The Laboratory RABBIT

Second Edition





Mark A. Suckow
Valerie Schroeder

CRC Press
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A Volume in The Laboratory Animal Pocket Reference Series

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The Laboratory Animal Pocket Reference Series

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CRC Press
Taylor & Francis Group
Boca Raton London New York

CRC Press is an imprint of the
Taylor & Francis Group, an **informa** business

CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

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Version Date: 20140512

International Standard Book Number-13: 978-1-4200-9106-9 (eBook - PDF)

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dedication

M.A.S.: To my family: Sue, Brianne, Abby, Pat, and Sadie.
V.A.S.: I would like to thank Dr. Mark Suckow for his confidence in my abilities and the opportunity to work on this project. In addition, I thank my co-workers who assisted in ways large and small. A special thanks to my husband, Mark, for his patience and encouragement and unflagging support of my career in animal research.

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preface

The use of laboratory animals, including rabbits, continues to be an important part of biomedical research. In many instances, individuals performing such research are charged with broad responsibilities, including animal facility management, animal husbandry, regulatory compliance, and performance of technical procedures directly related to research projects. In that regard, this handbook was written to provide a quick reference source for investigators, technicians, and animal caretakers charged with the care and use of rabbits in a research setting.

This handbook is organized into six chapters focusing on biological features of the rabbit; husbandry and care; management; veterinary care; experimental methodology; and additional informational resources. Basic information and common procedures are presented in detail. Other information on less commonly used techniques or methods beyond the scope of this book is referenced extensively so that the reader is directed toward additional information without having to wade through a burdensome volume of detail here. Thus, this handbook should be viewed as a basic reference source and not as a complete review of the biology and use of the rabbit. This second edition of *The Laboratory Rabbit* provides updated material and references. In addition, we have added a large number of color figures.

A final point to be considered is that all individuals performing procedures described in this handbook should be properly trained. The humane care and use of rabbits is improved by initial and continuing education of personnel and will facilitate the overall success of programs using rabbits in research.

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authors

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important biological features

introduction

The rabbit has proven to be a valuable animal in research and testing. The domestic rabbit belongs to the taxonomic order Lagomorpha. Although the rabbit appears rodent-like with respect to some morphologic features, protein sequence data have led some to suggest that rabbits may be more closely related to primates than to rodents.[1] The scientific name of the rabbit is *Oryctolagus cuniculus*. An adult male rabbit is called a **buck**, an adult female rabbit is called a **doe**, and an immature rabbit is called a **kit**.

Common uses of rabbits in research include polyclonal antibody production, biomedical device testing and development, atherosclerosis research, and teratogenicity testing of pharmaceutical compounds.

Breeds

The most common breed used in research is the albino New Zealand White. Less commonly used breeds include the Dutch Belted and the Flemish Giant. Special genetic strains are also available, such as the Watanabe rabbit, which has inherited hyperlipidemia.

Behavior

Rabbits are generally timid and non-aggressive, although an occasional animal will display aggressive defense behavior, including thumping of the cage floor with the rear feet, charging the front of

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the cage, and biting. Adult males frequently are more aggressive than females, although females will aggressively defend their territory, particularly when young are present. Though generally social, overly aggressive animals may need to be housed individually. Adults often urinate and defecate habitually in specific locations of the cage. Although the rabbit is naturally nocturnal, laboratory-housed rabbits exhibit diurnal patterns of behavior.[2] Rabbits may be able to distinguish between individual humans, at least in terms of individuals associated with food availability.[3]

anatomic and physiologic features

Important and unique anatomic and physiologic features of the rabbit include the following:

Heart

- The rabbit heart lacks a tricuspid valve, with the right atrioventricular valve having only two cusps.[4]

Dentition

- The dental formula of rabbits is 2 (2/1 incisors, 0/0 canines, 3/2 premolars, and 3/3 molars).
- The teeth are all continuously erupting and will overgrow if malocclusion occurs.
- A set of small incisors directly behind the front incisors is referred to as the **peg teeth.**

Skeleton

- The overall skeleton is relatively fragile, comprising only 7% of the total body weight. In contrast, the skeleton of the cat contributes 13% to the total body weight in that species.[5]
- Skeletal fragility predisposes rabbits to fracture of the lumbar spine if not restrained properly.

Cutaneous Structures

- The **ears** are long, slender, and highly vascular, serving both thermoregulatory and auditory functions. Rabbits should NOT be grasped or restrained by the ears, since the ears are

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sensitive and easily damaged. Because of the vascularity, the ears are a frequent site for administration of compounds intravascularly and for obtaining blood samples.

- The **dewlap** is a large fold of skin present on the neck of some rabbits. This area frequently accumulates moisture and is predisposed to dermatitis.
- Bucks have no nipples, while does have 8 to 10.
- In the laboratory, New Zealand White rabbits are typically used. They are albino, thus they lack pigment and the eyes appear red due to the vasculature at the back of the eye.

Gastrointestinal System

- The **cecum** is very large and comprises approximately 40% of the total digestive tract.
- The **sacculus rotundus** is a pale-appearing accumulation of lymphoid tissue located at the junction of the cecum and the ileum.
- **Peyer's patches**, pale accumulations of lymphoid tissue located along the ileum, are relatively large in rabbits compared to other species.
- The **cecal appendix** is a large accumulation of lymphoid tissue located at the distal end of the cecum.
- The stomach is not normally empty in a healthy rabbit and has a very acidic pH of 1 to 2. Rabbits cannot regurgitate stomach contents.[6]
- Rabbits normally produce both dry and moist forms of feces. During the daytime, dry feces composed largely of indigestible fiber is produced, while at night soft, moist **night feces** is produced. Night feces, largely a product of cecal fermentation, is an important source of B-complex vitamins and protein and is normally ingested (coprophagy) by the rabbit.

Urogenital System

- The **inguinal canals**, connecting the abdominal cavity to the inguinal pouches, do not close in the rabbit. For this reason, the superficial inguinal ring should be closed following orchiectomy by open technique to prevent herniation.[6]

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- **Inguinal pouches** are located lateral to the genitalia in both sexes. The pouches are blind and contain scent glands that produce white to brown secretions that may accumulate in the pouch.
- The **urethral orifice** of the buck is rounded, whereas that of the doe is slit-like. This feature is useful for distinguishing the sexes.
- The reproductive tract of the doe is characterized by two uterine horns that are connected to the vagina by separate cervices.
- The placenta is hemochorial, in which maternal blood flows into sinus-like spaces where the transfer of nutrients to fetal circulation occurs.[7] Passive immunity is transferred to the young via the yolk sac prior to birth rather than by the colostrum or the placenta.
- The urine is normally cloudy due to a large amount of calcium carbonate and ammonium magnesium phosphate (triple phosphate) crystals. Normal urine color may range from yellow to red or red brown. The pH of rabbit urine is typically alkaline.

normative values

Basic Biologic Parameters

Typical values for basic biologic parameters (**Table 1**), clinical chemistry (**Table 2**), cerebrospinal fluid (**Table 3**), interstitial fluid (**Table 4**), respiratory and cardiovascular function (**Table 5**), hematology (**Table 6**), and reproduction (**Table 7**) are presented below.

Note: Values shown are representative of those in New Zealand White rabbits. Significant variation of values may occur between individual rabbits, breeds, and laboratories. It is imperative that individual laboratories establish normal values for their specific facility.

Clinical Chemistry

Approximate values for clinical chemistry parameters are shown in **Table 2**. Values can be expected to vary between individual rabbits, breeds, and laboratories, and with sampling method. It is imperative that laboratories establish normal values for their specific facility.

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TABLE 1 Basic Biologic Parameters of the Rabbit

Parameter	Typical value	Reference(s)
Diploid chromosome number	44	8
Life span (years)	5–7	9
Number of mammary glands	8 or 10	5
Body weight (kg)	2–5	9
Body temperature (°C)	38–40	9
Metabolic rate (kcal/kg/day)	44–54	10
Food intake (g/kg/day)	50	9
Water intake (ml/kg/day)	50–100	9
Fecal production (g/day)	15–60	11
GI transit time (hours)	4–5	5
Urine volume (ml/kg/day)	50–75	9
Urine specific gravity	1.003–1.036	9
Urine pH	8.2	9

TABLE 2 Clinical Chemistry Values of the Rabbit

Parameter	Typical value	Reference(s)
Total protein (g/dl)	5.0–7.5	9, 12–15
Globulin (g/dl)	1.5–2.7	9
Albumin (g/dl)	2.7–5.0	9, 12, 13, 15
Acid phosphatase (IU/L)	0.3–2.7	9
Alkaline phosphatase (IU/L)	10–86	9, 14
LDH (IU/L)	33.5–129	9, 15
Gamma glutamyltransferase (IU/L)	10–98	9
Aspartate aminotransferase (IU/L)	20–120	9, 14
Creatinine kinase (IU/L)	25–120	9
ALT (SGPT) (IU/L)	25–65	9, 14, 15
Sorbitol dehydrogenase (U)	170–177	15
Blood urea nitrogen (mg/dl)	5–25	9, 12, 14, 15
Creatinine (mg/dl)	0.5–2.6	9, 12, 14, 15
Glucose (mg/dl)	74–148	9, 12, 14, 15
Sodium (meq/L)	125–150	9, 12, 14, 15
Chloride (meq/L)	92–120	9, 12, 14, 15
Potassium (meq/L)	3.5–7.0	9, 12, 14, 15
Phospholipids (mg/dl)	4.0–6.0	9, 12, 14
Total bilirubin (mg/dl)	0.2–0.5	9
Uric acid (mg/dl)	1.0–4.3	9
Amylase (IU/L)	200–500	9
Serum lipid (mg/dl)	150–400	9
Phospholipids (mg/dl)	40–140	9, 15
Triglycerides (mg/dl)	50–200	9, 14
Cholesterol (mg/dl)	10–100	9, 12, 14, 15
Corticosterone (μg/dl)	1.54	15

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Cerebrospinal Fluid

Procedures for sampling cerebrospinal fluid are described in Chapter 5. Only very few white cells are present in normal cerebrospinal fluid. Presence of red blood cells in the sample often indicates contamination by blood during the sampling procedure.

TABLE 3 Cerebrospinal Fluid Cellular Values of the Rabbit

Parameter	Typical value	Reference(s)
White blood cells (cells/mm^3)	0–7	16
Lymphocytes (%)	40–79	16
Monocytes (%)	21–60	16

TABLE 4 Values for Interstitial Fluid of the Rabbit

Parameter	Typical value	Reference(s)
Colloid osmotic pressure (mmHg)	13.6	17
Viscosity (relative to water = 1)	1.9	17
Protein (g %)	2.7	17
Globulin (g %)	1.2	17
Albumin (g %)	1.5	17

Cardiovascular and Respiratory Function

Cardiovascular and respiratory function is often altered with anesthesia or disease. Normal values of cardiovascular and respiratory function are presented in **Table 5**.

TABLE 5 Values for Cardiovascular and Respiratory Function of the Rabbit

Parameter	Typical value	Reference(s)
Respiratory rate (breaths/min)	32–60	9
Heart rate (beats/min)	200–300	9
Tidal volume (ml/kg)	4–6	9
pO_2 (mmHg)	85–102	18
pCO_2 (torr)	20–46	9,18
HCO_3 (mmol/L)	12–24	9
Arterial oxygen (% volume)	12.6–15.8	18
Oxyhemoglobin (%)	91–93	18
Arterial systolic pressure (mmHg)	90–130	9, 19
Arterial diastolic pressure (mmHg)	80–90	9, 19
Arterial blood pH	7.2–7.5	9, 18

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Hematology

Approximate ranges for hematologic parameters are shown in **Table 6**. Some variation of values can be expected to occur between individual rabbits, breeds, and laboratories. It is imperative that individual laboratories establish normal values for their facility. Noteworthy hematologic features include the following:

- The rabbit neutrophil contains eosinophilic granules and is commonly referred to as the **heterophil** or **pseudoeosinophil** (**Figure 1**). It is often mistaken for the similar-appearing eosinophil, although the heterophil is distinguished by smaller, lighter granules.
- Acute stress in rabbits results in leukopenia, in contrast to leukocytosis in most other mammals.[4]
- Hyposegmented neutrophils can occasionally be microscopically observed in rabbit blood samples. This condition, known as the Pelger-Huet anomaly, is inherited as a partial dominant trait in rabbits.

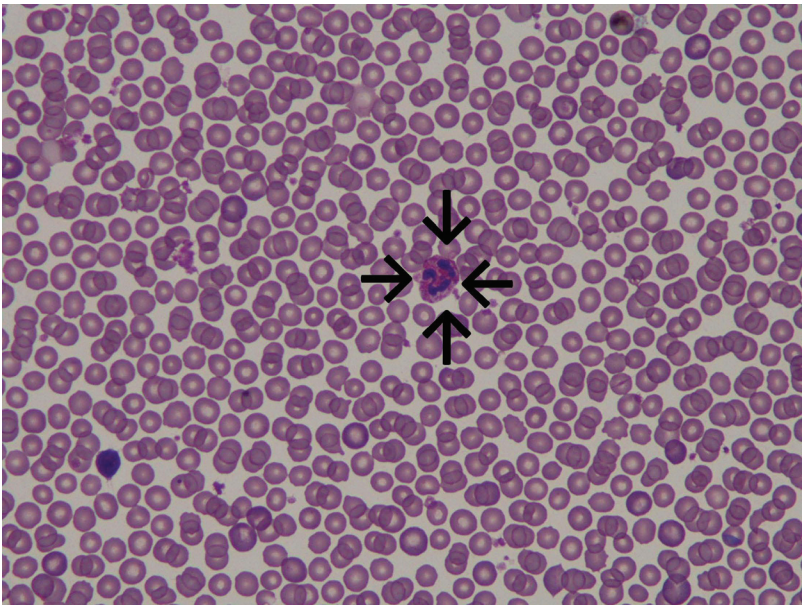


Figure 1. Heterophil (between arrows) in rabbit blood smear.

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TABLE 6 Hematologic Values of the Rabbit

Parameter	Typical Value	Reference(s)
Packed cell volume (%)	34–43	9, 12, 14, 20
Red blood cells (10^6/ul)	5.3–6.8	9, 12, 14, 20
White blood cells 10^3/ul)	5.1–9.7	9, 12, 14
Hemoglobin (g/dl)	9.8–14.0	9, 12, 14, 20
Neutrophils (%)	25–46	9, 14
Lymphocytes (%)	39–68	9
Eosinophils	0.1–2.0	9, 14
Basophils	2.0–5.0	9, 14
Monocytes (%)	1.0–9.0	9, 14
Platelets (10^3/ul)	158–650	9, 14
Reticulocytes (%)	1.9–3.8	9
MCV (fl)	60–69	9, 20
MCHC (%)	31–35	9, 14
MCH (pg)	20–23	9, 20
Blood volume (ml/kg)	55–65	9
Plasma volume (ml/kg)	28–50	9

Reproduction

Although high-quality rabbits are readily available from commercial vendors, they can be bred with relative ease. Detailed information on the reproductive biology of rabbits can be found elsewhere.[21] Important aspects of rabbit reproduction include the following:

- Puberty usually occurs between 5 to 7 months of age in New Zealand White rabbits. For does, the breeding life lasts an average of 1 to 3 years, although some remain productive for up to 5 or 6 years. Bucks typically remain reproductively useful for 5 to 6 years.
- Females do not have distinct estrous cycles, demonstrating instead a rhythm of receptivity punctuated by periods of anestrus. Receptivity is often signaled by the vulva becoming swollen, moist, and dark pink or red.
- Bucks may be mated to more than one doe. Commonly, a single buck is sufficient to service 10 to 15 does.
- The doe is brought to the buck's cage for breeding, since the female rabbit can be extremely territorial and may attack the male if he is brought to her cage.
- Ovulation is induced and occurs approximately 10 to 13 hours after copulation. Ovulation can also be induced by

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administration of luteinizing hormone,[22] human chorionic gonadotropin,[23] or gonadotropic releasing hormone.[24]

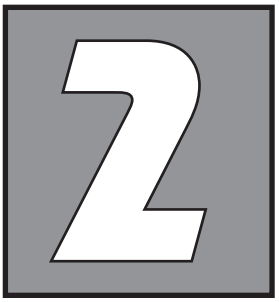
- Pregnancy can often be confirmed as early as day 14 of gestation by palpation of fetuses within the uterus, and radiographically by day 11.
- A nesting box with bedding material such as straw or clean, shredded paper should be provided to the doe several days prior to the expected kindling (birthing) date. The doe will usually line the box with her own hair. Boxes approximately 20 x 11 x 10 inches are useful for this purpose. Care should be taken not to place the nesting box in the corner of the cage or pen where the doe typically urinates.
- A number of breeding strategies have been tried with success, including natural breeding, artificial insemination, and embryo transfer.[21,25,26]
- Average gestation length and litter and kit size are summarized in **Table 7**. Values shown are typical of the New Zealand White rabbit and can vary between breeders.
- Kindling normally occurs during the morning and takes approximately 30 to 60 minutes.[27]
- Both anterior and breech presentations are normal.[27]
- The doe normally nurses the kits once daily for only several minutes. Orphaned kits can be fed kitten milk replacer.[27]
- Nursing may last 5 to 10 weeks. Kits may begin consuming solid food by 3 weeks of age, with weaning generally occurring by 5 to 8 weeks of age.
- The ears of kits open at 8 days of age, and the eyes at 9 to 11 days.

TABLE 7 Reproductive System Values of the Rabbit

Parameter	Typical value	Reference(s)
Gestation length (days)	31–32	9
Litter size (kits/litter)	7–9	9
Birth weight (g)	30–100	9

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husbandry

Good husbandry is the cornerstone of a successful laboratory animal care and use program. An effective husbandry program should address the housing, social, and nutritional needs of the rabbit,[28] as well as issues related to sanitation and record keeping.

housing

Housing of domestic laboratory rabbits should take into consideration both the **macroenvironment** (the space involving the entire room) and the **microenvironment** (the area immediately surrounding the animal).

Macroenvironment

The macroenvironment consists of the following elements:

1. **Location**. An optimal location for a room housing rabbits will be located at a site
   - where the least noise possible is present from sources such as dogs or cage wash operations
   - in close proximity to investigators and personnel responsible for care of the rabbits
   - that facilitates movement of caging equipment to and from the cage wash area

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2. **Equipment**. Equipment within the rabbit room should be:
   - what is essential for daily operations related to the care and research use of the animals
   - kept out of the reach of the rabbits and stored in a manner that facilitates sanitation

3. **Construction materials**. The following points should be considered regarding materials used in a rabbit room:
   - all surfaces of floors and walls must be capable of withstanding cleaning and disinfection procedures
   - the floors should allow movement of cages with minimal effort

4. **Environmental control**. It is important that environmental variables such as temperature, humidity, and light cycle remain consistent throughout the duration of a study.
5. **Design**. Rooms housing rabbits should be configured in such a way that:

   - sufficient space is available so that cages are easily maneuvered and operations such as cage changing are easily performed
   - the slope of the floor is toward the drain, yet not so steep as to interfere with the stability of the rabbit cages

Microenvironment

The caging system for the rabbits should provide safe and secure quarters for the animals and facilitate feeding and waste removal. Typically, several cages are secured on a cage rack equipped with casters (**Figure 2**). Appropriate caging should take into consideration the following:

1. **Size**. Cages should be large enough to allow the rabbit to freely move about and stretch out when lying down. In addition, attention should be paid to regulatory specifications for cage size. Rabbit cage size standards as described in the *Guide for the Care and Use of Laboratory Animals*[29] and the Regulations of the Animal Welfare Act[30] are shown in **Table 8**. Standards from both of these sources are the same.

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Figure 2. Rabbit cage rack with six cages.

2. **Cage materials**. Cages should be constructed of materials that are resistant to corrosion, strong enough to support and contain the animal, and facilitate disinfection. Stainless steel fulfills all these needs and is the most widely used material for rabbit cages. Heavy-duty plastics have also been used successfully for rabbit caging.
3. **Design**. Important cage design features include:

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TABLE 8 Cage Sizes for Rabbits

Body weight pounds (kilograms)	Floor area/rabbit feet^2 (meters^2)	Interior cage height inches (centimeters)
<4.4 (<2)	1.5 (0.14)	14 (35.56)
4.4–8.8 (2–4)	3.0 (0.28)	14 (35.56)
8.8–11.9 (4–5.4)	4.0 (0.37)	14 (35.56)
>11.9 (>5.4)	5.0 (0.46)	14 (35.56)

Summarized from the Guide for the Care and Use of Laboratory Animals[29] *and the Regulations of the Animal Welfare Act.*[30]

- doors that should open easily for personnel yet be secure enough to prevent escape of the rabbit. In this regard, a sliding latch on the outside of the door is effective
- walls and tops of cages that vary between solid and mesh styles; however, the openings must be sufficient to allow proper ventilation and observation
- wall and floor junctions that should be rounded and lack crevices so as to minimize accumulation of waste materials
- floors that may be slatted, expanded metal mesh, or solid bottom with perforated holes for the removal of feces and urine. In the case of wire mesh, it is recommended that the openings be 1 inch by ½ inch.[31] It is important to assure that the floor surface is non-slippery, as hip dysplasia can result in rabbits raised on floors with insufficient traction[32]
- watering devices, which include metal or ceramic bowls, bottles attached to the cage exterior, and automatic watering systems. Rabbits often overturn bowls or contaminate the water contained therein with urine or food material. Water bottles are effective, but care must be taken to assure that the bottle is firmly seated in its holder and that the sipper tube protrudes far enough into the cage. Automatic watering systems are less labor intensive, but adequate water flow from the sippers needs to be verified daily
- feeding devices, including bowls and feed hoppers attached to the cage exterior. To minimize contamination by urine or feces, feed should not be placed directly on the bottom of the cage

Environmental Conditions

It is important that the environment be maintained under stable conditions that promote the health of the rabbit. In this regard, important variables to be controlled include the following:

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1. **Temperature**. Rabbits tolerate a fairly wide range of ambient temperatures, particularly cool temperatures. The recommended ambient temperature range for rabbits is 60.8° to 69.8°F.[29]
2. **Illumination**. Although optimal lighting conditions for rabbits are unknown, common practice employs a 12- or 14-h light to a 12- or 10-h dark cycle. Light should be sufficient to allow daily observation of rabbits within their cages. Standard illumination intensities of 75 to 100 foot candles have been associated with retinal damage in albino rodents,[33,34] thus housing at lower light intensity may benefit the New Zealand White rabbit. Non-albino breeds of rabbits are presumably less likely to develop similar abnormalities under standard light intensities.
3. **Ventilation**. Ventilation should be adequate to minimize room ammonia concentration, since levels >50ppm can increase susceptibility of rabbits to respiratory disease caused by *Pasteurella multocida*.[35] For this reason, recirculation of room air is not advisable. Ventilation rates of 10 to 15 room changes per hour are commonly employed for rabbit rooms.[29]
4. **Humidity**. Recommended values for relative humidity are 40% to 60%.[29]
5. **Noise**. Rabbits may be startled by sudden, sharp noise. Physiologic changes have been noted in rabbits exposed to elevated noise.[37] Personnel should exercise care to minimize noise in the presence of rabbits.

environmental enrichment

Typical caging situations provide limited opportunity for rabbits to interact socially or with their environment. In this regard, efforts to modify the environment to encourage increased interaction may include:

1. **Group housing**. Group housing allows the rabbits the opportunity and space to more readily express their behavioral repertoire.[37] For example, group-housed female rabbits demonstrate behaviors such as mutual grooming and small-group socialization not possible for single-housed rabbits.[38] Group-penned females allowed to chose between single or paired housing prefer being in the same cage with other rabbits.[39]

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Group housing of male rabbits should be conducted with care to avoid fighting. Group-penned female and castrated male rabbits were more active, but agonistic behavior such as biting was noted even after dominance hierarchies were established.[40] Rabbits demonstrating aggression toward others should be separated from the group.

2. **Exercise**. Single-housed rabbits can be allowed to exercise in temporary floor pens. This allows for normal postures such as sitting up on the hind legs, stretching, and running. Strengthening of lumbar muscles could possibly decrease the likelihood of spinal dislocations.
3. **Holding and petting by personnel**. Acclimation of rabbits to routine handling and grooming facilitates manipulation when the animals are in a study. This reduces fractious behavior and anxiety in the rabbit.
4. **Enrichment objects**. Provision of novel objects, such as empty, cleaned soft-drink cans, balls, rattles, Nylabones® and wood blocks encourages animal movement around the cage and investigation of objects.[41] Rabbits generally interact with such objects by chewing.[39] Experience has shown that rabbits will move the objects by nudging, carrying, and tossing, depending on the shape and weight. All objects used in this manner should be free of sharp edges and be subject to minimal splintering. Additionally, objects must be easily sanitized. Enrichment objects must be replaced when they are worn or splintered, develop sharp edges, or become too soiled to clean.[42]
5. **Enrichment foods**. Novel food items, such as broccoli, apples, and alfalfa, can be offered. These items may supplement the normal feed ration; however, overfeeding of such treats may result in obesity. Introducing novel foods may entice anorexic rabbits to eat.[41]

nutrition

Rabbits are herbivorous animals, and specific nutritional requirements depend upon age, health status, and reproductive state.[43,44] Information on rabbit nutrition is presented in greater detail elsewhere.[44] A number of high quality, nutritionally adequate commercial

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diets are readily available. The following points should be considered regarding nutrition in rabbits:

1. **Amount of feed**. The recommended amount to be fed varies with the individual diet and the rabbit. Young, growing rabbits may be fed ad libitum, whereas mature rabbits may need to be limit fed, especially if they are singly housed with limited opportunity for exercise. Experience has shown that 100 to 120 grams of a typical commercial pelleted diet is sufficient to maintain the health and weight of an average adult New Zealand White rabbit.
2. **Presentation of feed**. Feed is normally offered to rabbits in a bowl or a J-feeder attached to the side of the cage. It is important to offer feed in such a way that contamination by urine or feces does not occur. For this reason, J-feeders are preferred over bowls placed on the cage floor. The feeder should be regularly cleaned to remove feed dust, which may decrease palatability of the food. Feed may become caked and moldy at the bottom or bend of the "J" if the feeder is not thoroughly cleaned on a regular basis. Bowls and J-feeders should be emptied daily to avoid placing new food on top of contaminated or wet feed and to prevent the buildup of feed dust.
3. **Fiber**. Although fiber digestibility in the rabbit is low,[45,46] fiber is an important component of the rabbit's diet and appears to play a role in the prevention of problems associated with the digestive tract. Recommendations for fiber range from 10% to 20% of the diet, although many diets contain fiber levels closer to the latter. Additional fiber can be provided in the form of alfalfa, apples, broccoli, or other palatable plant material. Most pelleted diets are formulated using alfalfa hay, and it is to be noted that alfalfa contains higher calcium levels than other hays such as timothy.
4. **Calcium**. In contrast to most other animals, the serum calcium level is not homeostatically regulated, but rises in direct proportion to increases in dietary calcium intake.[47] Vitamin D also plays a role in calcium absorption. Vitamin D toxicity has been reported in rabbits and is characterized by extensive calcification of soft tissues[48,49] (**Figure 3**). Urinary excretion of calcium is a major route of elimination in rabbits, whereas most other mammals excrete calcium via the bile.

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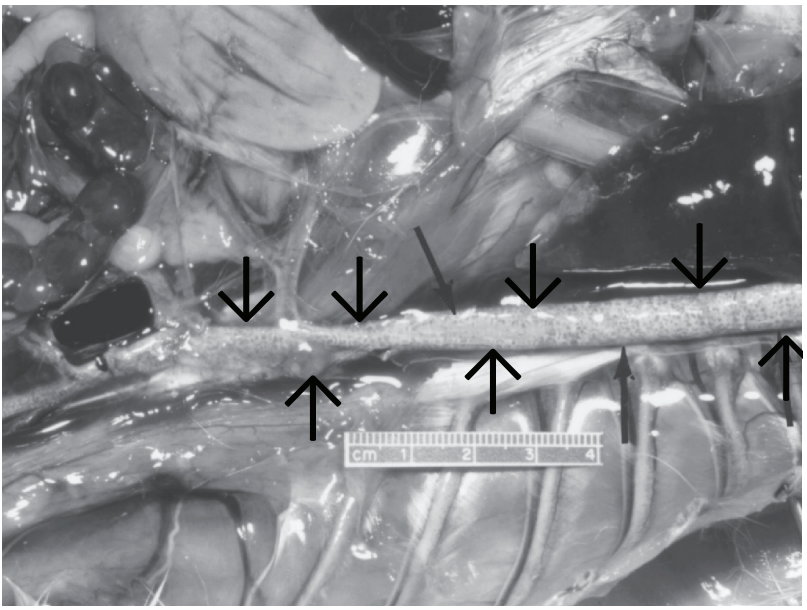


Figure 3. Rigid, calcified aorta (indicated by arrows) from a rabbit with hypervitaminosis D.

5. **Vitamin A**. Both vitamin A deficiency and toxicity have been associated with reproductive problems in rabbits.[43,50-52] Disorders are characterized by fetal resorption, abortion, stillbirth, and hydrocephalus. The precise vitamin A requirement for rabbits has not been determined, although 10,000 IU per kilogram of diet is considered adequate.[48]
6. **Vitamin E**. Vitamin E deficiency in rabbits has been associated with muscular dystrophy, abortion, stillbirth, and neonatal death in rabbits.[52-54] The precise vitamin E requirement for rabbits is not known.
7. **Storage of feed**. In general, commercial pelleted rabbit feed will retain acceptable nutritive levels for approximately 180 days (6 months) after milling. For this reason, most reputable feed suppliers indicate the date of milling on the outside of feed packages. If the date is encoded, the feed supplier can be contacted for code interpretation. Feed should be used no later than 180 days after the milling date.

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Feed should be stored in a room that is neither excessively hot nor humid. Storage of feed should be separate from that of potentially hazardous substances such as insecticides or chemicals used for cleaning and disinfection. Feed should be stored off the floor and away from the wall in order to facilitate sanitation and ventilation. The distances from the wall and off the floor are adequate when a broom or vacuum cleaner can fit behind and underneath the food, and when food can be easily moved for cleaning and it is easy to see when cleaning is necessary. In this regard, plastic pallets are useful. Open bags of feed should be stored in containers with tightly fitted lids to minimize vermin contamination. Storage procedures should facilitate display of specific information regarding the date of milling or the expiration date of the feed. Spilled feed should be promptly cleaned up and discarded.

8. **Coprophagy**. Rabbits normally produce and consume, at night, soft feces produced by the fermentative processes in the cecum. Referred to as "night feces," this material is an important source of protein and B vitamins for the rabbit.
9. **Water**. Rabbits should be provided a constant source of fresh, clean, potable water. Water intake averages 50 to 100 mL/kg of body weight per day for rabbits, although growing, pregnant, or lactating rabbits require additional water. To some degree, water consumption is also influenced by the amount and type of feed, with increased intake being associated with high-fiber diets.[43] Water can be provided by means of water bottles attached to cages, automatic watering systems, or bowls placed in the cage. As a caution, water bowls placed in cages and not secured must be checked frequently, as rabbits will overturn or contaminate the water.

sanitation

Effective sanitation is a crucial part of a sound husbandry program.[55] The chief objective of sanitation is to maintain the cage and room free of debris and waste that could provide a substrate for microorganisms and attract and harbor vermin. To achieve this objective, issues such as frequency and methods of sanitation must be considered.

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Frequency

Frequency of cage and room sanitation may depend upon factors including the number of animals per room, efficiency of the ventilation system, and individual animal behavior. In general, experience has shown that effective sanitation may be achieved using the following schedule:

1. **Daily**. Remove feces and urine from the litter tray and sweep or damp-mop the animal-room floors.
2. **Weekly**. Transfer rabbits to clean, disinfected cages. The optimal changing interval is weekly, although some facilities change cages biweekly or monthly. Litter trays should be disinfected weekly to prevent a buildup of urine scale. Contact bedding from solid-bottom cages should be replaced weekly or as needed. These procedures should be performed more frequently if necessary to provide adequate sanitation.
3. **Monthly**. Cage racks need to be replaced with clean racks. Some facilities opt to replace cage racks at the same time they replace the cages. A convenient time to clean the room is when the animals are placed in clean racks and cages. Monthly room cleaning regularly includes mopping all surfaces (ceiling, walls, and floor) and disinfecting waste and feed containers. Any sinks should be cleaned monthly as well.
4. **End of study**. Animal rooms should be cleaned and disinfected at the conclusion of animal studies or whenever the room is emptied of animals.

Methods

The following method can be followed for disinfection of caging equipment:

1. **Remove gross debris**. Remove all grossly visible debris such as hair, feces, and urine scale before beginning chemical disinfection (**Figure 4**). Brushing and rinsing with water are often sufficient to accomplish this step, although a detergent may be added to loosen or dissolve debris. Removal of urine scale may require washing or soaking equipment in a preparation containing an acid such as phosphoric acid or citric acid. Individuals performing these procedures should wear

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Figure 4. Use of high-pressure water to remove waste material from rabbit cage pan. Note that the operator is wearing appropriate protective equipment.

protective equipment to minimize the risk of chemical or thermal injury to the skin, eyes, and nasal passages. Hearing protection is also advisable, because of the intensity of noise that may be generated by cage-washing operations.

2. **Disinfection of surfaces**. Disinfection is generally performed by application of a chemical detergent and disinfectant followed by a water rinse. A variety of disinfectant chemicals are available from a number of vendors. Any application of chemicals to cages or equipment should be followed by thorough rinsing with water to minimize exposure of animals to potentially harmful chemical residues. Alternatively, hot water may be used to disinfect equipment. Typically water at a temperature of 180°F is used for this step, although procedures using water at lower temperatures with longer sanitation times have been shown to be similarly effective.[56] Although sanitization may be effectively performed manually,[57] the use of automatic cage washers is an efficient means to perform this function.

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Note: Personnel should wear protective equipment such as protective, chemically resistant gloves, aprons, and safety goggles or face shield when handling chemicals used for sanitation.

The following method can be used for disinfection of animal rooms:

1. **Remove gross debris**. Removal of all gross waste is accomplished by sweeping up loose materials. Many disinfectants are inactivated by organic debris. For areas of stubborn soiling, a detergent can be applied to loosen and dissolve debris, followed by manual scrubbing with a brush.
2. **Disinfection of surfaces**. Common disinfection practices include:

   - mopping with a disinfectant
   - foaming the interior surfaces with a disinfectant
   - using a pressure sprayer
   - applying sterilization chemicals such as chlorine dioxide, formaldehyde, hydrogen peroxide, or paracetic acid[58]

The use of the double-bucket method is recommended when mopping. This allows one side to have a disinfectant detergent and the other to contain clean rinse water. The length of contact time for disinfectant solutions varies depending on the dilution in water, the type of chemical, and the level of sanitation to be achieved. Many require rinsing with water before returning animals to the area.

Note: Animals should be removed from rooms or protected in such a way that they do not become wet or exposed to chemicals during cleaning.

Quality Control of Sanitation

It is important that the overall efficacy of disinfection procedures be assessed periodically. Several methods may be employed in this regard:

1. **Temperature indicators**. Temperature tape monitoring utilizes tape applied to equipment undergoing thermal disinfection. The tape changes color when exposed to temperatures and times consistent with disinfection (**Figure 5**). Monitoring cage-wash temperature with temperature tape is often performed each day the cage-washing machine is used. Used

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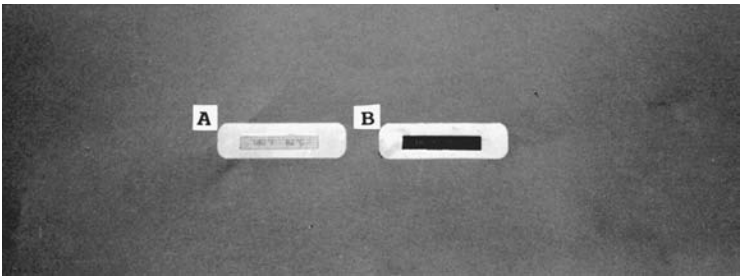


Figure 5. Temperature tape before (A) and after (B) exposure to 180°F water.

tapes should be maintained in a log as a record demonstrating that an acceptable cage-wash temperature was reached.

2. **Microbiological monitoring**. Microbiological monitoring involves bacterial culture of equipment and room surfaces. Surfaces to test include animal room surfaces, cages, cage racks, water bottles, sipper tubes, feeders, and any other equipment that undergoes disinfection. Surfaces may be cultured using RODAC (Replicate Organism Detection and Counting) plates. Surfaces can be swabbed and then plated, or the RODAC plate can be gently touched against any flat surface (**Figure 6**). RODAC plates are incubated and bacterial



Figure 6. Application of a RODAC (Replicate Organism Detection and Counting) plate to an interior wall of a cage.

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colonies counted 48 hours later. Moderate or heavy bacterial growth indicates weakness in the disinfection process and necessitates evaluation of disinfection procedures and equipment.

transportation

On occasion, live rabbits must be transported between facilities or institutions. Important aspects of transportation include the shipping container, provision of food and water during transit, observation of rabbits during transit, and environmental factors. In the United States, specific requirements for transportation of rabbits are described in the Regulations of the Animal Welfare Act.[30]

1. **Shipping container**. The shipping container should be constructed of material durable enough to securely contain and protect the rabbit and withstand damage that could result in animal injury. Sufficient space should be provided to allow the rabbit to make normal postural adjustments. Containers should be designed to allow adequate ventilation of the interior of the container, yet protect the rabbit from drafts.
2. **Food and water**. The need to provide food and water during transportation depends on the length of time and conditions of shipping. The Regulations of the Animal Welfare Act state that food and water need to be provided in instances when transit will last longer than 6 hours.[30] If relatively warm temperatures are anticipated during shipping, however, it may be beneficial to provide a water source for rabbits in transit for less than 6 hours.
3. **Observation**. Frequent observation of rabbits during transportation is recommended. The Regulations of the Animal Welfare Act require observation every 4 hours.[30] Adequacy of ventilation, ambient temperature, and general condition of the rabbit should all be assured during observations. Any factors resulting in stress to the animal should be corrected as soon as possible. Animals exhibiting health problems should receive prompt veterinary care.
4. **Environment**. Maintaining the microenvironment of the primary enclosure during shipment of rabbits is of great importance. In this regard, the ventilation system should

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allow adequate fresh air into the shipping container and minimize drafts. Extremes of temperature should be avoided. Addition of absorbent bedding will aid in waste management during shipping.

record keeping

Accurate records are of vital importance to a good husbandry program. Records should be maintained in such a manner that they are easily accessible to and understood by those who need them and easily completed by those annotating them. Records should be maintained so that they are protected from theft, animals, or damage due to moisture. It is important that all personnel clearly understand what specific information is to be recorded and the need for such records.

Identification of individual rabbits facilitates accurate record keeping procedures. Common methods used to identify individual rabbits include cage cards, plastic ear tags, tattoos (**Figure 7**), and implantable electronic microchip devices. Many vendors of research rabbits supply animals individually identified by one of these means. In the



Figure 7. Identification tattoo on the inner surface of the ear of a rabbit.

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case of some vendors, breeding records based on animal identification can be used to determine the pedigree of individual animals.

Following are some of the basic records that should be maintained by an animal research facility:

1. **Health records.** Daily records of animal health facilitate good animal care. Whether one keeps health records for individual animals or for rooms of animals is a matter of individual preference and requirements of the research. Daily entries might note the rabbit's appetite, urine and feces output, and any specific abnormalities. Additionally, experimental manipulations and administration of medications should be recorded. Information regarding abnormal animals should be promptly communicated to the attending veterinarian. A monthly record of physical examination including weight and body condition for animals in long-term studies can be a useful tool. This allows for identification of trends in weight loss and gain. The ears, teeth, and nails should also be examined and cleaned or trimmed as needed to maintain the comfort and well-being of the rabbit.
2. **Census**. Information concerning the number of animals in individual rooms and the overall facility is helpful in planning the daily workload. Census information maintained in a room or on the outside door and logged into a permanent record according to protocol approval number or principal investigator is often useful.
3. **Work records**. Records of routine husbandry tasks carried out in animal rooms should be maintained. Basic relevant information could include cage and rack changes, room temperature and humidity, sanitation of room surfaces, cleaning of sinks, changing of room air filters, replacement of sponges and mop heads, and cleaning of waste receptacles and feed barrels. The date and initials of the individual performing the daily/weekly/monthly tasks should be part of the log.

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3

management

regulatory agencies and compliance

Specific regulatory agencies and requirements may vary with locale; however, in the United States the following are the primary organizations with regulatory oversight or accreditation responsibilities for programs of research, teaching, or testing involving rabbits:

U.S. Department of Agriculture

- Oversight responsibility is described in the **Animal Welfare Act** (P.L. 91-579, 94-279, 99-198).[59]
- Specific regulatory requirements are described in the **Regulations of the Animal Welfare Act.**[30]
- Registration with the USDA and adherence to USDA regulations are required by all institutions, except elementary and secondary schools, using rabbits in teaching, testing, or research in the United States.

National Institutes of Health, Public Health Service (PHS)

- Oversight responsibility is described in the **Health Research Extension Act of 1985** (P.L. 99-158).[60]
- Policy is described in the **Public Health Service Policy on Humane Care and Use of Laboratory Animals.**[61]

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- Adherence to the PHS Policy is required of those institutions conducting research using funds from PHS.
- Principles for implementation of PHS policy are those described in the *Guide for the Care and Use of Laboratory Animals.*[29]

U.S. Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA)

- Policies are described in the **Good Laboratory Practices for Nonclinical Laboratory Studies** (CFR 21 (Food and Drugs), Part 58, Subparts A–K; CFR Title 40 (Protection of Environment), Part 160, Subparts A–J; CFR Title 40 (Protection of Environment), Part 792, Subparts A–L).
- In general, standard operating procedures must be outlined and rigorously followed and supported with detailed records.
- Adherence is required when using rabbits in studies used to request research or marketing permits as part of the approval process for drugs or medical devices intended for human use.

Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International)

- AAALAC International is a nonprofit organization designed to provide peer-review-based accreditation to animal research facilities.
- Basis for accreditation is adherence to principles described in the *Guide for the Care and Use of Laboratory Animals.*[29]
- Accreditation is voluntary.

In addition to the above regulatory bodies, state and local regulations may exist. This is particularly true for research facilities outside of the United States, where specific federal regulatory requirements may differ from those in the United States.

Institutional Animal Care and Use Committee (IACUC)

The basic unit of an effective animal care and use program is the Institutional Animal Care and Use Committee (IACUC). The USDA, Public Health Service (PHS), and AAALAC-International require an

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IACUC at any institution that falls under their purview and uses rabbits in research, teaching, or testing. Important points regarding the composition of the IACUC include:

- **Number of members.** USDA regulations require a minimum of three members, while the PHS policy requires a minimum of five members.
- **Qualifications of members.** The IACUC should include the following:
  - A chairperson
  - A doctor of veterinary medicine who has training or experience in laboratory animal medicine or science, and responsibility for activities involving animals at the research facility
  - An individual who is in no way affiliated with the institution other than as an IACUC member. At some institutions this role has been fulfilled by clergypersons, lawyers, or local humane society or animal shelter officials.

In addition, PHS policy requires the following members:

- A practicing scientist with experience in animal research
- One member whose primary concerns are in a nonscientific area. This individual may be an employee of the institution served by the IACUC
- It is acceptable for a single individual to fulfill more than one of the above categories.

Responsibilities of the IACUC

The written regulations should be consulted for an in-depth description of IACUC responsibilities. In general, the IACUC is charged with the following:

- reviewing proposed protocols for activities involving use of animals in research, teaching, and testing. Written protocols must be approved by the IACUC before animal use may begin
- inspecting and assuring that the animal research facilities and equipment meet an acceptable standard
- assuring that personnel are adequately trained and qualified to conduct research using animals

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- assuring that animals are properly handled and cared for
- assuring that the investigator has considered alternatives to potentially painful or stressful procedures and has determined that the research is nonduplicative
- assuring that sedatives, analgesics, and anesthetics are used when appropriate
- assuring that proper surgical preparation and technique are utilized
- assuring that animals are euthanized appropriately

occupational health and zoonotic diseases

Domestic rabbits purchased from reputable vendors pose virtually no risk of infectious zoonotic disease, unless experimentally infected with zoonotic pathogens. The aspects of a comprehensive program for occupational safety and health for individuals working with laboratory animals has been described.[62] In general, personnel should wear a clean lab coat or coveralls when working with research animals. Further, to mitigate risk associated with allergen exposure, individuals should wear disposable gloves and should consider measures for respiratory protection. Occupational health programs for personnel handling rabbits should be developed based on risk assessment and with consideration for the following potential health issues:

- **Puncture, bite, and scratch wounds.** Rabbits will infrequently bite; scratch wounds, however, while often inflicted unintentionally, are considerably more common. Puncture wounds may result from handling equipment with sharp edges or points. For this reason, personnel should have current tetanus immunization.
- **Ringworm.** Ringworm results from infection of cutaneous tissue with fungi called dermatophytes. Any rabbit demonstrating characteristic ringworm lesions as described in the veterinary care section (Chapter 4) of this handbook should be considered a possible source of human infection.
- **Allergy.** Allergies to rabbit dander are not uncommon in personnel exposed to rabbits.[63] Personnel may experience respiratory symptoms such as sneezing and rhinitis or skin symptoms such as redness, swelling, and pruritis following exposure. As

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with may other allergies, extreme sensitivity to rabbit dander can result in anaphylaxis and thus represents a serious occupational hazard for some individuals. It is advisable for sensitive personnel to wear a particulate filter mask or fitted respirator, gloves, and a clean launderable lab coat or coveralls (**Figure 8**). Ideally, sensitive personnel should be reassigned to job tasks that eliminate the possibility of exposure to allergens. The advice of an occupational health specialist should be sought and followed if reassignment away from rabbit areas is not possible. In addition, it is advisable for such individuals to undergo periodic respiratory-function testing.

- **Experimental biohazards.** Some studies may involve purposeful infection of rabbits with known human pathogens. In such cases, it is recommended that standard operating procedures for safe handling of biohazardous materials and infected animals be established and followed. Guidelines for use of biohazardous agents are discussed in detail elsewhere.[64]



Figure 8. An animal caretaker wearing disposable gloves, mask, and launderable long-sleeve smock to decrease exposure to allergens during animal handling.

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veterinary care

basic veterinary supplies

The following basic supplies are useful for the clinical care of rabbits:

- A stethoscope
- Disposable syringes, ranging in size from 1 mL to 12 mL
- Disposable hypodermic needles, ranging in size from 21 to 26 gauge (diameter) and 5/8 to 1½ in. (length)
- Blood collection tubes with no additive (for serum) or added EDTA (for whole blood)
- Gauze sponges
- Small animal rectal thermometer
- Lubricating jelly
- Disinfectant such as povidone-iodine solution
- Sterile fluid such as lactated Ringer's solution or 0.9% sodium chloride
- Nail clippers
- Bacterial culture swabs in transport media
- 8-French infant feeding tubes for oral gavage

Additional supplies should supplement those listed above, depending upon the needs of the facility.

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physical examination of the rabbit

A physical examination should be performed on rabbits upon arrival at the facility and on rabbits exhibiting any abnormalities. Findings should be recorded in the medical records for the animal. Physical examination of the rabbit is performed in the following manner:

1. General assessment of behavior of the animal within the cage and during removal from the cage. Findings such as lethargy or aggressiveness should be noted.
2. The feces and urine in the cage pan should be inspected, and abnormal consistency, color, or odor noted.
3. The feed bowl or hopper should be checked to evaluate the rabbit's appetite.
4. The coat should be examined for hair loss, open or closed skin lesions, and abnormal masses.
5. The bottom of the feet should be examined for open or closed lesions. Overgrown toenails should be clipped.
6. The eyes should be examined for discharge or abnormal coloring of the conjunctiva.
7. The nose should be examined for discharge.
8. The lips and mouth should be examined for lesions and overgrown incisors.
9. The ears should be examined for accumulation of dry, brown, crusty material, which is suggestive of ear mite infestation.
10. A stethoscope should be used to listen for abnormal respiratory sounds, which may indicate pneumonia.
11. The abdomen should be palpated for abnormal masses within the abdominal cavity. This is performed by standing directly behind the rabbit and firmly pressing the fingers of both hands into the cranial part of the abdomen and slowly drawing the fingers back caudally, being sure to palpate both ventral and caudal aspects of the abdomen (**Figure 9**).
12. The perineal region is examined for fecal or urine staining, vulvar discharge, and for any other lesions.
13. The body temperature may be measured rectally by inserting, for 2 to 3 minutes, a small-animal glass rectal thermometer with a small amount of lubricating jelly applied to the

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Figure 9. Palpation of the abdomen of a New Zealand White rabbit.

bulb. Alternatively, the body temperature may be measured from the ear by use of an infrared tympanic thermometer, although values obtained by this method may vary from the rectal temperature.[65] The normal body temperature for rabbits, as measured by rectal thermometer, is 38° to 40°C (100.4° to 104°F), with some variation related to ambient environmental conditions.

quarantine

Groups of rabbits arriving from the vendor should be isolated for several days. Although physiologic stabilization occurs within 48 hours,[66] subclinical disease may require longer periods to demonstrate clinical manifestations.

common clinical problems

Rabbits can develop a variety of clinical problems, as described below. Many of these diseases can be avoided by using specific-pathogen-free (SPF) rabbits from reputable vendors.

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General Signs Suggestive of Illness

- Loss of appetite and weight loss
- Unkempt appearance, hair loss or thinning (**Figure 10**)
- Lethargy and inactivity
- Nasal or ocular discharge
- Diarrhea (**Figure 11**)

A summary of clinical disease associated with specific etiologic agents is presented in **Table 9**, and additional information for some of these diseases and agents follows.

Control of infectious disease in rabbits involves strict sanitation and isolation or removal of sick animals. Ideally, rabbits should be housed in such a way that contact between SPF rabbits and rabbits harboring potential infectious pathogens is minimized. Often, this is best achieved by maintaining SPF rabbits using barrier facilities and procedures.[67] Such procedures generally involve maintenance of the room under positive air pressure through high-efficiency particulate air (HEPA) filters, restriction of access to only those personnel essential to the care and use of the rabbits, donning of disposable gloves and clean laboratory coats and coveralls, which are worn only in the

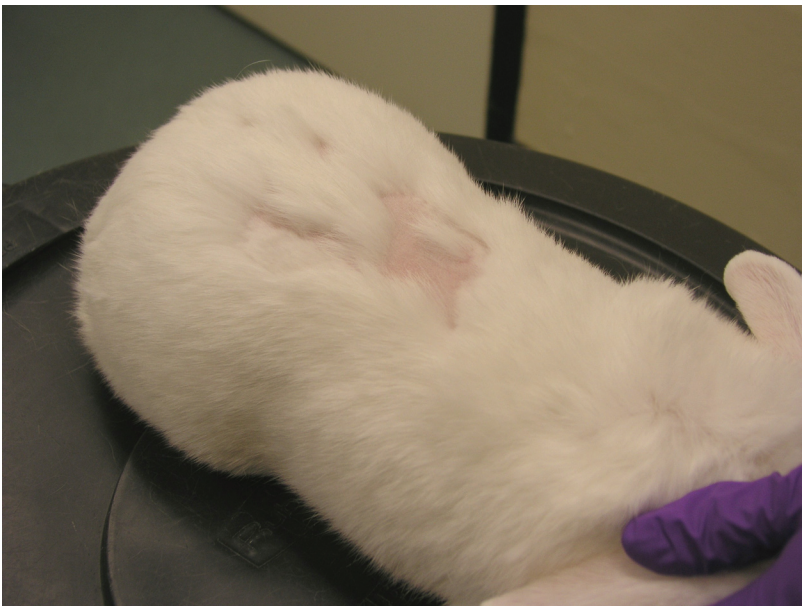


Figure 10. Alopecia on the back of a rabbit.

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TABLE 9 Common Diseases of Rabbits

Clinical signs	Etiologic syndrome
Diarrhea, distended abdomen, anorexia	Coccidiosis
Diarrhea, anorexia, high death rate	Clostridial enterotoxemia
Nasal and/or ocular discharge, anorexia, labored breathing, abscessation, reduced reproductive ability, head tilt and circling	Pasteurellosis
Ulcers and crusts on nostrils, mouth, eyelids, vulva, and prepuce	Venereal spirochetosis
Bloody vulvar discharge, anorexia, weight loss, reproductive failure	Uterine adenocarcinoma
Patchy hair loss, thinning of hair	Hair pulling
Crusty, pruritic hairless lesions on face or ears	Dermatophytosis
Ulcerated lesions on bottom of feet, reluctance to move	Ulcerative pododermatitis
Accumulation of brown, crusty matter in ears, head shaking, ear scratching	Ectoparasitic otitis externa (ear mites)
Hind limb paresis/paralysis	Lumbar spinal fracture
Anorexia, weight loss, ptyalism	Dental malocclusion
Sudden anorexia, reduced fecal output	Trichobezoar
Tenderness in perineal region	Urine scald dermatitis
Enlargement of the eye	Buphthalmia

barrier, requirements that any rabbits leaving the barrier are not permitted to return to the barrier, thorough disinfection of supplies before entry into the barrier, and, in some cases, use of autoclavable feed.



Figure 11. Rabbit with diarrhea.

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Note: The risk of infectious disease can be minimized by using specific-pathogen-free (SPF) rabbits exclusively.

The diseases and treatment/prevention strategies discussed here represent the problems most likely to be seen in a typical laboratory rabbit. More complete reviews of rabbit diseases can be found elsewhere.[5,68,69] Treatment of rabbits for disease should be implemented under the direction of a qualified veterinarian following appropriate diagnostic measures. A list of drugs commonly used in rabbits is provided in **Table 10**.

Coccidiosis

- Caused by several species of the protozoan parasite *Eimeria*, including *E. stiedae* (hepatic isolate), *E. magna* (intestinal isolate), and *E. irresidua* (intestinal isolate).
- Infection may be subclinical or may cause mild to severe diarrhea. In young rabbits, the diarrhea associated with coccidiosis may be lethal.[70]
- If the liver is affected, the abdomen may have a pendulous appearance. Numerous yellow or white spots are often present on and in the liver.

TABLE 10 Drug Dosages for Rabbits

Drug	Dosage information	General application	Reference
Cephalexin	15-20 mg/kg PO/BID	Bacterial infections	108
Dexamethasone	0.5-2 mg/kg, IM	Shock, anti-inflammatory	68
Doxapram	2-5 mg/kg IV	Stimulation of respiratory activity	108
Enrofloxacin	5 mg/kg IM/BID	Bacterial infections	79
Gentamicin	5-8 mg/kg SC/SID	Bacterial infections	77, 109
Griseofulvin	25 mg/100 g PO, repeat in 10 days	Dermatophytosis	90
Ivermectin	200–400 μg/kg SC twice, 14–18 d apart	Ectoparasitism	91-93
Oxytocin	1–2 units IM or SC	Stimulation of uterine contractions	110
Prednisone	0.5–2 mg/kg IM or SC	Anti-inflammatory	58
Procaine penicillin G + benzathine penicillin G	84,000 IU/kg SC once weekly for three weeks	Venereal spirochetosis	88
Selamectin	6–18 mg/kg topically	Psoroptic ear mange	96
Sulfamethazine	100 mg/kg PO	Coccidiosis	111
Tilmicosin	25 mg/kg, SC	Bacterial infections	86

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- Diagnosis is by examination of fecal flotation preparations for coccidial oocysts.
- Various sulfonamides will ameliorate but not eliminate infection.[71]
- Control involves strict sanitation.

Clostridial Enterotoxemia

- Caused by the spore-forming, toxin-producing, anaerobic bacteria *Clostridium spiroforme*.[72]
- Weanlings are more susceptible than adults.
- Causes moderate to severe diarrhea, frequently resulting in death.
- Diagnosis is by histopathologic examination of the cecum and colon for inflammation, isolation of *C. spiroforme* under strict anaerobic culture conditions, microscopic examination of feces for coiled Gram-positive organisms, or by assay of cecal contents for *C. spiroforme* iota toxin.[73]
- Feeding of diets with high fiber (approximately 20% fiber) may serve to prevent the disease.
- Cholestyramine administered daily by gavage (2 g/20 mL of water) may help prevent death of individuals in the event of an outbreak.[74]
- Rigorous disinfection can help control the disease. Prevention is key to control, particularly since antimicrobial resistance is common among rabbit colonies.[75]

Pasteurella Multocida Infection

- This Gram-negative bacterium is the most common bacterial pathogen of rabbits.
- Infection may be subclinical or may cause various combinations of clear to thick nasal discharge, clear to thick ocular discharge, anorexia, lethargy, and respiratory distress due to pneumonia.[76]
- Infection may also result in abscesses in subcutaneous tissues and other sites, torticollis (head tilt; **Figure 12**) and circling related to infection of the inner ear, and septicemia.

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Figure 12. Torticollis (head tilt or wry neck) due to inner ear *P. multocida* infection.

- Diagnosis is by bacterial culture of the nasal cavity or other affected tissues.
- Antibiotic treatment may include penicillin.[77] Some investigators have found enrofloxacin to be highly effective at elimination of *P. multocida* infection,[78,79] while others have found it to be ineffective.[80] Although *P. multocida*-free kits can be derived by treatment of infected does with enrofloxacin,[81] use of enrofloxacin in pregnant does may not be advisable, since the drug readily crosses the placenta[82] and is excreted in milk[83] in rabbits. In other species, enrofloxacin has been associated with cartilage damage in the young.[84,85] Tilmicosin has also been successfully used for treatment of pasteurellosis in rabbits.[86]
- Eradication of *P. multocida* from an entire colony can be attempted by various management and therapeutic procedures.[87]

Venereal Spirochetosis

- Caused by the spirochete bacteria *Treponema cuniculi*.
- Transmitted by direct contact with an infected rabbit.
- Infection may be subclinical or may result in raised, crusted or ulcerated lesions on the genitalia, perineal region, nose, mouth, and eyelids.

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- Diagnosis is by darkfield microscopic examination of lesion scrapings.
- Condition may resolve spontaneously within several weeks to months, or it can be treated with a combination of benzathine penicillin and procaine penicillin.[88]

Uterine Adenocarcinoma

- Spontaneous, highly metastatic neoplasm common among does older than two years.
- Clinical signs include anorexia, weight loss, reduced reproductive performance, and bloody vulvar discharge. Labored respiration can result from metastasis to the lungs.
- Diagnosis is usually by palpation of abnormal masses with the abdominal cavity.
- Affected animals should be humanely euthanized.

Hair Pulling

- Presumably due to nest-building behavior, boredom, or seasonal molting.
- Environmental enrichment strategies may relieve hair pulling related to boredom.

Dermatophytosis (Ringworm)

- In rabbits, most commonly caused by the fungus *Trichophyton mentagrophytes*. Less commonly, *Microsporum canis* has been implicated.[89]
- Infection may be subclinical or characterized by hair loss, reddening of skin, and crusts or scabs on the face, ears, and forelimbs. Rabbits may vigorously scratch at lesions.
- Diagnosis is made by clinical appearance, culture of hairs at the lesion margins on dermatophyte test media (DTM), or by microscopic examination of lesion skin scrapings mounted in 10% KOH for typical dermatophyte organisms.
- Transmissible to humans.
- Treatment includes application of antifungal creams to lesions or systemic treatment with griseofulvin.[90] Affected rabbits can also be successfully treated with 1% copper sulfate applied as

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a dip or with a dilution of a metastabilized chlorous acid/chlorine dioxide compound applied as either a dip or a spray.[91]

Ulcerative Pododermatitis

- Frequent in heavy rabbits housed on wire mesh floors.
- Characterized by open, ulcerated lesions on the bottom of the feet (**Figure 13**). Although any of the feet can be affected, the rear feet are more commonly involved, since rabbits bear most of their weight on the rear limbs and will occasionally stamp their rear feet when they feel threatened.
- Treatment includes cleaning the lesion and applying topical antibiotic, and providing rabbits with a Plexiglas resting board or other type of resting mat. Alternatively, affected rabbits may benefit from housing in a solid-bottom cage with wood shavings provided as bedding material.



Figure 13. Underside of foot of rabbit demonstrating open lesion typical of ulcerative pododermatitis (sore hocks).

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Ectoparasitic Otitis Externa

- Caused by infestation with *Psoroptes cuniculi*, the rabbit ear mite.
- Characterized by presence of dry, brown, crusty material adherent to the inner surface of the ear. Rabbits with intense pruritis may scratch their ears or shake their heads.
- Diagnosis is confirmed by observation of *Psoroptes* organisms upon microscopic exam of swabs of the accumulated crusty material. Mites are large and may be seen with the naked eye.
- Treatment may include instillation of 1 to 2 mL of mineral oil containing an insecticide or acaricide into the ear canal. Alternatively, ivermectin is effective;[92-94] however, it should be noted that ivermectin may have an immunopotentiating effect in rabbits.[95] Selamectin applied topically has also been demonstrated to be effective.[96]
- Topical treatment with a 2.5% solution of *Eugenia caryophyllata* essential oil has been shown to be effective.[97]

Fracture of the Lumbar Spine

- Relative strength of the hind limb musculature to the weakness of the lumbar spine predisposes rabbits to fracture or the lumbar spine when they jump or thrash during handling.
- Characterized by partial or complete hind limb paresis or paralysis, loss of control of urinary bladder function, and diminished anal sphincter tone.
- Diagnosis can be confirmed by radiography.
- Affected animals generally should be euthanized.
- Extremely valuable animals can be maintained by providing intensive nursing care, including expression of the bladder several times daily, daily cleaning of the animal, provision of a resting cushion and frequent changing of the rabbit's position to prevent decubital ulcers, and assuring adequate ingestion of food and water.

Dental Malocclusion and Overgrown Teeth

- Continuously erupting teeth of the rabbit need to wear against one another. If occlusion is not proper, the teeth will overgrow (**Figure 14**).

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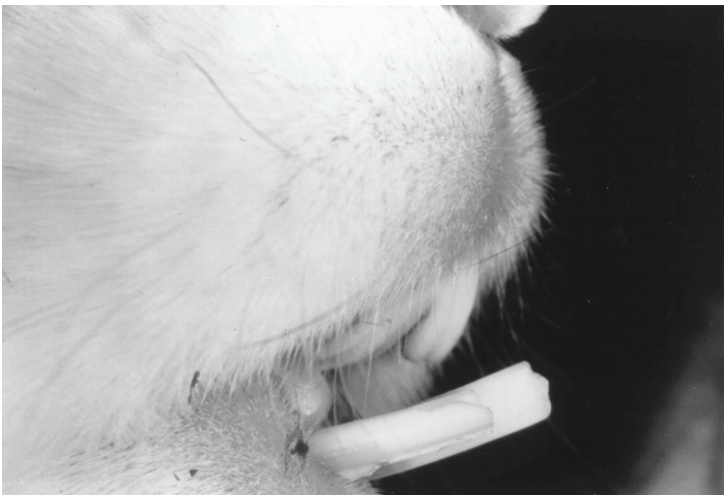


Figure 14. Rabbit with overgrown incisors due to malocclusion.

- Due to inherited mandibular prognathia (most common cause) or to fractured or missing teeth.
- Characterized by weight loss, difficulty with mastication, and ptyalism.
- Overgrown teeth should be periodically (every 4 to 8 weeks) clipped or trimmed to assure occlusal leveling, preferably with a dental bur.[98] The use of nail clippers is not recommended, since the teeth can crack.

Trichobezoar

- Fastidious grooming habits predispose rabbits to ingestion and subsequent accumulation of hair in the stomach or pylorus. Vomition of accumulated hair or other material by the rabbit is precluded by the annular gastric musculature at the base of the esophagus.
- Most rabbits with gastric trichobezoars remain clinically normal.[99] However, a few may experience anorexia, weight loss, and decreased fecal output if the trichobezoar obstructs the flow of ingesta to a significant degree. Death may result if the obstruction is prolonged.[100] Occasionally, gastric rupture with subsequent peritonitis may occur.[101]
- Diagnosis is confirmed by palpation of an abnormal, doughy mass in the cranial abdomen. Contrast radiography is not consistently conclusive.[102]

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- Treatment may include the administration of 10 to 15 mL of mineral oil by oral gavage (see Chapter 5 for the oral gavage technique), although some authors suggest administering 5 to 10 mL of fresh pineapple juice for 3 to 4 days.[5]
- Surgical gastrotomy may be necessary in some cases; however, rabbits that have been anorexic for extended periods often do not survive surgery due to their poor physiologic condition. In addition, gastrotomy may predispose the rabbit to subsequent reformation of gastric trichobezoar.[99]
- High-fiber diets may be useful in the prevention of trichobezoar.[103]

Dermatitis due to Urine Scald

- Sediments from calcium salts excreted in the urine form a viscous material when accumulated in the thick hair of the hindquarters of rabbits. This material is irritating to the skin and results in dermatitis.
- Conditions that interfere with the normal flow of the urine away from the hair and skin of the rabbit may initiate urine scald. Such conditions include lumbosacral fractures, urinary incontinence, poor husbandry and failure to remove urine-soaked bedding, cage size or configuration that results in urine reflecting back onto the rabbit, and any condition that impairs the rabbit's ability to properly move and groom (e. g., obesity and pododermatitis).[104]
- Primary conditions that result in urine scald should be identified and corrected.
- Treatment includes clipping of hair around affected area and daily cleaning with an antiseptic solution. Because the inflamed skin may be very sensitive, the rabbit may need to be sedated or tranquilized. Further, systemic antibiotics or topical antibiotic creams can help prevent secondary bacterial infections of the inflamed skin. If needed, pain-relieving analgesics are merited in cases of severe dermatitis. Further, induction of dieresis by administration of subcutaneous or oral fluids (100 mg/kg/day), or by increasing voluntary water intake by supplementing the diet with leafy green vegetables and providing fruit juice can be helpful.[104] Reducing the amount of dietary calcium by substituting timothy hay for alfalfa hay is another beneficial strategy.

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Buphthalmia

- An inherited, autosomal recessive trait.
- Clinical signs may include an enlarged and bulging eye, increased size of the anterior chamber of the eye, bluish or cloudy appearance of the cornea, and conjunctivitis.[105]
- Affected animals may have increased intraocular pressure as early as 3 months of age.[106] Intraocular pressure in rabbits can be accurately measured using either a Schiotz tonometer or a noncontact tonometer.[107]
- The enlarged eye is subject to trauma and drying. Periodic application of ocular lubricants may lessen the likelihood of drying.

treatment of disease

Drug Dosages

Treatment of sick rabbits should be implemented under the direction of a qualified veterinarian, following appropriate diagnostic measures. A short list of drugs that can be used in rabbits is provided in **Table 10**. Dosages in this table are expressed per unit of body weight as shown. Abbreviations for route of administration are PO (oral), IV (intravenous), IM (intramuscular), and SC (subcutaneous). Abbreviations for frequency of administration are SID (once daily), and BID (twice daily).

General Treatment of Diarrhea

Rabbits may quickly become dehydrated following diarrhea, and treatment should aim to replace lost fluid and electrolytes, regardless of the precise etiology. The severity of dehydration can be assessed by the "skin tent" test, in which a fold of skin on the dorsum of the neck is lifted and released. Ordinarily, the skin should return to its position within 1 to 2 seconds; however, if the animal is dehydrated, the return to normal position will take longer.

In general, appropriate replacement fluids should be isotonic and contain an excess of bicarbonate (40 to 50 mEq/L), since diarrhea may precipitate acidosis. If the animal is also anorexic, dextrose may be added to provide caloric supplementation. It is important to assess hydration of the animal while it is receiving fluids,

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since over-administration of fluids can lead to serious complications. As a general guideline, fluids may be given in increments of 30 to 40 mL/kg of body weight until normal hydration is achieved. Fluids are most easily administered subcutaneously. Intravenous administration is an alternative route.

Animals experiencing fluid and electrolyte loss often become hypothermic as they lapse into shock. For this reason, it is important to maintain the body temperature of animals with severe diarrhea. To this end, such rabbits can be provided abundant, clean bedding or towels. Supplemental heat can be provided by means of a heat lamp positioned a minimum of 10 to 12 inches from the animals or by means of a heat blanket. Close attention should be paid to animals on heat blankets, since malfunctioning blankets can cause severe thermal burns to animals. Heat blankets using a circulating warm water system provide a safe and effective source of supplemental heat.

If diagnostic efforts implicate a specific etiology as the cause of diarrhea, specific treatment directed against that etiology should be pursued under the direction of a veterinarian.

General Treatment of Anorexia

Rabbits may experience anorexia for a number of reasons; however, the specific cause is not always discernible.[112] Although any specific cause should be appropriately eliminated following diagnostic identification, it is also appropriate to employ nonspecific measures to encourage rabbits to eat and thereby overcome anorexia. Some rabbits appear to have strong food preferences and can be coaxed into eating by offering them sliced apple, broccoli, alfalfa, carrots, carrot greens, or cabbage. Some rabbits prefer food covered with a few drops of molasses. If the rabbit has ceased drinking, fluid supplementation may be necessary. Administration of 30 to 40 mL/kg/day of lactated Ringer's solution with dextrose can be given subcutaneously. Although anorexia will resolve quickly in some rabbits, others may consume a small amount of preferred food for longer periods, even 1 or 2 weeks, before fully recovering. A method for nutritional supplementation via an implanted esophagostomy tube may be useful for severely anorectic rabbits.[113] Alternatively, a percutaneously placed gastrotomy tube can be used for nutritional support.[114] Animals that experience significant loss of body condition in the face of prolonged, unresolving anorexia should be humanely euthanized.

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General Treatment of Open Skin Lesions

Rabbits may develop open skin lesions for a variety of reasons, including trauma, urine scald, abscesses related to bacterial infection, and abscesses related to the use of Freund's complete adjuvant for polyclonal antibody production. In all cases, it is important to keep the lesion free of contaminating debris. In addition, it is advisable to clean all open lesions at least every other day with an antiseptic solution.

Whether or not the inciting cause of the lesion was a bacterial pathogen, any open wound is susceptible to secondary bacterial infection. For this reason, application of a topical bacterial ointment should be considered. In addition, it is advisable to perform bacterial culture on lesions that demonstrate drainage suggestive of infection. Systemic antibiotic therapy should be based on the outcome of culture and antibiotic sensitivity testing.

It is unwise to attempt to suture or otherwise close draining lesions. On the contrary, drainage should be permitted as part of the normal healing process.

Disease Prevention through Sanitation

Practicing proper sanitation is the best way to control many diseases of the rabbit. Rabbit cages should be routinely cleaned and disinfected as described in Chapter 2. Efforts should be made to prevent excessive accumulation of feces, urine, and dander, both in the cage and in the room. Instruments and equipment used on more than a single animal should be cleaned and disinfected between rabbits. In addition, use of disposable gloves will facilitate control of infectious disease. Personnel should wash their hands with an antiseptic soap after handling rabbits suspected of harboring infectious agents. Optimally, rabbits infected with pathogens should be isolated from non-infected animals.

anesthesia and analgesia

Procedures that may produce more than momentary pain should include the appropriate use of anesthetics and/or analgesics. **General anesthesia** is appropriate for highly invasive or otherwise painful procedures, while local anesthesia may be used when desensitization of a small, localized anatomic site is appropriate. Procedures that

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may produce pain lasting beyond the duration of anesthesia, such as those involving major surgery, should include the use of **analgesics** for post-procedural pain relief.

Principles of General Anesthesia

Procedures that produce more than momentary pain should involve the use of anesthetics. A number of commonly used anesthetic compounds and regimens are described below and briefly summarized for quick reference in **Table 11**. More detailed reviews of rabbit anesthesia can be found elsewhere.[115] Only the minimal amount of anesthesia needed to maintain an acceptable level of anesthesia should be used. Great variation may exist between individual rabbits in terms of the amount of anesthetic needed to induce a surgical depth of anesthesia and duration of anesthetic effect. In general, the animal should be first given a low dose of the anesthetic and additional

TABLE 11 Common Anesthetic Drugs for Rabbits

Agent	Dosage/route	Approximate duration	Reference
Thiopental	15–30 mg/kg, IV	5–10 min.	116
Pentobarbital	20–40 mg/kg, IV	30–45 min	117
Ketamine + xylazine	35 mg/kg + 5–10 mg/kg, IM	35–90 min	118, 119
Ketamine + xylazine + acepromazine	35 mg/kg + 5 mg/kg + 0.75 mg/kg, IM	60–100 min	118
Ketamine + xylazine + butorphanol	35 mg/kg + 5 mg/kg + 0.1 mg/kg, IM	80–100 min	120
Tiletamine/zolazepan + xylazine	15 mg/kg + 5 mg/kg, IM	70 min	119
Propofol	1.5 mg/kg IV, then 0.2–0.6 mg/kg/min by IV infusion	Varies with time of infusion	121
	10 mg/kg, IV	2–3 minutes	122
Tiletamine/zolazepam	10 mg/kg, IN	45 min	123
Ketamine + midazolam	25 mg/kg + 1.0 mg/kg, IN	50 min	123
Ketamine + xylazine	10 mg/kg + 3 mg/kg, IN	35 min	123
Isoflurane	1%–3% given by inhalation	Varies with length of exposure	115
Sevoflurane	3%–4% given by inhalation	Varies with length of exposure	
Desflurane	2% given by inhalation	Varies with length of exposure	150

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doses administered if needed. Anesthetics and analgesics are most appropriately used under the guidance of a qualified veterinarian.

Abbreviations for route of administration are PO (oral), IV (intravenous), IM (intramuscular), SC (subcutaneous), and IN (intranasal).

Characteristics of Commonly Used Injectable Anesthetics

Ketamine hydrochloride

- Dissociative anesthetic.
- Produces poor muscle relaxation, copious salivation, and lacrimation.
- May produce moderate decreases in cardiopulmonary function when used with xylazine.[124,125]
- Rabbits may self-mutilate if ketamine is injected intramuscularly too close to major nerves, such as the sciatic.[126]
- Yohimbine (0.2 mg/kg, IV) can be used to reverse ketamine/xylazine anesthesia.[127]

Xylazine

- Alpha-2 adrenergic agonist.
- Produces good muscle relaxation.
- Produces depression of cardiac output and hypothermia. Death due to acidosis following ketamine/xylazine anesthesia can occur in rabbits.[128]

Tiletamine/Zolazepam

- Tiletamine is similar to ketamine, while zolazepam is a diazepinone tranquilizer.
- May cause renal disease when used alone at anesthetic levels,[129] but lower dosages combined with xylazine are safe.[119] The nephrotoxicity of the drug has been attributed to the tiletamine component.[130]
- Lower dosages administered intranasally are effective.[123]
- Produces good muscle relaxation, but decreased cardiac output.

Pentobarbital and thiopental

- Barbituric acid derivatives.

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- Thiopental is ultra-short acting and is useful for short procedures, including introduction of an endotracheal tube for administration of inhalation anesthesia. Longer-lasting anesthesia may be produced by means of a slow thiopental IV infusion drip.
- Pentobarbital produces longer-lasting anesthesia than thiopental and may be given as a bolus or as slow IV drip.
- Both produce good muscle relaxation, but with significant respiratory depression, hypothermia, and hypotension.
- Both should be administered slowly, since some animals may succumb quickly to the adverse affects of the drug and may not need the total calculated dose.
- Always administer barbiturates intravenously, since IM or SC administration may result in irritation and possibly tissue necrosis at the injection site.

Propofol

- Substituted phenol derivative.
- Induces short-duration anesthesia following IV administration.[122,131] Good for quick procedures, including endotracheal intubation.
- Propofol should not be used for long-term anesthesia due to adverse effects on the cardiopulmonary system.[132]

Principles of Gas Anesthesia

Administration of gaseous anesthetics allows more precise control of the depth of anesthesia and facilitates artificial ventilation when the animal has been intubated. More complete descriptions of the principles of gas anesthesia can be found elsewhere.[133,134]

Administration of gaseous anesthetics generally requires specialized equipment such as an anesthetic vaporizer system that regulates the flow of anesthetic and oxygen. In addition, a scavenger system for waste anesthetic gases is necessary, since exposure to such gases poses a health risk to personnel. A variety of small animal anesthesia systems are commercially available.

Gaseous anesthetics may be administered through a face mask or a tube that has been passed into the trachea (endotracheal intubation). Similarly, anesthetic gases may be administered via a laryngeal mask airway (LMA), a device intermediate between the face mask

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and endotracheal tube.[135-137] The facemask, endotracheal tube, or LMA is connected to the anesthesia system and the controls are set to deliver a specific concentration of anesthetic (**Figure 15**). Because rabbits may resist placement of the face mask, endotracheal tube, or LMA, and because rabbits often hold their breath when exposed to gas anesthetics,[138] it is advisable to first sedate or lightly anesthetize the animal with an injectable agent. It is important to insert the endotracheal tube gently, since rabbits may be predisposed to severe tracheal injury during intubation.[139]

If a face mask is used, the mask is gently fitted over the rabbit's face (**Figure 16**) and then secured with gauze tape tied around the back of the head once the animal is anesthetized. Placement of an endotracheal tube is discussed below. Alternatively, anesthesia can be induced by placing the animal in a gas anesthesia chamber, which connects to the anesthesia system for delivery of the anesthetic gas. Once the rabbit has been lightly anesthetized, it is removed from the chamber and either the face mask, endotracheal tube, or LMA may be fitted. Both Bain's circuit and T-piece circuit arrangements can be used.

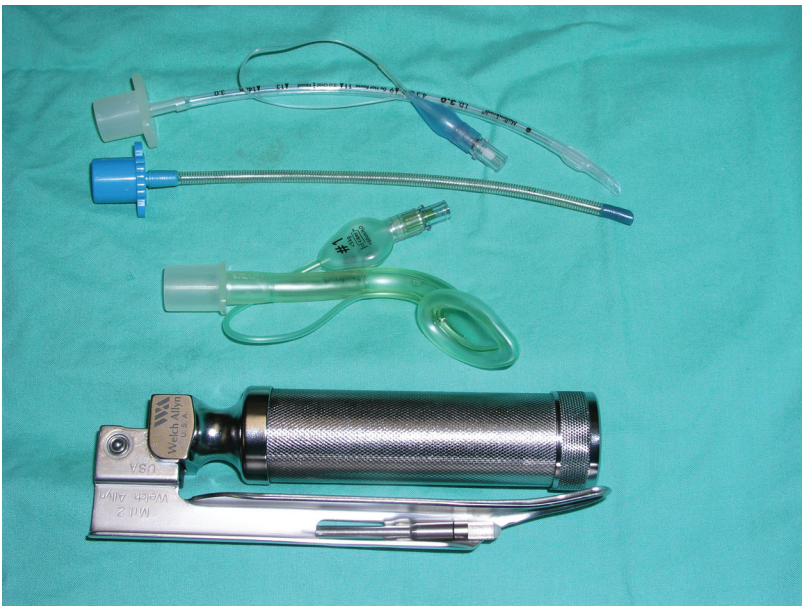


Figure 15. Equipment for airway maintenance during inhalation anesthetic delivery. From the top down: cuffed endotracheal tube, non-cuffed radio-opaque endotracheal tube, pediatric laryngeal mask airway, laryngoscope for visualization of pharynx and epiglottis.

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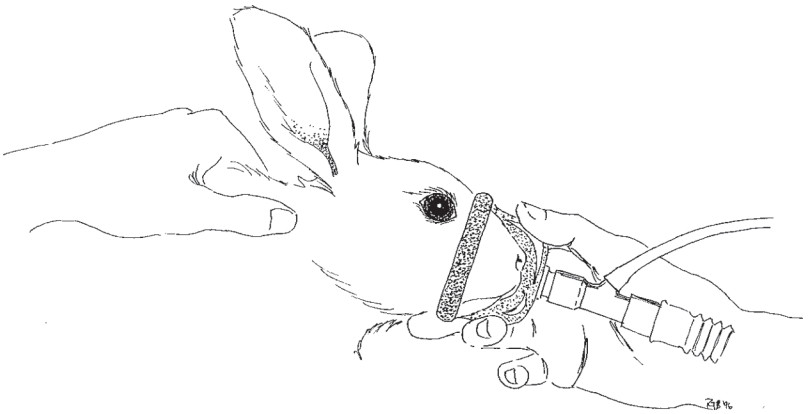


Figure 16. Placement of facemask apparatus on a rabbit for anesthesia.

The flow rate depends on the size of the rabbit, but rates of 2.5 to 7.5 L/min are commonly used. More detailed descriptions of gas anesthesia in rabbits specifically can be found elsewhere.[115,133]

Equipment for Endotracheal Intubation

- Laryngoscope with size 1 Wisconsin blade if the rabbit is >3 kg or size 0 if <3 kg
- Endotracheal tube of 2.5 to 4.0 mm internal diameter. The length of the endotracheal tube should approximate the distance from the nose of the rabbit to a point several millimeters anterior to the thoracic inlet. Freezing the endotracheal tube prior to use will stiffen the tube and facilitate intubation.[140]
- Water-soluble sterile lubricant
- Syringe to inflate endotracheal tube cuff
- Optional: lignocaine spray or 2% viscous lidocaine

Procedure for Endotracheal Intubation

1. The rabbit is lightly anesthetized with an injectable anesthetic.
2. The rabbit is placed on its sternum, and the head and neck extended. Insertion of the endotracheal tube may be facilitated by positioning the operator behind the rabbit and extending the head and neck of the rabbit upward.[141]

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3. The laryngoscope is placed over the tongue and toward the back of the mouth to improve visualization of relevant structures.
4. Pressure is exerted on the tongue with the laryngoscope blade to open the epiglottis, which covers the opening to the trachea (**Figure 17**).
5. To inhibit laryngeal spasm, the larynx can be sprayed with lignocaine or the endotracheal tube can be coated with viscous lidocaine. A small amount of water-soluble sterile lubricant should be applied to the endotracheal tube to ease passage into the trachea.
6. The endotracheal tube is advanced into the trachea and the stylet removed, if a tube with a stylet is being used. Passage of the tube to the side of the laryngoscope channel will permit continued visualization of the larynx as the tube is advanced.[142]
7. The cuff of the tube is inflated, if a cuffed tube is being used.
8. Location of the tube within the trachea, rather than the esophagus, is confirmed by detecting passage of air through the tube as the rabbit breathes.
9. The external end of the tube is connected to the gas anesthesia system.

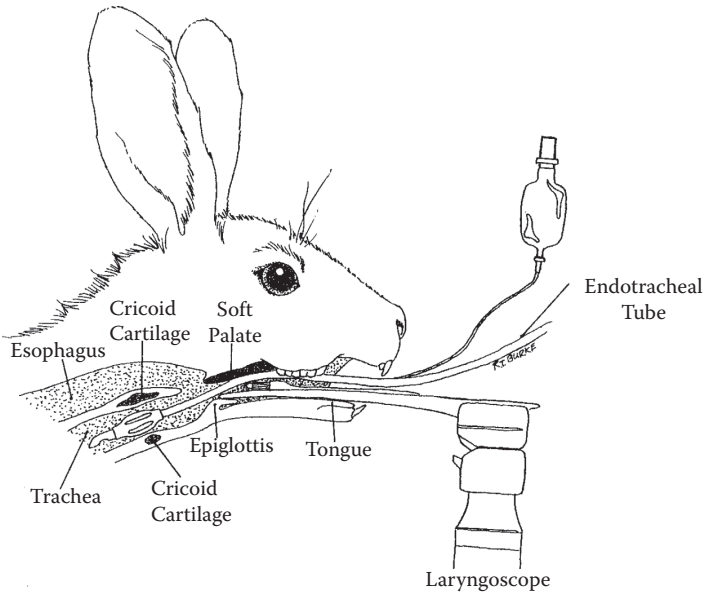


Figure 17. Endotracheal intubation of the rabbit.

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10. Following anesthesia, the tube is removed gently once the rabbit exhibits the gagging reflex.

Alternative Procedures for Endotracheal Intubation

- Blind intubation without a laryngoscope[143-146]
- Oral intubation using a fiber-optic laparoscope[147] or endoscope[148]
- Percutaneous tracheal catheterization[149]

Characteristics of Commonly Used Gas Anesthetics

Isoflurane

- Advantages: produces effective anesthesia, with less potential for untoward effects than halothane.
- Disadvantages: may induce respiratory depression and hypotension.
- Usually administered at concentrations of 1% to 3%.

Sevoflurane

- Advantages: relatively rapid anesthetic induction and recovery; less pungent and irritating than isoflurane.
- Disadvantages: may induce respiratory depression and hypotension.
- Usually administered at concentrations of 3% to 4%.

Desflurane

- Advantages: produces effective anesthesia with good muscle relaxation; with rapid induction, results in less cardiac depression compared to isoflurane.[150]
- Disadvantages: may induce respiratory depression and hypotension.
- Effective at concentrations of 2%.

Principles of Local Anesthesia

Local anesthesia involves desensitization of specific, defined sites, often involving the skin and subcutaneous tissues. Cutaneous biopsy and percutaneous blood sampling are examples of procedures that

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might involve local anesthesia. Injectable lidocaine and lignocaine-prilocaine cream are useful local anesthetics in the rabbit.

Lidocaine

- Produces excellent local tissue desensitization.
- Induction of local anesthesia involves infusion of a small volume by needle and syringe, usually 0.5 to 1.0 mL of 1% or 2% lidocaine, directly into or around the site of interest.

Lignocaine–Prilocaine cream

- A commercial preparation of lignocaine-prilocaine cream (EMLA cream, AstraZeneca, Inc., Wilmington, DE) can be used for skin desensitization prior to venipuncture of the rabbit marginal ear vein.[151]
- Cream is applied to the site and covered with an occlusive bandage. Desensitization takes place over approximately 1 hour.

Sedation and Tranquilization of Rabbits

Rabbits that resist handling or manipulation may need to be sedated or tranquilized. **Sedatives** produce drowsiness and reduce apprehension, while **tranquilizers** produce a calming effect without drowsiness. Most drugs used in this regard do not have a true analgesic effect but rather produce mental calming and increased tolerance for handling and other external stimuli. Agents frequently used for sedation or tranquilization of rabbits are listed in **Table 12**.

TABLE 12 Common Agents for Sedating/Tranquilizing Rabbits

Agent	Dosage/route	Reference(s)
Acepromazine	0.75–5.0 mg/kg, IM	152, 153
Xylazine	3–9 mg/kg, IM	154
Diazepam	4–10 mg/kg, IM	155
Hypnosis	See “Manual Restraint” Chapter 5	156, 157

Analgesia

Any procedure that could potentially result in post-procedural pain should involve the use of an analgesic. Signs of pain in the rabbit include decreased food and water consumption, reluctance to move, vocalization manifested as shrill cry, and subtle or obvious changes

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in attitude. Not all rabbits will exhibit overt indications of pain following painful procedures, thus analgesics should be routinely used for potentially painful procedures. Information for commonly used analgesics in rabbits is summarized in **Table 13**.

TABLE 13 Analgesics Commonly Used in Rabbits

Agents	Dosage/route	Degree of pain relieved, duration	Reference
Aspirin	100 mg/kg, PO in solution	Mild to moderate, 4 hours	158–160
Butorphanol tartarate	0.1–1.5 mg/kg, IV 1.0–7.5 mg/kg, SC or IM	Mild to moderate, 4 hours	161, 162
Butorphanol + xylazine	5 mg/kg + 4 mg/kg, IM	Moderate, 2 hours	115
Buprenorphine	0.01–0.05 mg/kg, SC or IV	Severe, 6–12 hours	115, 161
Fentanyl	25 μg/h transdermal patch	Severe, 24 hours*	163
Meloxicam	0.2 mg/kg, SC	Moderate to severe, 24 hours	164
Morphine	2.5 mg/kg, SC	Severe, 2–4 hours	115, 161

* *Blood levels peaked at 24 hours; however, there is no data evaluating analgesic value in rabbits.*

Perianesthetic Management

Because anesthesia can have a major physiologic impact, it is important that animals undergoing anesthesia receive proper supportive care before, during, and after the procedure.

Care Prior to Anesthesia

Only healthy animals should be subjected to anesthesia for elective procedures. The following steps should be taken to assure that the animal is healthy prior to anesthesia.

- Evaluation of a blood sample for hematologic abnormalities.
- A brief physical examination including rectal temperature measurement and auscultation of the heart and lungs should be performed to assess the overall health status and to detect any signs of illness, particularly pasteurellosis or other respiratory disease.

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- The animal should be weighed so that the accurate dose of anesthetic may be determined.

Note: Many species are fasted prior to anesthesia in order to minimize the potential for aspiration of vomited material during anesthesia; rabbits, however, are unable to vomit, so fasting is unnecessary.

- Subcutaneous fluids should be administered to prevent dehydration during the procedure. Sterile lactated Ringer's solution or 0.9% NaCl are appropriate fluids and can be easily administered subcutaneously at a dosage of 10 to 15 mL/kg of body weight for each anticipated hour of anesthesia.
- To minimize production of respiratory secretions, which may interfere with respiration, glycopyrrolate (0.1 mg/kg SC or IM) may be administered prior to anesthesia.[165]

Note: Although atropine is often used in other species to prevent excessive respiratory tract secretions, it is ineffective in many rabbits because of rapid enzymatic degradation.[166]

Care During Anesthesia

The anesthetized rabbit should be closely monitored to determine that the anesthetic depth is sufficient and to assure that the animal remains physiologically stable. In this regard, the following procedures should be followed:

1. The depth of anesthesia should be monitored prior to and during surgical or other experimental manipulations. Useful parameters to measure anesthetic depth include:
   - **Jaw Tone**. Loss of resistance to opening of the mouth is one measure of anesthetic depth.
   - **Changes in heart and respiratory rates and character.** With some anesthetic regimens, increases in heart and respiratory rate and depth can indicate an insufficient level of pain insensation.
   - **The pedal reflex.** With the leg extended, one toe is firmly pinched. In general, surgical depth of anesthesia can be assumed if the rabbit does not vocalize or attempt to withdraw the limb, although the reliability of this reflex can vary between rabbits.

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- **The ear pinch.** Failure of the rabbit to arouse following pinching of the ear indicates a relatively deep level of anesthesia.

2. Adequacy of cardiovascular function should be monitored by means that might include:
   - monitoring of heart and respiratory rate and character
   - electrocardiographic (ECG) pattern
   - blood gas levels and pH
   - blood pressure[115]

3. Body temperature of the rabbit should be maintained to prevent hypothermia, particularly if undergoing experimental surgery involving exposure of a body cavity. Appropriate measures for this include:
   - placement of the animal on blankets or heat blankets. External heating devices such as a warm-water blanket or a forced-air warming unit are important aids in maintaining normal body temperature of rabbits under general anesthesia.[167]
   - administration of warm fluids
   - increasing the ambient temperature of the room

Care Following Anesthesia

It is critical that steps be taken to assure that the rabbit returns to a normal physiologic state following anesthesia. In this regard, the following measures should be taken:

- Monitoring of rectal temperature to assure that the rabbit does not become hypothermic. Hypothermic rabbits can be covered with blankets, placed on heat blankets, or placed at least 10 to 12 inches beneath a heat lamp until the body temperature has returned to normal.
- Monitoring of pulse and respiratory rate and character
- Administration of supplemental fluids if needed

Note: A qualified veterinarian should be consulted if recovery from anesthesia is prolonged or otherwise abnormal.

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aseptic surgery

All survival surgery in rabbits should involve aseptic techniques and preparation of the surgical site. Generally, this involves the following procedures and principles:

1. Hair at the surgical site is shaved with an electric clipper.
2. The skin is scrubbed thoroughly with an antiseptic.
3. The surgical site is isolated with sterile surgical drapes.
4. Sterile surgical instruments are used for all surgical procedures.
5. Individuals performing surgery or directly assisting the surgeon wear sterile surgical gloves, gown, caps, and facemasks.
6. Principles of aseptic surgery are described in greater detail elsewhere.[168-172]

Note: Nonsurvival surgical procedures (those that do not involve recovery from anesthesia) of short duration need not be aseptic.

postsurgical management

Following surgery, animals should be monitored frequently until the experiment has been completed. Particular attention should be paid to the following:

- Any change in behavior or appetite should be noted. Changes may indicate that the animal is in pain or experiencing other complications.
- The edges of the surgical incision should remain neatly apposed following surgery. Surgical sites must be examined to assure that rabbits do not remove sutures. Equipment such as **Elizabethan** or **cervical collars** (**Figure 18**) are useful to restrict the ability of the rabbits to bite sutures, but do no interfere with the rabbits' ability to eat. **Tissue glue** is a useful alternative to sutures in rabbits, since the lack of a suture often diminishes the interest of the animal in the incision site.

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Figure 18. New Zealand White rabbit wearing a cervical collar.

- Signs of infection at the surgical site in the days and weeks after surgery. Signs of infection include
  - thick, white, yellow, or green discharge
  - abnormal warmth or redness
  - elevated body temperature

Any discharge should be cultured for bacteria, and antibiotic therapy begun under the guidance of a qualified veterinarian.

euthanasia

Euthanasia of animals should be conducted in a humane and professional manner. The specific method chosen should produce a quick, painless death. Individuals euthanizing rabbits should be properly trained in the euthanasia technique to be used. In general, animals

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should be euthanized out of the sensory range of other animals. Death should always be confirmed by stethoscopic auscultation for absence of a heartbeat. Specific methods of euthanasia for rabbits are summarized in **Table 14**. A complete summary of recommendations for euthanasia has been published by the American Veterinary Medical Association.[173]

TABLE 14 Common Methods for Euthanasia of Rabbits

Method	Route/technique	Comments
Pentobarbital overdose	150 mg/kg IV or IP	Use of pentobarbital requires Drug Enforcement Agency Registration
Carbon dioxide overdose	Inhalation of 60 to 70% CO_2 in an appropriate chamber	Compressed CO_2 in a cylinder, NOT dry ice, should be used as CO_2 source
Cervical dislocation	Neck is hyperextended and twisted, separating cervical vertebra	Do NOT perform on unanesthetized rabbits, nor those weighing >1 kg

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5

experimental methodology

Rabbits have been used in myriad different ways in research. Although it is impossible to cover all the techniques that have been used, some of the more common methods and principles for handling rabbits during experimentation are presented here. It is important that personnel performing experimental manipulations on animals are properly trained in those procedures.

restraint

It is critical that rabbits be properly restrained to ensure safety of both the animal and the handler. The relative strength of the hind limbs of the rabbit to the fragility of the skeleton may translate into fracture of the lumbar spine if the rabbit's weight is not supported properly. Rabbits should never be carried by the ears. In addition, improperly held rabbits may inflict scratches on the handler with their rear feet.

Note: The rear quarters of the rabbit must be supported during restraint.

In general, rabbits should be restrained for only the minimum amount of time needed to perform any experimental manipulation. Restraint methods include manual restraint, use of restraint devices, and chemical restraint. A variety of restraint devices have been developed for rabbits, some of which are available commercially. Most restraint devices are designed to hold the rabbit securely while allowing access to sites for administration of compounds or sampling. It is important that such equipment be sanitized following each use, since infectious disease can be transmitted between rabbits via equipment.

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Manual Restraint Methods

Lifting

- A rabbit can be picked up or lifted out of the cage by gently, but firmly, grasping the scruff of the neck with one hand and supporting the weight of the animal with the other hand (**Figure 19**). Never lift a rabbit by its ears.
- Aggressive rabbits may resist grasping and may even charge toward the handler. In such instances, a cloth towel can be gently thrown over the rabbit's head and body. This will temper the rabbit's aggression and allow the handler to grasp the scruff and lift the rabbit out of the cage in the manner described above.

Carrying

- The rabbit is picked up by placing one hand underneath the rear quarters of the rabbit to support the weight of the



Figure 19. Holding a rabbit by the scruff of the neck with one hand while supporting the rear quarters with the other hand.

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hindquarters (**Figure 19**) and grasping the scruff with the other hand. Alternatively, the rabbit can be securely held with its head tucked into the crook of the weight-supporting arm (**Figure 20**).

Holding

- Examinations and non-painful procedures can be performed using minimal restraint. Placing a hand over the head and eyes will prevent the rabbit from going forward, and a hand on the hindquarters will prevent the animal from backing away (**Figure 21**). Using less restraint can decrease anxiety and distress for minor procedures such as grooming, nail trimming, and topical drug applications.

Hypnosis[156]

- The rabbit is grasped by the scruff and gently placed on its back. The ears are placed forward over the eyes, the chin is firmly flexed against the neck, and the body is stretched out by grasping the hind legs. After several minutes, the legs are



Figure 20. Holding a rabbit by tucking the head under the elbow, supporting the body under the hindquarters with one hand and distributing the weight along the forearm of the handler.

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Figure 21. Manual restraint by covering the eyes and placing a hand over the hindquarters.

released, and the thorax and abdomen are gently stroked, resulting in a hypnotic trance. The resulting length and degree of immobilization are inconsistent between rabbits, but may permit short procedures lasting no more than several minutes to be performed. Wide variations between rabbits with respect to analgesic effect argue against use of this technique for invasive, potentially painful procedures.[157]

Mechanical Restraint Devices

Rigid restraints

- The restraint device is usually constructed of rigid metal, acrylic or polycarbonate materials. These are generally adjustable to accommodate a range of rabbit sizes and weights.
- They generally open from the top and allow the rabbit to be placed with the head in a slot or opening. The top is replaced and secured. The end is adjusted forward to prevent the animal from kicking or backing out of the restraint.
- These restraint devices have a variety of openings and panels to allow access to the normal injection and administration sites.

Soft restraints

- These restraints are composed of a durable fabric such as nylon, canvas, or a combination of the two. These restrainers

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are fashioned as a bag or wrap with zippers and/or Velcro closures to secure the rabbit inside and allow for access to normal injection and administration sites (**Figure 22**).

- They open from the top and allow the rabbit to be placed into the bag and the head to be positioned into an opening that is adjusted with Velcro tabs or metal hook and eye closures. The bag is then closed, resulting in the rabbit being swaddled, thus reducing struggling.

sampling techniques

Rabbits are frequently used in studies that require sampling of blood, urine, cerebrospinal fluid, or bone marrow. Common methods for obtaining such samples are presented below.

Blood

Frequently, large-volume blood samples are required of rabbits, particularly those used for polyclonal antibody production. General principles for blood sampling include:



Figure 22. Rabbit in a soft restraint bag.

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- **Volume of sample**. If too much blood is removed at a single time, the animal may experience hypovolemic shock and could die. If blood sampling is too frequent, the animal may become anemic. In general, 10% of the circulating blood volume can be removed every 3 to 4 weeks, or 1% at more frequent intervals of 24 hours or more, with minimum adverse effect to the rabbit.[174] The circulating blood volume is approximately 55 to 70 mL/kg of body weight; thus 6 to 7 mL/kg of body weight can be safely removed every 3 to 4 weeks. It is best to alternate sample sites each time blood is withdrawn.
- **Sampling vials**. Samples needed for evaluation of whole blood are generally collected in vials containing an anticoagulant. Samples needed for collection of plasma are collected in vials containing EDTA, heparin, sodium citrate, or potassium oxalate, depending on the experimental use. Samples for harvest of serum are collected in vials containing no anticoagulant. Blood sampled for processing to plasma or serum can be centrifuged at approximately 800 to 1000 x g for 10 to 15 minutes and the liquid fraction harvested as the sample. Alternatively, the liquid fraction (serum) will generally separate from the clotted cellular fraction if the sample is left at room temperature for approximately 30 minutes.

Note: Hypodermic needle diameter increases with decreasing gauge number.

Vascular catheterization

In situations requiring repeated blood sampling from rabbits, implantation of a vascular catheter may be merited. Placements of vascular catheters with subcutaneous ports require a survival surgery under general anesthesia. These techniques have been described for catheterization of various sites, including:

- the marginal ear vein[175-178]
- the central ear artery[179]
- the right anterior vena cava[180]
- the right atrium of the heart[181]

Subcutaneous vascular access ports allow chronic vascular access without an exposed catheter.[182] Although vascular catheters can be maintained for periods of months or even longer, catheter-tract

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bacterial infections and bacteremia are common complications,[183,184] which generally depend upon removal of the catheter for successful resolution.[185] In this regard, use of aseptic technique in catheter implantation and frequent cleaning and flushing of catheters are fundamental to successful long-term catheter maintenance.[181] Patency of catheters can be maintained by flushing 0.5 to 1 mL of sterile heparinized saline (100 IU/mL) through the catheter every other day.

Secondary renal and peripheral vascular abnormalities can result from long-term vascularization in rabbits.[186]

Note: Chronic vascular catheterization facilitates repeated blood sampling and intravenous compound administration but requires regular maintenance to avoid associated health problems.

Percutaneous blood sampling

Percutaneous sampling usually involves percutaneous vascular access by means of a syringe and sterile hypodermic needle. The bore of the needle should be just less than the diameter of the vessel to insure rapid blood withdrawal. As with all sharps, disposal in an appropriate puncture-resistant container designed for sharps is recommended. To minimize the risk of needle-stick injuries, the needle, still attached to the syringe, should be disposed of without recapping the needle. To prevent aerosolization of materials in needles, never cut or bend a needle for disposal.

Marginal ear vein or central ear artery (Figure 23)

These are the most commonly used sites for sampling of blood from rabbits. The following points should be considered:

- The artery is preferred for larger volume samples.
- Sampling of blood from the marginal vein should be performed as close to the base of the ear as possible, whereas sampling from the central artery should be performed nearer to the tip of the ear. If initial attempts at venipuncture at these sites are unsuccessful and result in hematoma formation, additional attempts can be made distally toward the tip of the ear for the vein and proximally toward the base for the artery.
- The sedative **acepromazine maleate** not only calms difficult rabbits, but is also vasodilatory at intramuscular (IM) dosages of 1 to 5 mg/kg body weight.[174] Other methods to achieve vasodilatation include wrapping the ear for several minutes

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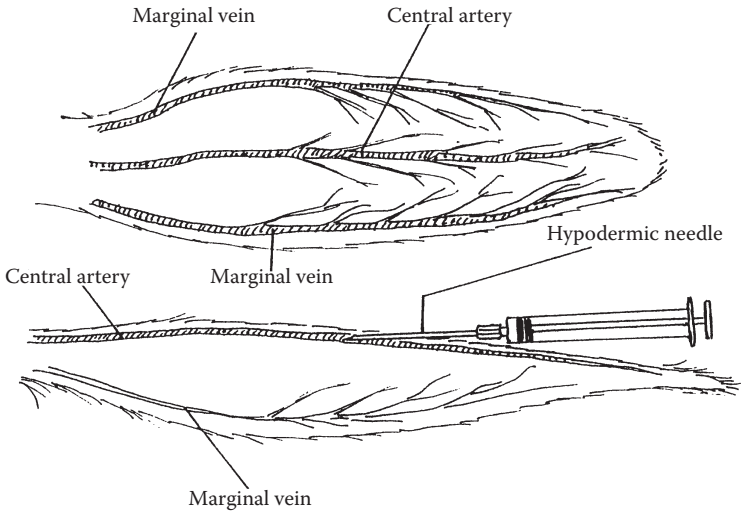


Figure 23. Location of the ear vessels from a dorsal view (top) and from a lateral view, indicating relative orientation of the needle during sampling of blood from the central artery (bottom).

in a towel soaked with warm water or by vigorously rubbing or massaging the ear for 30 to 60 seconds. The use of topical irritants has fallen out of use because of problems arising from the health risks to personnel.

Procedure

1. The hair is shaved to assist in identifying the vessels. The skin is cleaned with a non-irritating, non-astringent disinfecting agent to minimize the chance of introducing skin-associated bacteria into the blood stream and to avoid the constriction of the vessels caused by cooling during the evaporation of alcohol.
2. Locate the vessel and select an appropriately sized needle (25 to 20 gauge) and syringe (3 to 12 mL). Break the seal on the syringe plunger before beginning to facilitate blood flow.
3. Restraint is a crucial component for successful venipuncture. The rabbit should be placed in lateral recumbancy such that the ear selected is on the down side of the rabbit. Restrain by holding the rabbit's head at the jaw line. An index finger can be placed between the ears to lift the top ear for better visualization of the other ear.

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4. Hold the ear taut and straight to stabilize the ear during venipuncture. The needle is inserted with the bevel facing up. Place the needle directly on the vessel to insert. The thumb can be used to steady the syringe during blood withdrawal.
5. Once in the vessel, blood should immediately flash into the hub of the needle and begin to fill the syringe. If the plunger is pulled back too aggressively, the vessel may collapse and blood flow will cease. Likewise, a repeated back and forth motion of the plunger can cause the blood to clot in the needle.
6. The key to successful blood withdrawal is to keep the needle steady to prevent hematoma formation. Should the vessel collapse or narrow, rub the base of the ear or flick the vessel to stimulate vasodilatation and blood flow.
7. Apply pressure over the puncture site as the needle is withdrawn. After several minutes, should the puncture continue to bleed, hold off the vessel at the base of the ear to allow the clot to form at the puncture site. Monitor the rabbit for bleeding after it is returned to the cage.

Indwelling catheter in central ear artery

Temporary intravenous catheters are often used for ready access during surgical procedures. The catheters come in a variety of sizes and lengths and can be radiolucent or radio-opaque. Catheter types vary but are generally configured over the needle, where the needle acts as a stylet to stabilize the catheter during placement. They are designed to be removed or replaced after a period of 2 to 3 days. The placement method is similar to the method for blood withdrawal, with the following changes:

1. The ear should be cleaned using an antiseptic such as povidine iodine solution to decrease the chance of skin bacteria being introduced with the catheter.
2. Select a catheter size that is small enough to allow easy passage into the blood vessel. Once the needle and catheter are in the vessel, gently advance the catheter without advancing the needle. The catheter should be placed such that the entire length, to the hub, is within the vessel. The needle is removed, a cap or lock placed on the catheter hub (**Figure 24 a**), and the hub taped to the ear just before flushing. (**Figure 24 b**)

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3. The ear must be maintained in a straight position to avoid kinking the catheter or perforating the vessel wall by the catheter tip. A splint can be formed to hold the ear straight using rolled cotton covered with gauze, a padded tongue depressor, dense sponge foam, or a Styrofoam cone. One should wrap

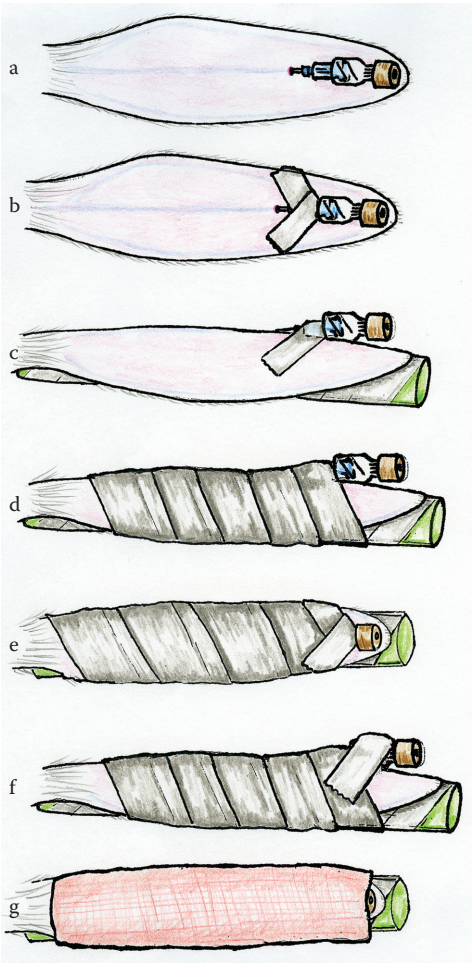


Figure 24. Indwelling catheter in the central ear artery. Sequence of securing indwelling catheter after placement. a: Catheter is capped. b: Catheter hub is secured to the ear. c: Ear splint is inserted and pinna positioned. d: Tape is applied to the ear in a spiral starting at the tip. e: Injection cap is secured with tape (dorsal view). f: Injection cap is secured with tape (lateral view). g: Protective wrap is placed over exposed cap.

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the splint with tape, sticky side out, to secure it to the inner surface of the pinna. The splint is positioned in the ear canal after the catheter is placed in the blood vessel (**Figure 24 c**).

4. The catheter is flushed with a heparin saline solution prior to taping. The patency is confirmed by visual inspection of the ear vessels while flushing; the vessels should blanch as the saline replaces the blood. If the catheter is not within the vessel, a bleb or blister will form within the skin around the vessel and resistance will be felt as the saline is being injected, indicating that the needle is not within the blood vessel.
5. The catheter is secured using paper tape or a perforated tape such as Transpore.™ These tapes can be easily removed from the hair (**Figure 24 d**). Do not crease the ear when taping to the splint. Apply the tape starting at the catheter and working toward the body. Apply in a spiral pattern to prevent a stricture that might occlude blood flow. Secure the catheter cap with tape (**Figure 24 e–f**).
6. A self-adhesive elastic wrap is used to protect the exposed catheter cap, or a stockinet sleeve can be used to prevent trauma to the ear from head shaking (**Figure 24 g**).

Jugular vein

Procedure

1. The jugular vein cannot be externally visualized in rabbits, thus jugular puncture is made following location of the vessel based on anatomical landmarks and palpation. The fur is shaved on the neck to facilitate identification of the vessel.
2. The rabbit is positioned in dorsal recumbancy and the neck extended. This is best achieved when the rabbit has been lightly anesthetized or sedated (see Chapter 4, **Table 11** for drug dosages). The site is cleaned and disinfected using alcohol and an antiseptic such as povidine iodine solution to minimize the chance of introducing skin-associated bacteria into the blood stream.
3. The vessel is palpated in the neck, after the assistant restraining the rabbit has occluded the vessel, by pressing with the thumb at the thoracic inlet.[176] The vessel will fill with blood and be easily felt under the skin, and often it will be engorged enough to visualize.

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4. Hold the rabbit's head, and turn the nose slightly away from the vessel. Insert the needle into the vessel toward the heart and withdraw blood. Before removing the needle, release the pressure at the thoracic inlet. Apply direct pressure over the venipuncture and release the head. The muscles in the neck will assist in achieving hemostasis.

Cardiac puncture

Cardiac puncture should be used for obtaining large volumes of blood when sampling is to be immediately followed by euthanasia.

Procedure

1. The rabbit must be anesthetized for this non-survival procedure. See Chapter 4, **Table 11** for anesthetics types and dosages.
2. The rabbit is placed in dorsal recumbancy. Positioning can be facilitated by using a V-trough and securing the limbs using soft cotton ties. The forelegs should be stretched forward on each side of the head.
3. The hair over the needle puncture location is wetted with alcohol or other disinfectant. This assists in locating the intercostal space for needle insertion.
4. A long, large-bore needle, such as an 18-gauge, 1½-inch needle, attached to a syringe is used for cardiac puncture. Use a 50- to 60-cc syringe if exsanguination is required.
5. The needle is inserted on the left side of the chest between the ribs at the point where maximal palpable heartbeat intensity is detected, and then directed toward the sternum. An alternate approach is to insert the needle, bevel up, in the notch to the left of the xiphoid process. The needle is directed in a cranial direction at about a 30° angle toward the back (**Figure 25**).
6. Alternately, the anesthetized rabbit may be positioned on its right side. The area for needle insertion can be generally identified on the left side of the chest where the point of the elbow touches the chest. Find the point of maximal palpable heartbeat intensity and insert the needle between the ribs, directing it toward the sternum. Because of laevoversion of the heart in some rabbits, cardiac puncture may be facilitated in those animals by placing the rabbit in left lateral recumbancy and inserting the needle through the right chest wall.

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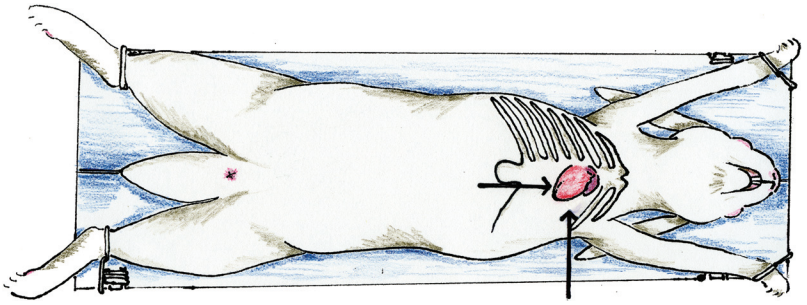


Figure 25. Restraint and positioning of the rabbit for cardiac puncture. Arrows indicate needle insertion points lateral intercostal approach or sternal approach.

Note: Cardiac puncture is performed only on animals immediately prior to euthanasia, because of the risk of cardiac tamponade and laceration of pleural viscera.

Urine

The method of urine collection depends on the use of the sample and the need for sample free from contamination with bacteria, feces, or other debris. Urine should be collected in a clean or sterile, dry container and stored under refrigeration if the sample is not to be used within several hours.

Voided sample collection

- **Voided** urine can be sampled directly from a clean pan placed beneath the rabbit housed on a wire grid. Paper or other absorbent materials must be omitted to permit collection. The urine can be poured, pipetted, or drawn up with a sterile syringe from the collection pan.
- **Manual Expression.** Voided urine can alternatively be collected by manual expression of the urinary bladder. For this method to be successful, the urinary bladder must be relatively full. The bladder is palpated in the caudal abdomen and gentle digital pressure applied to express urine from the bladder. The pressure should be firm and constant. The collection container should be positioned to catch the voided urine. If after several minutes urine is not produced, relax the pressure to prevent trauma.

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- Urine to be sampled over extended periods of time can be collected by means of a metabolism cage. Such cages employ a mechanism that diverts the urine into a collection receptacle separate from feces.

Pure or sterile sample collection

Urinary catheterization

1. Preferably, rabbits are first sedated or lightly anesthetized. The equipment needed is a sterile water-soluble lubricant, and a sterile, 9-French flexible catheter. Insert catheters only as far as necessary into the bladder. Long catheters should be measured against bladder distance to avoid knotting of the catheter in the bladder.
2. In male rabbits, the animal should be restrained in a sitting position, which allows access to the penis (**Figure 26**). Treatment of male rabbits with the sedative acepromazine (5 mg/kg IM) frequently stimulates temporary protrusion of the penis from the prepuce and could facilitate urinary catheterization of bucks. The penis is extruded and the



Figure 26. Restraint position for urinary catheterization of the male rabbit.

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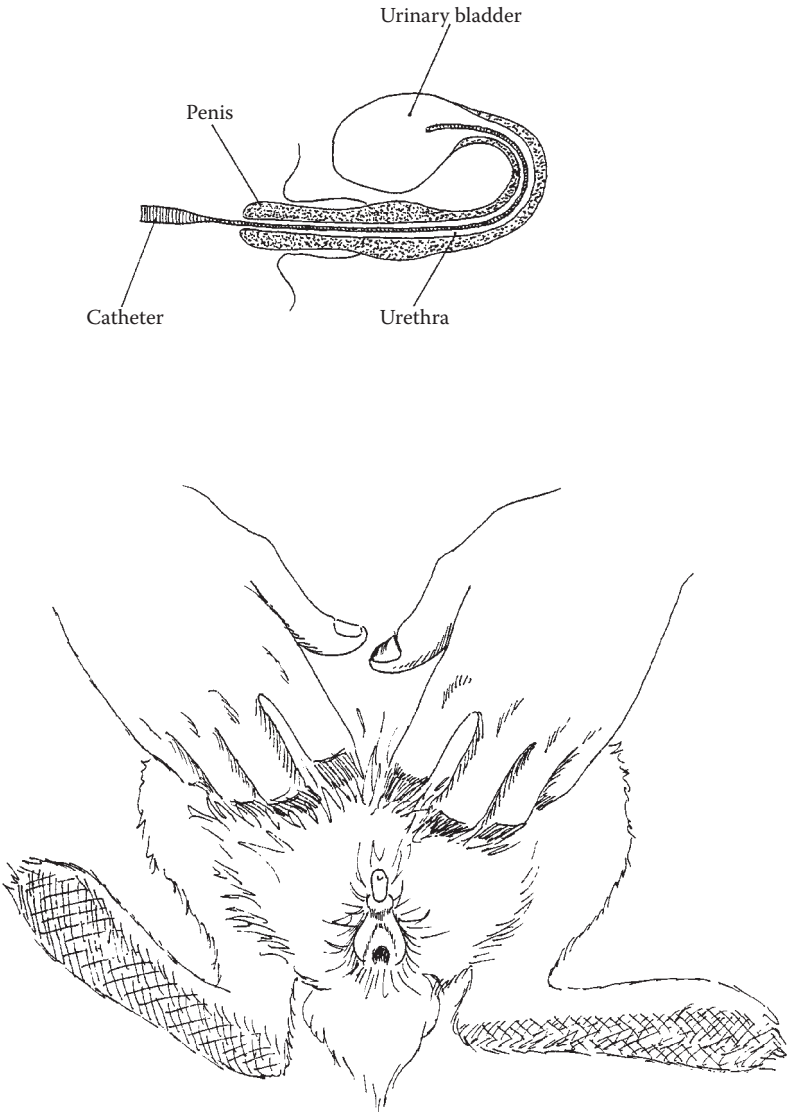


Figure 27. Orientation of the catheter in the urinary tract (top); and extrusion of the penis and palpation of the urinary bladder (bottom).

lubricated catheter is directed into the urethra and downwards (**Figure 27**).

3. In female rabbits, the animal is positioned on the sternum (**Figure 28**). The tail is reflected dorsally to allow visualization

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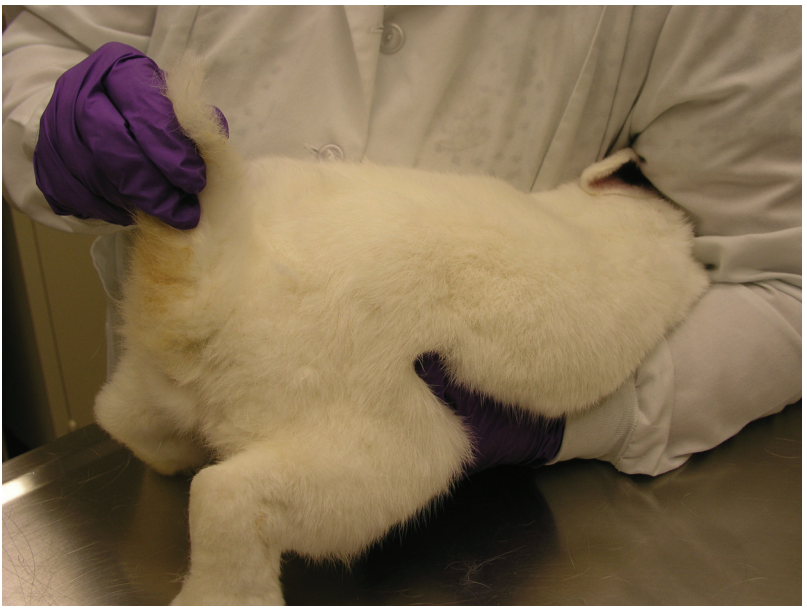


Figure 28. Restraint position for urinary catheterization of the female rabbit.

of the genital area. The lubricated catheter is advanced along the floor of the vagina where the urinary opening is located. The urinary papilla must be gently reflected dorsally with the catheter tip to allow passage into the urethra (**Figure 29**).

4. Once the catheter has entered the urinary bladder, urine should flow through the catheter following gentle manual compression of the caudal abdominal region. Gentle aspiration pressure from an attached syringe can be used.
5. Once the sample has been collected, gently remove the catheter.

Cystocentesis

1. Cystocentesis is a procedure in which a hypodermic needle attached to a syringe is passed through the abdominal wall and into the urinary bladder. This procedure should be performed on a rabbit with a palpable urinary bladder. Before beginning, palpate the caudal abdomen and locate the bladder. If this is not successful, wait approximately an hour and try again.

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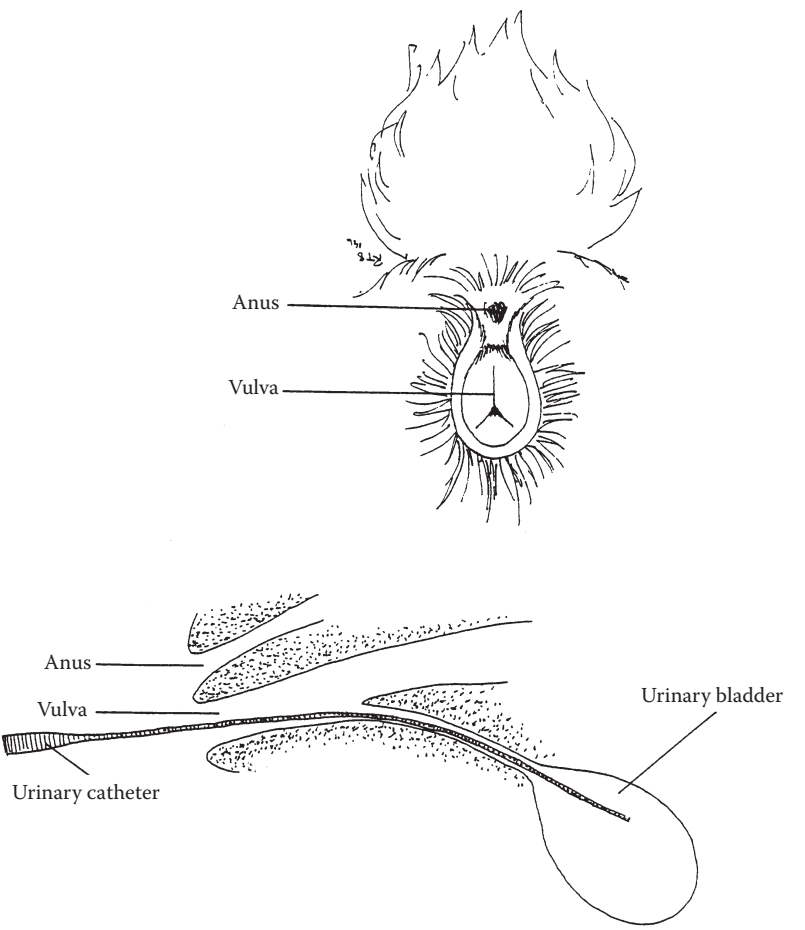


Figure 29. Location of the vulva (top) and orientation of the catheter in the urinary tract during catheterization of the female rabbit (bottom).

2. Preferably, the rabbit is first sedated or lightly anesthetized and placed in dorsal recumbancy. To facilitate positioning, a V-trough can be used with soft cotton ties placed on the legs to secure the limbs into position.
3. The caudal aspect of the abdomen is shaved and prepared as for aseptic surgery.
4. The bladder is located on the midline of the body just above the pubic bone in the pelvic girdle (**Figure 30**). Using the pubic bones as a landmark, palpate the abdomen to locate

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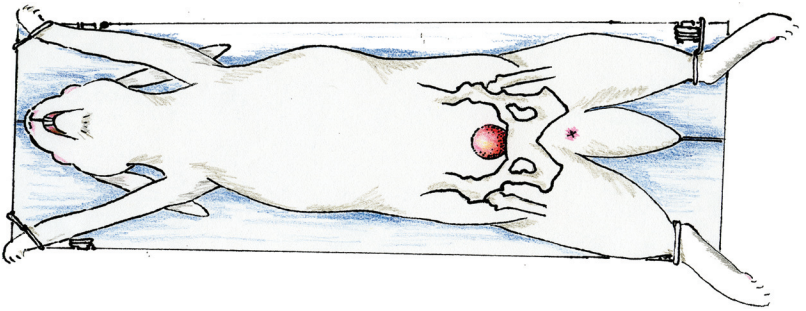


Figure 30. Restraint and positioning for cystocentesis. Note the position of the urinary bladder in relationship to the pelvic girdle, just above the pubis on the midline.

the urinary bladder. The urinary bladder is stabilized manually between the thumb and index finger of the free hand during collection (**Figure 31**). Using a 5- to 10-cc syringe with a 20- to 22-gauge hypodermic needle attached, insert the needle, perpendicular to the spine, through the skin and into the bladder. Hold the needle very still as urine is withdrawn from the bladder, as the distended bladder wall is thin and easily

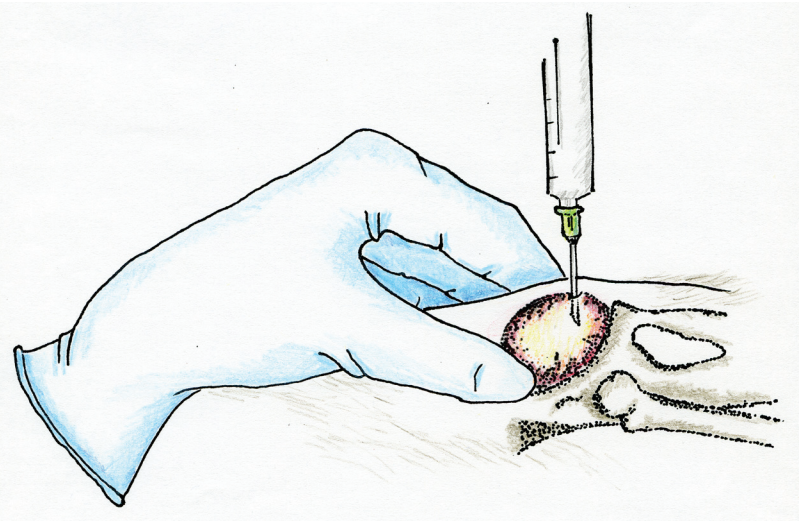


Figure 31. The bladder is stabilized with one hand while the needle is inserted into the urinary bladder on the midline, perpendicular to the spine.

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torn. Use gentle aspiration pressure from an attached syringe to collect the sample.

5. Remove the needle and apply pressure to provide hemostasis to any skin bleeding.

Cerebrospinal Fluid

Collection of cerebrospinal fluid (CSF) from rabbits requires the insertion of catheters or spinal needles. A common site is the cerebromedullary cistern. This is an enlargement of the fourth ventricle at the atlanto-occipital junction. Single CSF samples of 1.5 to 2 mL in volume are relatively easy to obtain by needle and syringe from this location.[187] Since significant damage to structures of the nervous system can occur if the rabbit is not completely immobile during the insertion of needles or catheters for CSF collection, anesthesia of the rabbit is necessary. Any time CSF samples are collected, aseptic technique and aseptic preparation of the sampling site are required.

Sampling from the cerebromedullary cistern

Procedure

1. The rabbit is anesthetized. (See Chapter 4, Table 11, for anesthetic regimens.)
2. The dorsal cervical area of the rabbit is shaved and prepared as for aseptic surgery.
3. The rabbit is placed in lateral recumbancy. With a firm grasp and placement of the thumb on the bony occipital protuberance, the head is flexed toward the chest while taking care not to obstruct the airway (**Figure 32**).
4. A 22-gauge, 1.5-in. spinal needle is slowly inserted approximately 2 mm caudal to the occipital protuberance and advanced slowly in the direction of the rabbit's mouth. It should be remembered that the epidural space of the rabbit is only 0.75 to 2.5 cm beneath the surface of the skin[188,189] in the lumbosacral region and likely is at a similar depth in the cervical region. The needle is kept parallel with the table surface, with slight rotations of the rabbit's head to maintain alignment as needed.
5. A slight decrease in resistance may be felt as the needle enters the cistern. The stylet is then removed and the CSF flow is usually apparent at the hub of the needle.

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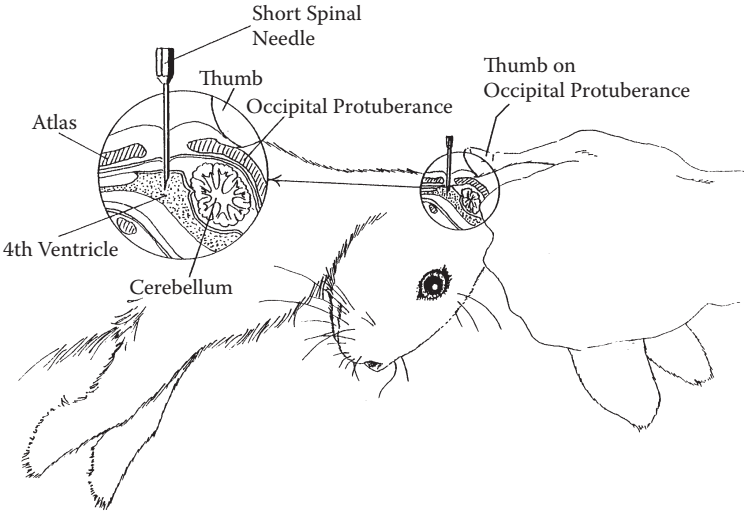


Figure 32. Sampling of cerebrospinal fluid from the rabbit. The needle passes into the 4th ventricle lateral to the spine.

6. CSF can then be harvested by gentle suction from an attached syringe. Small blood vessels are often lacerated during needle insertion, thus contamination of the sample with blood may occur with this technique.

Other sites for CSF access

- **The cisterna magna**. Catheterization of this site permits repeated chronic sampling of CSF. The advantages of such procedures are that CSF can be sampled in a nonanesthetized animal and that CSF samples obtained in this way are generally free of blood contamination.
- Methods for chronic CSF sampling from the cisterna magna include implantation of a catheter with sampling through an implanted subcutaneous access port[190] or implantation of a catheter through a surgically created hole in the skull. CSF is sampled through this catheter, which is anchored externally on the top of the head.[191]
- **Lumbar subarachnoid space**. This site can be used to sample CSF through an implanted catheter that is tunneled subcutaneously to exit externally through the skin.[192]

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- **Third ventricle**. Placement of a permanent stainless steel cannula into the third ventricle through a surgically created hole in the skull has been used as a means to collect multiple CSF samples from the unanesthetized rabbit.[193]

Bone Marrow

Sampling of bone marrow from rabbits should be performed with the animal properly anesthetized. Aseptic technique, including site preparation, should be followed. Sample sites include:

- **Proximal end of the tibia** by means of percutaneous aspiration using a 15-gauge needle.[194]
- **Humerus** by means of percutaneous aspiration using a Rosenthal pediatric needle.[195]
- **Femur** by means of percutaneous aspiration using a Rosenthal pediatric needle.[195] Alternately, marrow can be obtained through a surgical approach involving resection of the femur.[196] While this technique allows direct access to sterile marrow, the weakened femur is at risk of postsurgical fracture due to the weight-bearing function of the rear limb.

compound administration techniques

A variety of routes exist for administration of both test compounds and medications to rabbits. As with sampling techniques, it is important that the rabbit be securely restrained. When possible, rabbits should be sedated or lightly anesthetized to minimize any potential pain or distress. Routes of administration include the following:

Intravascular (IV)

Intravascular administration of compounds results in quick delivery to target tissues. Unless specifically required by experimental protocol, substances given intravascularly should be administered slowly, so that the consequences of an unexpected adverse reaction can be minimized. The following points for intravascular compound administration should be considered:

Common sites: marginal ear vein and jugular vein. The high pressure within the central ear artery precludes practical use of that vessel for compound administration by needle and syringe.

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Liquid compounds may be administered by needle and syringe using essentially the same approach as for blood sampling from these sites. The procedure is as follows:

1. Before injection of the compound, the syringe plunger should be pulled back slightly to confirm that the needle is indeed within the vessel. Intravascular location is confirmed by the presence of blood in the hub of the needle and the tip of the syringe shaft. Formation of a bleb or blister within the skin around the vessel as compound is being injected indicates that the needle is not within the blood vessel.
2. The compound is administered slowly. If the rabbit develops complications such as respiratory distress, additional compound should not be administered.

Chronic intravascular administration of compounds may be best performed through implanted catheters. Sites and techniques for catheters include:

- **Posterior facial vein**[175]
- **Marginal ear vein** using polyethylene tubing (inner diameter = 0.011 in., outer diameter = 0.024 in.) attached to a 2.8-French vascular access port affixed to the ear with cyanoacrylic adhesive[176]
- **Jugular vein,** used for chronic serial infusion by means of a surgically implanted vascular access port[182]

Continuous infusion in mobile, unrestrained rabbits can be performed using a swivel-tether system and catheterization of either the common carotid artery[149] or the marginal ear vein.[197,198]

Intramuscular (IM)

Intramuscular injection sites include the large gluteal muscles on the back of either of the rear legs (**Figure 33**) or the perilumbar musculature of the back (**Figure 34**).

Gluteal muscle injection

1. Depending on the viscosity of the compound, the smallest-bore needle possible should be used. Generally, 22- to 25-gauge needles are useful for this application.

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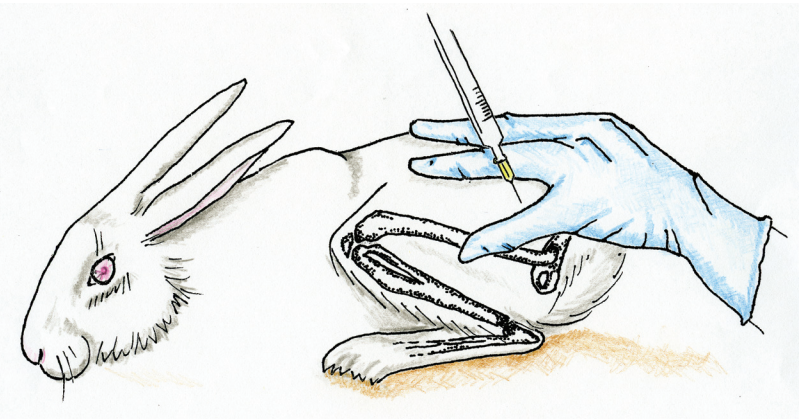


Figure 33. Administration of an intramuscular injection into the gluteal muscles of a rabbit.

2. It is important that nerves and blood vessels be avoided when giving IM injections. Position the animal on a flat surface in a normal posture with the hind legs beneath the animal. Place your hand on the animal's rump so that you can feel the iliac

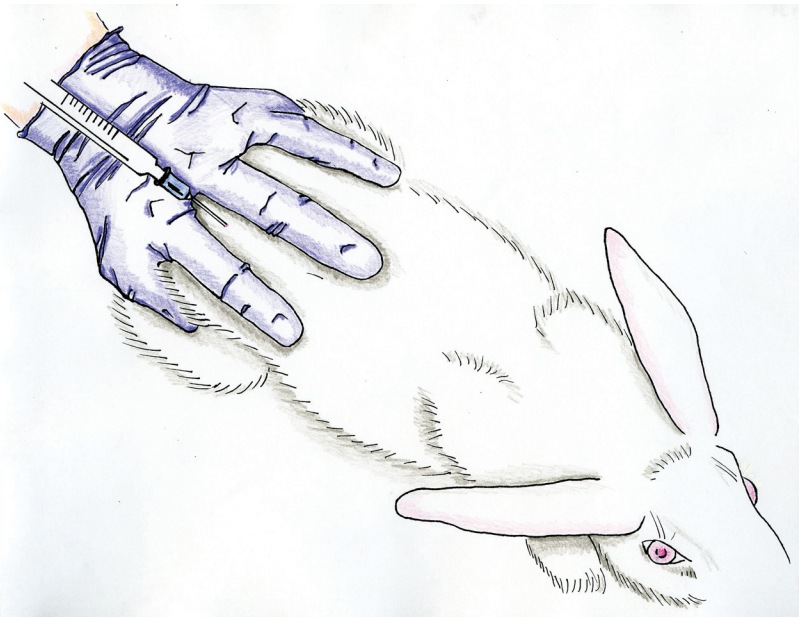


Figure 34. Administration of an intramuscular injection into the perilumbar muscles of the back in the rabbit.

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crests beneath your palm. Slide the thumb over the top of the hip and into the groove on the lateral surface of the thigh muscle. This groove is the natural separation between the *tensor fascia lata* and the gluteal muscles. The muscle mass of the *gluteus medius* is immobilized between the index finger and the thumb. Placing the thumb into the muscle groove prevents accidental injection into or around the sciatic nerve.

3. The skin can be swabbed with alcohol and the needle is inserted, bevel up, perpendicular to the skin and into the muscle close to the "V" formed by the thumb and index finger. This will ensure injection into the *gluteus medius* (**Figure 33**).
4. The syringe plunger is gently pulled back to ensure that the needle is not within a blood vessel. If intravascular, a small amount of blood may appear in the syringe or the hub of the needle, requiring the needle to be repositioned.
5. In general, volumes no greater than 0.5 mL should be injected into a single intramuscular site.

Lumbar muscle injection

1. Depending on the viscosity of the compound, the smallest-bore needle possible should be used. Generally, 22- to 25-gauge needles are useful for this application. Because the needle must penetrate the lumbrosacral fascia, the larger-gauge needle may be necessary.
2. It is important that nerves and blood vessels be avoided when giving IM injections. Position the animal on a flat surface in a normal posture with the hind legs beneath the animal.
3. The rabbit may be restrained by positioning close to the body with the head under the elbow. Alternatively, a canvas or nylon bag restraint maybe used to prevent excessive movement. Place a hand over the animal's rump so that you can feel the iliac crests beneath your palm. Put the middle finger on the spine and slide the hand forward until the thumb and pinkie finger are in the flank. The index and ring fingers will isolate the lumbar muscles on each side of the spine.
4. The skin can be swabbed with alcohol and the needle is inserted perpendicular to the skin, lateral to the spine and into the muscle between the middle finger and finger on either side. Injecting in this manner will prevent injection into the spinal column and will ensure injection into the *longissimus lumborum* muscle (**Figure 34**).

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5. The syringe plunger is gently pulled back to ensure that the needle is not within a blood vessel. If intravascular, a small amount of blood may appear in the syringe or the hub of the needle, requiring the needle be repositioned.
6. In general, volumes no greater than 0.5 mL should be injected into a single intramuscular site.

Subcutaneous (SC)

Subcutaneous administration of compounds by needle and syringe is easily accomplished in rabbits because of the pliable skin and large subcutaneous space on the dorsum (top) of the neck and back of the rabbit.

Procedure

1. The smallest-bore needle possible should be used depending upon the compound viscosity. Generally, 21-gauge or greater (smaller diameter) needles are useful.
2. A fold of skin on the dorsal neck or back is lifted, forming a tent, and the skin can be swabbed with alcohol.
3. The needle, with attached syringe, is inserted at a right angle to the skin fold (**Figure 35**). Care must be taken so that the needle is not passed completely through the skin fold to exit the other side.
4. The syringe plunger is gently pulled back to ensure that the needle is within the subcutaneous space and not a blood vessel. If intravascular, a small amount of blood may appear in the syringe or the hub of the needle; if the needle has passed completely through the skin fold, there will be a large volume

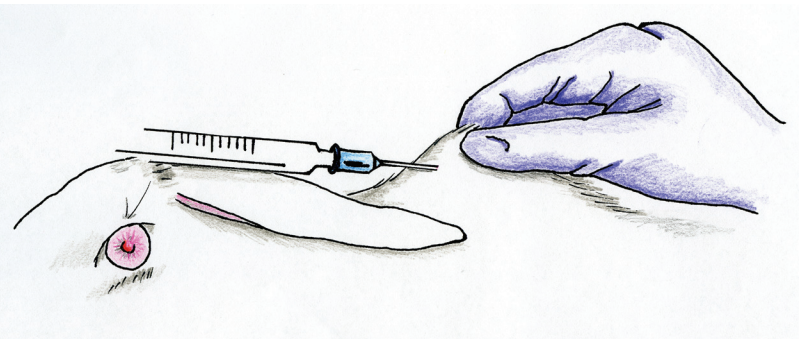


Figure 35. Subcutaneous injection in the rabbit.

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of air drawn into the syringe. If either of these conditions occurs, the needle must be repositioned.

5. Relatively large volumes (generally 10 to 20 mL per subcutaneous site) can be injected subcutaneously, although excessive volumes that greatly distend the skin should be avoided. Subcutaneous injection of antigens for polyclonal antibody production usually utilizes volumes of 0.10 to 0.50 mL per site.[199]

Intradermal (ID)

Intradermal injection is frequently used for immunization with specific antigens in the course of polyclonal antibody production. The skin on the dorsal thorax and abdomen (the back) are the commonly used sites.

Procedure

1. The hair is shaved to adequately view the injection site.
2. The skin is swabbed with alcohol, and a small-bore needle (25- to 27-gauge), bevel side up, attached to a tuberculin syringe is used to penetrate into the dermis while the skin is held taut (**Figure 36**). Alternately, the needle may be inserted subcutaneously and directed up toward an intradermal location.
3. A small blister-like bleb forms within the skin on injection, confirming the intradermal location.
4. Small volumes of approximately 0.05 to 0.1 mL per site may be administered in this manner.

Intraperitoneal (IP)

Compounds are occasionally administered to rabbits intraperitoneally; however, the risk of accidental puncture of and injection into abdominal organs exists. The site for injection is the lower (caudal) right abdominal quadrant.

Procedure

1. Normally a 20- to 22-gauge, long needle (1 inch or greater) is used.
2. The rabbit is placed on its back, which may require sedation in some rabbits.

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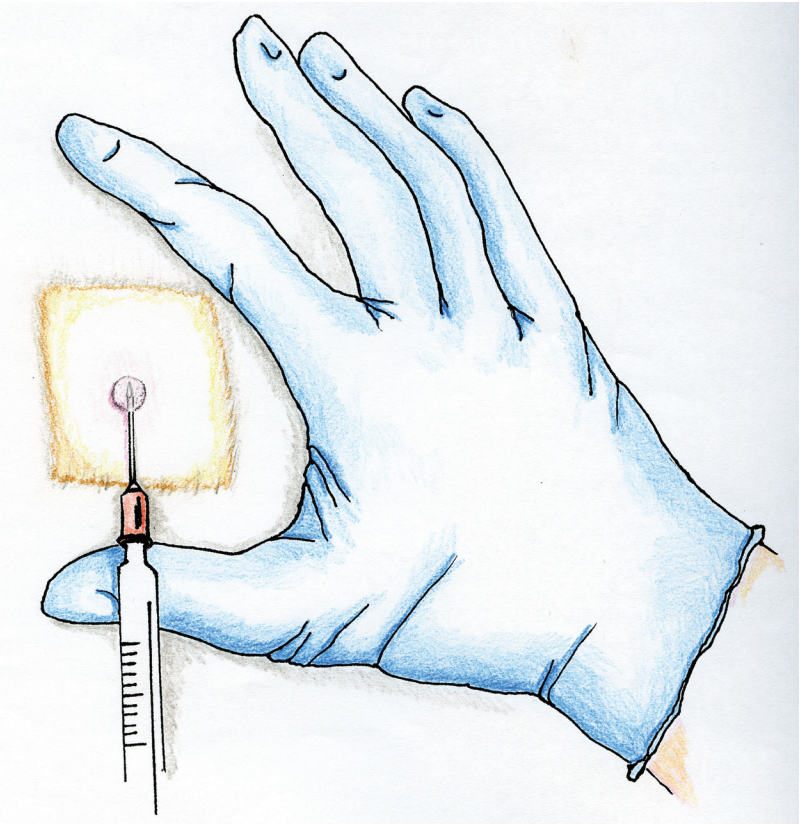


Figure 36. Intradermal injection in the rabbit.

3. The rabbit's hindquarters are held at a 30° to 45° angle to the horizontal while the rabbit is on its back.
4. The needle is inserted into the lower right abdominal quadrant just lateral to the midline and directed at an approximate 45° angle to the body wall.
5. The syringe plunger is gently pulled prior to injection to ensure that neither viscera nor blood vessels have been penetrated. For example, aspiration of yellow fluid implies that the needle has penetrated the urinary bladder, while green fluid suggests that the intestinal tract has been penetrated. Unexpected contamination by such materials necessitates discarding the compound to be given and obtaining a fresh sample.

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6. Once the injection is made, remove the needle at the same angle it was inserted to minimize muscle trauma. The rabbit can be returned to the upright position.

Implantable Osmotic Pumps

Osmotic pumps are small, self-contained devices that are designed to deliver substances at a specific rate under the force of osmotic pressure. The pump can be implanted surgically into subcutaneous sites or into the abdominal cavity. Consult with the manufacturer for specific implantation protocols.

Oral (PO)

Oral administration is possible with liquid, semi-liquid, dry, or paste forms of compounds. The form and consistency of a compound as well as the accuracy of dosages will determine the method of oral administration.

Compounding diets and drinking water

Incorporation of compound into drinking water or food can be used when oral delivery of compounds need not be very precise. Adding to drinking water is feasible when the compound is water soluble. If the additive is light sensitive, an opaque sleeve can be placed around the bottle. Water bottles should be changed at least twice a week, more often if the compound degrades quickly or is temperature sensitive. Diets can be commercially formulated to include a compound in a pelleted or powdered form. The pelleted form is preferred as it mimics the commercial diet usually fed as a control.

Syringe method

Small liquid volumes may be administered using a syringe to place the compound into the oral cavity of the animal.

Procedure

1. The rabbit is restrained in a canvas or nylon bag to prevent struggling.
2. The rabbit's head is grasped over the top, with the fingers and thumb on the lower mandible. The head is tilted up slightly.
3. A syringe without a needle or an oral dosing syringe containing the compound is placed in the corner of the rabbit's mouth through the diastema (the space between the incisors

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and premolars). The compound is injected into the mouth at a rate slow enough to allow the rabbit to swallow naturally.

4. Caution: pushing the material into the mouth too rapidly can result in choking or aspiration if the compound is in liquid form, as well as loss of the measured dose if it is expelled from the mouth.

Oral gavage

Oral gavage is used if the compound is unpalatable or is unstable at room temperature, or if a precise concentration or volume of liquid must be administered.

Procedure

1. Fractious rabbits may need to be sedated for oral gavage.
2. A rubber infant feeding tube (8-French) is usually used. The total length of the tube to be inserted can be estimated as the length from the mouth to the last rib and should be marked on the tube before insertion is begun.
3. A speculum is placed in the rabbit's mouth to prevent chewing the gavage tube. Speculums can be purchased that are made of hardened nylon or stainless steel,[200] or made using Plexiglas, wooden tongue depressors, or plastic syringe cases (**Figure 37**). The advantage of non-porous materials is that they can be sterilized. The speculums constructed from wooden tongue depressors and plastic syringe cases are disposable after a one-time use.
4. The gavage tube is lubricated, if necessary, with a non-toxic, water-soluble lubricant. The tube is then passed through the speculum into the mouth of the rabbit. The esophagus is dorsal to the trachea, thus the tube should be angled up as it passes into the pharynx. When the rabbit demonstrates the gag reflex, the tube is advanced into the esophagus and on into the stomach (**Figure 38**).
5. The location of the tube in the stomach must be confirmed to avoid accidental administration of compound to the respiratory tract. This is accomplished by examination of the tube for air passage as the rabbit breathes. By placing the end of the tube in a small volume of water, air bubbles will be apparent if the tube is in the trachea; likewise a mirror can be used to check for fogging, which indicates placement in the

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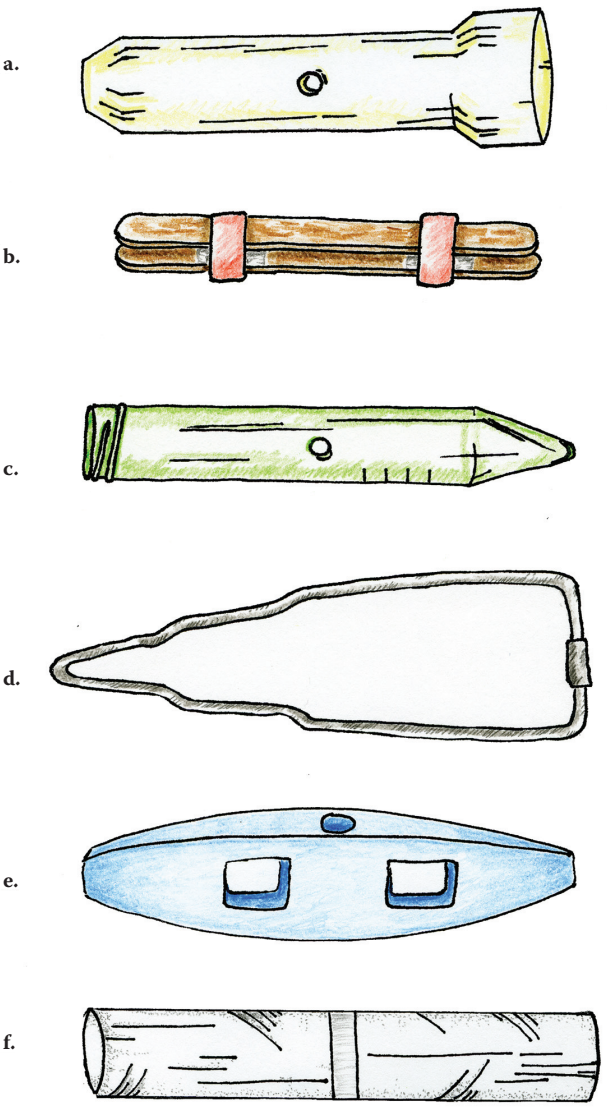


Figure 37. Mouth gags and speculums for oral gavage. a: Plastic syringe case with hole drilled to accommodate feeding tube. b: Wooden tongue depressors taped together with spacers of cotton pledgets. c: A 15-mL plastic centrifuge tube with hole drilled to accommodate feeding tube. d: Avian speculum. e: Feline mouth gag. f: Plexiglas® rod with hole drilled to accommodate feeding tube.

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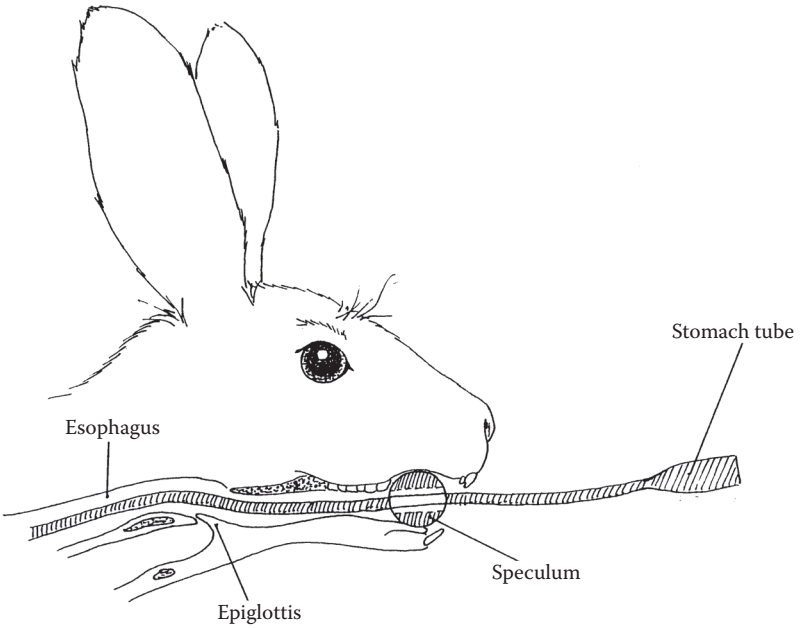


Figure 38. Orientation of the stomach tube for oral gavage in the rabbit.

trachea. Another method is to either inject a small amount of sterile saline, which will cause coughing if the tube is in the trachea, or to aspirate to check for ingesta.

6. The compound is slowly administered by a syringe attached to the stomach tube. Volumes as large as 10 mL/kg can be safely administered in this way. It is advisable to subsequently administer a small volume of water to rinse any residual compound into the stomach.
7. After administration, the tube is kinked to prevent flow of residual material in the tube into the respiratory tree as it passes through the pharynx, and the tube is slowly withdrawn.

Additional methods for oral dosing

Additional methods include **capsule administration**[201,202] and **surgical pharyngostomy**,[203] which are not described here. Surgical pharyngostomy is usually reserved for long-term or continuous administration of compounds.

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polyclonal antibody production

Rabbits are commonly used for production of antibody to a variety of antigens. Typically, the antigen of interest is administered to the rabbit several times, and the antibody-containing serum is later harvested. Because antibody to more than a single epitope of the antigen may be generated, antibody obtained in this way is referred to as polyclonal.

Key Points

1. The exact amount to be administered varies with the antigen; however, 500 to 1000 μg of antigen per immunization is commonly used.[204]
2. Following initial immunization, booster injections are typically administered every 4 to 6 weeks, although the optimal time period may vary widely between antigens. It is preferable not to give booster injections until the serum antibody response begins to wane.
3. Because some rabbits may mount only a weak antibody response to the administered antigen, it is useful to immunize at least two or three rabbits for each antigen.
4. Booster immunizations can be given using essentially the same procedures as for the initial immunization. If Freund's complete adjuvant was used for the initial immunization, it should not be used for subsequent booster immunizations. Rather, Freund's incomplete adjuvant could be used for booster immunizations (see following section on adjuvants).
5. Once immunized, rabbits may produce sufficient levels of antibody, often followed by a booster, to warrant maintaining them for periods of time lasting up to several years. For this reason, it is advisable to use specific-pathogen-free rabbits to minimize the risk of loss of valuable rabbits to infectious disease.
6. Common routes of antigen administration are injection intradermally, subcutaneously, or intramuscularly. Intravenous administration can also be used; however, antigens given by this route may induce anaphylactic shock, particularly upon booster administration.

Adjuvants

Adjuvants are nonspecific stimulants of the immune system that are coadministered with antigens to promote a stronger antibody

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response to that antigen. The optimal immunization regimen and adjuvant appears to vary with individual antigens. Substances commonly utilized as adjuvants for polyclonal antibody production include the following:

- **Freund's complete adjuvant** (FCA), which is the most commonly employed adjuvant and consists of a water-in-oil emulsion containing killed *Mycobacterium tuberculosis.* The antigen is thoroughly mixed with an equal volume of FCA to form an emulsion. The emulsion should be thick enough that it does not disperse when a drop of it is placed on the surface of a saline solution. FCA results in a chronic granulomatous response at the injection site,[205] which in the case of intradermal injections is often manifested as swelling and ulceration of the skin. When FCA is used as an adjuvant, only very small volumes should be injected per intradermal site.[206] A suggested maximal volume is 0.05 mL.[199] FCA should be used only for the first immunization, since severe hypersensitivity reactions may result if FCA is used for booster immunizations. Instead, booster immunizations may contain no adjuvant or Freund's incomplete adjuvant (FIA), which does not contain mycobacterial cells. For many antigens, use of FCA in the initial injection and FIA in booster injections consistently enhances the antibody response.[207,208]
- **Oil-in-water adjuvants,** which produce minimal inflammatory lesions and are an alternative to FCA. Many oil-in-water emulsions contain a synthetic block copolymer, monophosphoryl lipid A, a surfactant, and a detergent. The methods for use are similar to those for FCA.
- **Aluminum hydroxide** (alum), which can be used as an adjuvant by allowing adsorption of antigens onto an aluminum salt.[209,210] Use of alum will not result in inflammatory lesions such as those seen following use of FCA.

Collection of Antibody

The optimal time to collect serum for antibody harvest varies greatly with antigen, adjuvant, and route of administration. The level of antigen-specific antibody can be measured by assaying a small serum sample 7 to 14 days after immunization and harvesting a larger volume of serum when a significant rise in antibody is noted. In general, one can

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expect high antibody levels approximately 10 days after each boost. Blood sampling procedures are described earlier in this chapter.

Subcutaneous chamber method

Polyclonal antibody may also be produced and collected by means of a surgically implanted subcutaneous chamber.[211-213] The technique involves subcutaneous implantation of a perforated, hollow, plastic golf ball, which becomes encased within the tissue after several weeks. Antigen is percutaneously injected into the chamber through the perforations of the golf ball. Likewise, fluid rich in antigen-specific antibody is harvested percutaneously. The method allows collection of 12 to 22 mL of such fluid weekly. Adjuvants are not needed with this method.

necropsy

Many types of studies require the postmortem examination of organs and tissues (necropsy). In addition, necropsy is frequently performed to diagnose disease problems.

Equipment

Basic equipment needed to conduct a necropsy (**Figure 39**) on a rabbit includes the following:

- Latex or rubber gloves, lab coat, and facemask, eye goggles, or other protective eyewear.
- A small metric ruler
- Toothed and serrated tissue forceps
- Scalpel blades and handles
- Utility scissors
- Dissecting and small operating scissors
- A probe
- Bonecutting forceps
- Sterile swabs for bacterial culture of tissues
- Syringes (1 and 10 mL) with both large-bore (18-gauge) and small-bore (25-gauge) hypodermic needles

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Figure 39. Basic necropsy equipment for rabbit post-mortem examinations. From the top: bacterial culture swab, disposable scalpel handle and blade, two syringes with needles. From the left: rat-tooth thumb forceps, serrated thumb forceps, operating scissors, dissecting scissors, utility scissors, bone-cutting forceps, blunt probe, metric ruler.

- Saline for washing of structures and paper towels for absorption of blood and other fluids are useful.
- Spray bottle of disinfectant
- Additional equipment may be useful and can be added to this basic kit.

Note: Cutting surfaces of instruments will likely need to be honed periodically to maintain a sharp edge.

The necropsy is best performed in a dedicated necropsy room and on a surface that will facilitate drainage of blood and fluids and can be easily cleaned and sanitized. Stainless steel necropsy tables are optimal, and some are designed with downdraft airflow to draw infectious agents and noxious odors away from personnel. If that type of equipment is unavailable, an area that is isolated from other animals, personnel areas, and feed and bedding storage could be used,

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provided that the area can be appropriately cleaned and sanitized following each use.

Formaldehyde, which is commonly used in diluted form as a tissue fixative, can cause allergic reactions and irritation of surfaces lined by mucous membranes.[214,215] In addition, formaldehyde is considered to be a human carcinogen.[216] For these reasons, steps to limit exposure of personnel to formaldehyde should be taken, including adequate ventilation of the necropsy and tissue processing areas.

Personnel conducting necropsies should wear a clean lab coat, latex or rubber gloves, a facemask, and protective eyewear. Although specific-pathogen-free rabbits harbor few infectious agents that would pose a risk to humans, this equipment will further decrease exposure of personnel to airborne allergens and formaldehyde, as well as protect clothes from soiling with blood or other material.

Necropsy Procedure

Ideally the rabbit should be necropsied immediately after death. Alternatively, carcasses may be stored for a short time (several hours) under refrigeration to delay tissue decomposition. Carcasses thus stored should be kept in refrigerators not used for storage of food for animals or personnel. Freezing of carcasses can significantly interfere with meaningful necropsy. An in-depth description of necropsy methods for the rabbit can be found elsewhere.[217] A standardized necropsy form can facilitate the recording of observations and findings as well as ensure consistent methods between examiners. General procedures for necropsy of a rabbit are as follows:

1. The rabbit is first examined externally for abnormalities such as discoloration, hair loss, wounds, masses, nasal or ocular discharge, and fecal or urine staining of the perineum. In addition, the oral cavity is examined, with particular attention paid to the teeth.
2. The skin is incised along the ventral midline, beginning at the lower jaw and continuing along the midline caudally to the pubis (**Figure 40**). The animal's fur can be sprayed with water or a liquid disinfectant to minimize airborne hair. The scalpel blade can become dulled by cutting through hair; utility scissors can be used instead to cut through the skin.

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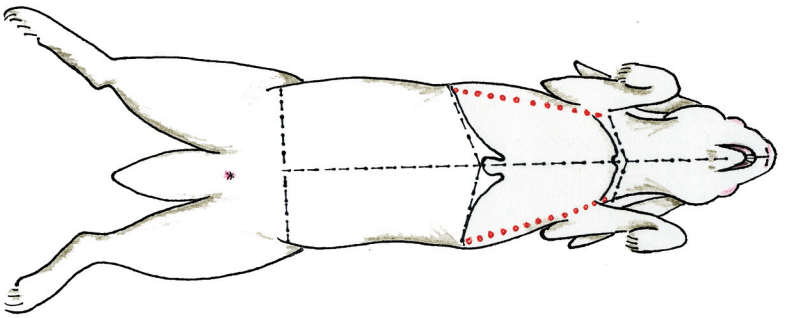


Figure 40. Incision lines for skin and muscle layers are indicated with a dashed line. The lines for cutting the ribs to expose the thoracic cavity are indicated with dotted lines.

3. The skin is then incised laterally from the midline just above the hips, immediately below the thorax, and anterior to the forelegs, then gently reflected laterally, and the subcutaneous tissues and underlying musculature is examined.
4. The abdominal wall is then incised and the abdominal cavity exposed using the dissecting scissors in the same manner as the skin (**Figure 40**).
5. The organs and peritoneal surfaces are examined for abnormal coloration, size, and presence of masses, traumatic damage, or any other abnormal appearance. Depending on the time between death, the carcass storage conditions, and necropsy, the tissues may appear abnormal due to postmortem autolysis, a natural process involving degradation of tissues after death and unrelated to disease processes.
6. The thoracic cavity is exposed by cutting the diaphragm and then clipping the ribs on the frontal plane using the bone cutting forceps (**Figure 40**). The clipped portion of the rib cage is then lifted off and removed or reflected laterally.
7. The lungs, heart, and pleural surfaces are examined for abnormalities as for the abdominal cavity. The organs are removed for inspection by cutting the trachea and cutting all attachments of trachea, lungs, and heart caudally to the diaphragm.
8. Abnormal fluids should be sampled for cytology and bacterial culture, and the volume and appearance of such fluids noted and recorded.

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9. Other masses or abnormal tissues can be cultured using bacteriological culture swabs if infection is suspected.
10. Samples of tissues can be preserved in 10% neutral buffered formalin and saved for later histopathology processing and evaluation. Smaller samples allow quicker penetration of formalin and are therefore preferred. If whole organs are saved, they should be sliced in 1-cm-thick pieces for preservation in formalin solution.

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6

resources and additional information

Because this volume is intended to be a handbook, coverage is not exhaustive for most topics. In this regard, provided here are additional resources for information related to the care and use of laboratory rabbits.

organizations

A number of professional organizations exist that can serve as initial contacts for obtaining information regarding specific issues related to the care and use of laboratory rabbits. Membership in these organizations should be considered, since it allows the laboratory animal science professional to stay abreast of regulatory issues, improved procedures for the use of animals, management issues, and animal health issues. Relevant organizations include the following:

American Association for Laboratory Animal Science (AALAS), www.aalas.org, serves a diverse professional group, ranging from principal investigators to animal care technicians to veterinarians. The journals *Comparative Medicine* and *Journal of the American Association for Laboratory Animal Science* are both published by AALAS and serve to communicate relevant information. AALAS sponsors a program for certification of laboratory animal science professionals at three levels: assistant laboratory animal technician (ALAT), laboratory animal technician (LAT), and laboratory animal technologist (LATG). Further, a certification program for managers of

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animal resource programs has been developed. An extensive online resource, the AALAS Learning Library, offers subscribers an extensive menu of courses relevant to laboratory animal science. The association also sponsors an annual meeting and several electronic listserves, including TechLink for animal technicians, CompMed for professionals working in comparative medicine and biomedical research, and IACUC-Forum for IACUC members and staff. Local groups have also organized into smaller branches.

Laboratory Animal Management Association (LAMA), www.lamaonline.org, serves as a mechanism for information exchange between individuals charged with management responsibilities for laboratory animal facilities. In this regard, the association publishes the *LAMA Review* and sponsors an annual meeting.

American Society for Laboratory Animal Practitioners (ASLAP), www.aslap.org, is an association of veterinarians engaged in laboratory animal medicine. The society publishes a newsletter to foster communication between members and sponsors sessions at the annual AALAS meeting and the annual meeting of the American Veterinary Medical Association.

American College of Laboratory Animal Medicine (ACLAM), www.aclam.org, is an association of laboratory animal veterinarians founded to encourage education, training, and research in laboratory animal medicine. The ACLAM board certifies veterinarians in the specialty of laboratory animal medicine. The group sponsors the annual ACLAM Forum with its continuing-education meetings, along with sessions at the annual AALAS meeting.

Laboratory Animal Welfare Training Exchange (LAWTE), www.lawte.org, is an organization of people who train in and for the laboratory animal science field. By sharing ideas on methods and materials for training, members can learn together how best to meet the training and qualification requirements of national regulations and guidelines. LAWTE holds a conference every two years for trainers to exchange information on their training programs in the United States and abroad.

Institute for Laboratory Animal Research (ILAR), www.dels.nas.edu/ilar. The mission of ILAR is to evaluate and disseminate information on issues related to the scientific, technological, and ethical use of animals and related biological resources in research, testing, and education. Using the principles of refinement, reduction, and

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replacement (3Rs) as a foundation, ILAR promotes high-quality science through the humane care and use of animals and the implementation of alternatives. Through the reports of expert committees, the ILAR Journal, web-based resources, and other means of communication, ILAR functions as a component of the National Academies to provide independent, objective advice to the federal government, the international biomedical research community, and the public.

Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC, International), www.aaalac.org. AAALAC is a nonprofit organization that provides a mechanism for peer evaluation of laboratory animal care and use programs. Accreditation by AAALAC is widely accepted as strong evidence of a quality research animal care and use program.

publications

A number of published materials are valuable as additional reference materials, including both books and periodicals.

Books

The following books may be worthwhile sources of additional information:

1. *The Laboratory Rabbit*, edited by P. J. Manning, D. H. Ringler, and C. E. Newcomer, 1994. Academic Press, Inc. Note that this book is undergoing revision and will be revised as a combined volume, *The Laboratory Rabbit, Guinea Pig, Hamster, and Other Rodents*, to be published by Academic Press, Elsevier, Inc.
2. *Pathology of Laboratory Rodents and Rabbits*, 3rd edition, by D. H. Percy and S. W. Barthold, 2007. Wiley-Blackwell, Inc.
3. *Formulary for Laboratory Animals*, 3rd edition, by C. T. Hawk, S. Leary, and T. Morris, 2005. Wiley-Blackwell, Inc.
4. *Clinical Laboratory Animal Medicine: An Introduction*, 3rd edition, by K. Hrapkiewicz and L. Medina, 2006. Wiley-Blackwell, Inc.
5. *The IACUC Handbook*, 2nd edition, edited by J. Silverman, M. A. Suckow, and S. Murthy, 2007. CRC Press/Taylor & Francis Group.

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6. *Handbook of Laboratory Animal Science: Essential Principles and Practices, Volume I*, 2nd edition, edited by J. Hau and G. L. Van Hooiser, 2002. CRC Press/Taylor & Francis Group. Note that the 3rd edition of this book is to be published in 2010.
7. *Anesthesia and Analgesia in Laboratory Animals*, 2nd edition, edited by R. Fish, P. Danneman, M. Brown, and A. Karas, 2008. Academic Press, Elsevier, Inc.
8. *Making and Using Antibodies: A Practical Handbook*, edited by G. C. Howard and M. R. Kaser, 2007. CRC Press/Taylor & Francis Group.

Periodicals

1. *Comparative Medicine*. Published by AALAS.
2. *Journal of the American Association for Laboratory Animal Science*. Published by AALAS.
3. *Laboratory Animals*. Published by Royal Society of Medicine Press (www.rsmjournals.com).
4. *Lab Animal*. Published by Nature Publishing Group (www.lab-animal.com).
5. *ILAR Journal*. Published by the Institute for Laboratory Animal Research (www.dels.nas.edu/ilar).
6. *ALN Magazine*. Published by Vicon Publishing, Inc. (www.animallab.com).

Electronic Resources

CompMed. Available through AALAS (www.aalas.org), CompMed is a listserve for biomedical research. CompMed is limited to participants who are involved in some aspect of biomedical research or veterinary medicine, including veterinarians, technicians, animal facility managers, researchers, and graduate/veterinary students. AALAS membership is not required to subscribe to CompMed.

TechLink. Also available through AALAS, TechLink is a listserve created especially for animal care technicians in the field of laboratory animal science. Open to any AALAS national member, TechLink serves as a method for laboratory animal technicians to exchange information and conduct discussions of common interest via e-mail messages with technicians in the United States and other countries around the world.

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IACUC.ORG. Produced by AALAS, IACUC.ORG (www.IACUC.org) is an information resource for members and staff of institutional animal care and use committees. It is a link archive where online resources are organized by menus and submenus. IACUC.ORG was developed as an organizational tool to quickly point to a topic of interest, such as protocol forms or disaster plans used by different institutions.

AALAS Learning Library. The AALAS Learning Library provides training that is essential for technicians, veterinarians, managers, IACUC members, and investigators working with animals in a research or education setting. The courses emphasize the appropriate handling, care, and use of animals, including rabbits.

LAWTE listserve. The Laboratory Animal Welfare Training Exchange (www.lawte.org) maintains a members-only listserve where individuals may seek information from colleagues. In addition, the site maintains a library of materials relevant to training of individuals in the proper handling and care of laboratory animals.

Rabbit Research Database. At this privately maintained site, users have access to a database that can search for research relevant to the nutrition, reproduction, physiology, immunology, and genetics of rabbits, particularly as these topics relate to rabbit production. A fee is required for access.

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references

1. Graur, D., Duret, L., and Gouy, M. 1996. Phylogenetic position of the order Lagomorpha (rabbits, hares and allies). *Nature* 379:333.
2. Jilge, B. 1991. The rabbit: a diurnal or nocturnal animal? *J. Exp. Anim. Sci.* 34:170.
3. Davis, H. and Gibson, J. A. 2000. Can rabbits tell humans apart? Discrimination of individual humans and its implications for animal research. *Comp. Med.* 50:483.
4. Brewer, N. R. 2006. Biology of the rabbit. *J. Am. Assoc. Lab. Anim. Sci.* 45:8.
5. Harkness, J. E. and Wagner, J. E. 1995. *The biology and medicine of rabbits and rodents*. Baltimore: Williams & Wilkins.
6. Gentz, E. J., Harrenstein, L. A., and Carpenter, J. W. 1995. Dealing with gastrointestinal, genitourinary, and musculoskeletal problems in rabbits. *Vet. Med.* 90:365.
7. Jones, T.C. and Hunt, R. D. 1983. *Veterinary pathology*, 5th edition, 1510. Philadelphia: Lea & Febiger.
8. Poole, T. 1987. *The UFAW handbook on the care and management of laboratory animals*, 6th edition, 418. Essex: Longman Scientific and Technical.
9. Gillett, C. S. 1994. Selected drug dosages and clinical reference data. In *The biology of the laboratory rabbit*, 2nd edition, ed. Manning, P. J., Ringler, D.H., and Newcomer, C.E., appendix. San Diego: Academic Press.
10. Kraus, A. L., Weisbroth, S. H., Flatt, R. E., and Brewer, N. 1984. Biology and diseases of rabbits. In *Laboratory Animal Medicine*, ed. Fox, J. G., Cohen, B. J., and Loew, F. M., chap. 8. Orlando: Academic Press.

Vet-ebooks.com

11. Kaplan, H. M. and Timmons E. H. 1979. *The rabbit: a model for the principles of mammalian physiology and surgery.* New York: Academic Press.
12. Burns, K. F. and De Lannoy, C. W., Jr. 1966. Compendium of normal blood values of laboratory animals, with indications of variations. *Toxicol. Appl. Pharmacol.* 8:429.
13. Fox, R. R. 1989. The rabbit. In *The clinical chemistry of laboratory animals*, ed. Loeb, W. F. and Quimby, F. W. New York: Pergamon.
14. Woolford, S. T., Schroer, R. A., Gohs, F. X., Gallo, P. P., Brodeck, M., Falk, H. B., and Ruhren, R. 1986. Reference range data base for serum chemistry and hematology values in laboratory animals. *J. Toxicol. Environ. Health* 18:161.
15. Loeb, W. F. and Quimby, F. W. 1989. *The clinical chemistry of laboratory animals*, Appendix. New York: Pergamon.
16. Curiel, T. J., Perfect, J. R., and Durack, D. T. 1982. Leukocyte subpopulations in cerebrospinal fluid of normal rabbits. *Lab. Anim. Sci.* 32:622.
17. Zurovsky, Y., Mitchell, G., and Hattingh, J. 1995. Composition and viscosity of interstitial fluid of rabbits, *ESP. Physiol.* 80:203.
18. Barzago, M. M., Bortolotti, A., Omarini, D., Aramayona, J. J., and Bonati, M. 1992. Monitoring of blood gas parameters and acid-base balance of pregnant and non-pregnant rabbits (*Oryctolagus cuniculus*) in routine experimental conditions. *Lab. Anim. Sci.* 26:73.
19. Sanford, T. D. and Colby, E. D. 1980. Effect of xylazine and ketamine on blood pressure, heart rate and respiratory rate in rabbits. *Lab. Anim. Sci.* 30:519.
20. Kabata, J., Gratwohl, A., Tichelli, A., John, L., and Speck, B. 1991. Hematologic values of New Zealand White rabbits determined by automated flow cytometry. *Lab. Anim. Sci.* 41:613.
21. Hafez, E. S. E. 1970. Rabbits. In *Reproduction and breeding techniques for laboratory animals*, ed. Hafez, E. S. E., chap. 16. Philadelphia: Lea & Febiger.
22. Kennelly, J. J. and Foote, R. H. 1965. Superovulatory response of pre-and post-pubertal rabbits to commercially available gonadotropins. *J. Reprod. Fertil.* 9:77.

Vet-ebooks.com

23. Williams, J., Gladen, B. C., and Turner, T. W. 1991. The effects of ethylene dibromide on semen quality and fertility in the rabbit: evaluation of a model for human seminal characteristics. *Fundam. Appl. Toxicol.* 16:687.
24. Foote, R. H. and Simkin, M. E. 1993. Use of gonadotropic releasing hormone for ovulating the rabbit model. *Lab. Anim. Sci.* 43:383.
25. DeBoer, K. F. and Krueger, D. 1991. A simplified artificial vagina for use in rabbits and other species. *Lab. Anim. Sci.* 41:187.
26. Fayrer-Hosken, R. A., Reynolds, D. C., and Brackett, B. G. 1987. An efficient rabbit artificial vagina and its use in assessing sperm fertilizing ability *in vitro. Lab. Anim. Sci.* 37:359.
27. Patton, N. M. 1994. Colony husbandry. In *The Biology of the Laboratory Rabbit*, ed. Manning, P. J., Ringler, D. H., and Newcomer, C. E., chap. 2. San Diego: Academic Press.
28. Joint Working Group on Refinement. 1993. Refinements in rabbit husbandry. *Lab. Anim.* 27:301.
29. Committee to Revise the Guide for the Care and Use of Laboratory Animals. 1996. *Guide for the Care and Use of Laboratory Animals*. Washington, D. C.: National Research Council, National Academy Press.
30. United States Department of Agriculture, Animal and Plant Health Inspection Service. 2005. *Animal Welfare Act and Animal Welfare Regulations*. Washington: U. S. Government Printing Office.
31. Hagen, K. W. 1974. Colony husbandry. In *The biology of the laboratory rabbit*, ed. Weisbroth, S. H., Flatt, R. E., and Kraus, A. L., chap. 2. Orlando: Academic Press.
32. Owiny, J. R., Vandewoude, S., Painter, J. T., Norridin, R. W., and Veeramachaneni, D. N. R. 2001. Hip dysplasia in rabbits: association with nest box flooring. *Comp. Med.* 51:85.
33. O'Steen, W. K. and Anderson, K. V. 1971. Photically evoked responses in the visual system of rats exposed to continuous light. *Exp. Neurol.* 30:525.
34. O'Steen, W. K. and Anderson, K. V. 1972. Photoreceptor degeneration after exposure of rats to incandescent illumination. *Z. Zellforsch. Mikrosk. Anat.* 127:306.

Vet-ebooks.com

35. Patton, N. M., Holmes, H. T., Caveny, D. D., Matsumoto, M., and Cheeke, P. R. 1980. Experimental inducement of snuffles in rabbits. *J. Appl. Rabbits Res.* 3:8.

36. Nayfield, K. C. and Besch, E. L. 1981. Comparative responses of rabbits and rats to elevated noise. *Lab. Anim. Sci.* 31:386.

37. Love, J. A. 1994. Group housing: meeting the physical and social needs of the laboratory rabbit. *Lab. Anim. Sci.* 44:5.

38. Whary, M., Peper, R., Borkowski, G., Lawrence, W., and Ferguson, F. 1993. The effect of group housing on the research use of the laboratory rabbit. *Lab. Anim.* 27:330.

39. Huls, W. L., Brooks, D. L., and Bean-Knudsen, D. 1991. Response of adult New Zealand White rabbits to enrichment objects and paired housing: *Lab. Anim. Sci.* 41:609.

40. Podberscek, A. L., Blackshaw, J. K., and Beattie, A. W. 1991. The behaviour of group penned and individually caged laboratory rabbits. *Appl. Anim. Behav. Sci.* 28:353.

41. Harris, L. D., Custer, L. B., Soranaka, E. T., Burge, J. R., and Ruble, G. R. 2001. Evaluation of objects and food for environmental enrichment of NZW rabbits. *Cont. Topics Lab. Anim. Sci.* 40:27.

42. Shomer, N. H., Peikert, S., and Terwilliger, G. 2001. Enrichment-toy trauma in a New Zealand White rabbit, *Cont. Topics Lab. Anim. Sci.* 40:31.

43. Cheeke, P. R., 1994. Nutrition and nutritional disease. In *The biology of the laboratory rabbit*, ed. Manning, P. J., Ringler, D. H., and Newcomer, C. E., chap. 14. San Diego: Academic Press.

44. Board of Agriculture and Renewable Resources, Subcommittee on Rabbit Nutrition, Committee on Animal Nutrition. 1977. *Nutrient requirements of rabbits*, 2nd rev. edition. Washington, D.C.: National Academy of Sciences.

45. Slade, L. M. and Hintz, H. F. 1969. Comparison of digestion in horses, ponies, rabbits, and guinea pigs. *J. Anim. Sci.* 28:842.

46. Cheeke, P. R. 1976. Nutrition of the domestic rabbit. *Lab. Anim. Sci.* 26:654.

47. Chapin, R. E. and Smith, S. E. 1967. Calcium requirement of growing rabbits. *J. Anim. Sci.* 26:67.

48. Stevenson, R. G., Palmer, N. C., and Finley, G. G. 1976. Hypervitaminosis D in rabbits. *Can. Vet. J.* 17:54.

Vet-ebooks.com

49. Ringler, D. H. and Abrams, G. D. 1970. Nutritional muscular dystrophy and neonatal mortality in a rabbit breeding colony. *J. Am. Vet. Med. Assoc.* 157:1928.

50. DiGiacomo, R. F., Deeb, B. J., and Anderson, R. J. 1992. Hypervitaminosis A and reproductive disorders in rabbits. *Lab. Anim. Sci.* 42:250.

51. Bondi, A. and Sklan, D. 1984. Vitamin A and carotene in animal nutrition. *Prog. Food Nutr. Sci.* 8:165.

52. St. Claire, M. B., Kennett, M. J., and Besch-Williford, C. L. 2004. Vitamin A toxicity and Vitamin E deficiency in a rabbit colony. *Cont. Topics Lab. Anim. Sci.* 43:26.

53. Ringler, D. H. and Abrams, G. D. 1971. Laboratory diagnosis of vitamin E deficiency in rabbits fed a faulty commercial ration. *Lab. Anim. Sci.* 21:383.

54. Yamini, B. and Stein, S. 1989. Abortion, stillbirth, neonatal death, and nutritional myodegeneration in a rabbit breeding colony. *J. Am. Vet. Med. Assoc.* 194:561.

55. Ooms, T. G., Artwohl, J. E., Conroy, L. M., Schoonover, T. M., and Fortman, J. D. 2008. Concentration and emission of airborne contaminants in a laboratory animal facility housing rabbits. *J. Am. Assoc. Lab. Anim. Sci.* 47:39.

56. Wardrip, C. L., Artwohl, J. E., and Bennett, B. T. 1994. A review of the role of temperature vs. time in an effective cage sanitization program. *Cont. Topics Lab. Anim. Sci.* 33(5):66.

57. Ryan, L. J., Maina, C. V., Hopkins, R. E., and Carlow, C. K. S. 1993. Effectiveness of hand cleaning in sanitizing rabbit cages. *Cont. Topics Lab. Anim. Sci.* 6:21.

58. Hitt, N. D. 2004. Moving on up: upgrading from an ABSL2 to ABSL3 facility. *Lab Anim. (NY)* 33:30.

59. Animal Welfare Act, United States P. L. 89-544, 1966; P. L. 91-579, 1970; P. L. 94-279, 1976; and P. L. 99-198, 1985 (The Food Security Act).

60. Health Research Extension Act, United States P. L. 99–158, 1985.

61. Public Health Service Policy on Humane Care and Use of Laboratory Animals, Office of Laboratory Animal Welfare 2002. Washington, D.C.: U. S. Department of Health and Human Services.

Vet-ebooks.com

62. Committee on Occupational Safety and Health in Research Animal Facilities. 1997. *Occupational health and safety in the care and use of research animals*. Washington, D.C.: National Academy Press, National Research Council.

63. Kaliste, E., Linnainmaa, M., Meklin, T., and Nevalainen, A. 2002. Airborne contaminants in conventional laboratory rabbit rooms. *Lab. Anim.* 36:43.

64. Centers for Disease Control and National Institutes of Health (CDC/NIH). 2007. *Biosafety in microbiological and biomedical laboratories.* Washington: U. S. Government Printing Office.

65. Chen, P. H. and White, C. E. 2006. Comparison of rectal, microchip transponder, and infrared thermometry techniques for obtaining body temperature in the laboratory rabbit (*Oryctolagus cuniculus*). *J. Am. Assoc. Lab. Anim. Sci.* 45:57.

66. Toth, L. A. and January, B. 1990. Physiological stabilization of rabbits after shipping. *Lab. Anim. Sci.* 40:384.

67. Scharf, R. A., Monteleone, S. A., and Stark, D. M. 1981. A modified barrier system for maintenance of *Pasteurella*-free rabbits. *Lab. Anim. Sci.* 31:513.

68. Carpenter, J. W., Mashima, T. Y., Gentz, E. J., and Harrenstein, L. 1995. Caring for rabbits: an overview and formulary. *Vet. Med.* 90:340.

69. Suckow, M. A., Brammer, D. W., Rush, H. G., Chrisp, C. E. 2002. Biology and diseases of rabbits. In *Laboratory animal medicine*, 2nd edition, ed. Fox, J. G., Anderson, L. C., Loew, F. M., and Quimby, F. W., chap. 9. San Diego: Academic Press.

70. Wilkinson, M. J., Bell, S., McGoldrick, J., and Williams, A. E. 2001. Unexpected deaths in young New Zealand White rabbits (*Oryctolagus cuniculus*). *Contemp. Top. Lab. Anim. Sci.* 40:49.

71. Pakes, S. P. and Gerrity, L. W. 1994. Protozoal diseases. In *The biology of the laboratory rabbit*, ed. Manning, P. J., Ringler, D. H., and Newcomer, C. E., chap. 10. San Diego: Academic Press.

72. Boriello, S. P. and Carman, R. J. 1983. Association of iota-like toxins and *Clostridium spiroforme* with both spontaneous and antibiotic-associated diarrhea and colitis in rabbits. *J. Clin. Microbiol.* 17:414.

73. Yonushonis, W. P., Roy, M. J., Carman, R. J., and Sims, R. E. 1987. Diagnosis of spontaneous *Clostridium spiroforme* iota enterotoxemia in a barrier rabbit breeding colony. *Lab Anim. Sci.* 37:69.

Vet-ebooks.com

74. Lipman, N. S., Weischedel, A. K., Connors, M. J., Olsen, D. A., and Taylor, N. S. 1992. Utilization of cholestyramine resin as a preventive treatment for antibiotic (clindamycin) induced enterotoxaemia in the rabbit. *Lab. Anim.* 26:1.
75. Agnoletti, F., Ferro, T., Guolo, A., Marcon, B., Cocchi, M., Drigo, I., Mazzolini, E., and Bano, L. 2009. A survey of *Clostridium spiroforme* antimicrobial susceptibility in rabbit breeding, *Vet. Microbiol.* 136:188.
76. Deeb, B. J. and DiGiacomo, R. F. 2000. Respiratory diseases of rabbits. *Vet. Clin. North Am. Exot. Anim. Pract.* 3:465.
77. Gaertner, D. J. 1991. Comparison of penicillin and gentamicin for treatment of pasteurellosis in rabbits. *Lab. Anim. Sci.* 41:78.
78. Okerman, L., Devriese, L. A., Gevaert, D., Uytterbroek, E., and Haesebrouck, F. 1990. *In vivo* activity of orally administered antibiotics and chemotherapeutics against acute septicaemic pasteurellosis in rabbits. *Lab. Anim.* 24:341.
79. Broome, R. L. and Brooks, D. L. 1991. Efficacy of enrofloxacin in the treatment of respiratory pasteurellosis in rabbits. *Lab. Anim. Sci.* 41:572.
80. Mahler, M., Stunkel, S., Ziegowski, C., and Kunstyr, I. 1995. Inefficacy of enrofloxacin in the elimination of *Pasteurella multocida* in rabbits. *Lab. Anim.* 29:192.
81. Suckow, M. A., Martin, B. J., Bowersock, T. L., and Douglas, F. A. 1996. Derivation of *Pasteurella multocida*-free rabbit litters by enrofloxacin treatment. *Vet. Microbiol.* 51:161.
82. Aramayona, J. J., Garcia, M. A., Fraile, L. J., Abadia, A. R., and Bregante, M. A. 1994. Placental transfer of enrofloxacin and ciprofloxacin in rabbits. *Am. J. Vet. Res.* 55:1313.
83. Aramayona, J. J., Mora, J., Fraile, L. J., Garcia, M. A., Abadia, A. R., and Bregante, M. A. 1996. Penetration of enrofloxacin and ciprofloxacin into breast milk, and pharmacokinetics of the drugs in lactating rabbits and neonatal offspring. *Am. J. Vet. Res.* 57:547.
84. Walker, R. C. and Wright, A. J. 1987. The quinolones. *Mayo Clin. Proc.* 62:1007.
85. Stahlmann, R. 1991. Cartilage damaging effect of quinolones. *Infection* 19:S38.
86. McKay, S. G., Morck, D. W., Merrill, J. K., Olson, M. E., Chan, S. C., and Pap, K. M. 1996. Use of tilcomisin for treatment of pasteurellosis in rabbits. *Am. J. Vet. Res.* 57:1180.

Vet-ebooks.com

87. DiGiacomo, R. F. 1994. Eradication programs for pasteurellosis in rabbitries. *Cont. Topics Lab. Anim. Sci.* 33:69.

88. Cunliffe-Beamer, T. L. and Fox, R. R. 1981. Venereal spirochetosis of rabbits: eradication. *Lab. Anim. Sci.* 31(5): 379.

89. Vogtsberger, L. M., Harroff, H. Hugh, Pierce, G. E., and Wilkinson, G. E. 1986. Spontaneous dermatophytosis due to *Microsporum canis* in rabbits. *Lab. Anim. Sci.* 36:294.

90. Hagen, K. W. 1969. Ringworm in domestic rabbits: oral treatment with griseofulvin. *Lab. Anim. Care* 19:635.

91. Franklin, C. L., Gibson, S. V., Caffrey, C. J., Wagner, J. E., and Steffen, E. K. 1991. Treatment of *Trichophyton mentagrophytes* infection in rabbits. *J. Am. Vet. Med. Assoc.* 198:1625.

92. Curtis, S. K., Housley, R., and Brooks, D. L. 1990. Uses of ivermectin for treatment of ear mite infestation in rabbits. *J. Am. Vet. Med. Assoc.* 196:1139.

93. Curtis, S. K. and Brooks, D. L. 1990. Eradication of ear mites from naturally infested conventional research rabbits using ivermectin. *Lab. Anim. Sci.* 40:406.

94. Bowman, D. D., Fogelson, M. L., and Carbone, L. G. 1992. Effect of ivermectin on the control of ear mites (*Psoroptes cuniculi*) in naturally infested rabbits. *Am. J. Vet. Res.* 53:105.

95. Sajid, M. S., Iqbal, Z., Muhammad, G., Sandhu, M. A., Khan, M. N., Saqib, M., and Iqbal, M. U. 2007. Effect of ivermectin on the cellular and humoral immune responses of rabbits. *Life Sci.* 80:1966.

96. Kurtdede, A., Karaer, Z., Acar, A., Guzel, M., Cingi, C. C., Ural, K., and Ica, A. 2007. Use of selamectin for the treatment of psoroptic and sarcoptic mite infestation in rabbits. *Vet. Dermatol.* 18:18.

97. Fichi, G., Flamini, G., Giovanelli, F., Otranto, D., and Perrucci, S. 2007. Efficacy of an essential oil of *Eugenia caryophyllata* against *Psoroptes cuniculi*. *Exp. Parasitol.* 115:168.

98. Legendre, L. F. J. 2002. Malocclusions in guinea pigs, chinchillas, and rabbits. *Can. Vet. J.* 43:385.

99. Leary, S. L., Manning, P. J., and Anderson, L. C. 1984. Experimental and naturally-occurring gastric foreign bodies in laboratory rabbits. *Lab. Anim. Sci.* 34:58.

Vet-ebooks.com

100. Wagner, J. L., Hackel, D. B., and Samsell, A. G. 1974. Spontaneous deaths in rabbits resulting from gastric trichobezoars. *Lab. Anim. Sci.* 24:826.

101. Lee, K. J. Johnson, W.D., and Lang, C. M. 1978. Acute peritonitis in the rabbit (*Oryctolagus cuniculus*) resulting from a gastric trichobezoar. *Lab. Anim. Sci.* 28:202.

102. Gillett, N. A., Brooks, D. L., and Tillman, P. C. 1983. Medical and surgical management of gastric obstruction from a hairball in the rabbit. *J. Am. Vet. Med. Assoc.* 183:1176.

103. Bergdall, V. K. and Dysko, R. C. 1994. Metabolic, traumatic, mycotic, and miscellaneous disease. In *The Biology of The Laboratory Rabbit*, ed. Manning, P. J., Ringler, D. H., and Newcomer, C. E., chap. 15. San Diego: Academic Press.

104. Donnelly, T. M. 2005. Wet fur and dermatitis in a rabbit. *Lab Anim. (NY)* 34:23.

105. Lindsey, J. R. and Fox, R. R. 1994. Inherited diseases and variations. In *The biology* of *the laboratory rabbit*, ed. Manning, P.J., Ringler, D. H., and Newcomer, C. E., chap. 13. San Diego: Academic Press.

106. Burrows, A. M., Smith, T. D., Atkinson, C. S., Mooney, M. P., Hiles, D. A., and Losken, H. W. 1995. Development of ocular hypertension in congenitally buphthalmic rabbits. *Lab. Anim. Sci.* 45:443.

107. Gupta, S. K., Saxena, R., Agarwal, R., Galpalli, N. D., Srivastava, S., and Agrawal, S. S. 2007. Estimation of intraocular pressure in rabbits using noncontact tonometer: a comparative evaluation with Schiotz tonometer. *Methods Find. Exp. Clin. Pharmacol.* 29:405.

108. Flecknell, P. A. 1987. *Laboratory animal anesthesia*, 129. London: Academic Press.

109. Bauck, L., Opthalmic conditions in pet rabbits and rodents 1989. *Compend. Contin. Educ. Pract. Vet.* 11:258.

110. Latt, R. H. 1976. Drug dosages for laboratory animals. In *CRC handbook of laboratory animal science,* vol 3, ed. Melby, E. C. and Altman, N. H., 567. Boca Raton: CRC Press.

111. Hawk, C. T., Leary, S. L., and Morris, T. H. 2005. *Formulary for laboratory animals*. Hoboken: Wiley-Blackwell.

112. Paul-Murphy, J. 2007. Critical care of the rabbit. *Vet. Clin. North Am. Exot. Anim. Pract.* 10:437.

Vet-ebooks.com

113. Makidon, P. 2005. Esophagostomy tube placement in the anorectic rabbit. *Lab Animal* (*NY*) 34:33.

114. Smith, D. A., Olson, P. O., and Mathews, K. A. 1997. Nutritional support for rabbits using the percutaneously placed gastrostomy tube: a preliminary study. *J. Am. Anim. Hosp. Assoc.* 33:48.

115. Wixson, S. K. 1994. Anesthesia and analgesia. In *The biology of the laboratory rabbit,* ed. Manning, P. J., Ringler, D. H., and Newcomer, C .E., chap. 6. San Diego: Academic Press.

116. Flecknell, P. A. 2009. *Laboratory animal anesthesia,* 3rd edition. London: Academic Press.

117. Bivin, W. S. and Timmons, E. H. 1974. Basic biomethodology. In *The biology of the laboratory rabbit,* ed. Weisbroth, S. H., Flatt, R. E., and Kraus, A. L., 79. Orlando: Academic Press.

118. Lipman, N. S., Marini, R. P., and Erdman, S. E. 1990. A comparison of ketamine/xylazine and ketamine/xylazine/acepromazine anesthesia in the rabbit. *Lab. Anim. Sci.* 40:395.

119. Poplilskis, S. J., Oz, M. C., Gorman, P., Florestal, A., and Kohn, D. F. 1991. Comparison of xylazine with tiletaminezolazepam (Telazol) and xylazine-ketamine anesthesia in rabbits. *Lab. Anim. Sci.* 41:51.

120. Marini, R. P., Avison, D. L., Corning, B. F., and Lipman, N. S. 1991. Ketamine/xylazine/butorphanol: a new anesthetic combination for rabbits. *Lab. Anim. Sci.* 42:57.

121. Blake, D. W., Jover, B., and McGrath, B. P. 1988. Haemodynamic and heart rate reflex responses to propofol in the rabbit. *Br. J. Anaesth.* 61:194.

122. LaBreck, J. C., An, Y. H., and Friedman, R. J. 1998. Chronic use of propofol for multiple minor procedures in the rabbit. *Contemp. Top. Lab. Anim. Sci.* 37:71.

123. Robertson, S. A. and Eberhart, S. 1994. Efficacy of the intranasal route for administration of anesthetic agents to adult rabbits. *Lab. Anim. Sci.* 44:159.

124. Sanford, T. D. and Colby, E. D. 1980. Effect of xylazine and ketamine on blood pressure, heart rate, and respiratory rate in rabbits. *Lab. Anim. Sci.* 30:519.

125. Wyatt, J. D., Scott, R. A., and Richardson, M. E. 1989. The effects of prolonged ketamine-xylazine intravenous infusion on arterial blood pH, blood gases, mean arterial pressure, heart and respiratory rates, rectal temperature and reflexes in the rabbit. *Lab. Anim. Sci.* 39:411.

Vet-ebooks.com

126. Beyers, T. M., Richardson, J. A., and Prince, M. D. 1991. Axonal degeneration and self-mutilation as a complication of the intramuscular use of ketamine and zylazine in rabbits. *Lab. Anim. Sci.* 41:519.

127. Lipman, N. S., Phillips, P.A., and Newcomer, C. E. 1987. Reversal of ketamine/xylazine anesthesia in the rabbit with yohimbine. *Lab. Anim. Sci.* 37:474.

128. Palmore, W. P. 1990. A fatal response to xylazine and ketamine in a group of rabbits. *Vet. Res. Commun.* 14:91.

129. Brammer, D. W., Doerning, B. J., Chrisp, C. E., and Rush, H. G. 1991. Anesthetic and nephrotoxic effects of Telazol in New Zealand White rabbits. *Lab. Anim. Sci.* 41:423.

130. Doerning, B. J., Brammer, D. W., Chrisp, C. E., and Rush, H. G. 1992. Nephrotoxicity of tiletamine in New Zealand White rabbits. *Lab. Anim. Sci.* 42:267.

131. Aeschbacher, G. and Webb, A. I. 1993. Propofol in rabbits 1. Determination of an induction dose. *Lab. Anim. Sci.* 43:324.

132. Aeschbacher, G. and Webb, A. I. 1993. Propofol in rabbits. 2. Long-term anesthesia. *Lab. Anim. Sci.* 43:328.

133. Flecknell, P. A. 2009. Anaesthesia. In *Laboratory animal anaesthesia*, 3rd edition, chap. 2. London: Academic Press.

134. Muir, W. W. and Hubbell, J. A. E. 2006. Inhalation anesthesia. In *Handbook of veterinary anesthesia*, 4th edition, chap. 9. St. Louis: C. V. Mosby.

135. Smith, J. C., Robertson, L. D., Auhll, A., March, T. J., Derring, C., and Bolon, B. 2004. Endotracheal tubes versus laryngeal mask airways in rabbit inhalation anesthesia: ease of use and waste gas emissions. *Contemp. Top. Lab. Anim. Sci.* 43:22.

136. Kazakos, G. M., Anagnostou, T., Savvas, I., Raptopoulos, D., Psalla, D., and Kazakou, I. M. 2007. Use of the laryngeal mask airway in rabbits: placement and efficacy. *Lab. Anim.(NY)* 36:29.

137. Bateman, L., Ludders, J. W., Gleed, R. D., and Erb, H. N. 2005. Comparison between facemask and laryngeal mask airway in rabbits during isoflurane anesthesia. *Vet. Anaesth. Analg.* 32:280.

138. Flecknell, P. A., Cruz, I. J., Liles, J. H., and Whelan, G. 1996. Induction of anaesthesia with halothane and isoflurane in the rabbit: a comparison of the use of a face-mask or an anaesthetic chamber. *Lab. Anim.* 30:67.

Vet-ebooks.com

139. Phaneuf, L. R., Barker, S., Groleau, M. A., and Turner, P. V. 2006. Tracheal injury after endotracheal intubation and anesthesia in rabbits. *J. Am. Assoc. Lab. Anim. Sci.* 45:67.

140. Jordan, T. 1996. Freezing endotracheal tubes. *Tech Talk* 1(2): 1.

141. Davies, A., Dallak, M., and Moores, C. 1996. Oral endotracheal intubation of rabbits (*Oryctolagus cuniculus*). *Lab. Anim.* 30:182.

142. Bechtold, S.V. and Abrutyn, D. 1991. An important method of endotracheal intubation in rabbits. *Lab. Anim. Sci.* 41:630.

143. Alexander, D. J. and Clark, G. C. 1980. A simple method of oral endotracheal intubation in rabbits (*Oryctolagus cuniculus*). *Lab. Anim. Sci.* 30:871.

144. Fick, T. E. and Schalm, S. W. 1987. A simple technique for endotracheal intubation in rabbits. *Lab. Anim.* 21:265.

145. Kruger, J., Zeller, W., and Schottmann, E. 1994. A simplified procedure for endotracheal intubation in rabbits. *Lab. Anim.* 28:176.

146. O'Roark, T. S. and Wilson, R. P. 1995. Use of the BAAM Mark VI for blind oral intubation in the rabbit. *Cont. Topics Lab. Anim. Sci.* 34(5): 87.

147. Worthley, S. G., Roque, M., Helft, G., Soundararajan, K., Siddiqui, M., and Reis, E. D. 2000. Rapid oral endotracheal intubation with a fibre-optic scope in rabbits: a simple and reliable technique. *Lab. Anim.* 34:199.

148. Tran, H. S., Puc, M. M., Tran, J-L. V., Del Rossi, A. J., and Hewitt, C. W. 2001. A method of endoscopic endotracheal intubation in rabbits. *Lab. Anim.* 35:249.

149. Bertolet, R. D. and Hughes, H. C. 1980. Endotracheal intubation: an easy way to establish a patent airway in rabbits. *Lab. Anim. Sci.* 30:227.

150. Hedenqvist, P., Roughan, J. V., Antunes, L., Orr, H., and Flecknell, P. A. 2001. Induction of anesthesia with desflurane and isoflurane in the rabbit. *Lab. Anim.* 35:172.

151. Flecknell, P. A., Liles, J. H., and Williamson, H. A. 1990. The use of lignocaine-prilocaine local anaesthetic cream for pain-free venepuncture in laboratory animals. *Lab Anim.* 24:142.

152. McCormick, M. J. and Ashworth, M. A. 1971. Acepromazine and methoxyflurane anesthesia of immature New Zealand White rabbits. *Lab. Anim. Sci.* 21:220.

Vet-ebooks.com

153. Freeman, M. J., Bailey, S. P., and Hodesson, S. 1972. Premedication, tracheal intubation and methoxyflurane anesthesia in the rabbit. *Lab. Anim. Sci.* 22:576.

154. Green, C. J. 1975. Neuroleptanalgesic drug combinations in the anaesthetic management of small laboratory animals. *Lab. Anim.* 9:161.

155. Hawk, C. T. and Leary, S. L. 1995. *Formulary for laboratory animals,* 7. Ames: Iowa State University Press.

156. Rapson, W. S. and Jones, T. C. 1964. Restraint of rabbits by hypnosis. *Lab. Anim. Care* 14:131.

157. Danneman, P. J., White W. J., Marshall, W. K., and Lang, C. M. 1988. An evaluation of analgesia associated with the immobility response in laboratory rabbits. *Lab. Anim. Sci.* 38:51.

158. Koch, K. L. and Dwyer, A. 1988. Effects of acetylsalicylic acid on electromechanical activity of *in vivo* rabbit ileum. *Dig. Dis. Sci.* 33:962.

159. Liles, J. H. and Flecknell, P. A. 1992. The use of non-steroidal anti-inflammatory drugs for the relief of pain in laboratory rodents and rabbits. *Lab. Anim.* 26:241.

160. Marangos, M. N., Onyeji, C. O., Nicolau, D. P., and Nightingale, C. H. 1995. Disposition kinetics of aspirin in female New Zealand White rabbits. *Lab. Anim. Sci.* 45:67.

161. Flecknell, P. A. 1991. Post-operative analgesia in rabbits and rodents. *Lab Animal.* 20:34.

162. Portnoy, L. G. and Hustead, D. R. 1992. Pharmacokinetics of butorphanol tartarate in rabbits. *Am. J. Vet. Res.* 53:541.

163. Foley, P. L., Henderson, A. L., Bissonette, E. A., Wimer, G. R., and Feldman, S. H. 2001. Evaluation of fentanyl transdermal patches in rabbits: blood concentrations and physiologic response. *Comp. Med.* 51:239.

164. Cooper, C. S., Metcalf-Pate, K. A., Barat, C. E., Cook, J. A., and Scorpio, D. G. 2009. Comparison of side effects between buprenorphine and meloxicam used postoperatively in Dutch Belted rabbits (*Oryctolagus cuniculus*). *J. Am. Assoc. Lab. Anim. Sci.* 48:279.

165. Olson, M. E., Vizzutti, D., Morck, D. W., and Cox, A. K. 1994. The parasympatholytic effects of atropine sulfate and glycopyrrolate in rats and rabbits. *Can. J. Vet. Res.* 57:383.

166. Linn, J. M. and Liebenberg, S. P. 1979. *In vivo* detection of rabbit astropinesterase. *Lab. Anim. Sci.* 29:335.

Vet-ebooks.com

167. Sikoski, P., Young, R. W., and Lockard, M. 2007. Comparison of heating devices for maintaining body temperature in anesthetized laboratory rabbits (*Oryctolagus cuniculus*). *J. Am. Assoc. Lab. Anim. Sci.* 46:61.

168. McCurnin, D. M. and Jones, R. L. 1993. Principles of surgical asepsis. In *Textbook of small animal surgery,* Vol. 1, 2nd edition, ed. Slatter, D. H., chap. 10. Philadelphia: W. B. Saunders.

169. Berg, R. J. 1993. Sterilization. In *Textbook of small animals surgery*, Vol. 1, 2nd edition, ed. Slatter, D. H., chap. 11. Philadelphia: W.B. Saunders.

170. Wagner, S. D. 1993. Preparation of the surgical team. In *Textbook of small animal surgery*, Vol. 1, 2nd edition, Slatter, D. H., chap. 12. Philadelphia: W. B. Saunders.

171. Powers, D. L. 1993. Assessment and preparation of the surgical patient. In *Textbook of small animal surgery,* Vol. 1, 2nd edition, ed. Slatter, D. H., chap. 13. Philadelphia: W. B. Saunders.

172. Hobson, H. P. 1993. Surgical facilities and equipment. In *Textbook of small animal surgery*, Vol. 1, 2nd edition, ed. Slatter, D. H., chap. 14. Philadelphia: W. B. Saunders.

173. American Veterinary Medical Association 2007. *AVMA guidelines on euthanasia*. www.avma.org/issues/animal_welfare/euthanasia.pdf (June).

174. Joint Working Group on Refinement. 1993. Removal of blood from laboratory mammals and birds. *Lab. Anim.* 27:1.

175. Hall, L. L., Delop, O. H., Roberts, A., and Smith, F. A. 1974. A procedure for chronic intravenous catheterization in the rabbit. *Lab. Anim. Sci.* 24:79.

176. Melich, D. 1990. A method for chronic intravenous infusion of the rabbit via marginal ear vein. *Lab. Anim. Sci.* 40:327.

177. Martin, F. R., Alguacil, L. F., and Alamo, C. 1991. A method for catheterizing rabbit vena cava via marginal ear vein. *Lab. Anim. Sci.* 41:493.

178. Clifford, R. H., Ruth, M. P., and Liberati, T. A. 2003. 24-hr intravenous infusion via the marginal ear vein in the New Zealand White rabbit. *Cont. Topics Lab. Anim. Sci.* 42:44.

179. Wallace, J., Gwynne, B., Dodd, J. R., and Davidson, R. 1988. Repeated arteriopuncture in the rabbit: a safe and effective alternative to cardiac puncture. *Anim. Technol.* 39:119.

Vet-ebooks.com

180. Conn, H. and Langer, R. 1978. Continuous long-term intra-arterial infusion in the unrestrained rabbit. *Lab. Anim. Sci.* 28:598.

181. Dennis, M. B., Jones, D. R., and Tenover, F. C. 1989. Chlorine dioxide sterilization of implanted right atrial catheters in rabbits. *Lab. Anim. Sci.* 39:51.

182. Perry-Clark, L. M. and Meunier, L. D. 1991. Vascular access ports for chronic serial infusion and blood sampling in New Zealand White rabbits. *Lab. Anim. Sci.* 41:495.

183. Hamory, B. H. 1987. Nosocomial bloodstream and intravascular device-related infections. In *Prevention and control of nosocomial infections*, ed. Wenzel, R. P., 283–319. Baltimore: Williams & Wilkins.

184. Penner, J., St. Claire, M., Beckwith, C., Besselsen, D., Wright, J., Fish, R., and Friskey, S. 1994. *Pseudomonas* sp. bacteremia associated with chronic vascular catheterization in rabbits. *Lab. Anim. Sci.* 44:642.

185. DaRif, C. A. and Rush, H. G. 1983. Management of septicemia in rhesus monkeys with chronic indwelling venous catheters. *Lab. Anim. Sci.* 33:90.

186. Danneman, P. J., Griffith, J. W., Beyers, T. M., and Lang, C. M. 1988. Renal and vascular damage associated with indwelling vascular access devices. *Lab. Anim. Sci.* 38:511.

187. Kusumi, R. K. and Plouffe, J. F. 1979. A safe and simple technique for obtaining cerebrospinal fluid from rabbits. *Lab. Anim. Sci.* 29:681.

188. Hughes, P. J., Doherty, M. M., and Charman, W. N. 1993. A rabbit model for the evaluation of epidurally administered local anaesthetic agents. *Anaesth. Intens. Care* 2:298.

189. Bozkurt, P., Tunali, Y., and Kaya, G. 1995. Depth of the rabbit epidural space. *Anaesth. Intens. Care* 23:119.

190. Tissot van Patot, M. C., Seim, H. B., and Tucker, A. 1995. Catheterization of the subarachnoid space in rabbits using a vascular access port. *J. Invest. Surg.* 8:371.

191. Vistelle, R., Jaussaud, R., Trenque, T., and Wiczewski, M. 1994. Rapid and simple cannulation technique for repeated sampling of cerebrospinal fluid in the conscious rabbit. *Lab. Anim. Sci.* 44:362.

Vet-ebooks.com

192. Haslberger, A. G. and Gaab, M. R. 1986. A technique for repeated sampling of pure cerebrospinal fluid from the conscious rabbit. *Lab. Anim. Sci.* 36:181.

193. Vistelle, R., Wiczewski, M., and Aurousseau, M. 1989. Continuous sampling of cerebrospinal fluid in the conscious rabbit. *Brain Res. Bull.* 22:919.

194. Sundberg, R. D. and Hodgson, R. E. 1949. Aspiration of bone marrow in laboratory animals. *Blood* 4:557.

195. Horan, P. K., Muirhead, K. A., Gorton, S., and Irons, R. D. 1980. Aseptic aspiration of rabbit bone marrow and enrichment for cycling cells. *Lab. Anim. Sci.* 30:76.

196. Powsner, E. R. and Fly, M. N. 1962. Aseptic aspiration of bone marrow from the living rabbit. *J. Appl. Physiol.* 17:1021.

197. Yu, C., Fiordalisi, I., and Harris, G. D. 1995. A unique swiveltether system for continuous i.v. infusions in freely mobile unrestrained rabbits. *Cont. Topics Lab. Anim. Sci.* 34(2):61.

198. Harris, G. D., Fiordlisi, I., and Yu, C. 1994. Intracranial pressure (ICP) during repair of diabetic ketoacidemia (DKA) in a rabbit model. *Pediatr. Res.* 35:203A.

199. Stills, H. F. 1994. Polyclonal antibody production. In *The biology of the laboratory rabbit*, ed. Manning, P. J., Ringler, D. H., and Newcomer, C. E., chap. 20. San Diego: Academic Press.

200. Brown, C. 2008. Intraoral examination in the rabbit *Lab Anim. (NY)* 37:405.

201. Vanatta, P. M. 1987. Capsule administration in the rabbit using a modified syringe. *Lab. Anim. Sci.* 37:367.

202. Eng, L. A., Carrig, C. B., Cordle, C. T., and Metz, C. B. 1987. Delivery of substances to the rabbit gastrointestinal tract by oral dosing with gelatin capsules. *Lab. Anim. Sci.* 37:239.

203. Rogers, G., Taylor, C., Austin, J. C., and Rosen, C. 1988. A pharyngostomy technique for chronic oral dosing of rabbits. *Lab. Anim. Sci.* 38:619.

204. Kendall, L. V. 2007. Production of polyclonal antibodies. In *Making and using antibodies*, ed. G. C. Howard and M. R. Kaser, chap. 4. Boca Raton: CRC Press.

205. Broderson, J. R. 1989. A retrospective review of lesions associated with use of Freund's adjuvant. *Lab. Anim. Sci.* 39:400.

Vet-ebooks.com

206. Halliday, L. C., Artwohl, J. E., Hanly, W. C., Bunte, R. M., and Bennett, B. T. 2000. Physiologic and behavioral assessment of rabbits immunized with Freund's complete adjuvant. *Cont. Topics Lab. Anim. Sci.* 39:9.

207. Johnston, B. A., Eisen, H., and Fry, D. 1991. An evaluation of several adjuvant emulsion regimens for the production of polyclonal antisera in rabbits. *Lab. Anim. Sci.* 41:15.

208. Smith, D. E., O'Brien, M. E., Palmer, V. J., and Sadowski, J. A. 1992. The selection of an adjuvant emulsion for polyclonal antibody production using a low-molecular-weight antigen in rabbits. *Lab. Anim. Sci.* 42:599.

209. Glenny, A. T., Pope, C. G., Waddington, H., and Wallace, U. 1926. Immunological notes, *J. Pathol.* 29:31.

210. Baldridge, J., Algate, P., and Mossman, S. 2007. Adjuvants. In *Making and using antibodies*, ed. G. C. Howard and M. R. Kaser, chap. 3. Boca Raton: CRC Press.

211. Hillam, R. P., Tengerdy, R. P., and Brown, G. L. 1974. Local antibody production against the murine toxin of *Yersinia pestis* in a golf ball-induce granuloma. *Infect. Immun.* 10:458.

212. Clemons, D. J., Besch-Williford, C., Steffen, E. K., Riley, L. K., and Moore, D. H. 1992. Evaluation of a subcutaneously implanted chamber for antibody production in rabbits. *Lab. Anim. Sci.* 42:307.

213. Ried, J. L., Walker-Simmons, M. K., Everard, J. D., and Diani, J. 1992. Production of polyclonal antibodies in rabbits is simplified using perforated plastic golf balls. *Biotechniques* 12:660.

214. Misiak, P. M. and Miceli, J. N. 1968. Toxic effects of formaldehyde. *Lab. Manage.* 24:63.

215. Greenblatt, M., Swenberg, J., and Kang, H. 1983. Facts about formaldehyde. *Pathologist* September:648.

216. Formaldehyde Panel. 1980. Report of the Federal Panel on Formaldehyde. National Toxicology Program, Research Triangle Park, NC.

217. Feldman, D. B. and Seely, J. C. 1988. *Necropsy guide: rodents and the rabbit,* chap. 6. Boca Raton: CRC Press.

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ISBN: 978-1-4200-9105-2
90000
9 781420 091052

CRC Press
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an **informa** business
www.crcpress.com

6000 Broken Sound Parkway, NW
Suite 300, Boca Raton, FL 33487
270 Madison Avenue
New York, NY 10016
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