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Chapter 9

Dogs and Cats as Laboratory Animals

Daniel H. Ringler and Gregory K. Peter

I. Introduction 241
II. Types and Sources of Dogs and Cats 242
A. Introduction 242
B. Random Source 242
C. Conditioned for Research 243
D. Bred for Research 243
III. Housing 243
IV. Conditioning 244
A. Conditioning the Random Source Dog 244
B. Conditioning the Random Source Cat 247
C. Prevention of Respiratory Disease Transmission 248
D. Canine Devocalization 249
V. Canine and Feline Breeding Colony Management 250
A. Introduction 250
B. Preventive Medicine in a Breeding Colony 250
C. Breeding Considerations—Canine 252
D. Breeding Considerations—Feline 253
E. Diseases Affecting Reproductive Success—Canine 254
F. Diseases Affecting Reproductive Success—Feline 256
VI. Nutrition and Feeding 257
VII. Diseases 258
A. Introduction 258
B. Infectious 258
C. Parasitic 263
D. Iatrogenic 265
E. Neoplastic 266
VIII. Selected Normative Data 267
References 268

I. INTRODUCTION

Dogs and cats have been used in biomedical research for centuries based on the early belief, then proved fact, that their anatomy, physiology, and response to disease was similar to man's. These studies have made phenomenal contributions to the health and welfare of both man and animals. Most of our knowledge of physiology, pathology, immunology, surgery, biochemistry, nutrition, pharmacology, toxicology, and control of disease is based on animal studies. Many of the discov-

ISBN 0-12-263620-1

eries of Harvey, Pasteur, Bernard, and other early leaders in biomedical science resulted from work with dogs and other animals. In past centuries the use of dogs and cats in research was based primarily on size, availability, and simplicity of care. During the early part of this century, extensive use of dogs in physiologic and surgical research was also based primarily on these criteria.

Today, dogs or cats are often the species of choice in animal research because they spontaneously exhibit or can be induced to exhibit aspects of diseases that afflict humans. In effect the animals serve as models of human disease. A comprehensive text deals with the various aspects of spontaneous animal models of human disease (Andrews *et al.*, 1979). The use of the dog as a research model in immunology, hematology, and oncology has recently been summarized (Shifrine and Wilson, 1980). The relevance and appropriateness of selected mammals, including the dog and cat, as models of human aging have been examined (Committee on Animal Models for Research on Aging, 1981). A symposium to examine the past, present, and future contributions of animals to human health and welfare has been held [National Academy of Sciences—National Research Council (NAS—NRC) 1977]. It seems apparent that dogs and cats will continue to play a vital role in biomedical research in the future.

A recent survey of laboratories in the United States indicates that approximately 180,000 dogs and 55,000 cats are acquired for biomedical research and testing each year [Institute of Laboratory Animal Resources (ILAR), 1980]. Of these, only 25% of the dogs and 8% of the cats are bred specifically for research by commercial breeders. The remainder, some 140,000 dogs and 50,000 cats are obtained from pounds and animal shelters. These animals are generally referred to as "random source" animals in order to distinguish them from the animals that are bred specifically for research. These random source animals present a particular challenge to laboratory animal veterinarians who often have the responsibility for conditioning these animals for use in research.

II. TYPES AND SOURCES OF DOGS AND CATS

A. Introduction

Dogs and cats for use in research are available from a number of commercial breeders and animal dealers licensed under the Federal Animal Welfare Act. A directory of commercial breeders is published periodically (ILAR, 1979). The directory and additional information on sources of animals and model copies of procurement specifications for dogs and cats are available.* A listing of licensed animal dealers in the United States can be obtained from the United States Department of Agriculture.†

B. Random Source

Dogs and cats that are available for research may be classified into several types according to the source from which they are procured. The types are (1) random source, (2) conditioned for research, and (3) bred for research.

Random source dogs and cats are generally acquired from federally licensed animal dealers, pounds, or individuals. Their history and disease status is generally unknown, and they may be incubating a wide variety of infectious diseases. In the dog, the most common of these include canine distemper, canine parvovirus, parainfluenza SV5, canine adenovirus-type II, and *Bordetella bronchiseptica* infections. Typically, newly received dogs begin to show clinical signs of respiratory disease during the first or second week after arrival in the research facility. The time of onset of these diseases usually is dependent on the time since animals from different sources were first grouped together. If the holding period during which the animals are aggregated prior to receipt in the research facility is as long as 10 days then signs of respiratory infection will tend to occur during the first week after arrival. If the holding period is 4–5 days, then clinical signs are usually seen during the second week after arrival. Dogs that do not exhibit signs of respiratory infection during the first 30 days after arrival rarely have serious respiratory disease later.

Like dogs, cats newly received from pounds and animal dealers may be in the incubative stage of a wide variety of infectious diseases. The most common are feline panleukopenia, rhinotracheitis, calicivirus infection, and pneumonitis (*Chlamydia psittaci*). Infestation with fleas, ear mites, and intestinal parasites also is common. Fox and Beaucage (1979) have shown that newly received cats may carry salmonellosis. Several of these dog and cat pathogens are also hazardous to humans. The zoonotic implications of dog and cat diseases are described in Chapter 22 on zoonoses. Typically, newly received cats show signs of panleukopenia during the first week after arrival, and the respiratory disease complex is manifest during the second or subsequent weeks. Generally, random source cats must be quarantined and conditioned for 30–60 days to ensure that they are healthy, well-nourished, tractable, and adapted to confinement.

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C. Conditioned for Research

Random source dogs and cats that have been through a quarantine and conditioning period are available commercially. Alternatively, they can be quarantined and conditioned in the research facility prior to their inclusion in research projects. In either case, the objective of conditioning is to produce stable disease-free animals that will react uniformly in research. The conditioning process is described more fully in Sections IV,A and B. Model procurement specifications for conditioned random source dogs and cats are available from the Institute for Laboratory Animal Resources (see footnote to Section II,A).

D. Bred for Research

Dogs or cats that are bred specifically for research are more uniform and have fewer health problems that random source animals. Other desirable attributes are as follows: pedigrees are generally available, animals may be vaccinated and free of both infectious diseases and parasites, and the animals are accustomed to cage life. Disadvantages of dogs bred for research include cost, shyness, and the small size of the beagle that is most readily available. This size problem has become less severe as hound-type dogs have become increasingly available. Cats that are bred for research may be intractable. Most difficulties in temperment of both dogs and cats can be alleviated by adequate socialization in the supplier's colonies. When procuring dogs or cats that are bred specifically for research, it is important to specify that the animals must be adequately socialized.

III. HOUSING

Construction criteria for research facilities housing dogs or cats are much the same as those for facilities housing other species. These criteria are described in the "Guide for the Care and Use of Laboratory Animals" (ILAR, 1978b) and are treated in some detail in Chapter 17 on design and management of animal facilities. Other useful references include "Dogs—Standards and Guidelines for the Breedings Care and Management of Laboratory Animals" (ILAR, 1973), "Laboratory Animal Management—Cats" (ILAR, 1978d), and "Laboratory Animal Housing" (ILAR, 1978c). In this chapter, only those issues that pertain to primary enclosures (cages or pens) for dogs or cats will be addressed.

The primary enclosure is one of the most important factors in the environment of dogs and cats housed in the research laboratory. It influences the well-being of the animals as well as their biological responses. Criteria for evaluating a caging system have been identified (ILAR, 1978b) and include animal comfort as a primary consideration. Physical comfort includes such factors as keeping the animal dry, clean, and at an appropriate temperature; providing sufficient space to permit normal postural adjustments; avoiding unnecessary physical restraint; and preventing overcrowding. In addition, the primary enclosure should be designed to facilitate effective sanitation and should be maintained in good repair. Finally, the enclosure should meet the investigator's research requirements.

The need for exercise or additional physical activity especially for dogs has been the subject of controversy in laboratory animal science. Although experimental evidence is scant, it has generally been concluded that confinement in a cage or pen has minimal influence on the amount of exercise that a dog or cat engages in and does not necessarily affect the animal's well-being (ILAR, 1978b). Hite *et al.* (1977) compared beagles housed in standard size cages with those housed in cages three times larger and found no beneficial or adverse effects related to cage size. Newton (1972) studied calcium kinetics and myofibrillar specific enzyme activity and showed no difference between caged and exercised dogs. Since there is a remarkable lack of experimental evidence regarding the effects of cage confinement, the need for supplementary exercise or large enclosures remains a matter of experienced judgement.

In research facilities dogs and cats are usually housed in indoor cages or floor pens. Outdoor housing and indoor–outdoor runs have found less favor in recent years due to a number of factors, including (1) less standardization of environmental conditions; (2) difficulty in preventing access by birds, insects, and wild animals; (3) noise control difficulties in urban areas; (4) inefficient utilization of space; and (5) difficulty in providing suitable outdoor space in association with the usual multistory research facility. However, outdoor or indoor–outdoor housing may be suited to some types of facilities in rural locations.

Within research facilities dogs and cats may be housed individually or in groups. Individual housing is generally preferred during both conditioning and experimental periods because it permits easier observation and handling. Consumption of food and water and production of feces and urine can be monitored more easily.

Generally accepted recommendations for dog and cat cage size are provided in the "Guide for the Care and Use of Laboratory Animals" (ILAR, 1978b) and the legal requirements are specified in the regulations of the Federal Animal Welfare Act [Code of Federal Regulations (CFR), 1982]. The regulations are available from the United States Department of Agriculture (see footnote to Section II,A). Those who design or select commercially available cages should be familiar with applicable portions of these documents.

Table I

Cage Space Recommendations for Dogs and Cats[a]

Animal	Weight (kg)	Type of housing	Floor area/animal	Cage height[b]
Dog[c]	15	Pen or run	0.74 m^2 (8.0 ft^2)	[d]
	15–30	Pen or run	1.11 m^2 (12.1 ft^2)	[d]
	30	Pen or run	2.23 m^2 (24.0 ft^2)	[d]
	15	Cage	0.74 m^2 (8.0 ft^2)	81.3 cm (32 in.)
	15–30	Cage	1.11 m^2 (12.1 ft^2)	91.4 cm (36 in.)
	30	Cage	[c]	[d]
Cat	4	Cage	0.28 m^2 (3.0 ft^2)	61.0 cm (24 in.)
	4	Cage	0.37 m^2 (4.0 ft^2)	61.0 cm (24 in.)

[a]Modified from the "Guide for the Care and Use of Laboratory Animals" [Institute of Laboratory Animal Resources (ILAR) 1978b].

[b]From the resting floor to the cage top.

[c]In order to be in compliance with the regulations of the Animal Welfare Act the required floor area may be computed by the following equation: (length of dog in inches + 6) × (length of dog in inches + 6) ÷ 144 = required square feet of floor space. The length of a dog is the distance from the tip of the nose to the base of the tail.

[d]It is generally accepted that cage or pen height should be at least equal to the height of the dog at the shoulders plus 6 in.

The cage space recommendations from the "Guide for the Care and Use of Laboratory Animals" are provided in Table I. In addition to these recommendations, the Guide emphasizes that cage and pen areas other than those suggested should be considered equally acceptable if they provide equivalent comfort for the animals. However, one must recognize that legal specifications apply to the housing of dogs and cats and are stated in the regulations of the Federal Animal Welfare Act (CFR, 1982). In general, cages that meet the size and construction recommendations of the Guide also meet the regulations of the Animal Welfare Act. However, several additional requirements incorporated into the regulations include (1) limitation to not more than 12 nonconditioned dogs or 12 nonconditioned cats in the same primary enclosure, (2) provision of litter boxes for cats, and (3) solid resting surfaces sufficient to accommodate all cats in the primary enclosure, these resting surfaces must be elevated if the primary enclosure houses two or more cats.

IV. CONDITIONING

A. Conditioning the Random Source Dog

Conditioning is the process whereby a newly arrived random source animal is freed of all parasites and infectious diseases and is acclimated to the laboratory environment. During the conditioning period the animal should achieve a defined health status consistent with the requirements of the particular experimental design.

Conditioning programs for dogs vary widely in length and complexity among research facilities. Most programs consist of physical examination; internal and external parasite control; vaccination for respiratory diseases, infectious canine hepatitis, canine parvovirus, and leptospirosis; laboratory examination for heartworm; and specific treatment of disease present during the conditioning period. In some programs the dogs are held for as little as 14 days prior to release to research projects. In our experience this holding period is insufficient because 5–10% of the dogs begin to exhibit clinical signs of respiratory disease following the 14 day holding period. Most research facilities have been more successful with a conditioning program that lasts at least 30 days. A model conditioning program is provided in Table II.

Table II

Conditioning Program for Random Source Dogs

Arrival procedures
1. Physical examination by veterinarian or animal health technician. Rejection of animals that are immature, aged, emaciated, or ill or those that fail to meet specific criteria (age, sex, disposition, hair length, etc.)
2. Weigh, sex, maintain identification, and initiate individual health record
3. Vaccinate for canine distemper, canine parvovirus, canine adenovirus type I (infectious canine hepatitis), canine parainfluenza and *Bordetella bronchiseptica*
4. Total immersion dip in insecticide solution for ectoparasites
5. House singly in floor pens with wood chip bedding. Alternatively animals can be dried and housed in cages or pens without absorbent bedding
6. Provide food and water

Postarrival procedures
1. Blood sample for heartworm microfilaria examination
2. Identify permanently if research protocol requires
3. Devocalize (optional)
4. Examine feces for intestinal parasites and ova and treat as indicated or, alternatively, administer a broad spectrum anthelmintic at 14-day intervals
5. Monitor food and water consumption daily
6. Observe each animal daily for signs of illness and provide veterinary medical care for ill animals. Alternatively, euthanize ill animals

Prerelease procedures
1. Physical examination
2. Repeat heartworm microfilaria examination if specific studies necessitate.
3. Examine feces for intestinal parasites and ova
4. Hematology and clinical chemistry examinations as required for specific studies

General considerations

Newly received dogs should be isolated as a group. Special precautions should be taken to ensure that personnel, fomites, and the ventilation system do not transmit infectious agents to previously conditioned dogs (see Section IV, C)

Arrival procedures usually include physical examination, dip in insecticide for external parasites, temporary identification, appropriate housing, and provision of food and water. It may be advisable to limit food consumption during the first several days until animals become accustomed to having laboratory diets provided *ad libitum*. At or shortly after arrival, animals should be immunized against canine distemper, canine parvovirus, canine adenovirus, canine parainfluenza, and *Bordetella bronchiseptica*.

Controlled studies have demonstrated that morbidity and mortality is significantly lower in newly received random source dogs that are immunized on arrival. Doyle *et al.* (1979) found that immunization against canine distemper, infectious canine hepatitis, and canine parainfluenza virus reduced the incidence of respiratory disease from 28 to 21% and the mortality from 25 to 14%. Appel (1970) has shown that virulent canine distemper virus spreads to the brain and epithelial tissues on about the ninth day after exposure. In order to be protective, the serum neutralizing antibody titer must be higher than 1 : 100 before the virus reaches the brain and epithelial tissues. Thus, the failure of vaccine to protect newly received dogs from distemper is in all likelihood due to exposure prior to vaccination.

Heartworm infection can interfere with pulmonary arterial circulation (Fig. 1) and result in cor pulmonale. Pulmonary arteries can be completely occluded by intimal proliferation (Fig. 2) and thrombosis induced by embolization of dead parasites. Early in the conditioning period, blood samples should be examined for microfilaria of the canine heartworm *Dirofilaria immitis*. The most commonly used methods are the modified Knott's technique or the filter technique. They are usually repeated during the holding period to help ensure detection of heartworm infection. Difficulties arise in detecting heartworm infestation when dogs harbor adult worms but are amicrofilaremic. These are called occult infections. The prevalence of occult infection has been reported to range between 10 and 60% (Rawlings *et al.*, 1982). Occult infection occurs in prepatent infections, unisexual infections, or where adult worms have been rendered sterile with drugs used in heartworm treatment. In these three types of occult infection no microfilaria are produced. A fourth type, "immune-mediated amicrofilaremia," occurs when microfilaria are produced by the adults but are rapidly cleared from the circulation, presumably due to presence of anti-microfilarial antibody (Wong and Suter, 1979). Currently there are several serologic methods being developed for detecting these antibodies or *Dirofilaria immitis*-related antigens in the serum. For the most part, these tests are still being evaluated, and their sensitivity and specificity has not been documented. Currently, we are utilizing several of these tests to improve our capability to detect heartworms in dogs used in research.

Animals generally are identified permanently with an ear tattoo, ear tag, or identification collar. In accord with the regulations of the Federal Animal Welfare Act, the research facility must retain the ability to correlate the permanent identification of the animal with information on the source of each animal.

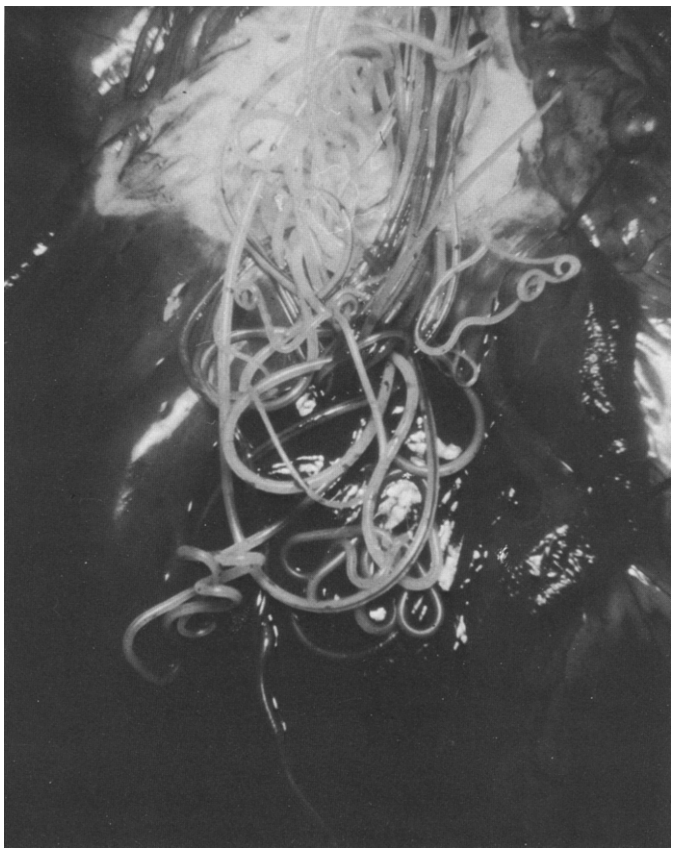

Fig. 1. Canine heartworm infection. Adult heartworms in the right ventricle and pulmonary artery of a newly received random source dog.

Diarrhea is an occasional clinical finding in newly received random source dogs and cats, especially those that have been exposed to crowded unsanitary conditions. Many animals improve spontaneously within a few days as they become adjusted to the quarantine facility and laboratory diet. General treatment measures that should be considered include maintenance of fluid, electrolyte, and acid–base homeostasis and dietary restriction. Initially, the GI tract should be rested by withholding food for 24 hr or more. When feeding is resumed, small amounts of bland food should be fed frequently.

If diarrhea persists, a specific etiologic diagnosis should be made to facilitate therapy and to protect other animals in the facility. Many of the bacterial, viral, protozoal, mycotic, and helminth agents that cause disease in newly received dogs and cats are listed in Table III. Differential diagnosis and treatment of diarrhea due to these etiologic agents is beyond the scope of this chapter. For additional information the reader should consult veterinary texts that deal with the subject in more detail

Fig. 2. Canine heartworm infection. Proliferation of intima in pulmonary artery in response to adult heartworms within the lumen. Hematoxylin and eosin. × 25.

(Anderson, 1980; Ettinger, 1983; Kirk, 1980; Kirk and Bistner, 1981).

Several of the enteric pathogens of dogs and cats are also human pathogens. Dogs or cats may serve as a reservoir for salmonella (Morse and Duncan, 1975), yersinia (Wilson *et al.*, 1976), and campylobacter (Fox, 1982). The public health aspects of these diseases are discussed in more detail in Chapter 22 on zoonoses.

Control and elimination of helminth parasites is usually achieved through treatment of all animals in the group with anthelmintics at specified intervals. Alternatively, fecal flotations and sedimentations may be performed and individual animals treated as indicated. A program for group treatment with anthelmintics should be based on an adequate survey of the incidence of intestinal parasites in newly received dogs (Table IV). An effective regimen is dichlorvos on day 3, niclosamide

Table III

Enteric Pathogens of Newly Received Random Source Dogs and Cats

Bacterial
Bacillus piliformis (Tyzzer's disease)
Campylobacter jejuni
Clostridium spp.
Enteropathogenic *E. coli*
Salmonella spp.
Shigella spp.
Staphylococci
Yersinia enterocolitica
Viral
Coronavius
Canine
Feline
Parvovirus
Canine
Feline panleukopenia virus
Rotaviruses
Astrovirus

Table III (*Continued*)

Protozoal
Coccidia
Giardia
Trichomonads
Entamoeba histolytica
Balantidium coli
Mycotic
Aspergillus spp.
Candida albicans
Histoplasma capsulatum
Phycomycetes
Helminths
Ascarids
Cestodes
Hookworms
Strongyloides stercoralis
Whipworms

Table IV

Prevalence of Helminths in Selected Dog Populations

Geographic location	Animal[a] source	*Toxocara canis*	*Toxascaris leonina*	*Trichuris vulpis*	*Ancylostoma caninum*	*Dipylidium caninum*	*n*	Reference
Utah	R	26.0[b]	6.0	—	—	2.0	50	Sawyer *et al.* (1976)
Ohio	R	19.2	10.2	42.2	60.8	—	500	Strietal and Dubey (1976)
New Jersey	R	22.5	5.4	75.6	72.0	28.6	2737	Lillis (1967)
Indiana	R	18.3	8.7	51.9	58.7	16.3	104	Kazakos (1978)
Montreal, Quebec	P	34.0	11.4	1.2	2.5	—	332	Ghadirian *et al.* (1976)
Halifax, Nova Scotia	R	26.0	1.3	1.3	8.0	0.6	474	Malloy and Embil (1978)
New Orleans, Louisiana	P	6.5	—	19.0	46.0	—	325	Vaughn and Jordan (1960)
Indiana, Ohio	R	21.0	4.1	—	—	—	1465	Ehrenford (1957)
Bermuda Islands	P	38	—	3.0	54.1	9.3	366	Williams and Menning (1961)
Iowa	P	3.0		1.2	5.3	—	33594	Lightner *et al.* (1978)
Michigan	R	13	3	13	40	—	74	Peter (1983)

[a]R, random source animals; P, pet animals.
[b]All values are percent.

on day 7, dichlorvos on day 14, and dichlorvos again on day 28.

All dogs should be observed daily by a veterinarian or animal health technician. Any dog exhibiting signs of disease should be subjected to appropriate physical and clinical pathologic diagnostic procedures followed by specific therapy for all conditions except respiratory disease. Because of the high incidence of respiratory disease, up to 70%, and the uniformity in the clinical presentation, it may be advisable to treat all affected animals with broad spectrum antibacterials for several days and perform extensive diagnostic procedures only on dogs that do not respond to treatment. We have found that a combination of sulfadimethoxine (25 mg/kg q24h po, iv, or im) and oxytetracycline (25 mg/kg q8h, po) is an effective antibacterial combination for initial treatment. Other broad spectrum agents may be equally effective.

B. Conditioning the Random Source Cat

Random source cats, those obtained from animal shelters and animal dealers, may be infected with a wide variety of infectious agents. The most life threatening of these is feline panleukopenia virus. In addition, the feline respiratory disease complex produces high morbidity during the first few weeks after receipt. Flea, ear mite, and intestinal parasite infestations also are common. Typically, newly received cats begin to show clinical signs of panleukopenia during the first week after arrival, and the respiratory disease complex is manifest during the second or subsequent weeks. The time of onset of these infectious diseases is in all likelihood dependent on the elapsed time following comingling of animals from different sources.

In an ideal situation, random source cats should be vaccinated for feline panleukopenia, rhinotracheitis, calicivirus, and pneumonitis (*Chlamydia psittaci*) and isolated until immunity developes. Only then should they be assembled into groups from disparate backgrounds. Occasionally arrangements can be made with animal shelter directors or animal dealers to vaccinate cats on arrival in their facilities and then provide some measure of isolation until immunity has developed. In any case, cats should be immunized at the earliest possible time in the hope that immunity will develop prior to exposure to these pathogens.

Conditioning programs are directed toward elimination of infectious agents and parasites and acclimation of the animals to the laboratory environment. Programs for achieving these objectives vary widely in length and sophistication among research facilities. Some programs hold cats for only 7–14 days prior to release to research projects. Most find that this period is insufficient because many cats will exhibit clinical signs of upper respiratory disease following a 14-day holding period. Typically, the respiratory disease complex spreads through a newly received group with a few cats continuing to show upper respiratory signs even after 14 days. Most cat conditioning programs have been more successful if the conditioning period is extended to 30–60 days.

A model conditioning program is illustrated in Table V. Several aspects of the program will be discussed here. The physical examination following arrival should be directed toward selecting the healthiest, most vigorous cats for conditioning. It is usually not cost effective to proceed with diagnosis and treatment of cats that are ill on arrival or those that become ill during the first few days of the conditioning period. These animals should be euthanized. If the newly received cats from different sources have been housed together for several days then one can expect 10–40% mortality due to panleukopenia during the conditioning period. Vigorous fluid, antibiotic, and supportive treatment of individual cats that exhibit signs of

Table V

Conditioning Program for Random Source Cats

Arrival procedures
1. Physical examination by veterinarian or trained technician. Reject animals that are immature, aged, ill, or those that fail to meet specific research criteria (age, sex, disposition, hair length, etc.)
2. Weigh, sex, identify, and initiate individual health records
3. Initiate administration of a broad spectrum antibiotic for 10–14 days
4. Vaccinate for rhinotracheitis, calicivirus, and panleukopenia. (Intranasal vaccine preferred; vaccination for feline pneumonitis, *Chlamydia psittaci*, may also be helpful)
5. Provide food and water

Postarrival procedures
1. Dust or spray each cat with a topical insecticide
2. Examine ears for ear mites and treat as necessary
3. Examine feces for intestinal parasites and ova and treat as indicated or alternatively, administer a broad spectrum anthelmintic at 14-day intervals
4. Monitor food and water consumption daily
5. Observe each animal daily for signs of illness and provide veterinary medical care for ill animals. Alternatively, euthanize ill animals

Prerelease procedures
1. Physical examination
2. Examine feces for intestinal parasites and ova
3. Hematology and clinical chemistry examinations as required for specific studies

General considerations
1. Newly received cats should be isolated as a group. Special precautions should be taken to ensure that personnel, fomites, and the ventilation system do not transmit infectious agents to previously conditioned cats (See Section IV,C)
2. All long-term cats should receive yearly booster vaccinations for panleukopenia, rhinotracheitis, calicivirus. In endemic areas vaccination for pneumonitis (*Chlamydia psittaci*) should be added to this regimen

panleukopenia is often not cost effective, and euthanasia should be considered.

The feline respiratory disease complex affects many newly received cats. The complex consists primarily of feline viral rhinotrachetitis virus or feline calicivirus infection. These agents are readily transmitted among cats individually housed in a room, and often a majority of the animals within a group will have respiratory signs. The husbandry staff must observe the precautions outlined in Section IV,C or the disease will spread from room to room. The intensity of treatment depends on the severity of clinical signs and the length of time that the group has been conditioned. Animals that are nearing the end of the conditioning period are more valuable because of the accumulating costs of daily maintenance and conditioning procedures. Often it is not cost effective to institute extensive treatment and nursing care for respiratory disease during the early portion of the conditioning period since the cost of drugs, supplies, laboratory tests, and nursing care can quickly exceed the cost of a replacement animal. Animals that show extensive clinical signs early in the conditioning period should be euthanized rather than treated. Of course, all ill animals must receive adequate veterinary medical care or be euthanized.

We have found that prophylactic tetracycline (25 mg/kg q12h po or 7 mg/kg q12h im) for 10–14 days beginning on the first day of conditioning is very helpful in reducing the severity of respiratory disease. *Chlamydia psittaci*, the causitive agent of feline pneumonitis, is uniformly sensitive to tetracycline, and secondary bacterial pathogens associated with viral respiratory diseases may also be susceptible.

Treatment of all but the most severely ill cats includes broad spectrum antibiotic therapy, fluid therapy, parenteral vitamins, and ocular care. It is beyond the scope of this chapter to provide detailed recommendations on the treatment of the feline respiratory disease complex. Stein (1980) has described treatment in some detail, and Section VII,B,2 provides additional information on the feline respiratory disease complex.

Ectoparasites, primarily fleas and ear mites, commonly infest newly received cats. Standard methods of treatment can be used during the conditioning period; however, later, when the animals are in experimental use, insecticides must be used with care since exposure, even to low concentrations, can induce or inhibit hepatic microsomal enzyme activity and alter the animal's biologic responses.

Gastrointestinal parasites should be eliminated during the conditioning period. There are two basic methods for eliminating these parasites. The first involves fecal examination of each animal and subsequent therapy at appropriate intervals until a series of negative fecals are obtained. The other involves routine treatment of all newly received cats with a broad spectrum anthelmintic such as dichlorvos at 10–14 day intervals then fecal examinations for parasites and ova at the end of the conditioning period. The choice of methods will be dependent on the prevalence of intestinal parasites in the newly received cat population (Table VI), the cost of laboratory tests, and the costs associated with therapy.

C. Prevention of Respiratory Disease Transmission

The most practical method of avoiding transmission of viral or chlamydial respiratory infections among dogs or cats is to receive, quarantine, and house them in individual cages with only a small number of animals per room. The husbandry staff must use strict rules of hygiene to prevent contamination from animal to animal and room to room. Procedures should include hand washing between handling ill animals, then hand washing and an outer clothing change between rooms. There should be no recirculation of air nor transfer of supplies and equipment between rooms. Cages and equipment should be disinfected between uses. Scott (1980a) tested 35 viricidal disinfectants against three feline viruses. Household bleach (5.6% sodium

Table VI

Prevalence of Helminths in Selected Cat Populations

Geographic location	Animal source[a]	*Toxocara cati*	*Toxascaris leonina*	*Capillaria* sp. and/or *Trichuris* sp.	*Ancylostoma* sp.	*Dipylidium caninum*	*n*	Reference
Utah	R	43[b]	—	—	—	1	100	Sawyer *et al.* (1976)
Ohio	R	25	—	1.3	9.4	—	1000	Christie *et al.* (1976)
New York	P	10	—	—	2	—	100	Dorman and Strand (1958)
New Jersey	R	55.7	—	—	84.6	10.4	1450	Lillis (1967)
Missouri	P	24.4		2.6	6.4	—	1294	Visco *et al.* (1978)
Illinois	P	41	6	3	6	—	34	Guterbock and Levine (1977a)
	L	29	5	2	8	—	124	
	R	35	9	7	14	—	57	
Halifax, Nova Scotia	R	25.1	0.3	0.3	—	—	299	Malloy and Embil (1978)
Bermuda Islands	R	17.9	—	10.3	27.8	12.8	39	Williams and Menning (1961)
Iowa	P	3.3		—	1.7	—	11995	Lightner *et al.* (1978)
Michigan	R	30.0	—	—	41.8	1.8	55	Peter (1983)

[a]R, random source animals; P, pet animals; L, laboratory colony.
[b]All values are percentages.

hypochlorite) diluted 1 : 32 was found to be the most effective and practical broad-spectrum viricidal product. To increase activity, this dilute bleach can be combined with detergents.

Animal husbandry personnel should provide daily care for long-term stable animals early in the day, then proceed to care for conditioning animals next, then newly received animals later in the day. Alternatively, staff members should work only in one colony. Of course, newly received dogs or cats should not be introduced into stable colonies until long-term observation and laboratory tests provide relative assurance that they do not harbor communicable respiratory diseases.

D. Canine Devocalization

In a research animal facility it is important to control environmental variables. One of the variables that is especially difficult to control is the noise of barking dogs. This noise, which can be extremely intense, is undesirable because of its effects on personnel and dogs in the facility as well as on personnel and research animals in adjacent areas. Every effort should be made to reduce sound transmission to other animal housing areas and human occupancy areas such as laboratories and patient-care facilities. Physical and acoustical separation of dog housing areas is usually the best method of reducing noise in adjacent areas. Within the dog housing area, sound control is especially difficult, since the use of acoustical materials in animal housing rooms often presents problems in sanitation and vermin control.

If noise from a dog housing area cannot be controlled through construction and acoustical absorption techniques, it may be necessary to utilize surgical techniques to reduce the intensity of sound produced. Several surgical procedures have been developed to reduce the level of noise produced when dogs bark. These procedures entail sectioning of the vocal cords and removal of the ventricular folds or adjacent mucosa.

The humane aspects of these "devocalization" or "debarking" procedures should be thoughtfully considered. The procedure requires general anesthesia and may cause laryngeal discomfort during the immediate postoperative period. Most dogs eat and drink normally following the immediate postoperative period, and many dogs continue to vocalize with lower intensity and pitch within a few days of the surgery. It is not apparent that there are any long-term detrimental physical or behavioral effects following the procedure.

Removal or sectioning of the vocal cords endoscopically (Anderson, 1955; Young and Sales, 1944) is the least satisfactory and frequently results in only transient devocalization. Transection of the vocal cords with electrocautery (Kraus, 1963) produces more permanent results with less hemorrhage. An extensive surgical method for devocalization that incorporates total removal of the vocal ventricular folds is described by Yoder and Starch (1964). This procedure is the longest lasting and provides the greatest sound reduction, but it requires considerably more surgical time than the other procedures. This can be an important consideration if many dogs must be devocalized.

A procedure developed by Raulston *et al.* (1969) utilizes a combination of transection of the cord with electrocautery and removal of the laryngeal saccular mucosa by means of a burr in a manner used in horses with recurrent laryngeal nerve paralysis. Results are longer lasting and more satisfactory than with

cautery alone. It is a very rapid method, allowing the devocalization of 40–50 dogs per hour, excluding anesthetization time.

V. CANINE AND FELINE BREEDING COLONY MANAGEMENT

A. Introduction

In the medical management of breeding colonies, the veterinarian must emphasize as the ultimate goal, the prevention of disease and the production of healthy animals for research. As in producing domestic food animals, a "herd-health" approach is required. The need for treatment of individual cases usually indicates a failure in husbandry or preventive medical programs. The economic costs and the medical benefits of instituting preventive or therapeutic measures must be taken into account when changes in medical care and colony management are contemplated. To aid in diagnosing disease entities and making managerial decisions concerning animal health, access to reliable diagnostic laboratories is essential. The need for diagnosis and treatment of disease should, however, be minimal if sound husbandry and preventive medical programs are implemented, supervised, and properly revised as new problems arise.

B. Preventive Medicine in a Breeding Colony

1. Environment

Although the actual physical plant for a breeding colony will vary depending upon specific needs and circumstances, there are some general principles that have been identified. These principles are discussed in Section III of this chapter and in Chapter 17 on design and management of animal facilities. Special attention must be directed to the adequacy of temperature and humidity control and ventilation in indoor facilities (ILAR, 1973, 1978c,d). Morbidity in the young can often be directly linked to inadequate ventilation or poor temperature and humidity control. There should be at least ten air changes an hour or more depending on temperature, humidity, and population densities. Morbidity can also be reduced by a physical plant that promotes rodent and insect control. Suspended wire cages help eliminate the oral–fecal transmission of intestinal parasites. The underlying theme of these measures is to provide a stable environment that lowers morbidity and mortality from disease by preventing stress and persistent contact with waste matter and potential pathogens.

The facility might include the following separate areas: (1) a housing and mating area for adult males in which each male has an individual territory, (2) a whelping/nursery area to which the female is taken prior to parturition, (3) an area in which weanlings can be raised and adults can be housed, (4) a surgical suite, (5) a diagnostic laboratory, (6) an isolation ward for sick animals and possibly a separate quarantine area for newly arrived animals, and (7) an administrative office area. An additional area for holding animals before shipment is convenient but not necessary.

A proper social environment is also important. The adaptability of a dog or cat to the laboratory setting, as to the home, is dependent upon regular human contact (Fox, 1965). Failure to supply this need can render an animal behaviorally useless as an experimental animal. Animals that exhibit undesirable behavioral traits even after adequate socialization should be culled from the breeding program.

2. Nutrition

Any good quality commercial food meeting the National Academy of Science–National Research Council (NAS–NRC) recommendations for nutrients (1974, 1978) can serve as the maintenance diet for the colony. Adults can be fed one or two times a day or *ad libitum*. Most dogs and cats do well on *ad libitum* feeding. Those that become obese may need to be hand fed. Puppies and kittens can be offered canned food or a moistened gruel of dry food starting at 4 weeks. Weaning usually takes place at 6 weeks, although this may vary depending on litter size. If *ad libitum* feeding is not implemented at this time, more frequent feedings (e.g., three to four times a day) are necessary for the first 3 months followed by decreasing to adult frequency of 1–2 times/day by 8 to 12 months of age.

During gestation nutritional requirements increase. The bitch and queen should be fed approximately 50% more than maintenance levels. During lactation, they should be fed *ad libitum* as they will consume two and one-half to three times as much food due to the energy demand of feeding a litter. They may lose weight, despite this increase in consumption.

Orphaned young or young removed from the mother for any reason should be fostered if possible. If hand-raising is required, a commercial milk replacer such as Esbilac (bitch milk replacer) or KMR (kitten milk replacer), Borden Inc., Norfolk, Virginia, should be fed and the orphan's weight monitored frequently to ensure adequate nutrition (Small, 1980).

Clean water should be made available at all times. If supplied in a bowl or bucket, the container should be rinsed and refilled daily and sanitized weekly. Automatic watering systems obviate this need but require weekly disinfectant flushing and daily inspection to assure proper functioning.

3. Immunization

a. Introduction. A routine vaccination schedule for both adults and young should be implemented. Modified live viral

vaccines should be used with caution in pregnant animals since the may cause congenital defects. It is prudent, therefore, to assure that vaccinations with these products are current before mating occurs. This will help ensure adequate colostral antibody to protect the young. All new arrivals in a colony should have current vaccinations. A period of quarantine and conditioning is necessary to prevent the introduction of a diseased or susceptible animal. See Sections IV,A and B for more complete descriptions of quarantining and conditioning programs for newly arrived animals.

b. Canine. In the canine colony, puppies should be immunized against distemper, infectious canine hepatitis (canine adenovirus type 1), leptospirosis, canine parainfluenza virus, and canine parvovirus at 6–8, 10, and 12–14 weeks of age. The exact timing of the first vaccination should coincide with the decline of maternal antibody levels. In most puppies this occurs at approximately 8–9 weeks, but a more precise time can be determined by analyzing serum titers. If the pup has not received colostrum, the vaccine regimen should be begun at 4 weeks of age. The use of measles virus vaccine in pups less than 6 weeks of age for protection against distemper virus is probably not necessary when the dam is revaccinated annually and the pup has received colostrum.

The recent concern over parvovirus infections and its potential disastrous effects in a colony situation warrant its inclusion in a vaccination program. The vaccine is available in combination with the above-mentioned products and can be administered on the same schedule. There is some indication that the canine origin products may provide greater protection than those of feline origin (Carmichael *et al.*, 1981).

Both parenteral and intranasal vaccines are currently available against *Bordetella bronchiseptica.* Although the vaccines may not totally protect dogs against "kennel cough," as there are several etiologic agents implicated, it can decrease the morbidity and severity of this disease complex (Shade and Goodnow, 1979).

In an indoor colony, rabies immunization is not necessary, since the likelihood of exposure is minimal; however, it may be advisable to immunize dogs that are housed outdoors or are being shipped to an outdoor facility. If shipment involves export or interstate transport, rabies immunization may be necessary to comply with shipping regulations.

c. Feline. In the feline colony, kittens should be immunized at 8 and 12 weeks, and adults should be reimmunized annually. Modified live vaccines against feline panleukopenia, feline viral rhinotracheitis (FVR), and feline calicivirus (FCV) are preferred. Intranasal vaccination for FVR and FCV can induce rapid immunity in the face of an outbreak. The inclusion of a vaccine against feline pneumonitis (FPN), a less common chlamydial disease, is warranted if the etiologic agent is present in the colony. Although not affording complete protection, vaccination against FPN can decrease the duration and severity of signs (Mitzel and Strating, 1977) and may eliminate the chronic disease seen in susceptible animals. Vaccination against rabies, as with canines, is not usually necessary unless it is required by shipping regulations.

4. Parasites

Parasite control is an important aspect of preventive medicine in breeding colonies. Parasites constitute a variable in research, and most responsible investigators specify that research animals should be free of both internal and external parasites.

External parasites can be controlled by routine environmental sanitation and regular dipping, spraying, or dusting with appropriate parasiticidal agents. Lindane is commonly used in dogs, but is toxic for cats. Carbaryl or rotenone compounds are safe for cats. Ear mites can be controlled with routine instillation of a 3 : 1 mixture of mineral oil and a commercial rotenone product (Canex, Pittman-Moore, Inc., Washington Crossing, New Jersey). Generalized demodectic mange in dogs possibly reflects a genetic predilection and an associated deficiency in cell-mediated immunity which may necessitate culling the animal (Muller and Kirk, 1976). Astute observation by the colony staff can allow early institution of more effective preventive medical procedures and medical management of these conditions before they become a major problem.

The control of internal parasites also depends on environmental considerations and parasiticidal therapy. Suspended caging, flea, and rodent control and strict sanitation help break the life cycle of these parasites. The various groups of animals in the facility should be routinely surveyed for internal parasites utilizing direct fecal smears and fecal flotations to detect ova or parasites. The frequency should be based on cost-effectiveness. The appropriate therapeutic agent should be administered as dictated by these examinations.

5. Record Keeping

The keeping of thorough, accurate records cannot be overemphasized. The medical and breeding information contained in them is invaluable in formulating and assessing preventive medical measures and breeding practices. A small computer for storing and processing the potentially large amount of data generated can be cost-effective and facilitate information retrieval.

The information on each animal should contain, above all, a record of permanent proper identification such as a tattoo number. Physical characteristics such as size, conformation, congenital abnormalities, and growth rate should be noted. Heritage and the progress of littermates offer valuable information on genetic constitution. For adults, behavioral information on disposition, maternal instinct, mating behavior, and libido

are important parameters. Other important breeding and birthing characteristics include date and length of estrus, results of semen examinations, previous gestation lengths, occurrence of dystocia, time of labor, litter size and viability including stillbirths, postparturitional vaginal discharges—character and duration, lactation, and number of pups weaned. Medical histories should include vaccinations, illnesses, diagnoses, therapy, surgical procedures and laboratory data generated by the clinical examination at the time of each illness. Records kept with diligence can be useful in assessing cases of subfertility, disease transmission and prevalence, husbandry deficiencies, and many other problems amenable to improved colony and medical management.

C. Breeding Considerations—Canine

1. Estrus and Mating

The bitch has a monestrous estrous cycle with heats occurring throughout the year, but predominantly in January or February and again in July or August. This is highly variable between breeds and individuals with the time between cycles ranging from 4 to 18 months. For an individual bitch, however, this time interval is usually consistent, and records can help predict the onset of estrus. Estrus is usually detected by regular clinical observation of the vulva for swelling and the serosanguinous discharge typical of proestrus. Vaginal smears to detect estrus, although accurate, are labor intensive and unnecessary in most situations.

Estrus can be induced during the anestrous period with a combination of pregnant mare serum gonadotropin (PMSG) and human chorionic gonadotropin (HCG) or pituitary gonadotropins of sheep origin (Evans, 1980). Induction can be desirable from a management aspect if whelping synchronization is important. Bitches that exhibit prolonged anestrus or incomplete estrus should be culled from the breeding colony.

The prevention of estrus can at times be desirable. Animals to be shipped or those that are group-housed are examples. The blocking of estrus can be accomplished by the use of either a progestational agent such as megestrol acetate (Ovaban, Schering Corp., Kenilworth, New York) (Buke and Reynolds, 1975) or an androgenic agent such as mibilerone (Cheque, Upjohn Co., Kalamazoo, Michigan) (Sokowlowski, 1978; Sokowlowski and Gerg, 1977; Upjohn Co., 1978).

A bitch may be bred on her first heat after 1 year of age and on every cycle thereafter if the duration of anestrus is greater than 8 months. If the intercycle duration is less than this, she should be rested every third cycle (Kirk, 1970).

The male dog is usually brought into service at 1 year but can begin as early as 8 months. He is fertile and able to inseminate females throughout the year.

Mating is accomplished by placing the bitch with the stud every other day during estrus until she refuses to accept him. If natural mating does not occur, artificial insemination can be performed (Seager, 1977). Semen should be collected at regular intervals for semen evaluation. Studs should not service more than one or two bitches per week nor be collected more often than every other day. The usual ratio of males to females is 1 : 10–15 which allows for the relatively long anestral periods.

2. Pregnancy and Parturition

Pregnancy diagnosis is most easily accomplished by abdominal palpation at 21–28 days postmating or radiography after 43 days. A negative finding may indicate failure to conceive, fetal resorption, early abortion, or stud infertility. As always, carefully kept records can assist in delineating the reasons for "misconception."

Gestation length varies between bitches but is consistent for any individual. The average duration is approximately 63 days. The pregnant bitch should be moved to the whelping area 10 to 14 days prior to her expected date of delivery. Adaptation to her surroundings and the avoidance of stress are important to ensure a normal delivery. If she is upset, gestation may be prolonged. A whelping box, preferably disposable and/or nesting paper should be provided.

The first signs of impending parturition are usually behavioral. The bitch seeks seclusion or the company of a keeper to whom she is very attached. She may exhibit nest building behavior and appear apprehensive especially if she is nulliparous. Anorexia and even emesis may be evident. A decrease in body temperature the day before parturition is not as reliable in predicting impending parturition as the palpable relaxation of the pelvic musculature and ligaments. The most reliable method of predicting parturition is to observe these changes in each animal and record them for future reference.

The first stage of parturition, consisting of uterine contractions which increase in frequency and strength, lasts 6–12 hr. This varies by breed and may be longer in nulliparous bitches. The second stage is indicated by obvious tenesmus coincident with the contractions. This increases the intrauterine pressure and causes the rupture of the fetal membranes and expulsion of the pups. The membranes are usually delivered within 15 min of the birth of the pup, although they may be delivered together. Usually, 30–45 min elapse between the birth of subsequent puppies. There may be a green vaginal discharge which is normal as a result of membrane rupture, but if there is an excessive delay before a puppy is delivered, a vaginal exam is indicated. Uncomplicated, the whelping of the entire litter may take only 2 hr in smaller breeds and as long as 12 hr in larger breeds.

If a delay in delivery is evident, determination of the cause

dictates the action taken. Malposition may be corrected by digital manipulation *per vaginum*. If the fetus is too large or cannot be rotated into a normal presentation, then a cesarian section must be performed. Smith (1974) describes in detail the surgical procedure. This action should never be postponed until the bitch is exhausted as the surgery is risk enough. If uterine inertia develops, either primary or secondary to obstruction, as many as three oxytocin injections (5–10 U, im or iv) 20 min apart can be administered to stimulate uterine activity. If uterine enertia persists a cesarian section should be performed.

Upon the completion of whelping, abdominal palpation and vaginal examination to ensure that no pups remain should be followed by an oxytocin injection (5–10 U, im or iv) to help control postparturient hemorrhage, contract the uterus, and stimulate milk letdown. The umbilical cord should be dipped in an iodophor disinfectant solution.

Following birth, bitches usually lick their pups vigorously. This stimulates respiration and circulation and removes the membranes and fluids. If pups are delivered by hysterotomy, they should be dried vigorously with a soft terrycloth towel and placed in an incubator until the bitch has recovered. Orphan puppies should receive colostrum if at all possible. They can be maintained on a commercial milk replacer, until they can be fostered to a receptive dam. If they are not fostered, they must be hand raised. This entails the use of an incubator, frequent feedings, and the stimulation of urination and defecation (Olson and Olson, 1971). It is far easier and more efficient to foster whenever possible.

D. Breeding Considerations—Feline

1. Estrus and Mating

The queen is seasonally polyestrous with two to three cycles between mid-winter (January) and early fall (September). Behavioral changes, such as posturing with the pelvis extended and the tail deflected laterally and vocalization, may be evident especially while being handled, but there is no characteristic vulvar swelling or vaginal discharge. Vaginal cytology should be used with care in determining the proper time for mating, because collection of the cytologic sample may actually induce ovulation and pseudopregnancy.

Induction of estrus can be accomplished by housing the anestrous female in close contact with normally cycling females (Colby, 1980) or by administering exogenous gonadotropins (Cline *et al.*, 1980; Colby, 1970; Wildt *et al.*, 1978). Increasing the light to 14–18 hr per 24-hr period may enhance the percentage of cycling queens (Scott and Lloyd-Jacob, 1959).

The queen is always taken to the male's territory, because of the male's strong sense of territoriality. Libido in the male can be easily suppressed by confinement, the presence of another male, unfamiliar surroundings, or an exceptionally aggressive female. Receptivity of the female lasts from 1 to 4 days and induced ovulation occurs 24 hr after mating. Repeated matings are recommended to ensure success. If not mated, the cycle lasts 10 to 14 days followed by another in 2 to 3 weeks.

Semen collected by electroejaculation (Platz and Seager, 1978) can be examined in the laboratory to evaluate fertility of the male and/or it can be used for artificial insemination (Sojka *et al.*, 1970).

2. Pregnancy and Parturition

Pregnancy diagnosis by abdominal palpation is reliable 17–21 days postmating. Implantation sites are firm, marble-sized swellings that can be palpated early in this period. The uterus becomes larger and softer to palpation after day 21. The skeletons of the fetuses can be visualized radiographically after about 43 days.

Gestation requires approximately 63–65 days in the cat. As with the bitch, it is advisable to move the queen to a kindling environment before parturition. It should be quiet, dark, and contain a kindling box.

As parturition draws near, mammary development begins. It is especially noticable during the last 3 days of gestation and milk can be expressed 24 hr before parturition. Other signs of impending birth include mucous vaginal discharge, vulvar enlargement, decreased body temperature, and behavioral changes characterized by seclusion seeking or the strong attachment to a certain handler.

The normal interval between expulsion of kittens can vary from minutes to hours but because of the length of the estrous cycle and the general practice of repeat breedings, kittens may be born in more than one group with days intervening. Thus, delay in expulsion of fetuses does not necessarily mean dystocia. A careful examination of the breeding history and the queen can be helpful in determining whether dystocia exists. If a particular queen has a history of dystocia, a prepartum exam including palpation and radiography may be necessary to determine the need for cesarian section. In the queen, this is usually not necessary as dystocia is not as common as in the dog. Usually digital manipulation is the only assistance necessary. It is not customary to use oxytocin to aid uterine motility and milk letdown in the feline. Oxytocin (0.5–3.0 U, im or iv) may be useful if placental membranes are retained or there is extensive postparturient hemorrhage. A postpartum exam is essential to determine if all kittens have been expelled and the membranes passed. The umbilical cord should be dipped in an iodophor disinfectant solution. Finally, the quality of maternal behavior should be observed and recorded.

E. Diseases Affecting Reproductive Success—Canine

1. Introduction

Reproductive success is best measured by the number of healthy pups reaching puberty. Mortality generally occurs before weaning, especially during the first week in which stillbirths, congenital abnormalities, physiological immaturity, and trauma account for a large number of deaths. Thereafter, the major causes of morbidity and mortality are pneumonia and gastrointestinal disease, which may be exacerbated during the stress of weaning.

Neonates are extremely prone to hypoglycemia, hypothermia, and dehydration. Therefore, malnutrition of either the bitch or the neonate or anorexia due to illness can be life-threatening. Much of the treatment of disease in the neonate consists of supportive as well as specific therapy.

Adult animals are culled primarily due to reproductive problems, chronic skin and ear infections, and trauma. The following summary is not meant to be conclusive, but highlights some of the specific health problems seen in breeding colonies.

2. Diseases of the Young

a. Canine Herpesvirus (Puppy Viremia). Canine herpesvirus infection is an acute fulminant disease that usually affects puppies from 1 to 3 weeks of age. Older dogs are usually unaffected or may exhibit signs of a mild upper respiratory disease. The virus is transmitted *in utero* or as the puppy passes through the birth canal and contacts virus-containing vaginal fluids. Susceptibility to fatal viremia is greatest during the first week of life. The clinical signs include sudden onset, constant crying, cessation of nursing, and death within several hours. The entire litter is commonly affected, and it is usually the primiparous litter. Subsequent litters may not be affected, as self-immunization in the colony usually occurs. Therefore, the occurrence of canine herpes infection in a litter is not a common reason for culling a bitch.

Necropsy reveals pathognomonic renal cortical hemorrhages with necrotic centers. There may be similar hepatic lesions (Fig. 3) and bronchopneumonia. Confirmation of the diagnosis is by histologic observation of basophilic intranuclear inclusions in necrotic areas of parenchymal organs or by viral isolation (Smith *et al.*, 1972).

Successful treatment depends on the early recognition of clinical signs and consists of placing pups in an incubator for 24 hr. The temperature should be 100°F for the first 3 hr and 95°F thereafter. A relative humidity of 60% and frequent oral fluids (5% glucose) help prevent dehydration. Surviving puppies may develop chronic renal disease at an early age (Mosier, 1977).

b. Toxemia and Septicemia. "Toxic milk syndrome" has been associated with uterine subinvolution in the bitch. The

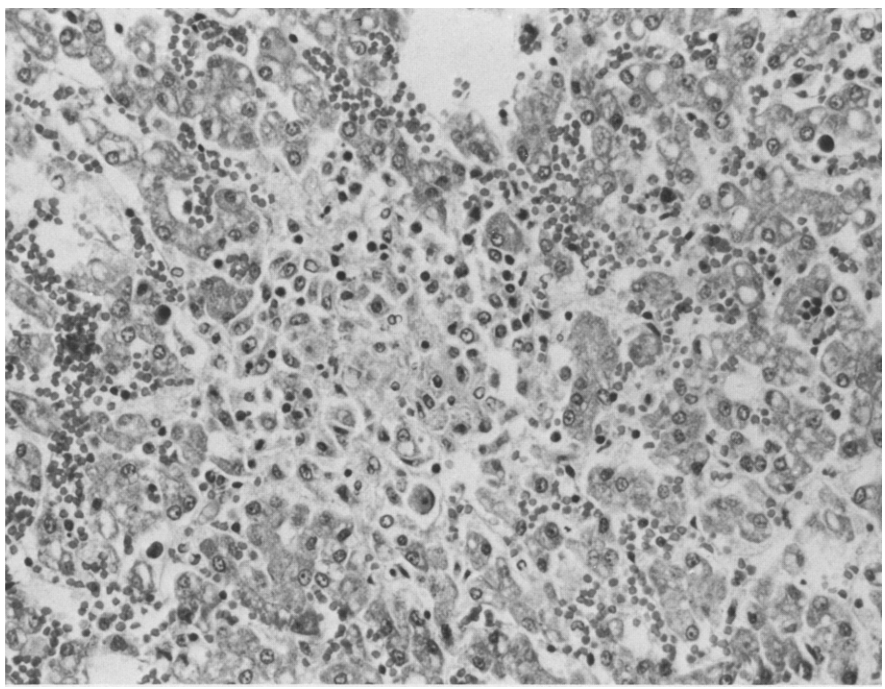

Fig. 3. Canine herpesvirus infection. Necrotic focus in liver of 11-day-old puppy. Hematoxylin and eosin. × 160.

first indication of a medical problem may be crying, bloated, 4- to 14-day-old puppies with red, edematous rectums. The bitch may exhibit a greenish vaginal discharge indicating metritis. Treatment consists of removing the puppies and placing them in an incubator at 85°–90°F and oral gavage with 5% glucose until the bloat has receded. This is followed by feeding commercially available milk replacer for a 24-hr period. Treatment of the bitch is instituted with an intrauterine antibacterial/estrogen infusion (Utonex, Upjohn Co., Kalamazoo, Michigan) followed by oral ergonovine (0.2 mg t.i.d. for 2–3 days) and systemic antibiotic therapy for 7 to 10 days. The pups can be returned after 24 hr. Routine administration of oxytocin postpartum has been effective in preventing this condition. Good nutrition and regular exercise may also be helpful in ensuring proper uterine involution during subsequent breedings.

Puppy septicemia occurs most frequently during the first 5 weeks of life. During the first 48 hr of life, the syndrome is characterized by crying, bloating, cessation of nursing, with resultant hypothermia, hypoglycemia, and dehydration. Death usually ensues within 12 hr of onset. Older puppies present with distended abdomens, hyperpnea, and crying and die within 18 hr. Signs may appear in only one pup, but many times the entire litter becomes progressively involved. Visceral congestion and intestinal distension with gas are found postmortem. The condition is often associated with metritis and/or mastitis in the bitch. Environmental factors such as high humidity, poor ventilation, and bacterial contamination due to poor sanitation are implicated as predisposing factors. Blood cultures from puppies have revealed *Streptococcus, E. coli,* and *Klebsiella* as common agents (Glickman, 1980).

Treatment consists of moving the pups to an incubator, relieving the bloat, administering subcutaneous lactated Ringer's solution, and oral dosing with a broad-spectrum antibiotic. It is best to prevent the problem through improved sanitation and husbandry. Ensuring colostrum consumption may also be helpful. In some colonies where the problem is consistently linked to a particular bacterial agent, autogenous bacterins may be useful. Bitches who have repeated episodes of metritis and/or mastitis should be culled.

c. Gastrointestinal Disease. In young dogs, morbidity and mortality due to gastrointestinal disease can be significant. Diarrhea and vomiting are commonly seen following weaning and are probably related to dietary changes and stress. These signs usually resolve spontaneously. If not, the diarrhea usually responds to dietary management (addition of cooked rice) and neomycin/anticholinergic therapy.

Persistent cases requiring diagnosis and treatment usually have an infectious etiology that can include parasites, bacteria, and viruses. Although diseases caused by parasites should be minimal in a well-managed colony, initial fecal flotation and direct smears are indicated in diagnosing gastrointestinal disorders. Positive results dictate the appropriate therapy and the need for subsequent fecal examination. The bitch should be similarly examined as she is the probable source of the infestation.

Parvoviral enteritis is potentially a serious threat to young dogs in colonies. Mortality can be very high in 5- to 12-week-old puppies. Lethargy, anorexia, diarrhea, and vomiting with rapid dehydration is the common clinical presentation. Panleukopenia or lymphopenia may be present early in the course of the disease. Coronavirus enteritis presents a similar clinical picture but usually without panleukopenia or lymphopenia. These conditions can be differentiated histologically in the laboratory (see Section VII,B,3 for additional information on canine parvovirus). Parvovirus vaccine is effective and should be included in a routine immunization program for both bitches and puppies.

d. Respiratory Disease. Prevention of pneumonia requires rigorous environmental control and a complete immunization program. Vaccination against canine distemper, parainfluenza, canine adenovirus I (infectious canine hepatitis) or canine adenovirus II, and *Bordetella bronchiseptica* can prevent much of the respiratory disease in a colony; however, the most critical factor is environmental control.

Tracheobronchitis, or kennel cough, caused by *Bordetella bronchiseptica* and canine parainfluenza in synergy is a common syndrome seen in group-housed dogs. It is usually a mild disease in older dogs requiring little medical attention, but in pups from 4 to 12 weeks of age, the disease can be more severe. Secondary invaders (*Pasteurella, Streptococcus, Klebsiella, Proteus, Hemophilus, E. coli,* mycoplasmas) in addition to the combination of primary etiologic agents (*Bordetella bronchiseptica* and canine parainfluenza virus) can cause life-threatening disease in affected pups. Therapy consists of broad spectrum antibiotic therapy. Severe congestive cases may respond to nebulization with a mucolytic agent and gentamycin. These dogs may suffer permanent lung damage (see Section VII,B,1 for additional information on canine respiratory diseases).

e. Miscellaneous Diseases. Pustular dermatitis occurs in pups before weaning. It usually affects the entire litter. Predisposing factors, such as high humidity and poor santitation, allow bacteria, usually staphyococci, to colonize the skin. Lesions occur predominantly on the head and neck. Topical therapy consists of cleansing the skin and administration of an antibiotic ointment.

Puppies are born hypoprothombinemic and can hemorrhage easily. Severing of the umbilical cord too close to the body wall can result in intraperitoneal hemorrhage and death. The prevention of bleeding tendencies in general can be accom-

plished by the administration of vitamin K_1 to the bitch during the last 30 days of gestation and to the newborn pups.

Trauma in the neonate is usually caused by the inexperienced bitch. If she is traumatic during removal of the fetal membranes, not only hemorrhage but umbilical herniation or evisceration can result. Excitable or inattentive bitches may unknowingly crush their young or provide poor care. They should be culled from the colony.

3. Diseases of the Adult

a. Brucellosis. Disease due to *Brucella canis* is suspected whenever there is a clinical history of abortion, infertility, testicular abnormalities, or lymphadenopathy. The disease, however, can be insidious with very low morbidity.

This systemic disease produces a prolonged bacteremia (up to 2 years) without fever. Transmission can occur at mating and by contact with aborted fetal membranes or vaginal discharges. Early embryonic death may occur and be interpreted wrongly as misconception. Later, abortion may occur in the last one-third of gestation followed by a prolonged vaginal discharge. Stillbirths can occur or live puppies may be weak and die soon after birth. If they survive they are often bacteremic and exhibit lymphadenopathy. Adult males affected with this disease can have epididymitis, orchitis, prostatitis, testicular atrophy, and lymphadenopathy.

The disease also affects humans. The zoonosis is characterized by headaches, weight loss, lymphadenopathy, and flulike symptoms—chills, weakness, sweating, muscular aches, and malaise (see Chapter 22 for a more comprehensive discussion of this zoonotic disease).

Control of brucellosis in a colony situation requires rigorous serological screening and culling (Moore *et al.*, 1968; Pickerill and Carmichael, 1972). A convenient and rapid slide agglutination test is available (Canine Brucellosis Diagnostic Test, Pittman-Moore, Inc., Washington Crossing, New Jersey), but can give false positive results due to nonspecific agglutination reactions (Brown *et al.*, 1976). If the slide agglutination is positive then tube agglutination and blood culture are indicated to confirm the diagnosis. Suspect dogs should be isolated, and if positive serology is confirmed by the tube agglutination, they should be destroyed. Three consecutive negative monthly tests in all dogs indicate that the colony is free from infection. New arrivals should be quarantined and undergo two or three negative tests at monthly intervals before entering the colony. During an attempt to eradicate the disease, daily cleaning and disinfection of the facility is helpful. Once free of the disease, a colony should be periodically tested with the rapid slide test to ensure that contamination has not occurred.

b. Mastitis. Mastitis usually occurs only when nursing ceases abruptly and the udder becomes engorged. Death of a litter or sudden removal of the pups may precipitate the condition. If mastitis occurs while the pups are nursing, it can be a threat to the puppies' health, especially if the milk is frankly purulent. The puppies should be removed or denied access to the infected glands by the use of bandages. The bitch's milk should be cultured to determine specific antibiotic therapy, and broad spectrum systemic antibiotics should be administered pending laboratory results. Hotpack applications and manual milk removal will hasten recovery and relieve discomfort. Recurrence on subsequent lactations is not uncommon, and repeated mastitis may constitute a reason for culling the bitch.

c. Metritis. Metritis usually occurs in the first week postpartum. Early recognition and prompt therapy shorten the disease course and prevent subsequent decreased breeding efficiency. The toxemic bitch with metritis is usually depressed, anorexic, febrile, and has decreased milk production. An excessive or abnormal vaginal discharge may be present. It is usually fetid, watery, and red. If the placenta is retained, the discharge may be green to black. Nursing pups may be listless, cry, and may have red edematous rectums. They may also exhibit other signs of septicemia/toxemia discussed earlier.

Therapy consists of administration of an ecbolic, either oxytocin or ergonovine; intrauterine infusion of an antibacterial/estrogen solution (Utonex, Upjohn Co., Kalamazoo, Michigan); and systemic antibiotics. Metritis may not necessarily recur after subsequent parturitions. Routine oxytocin injections several hours after whelping may reduce the incidence of metritis in the breeding colony.

F. Diseases Affecting Reproductive Success—Feline

Introduction

Many of the disease conditions affecting reproduction can be lessened by vaccination (panleukopenia, viral rhinotracheitis, calicivirus), and others can be eliminated by testing and culling (feline infectious peritonitis, feline leukemia virus). The prevention of disease in general requires good husbandry practices and prompt recognition and treatment of health problems. The following discussion will deal briefly with disease entities encountered in the feline breeding colony.

a. Panleukopenia. Disease due to feline panleukopenia virus is rare in breeding colonies due to the efficacy of vaccination. Vaccination of queens should occur before mating, since vaccination during pregnancy may have untoward effects on developing fetuses. To be effective, vaccination of the young must occur after maternally acquired antibody has diminished and prior to natural infection. The ideal time may vary from 3 to 16 weeks depending on the level of maternally acquired immunity. It is customary to vaccinate kittens at 8, 12, and 16

weeks and annually thereafter. Affected kittens may die acutely or become progressively depressed, anorectic, and dehydrated. Infected pregnant queens may experience abortions, stillbirths, and neonatal deaths. Kittens may have cerebellar hypoplasia if they are exposed to the virus *in utero*.

b. Respiratory Disease. Vaccination against the common causes of respiratory disease, viral rhinotracheitis, and calicivirus is mandatory. Vaccination against feline pneumonitis is less effective but may be indicated if the disease is enzootic. The major threat to reproductive success is transmission of rhinotracheitis or calicivirus infection to kittens by queens who are carriers. Feline viral rhinotracheitis viremia in the pregnant female may also cause abortions in addition to respiratory signs (Benirschke *et al.*, 1978).

Animals affected with upper respiratory disease should be isolated from the colony while being treated. Carrier queens that repeatedly infect their litters with rhinotracheitis or calicivirus should be culled (see Section VII,B,2 for additional information on feline respiratory diseases).

c. Feline Leukemia Virus. Feline leukemia virus (FeLV) can cause fetal resorption and abortion. Infertility due to persistent anestrus may also occur. Kittens exposed to FeLV may develop thymic atrophy and immunologic incompetence leading to increased susceptibility to other diseases. Methods to rid a colony of animals infected with FeLV are discussed in Section VII,E,1.

d. Feline Infectious Peritonitis. Feline infectious peritonitis (FIP) is an insidious infectious disease caused by a coronavirus which infects cats of all ages. Initial infection may be asymptomatic or manifest as another mild upper respiratory disease. Feline infectious peritonitis is strongly implicated in the kitten mortality complex discussed below. Cats with FIP should be removed from the colony using methods outlined in Section VII,B,4.

e. Kitten Mortality Complex. The kitten mortality complex (KMC) is a relatively newly described disease entity seen in catteries and breeding colonies (Norsworthy, 1979; Scott *et al.*, 1979). The etiology is unknown; however, feline leukemia virus or feline infectious peritonitis virus may play a role. The complex presents as a high frequency of reproductive failures and kitten deaths in successive pregnancies. Reproductive failure is characterized by fetal resorption, abortion in the last half of gestation, and stillbirths. Some queens appear to be repeat breeders, indicating the possibility of early embryonic death.

Commonly kittens are born weak and die soon after birth or are healthy for a few weeks then gradually become anorectic, depressed, lose weight, and die. There are no specific lesions seen other than those attributable to malnutrition. Some kittens as well as adults may die as the result of acute congestive cardiomyopathy. A histologic diagnosis of FIP has been made in some kittens involved in outbreaks of this complex (Scott *et al.*, 1979). It is usually the granulomatous form. When kittens are affected, adults may also exhibit mild chronic upper respiratory disease. Both adults and kittens exhibit intermittent low grade fevers. Endometritis is commonly seen in breeding colonies afflicted with KMC.

Little is known about this complex at the present time. Prevention may very well depend on the maintenance of an FIP-free colony. At present, treatment is symptomatic.

f. Metritis. Metritis occasionally occurs in the queen following parturition. Causes include retained placental membranes and lack of aseptic technique during assisted delivery. Treatment of the kittens and the queen are similar to that described for canines in Section V,E,3,c.

VI. NUTRITION AND FEEDING

Nutritionally complete commercial diets are available for dogs and cats, and in most research facilities they are fed *ad libitum* unless obesity or research requirements demand controlled dietary intake. Standard diets for dogs should contain the nutrients specified in the National Research Council document "Nutrient Requirement of Dogs" (NAS–NRC, 1974). Nutrient requirements for cats are outlined in the National Research Council document "Nutrient Requirements of Cats" (NAS–NRC, 1978). Laboratory animal veterinarians should have these references available.

Consistent reproducible experimental results require control over as many variables as possible, including the diet. Deficiencies or imbalances of nutrients can influence the manner in which animals respond to a given experimental manipulation. A monograph, "Control of Diets in Laboratory Animal Experimentation," summarizing the most important aspects of dietary control in animal experimentation is available from the National Academy of Sciences (ILAR, 1978a). Some of the most important points include nutritional adequacy, imbalances associated with diet modifications, ingredient variation, contamination, effect of environmental factors, and reporting responsibilities concerning diets.

Most commercially available balanced dog or cat diets are so-called closed-formula diets. These diets must meet labeled specified minimum values for protein and fat and maximum values for ash and fiber, but they do not necessarily provide exact nutrient levels or constancy of ingredient composition from batch to batch. Ingredient composition varies depending on the cost relationships of the various ingredients as the manufacturer attempts to achieve the label requirements at the lowest ingredient cost. If more precise dietary control is re-

quired, then open-formula (also called fixed-formula) diets can be purchased from any of a number of commercial manufacturers of special laboratory animal diets. In these diets the ingredients are identified and the percentage of each ingredient is kept constant from batch to batch.

In some experimental designs where nutritional intake must be controlled even more strictly, it may be necessary to provide semipurified diets. These diets are compounded from purified protein or amino acids, lipid, carbohydrate, vitamins, and minerals (NAS–NRC, 1974, 1978). Semipurified diets are also available commercially.

The date of diet manufacture should be known by the user. Preferably the manufacture date should be clearly marked on each bag of diet. In most facilities, diets, if stored under normal room temperature conditions, may be fed up to 6 months after the manufacture date. A system to ensure that diets are properly rotated and only fresh diets are fed should be in operation in each research facility. Of course, shelf-life of food is lengthened if food is stored at refrigerator temperatures; however, refrigeration of standard animal diets is not customary.

Because chemical (heavy metals, pesticides, estrogens, and aflatoxins) and microbiological (*Salmonella* sp. and *E. coli* type 1) contaminants have been found in animal food, some studies may require assays for particular contaminants (Newberne and Fox, 1978). Several commercial companies provide this service. Alternatively, batches of diet can be preanalyzed for contaminants, such as drugs, estrogens, heavy metals, and pesticides. Manufacturers then certify that the batch of diet contains less than certain minimum amounts of these contaminants. This type of preanalyzed diet is often used when animal studies must comply with the Good Laboratory Practices program of the Food and Drug Administration.

The regulations of the Federal Animal Welfare Act provide certain specifications for feeding and watering dogs and cats. They must be fed clean, wholesome palatable food at least once each day from food containers that minimize contamination by excreta. Water must be offered for a 1-hr period twice daily. Food and water containers must be kept clean and must be thoroughly sanitized at least once every 2 weeks. See Chapter 2 for a more complete discussion of the regulations of the Federal Animal Welfare Act.

VII. DISEASES

A. Introduction

Since many dogs and cats in research facilities are newly received from animal shelters, the laboratory animal veterinarian is confronted with the same spectrum of disease that confronts the private veterinary practitioner. The range of disease encountered extends from infectious diseases and congenital anomalies of the young to disease of the aged and includes metabolic, traumatic, and neoplastic conditions. The diagnosis, medical management, and epidemiology of these diseases is beyond the scope of this chapter and is dealt with in detail in several excellent veterinary texts (Ettinger, 1983; Kirk, 1980; Kirk and Bistner, 1981). While examining newly received dogs and cats the laboratory animal veterinarian should be ever alert for animals with diseases that might serve as animal models of human disease.

In the research facility, the primary veterinary medical focus is on preventive medicine and on dealing with iatrogenic (investigator induced) lesions. Newly received dogs and cats with spontaneous medical difficulties should be identified during the quarantine and conditioning period (see Section IV for a more comprehensive discussion of quarantining and conditioning procedures). The decision to treat or euthanize ill animals is a matter of professional judgment based on prognosis, humane considerations, cost-effectiveness of therapy, and protection of the long-term animals in the facility from communicable diseases.

Once research studies have begun, the decision to isolate ill animals or to treat spontaneous or iatrogenic disease must be made in consultation with the study director. The effect of isolation or therapy on the research study must be weighed against the pain and discomfort that the animal might experience or the threat that the disease might entail for other animals in the study. The decision to treat, withhold treatment, isolate, or euthanize the animal is usually a difficult one that calls for cooperation and trust between the laboratory animal veterinarian and the study director. Resolution of this potential conflict is facilitated if the veterinarian becomes familiar with the study and the study director becomes familiar with the humane and veterinary medical considerations.

In the following sections we will discuss those diseases of the dog and cat that are somewhat unique to the research facility or those that present unusual complications for research. For detailed discussion of the diagnosis, medical management, and epidemiology of disease entities the reader should refer to veterinary texts on the subject (Ettinger, 1983; Kirk, 1980; Kirk and Bistner, 1981).

B. Infectious

1. Respiratory Infections of Random Source Dogs

Severe and often fatal respiratory infection is the most important disease problem encountered in newly received random source dogs (Fig. 4). Studies indicate that up to 70% of newly received dogs may have clinical signs of respiratory disease, and a mortality rate of up to 20% is not uncommon (Bey

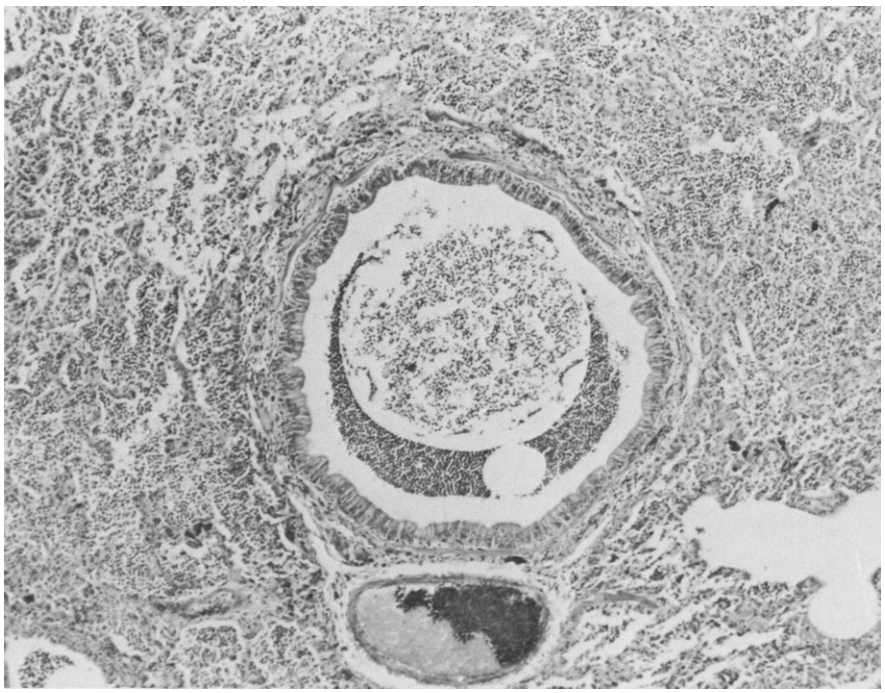

Fig. 4. Canine bronchopneumonia. Typical acute inflammatory exudate, primarily neutrophils, in bronchus and alveoli of a random source dog during quarantine period. Hematoxylin and eosin. × 40.

et al., 1981; Binn *et al.*, 1970b). The affected dogs exhibit mucopurulent nasal discharge, conjuctivitis, cough, dyspnea, depression, and anorexia. Some animals respond favorably to intensive antibiotics and supportive therapy, while others are refractory and the disease progresses to life-threatening bronchopneumonia.

Canine distemper virus has been identified as a major pathogen in this disease complex (Fig. 5). Histopathologic studies have confirmed the diagnosis of canine distemper in most fatal infections (Binn *et al.*, 1979). It has also been shown that dogs seronegative to canine distemper virus or adenovirus are much more likely to succumb to respiratory disease during the conditioning period (Binn *et al.*, 1970b, 1979). In the later study, 74% of the dogs without protective antibody to canine distemper developed respiratory disease, and 33% died. In contrast, only 24% of the dogs with protective antibody became ill and 4% died. Prevention of canine distemper appears to be the key to controlling severe, prolonged, and often fatal respiratory disease. Newly arrived dogs that have antibody to canine distemper also have a prevalence of antibody to infectious canine hepatitis virus (canine adenovirus type 1) twice that of dogs seronegative to canine distemper virus (Binn *et al.*, 1970b). The parallel titers in all likelihood indicate that these dogs have been vaccinated with a bivalent vaccine.

Doyle *et al.* (1979) found that immunization of newly received random source dogs against canine distemper, infectious canine hepatitis, and canine parainfluenza virus on arrival reduced the incidence of respiratory disease from 15 to 2% and the mortality from 16 to 6%. Appel (1970) has shown that to be effective, immunization against canine distemper must occur before exposure to virulent canine distemper virus occurs.

Although canine distemper is the major pathogen of newly received random source dogs, several other agents have been isolated from sick dogs during the conditioning period. Canine parainfluenza virus and canine adenovirus type 2 are the most prevalent. Both of these agents can produce respiratory disease, but it is generally concluded that they are not major pathogens (Binn *et al.*, 1970b). Rosendal (1978) isolated *Mycoplasma cynos* from the lungs of dogs with distemper and demonstrated experimentally that *M. cynos* could cause severe pneumonia.

Streptococcus zooepidemicus can cause acute necrotizing pneumonia in newly received random source dogs (Garnett *et al.*, 1982). The clinical course is often peracute and results in death without clinical signs. Dogs that are less severely affected have cough and moist rales often with purulent nasal discharge and tonsillitis. Necropsy lesions include diffuse hemorrhagic pneumonia and septic thrombi in the kidneys, lymph nodes, spleen, brain, and adrenal glands. Pencillin therapy is often effective if instituted early in the disease course.

Clinical tracheobronchitis (kennel cough) is often seen whenever dogs are group-housed. The clinical syndrome is characterized by a dry hacking cough but in rare instances productive cough, pneumonia, and nasal or ocular discharge may

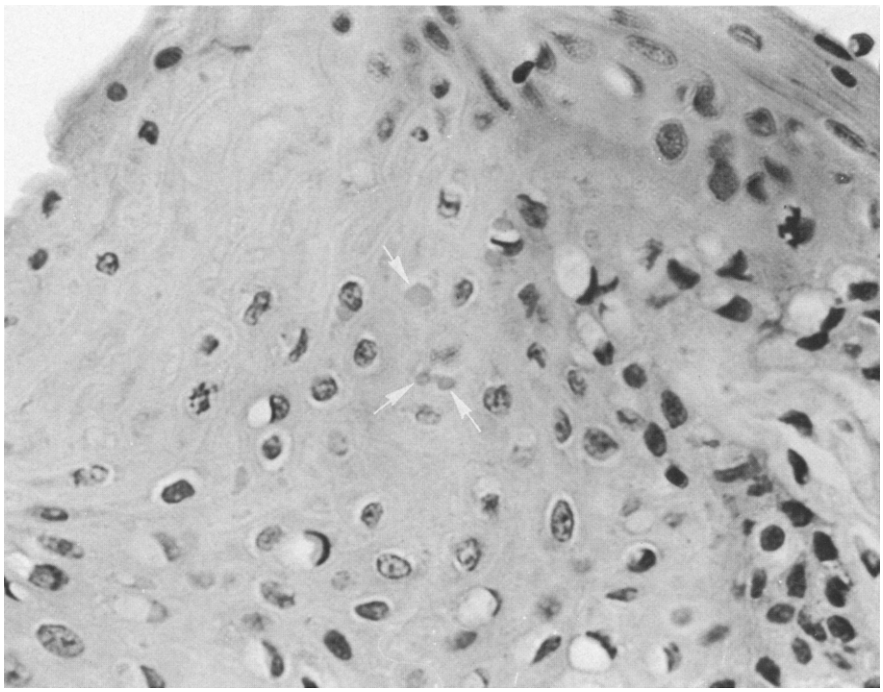

Fig. 5. Canine distemper. Inclusion bodies (arrows) in cytoplasm of epithelium of tongue. Random source dog during the quarantine period. Hematoxylin and eosin. × 400.

occur. The etiology of kennel cough is complex with both a bacterium (*Bordetella bronchiseptica*) and a virus (canine parainfluenza virus) playing a role. The disease is self-limiting unless infection with additional respiratory pathogens, especially canine distemper virus, ensues (Konter *et al.*, 1981). Live avirulent vaccines against both *Bordetella bronchiseptica* (Bey *et al.*, 1981) and canine parainfluenza (Konter *et al.*, 1981) are now commercially available.

Viruses less frequently isolated from the pneumonic canine lung include reovirus type 1 (Massie and Shaw, 1966), canine herpesvirus (Binn *et al.*, 1967), minute virus of canines (Binn *et al.*, 1970a), canine coronavirus (Binn *et al.*, 1975), and reovirus type 2 (Binn *et al.*, 1977). The role of these viruses in respiratory disease of random source dogs is unclear. Canine herpesvirus is rarely isolated, and serological studies indicate little spread of the virus. Minute virus of canines occurs with somewhat greater frequency, but it is rarely isolated from fatal cases, and very few sick dogs have rising titers to the virus. Canine coronavirus is frequently present in the small intestine, but is only rarely isolated from the lungs of sick dogs.

A complete program for immunization of group housed dogs against respiratory pathogens is necessary. In young animals the program should begin at 6–8 weeks or as soon as maternal antibody declines, if that is known. Live avirulent respiratory pathogens that should be included are canine distemper, infectious canine hepatitis (adenovirus type 1) or adenovirus type 2, canine parainfluenza, and *Bordetella bronchiseptica*. Annual revaccination is recommended.

2. Respiratory Infections of Random Source Cats

Newly received random source cats are beset by a wide variety of respiratory pathogens. The two most important are a herpesvirus, feline viral rhinotracheitis (FVR), and a picornavirus, feline calicivirus (FCV) (Scott, F. W., 1977). Other agents, such as the etiologic agent of feline pneumonitis (*Chlamydia psittaci*) and feline reovirus, may cause primary disease. Palmer (1980) indicates that 40–45% of feline upper respiratory infections are due to FVR, 40–45% are due to FCV, and about 4% are caused by *Chlamydia psittaci*. Numerous bacteria including mycoplasma are secondary invaders. Feline respiratory disease due to one or a combination of these agents is characterized by similar clinical signs, and clinical differentiation of them is not easy. Control of these infections is a difficult problem in research facilities just as it is in catteries and veterinary hospitals.

Sneezing, coughing, fever, and hypersalivation are the first signs observed in FVR, followed by photophobia, chemosis, serous ocular and nasal discharge, and depression. Occasionally, eye involvement is unilateral, but bilateral involvement usually follows in a few hours. As the disease progresses, both ocular and nasal discharges may become purulent and form

crusts. Eye involvement may proceed to ulcerative keratitis. Nasal exudate may occlude the nares and cause mouth breathing and anorexia. In summary, FVR is characterized by severe upper respiratory infection, especially in kittens, and ulcerative keratitis. Oral ulcers and pulmonary lesions are uncommon with FVR infection.

Feline calicivirus (FCV) infections are generally milder than FVR, although there is a wide difference in pathogenicity of FCV strains. In the mildest form, clinical disease is characterized by fever and ulcers on the tongue, hard palate, and nasal commissure. More virulent strains cause severe pneumonia that may be complicated by secondary bacterial invasion. Thus, FCV infection is characterized by oral ulcers and pneumonia. Conjunctivitis, rhinitis, and tracheitis are not usually seen in FCV infections.

Feline calcivirus has a short, less than 48 hr, incubation, and the primary disease rarely persists more than 5–7 days. Feline viral rhinotracheitis, on the other hand, has an incubation period of 2–4 days and the primary disease may persist for 10–14 days.

Feline pneumonitis (FPn), caused by *Chlamydia psittaci*, is characterized clinically by sneezing and coughing accompanied by serous then mucopurulent ocular and nasal discharge and fever. The signs may persist for 2–3 weeks; however, the disease is usually mild.

Reovirus infection is usually mild, with signs restricted to mild conjuctivitis and possible pharyngitis.

Differentiation of these infections is beyond the capability of most diagnostic laboratories. The diagnosis may be accomplished by isolation of the etiologic agent or by detecting rising antibody titer. Histologically FVR produces intranuculear inclusions in respiratory epithelium. In FPn, *Chlamydia psittaci* produces characteristic intracytoplasmic inclusions in respiratory or ocular epithelial cells.

Differential diagnoses should include underlying neoplastic, bacterial, or mycotic agents, and the possibility of feline leukemia virus acting as an immunosuppressor should not be overlooked.

Treatment of feline respiratory disease is primarily symptomatic. In FVR and FCV the etiologic viruses are responsible for the clinical signs and secondary bacterial infection is of lesser significance. Therapy includes fluids, ocular care, broad-spectrum antibiotics to combat *Chlamydia psittaci* and secondary bacterial invaders, and vitamins. The severely ill cat may require blood transfusions, inhalation therapy, and pharyngostomy to facilitate stomach-tube alimentation. Stein (1980) and Kirk and Bistner (1981) have described these therapeutic techniques in some detail.

The disease is spread from cat to cat by direct contact, fomites, or aerosol droplets. In natural cases infection is either oral or intranasal. Actively infected cats excrete etiologic agents in the saliva and nasal and ocular discharges. Calicivirus is also excreted in the feces and urine. The procedures outlined in Section IV,C should be followed to ensure that the agents are not transmitted by fomites or aerosol droplets.

After recovery, an important aspect of the spread of respiratory disease is the presence of a carrier state. Cats infected with either FVR or FCV may continue to shed the virus for many months. Severe stress or other diseases may cause carrier animals to again excrete virus months or even years later. Queens who have been infected as kittens may in turn infect their kittens.

According to Scott (1977), prevention of feline upper respiratory disease depends on: (1) exclusion of infected cats, (2) reduction of the concentration of virus in the environment, and (3) immunization of cats by vaccination.

In the research facility the first can be accomplished by housing newly received cats separately from those being conditioned or those in stable long-term colonies. Cats should not be transferred from room to room unless all cats in the room have been quarantined for 30 days and have been free of respiratory signs for a minimum of 2 weeks.

The concentration of virus in the environment can be reduced by frequent washing of cages and equipment and ensuring excellent personal hygiene by the husbandry staff (see Section IV,C for a more complete description of measures that reduce transmission of respiratory pathogens).

The most effective method of preventing infection is by immunization. Excellent vaccines that protect against FVR and FCV are commercially available. According to Mitzel and Strating (1977), vaccines for feline pneumonitis are less effective. All cats should receive annual booster vaccinations for FVR and FCV, usually combined with feline panleukopenia. Scott (1980b) provides an update on feline immunization.

3. Canine Parvovirus

Canine parvovirus (CPV) infection can cause high morbidity and moderate mortality in commercial and research canine breeding colonies. Merickel *et al.* (1980) describe an outbreak of acute canine parvoviral enteritis in a closed beagle research colony. During the 2-month episode, 66 of 183 puppies (36%) became ill and 22 died while only 4 of 1657 adults were affected and 3 died. This tendency for morbidity and mortality to be much higher in the young is characteristic. Similar episodes have been reported from several areas in the United States as well as Canada, Australia, and Europe (Pletcher *et al.*, 1979).

The disease is very similar to feline infectious enteritis (feline panleukopenia) and is characterized clinically by anorexia, depression, diarrhea, vomiting, rapid dehydration, and panleukopenia. Histological lesions include villous atrophy and crypt epithelial necrosis in the small intestine with crypts lined

by large, irregularly shaped epithelial cells (Pletcher *et al.*, 1979). There is lymphoid necrosis in the spleen, lymph nodes, and Peyer's patches. Young dogs may die suddenly due to severe primary nonsuppurative myocarditis (Hayes *et al.*, 1979).

The diagnosis may be confirmed by detection of CPV antibody in feces or by ultrastructural identification of parvoviral particles in feces. If myocarditis is present, parvoviral particles may be found in myocardial intranuclear inclusions.

Treatment is directed toward restoration of fluid and electrolyte balance. Often, dehydration, acidosis, and hypokalemia are severe. Broad spectrum antibiotic coverage is indicated to prevent secondary bacterial sepsis.

Canine parvovirus infection can now be prevented by vaccination with any of a number of commercially available vaccines. Immunization against CPV infection should be a standard practice in canine breeding colonies or wherever young dogs are used in research. Bitches should be immunized prior to mating, since the vaccine may cause congenital malformations if immunization occurs during pregnancy. Young dogs less than 3 months old should not be exposed to random source dogs, since infection may occur during this critical time of diminishing maternally acquired antibody. To be effective, vaccination against CPV must occur after maternally acquired antibody has diminished and before virulent infection takes place. The ideal time can vary from 3 to 16 weeks of age depending on the level of maternally acquired immunity. In critical situations, the timing of vaccination should be based on a hemagglutination inhibition titer nomogram that can be developed if the titer of the bitch or pups is determined.

4. Feline Infectious Peritonitis

Feline infectious peritonitis (FIP) is an important multifaceted infectious disease that affects both domestic and wild cats. Weiss and Scott (1980) have comprehensively described the etiology, epizootiology, pathogenesis, diagnosis, treatment, and control of FIP. Briefly, the disease, caused by a coronavirus, is characterized by chronic weight loss, depression, and fever that is nonresponsive to antibiotics. About one-half of those clinically affected have peritoneal exudate, about one-third have both peritoneal and pleural exudate, and about one-half have neither. Frequently, there are protean organ-specific signs due to perivascular pyogranulomatous lesions and vasculitis involving liver (Fig. 6), kidney, pancreas, eyes, brain, heart, and lungs. Depending on the organs affected, the clinical syndrome can vary widely.

Surveys indicate that 20% or more of cats in the United States are serologically positive for FIP (Horzinek and Osterhaus, 1979). Thus, many cats entering research facilities through public pounds or animal shelters will be infected. Identification of these animals is aided by the indirect fluorescent antibody test (IFAT) that can be utilized to detect FIP antibody titers. The interval between initial exposure and seroconversion is 2–6 weeks according to Weiss and Scott (1980).

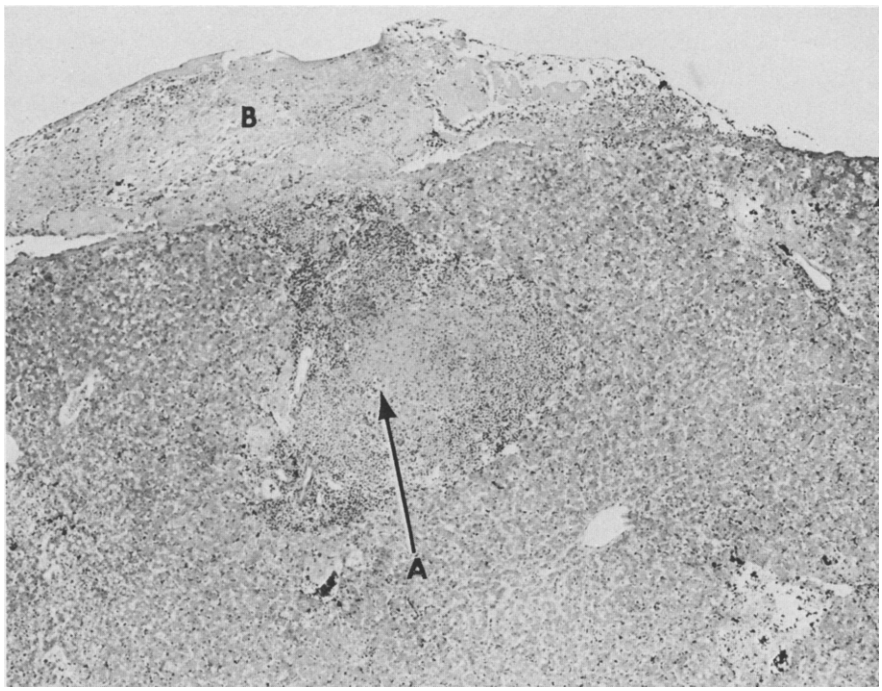

Fig. 6. Feline infectious peritonitis infection. Pyogranuloma in liver (A) with fibrinopurulent exudate adherent to serosal surface (B). Hematoxylin and eosin. × 25.

Cats with IFAT titers should be excluded from breeding colonies and long-term research projects. This can be accomplished by quarantining all new arrivals and obtaining two negative IFAT titers on the entire group over a 30-day interval. Periodically, breeding colonies should be retested to ensure that the agent has not been inadvertantly introduced.

Recently, an enteric feline coronavirus has been found to be ubiquitous in some cat populations (Pederson *et al.*, 1978). The virus is shed in the feces of many seropositive cats and may cause enteritis in kittens. Although the enteric coronavirus differs from FIP virus in pathogenicity, it is closely related antigenically. Thus, IFAT titers may not distinguish between animals infected with FIP virus and those infected with feline enteric coronavirus. Hopefully, kinetic-based enzyme-linked immunosorbent assays may aid in distinguishing between these populations (Barlough *et al.*, 1983).

5. *Salmonella* Infections of Random Source Cats

Newly received random source cats harbor a wide variety of pathogens, some of which may have zoonotic potential. It has been demonstrated that cats can serve as a reservoir of *Salmonella* for infection of animal technicians, investigators, and other animals. In a survey of newly received random source cats, Fox and Beaucage (1979) found that 10.6% of 142 cats received from commercial vendors had *Salmonella* in their feces. Timoney *et al.* (1978) described an outbreak of *S. typhimurium* in young cats in a veterinary hospital. A morbidity of 32% and a mortality of 61% was observed.

Laboratory animal veterinarians should be aware that cats can serve as a reservoir of *Salmonella* in the research facility. Screening of newly received cats for enteric *Salmonella* before they are released from quarantine should be considered.

6. Dermatomycosis

Dermatomycosis or "ringworm" can be a significant endemic problem in colonies of cats used in research. The vast majority of cases are caused by *Microsporum canis,* while only a few percent are caused by *M. gypseum* or *Trichophyton mentagrophytes* (Muller and Kirk, 1976). Young animals are more frequently clinically affected than adults. Baxter (1973) reports that 70% of clinically significant cases involve kittens, while only 30% involve adult cats. Adult cats, however, can serve as inapparent carriers. Dermatophytes are transmitted from animals to humans (refer to Chapter 22 for additional information on the zoonotic implications of this disease).

The classical presentation in the cat consists of facial dermatitis with circular areas of alopecia. Lesions may also appear as scaly, nonerythematous patches or raised erythematous plaques, with protruding stubbled hairs. The distribution of lesions frequently includes the feet. The lesions may be self-limiting (2–4 weeks) or persist for years. They may progress to folliculitis–furunculosis and secondary pyoderma.

The diagnosis of dermatomycosis suggested by history and clinical examination can be confirmed using several methods. The use of a Wood's lamp to detect fluorescence of infected hairs is equivocal, as approximately 40% of *M. canis* infections are negative by this method (Muller and Kirk, 1976) and many other substances fluoresce as well. The yellow-green color under fluorescent light is most evident on the intrafollicular portion of the short-stubble hairs. As with the Woods lamp, microscopic examination of hairs cleaned with potassium hydroxide is rarely effective as the sole means of confirming the diagnosis. Fungal culture of the short-stubble hairs and skin biopsy are more definitive. Skin biopsy usually reveals acanthosis, parakeratosis, hyperkeratosis, and an inflammatory infiltrate in the upper dermis. Special stains, such as methenamine silver, may facilitate visualization of spores and mycelia in the keratinized portion of the skin and/or the hair follicle (Fig. 7).

An effective treatment is oral administration of griseofluvin with oil or after a meal at a dose of 30–60 mg/kg body weight daily for 4–6 weeks or for at least 2 weeks after a clinical cure. Once a response is seen, the dosage can be reduced to 10–15 mg/kg (Muller and Kirk, 1976). This drug should not be given to pregnant animals.

Shaving the affected area and cleansing it with a provodine iodine wash, dipping with captan 1–2 times/week, and application of fungicidal or fungistatic ointments may also be helpful.

Prevention of dermatomycosis in exposed animals with a single massive dose (200 mg/kg) of griseofulvin has proved effective (Muller and Kirk, 1976). Dawson and Noddle (1968) suggest that all new arrivals in a cat colony should be examined with a Woods lamp and material obtained from brushing the cat with a toothbrush should be cultured for dermatophytes. These animals should remain in quarantine pending culture results. Any positive animals should be isolated in individual cages in a room with a separate ventilation system. They should be treated and cared for by personnel wearing protective clothing and plastic goves. Cages, work surfaces, walls, and floors should be sanitized thoroughly since dermatophytes can persist in a dry environment for up 13 months (Dawson and Noddle, 1968). Addition of animals to a stable colony should occur only after freedom from infection is assured.

C. Parasitic

1. Introduction

The prevalence of parasitic infestation in newly received dogs and cats is generally dependent on the type of animal acquired, i.e., random source, conditioned for research, or

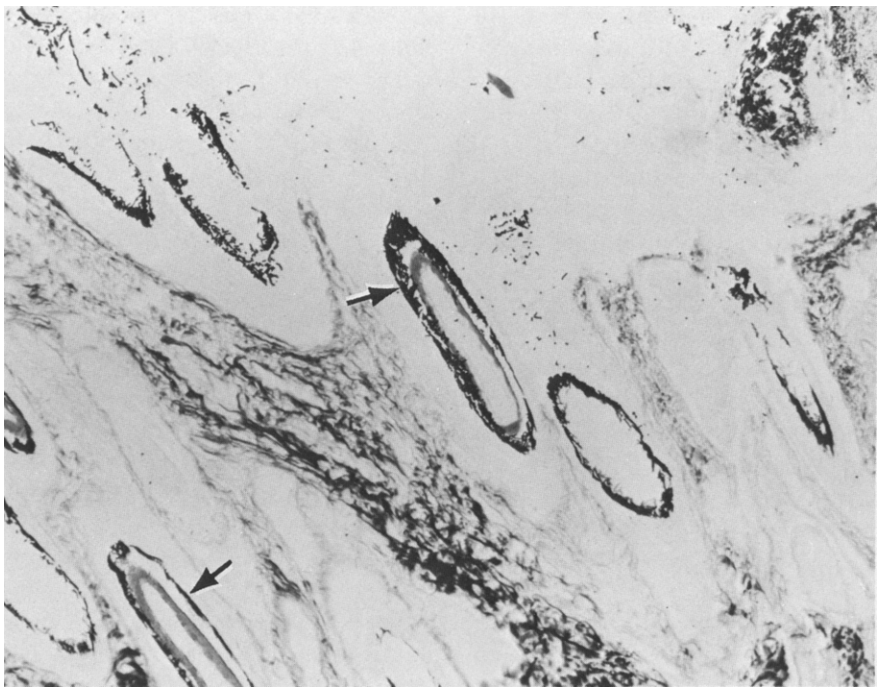

Fig. 7. Feline ringworm. Skin biopsy with fungal elements (arrows) within hair follicles and surrounding hair shafts. Methanamine silver. × 63.

bred for research. Newly received random source animals reflect the prevalence of parasitic infestation in animals acquired from animal shelters. Studies by Kazacos (1978) and Guterbock and Levine (1977a) have shown that the prevalence of intestinal helminths in these animals ranges between 35 and 87%. We find that the prevalence of helminth infestations can be reduced considerably by treatment of the entire group with broad spectrum anthelmintics at 2 week intervals (see Sections IV,B and C for more specific recommendations). The need for treatment of the entire group during the conditioning period should be based on a survey of intestinal parasites in incoming animals and on cost-effectiveness considerations. Other important aspects of the intestinal parasite control program are room and cage sanitation and caging to prevent fecal–oral transmission of parasite ova.

The prevalence of intestinal parasites in newly received animals that are conditioned for research or bred for research is much lower. However, these animals should be quarantined and screened with fecal flotations and sedimentations prior to admission to long-term housing rooms. Animals in long-term projects should be screened at quarterly intervals to ensure that they are free of intestinal parasites.

External parasites of newly received dogs are generally controlled through total body immersion in an appropriate insecticide solution. Newly received cats are generally dusted with carbaryl or rotenone compounds. Ear mites in both dogs and cats can be controlled with routine instillation of a 3 : 1 mixture of mineral oil and a commercial rotenone product (Canex, Pittman-Moore, Inc., Washington Crossing, New Jersey).

Control and treatment of the wide variety of internal and external parasites is beyond the scope of this chapter. Readers should refer to veterinary medicine texts (Kirk, 1980) and veterinary parasitology texts (Georgi and Theodorides, 1980) for specific recommendations.

2. *Filaroides hirthi*

Filaroides hirthi, a filarid lung worm of the dog, is a widespread pulmonary parasite in commercial beagle colonies (Georgi *et al.*, 1977; Hirth and Hottendorf, 1973). Georgi *et al.* (1979) found that first stage larvae or embryonated eggs are infective and that coprophagy in puppies is the common route of transmission and auto-infection. In natural infections there are usually only a few worms within the pulmonary parenchyma and no clinical signs, but with concurrent stress, such as that encountered in some research projects, fulminating verminous pneumonia can develop (August *et al.*, 1980; Craig *et al.*, 1978). The major lesions caused by this parasite are focal granulomas in response to dead adult worms in the lungs. These lesions, although not life-threatening, may be confused microscopically with those produced by oncogenic agents, drugs, and other pathogenic organisms (Georgi, 1976). Even subclinical lesions such as these are undesirable in animals used in research, since they may confound research results.

Diagnosis can be accomplished by detecting larvae in feces with fecal flotation techniques using $ZnSO_4$ (specific gravity = 1.18) (Ehrenford, 1957), or $NaNO_3$ (specific gravity = 1.2) (Appel, 1970). A large 10- to 15-gm sample of feces should be used with either technique. Bronchial wash may also yield embryonated eggs in heavy infestations.

Most anthelmintics (piperazine, dichlorvos, thiabendazole, levamasole, and dithiazanine iodide) are not effective. Administration of two courses of albendazole (50 mg/kg body weight) for 5 days at 3-week intervals to infected dams is very effective. It prevents vertical transmission and renders subsequent litters free from infection (Georgi *et al.*, 1979). A single course of therapy in experimentally infected dogs killed or sterilized all worms (Georgi *et al.*, 1978). The parasite is not transmitted *in utero*. In infected colonies, transmission can be controlled by use of albendazole, caging animals separately, and reducing fecal contamination of the environment.

D. Iatrogenic

1. Introduction

It is inherent in the nature of experimental work with animals that during experimentation alterations in physiology may be induced. As a consequence, the laboratory animal veterinarian is often presented with clinical cases that result from or are a side effect of experimental procedures. These are called iatrogenic conditions or lesions. Animals in renal failure as a result of experimental hypertension or animals in hypoglycemic shock as a result of induced diabetes are examples of clinical conditions that are a consequence of the experimental alteration. Other clinical problems arise that are not directly attributable to the intended experimental alteration. For example, dogs with experimental gastric fistulas may become alkalotic due to chronic loss of gastric acid or cats with recording electrodes surgically implanted in the central nervous system may develop meningoencephalitis due to postsurgical infection.

If experimental procedures are carefully planned and carried out, many iatrogenic complications can be prevented. The laboratory animal veterinarian can often make a significant contribution by discussing possible iatrogenic complications with investigators prior to initiation of experimental procedures.

2. Medical Management of Chronic Indwelling Central Venous Catheters

Many experimental protocols necessitate continous or repeated access to arteries or veins for blood sampling, drug administration, or pressure measurement. Chronic indwelling central venous catheters that are necessary to achieve these ends can cause many clinical problems. Hysell and Abrams (1967) identified some of the complications seen in laboratory animals with chronic indwelling central venous catheters. Direct physical trauma from the catheter may cause damage of the vascular wall and intravascular thrombus formation at the catheter tip (Fig. 8). If venous thrombi dislodge they become embolic to the lungs and may cause either minor or massive pulmonary infarction. When arterial, especially aortic, thrombi dislodge they may cause infarction of any organ; however, most clinical problems are caused by infarction of the brain, spinal cord, kidney, or gut. Intracardiac catheters may cause valvular insufficiency, vegetative valvular endocarditis, or artrial thrombosis.

Often catheters and resultant thrombi become septic as the catheter provides a direct link between the external environment and the bloodstream of the animal. Bacteria may enter the bloodstream either through the lumen of the catheter or through the tract around the catheter. Maki *et al.* (1976) found that in humans, local inflammation of the skin site was strongly correlated with the incidence of catheter-related septicemia. In animals, we have concluded that the incidence of septicemia due to catheter tract infection is very much dependent on the distance between the skin entry site and the vessel entry site. If the catheter has a relatively long subcutaneous course before entering the vein then there is less likelihood that infection at the skin entry site will result in septicemia. Peters *et al.* (1973) have shown that an intravascular fibrin sleeve develops around

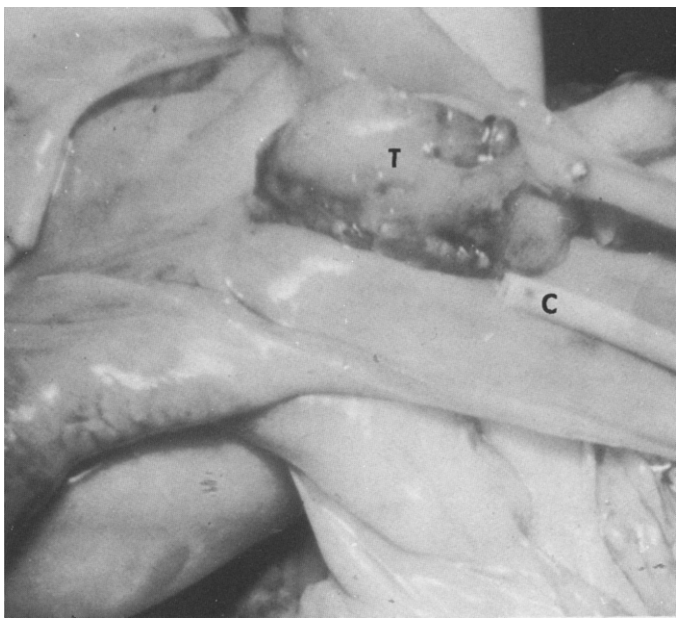

Fig. 8. Iatrogenic vascular thrombosis. Mural thrombus (T) at the tip of a chronic indwelling vascular catheter (C) in the posterior vena cava.

vascular catheters within 24–48 hr of implantation. This fibrin sleeve can become seeded with bacteria and serve as a locus from which septicemia can result. Several investigators including Maki (1976) have found that the incidence of bacterial colonization of the catheter tip is proportional to the time that the catheter is left in place.

The goal of the laboratory animal veterinarian should be to prevent, not treat, catheter-related sepsis. The education of investigators about the measures that are important in preventing catheter-related septicemia is critical. Sterile catheters must be implanted using sterile technique and extrinsic contamination of the infusion system and catheter tract must be prevented. Maki *et al.* (1973) and others have found that sources of bacterial contamination include (1) the animal's cutaneous flora, (2) the investigator's cutaneous flora, (3) contaminated infusion fluids, (4) contaminated disinfectants, and (5) autoinfection due to bacteremia seeded from a remote infected locus.

We have found that implantation of sterile catheters utilizing sterile surgical technique is the first important step in preventing septicemia. A healthy infection-free animal is prepared for surgery by shaving, scrubbing, and applying an iodine-containing disinfectant to both surgical site and the site where the catheter enters the skin. A gas sterilized catheter is placed using asceptic surgical technique by personnel that have received training in these techniques. The catheter should be coated with a tridodecylmethyl ammonium chloride (TDMAC)–heparin complex as described by Brenner *et al.* (1974) to reduce thrombogenesis. The TDMAC–heparin complex coating material is available from Polysciences, Inc., Warrington, Pennsylvania. Following placement, radiography should be utilized to ensure that the location of the catheter tip is correct. Prophylactic antibiotics should be administered one day before and for 3 days after surgery.

Following catheterization, the catheter entry site in the skin should be cleansed, disinfected, and treated with topical antibiotics and bandaged every 2–3 days for the duration of the implantation. Entry site care is especially important if the vessel cannulation site is near the skin entry site.

To prevent bacterial contamination of the catheter lumen the infusion system should be as simple as possible. Fewer connections allow for fewer possible entry sites for bacteria. The system should be opened as infrequently as possible, and all openings should be performed aseptically. During periods when vascular catheters are not being used, they should be flushed daily with heparinized saline solution (10 units heparin/ml), and this solution should remain in the catheter.

Since adypsia, anorexia, and depression are often the first signs of septicemia, the food and water consumption and behavior of animals with vascular catheters should be monitored daily. If adypsia, anorexia, or depression are present, physical examination and blood culture (from a remote site) should be performed promptly. Antibiotic therapy should be instituted immediately and continued for 10 days. Our choice of antibiotic is generally based on previous antibiotic sensitivity tests on organisms cultured from the blood of septicemic animals from that particular laboratory. We find that each laboratory tends to have characteristic organisms that repeatedly cause septicemia.

We have found that removal of the catheter is usually necessary in order to prevent recurrent septicemia once antibiotic therapy is stopped. Our clinical experience with dogs agrees with that of DaRif and Rush (1983) with monkeys. In their study, antibiotic therapy with the catheter left in place resulted in marked clinical improvement; however, blood culture 5 days after cessation of antibiotic therapy demonstrated that the animals were again bacteremic. These findings are in agreement with those of numerous investigators including Maki (1976) who have found that catheter removal is an essential step in successful medical management of septicemia in human hospital patients with vascular catheters.

E. Neoplastic

Feline Leukemia Virus

Feline leukemia virus (FeLV), a retrovirus, widely infects cats. Chronic FeLV infection causes a variety of lymphoproliferative, myeloproliferative and bone disorders, glomerulonephritis, anemia, and neoplasia. Immunosuppression results in increased susceptibility to many other pathogens. These lesions and other as yet unidentified effects may have a significant impact on biological functions in cats used in biomedical research.

Ladiges *et al.* (1981) have screened newly received random source cats on receipt at a large research institution and have found that 4.9% were viremic. Nine of 20 viremic cats selected for pathologic evaluation had lymphoma or myeloproliferative disease. This provides some indication of the role that FeLV can play in producing lesions even in cats used in short-term studies.

For some long-term studies and in research breeding colonies it may be necessary to identify FeLV-infected cats and eliminate them from the quarantine rooms or colony. According to Hardy *et al.* (1976) this can be accomplished by identifying viremic cats with the immunofluorescent antibody (IFA) test and removing them from the facility or colony. The IFA test detects FeLV gs antigens in peripheral blood leukocytes and platelets. A positive IFA test means that the cat is viremic. Unfortunately, exposed cats can incubate FeLV for 3 months before viremia is established.

The following procedure as described by Hardy *et al.* (1976) may be used to free a group or colony from FeLV. All cats housed as a group are tested at 3 month intervals, and all positive cats are eliminated from the group. When all cats in the

group have been IFA negative on two consecutive IFA tests after the last infected cat has been removed, the group is considered FeLV free. All new cats introduced into an FeLV free group must first undergo quarantine and two negative IFA tests at 3-month intervals.

Diagnosis and treatment of FeLV-related disorders is beyond the scope of this chapter. Pedersen and Mardewell (1980) have described diagnosis and treatment in some detail, and a text edited by Hardy *et al.* (1980) summarizes recent clinical and experimental information on FeLV.

VIII. SELECTED NORMATIVE DATA

Parameter	Cat		Dog	
	Value	Reference[a]	Value	Reference[a]
Adult weight				
Male	3.5 kg	1	10.5 kg	1
Female	2.5 kg	1	9.9 kg	1
Life span				
Usual	12 years	1	12 years	1
Maximum	28 years	2	20 years	2
Chromosome number	38	1	78	1
Food consumption	24 gm/kg[b]	3	18 gm/kg[c]	4
Body temperature	101.5°F(100.5–102.5°F)	1	102°F(100.2–103.8°F)	1
	38.6°C(38.1–39.2°C)	1	38.9°C(37.9–39.9°C)	1
Puberty				
Male	36 weeks	1	6–12 months	1
Female	5–12 months	1	6–12 months	1
Breeding life	6–8 years	1	6 years	1
Breeding season	January–October	1	All year	1
Ejaculate volume	0.03–0.3 ml	1	2–16 ml	1
Sperm/ejaculation	15–130 × 10^6	1	5 × 10^8	1
Type of estrous cycle	Polyestrus	1	Monestrus	1
Length of estrous cycle	2–3 weeks[d]	1	16–56 weeks	1
Duration of estrus	3–6 days	1	9–10 days	1
Ovulation mechanism	Induced	1	Spontaneous	1
Ovulation time	25–50 hr postcoitus	1	2–3 days postestrus	1
Ovulation rate	4 ova	1	6–8 ova	1
Pseudopregnancy	Uncommon (6 weeks)	1	Common (60 days)	1
Gestation	58–65 days	1	59–68 days	1
Litter size	3–5	1	1–12	1
Birth weight	110–120 gm	5	250 gm	1
Weaning age	3–8 weeks	1	3–8 weeks	1
Heart rate	110–140 beats/min	1	70–160 beats/min[e]	6
Normal heart axis	—		+40° to +100°	6
Blood pressure[f]				
Systolic	120 mm Hg	2	112 (95–136) mm Hg	2
Diastolic	75 mm Hg	2	56 (43–66) mm Hg	2
Cardiac output	—	—	1820–2660 ml/min[g]	7
Stroke volume	—	—	11.3–15.8 ml/min	7
Blood volume				
Plasma	40.7 (34.6–52.0) ml/kg	2	55.2 (43.7–73.0)ml/kg	2
Whole blood	55.5 (47.3–65.7) ml/kg	2	94.1 (76.5–107.3)mg/kg	2
Respiration frequency	26 breaths/min	1	22 breaths/min	2
Tidal volume	34 (20–42) ml	8	251–432 ml[h]	8
Minute volume	0.96 liters/min	8	4.1–6.1 liters/min[h]	8
Whole blood				
pH	7.35 (7.24–7.40)	2	7.36 (7.32–7.42)	2
CO_2	20.4 (17–24) m*M*/liter	2	21.4 (17–24) m*M*/liter	2

(*continued*)

VIII. SELECTED NORMATIVE DATA (*Continued*)

Parameter	Cat		Dog	
	Value	Reference[a]	Value	Reference[a]
Plasma				
CO_2 pressure	36 mm Hg	2	38 mm Hg	2
Protein	6.0–7.5 gm/dl[r]	9	6.0–7.5 gm/dl[r]	9
Fibrinogen	150–300 gm/dl	9	150–300 gm/dl	9
Total leukocyte count	5.5–19.5 × 10^3/ml	9	6.0–17.0 × 10^3/ml	9
Differential leukocyte count				
Neutrophils	(35–75%) 2.5–12.5[j]	9	(60–70%) 3.0–11.4[j]	9
Bands	(0–3%) 0–0.3[j]	9	(0–3%) 0–0.3[j]	9
Lymphocytes	(20–55%) 1.5–7.0[j]	9	(12–30%) 1.0–4.8[j]	9
Monocytes	(1–4%) 0–0.85[j]	9	(3–10%) 0.15–1.35[j]	9
Eosinophils	(2–12%) 0–0.75[j]	9	(2–10%) 0.1–0.75[j]	9
Basophils	rare	9	rare	9
Erythrocyte count	5.0–10.0 × 10^6/μl	9	5.5–8.5 × 10^6/μl	9
Hemoglobin	8–15 gm/dl	9	12–18 gm/dl	9
Reticulocyte count	0–1.0%	9	0–1.5%	9
Hematocrit				
PCV (Adult)	30–45%	9	37–55%	9
PCV (Young)	24–34%	9	25–34%	9
MCV	39–55 fl	9	60–77 fl	9
MCHO	30–36 gm/dl	9	19.5–24.5 gm/dl	9
Platelet count	3–7 × 10^5/μl	9	2–9 × 10^5/μl	9
Maximum volume of single bleeding	2% of body weight	9	2% of body weight	9
Myeloid/erythroid ratio	0.6–3.9/1.0	9	0.75–2.4/1.0	9
Urine				
pH	5.5–7.5	10	5.5–7.5	10
Normal specific gravity	1.030 (1.018–1.050)	10	1.025 (1.018–1.050)	10
Maximum specific gravity	1.060 +	10	1.080 +	10
Volume	22–30 ml/kg body weight/day	10	25–41 ml/kg body weight/day	10

[a]Key to references: 1, Mather and Rushmer (1979); 2, Altman and Dittmer (1972, 1973, 1974); 3, NAS–NRC (1978); 4, NAS–NRC (1974); 5, Scott (1970); 6, Bolton (1975); 7, Ettinger and Suter (1970); 8, Lumb and Jones (1973); 9, Duncan and Prasse (1977); 10, Osborne *et al.* (1972).

[b]Dry diet, active adult cats.

[c]Dry diet, consumed by a 22.7 kg dog.

[d]If not mated.

[e]Can be as high as 180 beats/min in toy breeds and 220 beats/min in pups.

[f]Aortic.

[g]In 10–31 kg dogs.

[h]Range includes variable sized dogs.

[i]Will be slightly lower in young animals.

[j]Total (× 10^3/ml).

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