diseases described in the laboratory animal literature are typically those seen in specific strains and ages most commonly used for research (i.e., SPF, genetically defined stocks of rodents, and New Zealand white rabbits) and are likely to differ substantially from common conditions of rodents purchased at the local pet store, chinchillas managed in a production setting or neutered geriatric house rabbits. Treatment of animals reared for food or fur production may be limited due to the impact of drug residues or damage to pelts. Thus, it is important to use professional judgment when evaluating the literature and to consider the differences in management and purpose when formulating an appropriate diagnostic and therapeutic plan for each case.

SOURCES OF INFORMATION

References for veterinarians who see rabbits and rodents in private practice are readily available. Web resources abound, but should be regarded with some caution if unreferenced or not evidence-based. LafeberVet (lafeber.com/vet/) is a useful, free online resource for veterinarians that requires an initial registration and provides excellent articles and videos on treating exotic companion animals, including small mammals. General references related to the practice of rabbit and rodent medicine are listed at the end of this chapter. Species-specific references are provided in the other chapters. This text emphasizes general references and indices of current literature rather than exhaustive literature reviews.

Knowledge about rabbits and rodents varies considerably among veterinarians. Even among the most knowledgeable and successful practitioners, recommendations for treatment vary, depending on personal experience and geographic area of practice, which may determine the nature of conditions seen as well as the general availability of therapeutics with which to treat different conditions. The Veterinary Information Network (VIN, www.vin.com) is a subscription-only online network that supports dialogue among veterinary practitioners,

including specialists in rabbit and rodent medicine. Membership in VIN also provides ready access to a searchable literature, webinar, and case database that includes many exotic species. Laboratory animal veterinarians have extensive training in these species, particularly in matters relating to biology, husbandry, and disease. Diagnostic laboratories specializing in rodent and rabbit diseases also can be helpful in suggesting appropriate work-ups or providing necropsy and specialized diagnostic services. Companion animal veterinarians may need to seek diagnostic laboratories that specialize in research rodent or rabbit health monitoring for specific testing of certain infectious agents, because many laboratories geared to domestic animals do not provide these tests. Similarly, diagnostic expertise and availability of specific, validated assays for use in meat or fur-bearing species is limited.

TAXONOMY AND HISTORY

Detailed taxonomy and history of domestication of rabbits and rodents can be found in Chapter 2. Until the early 1900s, rabbits and rodents were classified similarly; however, anatomic and physiologic studies indicated significant differences leading to reclassification of rabbits in their own distinct order. Rabbits are members of the family Leporidae in the order Lagomorpha, whereas rodents are members of the order Rodentia. Rats, mice, gerbils, and hamsters are in the suborder Myomorpha ("rat-like," a clade of Myodonta), while guinea pigs, degus, and chinchillas are classified in the suborder Hystricomorpha ("porcupine-like," a clade of Ctenohystrica). Differences in classification of rabbits and rodents relate to jaw musculature, dental anatomy and physiology, as well as to differences in nutrition, gastrointestinal function, reproduction, and molecular data. Rabbits and rodents belong to the monophyletic clade of the Glires.

Rabbits and guinea pigs have been used for food (and domesticated to the extent of captive production for this purpose) for centuries; however, during the last century, breeding of these species, as well as of chinchillas, commenced for other purposes. This included the widescale production of pelts (rabbits, chinchillas), use in biomedical research (primarily rabbits and guinea pigs), and as fancy show animals. Whereas mention is made of domestication of mice in Asia as long ago as 1100 B.C., modern fancy rats and mice were first domesticated in the late nineteenth century. Though rats were occasionally used for food in times of famine, their initial domestication was for the once popular sport of rat-baiting, in which several rats were placed in a pit and bets collected on how long it would take a terrier to decimate the captives. Fancy rats and mice are relatively popular, and are judged in shows based upon size, color, and behavior. As discussed, rats and mice are the predominant mammals worked with in biomedical research; development of inbred and outbred stocks in the early twentieth century preceded the current explosion of genetically engineered strains (see below). Hamsters and gerbils were more recently domesticated and were introduced as companion and research animals in the 1950s. All these species became popular as small mammal companions starting in the 1960s, concurrent with their availability in pet stores and from private breeders, and with growth of urban and suburban communities.

BEHAVIOR

An understanding of the natural behavior of these animals is essential if provision of appropriate husbandry and veterinary care is to be made. All of the species described in this text are prey species, and as such, they are generally stressed in the presence of a perceived predator, such as a cat or dog, and have developed adaptive behaviors to avoid predation. One of the most prevalent of these is the propensity for active behaviors to be concentrated either during the dark phase of the daily cycle (nocturnal activity), or during dawn and dusk transitions (crepuscular activity). This is most apparent in hamsters, which exhibit significant resistance to arousal during the light cycle, and is least apparent in guinea pigs, which scatter their activities over a 24-hour period. This fact may limit the ability of a clinician or owner to evaluate normal activity, in that the typical physical exam and evaluation will occur when the animal is less likely to be active, and may not be exhibiting evidence of pain. Behavioral evaluations are further complicated in that the "fight or flight" response initiated during an exam may override behaviors less conducive to overall survival. For this reason, evaluation during the dark phase and in the home cage can be beneficial for detecting subtle abnormalities. Evaluation in the home environment is often possible in a laboratory situation, and may be feasible when evaluating a colony-wide problem at a commercial breeding establishment. If animals must be moved from their normal area to an examination area, it is helpful to have a small, darkened, secure transport cage and to minimize sudden and loud noises in the area of the cage. Many practices have developed procedures for specifically accommodating these small mammal companions; for example, restricting appointments to times when no predator species will be present or partitioning waiting rooms (see below for welfare-friendly practice recommendations for small mammals).

Rabbits and rodents have highly developed senses of smell and hearing to aid in detection of predators. Therefore, it is likely less stressful to examine and house these animals outside the sight and smell of perceived predators. Prey species are often approached from above by predators, thus when picking up an animal, a slow, steady approach from the side will allow orientation to the movement. Rabbits and rodents are often calmed by a confident and encircling grasp, and by covering the eyes. This can be achieved by use of a towel or sleeve during the examination process.

In general, the amount of stress that may be induced by even minimally invasive clinical procedures should always be weighed against the benefit of intervention in rabbits and rodents to a far greater degree than is typically considered for dogs and cats. Stress can be minimized by thoughtful consideration of their natural behaviors, and by calm manipulations that take these behaviors into consideration.

REGULATORY CONSIDERATIONS

Rabbits and rodents worked with in biomedical research are subject to significant regulatory oversight. In the United States, the Animal Welfare Act (AWA), a Federal law promulgated by the Animal Welfare Division of USDA-APHIS, outlines provisions and standards expected for rabbits, guinea pigs, chinchillas, hamsters, and gerbils, as well as other mammals worked with in biomedical research. Rats of the genus *Rattus* and mice of the genus *Mus* specifically bred for use in research are exempt from AWA coverage. In 1998, USDA-APHIS issued a regulatory update advising that any retail pet store selling small mammals be licensed as a dealer subject to AWA regulations.

The Health Research Extension Act (HREA) provides standards for all vertebrate animals used in biomedical research funded by the United States Public Health Service (including the National Institutes of Health, Centers for Disease Control and Prevention, and Food and Drug Administration). Specific measures of the HREA are outlined in a document published by the National Academies Press (NAP) under the auspices of the Institute for Laboratory Animal Research (ILAR), a division of the National Research Council (NRC), entitled *The Guide for the Care and Use of Laboratory Animals,* and often referred to as "The Guide." Laboratory animal veterinarians, and those acting as veterinary consultants to facilities using animals in biomedical research, should be well versed in this document. This and other guidelines for use of animals in biomedical research are referenced at the end of this chapter.

Regulations regarding the use of laboratory animals also exist in many other countries, such as the UK, the E.U., Japan, and Australia. In Canada, the Canadian Council on Animal Care (CCAC) has developed guidelines for the care and use of animals in science. All vertebrate species, as well as cephalopods, are covered by these guidelines (www.ccac.ca). Any research institution holding animals and receiving Canadian federal funds for research must comply with CCAC guidelines and participate in periodic on-site assessments of their facilities and operations. Participation is optional for private institutions not receiving federal monies, but many organizations choose to comply with the CCAC guidelines to demonstrate a high level of commitment to humane animal care and use. The CCAC also has produced species-specific guidelines in recent years that detail specific requirements and expectations for care and housing of various animals, including rats and mice. Other small mammal species-specific guidelines may follow in the future.

Regardless of the national framework of regulatory oversight, many countries around the world, including the United States and Canada, have a requirement for a system of local ethical research oversight in the form of an Animal Care Committee or Animal Welfare Body. The main purpose of these bodies is to review the care and to safeguard the use of all animals housed in a facility for scientific purposes.

There is minimal specific legislation anywhere in the world that deals with the welfare requirements of rabbits raised for meat or rabbits and chinchillas raised for fiber and fur production. Whereas country-specific general transportation and slaughter regulations and guidelines apply to all animal species, rabbits are often combined with poultry when considering commercial production, with little regard for species-specific physiologic and behavioral differences and requirements. Canada has published and implemented a Code of Practice for the Care and Handling of Rabbits (http://www.nfacc.ca/codes-of-practice/rabbits), and this topic is also receiving increased attention in the E.U. by the European Food Safety Authority (EFSA).

GENETICALLY MODIFIED ANIMALS

Animals have been selectively bred for centuries to develop genetic characteristics desired by humans. Since the 1980s, advances in recombinant DNA technology have greatly accelerated the capacity to manipulate the genome of domesticated species, including that of mice, rats, and rabbits. This has been especially significant in mice, which have robust stem cells and blastocysts (early embryo stages) that are readily manipulated. In 1982, the first report of a genetically engineered mouse ("transgenic mouse") was demonstrated by inserting a growth hormone gene into the germline of an inbred mouse, resulting in an altered phenotype. Animals with the gene inserts weighed two to four times more than their nonmanipulated inbred siblings, providing a dramatic example of the utility of this technique. Further developments of this technology, and subsequent refinement of more sophisticated methods for specific gene targeting such as activation, deactivation or replacement with an experimental gene, have resulted in propagation of many thousands of strains of mice used in laboratory studies for investigations in such varied fields as infectious and congenital diseases, development and differentiation, toxicology, cancer, immunology, and neurobiology. Mice altered by one of these several methodologies are collectively known as genetically modified mice (GMM) (see Table 1.1 for examples).

The first widely used technique developed for insertion of foreign DNA into the germline of an animal was microinjection. With microinjection, early embryos (blastocysts) are

Table 1.1. Examples of some genetically modified mice (GMM) including production methods and uses in biomedical research.

Type of Modification	Procedure for Creation	Phenotype/Example
Oncogene expression, e.g., myc or ras	Microinjection	Expression evaluated in tissues for studies of tumorigenesis
Immune system alterations	Knockout or Clustered regularly interspaced short palindromic repeats (CRISPR)	Interferon, cytokine, interleukin or specific immunocyte knockouts with specific immunodeficiencies
Regulation of gene expression	Microinjection or knockout or CRISPR	Regulatory element mutations used to study fetoprotein expression
Creation of animal models of single-gene mutations	Knockout or CRISPR	Cystic fibrosis resulting from disabling cystic fibrosis transmembrane regulator gene in mice
Creation of models for study of HIV-AIDS	Microinjection	Mutated HIV transgene develops Kaposi's sarcoma skin lesions in mice
Development of sensitive tests for toxicologic screening	Microinjection or knockout or CRISPR	Mice expressing a marker gene with a disabled promoter region; reversion of the promoter to an active form following exposure to potential toxicants can be screened in vitro following tissue harvest

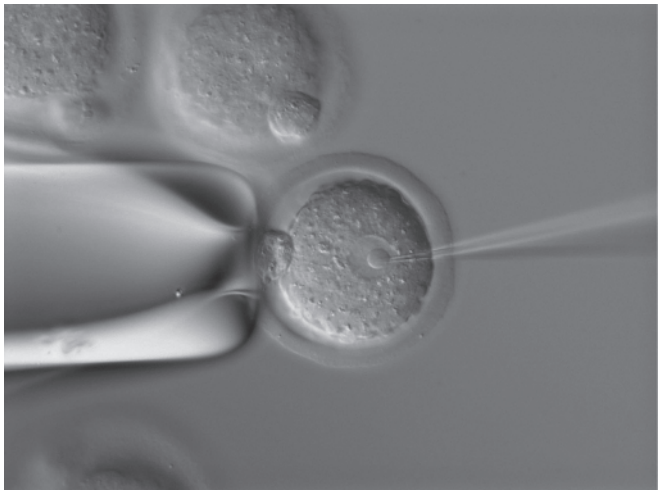


FIGURE 1.1. DNA being injected into an embryonic nucleus by microinjection. Courtesy of A. Bower and M. Baetscher.

removed from the female mouse and then, using a specialized microscope, a fine glass pipette is used to pierce the cell membrane and inject prepared DNA into one of the embryonic nuclei (Figure 1.1).

The injected embryos are then surgically implanted into another recipient female and pups are delivered at term and reared by the mother. Offspring are typically tested at or around weaning for evidence of incorporated microinjected DNA sequences. An experienced laboratory produces pups from 30% to 60% of injected embryos; 10–40% of these will be transgenic. This technique results in random insertion of multiple copies of DNA sequences (1–200 copies) into the mouse genome. Multiple rounds of breeding ensue onto an inbred strain to develop stable homozygous lines, which are then used for further experimental manipulations.

More sophisticated knock-out technologies were later developed using methods that specifically impair or insert new genes into a designated site within the genome. Two important discoveries preceded this technology: (1) the ability to grow mouse embryonic stem (ES) cells in culture, and (2) understanding the process of homologous recombination during DNA replication. Undifferentiated ES cells have the capacity to develop into any cell of the body when provided with appropriate cues; in the case of knock-out development, this includes mixing the stem cells with an early-stage embryo (blastocyst). Commonly, segments of DNA with the altered gene of interest are mixed in a culture with mouse ES cells. Cells are subjected to an electrical field that opens pores in the cell membrane (electroporation). Some of the electroporated ES cells take up foreign DNA; following cell division, homologous recombination occurs between the ES genome and foreign DNA in a small fraction of cells, resulting in inactivation of the gene of interest. Cells that have undergone recombination are selected, microinjected into blastocysts, and implanted into recipient female mice. A percentage of offspring will be born as chimeras, that is, with cells of both the wild-type embryo and the altered ES cells, and these can be detected visually if the ES cells and blastocysts are each generated from mice of different coat colors (Figure 1.2).

Genetic testing and breeding will eventually result in genetically characterized stable mouse lines. Experienced laboratories will produce approximately two lines per DNA targeting sequence attempted; it takes a year or more for this success. Even more sophisticated GMMs are being produced that conditionally express certain genes, allowing studies of the effects

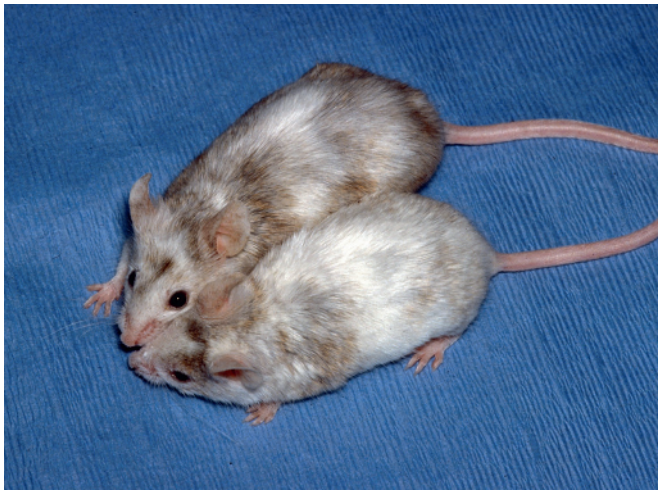


FIGURE 1.2. Two chimeric mice produced by knock-out technology. Courtesy of K. Pritchett-Corning.

of "turning on" or "turning off" a gene in a specific tissue or at a specific developmental stage, for example.

The effects of genetic modification are unpredictable and may result in subtle phenotypic alterations that may not be clinically obvious. Clinical veterinarians and veterinary pathologists have played an important role in developing, standardizing, and cataloging mutant phenotypes, which in combination with complete genome sequences results in understanding of molecular and genetic contributions to physiology, behavior, and many disease processes.

Recently developed gene editing technology using the CRISPR (clustered regularly interspaced short palindromic repeats)/Cas9 (generally shortened to just CRISPR) systems allows for increased precision when modifying DNA. The technique is based on the adaptive immune system of bacteria and makes use of the Cas9 endonuclease, which can cut DNA at precise locations specified by a synthetic RNA guide. In addition to this highly selective editing, the process can significantly shorten the time to when genetically modified animals are available for research because it does not involve injecting foreign DNA.

These molecular and cellular manipulations have generated tens of thousands of GMMs that either need to be propagated at low levels to keep the line viable or preserved via cryopreservation of sperm, embryos, or ova for future use. GMMs may be immunocompromised, have reduced fertility, or have increased morbidity or mortality, resulting in the need for more sophisticated monitoring and veterinary intervention. Veterinarians play an important role in developing management practices that consider the special needs of these animals and are advocates for their welfare and appropriate care.

Genetic engineering of rats has been much more difficult to master, though recent advances in embryonic stem cell technology hold promise for solving some of the technical difficulties that have hampered development of these animals. The unique physiology and behavior of rats compared to mice make them very useful for certain studies, particularly in cardiovascular disease, neurobiology, and behavior.

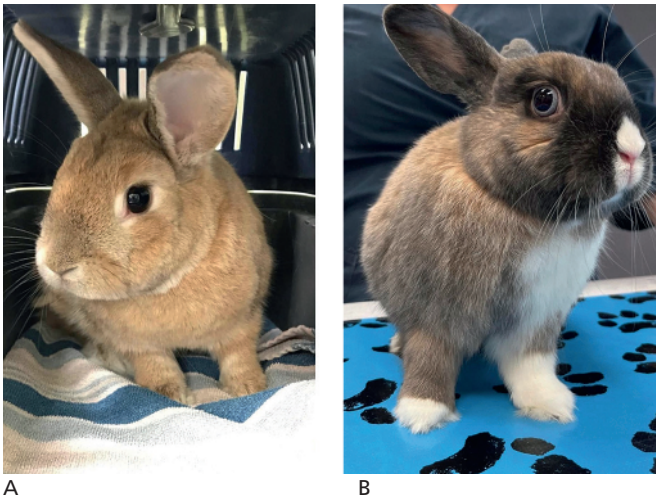
WELFARE-FRIENDLY CLINICAL PRACTICES FOR RABBITS AND RODENTS

Perhaps the most important consideration when working with companion rabbits and rodents in clinical situations is that they are prey species. With this in mind, many clinical practices, including those related to the overall clinic environment (e.g., waiting area, exam rooms, hospital ward), patient handling and restraint, physical examination, and clinical procedures, can be incorporated to reduce anxiety and enhance the welfare of these species.

Clinic Environment

It is important to optimize the client waiting area, exam rooms, and hospital ward for small mammals. Some clinics may specialize in or exclusively see small mammal pets or exotic companion mammals, such that avoidance of predator species is much more easily achieved. Rabbit/rodent-only clinics can operate similarly to those for cats, for example, with specific times of the day or week designated exclusively for these consultations. For mixed-species practices, it is important to provide a quiet seating area away from predator species such as dogs, cats, and ferrets, ideally with a visual barrier. Providing towels to cover carriers in the waiting area can help make rabbits and rodents feel more secure.

When possible, set aside an examination room exclusively for small mammal patients to minimize their exposure to predator odors. The exam room environment should be kept calm and quiet, and dimmer lights may be beneficial. Using a clean towel or nonslip mat on the table may help the animal feel more secure and will help reduce noise (Figure 1.3). Avoid excessively loud sounds (e.g., speaking volumes, background music, banging instruments) when examining the patient and be aware that the hearing ranges of these species can differ from that of humans.



A B

FIGURE 1.3. A: Example of suitable carrier for companion rabbit, B: Rabbit on a non-slip mat on examination table. Courtesy of CAEPC.

For example, rodents and rabbits are adapted to hearing higher frequencies that people cannot hear.

Rabbits and rodents should be hospitalized in a secure room separate from potential predators, such as ferrets. Caging should be escape-proof and safe for both the patient and the handler. Specialized top-opening cages and incubators designed for small mammal pets are readily available. For short hospital stays, some rodents can be hospitalized in the familiar surroundings of their home cage. Standard hospital cages designed for dogs and cats can sometimes be adapted for rabbits, guinea pigs, and chinchillas, although care must be taken to prevent falls as the cage door is swung open. The cage can be provided with a towel or blanket brought from the client's home, and the floor can be lined with a nonslip nontoxic material to provide a comfortable surface, such as a rubberized mat with small crosshatches that provides traction while allowing urine and feces to pass through. A litter box is usually needed for rabbits, preferably with the same substrate used at home, and a shallow resting tray with hay, shredded paper or other soft bedding can also be provided. A hide or shelter, such as an inverted tissue or cardboard box with an opening cut out, is essential for guinea pigs and chinchillas, and can also be used to facilitate restraint, as guinea pigs in particular tend to scatter when startled. Enclosures with mesh fronts that preclude animal escape and that can withstand chewing may be useful.

A supply of species-specific food pellets, good-quality hay, and critical-care formula for herbivores is needed for hospitalized rabbits and rodents. Providing fresh leafy greens and other vegetables may encourage eating. Owners should be consulted as to their pet's food preferences and can be asked to bring a small quantity of the animal's regular diet during periods of hospitalization to avoid gastrointestinal upset. Clean potable water should always be available, preferably in a hanging bottle to prevent soiling or in a non-tippable dish. An elevated dry area should be available as a refuge from damp bedding due to inadvertent leaking or spillage.

Physical Examination and Patient Handling

Clinic personnel must be competent in appropriate handling and restraint of rabbit and rodent companion animals to minimize stress and to avoid injury to the patient as well as the handler. Hands should always be washed thoroughly between patients, and a fresh lab coat should be worn if the last patient handled was a dog, cat, or ferret. The small mammal patient should be approached gently, quietly, and calmly. Recommendations for species-specific restraint methods are provided in Chapter 2. Rabbits, guinea pigs, and chinchillas have strong leg muscles and fragile skeletons, leaving them prone to fractures of their limbs, pelvis, or lower back. For this reason, it is especially important to handle and support them in a position that prevents them from kicking, jumping, or being accidentally dropped. Carriers that can be opened from above are often preferred to give the broadest exposure to the whole animal and ensure that the animal is aware of your presence.

The examination should begin by first observing the patient in its enclosure, focusing on its activity, mentation, respiratory rate and effort, as well as the appearance of any feces and urine present. Next, obtain the patient's body weight and use this opportunity to gauge the animal's temperament before performing the physical examination. Body weight is one of most important objective assessments of patient progress and is also essential for calculating appropriate doses of medications. Rodents are easily weighed in a container such as a plastic box or disposable paper bag or cup tared on a small digital gram scale. The carrier in which the patient is presented also may be used as the weighing container. Rectal body temperatures should not be obtained routinely as this may lead to excessive excitement.

Procedures

Fractious or distressed small mammals may benefit from mild sedation for examination or diagnostic testing. Extra caution must be taken when sedating sick or debilitated patients. Procedures such as blood draws that may be routinely performed on a conscious dog or cat may not be well tolerated in small mammal pets without sedation or anesthesia. For example, venipuncture in an awake guinea pig can be inherently difficult, and manual restraint for such a procedure can be very stressful for the patient. Therefore, sedation or anesthesia may be required.

In general, if the animal is alert enough to defend itself vigorously, it will tolerate sedation (with an appropriately selected drug protocol—see Chapter 3). Induction with gas anesthesia can be performed in a small induction box or inside a large facemask (for smaller patients), taking care to protect personnel from waste anesthetic gasses. Appropriate thermal support should be provided and body temperature should be closely monitored, taking particular care with heat-sensitive species, such as chinchillas, to avoid overheating.

EQUIPMENT NEEDS

Therapeutics and equipment available in a small animal practice can often be adapted for use in rabbits and rodents. Rabbits and cats are similar in size and can share some of the same equipment. Drugs, including anesthetics, and their dosages are discussed in other sections. Drugs must be used cautiously because virtually all use is extralabel in these animals. Very small dosages are often required, and it is sometimes necessary to carefully dilute the stock drug to generate a manageable injection volume. Appropriate diluent, storage conditions, and length of time the diluted drug is stable are important considerations, as is accurate labeling of the diluted drug. It is especially critical to be aware of use of drugs in meat rabbits to ensure that appropriate withdrawal times are followed prior to slaughter for human consumption.

Rodents weigh between 18 and 20 g (2/3 oz) for a mature female mouse to approximately 1 kg (2.2 lb) for obese or pregnant guinea pigs. These species should be weighed in grams or kilograms, depending on the patient size. Scales with up to a 1–2 kg capacity and with sensitivity to 5 g are essential, as is an appropriate weighing container for the animal. Larger rabbits may require scales of up to 10 kg capacity. The tare function on digital scales allows automatic deduction of the weight of the container (box, pet carrier, clean disposable paper bag, or coffee cup) or towel/blanket, if needed for patient comfort, from the digital measurement. Obtaining an accurate body weight is very important, not only for correct dosing of small rodents and rabbits but also for detecting changes in body weight, which are often the only objective data available for monitoring these small mammals over time. Equipment adapted to patient size should also be used, such as small needles, miniaturized surgical instruments, magnification devices (surgical loupes, endoscopes), and anesthetic monitoring equipment of appropriate sensitivity (equipment designed for research animals or human neonatal and pediatric devices). Other considerations include: (1) the need to perform oral examinations and tooth trimming in a small and narrow oral cavity; (2) requirements for administration of volatile anesthetics to small animals with high metabolic rates; (3) maintenance of core body temperature during anesthesia; (4) physiologic monitoring of rapid heart and respiratory rate in a small patient during anesthesia; (5) availability of appropriate dentistry tools; and (6) dilution of stock drugs with appropriate diluents to avoid inaccuracies and overdosing. Some recommended specialized items include those listed in Table 1.2.

MAJOR HUSBANDRY CONCERNS

Maintaining high husbandry standards is essential for reducing or eliminating factors that predispose animals to injury, disease, or development of abnormal behaviors and stereotypies. This includes establishing satisfactory methods for sanitation and providing escape-free, appropriately resourced, well-constructed caging. These concerns extend to animal housing for pets, as well as to research and commercial production settings.

Behavioral Management Considerations

Housing and husbandry approaches should provide for the behavioral well-being and physical comfort of the animals. It should take into consideration the normal behaviors, postures, and typical movements of each species as well as considering opportunities for animals to engage more with their environment and with those who care for them. Taking a more holistic approach helps to ensure that we better meet the needs of these animals and that they have a good life. Regardless of their end purpose, whether as a companion animal, research subject or for commercial production, small mammals typically spend the majority of their life in close contact with the cage environment, and it is important to ensure that this environment is optimized. Animals housed in a suboptimal environment without sufficient space, choice, and control, and opportunities for regular exercise, exploration, and cognitive stimulation may become bored, fight among themselves, and develop abnormal behaviors detrimental to their health and well-being, such as fur chewing and bar biting. Although ensuring the absence of disease is an important concern when caring for these animals, consideration and attention to their behavior is also very important as it provides insight into their emotional state. An umbrella model has been proposed to explain the concept of a holistic behavioral management program for research animals, and this concept can be adapted to other settings in which small rodents and rabbits are kept and maintained (see Figure 1.4). Expanding an animal's options for performing species-typical activities and behaviors can positively affect both physiologic and behavioral well-being (Figure 1.5). Strategies to consider include adding objects to chew and manipulate, which encourage fine motor activity; novel foods, which provide opportunities for variation in diet and foraging; and other resources that stimulate senses other than touch or taste, for example, those promoting exercise. It is important that objects added be used and enjoyed by the animals, that they can be consumed, sanitized or discarded at regular intervals, and that they do not introduce safety hazards that may impair animal health. Examples of species-specific recommended resources are provided in Chapter 2.

Rabbits and rodents are highly social species and do best when housed in pairs or groups whenever possible with the exception of female and mature male hamsters, breeding does with kits, and intact male rabbits, which often fight with severe consequences when housed with conspecifics. Most of these small animals naturally dig tunnels and live in burrows in the wild, and should be housed on solid flooring with absorbent substrate and adequate nesting material.

Housing

Primary enclosures (cages and pens) should be structurally sound, appropriate for the species housed, in good repair, free of sharp or abrasive surfaces, built for easy cleaning, and constructed to prevent escape and intrusion of other animals. They should also be large enough to incorporate all needed cage furnishings and other resources as well as providing for freedom of movement and normal postural adjustments, such as eating, mating, stretching without touching the cage top, jumping, and exercising. Unpainted wood, untreated metal, and other porous or unsealed materials that are difficult to sanitize should not be used for long-term housing of rabbits or rodents. Flooring and nesting materials that prevent escape, provide the capacity to burrow and maintain thermoneutrality, and allow for adequate sanitation should be used. While

Table 1.2. Special equipment needs for small mammal procedures.

A. Physical Examination/Blood Collection/Drug Administration Needs

Digital scales able to accurately weigh animals from 20 g to 10 kg
Towels/baskets/restraint devices (preferably dedicated to rabbits/rodents)
Small needles (22–28 gauge) and butterfly IV catheters
Small gauze pads and rolls, self-adhering elasticized bandages, medical tape
22–26 gauge IV catheters
Ball-tipped dosing needles—straight and curved (flexible plastic preferred) for oral gavage
0.5 mL, 1 mL, 3 mL, and various straight- and curved-tip syringes (low dead space syringes for blood draws and drug injections)
30 mL and 60 mL catheter tip syringes for feeding of rabbits
Microcollection tubes for blood samples (serum separator, heparin, ethylene diamine tetra acetic acid [EDTA])
Microtip swabs for microbiology culture
Otoscope with several sets of plastic cones for ear and cursory dental examinations
Small bivalve vaginal or nasal speculum with light
Sharp clippers (consider portable moustache clippers)
Pediatric stethoscope
Nebulization or oxygenation chamber
Small nail trimmer

B. Hospital In-Patient Needs

Secure caging with appropriate nesting and bedding material and environmental controls (preferably in a quiet ward or area separate from other species)
Food crocks that are difficult to tip over and have low sides for easy access
Water bottles with operational valves or sipper tubes
Food
- Herbivore critical care formula
- Different types of hay (timothy, oat, botanical, mixed, alfalfa)
- Species-specific pellets for rabbits and rodents
- Fresh leafy vegetables

Litter pans and litter appropriate for rabbits
Hide boxes, especially for guinea pigs and chinchillas

C. Anesthetic and Surgery Needs

Thermal support system (e.g., forced warm air system, water recirculating blanket, heating bags, microwavable heating pads), disposable hand warmers (also useful for vasodilation prior to blood collection)
Bubblewrap, tubular gauze, or stockinette for draping small rodents
Ophthalmic surgical or microsurgical instruments
Small metal wound clips (8 mm) and wound clip applicator
Appropriate gauge (3-0 to 5-0) suture materials with round/cutting/reverse cutting needles
Inhalant gas vaporizer with nonrebreathing assembly
Small face masks (commercially available or can be fashioned from syringe cases)
Small induction chambers (commercially available or can be made from appropriately sized plastic containers with rubber gasket seals)
Surgical restraint blocks
Small cuffed and uncuffed endotracheal tubes (2-0 and larger)
Transparent or light-weight paper surgical drapes
Curettes
2.7 mm rigid endoscope (for intubation)
Sterile cotton-tipped applicators
Surgical loupes (e.g., Surgitel®)
Appropriate size surgical retractor (e.g., Lonestar retractor®)
Micro-stream pediatric capnography
Pulse oximeter (designed for small mammal pets or research mice and rats)
Continuous temperature probe
Infusion pump

(*continued*)

Table 1.2 (Continued)

D. Dentistry Needs
Cheek dilator/spreader
Rabbit/rodent mouth gag
Dental unit with straight hand piece and rotating dental burrs/soft tissue protector
Rabbit incisor luxator
Rabbit molar luxator
All-purpose dental scaler/curette
Cheek teeth extraction forceps
Tongue depressors
Topical anesthetic gel

E. Nice to Haves (a.k.a. "Bells and Whistles")
Radiologic and ultrasound equipment
Stereoscope for microvascular surgery
CT scanner for skull imaging
Dental radiography unit
Rabbit/rodent dental platform
Laryngeal mask airways (e.g., V-gel®)
Ventilators for exotic species (e.g., Vetronics small animal ventilator®)
Doppler unit and cuffs
Endoscopic and video-recording system
Radiosurgery unit and forceps
Mouse/rat intubation platform and instruments
Non-invasive blood pressure monitor

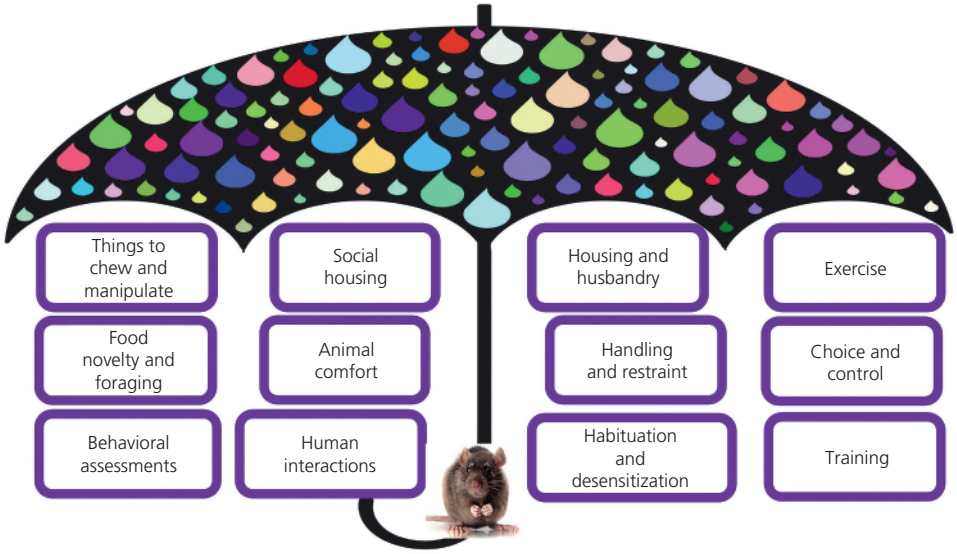


FIGURE 1.4. A proposed umbrella model of research animal behavioral management programs. Turner et.al., 1919 / MDPI / CC-BY-4.0.

wire or plastic mesh or perforated metal flooring is commonly used for meat rabbits to reduce disease burden and promote ease of sanitation, solid resting mats or surfaces are highly beneficial and promote animal comfort as well as reducing foot or hock lesions (pododermatitis, see Chapters 2, 4, and 5).

Physical Comfort

Animal caging should be dry, clean, well-ventilated but protected from drafts, and kept away from excessive noise and direct sunlight. Regulatory guidelines for institutional temperature and humidity ranges are provided within the US AWA, the ILAR Guide, and the CCAC guidelines (Table 1.3).

FIGURE 1.5. Example of thoughtfully planned housing for gerbils.

In general, the thermoneutral zone of rodents is 26–30 °C (79–86 °F), and these animals are comfortable in warm ambient temperatures. Rabbits prefer cooler temperatures because of their dense coat and may be more comfortable at 16–20 °C (61–68 °F) temperatures. Rabbits can tolerate much cooler ambient temperatures provided they are protected from drafts and are given abundant dry bedding. Cages should never be placed in direct sunlight to prevent overheating of these animals, none of which have efficient cooling mechanisms. Hairless and smaller rodents, such as mice, require higher ambient temperatures. Relative humidity in the environment should be maintained between 30% and 70%. Temperature or humidity extremes and variations can significantly contribute to discomfort and disease susceptibility, and should be closely monitored.

Room air changes in institutional animal facilities, using fresh or filtered air, are generally required to be at least 10–20 complete air changes per hour, although more recently, there has been a move to more performance-based indicators of sufficient ventilation. These rates of air exchange are recommended to reduce waste gasses, airborne particulates, and allergen load associated with a large number of animals housed at high density in research or production settings. Fewer air exchanges are certainly adequate for small numbers of companion rodents or rabbits in private homes. The size of the room, strain and sex of animal, number of animals present, number of animals per cage, type of cage, and sanitization interval affect ventilation requirements. For companion small mammals, enclosed cages such as covered aquaria should be avoided, as these may result in poor air circulation and a build-up of potentially toxic levels of ammonia and carbon dioxide. Aquaria left in direct sunlight can also result in hyperthermia and rapid death. In research facilities, a light intensity of 30 foot candles (323 lm/m^2) at 1 m above floor level (approximately equivalent to a dimly lit office) is adequate for routine housing and is recommended by the ILAR Guide. Less light is needed to maintain circadian rhythms, and higher illumination intensity may induce retinal degeneration in albino rats and mice. Animals maintained under conditions of continuous light or dark may become infertile.

Housing for small rodents, particularly mice in research facilities, has generated a unique industry, as methods to house large numbers of animals efficiently while limiting spread of adventitious pathogens have become increasingly important. Filter top caging was initially demonstrated to provide effective cage-level barriers to the spread of disease in the 1960s; however, the modern caging systems now used widely were first introduced in the 1980s. The most economical microisolation system is static, that is, air circulation between the room and cage is passive. This leads to a rapid build-up of high levels of ammonia and CO_2, necessitating frequent (typically semi-weekly) cage changes. Individually ventilated caging (IVC, also known as ventilated caging systems or VCS) is now widely available commercially and has largely replaced static cages in many facilities. Several companies produce IVC with different specifications. These may have high efficiency particulate air (HEPA) filtration for incoming or outgoing air or both. The benefits of IVC include: (1) provision of biosecurity by limiting spread of diseases between cages and from the cage to the environment; (2) very low accumulation of ammonia and CO_2 within cages, allowing for a longer interval between cage changes of at least 2 weeks; (3) a decrease in

Table 1.3. Temperature and relative humidity (RH) guidelines.

Species	United States Department of Agriculture Animal Welfare Act (USDA AWA)	Institute for Laboratory Animal Research (ILAR) Guide	Canadian Council on Animal Care (CCAC) Guidelines
Rabbits	Not specified	30–70% RH, 61–72 °F (16–22 °C)	40–70% RH, 16–22 °C
Guinea Pigs	60–85 °F	30–70% RH, 68–79 °F (20–26 °C)	40–70% RH, 18–22 °C
Hamsters	60–85 °F	30–70% RH, 68–79 °F (20–26 °C)	40–70% RH, 21–24 °C
Gerbils	Not specified	30–70% RH, 68–79 °F (20–26 °C)	40–70% RH, 15–24 °C
Chinchillas	Not specified	Not specified	Not specified
Mice	Not covered	30–70% RH, 68–79 °F (20–26 °C)	40–60% RH, 20–26 °C
Rats	Not covered	30–70% RH, 68–79 °F (20–26 °C)	40–60% RH, 20–26 °C

rodent allergens in the macroenvironment, with concomitant benefits to personnel; and (4) provision of protection of personnel and other animals from pathogens, that is, biosafety improvements.

IVC have also permitted increased use of rodents that are immunodeficient because of genetics or experimental manipulations, providing a protected environment for animals that could otherwise succumb to opportunistic infections. IVC do reduce intercage communication of mice and may create drafts for animals because of high air exchange rates, leading to reports of decreased breeding performance in some lines of mice. There is also discussion of the optimal cage change interval for IVCs in that cages may remain dry for extended periods because of the high air flow rates, but animals may be housed largely on dried feces with insufficient substrate. Intracage ammonia levels can be too high if cage change intervals are too long. Alternative systems that permit communication of animals between cages as well as reducing exposure of personnel to potential laboratory animal allergens (LAA) are ventilated cabinets with interior racks for caging.

Health Maintenance

Facilities and caging should be cleaned and sanitized when necessary, usually one to three bedding changes per week for mice, rats, guinea pigs, chinchillas, and rabbits, and longer intervals (up to biweekly) for hamsters, gerbils, and rodents held in individually ventilated cages (IVC). Ammonia gas, which increases susceptibility to respiratory tract disease, can be reduced by decreasing population density, use of IVC (to a limit), and by providing good sanitation and frequent bedding changes. In general, pelleted cellulose bedding is superior to wood or corncob for absorbing urine and lowering ammonia levels in cages. Bedding substrate and nesting material should be provided in a sufficient volume to permit digging, nest-building, and thermoregulatory choice. Vermin must be excluded from animal housing areas, as feral rats and mice may be a source of parasitic, viral, and bacterial pathogens. Different species and animals with unknown or non-SPF disease status should be housed separately, preferably in different rooms or in IVC. Professional and technical personnel or companion animal owners should examine animals at least daily for evidence of injury and disease. Stock and replacement animals should be obtained from reputable dealers or pet animal suppliers. Many animals in the pet trade are infected with one or more pathogenic organisms, and the stress and consequences of transport, marginal nutrition, mixing of species and sources of animals, inbreeding, and suboptimal environmental conditions may exacerbate underlying disease conditions.

Nutrition

Food should be stored in closed containers, kept at room temperature or below, and observed regularly for mold or vermin. Feeding and watering devices should be kept clean, be designed or placed so as to prevent fecal and urine contamination, be appropriate for the species and age of animal housed, and be accessible and functional. The shape of the animal's face may determine whether it can access feed and water devices, and this issue should be given close attention. Water should be fresh, clean, and available ad libitum and at all times. Specially designed watering bags with reusable valves are manufactured for use in laboratory animal facilities, and may provide ergonomic and labor benefits in certain circumstances while still providing continuous access to potable water. Gel-based diets ("gel cups") are frequently used when shipping rabbits and small rodents for extended distances, and also may be used to provide fluid and nutritional support for debilitated animals, animals recovering from surgery, or those adjusting to a new environment (Figure 1.6).

Rabbits and rodents should be fed a fresh, clean, nutritious, palatable feed on a regular basis and in an adequate quantity. Diets milled for laboratory animals typically include a milling date and should be used within 6 months of manufacture. Diets available for companion rodents are highly variable, and seed-based diets should be avoided in lieu of a pelleted chow manufactured by a reputable company for the specific species being fed. Discounted, outdated, or improperly formulated feeds, supplements, and vitamin formulations should be avoided. Colorful, attractive displays of rodent and rabbit feeds in pet stores should be scrutinized closely. The most common deficiencies encountered in pet store rabbit and rodent feeds are low protein content (under 16% crude protein), excessively long storage with subsequent nutrient decomposition, and inappropriate species use, particularly for guinea pigs, which require daily vitamin C in the diet. Smaller bags of food purchased more frequently are likely to provide more nutrients and vitamins to pets than large quantities of food that will take months to consume. Supplementation with grains, salt blocks, and vitamins is typically unnecessary

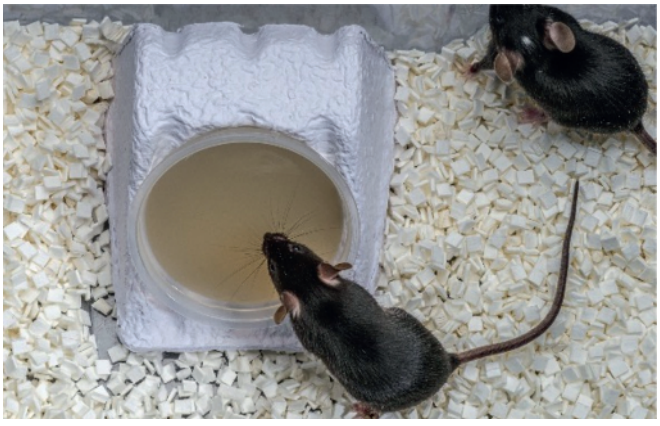


FIGURE 1.6. Mice provisioned with a gel cup in a Shepherd Shack®, providing both a shelter and ensuring successful acclimation of mice after shipping to a new facility. Courtesy of Shepherd Specialty Papers®.

if the diet is properly formulated. Treats, such as fresh fruits and vegetables, may be used to reinforce desired behaviors, but should never consist of more than 5–10% of the daily diet. Clean timothy or other grass-based hay is available prepackaged and should be provided ad libitum for pet rabbits, guinea pigs, and chinchillas. Many mice and rats will also consume and use hay when it is provided. Similarly, sterilized or gamma-irradiated timothy hay can be provided to research rabbits and rodents to promote gut health and reduce boredom. Free-choice hay is not commonly provided to meat rabbits because it reduces feed efficiency and slows animal growth, but some hay is helpful to improve gut health, maintain normal wearing of their teeth, reduce enteric disease, and reduce boredom and development of abnormal or stereotypic behaviors.

Although the nutritional requirements of rabbits and rodents have been investigated and reported, optimal nutrient levels for most species remain uncertain. Requirements known at present are available from feed company publications or from the publications of the US National Academy of Sciences' NRC. With the important exception of ascorbic acid deficiency in guinea pigs and caloric, water, and protein deficiencies in all species, malnutrition is uncommon in rabbits and rodents. Primary nutritional imbalances may be manifested as weight loss or failure to gain, increased susceptibility to disease, hair loss, poor hair coat, prenatal mortality, agalactia, infertility, anemia, deformed bones, central nervous system abnormalities, or a reluctance to move. Subclinical nutritional deficiencies, excesses or imbalances may contribute to secondary infections or metabolic disorders.

The most prevalent nutritional problem in companion rabbits and rodents, and in laboratory animals held long-term, tends to be obesity associated with ad libitum feeding of high-calorie foodstuffs, including treats, and insufficient dietary fiber. More specific information about nutritional requirements and nutritional-related diseases for each species, and for companion versus laboratory animals, is provided in Chapter 2.

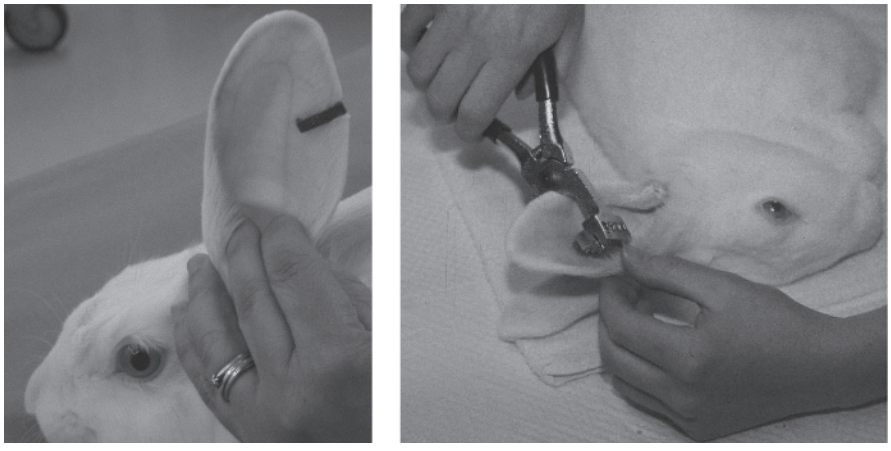
Identification

Animals worked with in research settings should be clearly identified using accepted methods—preferably those that are minimally invasive. Animals may be identified by cage cards, individual coat pattern, ear punch or notch, shaving hair patches, nontoxic marker or dye-staining on light colored fur or skin areas, (mice, rats, and hamsters), ear tag or stud, or tattooing, for example, ear, tail, footpad or shaved flank (Figures 1.7–1.9).

Microchip devices that store animal identification information in association with physical parameters such as temperature are used in some research facilities and for some small mammal companions. An example of an ear notch/punch code is shown in Figure 1.10. This method can be used for individually identifying the animal as well as for collection of tissue for DNA genotyping.

Cage cards with information specific to the animal and protocol are required in research settings, and use of bar codes on cards can assist with electronic census tracking. Permanent individual animal identification is often used together with

FIGURE 1.7. Example of instrument used for ear punching of mice. Note that the tissue obtained from the hole punch can also be used for subsequent genotype analysis.



A B

FIGURE 1.8. A: Ear tag in a rabbit, B: Rabbit sedated and positioned for ear tattoo identification. Courtesy of Ernest Olfert.

FIGURE 1.9. Tail tattoo in mouse. A: Mouse in tattoo cassette, B: Cassette inserted into tattoo device, C: Completed tail tattoo. Courtesy of S. Perrotta.

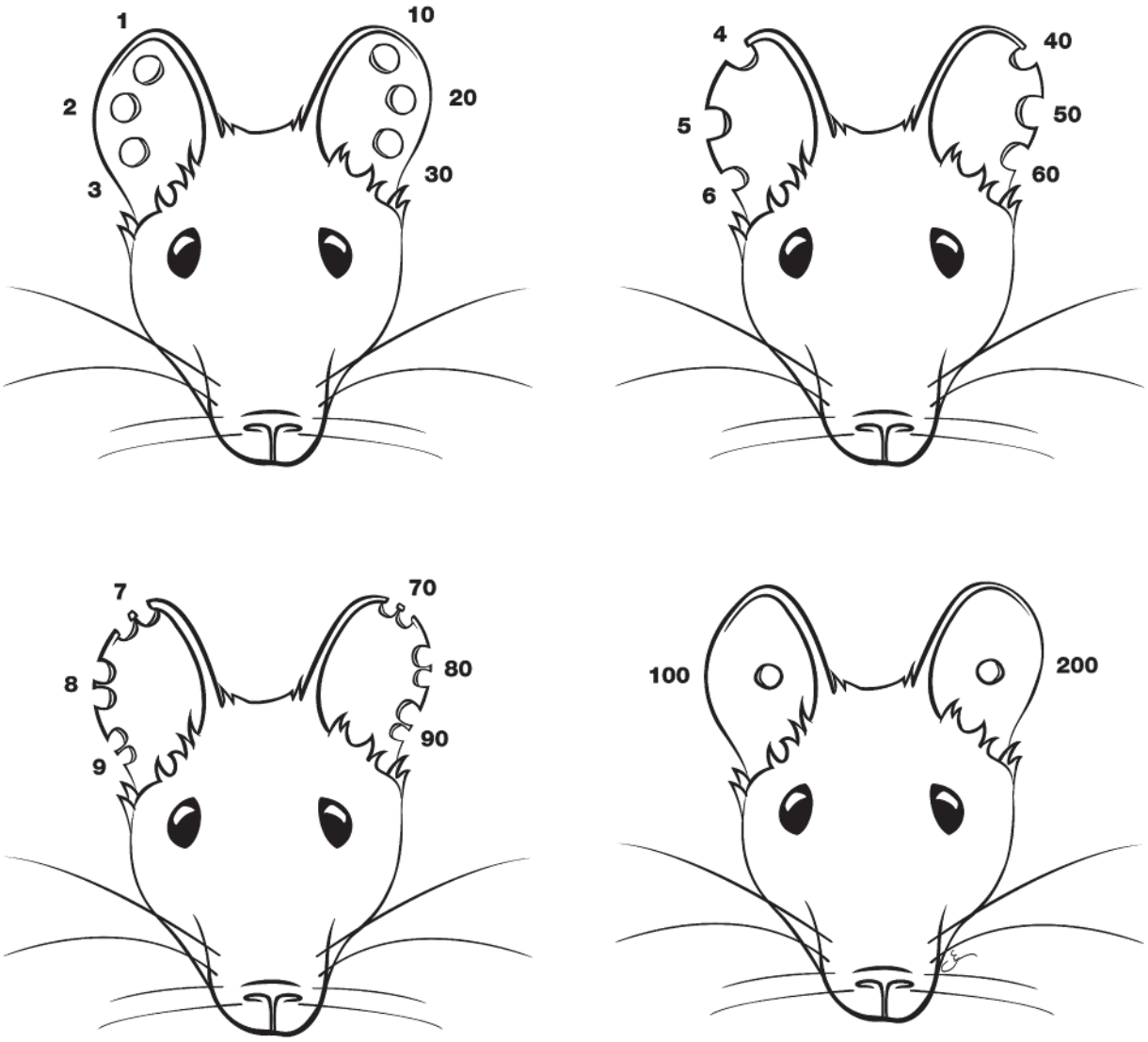


FIGURE 1.10. Standard ear notch punch codes for identification of rodents. The punch codes are combined to achieve the desired final number. Illustrations by Gianni A. Chiappetta.

cage cards since cards can be inadvertently mixed during cage cleaning and experimental manipulations.

FACTORS PREDISPOSING TO DISEASE

Certain organic or environmental factors increase the exposure or reduce the resistance of animals to disease. These factors must be considered by animal caregivers in disease prevention efforts. Factors that influence disease susceptibility include environmental, genetic, metabolic, experimental, and dietary variables. Attention to these factors is extremely important in rabbit and rodent husbandry as well as in disease prevention and control. Many aspects of husbandry are mandated or discussed in detail in regulations governing the care and use of laboratory animals, and provide suitable guidelines for companion and production animals.

Facility Cleaning, Disinfection, and Fumigation

Good sanitation and hygiene are essential in rabbit and rodent maintenance. Very high levels of sanitation are required in an SPF research colony that may contain animals with immunodeficiencies or those infected with certain pathogens on an experimental basis. This level may not be necessary for companion animal and production facilities, but can be used as a basis for animal care. Clean cages are particularly important during pregnancy, lactation, and weaning; after removal of sick animals; after surgical procedures; and preceding the introduction of new animals into the household or colony. Some species (including hamsters, some strains of mice, and primiparous animals of all species) are better left undisturbed immediately following parturition, as disturbances may affect maternal care.

Cages can be disinfected by washing with 82 °C (180 °F) water after removal of organic matter or by applying a disinfectant solution to all surfaces. Disinfectant wipes or solutions, for example, hydrogen peroxide, phenolic, quaternary ammonium or halogen-containing compounds, including hypochlorite or dilute bleach solutions, are available in grocery, farm supply or feed stores, or from specialty manufacturers. Label instructions for concentrated solutions should be carefully followed for best results. Clients are more likely to follow advice about disinfection if common household products, such as bleach, vinegar, or common disinfectant wipes, are recommended. Detergents and disinfectants must be rinsed thoroughly from cleaned cages and feeders, as residues may cause serious health effects and may alter experimental data. Research facilities typically use specifically designed cage wash equipment and detergents to facilitate consistent sanitation of cages, feeders, and water bottles. Companion animal food bowls and water bottles can often be sanitized in home dishwashers. If items are hand washed, kitchen dishcloths should never be shared between human and animal dishes to prevent transmission of potential zoonotic infectious agents between animals and their human caregivers.

Disinfectants should be selected for broad spectrum activity, rapid kill effect, cleaning capacity, solubility, stability, residual activity, and lack of odor and toxicity. Ideally, disinfectants should be effective in the presence of organic materials, detergents, hard water, at varying pH levels, and on porous, rough, or cracked surfaces. Some disinfectant preparations should be avoided because they cloud clear plastic cages or cage accessories. Unfortunately, no single disinfectant meets all these criteria, and selection must be based on specific requirements. The effects of disinfectants vary with time of exposure, temperature and concentration of solution, and ionic content of the diluent. Important categories of microorganisms that are weakly or unaffected by standard disinfectant solutions are bacterial spores, coccidial oocysts, parasite ova, prions, and nonenveloped viruses. *Pseudomonas* spp. can be more resistant to disinfection than other bacteria and frequently contaminate watering devices, necessitating careful disinfection of this equipment. Use of acidified water to decrease *Pseudomonas* spp. burden is described in the mouse husbandry section of Chapter 2. All of these agents can induce topical irritation, burns, eye injury, if inadvertently splashed into the eyes, and respiratory irritation, in animals and people, and they should be used following manufacturer's safety instructions in well-ventilated areas. Agents should never be combined.

Halogen-containing disinfectants, including hypochlorites and iodophores, are effective in acidic solutions, but they may stain or damage fabrics and have reduced activity in the presence of organic matter, soap, or detergent residues. A good, practical, and safe disinfectant for pet or food animal cages is a solution of 30 mL of a 5% sodium hypochlorite solution (laundry bleach) in one liter of water (1 oz. per quart). A fresh mixture should be prepared just prior to use and used on clean cages or equipment only, followed by thorough rinsing and allowing time for items to dry.

Phenol derivative compounds, the disinfectants least affected by environmental influences, kill the vegetative forms of most Gram-positive and Gram-negative bacteria after approximately 30 minutes of contact time, and they can be found in some cold sterilant solutions. One exception is *Pseudomonas* spp., which require longer exposures and higher concentrations. Germicidal activity is increased with increased concentration and temperature of the solution. Phenolic compounds, emulsified at 1–5% in weakly acidic, soapy water, have some antifungal, sporicidal, and virucidal activity. Phenolics are also found in many common disinfecting antiviral wipes. Because of a residual odor and potential toxicity, phenolic derivatives should not be used to disinfect feeders and waterers.

Quaternary ammonium compounds are effective against Gram-positive bacteria, and many fungi and viruses, but are considerably less effective in the presence of organic matter,

soaps, and an acidic pH. These compounds are useful for general purpose disinfection and for cleaning feeders and waterers, though as mentioned previously, devices should be thoroughly rinsed afterward. Residues of these compounds have been shown to impair reproductive performance in mice and have been implicated as a cause of death among suckling rabbits. Other disinfecting substances used less often and for resistant organisms such as bacterial spores, parvoviruses, parasitic ova, and coccidial oocysts include oxidizing disinfectants, formalin/formaldehyde, and ethylene oxide gas. Ammonia solutions are effective cleaning agents but are not typically effective against viruses.

The alkaline urine of rabbits, guinea pigs, and hamsters (above pH 8.0) contains phosphate and carbonate crystals that result in scale residues on caging. Acidic products, for example, dilute inorganic acids including white vinegar, can be used to dislodge the crystal accumulation. Some plastics are affected by alkaline detergents, which cause the transparent plastic cages to become cloudy and brittle. Acid detergent preparations are less destructive, but they will discolor aluminum.

Gas fumigation is an effective method for room and cage sanitization and for eliminating parasites and vegetative bacterial forms following removal of organic matter. Before gas fumigation is attempted, the room must be free of animals and people, airtight, warmed to at least 21 °C (70 °F), and wetted to raise the relative humidity to 80% or more. Vaporized hydrogen peroxide is used increasingly because it is noncorrosive, less toxic to people and animals, it requires minimal postprocess neutralization, and it produces ecologically friendly nontoxic waste products (water and oxygen). Formaldehyde gas has been used for fumigation for years and is generated by heating paraformaldehyde crystals in an alkaline solution on a hot plate. Chlorine dioxide or peracetic acid can also be used for fumigation. Because of the potential for severe toxicity with these alternative agents, provisions must be made for exhausting fumes from the room without the entry of personnel, and stainless steel and other equipment that may be corroded by fumigants should be removed before fumigation.

New methods of sterilization and newer chemical sterilants have been developed in response to emergence of antibiotic-resistant organisms present in hospital settings. These include new aldehydes, acids, and surfactant agents.

ALLERGIES TO RABBITS AND RODENTS

The high prevalence of allergies to laboratory animals (LAA) has been recognized for decades, and has been reported in 11–44% of people with repeated unprotected exposures to rabbits and rodents. This issue has not been widely discussed or evaluated in small mammal pet owners or among meat rabbit producers or rabbit abattoir workers. It is likely that exposure in a research animal setting under circumstances of repeated and frequent exposures to large numbers of animals, their dander, and their excreta contributes to the high prevalence of this health condition. The allergic reactions among people in frequent contact with animals involve both contact (dermal and ocular allergic dermatitis and conjunctivitis) (Figure 1.11) and inhalant (respiratory allergic rhinitis, bronchial hypersensitivity) syndromes. LAA may progress to asthma in up to 22% of affected persons and can result in anaphylaxis in severely allergic persons. The generation of immunoglobulin E (IgE) against antigens produced by laboratory animals is a prerequisite for diagnosis of LAA. Specific clinical signs include runny and itchy eyes and nose, a persistent cough, asthma or shortness of breath, or various skin manifestations, including wheal and flare reactions, hives, and pruritic rashes (urticaria). Sensitivity reactions may occur immediately, 15–20 minutes after exposure or many hours later. It is difficult to be in contact with animals without having contact with allergens, as even very small quantities of allergens can trigger a reaction. Allergens have also been detected on clothing and in the cars and offices of people who have had animal contact in other areas.

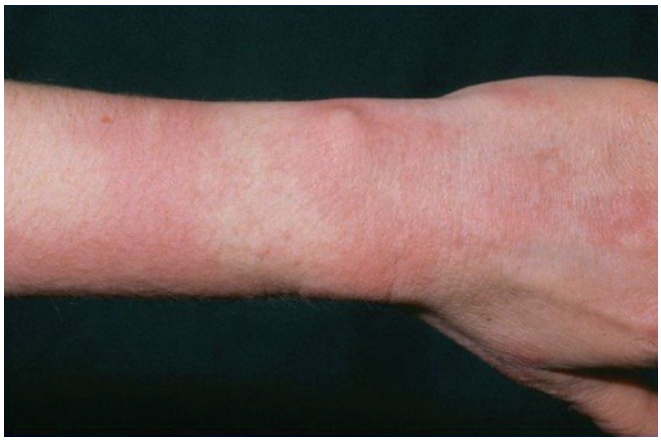


FIGURE 1.11. Generalized wheal-and-flare reaction on the arm of an individual with laboratory mouse contact allergies.

Predisposing factors for development of allergies to animal allergens unrelated to occupational exposures include atopy (clinical hypersensitivity of hereditary predisposition) and smoking. The intensity, frequency, and directness of contact are the most important associations related to development of LAA. Allergies are usually species-specific, that is, particular to one species of animal or another, but not strain-specific. Development of one allergy increases the probability that allergies to additional antigens may occur. Development of LAA has been recorded in association with exposures to rats, guinea pigs, rabbits, mice, hamsters, and gerbils; virtually any laboratory animal can induce allergies in exposed and predisposed individuals. The most difficult allergies to manage are those to rats and mice, but this likely reflects the fact that the numbers of these animals are greatest in most research animal

facilities. Many mouse and rat urinary proteins belong to a family called lipocalins. These proteins resemble antigens of schistosomes, which are human trematodes (flukes). These proteins are highly prone to triggering IgE production, which likely accounts in part for the high proportion of the population susceptible to LAA. Three distinct mouse allergens and two allergens of rats have been described and are found in hair, dander, urine, and serum. Allergens have not been as well characterized in other species, though at least two lipocalin-like proteins have been identified in rabbits and guinea pigs, and are present in urine, saliva, and dander.

Various animal factors influence the risk of exposure to LAA and examples of these follow. Female mice generate far fewer airborne allergens than do males. Airborne prealbumin and albumin are reduced when corncob bedding is used in place of wood shavings. Rabbit saliva is deposited on the fur during grooming. After drying, the allergens become airborne and serve as an important source of exposure. Allergens in aerosolized rat urine can be carried with ammonia gas. These exposures may be particularly dangerous because they can be associated with severe pulmonary congestion. Symptoms develop rapidly after sensitized persons enter rat facilities that have poor ventilation and infrequent cage cleaning. Proteinuria in rats increases with age; consequently, exposure to these animals puts people at higher risk for allergy development.

This discussion clearly illustrates that laboratory animal facilities should have occupational health programs in place that consider development of LAA as a risk of employment, and employees with predisposing factors should be identified and monitored periodically as part of the program. The need for occupational health awareness is well described in the ILAR Guide, and ILAR has also published a volume titled *Occupational Health and Safety in the Care and Use of Research Animals* to provide additional information on this topic. Veterinarians or owners with small mammal pets or production animals should be aware of the possibility of development of allergies, and should seek the advice of a physician if they believe they have an allergy to rabbits or rodents.

Prevention

Rabbit and rodent airborne allergens and particulates can be measured, allowing for association between environmental exposures and development of LAA. This technology has also allowed evaluation of husbandry methods that decrease ambient concentrations of airborne allergens. These studies are the basis for recommendations for reduced occupational exposures. Because nonoccupational risks can increase the risk of development of LAA, many laboratory animal facilities include a preemployment risk assessment as part of their occupational health program.

An effective LAA prevention program includes education and training; implementation of personal protective equipment (PPE), including gloves, designated work clothes, or laboratory coats, and respiratory protection; modification of work practices; and most importantly, use of various engineering controls to reduce the level of allergen exposures. Use of ventilated cages that are pressurized negative to the room and that are opened only in ventilated changing stations reduces mouse allergens 10-fold relative to nonventilated caging handled on conventional change tables. Increasing room ventilation rates and humidity, use of low-dust bedding, wetting bedding prior to dumping, use of ventilated dump stations, and using room-level air filtration are all measures that decrease allergen exposures.

Persons experiencing allergic symptoms with exposure to laboratory animals should be evaluated by a physician with experience in allergy diagnosis and management. Diagnostic tests that may be performed include skin tests or in vitro assays that detect IgE reactions to LAA. Pulmonary function measurements may be used to assess asthmatic symptoms. Possible management for sensitized individuals includes reduction of exposure, pharmacologic treatment, or immunotherapy. Early intervention is essential, as prognosis for control of symptoms and overall outcome is highly dependent upon disease severity at the time of diagnosis.

Small mammal pet owners can minimize allergen exposure by keeping the animals in well-ventilated areas, providing regular sanitation of cages and the surrounding environment to reduce allergen levels, using dust-free bedding, and ensuring appropriate hand and clothing hygiene after handling these pets. On farm, ensuring adequate ventilation is essential for reducing environmental allergens.

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