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Chapter 4

Common Infectious Diseases of Multiple-Cat Environments

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Domestic cats seem to suffer inordinately from a variety of infectious diseases. Cats are not immunologic cripples, however. They belong to one of the most successful families of carnivores ever evolved on earth. Cats and their wild relatives are found on many continents and in varied climates. In their own environment, and under usual conditions of population density and pressure, cats handle infectious diseases very well.

Cats are not intrinsically sensitive to infectious disease, but seem so as a reflection of their modern environments. These environments are often totally different from the environments in which cats evolved. The concept that environment is one of the most important factors in determining the incidence and severity of disease is one of the pillars of our knowledge of infectious diseases. Infectious agents usually do not kill or incapacitate a significant number of their hosts. To do so would deprive them of the environment essential to their own survival. Therefore, when disease occurs, it must be the exception rather than the rule.

The term "infection" is not synonymous with the term "disease." Infection occurs when the microbe invades the body. Disease is caused by tissue damage from the invading microbe or the host's own attempts to contain or destroy the infectious agent. Many infectious agents cause mild or inapparent disease. For instance, most cats infected with coronaviruses, caliciviruses, parvoviruses, herpesviruses, feline leukemia viruses or feline immunodeficiency viruses do not demonstrate disease following infection. However, if factors are favorable, these same agents can cause severe and often fatal disease. Therefore, control and prevention of infectious "disease" depends on understanding factors that enhance the disease-causing potential of a microbe.

Factors Influencing Disease

We are frequently confronted with infectious diseases manifested in many different forms. Unfortunately, we are usually only aware of the most severe form. This form is often described in textbooks as being the "classic" or "typical" presentation. In truth, the proportion of animals developing this form of disease is usually small. When a cat is exposed to a disease agent under normal conditions, mild self-limiting or clinically inapparent disease usually occurs. When host and environmental factors are unfavorable, primary illness is more apt to be severe, persistent infections are more common, aberrant or chronic forms of the disease are more prevalent, and the overall death rate is higher.

Consider the following situation in which a young kitten is born to a household pet. As in most households, the queen is the sole cat and only about one-third of the households in the neighborhood have cats and very few of them produce kittens. There are very few kittens in the neighborhood, therefore, at any time. When the kittens are 6-9 weeks of age, they are weaned and adopted by a neighbor, friend or relative. The kittens are given only a panleukopenia vacci-

nation and dewormed. They live in their new homes for years without any apparent illness. Yet, when blood samples are taken years later, they contain antibodies to a number of different pathogenic microbes.

Contrast this to kittens born in a large cattery, where 25 adult breeding cats and numerous kittens of varying ages are raised together in several rooms. These kittens typically develop a series of clinical illnesses, starting as early as 2 weeks of age. Some of the kittens die before they reach 16 weeks of age, and a proportion of the survivors manifest signs of chronic disease. The death rate also is much higher than for kittens raised in a single-cat household. What so drastically altered the course of disease in the cattery-reared kittens? This question can only be answered through an understanding of factors that influence the course of infection (Table 1).

Heritable or developmental anomalies of the immune system can greatly influence the course of infection. Certain types of anomalies cause the host to be deficient in cell-mediated immunity, deficient in the ability to make all or certain antibodies, deficient in specific complement components, or deficient in the normal function of phagocytic cells. Some of these deficiencies may lead to a greater incidence and severity of infections, but may still allow the animal to live an otherwise normal life. Some anomalies may be so severe that the animal dies of overwhelming infections while still a kitten. Fortunately, heritable anomalies of the immune system are relatively rare in cats (see chapter on genetic disorders).

Table 1. Factors that influence the outcome of infection.

Host Factors
• Developmental and heritable anomalies of the immune system
• Undefined heritable resistance factors
• Maternal immunity (passive systemic and passive local)
• Age at time of exposure
• Multiple illnesses
• Nutritional state
Environmental Factors
• Population density
• Sanitation
• Ventilation
• Interchange of animals from one population to another
Agent Factors
• Virulence of the pathogenic microbe
• Strain differences
• Dose of the pathogenic microbe
• Route of infection

Undefined heritable resistance factors are far more important causes of immunodeficiency in cats than defined genetic abnormalities. Undefined resistance factors, as the name implies, are difficult to pinpoint to a specific defect. In this situation, a group of cats is born with an immune system that seems intact, and the animals are normal by every conceivable test of immune function. In spite of this apparent normalcy, one member of the group may react far differently from another when exposed to a certain infectious agent. This increased susceptibility to certain diseases may extend beyond individuals to bloodlines within breeds or to entire breeds themselves. For instance, breeds of Siamese origin seem to suffer inordinately from chronic nasal infections. Abyssinian cats appear to have more problems with gum disease than other breeds. Persians suffer inordinately from clinically apparent dermatophyte infections, and comprise an inordinate proportion of purebred kittens that succumb to feline infectious peritonitis.

As important as these undefined genetic factors are to disease, most breeders totally ignore disease resistance when selecting breeding stocks and developing bloodlines. They are often more interested in esoteric traits such as coat color, body conformation and size. Unfortunately, the fixing of many of these traits involves inbreeding. Inbreeding, if done properly, has a limited deleterious effect on the host, as witnessed in the many inbred strains of mice. More often, however, inbreeding is not done with care, and lethal or sublethal genes accumulate in increasingly greater numbers. The net effect of inbreeding is often a decline in vigor. This decline in vigor is hardly ever due to specific defects in immunity, but rather to accumulation of more subtle and multiple genetic defects that are impossible to define.

Maternal immunity is an important factor in infectious diseases occurring in kittens between 4 and 16 weeks of age. Maternal immunity provides protection for the

kitten from infectious diseases that may occur during the critical period when the kitten's own immune system is developing. Maternal immunity is of 2 types: passive systemic immunity and passive local immunity.[2]

Passive systemic immunity is derived from antibodies given to the kitten by its mother in the first milk (colostrum) during the first day of life.[2] Antibodies are concentrated in the colostrum in the mammary glands of the queen and are given to the kitten during nursing. The intestinal tract of the kitten is permeable to antibody globulins for the first day of life; after this time they are no longer absorbed but rather are digested in the same manner as other dietary proteins. A kitten ingesting colostrum attains levels of antibodies in its blood equal to those of the mother. Because these absorbed antibodies only have a finite lifespan in the body of the kitten, they eventually disappear. One-half of the total remaining amount is metabolized during each subsequent 7-day period.

Maternally derived antibody levels in blood are usually very low by 6-8 weeks of age, and negligible by 12-16 weeks. Fortunately, by about 4 weeks of age, the kitten's immune system begins to function and antibodies produced by the kitten's immune system appear in the blood at progressively higher levels. The period between 4 and 16 weeks of age is a time when relatively more and more of the antibodies are of kitten origin and less and less of maternal origin. Passive systemic immunity is present, therefore, when the kitten needs it the most and is gradually replaced as it is no longer needed. Passive systemic immunity is active in killing microbes that enter the bloodstream via local sites of infection in the skin or mucous membranes of the respiratory, gastrointestinal or urogenital tracts.

Situations that prevent adequate transfer of antibodies from the mother to the young cause the newborn animal to be susceptible to infection. Because the bulk of passive systemic immunity is derived from colostrum during the first day of life, adequate nursing of kittens at birth is essential. Failure of kittens to receive sufficient colostrum leads to severe and often fatal systemic infections in the neonatal period (first 2 weeks of life).

Passive local immunity is provided continually by the queen for as long as the kitten nurses. After the colostral phase of lactation ends (by 72 hours after birth), the kitten receives what is known as "milk."[2] Milk, like colostrum, also contains antibodies, but at much lower levels. These antibodies are of 2 types, IgG and IgA.[2] IgG antibodies are degraded by stomach acids, while IgA resists digestion and appears unaltered in the stool. Antibodies in the milk protect against infections that begin on the surfaces of the oral and intestinal mucous membranes. Pathogenic organisms ingested with the food are immediately destroyed by the milk antibodies; IgG works preferentially in the mouth, oropharynx and esophagus, and IgA works preferentially in the stomach and intestines.

Because the vast majority of common kittenhood infections begin in the oropharynx, passive local immunity is very important in preventing disease. Passive local immunity works in concert, therefore, with passive systemic immunity; one prevents infections locally, while the other works within the bloodstream. Passive local immunity, like passive systemic immunity, is slowly replaced by active local immunity. As the kittens reach 2-6 weeks of age, increasingly more antibody is produced by the tonsils and gut-associated lymphoid tissues and is transported into the saliva and mucus by cells lining the gastrointestinal, respiratory and urogenital tracts.[2]

For passive local immunity to be protective, the milk must contain the required complement of specific antibodies, the antibodies must be present in the milk in adequate amounts, and the milk must be ingested in sufficient quantities by the kitten. As an example, if the queen's milk does not have antibodies to rotaviruses, then the kittens will not be protected against rotavirus infection. Likewise, even if antibody is present in the milk, it is of no protective benefit if it is not ingested in sufficient quantity. Passive local immunity is lost when the kitten is weaned. In catteries, weaning is usually sudden. In nature, however, weaning is a slow affair. After 4-6 weeks of age, the kittens receive progressively less milk from their mothers (and less immunity) and the milk that is ingested contains progressively fewer antibodies. In this way, there is a slow

and progressive exchange of passive local immunity for active local immunity.

Age resistance is also very important. The immune system of the newborn kitten is very immature. By 2-4 weeks of age, the kitten's immune system begins a stage of rapid maturation. The immune system is well developed by 14-16 weeks of age. Continued development, albeit at a slower pace than in kittenhood, continues well into late adolescence.

If a kitten is infected at a young age, it does not respond as well to the infection and the resulting disease is much more severe. A number of factors allow microbes to overcome maternal immunity in young kittens. One of these factors is failure of the queen to pass on specific maternal immunity to the kitten. Even if the kitten is provided with maternal immunity to a specific pathogenic microbe, maternal immunity can be overcome if the exposure is severe enough. The maternal immunity may be sufficient to prevent infection with small numbers of the microbe, but not sufficient to prevent infection with exposure to large numbers of the microbe.

One of the best examples of age resistance has been demonstrated for feline leukemia virus (FeLV) infection (see section on FeLV infection). Almost all kittens infected in the neonatal period of life (first 2 weeks) become persistently infected and die within a few months to a year or so. In contrast, only about 50% of 12- to 16-week-old kittens become persistently infected following exposure; the rest recover and are immune for the rest of their lives. Even among those that become persistently infected, the disease course is longer. Adult cats are even more resistant to infection, with 70-95% recovering following initial exposure.

Multiple illnesses present in a cat at one time often make the cat more susceptible to coincidental infection with other disease agents. Disease can sap the body of necessary nutrients, or directly suppress the immune system and increase disease susceptibility. For instance, feline herpesvirus infection can damage the mucous membranes of the nasal passages, upper and lower respiratory tract, and conjunctiva of the eyes, and allow secondary invasion by resident bacteria. This is evidenced by a change in the character of the inflammatory secretions from clear (serous) to cloudy (purulent). Feline leukemia virus infection can increase the severity of many other diseases, including feline infectious peritonitis, hemobartonellosis, toxoplasmosis, cryptococcosis, feline immunodeficiency virus infection, feline herpesvirus infection, and a number of bacterial infections (see section on FeLV). Feline panleukopenia virus infection is immunosuppressive (see section on panleukopenia). Feline calicivirus infection is rarely fatal by itself, while feline panleukopenia has moderate mortality. If cats are infected with both calicivirus and panleukopenia virus at the same time, however, mortality is very high.[1] Flea infestations frequently increase dramatically in sick cats (see section on fleas). The reason for this is not completely understood, but may be due to decreased grooming.

Nutritional status is very important in determining a cat's resistance to infection.[4] Products of the immune response are proteins derived from body stores or directly from food that is consumed. Nutritional problems are usually manifested in kittens, pregnant and lactating queens, feral cats living in overpopulated or low-nutrient environments, and cats living in large multiple-cat households. Kittens are affected particularly severely. Caloric requirements per unit of weight in young animals are several times greater than requirements of adults. Specific nutrients, such as protein, vitamins and minerals, are also much different for young animals. Relative or absolute malnutrition is common in enterprises where large numbers of young animals are reared. Kittens are at the lowest end of the social order and must compete more for food, and are often further drained of energy and nutrients by kittenhood diseases.

Population density is one of the most important factors in determining the severity of disease within a population and in individuals within the group. The greatest single source (reservoir) for pathogens of cats is other cats. Many diseases of cats are carried and shed by a proportion of asymptomatic or partially symptomatic cats. A high population density favors spread of such infections because it increases the number of potential carriers in the environment, brings carrier and susceptible cats into closer proximity to each other, increases the

degree of environmental contamination of food, water, air and soil, and increases the dose or amount of infectious agent passed from contagious to susceptible animals. Equally important, overcrowding of cats increases socially induced stresses and increases competition for food. The former leads to increased adrenal gland secretions, immunosuppression and decreased resistance, while the latter increases the likelihood for relative or absolute malnutrition.

The effects of increased population density can be counteracted in part by enhancing ventilation (to dilute air-borne contamination) and excrement removal, and designing barriers to reduce social stresses. Unfortunately, these steps become more time-consuming and expensive as the population density increases. Most catteries and other large multiple-cat households do not make the necessary adjustments to the environments, and disease problems increase progressively as the population density rises.

Increased population density has an interesting interrelationship with other factors. For instance, in a normal urban situation, only every third or fourth household owns a cat and very few of these cats produce kittens. Kittens born in such households usually have no contact with cats other than the queen until they are 3-4 months of age. Then they begin to socialize with cats out of their immediate environment. Exposure to other cats is usually fleeting and the chance for infection low. In contrast, kittens born in a cattery or other large multiple-cat households are exposed to other animals immediately and become infected as soon as their maternal immunity is overcome (usually 4-12 weeks of age). In addition to exposure at a relatively young age, cattery kittens are apt to be exposed to much greater amounts of pathogenic microbes.

Interchange of animals between populations is important in disseminating disease. Each population has its own viral, bacterial, parasitic and protozoal flora. Because of the severity of disease in such environments, older animals are often carriers of the very disease agents that they suffered so much from as kittens. Cats within a given cattery or area are most resistant to the pathogens to which they are continuously exposed. However, they may have very little exposure to strains of organisms found in other isolated populations of cats. Animals transported from one population to another are likely to spread new strains and types of infectious agents into their new homes. In turn, they are also exposed to myriad unfamiliar microorganisms. Once a new type of infection is introduced into such a population, unfavorable environmental and host factors ensure rapid spread.

The spread of infection between relatively isolated populations involves both the group of animals into which the new animal is placed and the new animal itself. The newly introduced animal is often under heavy stress as a result of being uprooted from its familiar surroundings, transportation to the new surroundings, and disruption of social orders. Upon arrival in the new cattery, the cat is immediately bombarded with a number of pathogenic strains of microorganisms that it has never previously contacted. This exposure, coupled with stress, often leads to a series of infections occurring at one time or in rapid sequence. If the diseases are severe, the animal might require extensive treatment or even die. With time, however, the newcomer also becomes resistant to the resident organisms.

Introduction of new types of microbes into a group of susceptible cats by a newcomer has more serious consequences than the opposite situation described above. In the previous situation, only the cat that was introduced is affected. In this situation, a larger number of resident animals is involved. Pathogenic microbes spread very rapidly in a closed group of animals, especially when they have no resistance to them. An explosive outbreak of disease often follows. The outbreak may involve most of the population, and cats of all ages. As the new microbe establishes itself in the environment, disease becomes less frequent and occurs mainly in kittens. This is because the older cats become immune. This protective immunity is passed on to the kittens by their mothers, but only lasts until 6-12 weeks of age. At this time, the kittens are the only susceptible animals in the premises.

Interchange of kittens is most apt to cause problems, followed by interchange of

adolescents, then adults <4 years of age, and least likely, aged cats. Kittens are most susceptible to disease, and are the worst carriers and shedders of pathogenic microbes. With time, their immunity becomes progressively stronger, and fewer remain carriers; those that remain carriers also shed fewer organisms. Therefore, if new cats are to be introduced into a cattery, the emphasis should be on adult cats, followed by adolescents, and then kittens that are at least 16 weeks of age. Kittens younger than 16 weeks of age are most likely to cause problems. When purchased, they should be isolated and slowly introduced into the cattery.

Environmental temperature and humidity are significant factors in infection. Certain species of animals have optimum temperature and humidity requirements for good health. Cats do best when the humidity is low and the temperatures relatively high. Cold, wet climates are the worst. The exact temperature and humidity are often less important than fluctuations of temperature and humidity. If temperature and humidity fluctuate wildly from week to week, disease may be more of a problem even though the minimums and maximums are within the suggested levels.

Temperature extremes may influence disease by inducing stress. This has been one explanation for outbreaks of the common cold in people following extremely cold bouts of weather. More often, however, extreme weather changes cause animals to congregate together. For instance, animals and people are often brought together in cramped, poorly ventilated quarters during inclement weather. Certain ranges of temperature and humidity may also favor persistence of microbes in the environment. Heat and dryness have a destructive effect, while cold and dampness have a protective effect on microbes. Certain temperatures and humidities may even favor certain stages of the microbe. Warm, damp weather favors survival of many nematode ova and larvae. The life cycle of the flea from egg, larva, pupa to adult is very temperature and humidity dependent.

Stress is a nebulous term and difficult to measure. It can result from infectious diseases, noninfectious diseases, sudden and severe changes in the weather, nutritional inadequacies, and emotional instability. Stress is mediated through the endocrine (in particular the adrenal glands) and autonomic nervous systems. The endocrine and autonomic nervous systems interact closely with each other, so that effects on one are manifested on the other. Ultimately, stress has a negative effect on the sense of well-being of the cat and its ability to fight disease.

Stress is usually not outwardly apparent. Stress has its effect in subtle ways and over long periods. A cattery may appear well kept and the cats outwardly happy. But beneath this veneer there may be an increased incidence of behavioral problems (see chapter on behavior) and infectious diseases. Just as it is frequently impossible for one person to evaluate the level of stress that another person is undergoing, it is also often impossible for a cattery owner to appreciate the stress levels among individual cats or in the cattery as a whole.

Virulence of the organism is the propensity for a given dose of microbes to cause disease. Organisms that do not cause disease, regardless of the infecting dose, are considered avirulent. An organism that causes minimal disease, even when given in large numbers, is considered of low virulence. Pathogenic microorganisms that cause severe disease, even when given in small numbers, are considered highly virulent.

If the host is heavily stressed or immunocompromised by other diseases, an organism that is usually of low virulence may cause severe disease. Some species, breeds or bloodlines of animals are more susceptible to a given dose of a particular strain of pathogen than others. An organism of low virulence to one cat may be highly virulent to another, therefore. Some microorganisms are more virulent for reasons intrinsic to the organism itself. Disease-causing agents contain genetic material that determines their structure. The genetic structure of the organism, may greatly influence the ability of the organism to cause disease. For instance, some strains of *E coli* bacteria have surface proteins that allow for attachment to intestinal cells and also produce certain types of enterotoxins. They are the strains that are invariably associated with diarrhea. Other strains lack these proteins and

are not pathogenic. Some strains of feline leukemia virus are of low disease-causing potential, while others almost selectively cause anemia or lymph node cancers after a short period of infection. Caliciviruses exist in dozens, and perhaps hundreds, of serotypes or strains. The various serotypes can cause different severities of disease and even different disease signs. Feline infectious peritonitis virus also exists in numerous strains; some are very virulent, while others are minimally pathogenic.

Differences of strains of pathogens play a role in infection. Strains are genetically distinguishable members of the same species of organism. Strictly speaking, one organism differs in strain from another if the host's immune system perceives them in a different manner. For example, a particular *E coli* infection of the intestine elicits antibodies against the infecting organisms. If these antibodies fail to prevent infection with another isolate of *E coli,* then the second strain of *E coli* is a different strain. Strains may also be defined by the type of disease they cause; an *E coli* that causes enteritis is sometimes referred to as an "enteropathic strain," while an *E coli* that does not cause enteritis is termed "non-enteropathic."

The occurrence of different strains of microorganisms poses a threat to the host. Not only must the host generate immunity to each type of organism, but it must respond to several different strains of the organism. Many cattery owners and veterinarians believe that if a cat is given a vaccination for calicivirus that it will be immune to all calicivirus infections. However, caliciviruses exist in many strains and a cat immunized with a calicivirus vaccine is only immune to those strains in the vaccine. If the vaccine protects against almost all strains, or against the most important or common strains will it be effective. If the vaccine protects only against a few strains or against strains that are not commonly seen in the vaccinated population, it will not be effective. If only one strain exists for a particular pathogen, immunity to one isolate protects against all other isolates.

In regard to dose, generally, the more of an agent that is taken into the body at the time of initial exposure, the more severe the resulting disease. In the case of some pathogens, there is even a threshold dose for disease. For instance, many pathogenic intestinal bacteria do not cause infection if they are ingested at low levels. However, as the level of ingestion rises, a point is reached where disease occurs. The most important way to decrease disease is to limit the dose of the organism. Optimally, the dose should be reduced to zero, or to a level below the infection threshold.

Route of infection is also important. Infectious agents may enter the body by several routes, such as by mouth (oral), inhalation into the upper and lower respiratory tracts, up the urogenital tract, or inoculation through the skin. Most pathogenic microbes enter the body by the route that is most conducive to causing disease. This is called the "natural route of infection." Even if the organism were to enter the body by another route, the infection is often the same. In some cases, however, the route may greatly influence the disease course. Feline herpesvirus does not produce disease when inoculated into the muscles or subcutaneous tissues. However, if it is placed on the mucous membranes of the nose or eyes, it causes disease. This is because herpesvirus does not replicate very well at the slightly higher temperatures in the core of the body. The mucous membranes, being slightly cooler because of exposure to the outside air, favor virus replication. This phenomenon was used to produce some of the early feline herpesvirus vaccines. If the vaccine was given by injection into the tissues, it did not need to be altered so much in virulence. If the same vaccine were put on membranes of the nose or eyes, it would cause disease, however. It is not surprising, therefore, that many of the early live feline herpesvirus vaccines actually caused the very disease they were supposed to protect against; if vaccine virus contaminated the fur at the site of injection, it was rapidly groomed onto the tongue, paws and eyes, where it would cause disease.

Proper and Improper Immunization

Infectious diseases are more common and severe in young animals, so this is the obvious age group requiring immunization. Unfortunately, vaccines are only available for a handful of infectious diseases. However, these diseases are among the most im-

portant. It is important to understand why vaccines are given in a certain way so that their effect can be maximized. The most important questions are the timing and number of vaccinations.

Most kittens begin their vaccinations at 6 weeks of age. This age was not picked for arbitrary reasons. Maternal immunity (in particular, passive systemic immunity) interferes with vaccination for the first 4-6 weeks of life. This inhibitory effect disappears between 6 and 16 weeks of age as maternally derived antibodies disappear from the blood. The immune system has no need to respond to a vaccine before this time, because maternal antibodies are already present. Even if maternal immunity were not present, kittens <4 weeks of age have poorly developed immune systems and are not capable of responding well to vaccines. For both reasons, vaccinations should not be started earlier than 6 weeks of age.

Maternal immunity is also why vaccines are given as a series of injections, starting at 6 and ending at 12-16 weeks of age. The last immunization is given at a time when virtually all maternal immunity has disappeared and the kitten is fully immunizable. For some kittens this is as early as 6 weeks of age, while for others it is up to 12-16 weeks of age (depending on the level of antibodies obtained from the queen). If it were easy and inexpensive to determine the time when maternal antibodies to a particular vaccine disappear, then it would be possible to immunize the kitten with one dose of vaccine. So what, you might ask! Just give the immunization at 12-16 weeks of age when it is certain that virtually any kitten will respond. If only one dose is given at 12-16 weeks of age, however, some kittens might go unprotected for many weeks (those that lost their maternal immunity early). As a logical solution, why not give a dose of vaccine at intervals throughout this 6- to 16-week age period? If a kitten loses its maternal immunity at 6 weeks of age, the first immunization will provide protection. If it loses its maternal immunity at 9 weeks of age, the first dose will not be effective, but the second will provide protection, etc. By giving a series of immunizations at 3-week intervals, each kitten is unprotected for a minimum of time.

What determines the interval between kittenhood vaccinations? Three weeks is usually the minimum period between immunizations. The reason is because of what is called the "booster effect." Once maternal immunity is gone, the next dose of vaccine evokes an immune response and antibody production. This initial response may be low, however. Following a second immunization several weeks later, the immune response may be greatly amplified or "boosted." This booster effect is not as apparent if the vaccinations are given too closely together. An interval of 2 weeks does not give the immune system enough time to become adequately prepared for a second stimulus. Three-week or longer intervals provide more time for such stimulation. If 4-, 5- or 6-week intervals give a better booster effect than 3 weeks, why not use these intervals instead? The 3-week interval between vaccinations is a reasonable compromise. Two weeks is too short, and if you wait much longer than 3 weeks, the kitten may go unprotected for too long.

Terminology

Before studying infectious diseases, it is important to understand a few useful terms. An *epizootic* refers to a sudden or explosive outbreak of disease within a group of susceptible animals. The equivalent used term for human disease is *epidemic*. The spread of the disease is rapid, the *morbidity* (disease incidence) and *mortality* (death rate) may be high, and animals of all ages are often affected. Epizootics usually follow introduction of a disease agent into a population that has had no previous exposure to the microbe. As the population adjusts to the new infection by genetic selection (survival of the fittest) and immunity is acquired, a high degree of resistance develops in the survivors. This resistance is passed genetically to the offspring and from queen to kitten in the form of passive systemic and local immunity.

Development of genetic resistance and acquired immunity to a particular pathogen does not necessarily translate to disappearance of the organism from the environment. Many agents persist very well in resistant populations without causing serious illness. In fact, they have reached the ideal host-parasite relationship. The parasite and

host live together, sometimes for months, years or even lifetimes. Animals that harbor pathogenic microorganisms are called *carriers*. Some carriers shed the organisms continuously from their bodies; such animals are called *active carriers*. Calicivirus and feline leukemia virus carriers actively shed these organisms and are therefore active carriers. In other instances, the organism remains in a dormant or inactive form in the host and is only shed under certain circumstances. Such animals are called *latent carriers*. Feline herpesvirus carriers are latent carriers most of their lives, but under conditions of stress or other types of immunosuppression, they may temporarily become active carriers and shed the organism.

Disease that persists within resistant populations of cats is usually of an *enzootic* nature. The human equivalent of this term is *endemic*. Enzootic disease occurs mainly in young animals that have not yet acquired active immunity. Enzootic disease does not usually occur in older cats because older animals are usually infected when young and are immune. Enzootic disease is associated with much less morbidity and mortality than epizootic disease. It is more sporadic in its occurrence. Many cattery owners with enzootic herpesvirus, chlamydial, mycoplasmal and coronavirus infections underestimate the magnitude of their disease problems because the disease incidence and severity are not sudden and dramatic. Over a long period, however, more death and suffering can result from enzootic disease than from epizootic disease.

Sporadic disease refers to clinical infections that occur in a small proportion of animals at indefinite and often long intervals. Enzootic feline infectious peritonitis is often a sporadic type of disease. *Incidental, accidental* or *spurious diseases* usually involve individual animals and occur when the animal accidentally contacts a reservoir of the agent. A cat that contracts salmonellosis while feeding on an infected bird is spuriously or accidentally infected. *Nosocomial* infections result from exposure to pathogens that usually reside in a clinic or hospital. Nosocomial agents are often highly drug resistant, because they often originate from animals that are being treated heavily with antimicrobial drugs. Since most animals are hospitalized because of illness, and ill animals are more susceptible to infection, nosocomial infections are most likely to be seen in a hospital setting.

Environmental or *occupational diseases* occur when susceptible animals contact pathogenic microorganisms within their environment. The infectious agents have free-living niches in nature and do not require infection of cats for their survival. Cryptococcosis, a yeast infection transmitted in pigeon or dove feces, occurs mainly in cats from cities where pigeons abound or in homes where pigeon or dove cotes are maintained. Cat-bite abscesses, which occur almost exclusively in cats allowed to roam free, are occupational in origin, in that biting is a behavior that is occupational among free-roaming cats.

Opportunistic infections are due to microbes that are minimally pathogenic under normal circumstances but cause disease in immunocompromised hosts. Opportunistic organisms may be part of the normal flora of the cat or residents of the environment. Periodontal disease caused by normal oral bacteria in cats with feline immunodeficiency virus or FeLV infections is opportunistic.

Vectors are species of lower animals that transmit pathogens to susceptible hosts. Vectors may be inanimate, such as a grass awns or splinters, or animate, such as fleas or ticks. Many animate vectors are efficient transmitters of infectious diseases because they are natural prey species of the cat and important for the life cycle of the disease agent. Tapeworm infections (*Dipylidium canis*) are transmitted by fleas; one part of the life cycle of the tapeworm is in the flea, and the other in the intestine of the cat. Small birds, lizards, amphibians and rodents may be reservoirs for certain stages in the life cycle of *Toxoplasma*.

THE ENVIRONMENT AND DISEASE

Several hundred different bacterial, fungal, rickettsial, chlamydial, mycoplasmal, L-form, viral, protozoal and parasitic diseases affect cats.[3] Cats are exposed to these diseases in 8 general ways: 1) spread from the queen to the kittens *in utero* (congenital infections) or during the first 2 weeks of life (neonatal infections); 2) fleeting oral, mucous membrane or skin contact with excre-

tions (feces, urine), secretions (saliva, nasal mucus, tears, sexual fluids, pus), or exfoliations (dander, hair) from other cats; 3) bites, from which infectious material in the saliva of one cat is inoculated directly into the tissues; 4) inanimate fomites in the environment, such as vegetation, soil and water, that are contaminated with microorganisms; 5) contact with animals upon which the cat preys or *vice versa* (other mammals, reptiles, amphibians, insects); 6) mutation of one pathogenic agent to another within the body of the cat; 7) as opportunistic infections due to normal host or environmental microorganisms that take advantage of an immunocompromised host; and 8) as hospital-acquired infections (nosocomial infections), usually as a result of some medical procedure and involving antibiotic-resistant organisms.

Table 2 lists many of the common infectious diseases found in cats in various parts of the world and their major mode of infection. After reviewing Table 2, it should become obvious that certain diseases of cats may be more concentrated in one environment than another. For instance, free-roaming cats are at risk for diseases transmitted by inanimate fomites, such as vegetation, soil and water, or by animate fomites or vectors (prey animals of the cat, animals that may feed on the cat, or animals the cat may contact in its wanderings). Cats kept strictly indoors would not be exposed to such diseases. Biting, a behavior almost exclusively of outdoor cats, is not apt to be an important factor in disease transmission in cats kept indoors in stable groups. Diseases like FIV infection and cat bite abscesses are likely to be uncommon, therefore, in indoor cats but prevalent among outdoor animals.

By and large, only those diseases listed in Table 2 with a mode of transmission of congenital or neonatal, direct cat-to-cat contact, pathogenic mutants of common infectious agents, or opportunistic infections are likely to be important in catteries or cattery-like environments (pounds, shelters, multiple-cat households). It is also important to note that vaccines are available for many of the common diseases seen in cattery environments, and that use of such vaccines may modify the severity of disease in the environment. The degree of modification depends, however, on how routinely they are used and how good the vaccines are in preventing infection. For instance, panleukopenia vaccine is considered highly effective and has virtually controlled the disease in catteries. Feline calicivirus, herpesvirus and chlamydial vaccines are much less effective in controlling their respective diseases in high-density, high-stress environments. Feline leukemia vaccines, as presently formulated, are only partially effective in preventing infection.

In addition to whether cats are kept mainly indoors or allowed to run free, other factors play a role in the type of diseases that tend to be found within certain environments. The presence of breeding animals also in an important factor, as breeding allows for diseases that transmit from queens to their kittens, and adds kittens to the disease equation. Kittens are especially important because they represent a highly susceptible population. Kittens are more easily infected and are more likely to show disease signs. Because kittens often become sicker than older animals, they shed much more of the pathogen and are a greater source of infectious agents for other cats, especially for other kittens. Such environments as purebred catteries and pounds are much more likely to have serious infectious disease problems than multiple-cat households that keep only neutered animals, therefore. Pounds and shelters that accept large numbers of kittens also suffer more disease problems than similar institutions that accept mainly older cats.

The multiple-cat household with the lowest level of disease is one in which cats are purchased from a relatively disease-free source and maintained strictly indoors for the rest of their lives. The worst environment is an overpopulated, improperly constructed, purebred cattery. Though the range of diseases that occur in catteries is relatively smaller, the severity of disease can be worse than in free-roaming cats.

Though the worst environment in terms of severity of disease is a purebred cattery, the worst environment in terms of both severity and diversity of infections is a large, multiple-cat household of dozens of neutered and intact cats acquired as strays or from the feral pool of animals. These households often collect 20-60 or more adults as well as kittens, and cats are kept both in-

Table 2. Infectious diseases of cats and their common mode of transmission.

Disease	Causative Agent	Mode(s) of Transmission
	Viruses	
Pox	Rodent poxvirus	O,P
Panleukopenia	Parvovirus	C,D
Rhinotracheitis	Feline herpesvirus, type 1	C,D,O
Pseudorabies	Pseudorabies virus	P
Rabies	Field strains of rabies virus	D,P
	Vaccine strains of rabies virus	F,O
Enteritis	Coronavirus, rotavirus, astrovirus	D
Calicivirus infection	Feline calicivirus	C(?),D
FIP	Feline infectious peritonitis virus	C,D,M,O
FeSFV infection	Feline syncytium-forming virus	B,C
FeLV infection	Feline leukemia virus	B,C,D,M
Viral sarcomas	Feline sarcoma virus	M
Feline AIDS	Feline immunodeficiency virus	B,D(?)
	Bacteria	
Pseudomonas infection	*Pseudomonas*	O
Enteritis	*Campylobacter*	D,O
	E coli	D
Salmonellosis	*Salmonella*	D,P,O
Staph infections	*Staphylococcus*	B,C,D,O
Strep infections	*Streptococcus*	B,C,D
Pasteurellosis	*Pasteurella multocida*	B,C
Bordetellosis	*Bordetella bronchiseptica*	D,O
Tularemia	*Francisella tularensis*	P
Tetanus	*Clostridium tetani*	F
Anthrax	*Clostridium anthracis*	F
Tyzzer's disease	*Clostridium piliformis*	P,O
Plague	*Yersinia pestis*	P
Abscesses	Anaerobic and aerobic bacteria	B
Listeriosis	*Listeria monocytogenes*	P
Leptospirosis	*Leptospira*	P
Nocardiosis	*Nocardia*	F
Dermatophilosis	*Dermatophilus*	F
Mycobacteriosis	*Mycobacterium*	F,P,O
Actinomycosis	*Actinomyces*	B,F
Serratia infection	*Serratia marcescens*	N
EF-4 pneumonia	Eugonic fermenter-4	O
	L-Forms	
Abscesses, arthritis	Unknown species	B(?),D,P(?)
	Mycoplasmas	
Conjunctivitis	*Mycoplasma felis*	C,D
Fetal death(?)	*Mycoplasma, Ureaplasma*	C
Arthritis	*Mycoplasma*	D,O
	Chlamydia	
Conjunctivitis	*Chlamydia psittaci* var *felis*	C,D
Infertility(?)	*Chlamydia*	C
	Rickettsiae	
Hemobartonellosis	*Hemobartonella felis*	B(?),C(?),O
Q-fever	*Coxiella burnetii*	C,P

B = bites
C = congenital or neonatal infection
D = direct contact
F = fomites
M = mutation of agent
N = nosocomial infection
O = opportunistic infection
P = prey animals

(Table 2 continued)

Disease	Causative Agent	Mode(s) of Transmission
	Fungi	
Coccidioidomycosis	*Coccidioides immitis*	F
Histoplasmosis	*Histoplasma capsulatum*	F
Blastomycosis	*Blastomyces dermatitidis*	F
Cryptococcosis	*Cryptococcus neoformans*	F,O
Dermatomycosis	*Microsporum, Trichophyton*	D,F
Sporotrichosis	*Sporothrix schenckii*	F
Aspergillosis, mucormycosis, candidiasis	*Aspergillus, Mucor, Candida*	F,O
Protothecosis	*Prototheca*	F
	Internal Parasites	
Toxocariasis	*Toxocara cati*	C,D,P
Heartworm infection	*Dirofilaria immitis*	P,O(?)
Lungworm infection	*Aelurostrongylus*	P,O(?)
Nasal worm infection	*Mammomonogamus ierei*	P
Trichuriasis	Trichurid worms	D,P
Trichinellosis	*Trichinella spiralis*	P
Hookworm infection	*Ancylostoma, Uncinaria*	D,P
Stomach worm infection	Trichostrongyloid worms	D
	Spiruroid worms	P
	Physalopterid worms	P
Strongyloidosis	*Strongyloides*	D,F
Fluke infection	Lung flukes	P
	Liver and biliary flukes	P
	Pancreatic flukes	P
Tapeworm infection	*Dipylidium, Joyeuxiella, Taenia, Diphyllobothrium, Spirometra*	P
Thorny-headed worm infection	Acanthocephalan worms	P
	External Parasites	
Ear mite infestation	*Otodectes cynotis*	D
Mange mite infestation	*Cheyletiella*	D
	Chigger mites	F
	Demodex	C,D,O
	Notoedres	D,O
	Sarcoptes	P,O
	Lynxacarus	D,O(?)
Lice	*Felicola subrostratus, Trichodectes*	D,P,O(?)
Flea infestation	*Ctenocephalides felis*	D
	C canis, Pulex irritans	P
	Echidnophaga	P
	Protozoa	
Coccidiosis	*Isospora*	D,P
	Besnoitia, Hammondia, Sarcocystis	P
Toxoplasmosis	*Toxoplasma gondii*	D,P,O
Cryptosporidiosis	*Cryptosporidium*	D,P(?),O
Babesiosis	*Babesia, Nuttallia*	P
Cytauxzoonosis	*Cytauxzoon felis*	P
Giardiasis	*Giardia*	D,P,O(?)
Trypanosomiasis	*Trypanosoma*	P
Leishmaniasis	*Leishmania*	P
Encephalitozoonosis	*Encephalitozoon*	C,D
Hepatozoonosis	*Hepatozoon*	P

B = bites
C = congenital or neonatal infection
D = direct contact
F = fomites
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P = prey animals

doors and outdoors. A certain subpopulation moves freely between the 2 environments. Cats in such households suffer both from the common enzootic types of diseases that are the bane of purebred catteries, as well as from the more exotic diseases transmitted among outdoor cats.

Certain diseases may be greatly amplified by the type of environment. For instance, feline leukemia virus infection is enzootic among free-roaming cats, and 1-7% of such animals are persistently infected at any given time (see section on FeLV infection). In the decades before the discovery of FeLV detection tests, FeLV was rampant among both purebred catteries and multiple-cat households. The ultimate source of the virus for these catteries and households was cats that were infected in nature, but the subsequent rapid spread and severity of the disease were a direct result of the husbandry practices employed. In the outdoor environment, the virus is transmitted both by direct contact with secretions and by biting. Because outdoor cats are at some distance from each other and intimate contact is therefore limited, contact transmission involves a relatively small amount of virus. Because the cats are usually older when they contact infected cats, and exposure is apt to be slight, most infected cats recover and only a small percentage remain persistently infected and capable of transmitting the infection. If a FeLV carrier cat is brought into an indoor or indoor/outdoor environment with a high density of cats, close contact between animals, a high level of stress, and shared use of food and litter containers, contact transmission is much more efficient and the exposure dose is much greater. Many of the cats are also younger, and therefore more susceptible to infection. As a result of these unfavorable environmental factors, FeLV infection is much more severe; instead of about 5% of cats becoming persistently infected as in the outdoors, 30% or more of infected cats remain infected for life.

Feline immunodeficiency virus (FIV), another retrovirus, is a problem in outdoor cat populations but not in catteries and multiple-cat households (see section on FIV infection). FIV is spread almost exclusively by bites, while FeLV is transmitted efficiently both by bites and close contact. Once an FIV-infected cat is brought into the home or cattery, biting behavior is suppressed and so transmission of FIV decreases. FIV infection is only a serious problem, therefore, in multiple-cat households that adopt stray cats or those from the feral outdoor population and that allow their cats to run more or less free after they are tamed.

Pounds tend to have disease problems similar to those in catteries because they both deal with a mixture of older cats and kittens, and their housing and husbandry are similar. Therefore, pound cats suffer mainly from diseases that are spread by cat-to-cat contact. Further, the diseases seen in pounds are more apt to be of an acute nature, rather than a chronic one. Panleukopenia, herpesvirus infections, and various enteric and upper respiratory diseases are the most important infections seen in pounds. Such chronic diseases as FIV and FeLV infections and FIP are not apt to be a problem because the cats are not kept long enough for these diseases to develop.

Shelters, on the other hand, tend to have much less turnover of animals. Cats brought to the shelter are often older animals from owners that are no longer able to care from them, or strays and feral cats brought to the shelter by well-meaning cat lovers. Because shelter cats are kept for longer periods, sometimes for a lifetime, chronic infectious diseases are likely to be as important as acute ones.

Another group of cats worth mentioning is farm cats. If farms provide food for wild and semi-wild cats, farm-cat populations can sometimes become very large. As the populations grow larger, a greater proportion of the animals is comprised of kittens and adolescents. When the kitten and adolescent populations become large enough to sustain an epizootic, outbreaks of disease tend to occur. Vaccination is usually not carried out, and there is very little protection against common diseases. Panleukopenia is a particularly severe disease in such environments, and outbreaks are often associated with considerable mortality in younger animals. A farm may have 60 or more cats one year, and only a dozen the next year. The population slowly increases again, awaiting the next major outbreak of disease. This phenomenon has actually been used to limit a feral-cat population on an isolated island and bird sanctuary in Africa.

The cat population decreased from 3409 cats in 1977 to 615 in 1982 after introduction of panleukopenia virus.[5]

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DISEASE-CAUSING MICROBES

Several different types of pathogenic microbes are involved in infectious diseases of cats.[1] These include viruses, bacteria, mycoplasmas, chlamydiae, rickettsiae and rickettsial-like organisms, fungi, protozoa and ecto- and endoparasites. Before discussing diseases caused by specific agents belonging to each group, it is appropriate to know something in general about each of these types of agents.

Viruses are small particles that contain a single type of nucleic acid, RNA or DNA, and lack the essential enzyme systems required for independent survival. Therefore, they are parasites of living cells. The nucleic acid of viruses is surrounded by a protein coat. The DNA or RNA and its surrounding protein are known collectively as the nucleocapsid. Some viruses contain an additional outer carbohydrate-protein coat known as an envelope. Panleukopenia and caliciviruses are nonenveloped viruses containing either DNA or RNA, respectively. Feline herpesvirus and feline leukemia virus are enveloped viruses containing DNA or RNA, respectively. Viral particles attach to susceptible cells, and the viral DNA or RNA is released. The viral nucleic acid commandeers the synthetic machinery of the cell to produce its own proteins and nucleic acids. These are assembled into intact virus particles that are released from the cells by cell rupture or by budding from the cell surfaces. Viruses cause disease in several ways: by destroying the cells they infect; by interfering with normal cell metabolic functions; by interfering with cellular nucleic acids; or by focusing the host's immune response on the infected cell.

Unlike viruses, most bacteria are visible with conventional light microscopes. Bacterium have a rigid outer cell wall, lack a distinct nucleus and contain a single strand of circular DNA. Bacteria divide by a process of binary fission, where a single bacteria splits into 2 equal daughter cells. Bacteria are not obligate parasites of living cells; they can live freely on simple nutrients found in their environments. Bacteria may live in soil, water or plants, or in more complex animals. Many bacteria live on normal body secretions in the orifices of the GI, respiratory and urogenital tracts, as well as on the skin and its appendages.

Mycoplasmal, rickettsial and chlamydial organisms are more similar to bacteria than to viruses. However, they tend to be smaller than bacteria and are often the same size as very large viruses. *Rickettsia* species and *Chlamydia* species have both RNA and DNA, while *Mycoplasma* contain circularized DNA like bacteria. *Chlamydia* and *Rickettsia* have fairly rigid cell walls, while *Mycoplasma* has a cell wall that is thin and nonrigid. All of these organisms are obligate parasites of living animal cells; *Chlamydia* and *Mycoplasma* live in higher animals and *Rickettsia* live in lower animals. The animal cells provide the essential nutrients and metabolites that they cannot provide for themselves.

Fungi are true cells containing a membrane-bound nucleus with several chromosomes. They are somewhat larger than bacteria, and contain a complex rigid cell wall. Some fungi are free-living in the environment and feed off of nonanimal products. Others, such as the dermatophytes, live on the skin and in the hair follicles of higher animals. Fungi are highly pleomorphic in shape, depending on the environment in which they are found. Under certain growth conditions, fungi form complex thread-like structures called mycelia or hyphae. Under certain conditions, often in animal tissues, they exist as yeast-like bodies. Fungi are different from lower organisms in that they have both sexual and asexual developmental stages. The resting, and often infectious, stage of fungal organisms is called the spore. Spores are compact and well-pro-

tected from environmental degradation by a thick outer protective cell wall.

Protozoa are unicellular organisms that are structurally similar to animal rather than plant cells. Protozoa that are pathogenic to animals receive most of their nutrition from metabolic products of host cells. The exception is the intestinal protozoal parasites that can feed on products of digestion. Protozoa receive their nutrition by pinocytosis (ingestion of nutrients through evaginations of the cell wall) or through mouth-like openings. Intracellular protozoan parasites receive their nutrition by diffusion. Protozoa have many structural adaptations that facilitate their survival. Some can change their plasma membranes into a thick, protective cyst wall. Many have acquired means to travel through their environment, which is usually fluid. Pseudopods are temporary extensions of the cell wall through which cytoplasm streams, thus propelling the organism slowly forward. Flagella and cilia are microtubular structures rooted in a basal body at one end of the organism and may be free or attached to the body wall, forming veil-like undulating membranes. Movement by use of flagella and cilia is very rapid.

A parasite is any organism that requires another animal or plant for all or part of its life cycle. However, the term has been applied mainly to large complex multicellular microbes, most of which are visible to the naked eye. Parasites belong mainly to the animal phyla Nemathelminthes (roundworms), Platyhelminthes (flatworms and tapeworms), Acanthocephala (spiny-headed worms) and Arthropoda. The last group contains 6-legged arthropods (insects) and 8-legged arthropods (arachnids).

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DISEASES OF THE MULTIPLE-CAT ENVIRONMENT

Cats are infected by a large number of different microbes (Table 2), but only relatively few account for most disease problems. This is especially true for cats kept mainly indoors. Infectious diseases that are important for environments like catteries are generally those whose transmission involves 4 of the 8 mechanisms listed in Table 1. These include such mechanisms as: mother-to-fetus transmission; fleeting oral, mucous membrane or skin contact with contaminated excretions, secretions or exfoliations; mutation of one pathogenic agent to another within the host's body; and organisms normally within the environment that take advantage of an immunocompromised host.

Common infectious diseases in these categories include those caused by feline panleukopenia virus, feline herpesvirus, feline calicivirus, feline coronaviruses (enteric coronavirus and FIP virus), feline rotavirus (and miscellaneous enteric viruses), feline leukemia virus, several bacteria (*E coli, Salmonella, Pasteurella, Bordetella, Campylobacter,* streptococci, anaerobic bacteria), *Chlamydia, Mycoplasma,* dermatophytes, several protozoa (coccidia, *Giardia,* cryptosporidia) and parasites (ascarids, tapeworms, fleas, ear mites). Several additional diseases should be familiar to cattery owners, not because they are problems in catteries, but because of public health or differential diagnostic considerations. These include feline immunodeficiency virus infection, cat scratch disease, and toxoplasmosis.

Kitten mortality is a final topic of importance to cattery owners. Kitten mortality does not have a single cause, and is not always due to infectious agents. The reminder of the chapter will consist of specific discussions of each of the aforementioned diseases.

Kitten Mortality

Kitten mortality is relatively high among purebred or domestic (laboratory) catteries, especially when compared with other species of animals bred in captivity. This fact has led many managers of laboratory animal facilities to conclude that cats are among the most difficult species to breed in captivity.[3,15]

Kitten mortality tends to occur during 4 periods: *in utero* (abortions, fetal resorptions); at the time of birth (stillbirths); in the neonatal period (0-14 days of age); or in the immediate postweaning period (6-12

weeks of age). Mortality after this period is relatively low.

Kitten mortality figures vary greatly from cattery to cattery, depending on various causative factors. Mortality figures also depend on whether the cattery is conventional (infectious disease agents present) or specific pathogen free (SPF) (infectious disease agents not present). Kitten mortality (0-1 year of age) among conventional purebred catteries in the United States for the years 1975-76 averaged 34.5%, with about one-third being stillborn.[13] One-half of the mortality among live-born purebred kittens occurred during the first 7 days of life and over three-fourths before 6 weeks of age. In a study of kitten mortality in a Persian/Himalayan cattery from 1972-1977, yearly kitten mortality varied from a low of 24% to a high of 63%.[9] Mortality in 2 conventional domestic cat colonies maintained for laboratory purposes was similar to that in conventional purebred catteries, approaching 40%.[11] Following application of increased disease preventive measures, kittenhood mortality decreased to 35% for 2 years, then increased to over 60% following a particularly severe winter.[12] An outdoor/indoor conventional cattery lost 21.6% of live-born kittens before weaning and had 7.9% stillbirths.[15]

Kitten mortality among SPF catteries is lower than in conventional catteries, largely because of decreased deaths from infectious diseases after 2 weeks of age. One SPF cattery had a 14.8% preweaning mortality, including stillbirths;[16] another had 8.9% total kitten mortality.[3] Almost all of the deaths occurred before 7 days of age. Kitten mortality in another SPF cattery ranged from 12.6% to 29.4%, depending on the number of litters previously produced by the queens.[4]

Fetal deaths are extremely difficult to measure, especially if they occur early in gestation and the fetuses are resorbed. Many abortions also go unnoticed because of the propensity of the queen to eat the products of conception. Moreover, if accurate pregnancy examinations are not done at various times after conception, it is impossible to even determine if resorption or abortion occurred. In one large survey of purebred catteries, 2.1% of all feline pregnancies reportedly ended with abortion, and 0.7% in resorptions.[13] These figures, especially for fetal resorptions, are undoubtedly low. Such figures refer to total death of all of the fetuses in a litter, and do not take into account death of a portion of a litter. The mean litter size for a primiparous cat is around 2.8 kittens/litter, while for multiparous queens it is 3.3-4.5 kittens per litter.[2-4,14,15] If a cattery is averaging far below these levels, conception is abnormally low or fetal loss high.

Stillbirths are surprisingly common in both conventional and SPF catteries. Stillbirths in 3 different conventional catteries varied from 7.0% to 10.2%.[9,13,15] Reported stillbirths in SPF catteries have ranged from around 3% to 10% of total kitten births.[3,7,16] Stillbirths have multiple causes, including dystocia and resulting hypoxia, congenital defects incompatible with extrauterine existence, nutritional disorders and congenital infections.

More than one-half of kitten deaths occur in the neonatal period of life. Most deaths in this period are listed along with "fading kittens" by cattery owners. The neonatal period includes the first 10-14 days of life. Deaths occurring during this period result from disorders acquired *in utero*, during the birth process or within the first few days of life. Death losses during the neonatal period are highest in the first 3 days of life and taper off rapidly thereafter. Only one-fourth of kitten mortality occurs between 2 and 6 weeks of age.

The next peak in kitten mortality occurs in the postweaning period, from 6 to 12 weeks of age. Deaths in this period contribute less than one-fourth of the total kitten mortality in conventional catteries. Mortality during this stage is mainly due to infectious diseases potentiated by weaning stress, exposure to pathogenic microbes in the immediate environment, and loss of passive local (lactogenic) and passive systemic (maternal) immunity. Mortality varies greatly with environmental and genetic factors. Mortality during this period is very low in SPF catteries, due mainly to the absence of pathogenic microbes.

Causes

Kitten mortality occurs for the following reasons: congenital anomalies; nutritional diseases resulting from improper diets fed

to the queens; abnormally low birth weight; trauma during or after birth (dystocia, cannibalism, maternal neglect); neonatal isoerythrolysis; infectious diseases; and miscellaneous factors.

Gross congenital anatomic abnormalities have been observed in 6.8-20% of live-born and stillborn kitten fatalities.[3,7,8,10,13,16] Anatomic anomalies often involve cleft palates, cranial deformities (some with cleft palate), agenesis of the small and large intestines, cardiac anomalies, massive umbilical or diaphragmatic hernias, anomalies of the kidneys and lower urinary tract and skeletal anomalies. Congenital defects of a microanatomic or biochemical type probably account for an equal number of kitten deaths. Such defects usually go unreported and are usually included under the headings of stillbirths, fading kittens or undetermined deaths.

Queens fed inadequate diets during pregnancy may produce diseased and weak kittens. The most serious dietary problem of the last decade has been taurine deficiency. Commercial and prescription diets deficient in taurine were inadvertently fed to millions of cats. Deficiencies in dietary taurine led to an increased incidence of fetal resorptions, abortions, stillbirths and kittenhood deaths.[18] The main manifestation of the deficiency was a disease of the heart known as congestive cardiomyopathy. The so-called "kitten mortality complex," mistakenly ascribed to feline infectious peritonitis virus, was probably due to taurine-deficient diets.[14] Taurine deficiency may also have explained the seemingly high kitten mortalities described in purebred catteries in the United States in 1975-76.[13] Taurine is an amino acid that is abundant in animal meat. Therefore, foods made from vegetable proteins must be heavily supplemented with the substance. Fortunately, modern cat diets have been heavily supplemented with taurine, thus minimizing the problem.

Below-normal birth weight has been associated with higher kittenhood mortality. The normal birth weight (taken during the first day of life) of conventional kittens in one study varied from 70 to 144 g, with a mean of 106.4 g.[5] Conventional newborn kittens in a second study had a mean birth weight of 113 g.[2] These were similar to figures for SPF kittens of 69-150 g with a mean of 109 g.[3] The birth weight of kittens is not affected by the sex of the kitten, litter size or weight of the mother.[3,7] Larger queens tend to have smaller kittens than smaller queens, but kitten sizes are still within the normal range.[7]

The causes of abnormally low birth weights have not been determined, but are probably multifactorial. Though often attributed to prematurity, most abnormally small kittens are born at term. Their small stature probably is due to genetic or congenital illness. As such, genetic, developmental, nutritional and infectious causes are probably associated with many abnormally small kittens. In one study, 60% of the kittens that died during the first 6 weeks of life were underweight at birth.[7] Not only is abnormally low birth weight associated with a higher likelihood of stillbirth and mortality during the first 6 weeks of life, but there is a tendency for a disproportionate number of underweight kittens to be chronic poor doers and to die at a younger age.[4]

Many kittens that succumb in the first few weeks of life are of normal size, but their growth lags and they are subnormal in weight at the time of death.[7] Therefore, it is important to not only weigh kittens at birth, but also to weigh them at frequent intervals up to at least 6 weeks of age.

Growth rates of conventional and SPF kittens are similar.[3,5,11] Growth rate is most rapid between birth and 15 days of life and then slows somewhat; growth is faster in males than females after 12-16 weeks of age and in kittens with lower normal birth weights, but is not appreciably affected by litter size or weight of the mothers.[5] By 6 weeks of age, most normal kittens should have mean body weights of around 600 gm. The mean body weights of male domestic cats at 40 weeks of age is around 4000 g (4 kg) and that of females 2800 g (2.8 kg).[11] Since growth over this entire period is relatively steady, female cats are expected to grow at the average rate of 10 g/day and males at a rate of 14 g/day. The weights of individual cats may vary by 10% or more from the mean, and some purebreds may be substantially lower, though the normalcy of such poor growth may be questioned.

Deaths due to trauma during birth or the first 3 days of life accounted for 5-10% of total kitten losses in 2 colonies.[3,16] Trauma

also accounted for 19% of total kitten mortality among 0- to 8-week-old kittens presented to Angell Memorial Animal Hospital.[8] One-half of the losses during the first week of life were due to cannibalism, dystocia or maternal neglect. Traumas occurring after this time were not defined. Dystocia occurs in less than 2% of births, and so is not the leading cause of traumatic death in kittens.[15] Cannibalism is often associated with nervous or high-strung queens. Cannibalism of sickly kittens is also common, so it may be incorrect to always implicate trauma as the direct cause of death. Maternal neglect is another major trauma to newborn kittens.[16] Like cannibalism, it is often not possible to differentiate maternal neglect of otherwise normal kittens from maternal neglect of sickly kittens, the latter being a programmed response of queens that is akin to cannibalism.

Neonatal isoerythrolysis occurs infrequently among domestic cats, but may be relatively frequent in certain purebred catteries.[1,6] Though the precise mechanism has not been determined, it appears that a proportion of queens with type-B red blood cell antigen, when bred to a blood group-A tom, are at risk. Cats with type-B blood make antibodies against type-A blood group antigen. These antibodies may be passed to the kitten in the colostrum, and if the kitten is blood group A, the antibodies cause rapid destruction of the kitten's red blood cells. Affected kittens are born in apparent good health but fade rapidly during the first 24-72 hours of life and die. The spleen is enlarged, the membranes pale and sometimes yellow-tinged, and the urine may be exceedingly yellow or wine-colored.[1,6] This condition is rare in domestic cats because of the rarity of type-B blood in most outbred cat populations. Less than 1% of the domestic cats in the United States and the Caribbean, 3% in England, 9.7% in Japan, 15% in France and 26.3% in Australia have type-B blood.[4] Therefore, the chance of a type-B domestic queen in the United States being bred to a type-A tom is low. However, this may not be the case in purebred cats; some breeds may have a very high incidence (up to 50%) of type-B blood.[4]

Infectious diseases account for a substantial proportion of kittenhood deaths in the neonatal and post-weaning period. Of 149 kittens between 0 and 24 weeks of life, 121 (81%) died of some infectious disease, most often respiratory or enteric infections.[10] This was similar to the death rate due to infectious diseases of 220 of 359 (61%) reported in 0- to 8-week-old kittens.[8] A few fetal deaths and stillbirths are also due to infections occurring *in utero*. Specific pathogen-free catteries have fewer problems with infectious diseases due to viruses, so kitten mortality is less than in conventional catteries. However, deaths due to ubiquitous bacterial pathogens still remain a problem in SPF catteries, mainly because husbandry is similar.

Common infectious agents that cause *in-utero* or neonatal infections and fetal deaths, stillbirths or fading kittens include hemolytic streptococci, *Mycoplasma* and related organisms, feline herpesvirus type 1, feline panleukopenia virus, feline leukemia virus, feline infectious peritonitis virus and *Toxoplasma*.[17] Additional pathogens that infect and kill neonates include *E coli, Pasteurella,* staphylococci, *Mycoplasma* and *Chlamydia.* Fleas are underestimated pathogens of kittens. Heavy flea infestations cause clinical or subclinical anemia in kittens. In turn, the anemia lowers the kittens' resistance to other pathogens. Common infectious agents of weanling kittens that may contribute to mortality are feline herpesvirus type 1, feline calicivirus, feline panleukopenia virus, feline enteric coronavirus, feline infectious peritonitis virus, feline leukemia virus, *Bordetella, Pasteurella* and *E coli.* Details of these various infections are given in subsequent sections.

Bacterial infection of the blood (septicemia) in neonates is very common and deserves special mention. Coliform septicemia alone has been reported as the cause of death in about 10% of kittens.[3,16] Streptococcal infections may also be a major cause of neonatal kitten deaths in catteries.[17] Kittens that receive insufficient maternal immunity at birth, due to inadequate nursing or poor antibody levels in the queen's colostrum, or kittens exposed to massive levels of pathogenic bacteria in the birth canal or from the mother's mouth or milk are most susceptible to bacterial septicemia. Problem bacteria include hemolytic streptococci, *E coli* (especially hemolytic strains), *Pasteurella multocida,* staphylococci and other miscellaneous enteric bacteria.[17] The bacteria gain access to the kitten's body through mu-

cous membranes of the oropharynx and intestinal or genitourinary tracts, or through the umbilical cord. Mucous membrane infection occurs from exposure to contaminated vaginal secretions (either before or during birth), infected milk (in the case of queens with mastitis), or from saliva (during cleaning of the kitten at the time of birth and chewing off the umbilical cord). The most common route of infection is the umbilical cord.

Infection of the umbilical cord is known as omphalophlebitis. Pathogenic bacteria from the mother's mouth are inoculated into the umbilical cord when the cord is chewed off. The queen normally severs the umbilical cord several centimeters from the body wall. The remnant of the umbilical cord dries up rapidly, which limits bacterial growth in the end of the cord and prevents movement of bacteria up the cord. If the umbilical cord is chewed off too short, especially at the body wall, passage of bacteria into the base of the umbilical cord is unimpeded. Alternatively, if the umbilical cord is left long by the queen and an excessive number of bacteria are deposited in the end of the cord, the chances of bacteria entering the viable portion of the umbilical cord remnant are greatly increased. The net result of the penetration of bacteria into the viable tissue at the base of the cord is an abscess. This abscess often forms just under the skin at the site where the umbilical cord enters the abdomen. Therefore, the umbilical abscess may grow unseen for some time.

Bacteria from the infected umbilical cord have direct access to the bloodstream via the remnant of the umbilical vein. This remnant venous structure stays semi-patent for several days after birth. Once in the bloodstream, the bacteria travel to the lung, spleen, liver, joints and kidneys. Bacteria that enter the body through mucous membranes also spread rapidly into the bloodstream, especially if the kitten's maternal immunity is low. Once again, the lungs, spleen, liver, joints and kidneys are target organs. Kittens with bacterial septicemia usually fade away and die during the first 3-7 days of life.

Some cattery owners sever the umbilical cord themselves, tie it off and dip it in antiseptic. It is uncertain how successful this is in preventing neonatal septicemia. Regardless, it is not a practice that should be routine. Overattention to the kittens and queen during birth by the owner often results in problems that are even more serious than omphalophlebitis. Kittens with umbilical cords chewed off flush with the abdominal wall should immediately receive an injection of short-acting (penicillin K) and long-acting (benzathine penicillin) penicillin, regardless of whether they appear normal or not. This greatly reduces subsequent mortality. The base of the umbilical cord should be periodically examined for swelling, purulent exudation and discoloration. If kittens are weighed daily and their growth rate suddenly falls behind that of littermates, the umbilicus should be hot-packed (with a warm wash cloth) for 10-15 minutes several times a day. This sometimes causes the abscess to appear and come to a head and drain.

Pneumonia is another leading cause of death among kittens.[9,10,15] Bacteria are the major cause of pneumonia in kittens <2 weeks of age, while viruses are more important in kittens >2 weeks.[10] Bacteria commonly involved in kitten pneumonia include *E coli, Bordetella, Pasteurella* and streptococci. *Mycoplasma* and *Chlamydia* may also be involved in neonatal kitten pneumonia. The main viral pathogens causing pneumonia in kittens are feline herpesvirus type 1 and feline calicivirus, with the former being far more important.[10] Bacteria may enter the body through the oropharynx or through the bloodstream. Therefore, bacterial pneumonia may be the sole manifestation of disease or only a part of more widespread septicemia.

Enteritis caused by bacteria or viruses is relatively infrequent in nursing kittens but may be a serious problem in kittens being bottle fed. Enteritis due to bacteria (*E coli, Campylobacter, Salmonella*), viruses (caliciviruses, coronaviruses, rotaviruses, astroviruses, toroviruses), and protozoan parasites (coccidia, *Giardia*, cryptosporidia) is much more common in kittens 4-12 weeks of age than in younger animals.

There are several miscellaneous and poorly understood causes of kitten mortality. For reasons that are not understood, kitten mortality is lowest in 5th litters; first litters and litters after the 5th parity have higher mortality.[7] Midsize queens tend to

have lower kitten losses than large or small queens.[7] Kitten mortality is twice as high in one-kitten litters as in larger litters; the lowest mortality is among litters with 5 kittens.[7] Higher mortality in first-litter queens may be due to maternal neglect, though the reason for optimum survival among 5th litters is not obvious. Small queens may be small because they are sickly, which would explain a higher mortality among their kittens. Higher mortality among overweight queens is more difficult to understand.

Pathologic and Clinicopathologic Features

Kitten mortality appears to be a common and often unavoidable problem with breeding catteries. However, preweaning kitten losses (live-born and stillbirths) >20% and postweaning losses (weaning to 7 months of age) >10% should be reason for concern. Further, disproportional losses to any one factor (for example, congenital defects, specific infectious diseases) greater than those described above are reasons for concern regardless of the overall mortality figures.

If kittenhood mortality is excessive, cattery owners should take the following steps: do not stop breeding, because this will not help diagnose the problem; keep accurate and detailed records of losses, pedigrees of dying kittens, diet and any drugs (vaccines, antifungals, antiparasitics, antibacterials) being administered to the cattery as a whole or to affected queens; and obtain accurate (complete) postmortem examinations on all kittens that die, regardless of age. If these steps are not carried out, it is very difficult to pinpoint the problem.

Obtaining complete and accurate necropsies is the most expensive and crucial aspect of a kitten mortality study. It is preferable to sacrifice the kitten and perform a fresh necropsy as soon as it becomes apparent that death is inevitable. Agonal changes in tissues and the effects of forced feeding and other therapeutic interventions can greatly complicate gross and histopathologic interpretations. For instance, forced feeding of a weakened kitten often results in aspiration pneumonia. Pneumonic lesions may obscure the true cause of the kitten's weakness. Kittens allowed to die often show terminal heart and lung problems, which may also obscure the true cause of death. Kittens that die before they can be euthanized should be immediately refrigerated; freezing ruins tissues for gross and histopathologic examination and should be avoided. If refrigeration of the body is delayed for several hours, especially in warmer weather, autolysis of the tissues can be severe and ruin pathologic studies.

Postmortem examination should be performed by competent people. When possible, necropsies should be done by certified veterinary pathologists or by clinical veterinarians working with such people. Though many practitioners would disagree, most clinical veterinarians are incapable of conducting proper gross, let alone microscopic, tissue examinations. Gross abnormalities are often subtle and go unnoticed by untrained eyes. Representative tissues should be taken as aseptically as possible and frozen for microbiologic (viral, bacterial, fungal cultures) or toxicologic studies, should they prove necessary. A wide sampling of tissues should also be preserved in formalin for histopathologic examination. Formalin-fixed tissues, along with detailed descriptions of gross lesions and clinical histories, should then be forwarded to certified veterinary pathologists for microscopic examination. If tissues indicate an infectious or toxic disease as the cause of death, samples of frozen tissues can then be submitted to competent microbiologists or toxicologists for further study.

After causes of death are determined, it should be possible to integrate all data and diagnose the problem. For instance, if cardiomyopathy was the major cause of death among kittens in a cattery, nutrition and genetics would be 2 major areas for further investigation. Was the outbreak of cardiomyopathy associated with a major change in diet or was it limited only to cats from certain bloodlines or breedings? If infectious diseases were a major cause of kitten losses, did those diseases follow any changes in cattery management? If congenital anomalies were the major problem, was there a possible genetic link, or were certain drugs used in the cattery before the outbreak?

Treatment and Prevention

As previously mentioned, a certain amount of kitten mortality is unavoidable. However, if kitten mortality is excessive, there are only 2 ways to attack the problem: by trial and error or by determining the exact cause and initiating the most appropriate control measures. Unfortunately, most cattery owners choose the first method. Though trial and error is sometimes effective, it is usually not the most efficient or effective technique.

Kitten mortality cannot be treated, but rather it must be diagnosed and prevented. Once the major causes are determined, a concerted effort must be made to eliminate the causative factors before the next breedings. Regardless of the cause of the kitten mortality, prevention ultimately involves either changes in cattery management (to control the spread of infectious diseases or correct nutritional deficiencies) or genetics. Unfortunately, these are 2 areas that cattery owners avoid changing if possible. Environmental changes often involve great costs and basic alterations in breeding practices and philosophies. Many cat breeders avoid the topic of genetic weaknesses altogether because conceding that their bloodlines are weak is an admission that their breeding program has failed. This admission is hard to take for people who have invested large amounts of money, reputation and time in their cats. An admission may also have local, regional, national and international implications, especially if cats of the affected breed or bloodlines have done well in shows.

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Feline Panleukopenia Virus Infection

Cause

Outbreaks of fatal enteritis have been recognized in kittens since the turn of the century. Zschokke suggested *E coli* as a possible cause.[38] The disease was recreated several decades later in healthy cats using filtrates of tissue from affected animals, thus refuting the role of bacteria.[37] The cause of feline enteritis was confirmed to be a virus in the early 1930s.[10,36] The virus was first isolated in tissue culture in 1965.[11] The true identity of the virus as a parvovirus eluded investigators until 1974.[15,17,20,22,34] The name panleukopenia was derived from the very low white blood cell (WBC) count of infected cats.[9]

Feline panleukopenia virus (FPLV) is very hardy and withstands heating to 60 C for 30 minutes.[18] Infectivity decreases only 100-fold after being heated to 75 C for 30 minutes.[12] Partially purified virus has been known to survive for 30 minutes at 80 C. There was no decrease in viral infectivity after storage at 4-25 C for 13 months and

100-fold decrease after storage at 32 C for 6 months.[26] Infectivity of FPLV is not affected by chloroform or acidity (pH 3).[12,14,33] The virus is resistant to most disinfectants, but can be inactivated by 0.5% formalin or 1:32 dilution of commercial hypochlorite (bleach) solution.[31]

Six strains of FPLV have been identified.[13] It grows in cat, mink and ferret cells but not in bovine, dog, monkey or human cells.

Feline panleukopenia virus was originally thought to be the parent of the canine parvovirus that originally appeared in dogs in the late 1970s. However, there are minor, but notable, genetic, antigenic, biochemical and host range differences between the 2 agents.[2,6,21,25,35,39,42]

Pathogenesis

Feline panleukopenia virus infects and causes disease in most Felidae. It infects Mustelidae, such as mink and ferrets, but causes only mild or inapparent disease in these species.[39,42] Procyanidae, including raccoons and coatimundi, are susceptible to infection and disease.[8,14,39,42] Feline panleukopenia virus replicates poorly in dogs and does not cause disease.[42] The red fox and skunk are resistant to infection with FPLV.[39] All other species are also resistant.

Feline panleukopenia virus is shed in the feces during acute illness and for several weeks after clinical signs abate. Low-grade chronic shedding by asymptomatic carriers, probably from the oropharynx, appears likely.[3] Unlike most other viruses of cats, FPLV survives for months or years off the host. Therefore, outbreaks may occur following contact with infected animals or contact with previously contaminated quarters.

Infection occurs in 2 basic forms: fetal and postnatal. Postnatal infection is usually by the oral route, though almost any route of exposure will suffice.[20] The incubation period is 2-10 days.[1,11,20,22,27,34] An initial fever spike occurs during the initial viremic phase. A second fever spike is often seen several days later when the WBC count drops. The virus probably replicates in the oropharynx and spreads systemically to target organs. Though the virus can replicate in virtually any body tissue, cells with high mitotic rates, such as intestinal epithelium or the crypts of Lieberkuhn, bone marrow stem cells and lymphoid cells are the principal targets.

Fetal infection usually occurs mid-gestation.[4,16,18,19] Virus enters the fetus from the maternal circulation. Queens giving birth to affected kittens are rarely clinically ill during pregnancy, suggesting that fetuses are infected by an inapparent primary, secondary or latent maternal infection.

Clinical Features

Classic postnatal FPLV infection usually occurs in kittens 6-14 weeks of age, though cats of all ages may be affected.[7] Because of widespread vaccination, the disease is less prevalent among pet cats and in catteries than in the past. Infection in rural cats often follows local population increases that generate large numbers of susceptible young animals. Conditions in pounds are also ideal for the disease; many unvaccinated older cats and weanling kittens are in close contact with carrier or clinically ill cats and younger susceptible kittens.

Feline panleukopenia virus infection results in inapparent, peracute or subacute disease.[7] There is also a congenital (fetal) form of the infection. Subclinical or inapparent infections are probably common, particularly in older kittens and adult cats.[11]

Peracute disease is characterized by sudden death 4-9 days after exposure and is usually observed in kittens. Infected animals are apparently healthy and then moribund a few hours later. This form is most often mistaken for poisoning. Diarrhea and vomiting are infrequent, but severe abdominal pain may be elicited on palpation. Fever usually goes undetected, and by the time clinical signs are manifested, shock is advanced and the temperature is often subnormal. Death usually ensues within hours. Acute illness is manifested by colic, fever, depression, anorexia and vomiting of a frothy bile-tinged fluid. Abdominal palpation elicits pain. Diarrhea, usually fluid and fetid, follows several hours to a day later. Untreated cats dehydrate rapidly and most die of shock within 24-96 hours.

Subacute disease is manifested by mild depression and diarrhea lasting several days. Chronic diarrhea lasting several weeks to months or more has been observed

after recovery in a small proportion of cats and is due to extensive bowel damage and secondary fibrosis, and not to persistent infection.

The course of the disease in fetal infections differs dramatically from that described for postnatal disease.[12,18,19,34] Fetal infection results in almost selective destruction of the Purkinje cell layer of the cerebellum, and to a lesser extent, the retina. Infected fetuses can be aborted but are usually born alive. Characteristic ataxia is noticed when infected kittens begin to walk. Ataxia is lifelong and associated with hypermetria, dysmetria and incoordination. Kittens with cerebellar hypoplasia are otherwise normal and many become affectionate and functional pets. Retinal involvement is usually of no clinical significance.

Pathologic Features

Gross lesions are observed mainly in the gut and bone marrow.[40] In mild cases, the bowel is fluid filled, and the jejunal and ileal mucosa is reddened. Mesenteric lymph nodes are enlarged, edematous and occasionally hemorrhagic. In severe cases, the mucosa is hemorrhagic and covered with fibrinous exudate. The bowel wall may be so severely affected that fibrinous exudate can be seen on serosal surfaces. The bone marrow may be gelatinous and liquid. The stomach and esophagus in vomiting animals are reddened and bile stained.

Microscopic changes are mainly seen in the mucosa of the small intestine, bone marrow and lymphoid tissues.[40] Necrosis of the intestinal mucosa, beginning in the crypt epithelium, is most prominent in the jejunum and ileum. In severe cases, the mucosa sloughs and is replaced by a fibrinous diphtheritic membrane. Epithelial cells within the crypts of Lieberkuhn are in various stages of damage, ranging from hydropic degeneration to lysis. Eosinophilic intranuclear inclusion bodies are seen within some infected cells.[9,22,23] Inclusion bodies are more evident when tissue is fixed in Bouin's or Zenker's fixatives than in formalin. Bone marrow shows varying degrees of myeloid destruction. Lymphoid tissue can be totally depleted of lymphocytes but show evidence of reticuloendothelial hyperplasia. Leukocytes are almost totally absent in peripheral blood.

Clinicopathologic Features

Leukopenia is a consistent feature of FPLV infection. The drop in the peripheral WBC count parallels the second fever spike and starts as early as 4-6 days post-infection. Cells remaining in the peripheral blood are predominantly lymphocytes. Disease severity tends to parallel the WBC count. Counts above 7000 cells/μl are infrequently associated with clinical signs, while counts of 500-2000 cells/μl are associated with severe disease.

Feline panleukopenia virus can be detected in feces by enzyme-linked immunosorbent assay (ELISA) and electron microscopy. Virus shedding is detected before onset of signs and for a week or more after signs disappear.

Treatment and Prevention

Cats with clinical FPLV infection should be treated supportively and vigorously. Food and water are withheld, especially if colic, vomiting and diarrhea are severe. A balanced fluid and electrolyte solution should be given IV as a continuous drip while clinical signs are present. Fresh whole blood should be given if plasma protein levels fall below 4 g/dl or the WBC count falls below 2000 cells/μl. Broad-spectrum antibiotics should be given parenterally to prevent sepsis and temporarily decrease bacterial overgrowth in the damaged bowel. Supportive treatment decreases mortality by 50% in severe infections.

Vaccination has proven very effective in controlling FPLV infection.[7,26,30] Attenuated live-virus vaccines produce rapid immunity in kittens. Killed-virus vaccines are somewhat slower in producing immunity, are more apt to be blocked by low levels of maternal immunity and induce lower neutralizing antibody titers. In practice, however, killed-virus vaccines provide adequate protection and remain the mainstay of most immunization procedures. Starting at 6-10 weeks of age, 2-3 doses of vaccine should be given at 3-week intervals. Vaccination should not be ended before 12 weeks of age because of the presence of interfering maternal antibodies in younger kittens. For maximum protection, a final immunization at 16 weeks of age has been recommended.[30]

The need for yearly booster immunizations is debatable. Though yearly boosters have been recommended by some groups, experience with disease in the field does not indicate a need for such intensive revaccination.[7] Older cats are much less susceptible to clinical disease, and most cats with access to the outdoors are probably naturally boosted by field exposure.

Infection and Immunity

Maternal antibodies prevent infection in kittens for 6-14 weeks.[24] Maternal FPLV antibodies have a half-life of 9.7 days, and there is a good correlation between passive titers of the kittens and the serum titer of the queen.[30] Passive immunity interferes with the immunizing ability of both live and inactivated FPLV vaccines.[5,24,30,32] Of kittens without maternal FPLV antibodies, 89% responded to vaccination. Only 12% of kittens with maternal titers greater than 1:10 responded. Modified-live FPLV vaccines are more likely to overcome low maternal titers than inactivated-virus vaccines.[30] Vaccination induces both virus neutralizing antibodies and cell-mediated immunity.[41,43]

Feline panleukopenia virus infection can have an immunosuppressive effect on kittens. Fetuses infected in mid-gestation are often born with cerebellar hypoplasia, but are normal otherwise. These kittens continue to harbor and shed virus for extended periods after birth.[19] Therefore, fetal infection induces a form of tolerance to the virus. Fetuses infected at 35 days of gestation have depressed T-lymphocyte-mediated immunity.[29] Infection at 45 days of gestation has no such effect.

Feline panleukopenia virus produces fever, leukopenia and lymphoid lesions when inoculated into germ-free cats, but very little enteritis and no mortality.[27] The mitotic activity of the crypt epithelium of germ-free cats is apparently lower than in conventional cats, thus providing the virus with fewer target cells. It is likely that many mild intestinal pathogens, such as *Giardia*, cryptosporidia, coccidia, ascarids and various enteropathic bacteria can increase the mitotic index of the crypt epithelium and predispose kittens to FPLV-induced disease.

Animal and Public Health Considerations

Feline panleukopenia virus is only infectious to Felidae, Mustelidae and Procyanidae. It is not a human pathogen.

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Feline Herpesvirus Type-1 Infection

Cause

Feline herpesvirus type 1 (FHV-1) was first isolated from nasopharyngeal and conjunctival secretions of a group of 5- to 10-week-old kittens with upper respiratory disease.[12] It was originally called feline rhinotracheitis virus in reference to the type of disease it caused.[9]

Feline herpesvirus type 1 is a double-stranded DNA virus.[5,6,11,14,15] It belongs to the group of alpha herpesviruses. The virus is inactivated by ether, chloroform and almost all common commercial disinfectants, antiseptics, sanitizers and detergents.[1,29,44,46] Infectivity is maintained at 4 C for 154 days or more, but is lost within 33 days at 25 C, 3 hours at 37 C and 4-5 minutes at 56 C.[36] The virus stores well at subzero temperature and withstands lyophilization.

Pathogenesis

Feline herpesvirus type 1 is found throughout the world and infects only domestic and closely related wild Felidae.[8] Healthy-appearing carrier cats and cats with clinically active infections are the principal sources of virus. Carrier cats are latently or actively infected, with considerable interchange between the 2 states. Latent carriers maintain the viral genome in tissues of the nasal passages but do not shed infectious virus.[20,21,23] Under situations of stress or corticosteroid administration, the genome can be activated and intact virus shed.[18,20-22] In a study of over 200 healthy cats in Australia, 1.5% were actively shedding FHV-1 and 25.8% were latent carriers.[17]

Kittens are infected from 3 major sources: the queen; other cats in the environment; or live-virus vaccines. Virus is infectious when placed on almost any mucous membrane, but is not infectious when injected IM.[40] It seems the virus does not replicate at the higher core temperature of the body. Latently infected queens may become transient virus shedders because of the stress of gestation, parturition or lactation.[23] Infection of kittens can occur *in utero*, neonatally or between the ages of 6 and 12 weeks, when maternal immunity wanes.

Asymptomatic or clinically ill kittens and older animals in the same environment constitute a second reservoir of virus. Social and environmental stresses in catteries, multiple-cat households and animal shelters lead to a high level of shedding in resident cats. Conversely, these same stresses lead to decreased resistance in newly introduced animals and make them more susceptible to infection from resident virus shedders.

Outbreaks of feline herpesvirus infection have occasionally followed use of live-virus vaccines in a cattery. This has also been observed on at least 2 occasions in groups of isolated specific-pathogen-free cats in the author's laboratory, thus confirming the vaccine as the source. The importance and frequency of this problem remains to be determined, however.

Contrary to earlier beliefs, infection requires intimate contact between shedding and susceptible cats. Licking, grooming, and eating and drinking from the same food dishes appear more important than aerosol exposure in spreading the infection. Airborne spread via large droplets occurs only over short distances, and sentinel cats that share the same air space but different quarters as virus shedders are infrequently infected.[23]

Virus can be recovered from the nasal passages and oropharynx within 24 hours after intranasal and conjunctival sac inoculation.[47] Recovery of virus from these sites diminishes between days 11 and 14, and ceases by day 15. The virus can be recovered from mononuclear cells in peripheral blood around day 8 postinfection.[47]

Feline herpesvirus type 1 infection has been experimentally reproduced by a number of researchers.[12,13,20-22,26-27,35] Clinical signs usually appear within 2 days in experimentally inoculated cats and persist for 10-14 days. Fever in germ-free cats occurs by the second day postinfection and disappears by the fourth day. A second fever spike follows in natural infections, probably as a result of complicating secondary bacterial involvement.[13,35,39,45]

Clinical disease is more common in environments with a high density of kittens and where stress and other exposure factors are unfavorable. High-incidence environments include catteries, boarding facilities, multiple-cat households, animal pounds and humane shelters. Clinical disease is much less common among relatively free-roaming, solitary household and yard cats.

Clinical Features

At least 7 naturally occurring clinical syndromes are attributed to FHV-1 infection: abortion; neonatal disease; classic rhinotracheitis in kittens; chronic conjunctivitis and keratitis; recurrent disease in older cats; chronic sinusitis; and miscellaneous syndromes.

The role of FHV-1 in abortion in queens was confirmed by experimental studies in which pregnant queens were inoculated IV with infectious virus.[25] Virus was found in the placenta and uterine vessels 6-9 days later. Virus was demonstrated at day 26 in the fetal liver and chorioallantoic membrane. Though abortion was seen occasionally in pregnant queens that had been intranasally infected, no virus was detected in the uterus, placenta or fetuses.[25] Abortion after intranasal inoculation was attributed to nonspecific debilitating effects of the infection. Others were also unable to show *in-utero* transmission following maternal infection.[23]

Neonatal disease seems to be associated with queens that fail to provide maternal immunity or infect their young at birth or shortly thereafter. Neonatal mortality was high among kittens born to queens infected intravaginally with FHV-1 late in gestation.[2] Some of these kittens were born with respiratory disease and the clinical appearance was reminiscent of canine herpesvirus infection. Kittens infected during this neonatal period usually faded away and died over several days.

Classic FHV-1 infection occurs in kittens 6-12 weeks of age, when maternal immunity has waned. Severity of signs varies greatly from outbreak to outbreak and animal to animal. Inapparent infections are common.[23] The most consistent manifestation is rhinitis with sneezing and nasal exudation. Sneezing is particularly pronounced in the early stages of infection. The nasal exudate is serous initially but rapidly becomes purulent and sometimes blood tinged (Figs 1-4). Kittens with mainly rhinitis may have a low-grade fever but usually continue to eat. Clinical signs usually disappear in 7-14 days. A few kittens in an outbreak show rhinitis, pharyngitis, glossitis, tracheitis, high fever, depression, anorexia, open-mouth breathing and drooling (Fig 3). Pneumonia may be seen at necropsy. Mortality, when it occurs, is usually among this latter group of animals. Recovery often takes 2 weeks or more.

Contrary to many published descriptions of the disease, conjunctivitis is less common in FHV-1 infection than rhinitis. When conjunctivitis does occur, it can be mild to severe, and is bilateral (Fig 2, 4). Minimal serous discharge is seen early in the infection but can become more copious and purulent with time. Photophobia, or squinting, is particularly characteristic of FHV-1 keratoconjunctivitis and is due to involvement of the corneal epithelium and possibly the associated nerves (Fig 4). Chronic low-grade conjunctivitis and rhinitis can persist for weeks or months in some cats. Herpetic ulcers can also be a troublesome complication of FHV-1 infection.[37]

Corneal lesions are acute or chronic. Corneal ulcers occurring during the acute stage of illness are often large, superficial and very painful (Fig 3). Chronic lesions are less painful and consist of clusters of small whitish plaques in the central cornea. Limbal blood vessels invade the area in an attempt to heal the ulcer, and pigment is deposited along their paths. Acute herpetic ulcers sometimes enlarge rapidly and perforate the cornea, especially if lesions are secondarily infected with bacteria, and corticosteroids are used topically.

Recurrent disease in older cats is infrequent. It occurs as a result of reinfection in the face of waning or short-lived primary immunity or from stress activation of a latent infection. Recurrent disease can be brought about by corticosteroid injections, social stress associated with cat shows or new environments, surgical stress, chronic debilitating diseases, or the immunosuppressive effects of disease, such as FeLV or FIV infections. Recurrent disease resembles primary disease but is much milder and does not last as long. However, severe re-

Figure 1. Mild recurrent rhinitis, characterized by a slight serous nasal discharge, in an adult cat with herpesvirus type-1 infection. The eyes and mouth are unaffected. Sneezing and nasal exudation lasted about 1 week before resolving.

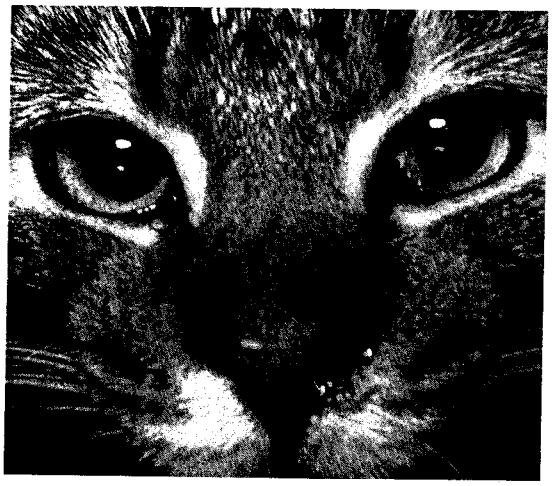
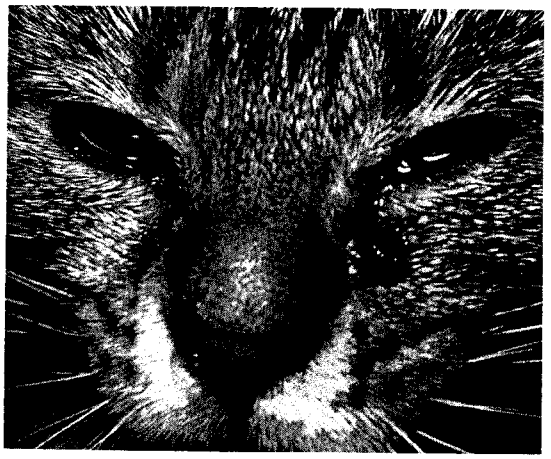


Figure 2. This cat with acute herpesvirus type-1 infection has rhinitis and painful keratoconjunctivitis, but no oral or pharyngeal lesions. Though not evident in this photograph, each eye has a large, superficial corneal ulcer. Such ulcers must be differentiated from the more punctate indolent ulcers associated with herpesvirus keratitis. (From *Virus Infections of Carnivores*, courtesy of Elsevier Science Publishing)



fractory chronic FHV-1 infection can occur in debilitated or immunosuppressed cats.

Chronic rhinitis and sinusitis can be sequelae of severe upper respiratory infections. This complication is much more common in Siamese and related breeds. Turbinate necrosis and damage to the mucosal linings caused by FHV-1 may render the nasal passages permanently prone to chronic infections with bacteria and mycoplasma that normally reside in the area.[26,35] Turbinate atrophy with nasal deformity and chronic epiphora from tear duct obstruction are other uncommon sequelae.

Several miscellaneous disorders have been associated with FHV-1 infection. The virus has been recovered from the brain of kittens, and has been implicated as a cause of CNS disease in experimentally and naturally infected kittens.[8,27] Ulcerative glossitis and skin ulcers due to FHV-1 have been observed in cats without respiratory signs.[30] Severe pancreatitis and pneumonia in a kitten have been associated with FHV-1 infection.[50]

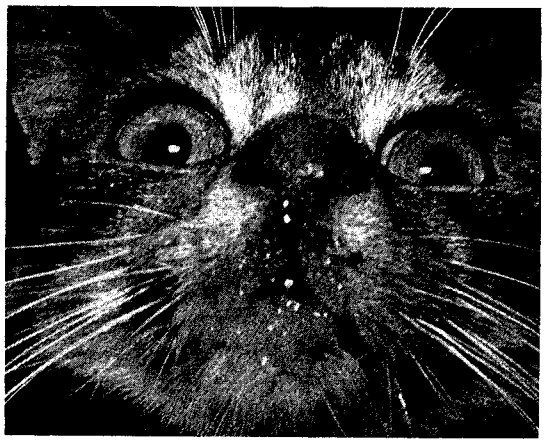
Pathologic Features

Following intranasal infection, the virus causes rapid cytologic infection of the nasal epithelium, with secondary spread to the conjunctival sac, oropharynx, trachea, bronchi and bronchioli. The earliest changes consist of mucosal edema, hyperemia and serous exudation. Focal necrosis of the mucosa follows and the discharges become mucopurulent. Regional lymph nodes and tonsils become enlarged, and small areas of atelectasis may be seen in the lungs.

Microscopic changes in infected epithelial cells resemble those described in cell cultures. Intranuclear inclusion bodies appear in epithelial cells in such areas as the nasal septum, turbinates, bronchi, bronchioli, tongue, conjunctiva and cornea. This is followed by disruption of the epithelium and secondary bacterial invasion. The submucosal tissues become edematous and infiltrated with polymorphonuclear cells. Lymphoid-cell infiltration follows during the recovery stage.

Bone necrosis has been described in kittens inoculated IV with FHV-1.[26] Adult cats do not demonstrate bone lesions following IV challenge, suggesting that growing bone is more susceptible to infection than mature bone. Bone lesions in intranasally infected kittens are limited to the nasal turbinates.[35] Atrophy of the turbinates and gross facial bone deformities may be sequelae of bone necrosis.

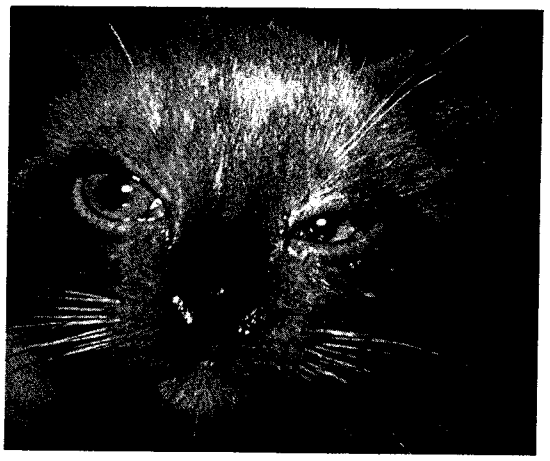
Figure 3. A young cat with herpesvirus type-1 infection. The eyes are unaffected, but the nares are encrusted with exudate. Glossitis and pharyngitis cause drooling. (From *Virus Infections of Carnivores*, courtesy of Elsevier Science Publishing)



Clinicopathologic Features

Feline herpesvirus infection should be suspected in any outbreak of respiratory disease in which rhinitis and sneezing are prominent clinical signs. Conjunctivitis as the only clinical sign is more apt to be due to *Chlamydia* or *Mycoplasma*, especially if

Figure 4. Rhinitis and keratoconjunctivitis in a kitten with herpesvirus type-1 infection. The serous oculonasal discharge often becomes purulent after several days. Squinting indicates painful eyes.



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it initially affects only one eye. Oral ulcers, especially if accompanied by fever and limping and in the absence of conjunctivitis and rhinitis, are more likely to be due to calicivirus.

Feline herpesvirus type 1 can be easily isolated from nasal exudates, conjunctival swabs or oropharyngeal swabs from clinically affected animals. Such material contains large amounts of virus. Cats with positive virus-neutralizing antibody titers should be considered active or latent carriers. However, some latent carriers may not have appreciable antibody titers. The latent carrier state can be detected by treating cats with corticosteroids for several days and culturing oropharyngeal secretions 4-10 days later.[23]

Leukocytosis with absolute neutrophilia is common in the first week of infection. Lymphocytosis may occur in the immediate postrecovery period.[47]

Treatment and Prevention

Treatment of severely affected individuals consists of: keeping the nostrils and eyes clear of discharges; oral or parenteral antibiotics to treat secondary infections; fluid and electrolyte replacement in severe dehydration; oral alimentation when necessary by stomach, nasal or pharyngotomy tube; and specific topical antiherpetic eye medications to treat corneal ulcers. Systemic or topical corticosteroid use should be avoided. Treatment is usually least effective in very young kittens and cats debilitated by other diseases, such as FelV and FIV infections. Recovery from primary infection usually takes a minimum of 2 weeks. Recurrent attacks are generally mild and last 3-10 days.

Feline herpesvirus type 1 is susceptible to systemic antiviral drugs, such as acyclovir and derivatives.[52] However, there is no clinical experience with use of such drugs in treating diseased cats.

Cats can be vaccinated against FHV-1 infection with vaccines containing killed virus, relatively virulent virus given parenterally, or attenuated virus given parenterally or intranasally.[4,32,38,42,51] Parenteral vaccination with killed- or live-virus vaccine gives good systemic immunity but weak local immunity. Such immunity lessens but does not abolish clinical signs resulting from a vigorous challenge with virulent virus and does not prevent latent infection. Experimental intranasal vaccination with avirulent live virus has prevented establishment of the latent carrier state.[38] However, this does not appear to be the case in field situations. Feline herpesvirus vaccines, regardless of type, should not be used as the sole means of disease prevention. In environments with unfavorable stress factors, exposure factors and husbandry practices, FHV-1 vaccines often do a poor job. Vaccination should only supplement good husbandry in such situations (see chapter on cattery design and management).

Live-virus FHV-1 vaccines have been implicated as a cause of outbreaks of upper respiratory disease in catteries. This is more likely to occur in catteries that have been previously free of disease, or catteries in which kittens are under severe stress or are genetically weak. Certain brands of vaccine are more likely to have this side effect than others. The phenomenon probably involves initial infection of a small proportion of vaccinated cats, with subsequent reversion to virulence of the relatively avirulent vaccine strain. At that point, the virulent virus is spread rapidly to other susceptible cats.

Infection and Immunity

The exact nature of FHV immunity is not known; cell-mediated as well as humoral mechanisms are probably involved in cats, as they are in other species.[43,49,51] Similar to other herpesviruses, FHV-1 frequently persists in a nonreplicative or latent state. Latent infections develop in as many as 80% of infected cats. Infectious or latent virus is found mainly in tissues of the head. Of 10 cats, 1 was an active shedder, 7 became active shedders after corticosteroid administration, and 2 cats treated with corticosteroids did not actively shed virus.[22] Feline herpesvirus type 1 was isolated from homogenates of nasal turbinates (9 of 10), soft palates (3 of 10), tonsils (3 of 10), oral mucosa (3 of 10) and tongue (2 of 10). It has been postulated that virus persists in the trigeminal nerve ganglia and other such structures.[22]

Latent carriers have been converted to active virus shedders by giving tham corticosteroids for several days or by stressing them with activities as minor as movement from one animal quarter to another.[20,21]

Virus activation also occurs in queens from stress of parturition and lactation, which may be an important source of infection for kittens.[23] When passive maternal immunity wanes, the kittens become infected.

There does not appear to be a good correlation between maternal virus-neutralizing antibody titers and duration of passive immunity in kittens.[23,41] Some kittens with high maternal titers to FHV-1 become infected, while others with low or undetectable titers resist. Maternal virus-neutralizing titers are usually 1:4 by 2-10 weeks. Kittens may become infected relatively early, while systemic maternal immunity is still present. This may allow the virus to establish itself in the body without clinical illness.[23]

Duration of immunity following experimental infection is variable.[48] Cats are solidly immune 21 days after infection, but most are again susceptible at 150 days. Recurrent disease is much milder and more transient than the primary disease. A similar situation occurs in nature. Recurrent bouts of transient rhinitis and conjunctivitis are common, especially in environments where primary disease is frequent and severe. Protection against recurrent disease is only partially mirrored by serum virus-neutralizing antibody levels.[48] Cats with higher antibody titers tend to be resistant, while previously exposed cats with lower or negative titers may or may not be resistant.

Animal and Public Health Considerations

Cats actively or latently infected with FHV-1 are only health hazards to susceptible domestic cats and closely related species. FHV-1 is not a human pathogen.

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Feline Rotavirus Infection

Cause

Rotaviruses are enveloped RNA viruses with a spoke- or wheel-like appearance, hence the name rotavirus (rota = wheel). Rotaviruses infect most species of mammals, including people. Feline rotavirus infects cats throughout the world. Of 50 cats examined in Louisiana, 23 were seropositive.[2] Similarly, 29 of 94 English cats had rotavirus antibodies.[3] Many normal cats presumably harbor and shed low levels of rotavirus in feces. Virus may also be voided by sick animals into the environment, where it can survive for up to 9 months in dried feces at room temperature.[4]

Clinical Features

Kittens are apparently infected early in life with rotaviruses, but disease signs are minimal or absent. Investigators induced transient diarrhea in 2 3-day-old kittens with fecal extracts.[3] One of the kittens was colostrum deprived while the other was not. Though enteritis was more severe in the colostrum-deprived kitten, both survived after a 1- to 2-day bout of relatively insignificant illness. In contrast to kittens, calves with low maternal globulin developed severe enteritis.[4] Therefore, it seems that rotavirus infection is less severe in carnivores, such as cats, than in herbivores.

Pathologic Features

Gross abnormalities are usually not found in the intestinal tract of affected animals. Virus can be identified by immunofluorescent antibody staining and

electron microscopy in epithelial cells of the jejunum and ileum.[1] Rotavirus can be easily detected in cat stools by electron microscopy or enzyme-linked immunosorbent assays using group-specific antisera.

Treatment and Prevention

Affected kittens seldom require treatment for rotavirus enteritis. If diarrhea is severe, oral food and water should be withheld for 24-48 hours and a balanced electrolyte solution given parenterally. Because the disease is generally of little clinical significance, there has been no impetus to develop vaccines or to devise husbandry procedures to limit its spread.

Animal and Public Health Considerations

As far as is known, feline rotavirus is infectious only to cats. Some animal rotavirus species occasionally cause mild enteritis in people. However, feline and human rotavirus isolates appear to be distinct.[1]

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Feline Enteric Coronavirus Infection

Cause

Feline enteric coronavirus (FECV) is one of the most common viral pathogens of cattery cats.[2,4,5,10,15] It is found in virtually every cattery and multiple-cat household, and infects virtually every cat in such environments. One-fourth or more of outdoor and pet cats have also been exposed to FECV. The virus is not an important cause of disease, however. Its importance lies with its extremely close relationship to the feline infectious peritonitis virus (FIPV).[1,7,13,14] Antibodies to FECV cannot be distinguished from antibodies to FIPV and *vice versa*. This has led to a great deal of confusion on the interpretation of FIP diagnostic tests.

Feline enteric coronavirus is extremely difficult to propagate in culture. To date, only one strain has been propagated *in vitro*, though others have been observed by electron microscope or fluorescent antibody testing.[2-4,11]

Feline enteric coronavirus infection has been studied in 2 relatively closed groups of cats. In the first group, FECV was found to be carried by many healthy seropositive cattery cats and shed in their feces.[10] Kittens in this cattery became seropositive to FIPV antigens at 5-16 weeks of age, usually without any signs of illness. A typical coronavirus was seen in the feces and was found to be distinct from FIPV in its disease-causing spectrum. Kittens in a second cattery also developed antibodies to FIPV antigens after weaning.[15] Adult cats in this environment were seropositive and specific-pathogen-free kittens housed with these animals also became seropositive without noticeable disease. About 25% or more of household pet cats also have antibodies detectable with FIPV tests; most of these cats were probably infected with FECV-type coronaviruses and not with FIPV.[5,10]

Pathogenesis

The major source of FECV is asymptomatic carrier cats that shed the virus in their feces.[10] Kittens in the acute stage of the infection also are a major source of virus within breeding catteries. The virus is passed from cat to cat mainly by the fecal-oral route, though the virus can be tracked from one area to the other by caretakers.[10] Kittens usually become infected between 5 and 16 weeks of age. Systemic passive and lactogenic immunity probably protects the kittens from infection until weaning.

Virus replication occurs predominantly in the small intestine.[3,10,11] There is a minor systemic spread of FECV during initial infection, but the focus of infection is the small intestine.

The acute infection stage of FECV usually goes unnoticed by the owner because of its mild and short course. Following the acute stage of infection, some infected cats

remain carriers for weeks, months or, in some cases, a lifetime. These chronic carriers shed very small amounts of virus as compared to cats in the acute and convalescent stages of the infection.

Clinical Features

Most experimentally infected cats do not develop clinical signs of disease. When present, disease signs are mild and self-limiting and occur 2-7 days after infection. Vomiting is a common initial sign of the infection. Diarrhea follows in 12-24 hours and lasts for 48-96 hours.[10] The stool may be soft and mucus-laden, or fetid and watery. Fatal hemorrhagic diarrhea is very uncommon.[4] Kittens with more severe enteritis may be depressed and anorectic for several days. A transient low-grade fever and leukopenia are often seen in clinically affected animals.[11]

Pathologic Features

Gross lesions in the intestinal tract are usually absent. In severely affected cats, mesenteric lymphadenopathy and edema of the bowel may be apparent.

Clinicopathologic Features

Feline enteric coronavirus should be suspected as the cause of any outbreak of transient enteritis in young cats. The diagnosis can be confirmed by examining stool specimens for virus by electron microscopy.

Serum antibodies appear within 1-2 weeks of infection. Though cats with higher antibody titers are more likely to shed the virus in their stool, there is no accurate serologic test to detect carrier cats.

Treatment and Prevention

Kittens with severe vomiting and diarrhea should not be given food or water for 48 hours and should be given a balanced electrolyte solution parenterally to counteract dehydration and to replace potassium, bicarbonate, sodium and chloride losses. Signs usually abate within 24-48 hours.

Elimination of FECV from catteries is extremely difficult. Serologic tests do not identify carriers, which makes it very difficult to remove or segregate affected animals from the premises. Even if the virus can be eliminated from the cattery, the widespread nature of the infection makes it difficult to keep the virus out.

Infection and Immunity

Though antibodies appear in the serum within a week or so of infection, local rather than systemic immunity is more likely to be involved in recovery and protection against reinfection. Following recovery from the initial infection, serum antibody titers may remain consistently elevated for months or years, or may wane after 2-8 months. Some cats may undergo cyclic and periodic increases and decreases in antibody titers. Circumstantial evidence indicates that cats with persistently high antibody titers are more likely to be carriers that cats that lose their antibodies after a few months. Cyclic increases and decreases of antibody titers probably correlate with infection, loss of the virus from the body, and reinfection.

Immunity to FECV does not extend to the closely related FIPV. In fact, cats with immunity to FECV are more susceptible to FIPV.[8,10,11]

Animal and Public Health Considerations

Feline enteric coronavirus is infectious only for domestic cats and related wild Felidae.

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Feline Infectious Peritonitis Virus Infection

Feline infectious peritonitis (FIP) is a relatively new disease of cats. The definitive reports of FIP were from the United States in the early 1960s.[27] It is doubtful the disease existed much before the early 1950s.[44] The reason for the sudden emergence of FIP is not known. It may be noteworthy that FIP appeared within a decade of the initial descriptions of transmissible gastroenteritis (TGE) of pigs in North America.[17] The causative agents for both diseases, though not identical, are closely related. The dramatic rise in incidence of FIP between 1950 and 1975 coincided with heightened interest in cats as primary pets, increased density of cats in urban areas and catteries, and emergence of such cattery-associated diseases as FeLV infection.[44] Feline infectious peritonitis is now essentially worldwide in distribution.[1,29]

Cause

Feline infectious peritonitis virus (FIPV) is a typical coronavirus with a sun- or crown-like appearance; hence the prefix corona. It is so closely related to TGE virus (TGEV) of swine and canine coronavirus (CCV)that they have all been described as strains of a single virus species.[28,57,64] However, there are distinct differences in the genetic structure of FIPV as compared to other coronaviruses, including TGEV.[10] Feline enteric coronavirus (FECV) is another closely related coronavirus included in this group.[53]

Pathogenesis

Feline infectious peritonitis is mainly a disease of domestic cats. It has also been recognized in the lion, mountain lion, leopard, cheetah, jaguar, lynx, caracal, sand cat and pallas cat.[6,8,14,48,60,61,66,68] Feline infectious peritonitis is seen in cats of all ages, but incidence peaks in cats between 6 months and 5 years of age.[44,48] There is no significant sex predisposition.

In the United States, FIP is more frequent in purebred than domestic cats, and in catteries or multiple-cat households rather than single-cat homes. The incidence of FIP in the United States appears to have plateaued over the last decade. In colder climates of Europe, FIP is seen more often among pet cats and appears to be increasing in frequency.

FIP losses occur as enzootics or epizootics, with the former being much more common. FIP losses are sporadic, unpredictable and infrequent in the enzootic form. Catteries with enzootic FIP may not have any deaths for years; then several cases might be seen in rapid succession. The disease may then disappear, only to reappear months or years later. Overall mortality from enzootic disease is usually 1-5%.

Much higher mortality has been seen in some groups of cats with epizootic FIP, sometimes approaching 25-50% of kittens and adolescent animals.[48,63] Epizootics of FIP seldom last for more than 6-12 months, are relatively uncommon and usually do not strike the same cattery more than once. Following an epizootic of FIP, the disease usually returns to the enzootic form. Enzootic FIP is probably associated with persistence of the same or similar strains of coronaviruses within a population, while epizootics are probably associated with first-time introduction of an FIPV-type coronavirus into the cattery or the introduction of a different strain of the virus.

The precise reservoir of FIPV in cats is not known. Some healthy or subclinically ill cats may harbor and shed FIPV over long periods.[55] Mounting evidence also suggests that FECV carriers may also serve as a reservoir for FIPV. FIPV appears to be a minor

mutant of the more ubiquitous FECV, and hypermutable regions have been observed in the closely related TGEV. Therefore, mutant FECV viruses (*ie*, FIPV) may be shed occasionally by FECV carrier cats or such mutants might be generated *in vivo* in kittens during the course of their FECV infections. FECV-type coronaviruses have been inadvertently introduced into at least 2 large SPF cat colonies. For the first several years no significant disease was seen, but eventually a few cases of FIP began to appear. There also seems to be a relationship between the severity of FECV infection within a cattery and the incidence of FIP. Catteries with a high proportion of cats with high coronavirus antibody titers are more likely to have FIP losses than catteries with cats having low or negative coronavirus antibody titers. There also appears to be a spectrum of FIPV strains, varying from extremely lethal to those that behave almost like FECV (Table 3).[55]

Regardless of the source of FIPV (FIPV carriers, FECV carriers or both), it appears that many cattery cats are infected early in life. Some kittens may be infected *in utero* or as early as the first 5 weeks or life. In some cases, disease is manifested within several days or weeks of infection, but in many cases, disease signs may not appear until many weeks or months later. The highly variable and often long latent period between infection and disease is one of the main reasons that FIP is so feared by cattery owners; it is often impossible to reconstruct whether the infection began in the cattery of origin or was acquired in the new environment after a kitten was sold.

The incubation period and clinical outcome of FIPV infection depend on several complex and incompletely understood factors, including strain of the virus and immunologic responsiveness of the host. The strain of virus is very important and related to immunologic responsiveness. Highly pathogenic strains of FIPV cause fatal FIP in almost all cats, regardless of age, route, inoculation or immunologic responsiveness (Table 3). However, these strains may be largely laboratory artifacts and atypical of most field strains.[55] Outbreaks of FIP with extremely high morbidity and mortality are very uncommon in nature, suggesting that such highly virulent laboratory strains are atypical. In contrast, other strains of FIPV never induce FIP when given by the oral route, though they are infectious and evoke serum antibodies. When given intraperitoneally, they are more virulent, but still only cause FIP in 50% or so of infected cats.[55]

The immunologic responsiveness of the cat also appears to be important in determining the clinical outcome of infection. Most strains of FIPV that exist in nature can be efficiently contained and eventually eliminated by normal cats. After infection, there is a rapid immune response and the virus is contained within local lymph nodes and eliminated over a few weeks or months. Cats that efficiently contain the virus during the initial stage of infection show no clinical signs of illness. However, if this immunity is in some way impeded, the virus is not contained and disease results. High levels of stress, concurrent infectious diseases, malnutrition or specific nutritional deficiencies, trauma (such as elective surgery), pregnancy/parturition/lactation, and genetic weaknesses occurring during the crucial containment period can lead to clinical disease.

The interrelationship of virus strain and host resistance is an important concept. If infected cats develop good resistance and the strain is of low virulence, disease is uncommon even though infection is frequent. At the opposite extreme, if the strain is of greater virulence and the cat's resistance is low, the incidence of FIP is high. This relationship explains why FIP is so unpredictable within catteries where the infection is common.

The initial site of FIPV replication in naturally occurring disease probably varies according to route of infection. Following parenteral infection (all routes other than oral), the virus probably replicates in macrophages within regional lymph nodes. After ingestion, the initial site of replication is probably the intestinal mucosa. Infection can also occur after experimental intratracheal inoculation of FIPV.[33,52]

Clinical disease is associated with dissemination of virus to target tissues via blood-borne phagocytes.[73] FIPV disseminates to tissue rich in phagocytic cells, in which FIPV replicates.[45] Sites particularly rich in target cells include Kupffer cells of the liver, visceral peritoneum and pleura, uveal tract, and the meninges and epen-

dyma of the brain and spinal cord. After dissemination, the ultimate course of disease depends on the type and degree of immunity that develops.

Virus containment is a function of strong cell-mediated immunity; humoral immunity is not protective. Many cats sequester FIPV for a prolonged time after initial infection. These subclinical or latent infections are usually caused by low-virulence strains of FIPV.[55] Maintenance of inactive infections is under immunologic control of the host. Situations interfering with established FIPV immunity can lead to disease.

Clinical Features

Feline infectious peritonitis refers to the principal clinical form of the disease, a transmissible inflammatory condition of the visceral mucosa and omentum.[74] A second form of the disease is characterized by granulomatous involvement of such parenchymatous organs as the kidneys, mesenteric lymph nodes, bowel wall, liver, pancreas, central nervous system and uveal tract of the eyes.[41,44] Granulomatous FIP is called "dry" or noneffusive because there is no inflammatory exudation into body cavities. Classic FIP, which comprises about 75% of cases, is termed "wet" or effusive.

The incubation period (time from infection to disease) of effusive FIP is 2-14 days under experimental conditions.[12,49,52,55] Experimentally induced noneffusive FIP has a longer incubation period. Though the incubation period for experimental FIP is relatively short and constant, the incubation period for FIP in nature can be as short as a few days or as long as a year or more. Feline infectious peritonitis in kittens 4-10 months old is often preceded by a long history of vague ill health and failure to grow at a normal rate. Affected kittens in the incubation stage of FIP may be more susceptible to other common feline diseases, indicating that their resistance is not normal.

At the time clinical signs of FIP are apparent, the disease is of the effusive (three-fourths of cases) or noneffusive (one-fourth of cases) type. However, cats with noneffusive FIP often go through a brief initial bout of effusive FIP weeks or months before death. Conversely, some cats suffer for weeks or months with low-grade noneffus-

Table 3. Variations in infectivity and virulence of various feline coronavirus isolates.

Strain	Infectivity*	Ability to Cause FIP following:	
		oronasal or oral inoculation	intraperitoneal inoculation
FECV-UCD	high	none	none
FECV-79-1685	high	none	none
FIPV-UCD2	high	none	extremely low**
FIPV-TN406 (high passage)	moderate to low	none	extremely low
FIPV-UCD3	high	none	moderate
FIPV-UCD4	high	none	moderate to high
FIPV-UCD1	moderate to low	moderate	high
FIPV-TN406 (low passage)	moderate to low	moderate to high	high
FIPV-79-1146	high	high	high
FIPV-Nor15	high	high	high

* Infectivity is defined as the ability to cause seroconversion following oral or oronasal inoculation.

**Extremely low = less than 1 case in 20-40 inoculated cats.

ive disease and then develop effusive FIP terminally.

The onset of effusive FIP is heralded by a chronic fluctuating fever often associated with a progressive decline in weight, activity and appetite over a 1- to 6-week period. Terminally, affected cats go into shock and die. Peritonitis and ascites are seen in over 90% of cats with effusive FIP; pleuritis with hydrothorax is a sole or accompanying feature in about 40% of cases (Table 4). Ascites leads to abdominal distention (Figs 5, 6) and hydrothorax to dyspnea (difficult breathing). Fluid distention of the pericardial sac, sometimes leading to cardiac tamponade and heart failure, is a rare occurrence.[81] Intact males frequently develop scrotal enlargement due to extension of peritonitis to the tunics surrounding the testes (Fig 5). Peritoneal and pleural exudates are characteristic of the disease. Involvement of other organ systems, such as the eyes and CNS, is clinically apparent in only 10% of cats with effusive disease, though a somewhat higher proportion may have microscopic lesions in these and other nonserosal sites (Table 4).

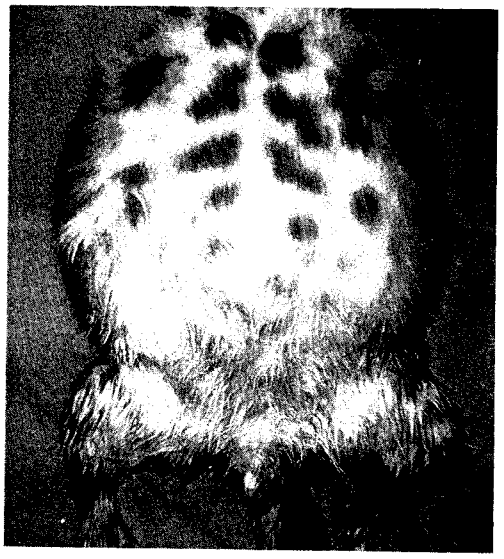
Cats with noneffusive FIP are ill 2-16 weeks or more. As in the effusive form, a chronic fluctuating fever accompanies the disease, along with a progressive decline in general body condition and appetite. Kittens with noneffusive FIP may fail to grow normally, and this may be the sole outward sign for weeks or months. In addition, signs referable to specific organ systems are seen. Peritoneal cavity lesions are found in 50% of cats with noneffusive FIP and pleural cavity lesions in 10% (Table 4). Unlike cats with the effusive form, one-third of cats with noneffusive FIP show signs referable to the central nervous system and have clinically apparent ocular disease (Table 4). Peritoneal cavity lesions in noneffusive FIP usually consist of irregular solitary or multiple masses within the kidneys, or hepatic or mesenteric lymph nodes (Fig 7). Granulomatous lesions in the liver, spleen, pancreas, omentum, serosal surfaces and intestinal walls are less frequent. Testicular enlargement is seen less frequently in cats with noneffusive FIP. Thoracic cavity lesions of noneffusive FIP are usually clinically silent. When present, they are usually on the pleural surface or heart (Fig 8).

Table 4. Variability in clinical signs of noneffusive FIP.

Clinical Signs Referable to Involvement of the:	Number of Cats
Peritoneal cavity	30
CNS	22
Eyes	14
CNS and eyes	8
Peritoneal cavity and eyes	7
Peritoneal and pleural cavities	4
Peritoneal and pleural cavities, CNS	3
Peritoneal and pleural cavities, eyes	2
Peritoneal cavity, CNS, eyes	2
Pleural cavity	1
Pleural cavity, CNS, eyes	1
Total	94

Central nervous system involvement is varied in its clinical expression and is much more likely to be associated with noneffusive FIP. Spinal signs, such as posterior paresis, incoordination, hyperesthesia, and palsy of the brachial, trigeminal, facial and sciatic nerves, have all been described.[25,36,38,44,65] Hydrocephalus, secondary to disease of the choroid and ependyma, has also been reported.[13,23,37] Cranial development can lead to dementia, personality changes (rage, withdrawal) or convulsive disorders. Cerebellar-vestibular signs, such as nystag-

Figure 5. Grossly distended abdomen of a kitten with effusive feline infectious peritonitis. Note the scrotal enlargement.



mus, head tilt or circling, have also been associated with FIP.

Ocular lesions can occur by themselves or in association with lesions in the CNS or peritoneal cavity.[48] Like CNS disease, ocular involvement is more common in noneffusive FIP (Table 4). Uveitis and chorioretinitis are the predominant ocular manifestat ions of the disease (Fig 9).[4,5,11,15,65]

Miscellaneous sites for lesions in noneffusive FIP include the nasal passages, tongue and distal small intestine. Granulomatous colitis due to FIPV has also been described.[82] *In-utero* infections with FIPV result in atypical disease. Pneumonia, pleuritis and hepatitis are the principal lesions in affected kittens.[40]

Pathologic Features

The pyogranuloma is the typical lesion of effusive FIP.[26,73,74] A pyogranuloma consists of necrotic debris and neutrophils, surrounded by a dense accumulation of phagocytic cells interspersed with a few lymphocytes and plasma cells. Considerable amounts of fibrin and protein-rich fluid are also deposited within and around the lesions.[73] Pyogranulomas appear as distinct

Figure 6. Over 600 ml of a yellow, mucinous effusion was removed from the abdomen of the kitten in Figure 5 at necropsy.

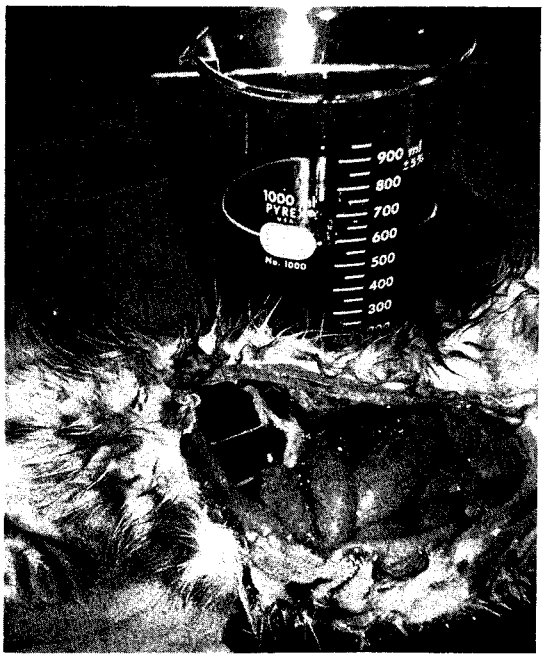


Figure 7. Mesenteric and hepatic lymph nodes and liver from a cat with noneffusive feline infectious peritonitis. The lymph nodes are enlarged and involved with granulomatous adenitis. The liver capsule contains raised, whitish foci 0.5-1 cm in diameter, extending into the underlying parenchyma.

or coalescing serosal plaques 0.5-2 mm or more in diameter (Fig 10). The visceral serosa of the thorax and abdomen is more likely to be involved. The omentum is often thickened, edematous and retracted into a compact mass. Though the pyogranulomatous process is usually surface oriented, a similar inflammatory reaction may extend

Figure 8. Lungs of a cat with noneffusive feline infectious peritonitis. A solitary, whitish granuloma is present on the edge of the left cranial lobe. Lymph node and liver lesions were also present in this cat (Fig 7).

into underlying tissues along penetrating veins. Focal lesions, often associated with phlebitis and a mixed inflammatory-cell infiltrate, may be seen deep in underlying muscle or organ parenchyma.

Lesions of noneffusive FIP are more typically granulomatous in nature, but nevertheless basically resemble the pyogranulomatous lesions of effusive disease. Granulomatous lesions vary in size, depending on the organ involved.[26,41,65] Ocular and CNS lesions more closely resemble the microscopic or small pyogranulomatous reactions seen in effusive FIP. Serosal, mesenteric and omental lesions also appear as small whitish plaques or nodules. Kidney, liver and mesenteric lymph node lesions are often very large, sometimes exceeding 5 cm in diameter. The outer zone of these granulomas is characteristically more fibrous, and the number of plasma cells and lymphocytes much greater than the pyogranulomas of effusive FIP. Edema, hyperemia, and fibrin and protein exudation are not as pronounced as in the pyogranulomatous lesions of effusive FIP.

Lymphoid lesions are common in effusive and noneffusive FIP. Splenic enlargement may be due to histiocytic and plasmacytic infiltration of the red pulp, hyperplasia of lymphoid elements in the white pulp, necrotizing splenitis with fibrin deposition and

Figure 9. Keratic precipitates on the inner cornea of a cat with noneffusive feline infectious peritonitis. A granuloma on the right side of the iris caused iridial discoloration and an irregular D-shape of the pupil.

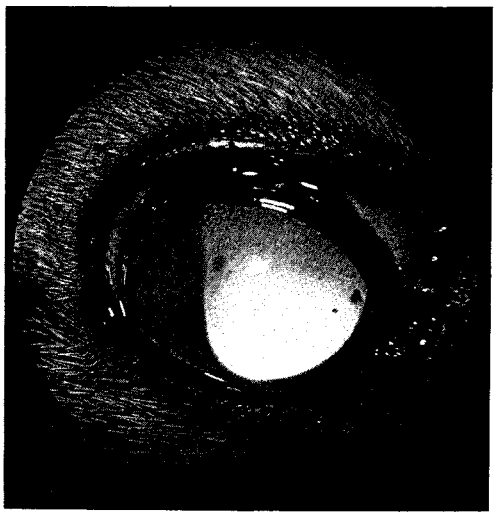
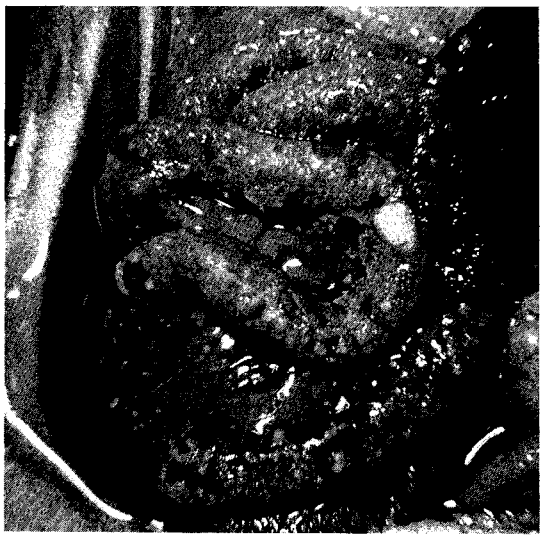


Figure 10. Abdominal viscera of a cat with effusive feline infectious peritonitis. The serosal surface of the intestines and spleen are covered with punctate, coalescing fibrinous plaques, the classic pyogranulomas of effusive FIP. Some peritoneal effusion remains, though most has been removed.



polymorphonuclear cell infiltrates, or by more organized pyogranulomatous reactions. Gross lymph node enlargement is usually limited to thoracic and abdominal nodes and is due to lesions resembling those described for the spleen.

Fluorescent antibody staining of tissue sections from cats with both forms of the disease shows FIPV in the lesions. In effusive FIP, a large amount of viral antigen is contained in phagocytic cells that make up the periphery of the pyogranulomas.[51,52,73] Less viral antigen is present in lesions of noneffusive FIP; it is usually found within a few macrophages adjacent to veins in the center of the lesions.

Clinicopathologic Features

Complete blood counts show similar changes regardless of the disease form. Leukocytosis with neutrophilia and lymphopenia is a common abnormality. In chronic disease, low-grade to moderately severe depression anemia is also seen.

Icteric serum or plasma, with or without evident jaundice of the tissues, is common in cats with FIP, especially the effusive form. In fact, FIP is the most common cause of an icteric serum or plasma in a cat

<3 years of age. The increased level of bilirubin in the blood is usually not due to liver involvement *per se*, but rather to microhemorrhage into tissues and extravascular destruction of red blood cells by phagocytic cells.

Total plasma protein levels are elevated in 50% of cats with effusive FIP and 75% of cats with noneffusive FIP. This increase is due to elevated levels of inflammatory and antibody proteins.

Disseminated intravascular coagulopathy occurs in cats with effusive FIP.[71] It is usually clinically inapparent but may contribute to the production and character of pleural and abdominal effusions.

Ascitic and pleural fluid from cats with effusive FIP is usually pale to dark yellow, and has a sticky, viscous consistency, somewhat like synovial fluid or egg white, with a high protein and WBC count.

Aqueous humor and CSF in cats with ocular or CNS disease also show similar increases in proteins and leukocytes. Synovial fluid from cats with effusive FIP is frequently inflammatory in character.

Following introduction of tests for detection of FeLV infection, 40-50% of cats with FIP were found to have concomitant FeLV infections.[9] With elimination of FeLV from many catteries and pet cat households, and the steady decline in the incidence of FeLV in the entire cat population, the proportion of cats with FIP and concurrent FeLV infections has greatly decreased. At the present, virtually all cases of FIP in purebred cattery-bred cats are FeLV negative, and FeLV infection is detected in 10% or less of domestic pet cats.

Many serum antibody tests have been used for diagnosis of FIP.[1,46] Unfortunately, they do not differentiate between cats infected with FECV and FIP, carrier cats and clinically ill animals, or FIPV shedders and nonshedders.[47,48] Antibody tests are only helpful if the clinician understands the serologic responses of cats experimentally infected with FIPV and related FECV.

When specific-pathogen-free, antibody-negative kittens are infected by oral or intratracheal instillation of FIPV, they react serologically in several ways, depending on the dose and strain of virus.[52,55] Some cats do not develop signs of infection after prolonged exposure and remain antibody negative. Infected cats that do not develop signs of illness show a flat antibody response, while cats that develop FIP show a progressive increase in antibody titer. Virus-neutralizing antibodies tend to correlate with immunofluorescent antibody (IFA) titers in both groups of cats.[49] Some infected cats, however, only develop virus-neutralizing antibodies, and IFA titers are negligible.[47]

Serologic responses are much more difficult to interpret in the field because of the great amount of antigenic similarity between FIPV and FECV, and ubiquitousness of FECV infection in nature. Investigators were unable to show differences in antibody specificity of serum from cats infected with FECV or with various high- and low-pathogenicity FIPV isolates.[3] For this reason, serodiagnosis of FIP in the field is fraught with a great deal of inaccuracy. However, currently used serologic procedures still have some usefulness. Immunofluorescent antibody titers $\geq$1:3200 are usually associated with FIP, frequently of the noneffusive type. Titers this high are uncommon in cats infected with FECV but may occur in healthy cats with subclinical or latent FIPV infections. Titers of 1:100-1:3200 are common in cats with effusive FIP and in a portion of cats with noneffusive disease. Unfortunately, IFA titers of 1:25-1:1024 are also seen in many cats that have had previous FECV infections or inapparent FIPV infections. Diagnosis of FIP in cats with titers in this range depends on the entire clinical and clinicopathologic picture. Positive coronavirus titers should alert clinicians to the possibility of FIP, while negative titers are often helpful in ruling it out. However, some cats with pathologically confirmed FIP have been seronegative by IFA, so a negative IFA titer is not always helpful. Seronegative cats are most likely to be younger and have fulminating effusive FIP. For these reasons, current FIP serologic tests should not be used as a sole diagnostic determinant of FIP in individual cats.

Because of the vagaries and nonspecific nature of FIP serology, FIP antibody testing should also not be used as a means to control FIP in catteries. Vast amounts of money are spent each year by cattery owners on FIP testing. In almost all cases, the results are uninterpretable. Virtually all catteries have 50-80% or more coronavirus seropositive cats. Most of the antibody posi-

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tivity is due to FECV strains and not to FIPV, and the tests do not differentiate one from the other. Moreover, antibody titers do not answer the critical questions: Has this cat been infected with FIPV? Will this cat succumb to FIP in the future? Is this cat carrying FIPV? Is this cat shedding FIPV? As a result of misguided test and elimination programs, more pedigreed cats in the United States probably die each year from FIPV antibody testing than from the actual disease. Ultimately, FIP must be diagnosed by clinical signs, clinicopathologic findings, and ante- or postmortem examination of tissues. Serologic testing should only be used as a general guide to diagnosis.

Treatment and Prevention

No treatment has proven uniformly and consistently effective. Cats that develop FIP usually die in 1-16 weeks. Nevertheless, several cats have reportedly gone into remission after treatment with various drugs. Some cats have gone into remission after treatment with tylosin and prednisolone.[7] This has sparked a decade of tylosin use for treatment of FIP. However, tylosin is now known to have no value whatsoever in treatment of FIP, and the fortuitous response in the original cats was probably due to self-cures or the prednisolone. Some cats went into remission after use of prednisolone and phenylalanine mustard or cyclophosphamide.[44] Another cat was successfully treated with prednisolone and phenylalanine mustard.[39] However, such treatments have also proven to be of limited effectiveness. In my experience, <5% of cats go into brief or sustained remission after treatment with immunosuppressive drugs. Successfully treated cats usually had milder illness, and were still eating and not overly debilitated when treated. Owners were also more apt to administer continuous supportive care in the form of fluid therapy, forced feeding and other such attentions. Debilitated animals inevitably die and drug therapy actually hastens their demise.

A number of dubious treatments have been used for FIP. The FIPV is very sensitive to interferons *in vitro*,[83] but these are ineffective *in vivo*. Various immunostimulants and megadoses of vitamins have also been advocated. These are equally ineffective. Spontaneous remission is a complicating factor in evaluating treatment success. Not every cat with FIP dies. Necropsy of older cats without overt signs of FIP has occasionally demonstrated fibrous lesions on the spleen and liver that indicate past FIP infection. Cats with ocular signs and no other systemic manifestations of FIP have occasionally gone into remission with just topical treatment. Cats with chronic fever, enlarged mesenteric lymph nodes that were histologically compatible with FIP, and high coronavirus titers have spontaneously gone into remission without treatment. Finally, small quiescent lesions in the spleen and mesenteric lymph nodes have been discovered in some infected cats during routine ovariohysterectomies. Therefore, it is sometimes difficult to ascertain whether a treatment is successful or if remission was naturally induced.

Currently, no vaccines are available to prevent FIP. Though FIPV immunizes baby pigs against TGE, initial attempts to immunize cats with TGE virus have been unsuccessful.[67,77] Immunization with killed FIPV has also proven uniformly unsuccessful.[34] Immunity derived from killed vaccines almost always renders cats more susceptible to challenge with the virulent live virus, and the resultant disease is usually more severe and fulminating. A genetically engineered vaccinia virus that expressed the envelope protein of FIPV has been recently tested.[87] It enhanced virulent FIPV infection rather than protecting cats.

Several research groups have been experimenting recently on the use of modified-live-virus vaccines for FIP.[86] When such attenuated virus is given oronasally to susceptible cats, a protective immunity against the virulent parental strain has been evoked. Such vaccines hold the best hope for biological control of FIP, but considerably more safety and efficacy testing remains before they can be licensed.

The incidence of FIP within catteries can be decreased by proper management. Mortality tends to increase as the population of animals, especially kittens, increases. Losses from FIP are also proportional to the severity of other kittenhood diseases, including herpesvirus, calicivirus, chlamydial, mycoplasmal, dermatophyte, parasitic and enteric infections. Kittens kept in crowded

catteries with a large number of other young animals suffer greatly from concurrent diseases. These diseases stress the kittens' immune system and are often associated with a temporary decrease in growth rate and an increase in susceptibility to disease in general. Feline leukemia virus infection, a bane of many catteries in the past, is the single most powerful potentiator of FIP in cats. Elimination of FeLV infection from many catteries has decreased the incidence of clinical FIP. Genetics also play an important role in FIP. Fragile strains of purebred cats are often more susceptible to FIP, probably because of decreased overall disease resistance. Death losses from FIP can sometimes be traced to certain breedings, and further breeding of pairs that produced affected kittens should be avoided. Breeding practices in catteries often result in an abundance of younger breeding animals. Younger animals are more apt to be carriers of disease agents than older animals; the carrier state is often only a protraction of acute illness. This is why catteries with breeding cats 4 years of age and older often have less disease than catteries with younger breeding stock.

Infection and Immunity

Immunity to FIPV appears to be largely cell mediated.[49,51,55] Humoral immunity is not protective or, in some cases, enhances disease.[48,49,51,55,72] The type and strength of immunity also determine the disease form (effusive, noneffusive, recovery or asymptomatic carrier state). Effusive FIP occurs in cats that mount a humoral immune response but fail to develop concurrent protective cell-mediated immunity.[55]

The duration of virus persistence in FIPV-recovered cats is not known. The disease can be reactivated in almost all cats within the first 2 months after infection, but not after 4-6 months.[55,80] This situation resembles that seen in latent FeLV infections.[56] Latency in FeLV infection is merely an extension of the recovery process and usually resolves within 6 months of the disappearance of viremia. This appears to be characteristic of many infectious diseases in which cellular immunity is important for recovery; the longer the period after recovery, the more difficult it is to demonstrate persistence of the agent. Immunity to many infections, including FIP, must be a slow, ongoing process that takes weeks, months or years. In some individuals, the agent may persist for a lifetime. In fact, persistence of the organism in the host may be an essential requirement for perpetuation of immunity.[49,55] Indeed, when latently infected kittens eliminate FIPV, they also lose their immunity.[55]

Animal and Public Health Considerations

Feline infectious peritonitis virus is a naturally occurring infection of domestic and wild Felidae. People are not hosts for the virus. Dogs and swine can be experimentally infected with FIPV; a mild to moderately severe TGE-like syndrome occurs in baby pigs.[76] However, it is doubtful that FIPV is a cause of naturally occurring enteritis in these species. Cats that carry FIPV or those with active disease should be considered infectious to other cats. Fortunately, only a very small percentage of cats naturally infected with FIPV ever develop disease. Further, by the time FIP is first diagnosed in a group of cats, the virus is usually well established. In practice, therefore, disease control by quarantine and isolation of individual animals seldom influences the natural course of disease in a group of cats.

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Feline Calicivirus Infection

Cause

The surface of feline calicivirus (FCV) is made up of cup-shaped depressions.[12] The prefix "calici" is derived from the Greek word *kalyx* for cup or chalice.

Feline calicivirus is not inactivated by lipid solvents, such as ether or chloroform. Infectivity is destroyed by heating to 50 C for 30 minutes. It is inactivated at a pH of 3 but becomes more stable as pH values increase. Infectivity is retained for at least 4 years at -65 C.[3]

Pathogenesis

Feline calicivirus causes disease mainly in domestic cats but has also been associated with illness in some wild Felidae.[11] Clinical illness is more common in catteries and multiple-cat households than in single-cat households. Clinical disease is most common in kittens, and in situations in which other infectious diseases are also likely to be problems. Infections with different serotypes probably occur throughout life but are not likely to be of great clinical significance. It is unlikely that many cats escape infection.

Feline calicivirus persists as an active asymptomatic infection in many recovered cats. In some areas, up to one-third of adult cats are silent oropharyngeal carriers. Virus can be isolated from the tonsillar tissues of recovered cats for at least 34 days.[6] Virus is shed almost continuously from the oropharynx by FCV carriers.[10,14] Maternal immunity protects kittens from infection for the first 3-9 weeks of life.[18] Kittens then become susceptible to infection by virus shed in the saliva of asymptomatic or clinically ill animals. Vaccination with live-virus vaccines is also a frequent cause of disease in kittens.[19,20]

The main route of infection is oral and the initial site of infection is the oropharynx. This localized primary infection is followed by transient viremia, with localization of virus in the epithelium of the nasal passages, conjunctiva, tongue, palate or other tissues. A diphasic temperature response follows experimental aerosol infection. The first temperature rise occurs about 24 hours after infection, and the second occurs between 96 and 168 hours. Recovery is rapid thereafter. Following experimental aerosol exposure, virus can be recovered from the conjunctival sac for 7 days, nasal passages and pharynx for at least 2 weeks, feces for 2 weeks, tonsils for 5 weeks and lungs for 10 days.

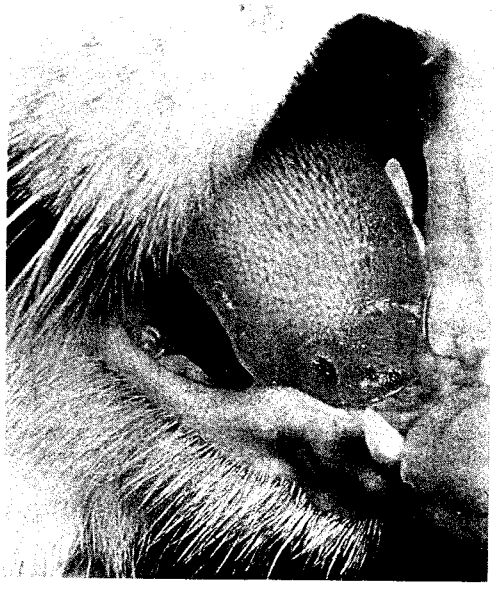
Clinical Features

The predominant clinical signs of naturally occurring FCV infection differ from one report to another. Upper respiratory disease is the principal form of infection described in the literature, but this form has only been partially recreated by massive aerosol exposure.[3] Conjunctivitis is not a common or pronounced feature of experimentally recreated disease and does not persist beyond 13 days. Rhinitis is also uncommon and is most severe by day 6 and disappears by day 10. Small vesicles occur in the palate and tongue of many experimentally infected cats. Vesicles rapidly rupture, leaving shallow erosions (Fig 11). Vesicles and erosions appear toward the end of the disease course and heal rapidly. Focal pneumonia is also a consistent lesion seen in kittens exposed to aerosols. The lungs are mottled with reddish areas of congestion and edema early in the course of infection. After several days, the pneumonic lesions consolidate to form elevated, firm areas in the lung that are pinkish-gray to pale red, have a patchy distribution and usually resolve by day 10.

Recent studies on naturally occurring and experimentally induced FCV infection indicate that upper respiratory disease is not the most common disease manifestation.[9] A transient fever associated with shifting lameness, and lasting 24-72 hours, is a far more common presentation. Oral ulcers are somewhat less frequent.

Caliciviruses have been isolated from feces of pound kittens undergoing epizootics of diarrhea. Though caliciviruses are asso-

Figure 11. Lingual ulcerations associated with acute calicivirus infection. (Courtesy of Dr. R.C. Povey, Langford, Inc, Guelph, Ontario)



ciated with so-called outbreaks of winter dysentery in people, their role in epizootic diarrhea in kittens remains to be determined.

The role of other disease agents in potentiating FCV infection and *vice versa* should not be underestimated. In a study of synergism between FCV and feline panleukopenia virus infections, mortality of 82% was observed in kittens infected with FCV and panleukopenia virus at the same time.[1] In contrast, mortality was only 10% in feline panleukopenia virus-infected cats and only 5% in cats infected with FCV alone. Feline herpesvirus type 1, *Mycoplasma, Chlamydia* and bacteria are all involved in kittenhood infections. The resulting syndromes are often caused by combinations of these and other disease agents.

The role of persistent calicivirus infections in chronic oral cavity disease (gingivitis, periodontitis, stomatitis) of cats is an area of interest. Australian researchers were the first to describe a high incidence of oral calicivirus in cats with chronic gingivitis and stomatitis.[13] Eight of 10 affected cats were culture positive, while 10 healthy controls were negative. Calicivirus infection was linked with FIV infection and chronic stomatitis in cats in the United Kingdom.[7] Seventy-nine and 92% of British cats with stomatitis in 2 different study groups were FCV infected, as compared to 19% of healthy appearing animals. However, 81% of the cats with stomatitis and 16% of the healthy cats were also infected with FIV. In a study of the relationship between gingivitis, periodontitis and stomatitis and chronic calicivirus or FIV in a household of 69 domestic cats in northern California, 27 of the cats had normal mouths and 42 had oral disease ranging in increasing severity from gingivitis (19 of 42), gingivitis and periodontitis (16 of 42), stomatitis and/or cheilitis (5 of 42), and gingivitis, periodontitis and stomatitis and/or cheilitis (5 of 42). Seventeen of the cats were chronic oral carriers of FCV, and 11 were persistent FIV carriers. Of these 28 carrier cats, 4 were coinfected with both viruses. Cats with FCV infection were no more or less likely to have oral disease than FCV-uninfected cats. However, all 11 of the FIV-infected cats had some degree of oral disease. Therefore, it appears that FCV infection alone is not a major cause of chronic oral disease in cats.

Pathologic Features

Focal, interstitial pneumonia is the most consistent lesion seen in experimental disease; rhinitis and conjunctivitis are uncommon and mild when present.[6] Fatal pneumonia is almost always due to complicating secondary bacterial invasion.[3]

Glossal and palatine ulcers are common in both experimental and naturally occurring disease.[4,6] Ulcers have rarely been observed on the footpads and perianal region.[8] The ulcers are derived from fluid-filled vesicles (2-5 mm in diameter) in the epithelium. Oral lesions are more apt to be seen in kittens eating abrasive dried food than in kittens consuming soft canned food.[4]

The cause of the characteristic limping is unknown. Nerves, muscles and joints appear microscopically normal.[9] The number of macrophages in synovial fluid is often increased, however. These macrophages may contain virus-antibody complexes.[19]

Clinicopathologic Features

FCV can be easily isolated on tissue culture from oral swabs of diseased and carrier cats, and from the blood of clinically ill animals.[9] The limping syndrome is associated with moderate to extreme increases in synovial fluid macrophages. The carpal and tarsal joints are most severely affected.

Treatment and Prevention

Fever, joint and muscle pain, and glossal and palatine ulcers disappear within 48-96 hours. Pneumonia, which is an uncommon sequela in nature, is usually due to secondary bacterial invasion of primary viral leions. Likewise, purulent nasal and ocular discharges are almost always associated with complicating bacterial, chlamydial or mycoplasmal infections. Antibiotics are valuable to counteract secondary infections. Though early reports of FCV infection emphasized the seriousness of the disease, the mortality of uncomplicated FCV infection is very low.[9,18]

Because it is virtually impossible to eliminate carrier cats from the environment, control of FCV infection is largely by vaccination. However, FCV can exist in many cat populations without causing serious problems.[18] Concurrent disease, stress and other factors may combine to potentiate disease severity in certain outbreaks.

Though current vaccine strains produce various degrees of cross-protection, the protection they afford is not necessarily against all field isolates.[9,19] The ease with which vaccine-resistant strains can be isolated from catteries indicates that serologic differences are more important than recently believed and immunization less effective than reported.

The effect of long-term calicivirus vaccination on the FCV carrier state was recently questioned. Feline caliciviruses have been isolated with the same frequency from the oral cavities of normal cats today as they were before vaccination was started over a decade ago.[19] The frequency of calicivirus isolation from cats with respiratory infections may even be higher today than in the past.[17] Caliciviruses have been isolated from the oral cavities of 20-30% of normal cats in catteries where vaccination is routinely practiced.[7] It is uncertain whether the strains in catteries are different from the vaccine strains, or if they are identical. It appears certain that both occur. Observations such as these bring into question the benefit of live-virus calicivirus vaccine programs in catteries as well as the general cat population.

Infection and Immunity

Feline calicivirus persists in the oropharynx of many cats and is actively shed in the saliva even with systemic immunity.[15-17] Carrier cats can be classified as low-, medium- or high-level virus shedders.[16] Susceptible cats can be infected in 2-3 days by high-level shedders, and in 11-13 days by low-level shedders. Unlike feline herpesvirus (rhinotracheitis), shedding is not influenced by stress.[16]

Maternal antibodies to FCV have a half-life of 15 days and persist in the serum of kittens for as long as 14 weeks.[5] Antibodies are virus neutralizing and very strain specific, especially when collected soon after infection. Maternal immunity to FCV appears to be incomplete.[2-4] Kittens with maternal immunity can often be infected as young as 3-9 weeks of age.[4,15,18] Even though virus can be isolated from the oropharynx, clinical signs and an active humoral immune response do not occur until maternal immunity declines several weeks later.[4,18] At this point, clinical signs are inapparent or relatively mild, and the resultant primary immune response develops slowly and reaches lower levels than in kittens free of maternal immunity at exposure. In contrast, kittens with very low maternal maternal titers rapidly become ill after infection and the disease is more severe.[4] The immune response also comes on more quickly after infection and reaches higher levels. Maternal immunity may lessen severity of disease in situations with a high level of exposure that occurs early in life.[18] In a small cattery where many of the cats were carriers, kittens showed few signs of illness due to FCV, even though they all became infected at an early age.

Animal and Public Health Considerations

Feline calicivirus is only infectious to domestic and some wild Felidae. It is not a human pathogen.

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Feline Leukemia Virus Infection

Cause

Feline leukemia virus (FeLV) was first identified in cats from a household that had lost several animals to lymphosarcoma.[34] In 1973, an indirect fluorescent antibody (IFA) test was developed that accurately detected viremia in infected cats.[22] The test was rapidly applied to clinical use, mainly as a diagnostic procedure for lymphosarcoma. As a result of clinical testing, FeLV was determined to be: horizontally spread from cat to cat; associated with a great many diseases other than lymphosarcoma; and carried and shed by many apparently healthy cats for long periods before illness developed.[5,9,18,21,24]

Feline leukemia virus does not survive long outside the cat.[12] It loses its infectivity within minutes or hours at room temperature. Some strains even lose considerable infectivity when stored at -70 C. Feline leukemia virus is destroyed within minutes at 56 C and is sensitive to most disinfectants.

Pathogenesis

Feline leukemia virus infects domestic cats throughout the world. Wild cats do not harbor the infection but can be infected when exposed to domestic cats. The incidence of infection is directly related to population density; rural cats have the lowest infection rate and affected cattery or multiple-cat household cats have the highest.[10,60] Urban areas, where many cats live in apartments, condominiums and tenement houses and are still allowed to roam outdoors also have a high incidence of infection.[8] Cats that live their life entirely within high rise apartments, as in New York City, have a very low incidence of infection.[21] These cats are rarely allowed to roam outdoors and have very little exposure to infected animals.

Feline leukemia virus is carried and shed by healthy, subclinically ill or chronically ill cats. In catteries with enzootic FeLV infection, about one-third of the cats are active carriers and shedders.[21,24] The incidence of active carriers in rural areas may be less than 1%, while in most high-density urban and suburban areas the incidence is 2-6%.[31,60] Infected cats have very high levels of virus in their blood and shed almost equal amounts in their saliva.[13,27] Smaller amounts of virus are also found in urine and feces.[27] Tears contain levels of virus about equal to blood levels.[25]

There are 2 basic routes of infection: horizontal via the passage of virus from infected to susceptible cats, and *in utero* from infected queens to their fetuses.[17,24] Though *in-utero* infection results in fetal or neonatal death in 80% of affected queens, 20% of kittens born to FeLV-infected mothers may carry the infection into later life.[48] Queens that have recovered from FeLV infection usually provide their offspring with maternal antibodies that protect them against infection in the first 12 weeks or so of life.[33]

Cats are exposed when they come into contact with infected animals, either while roaming outdoors or when infected and susceptible animals are housed together indoors. In Glasgow, Scotland, the infection rate among free-roaming cats increased progressively with time, and by 3-8 years of age, most cats had been exposed to the virus.[60] Active FeLV infections are uncommon in cats 10 years or older. Cats usually contract the infection early in life and recover or die before they reach later life.

Horizontal spread of FeLV infection requires prolonged intimate contact between cats. The reasons for this are the low stability of the virus in nature, the relatively large dose of virus required to infect by the oral route, and age resistance. Prolonged intimate exposure allows virus spread by mutual grooming and sharing of litter pans. A simple wire partition between cats is sufficient to prevent cross-infections if there is no physical contact between cats or their excretions. Bite wounds are an efficient mode of transmission because a large amount of virus can be injected directly into the body. Infection can also be spread via blood transfusions and reuse of dirty instruments for sequential surgeries.

Resistance to FeLV infection increases with age.[28] Following infection, 70-100% of neonates become persistently viremic for life. Kittens 8-12 weeks of age are much more resistant, and only 30-50% become persistently viremic following exposure.[53] Less than 10-20% of adolescent or adult cats become persistently viremic, and then only after exposure lasting as long as 1.5 years.[15] Age resistance can be virtually abolished by pretreating older cats with corticosteroids at the time of infection.[63] Presumably, natural forms of stress may do the same thing.

Following oral or oronasal instillation, the virus first replicates in regional lymphoid tissue of the oropharynx.[62,64] Virus can be detected within several days in a few circulating mononuclear cells in the blood. These cells apparently carry virus to the target organs in other areas of the body, such as the spleen, lymph nodes, and epithelium of the intestine, bladder and salivary glands. About the same time that virus appears in secretion or excretions from these organs, it also reaches cells in the bone marrow and appears in peripheral blood leukocytes and platelets. Viremia in weanling kittens seldom occurs sooner than 2-4 weeks after infection.[32,53] Viremia and virus shedding persist for less than 1-16 weeks in 70-90% or more of cats.[53] However, when viremia disappears, it usually does so in the first few days or weeks. Cats that remain viremic after 16 weeks usually remain persistently viremic for life, though on occasion viremia disappears after many months or years. Virus shedding usually stops when viremia disappears.[32] In a few instances, virus continues to be shed in tears, urine, milk or saliva for several weeks or months after cessation of viremia.[32,40,48] Eventually, however, even this virus shedding ceases.

Following recovery from viremia, virus persists as a latent infection in the bone marrow.[43,51,65] After 6 months, however, even latent infections become hard to demonstrate in most recovered animals.[51] In this regard, latency appears to be merely an extension of the postviremia recovery process for most animals. However, a small proportion of recovered cats may harbor infectious virus in a latent form for years and become viremic again months or years later. Latent infections can sometimes be converted to active infections by giving the cat glucocorticoids during the immediate postviremic period.[51,56,65] However, activation is very strain dependent, and latent infections with most field strains are activated only with difficulty.[51] Reactivation of latent infections can occur spontaneously up to 6-8 months following recovery in less than 10% of recovered cats.[51]

Most mortality resulting from FeLV infection occurs in persistently viremic cats.[44] Disorders associated with the persistently viremic state can be divided into several categories: *in utero* and neonatal deaths of kittens; lymphoid and myeloid neoplasms, aplastic or hypoplastic anemia, neuropathies or quasi-neoplastic syndromes; secondary or opportunistic infections due to acquired immunodeficiency; and immunologic disorders.

Clinical Features

Feline leukemia virus infection has 2 main clinical stages.[53] The initial stage occurs 2-6 weeks following infection and corresponds to the appearance of virus in the blood, saliva, urine and feces for the first time. This state of the disease is manifested by varying degrees in severity of fever, malaise, generalized lymphadenopathy, leukopenia, thrombocytopenia and anemia. These signs usually persist for 1-16 weeks before all clinical abnormalities disappear. Death is uncommon during this primary stage of disease; when it occurs, it is usually a consequence of sepsis, hemorrhage and anemia. These disorders are usually a result of profound leukopenia, thrombocytopenia and anemia.

Cats that survive the initial stage of infection make a real (true) or apparent (false) recovery.[53] True recovery is manifested by disappearance of virus from the blood, and eventually from other tissues as well. Cats that make an apparent or false recovery appear outwardly normal but remain persistently viremic for life. As a rule, cats that show either mild or inapparent signs during the initial stage of infection are usually among those that make a true recovery. The more severe the clinical signs are during the initial stage of infection, the more likely that the cat will become persistently infected.[53]

Cats that make a true recovery following initial infection usually suffer none of the long-term complications associated with FeLV infection. There is one exception, however. Completely recovered cats still suffer a higher incidence of lymphoid tumors than cats that never were infected.[11] This increased incidence is much less than in persistently viremic cats.

The secondary stage of FeLV occurs months or years after the primary stage and is heralded by the appearance of some FeLV-related disease. The secondary stage is ultimately terminated by death within 1-12 months. Mortality among persistently viremic cats is progressive and relentless, and averages about 50% each year that the cats remain infected. Therefore, most FeLV-infected cats die within 3 years.[44]

FeLV-related disease is either a direct consequence of infection (reproductive problems, lymphoid and myeloid neoplasms, miscellaneous neoplasms, aplastic or hypoplastic anemia, neuropathies or quasi-neoplastic syndromes) or an indirect consequence (immunodeficiency, immune-mediated disorders) of the virus infection itself.

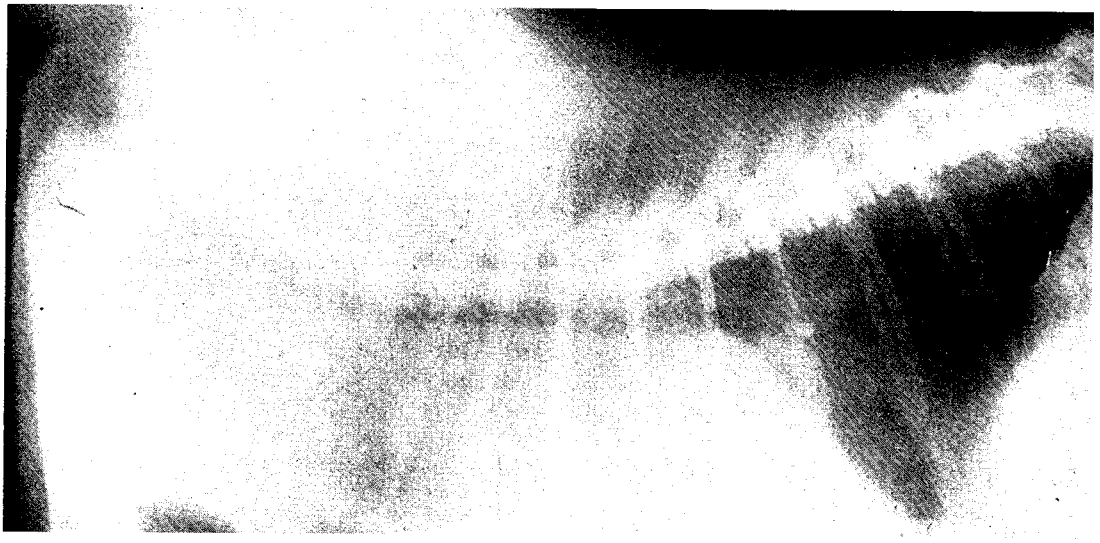
Reproductive problems in infected queens have been widely recognized but poorly documented. Abortion, fetal resorption, stillbirths and neonatal deaths occur in over 80% of viremic queens. However, some kittens are born apparently healthy, but are viremic and carry this viremia into later life. The cause of fetal losses has not been well studied. Virus can be recovered from most fetal tissues and the placenta.[30]

About one-half of FeLV infected cats die of cancer. Cancers related to FeLV-infected cats are of 3 types: lymphoid, myeloid or miscellaneous. Lymphoid tumors account for one-half to two-thirds of the FeLV-related cancer, myeloid tumors (often called myeloproliferative disease) account for about one-fourth to one-third, and miscellaneous cancers for the remainder. Most FeLV-related cancers occur from several months to 3 years or more following infection, and are usually seen in cats less than 6 years of age.[11]

Lymphoid neoplasms can be solid (lymphosarcoma) or more diffuse, with involvement of the blood (lymphocytic leukemia). FeLV-induced lymphosarcoma has been classified as multicentric, thymic, alimentary or miscellaneous.[16] Multicentric lymphosarcomas tend to occur in cats around 4 years of age, and about 90% are associated with FeLV. Thymic lymphosarcomas occur in cats around 2.5 years of age and about 80% are associated with FeLV. Alimentary lymphosarcomas are common in older cats but only about 25% of these cats have active FeLV infections. Miscellaneous lymphosarcomas involve the skin, eyes, kidneys or nervous system. Ocular and neural lymphosarcomas are usually associated with FeLV infection, whereas renal and dermal lymphosarcomas occur more often in FeLV-negative cats. Less than one-third of cats with lymphosarcoma have leukemia (abnormal lymphoid cells in the blood). Leukemia can occur with any of the solid forms of lymphosarcoma but is most frequently associated with multicentric disease.[16] However, some cats may have only blood and marrow involvement.

Cats with thymic lymphosarcoma usually show acute dyspnea and pleural effusion. Abnormal lymphoid cells may be detected in the pleural fluid. Grossly, the thymus often fills the entire cranial thorax and can encircle the heart (Figs 12, 13). Multicentric lymphosarcoma is often manifested by various combinations of generalized lymphadenopathy, anemia, hepatosplenomegaly and renal involvement; abnormal lymphocytes are often seen in the blood and/or pleural effusions. Neural lymphosarcoma is most commonly manifested as acute posterior paresis or paralysis (Fig 14). Generalized CNS disease or more focal peripheral nerve palsies are less commonly observed. Ocular lymphosarcoma can occur by itself or in association with other forms of the disease. Ocular lymphosarcoma is the most frequent

Figure 12. Lateral thoracic radiograph of an FeLV-infected cat with thymic lymphosarcoma. Note the lack of lung detail cranial to the heart, characteristic of a thymic mass. (From *Virus Infections of Carnivores*, Elsevier Science Publishing)



tumor in the eyes of cats and can involve the orbit, nictitating membrane, conjunctiva, cornea, fundus or iris and ciliary body (Fig 15).[71]

Myeloproliferative neoplasms arise from primitive stem cells, granulocytic precursors, erythroid precursors, or less commonly from megakaryocytes. Collectively, these myeloid cancers are called myeloproliferative diseases.[3,16,26] They tend to be seen during the first 6 years of life, with a peak incidence around 4 years of age. Abnormal cells often appear late in the course of disease and the initial clinical signs are usually referable to anemia, hepatosplenomegaly and sometimes icterus. About 70% of animals with myeloproliferative disease are persistently FeLV infected.

Myeloproliferative diseases have been classified into the following types: reticuloendotheliosis; erythremic myelosis; erythroleukemia; myelogenous leukemia; megakaryocytic leukemia; and myelofibrosis.[16] Reticuloendotheliosis is characterized by primitive undifferentiated stem cells in the blood and bone marrow.[14] Erythremic myelosis is a disorder characterized by an increased number of nucleated RBCs without a corresponding increase in more differentiated reticulocytes. The granulocytic cell series is normal. Erythroleukemia is similar to erythremic myelosis except that both immature erythroid and myeloid cells are present in the blood. Myelogenous leukemias induced by FeLV usually arise from precursors of polymorphonuclear neutrophils or monocytes. Eosinophilic, basophilic and mast-cell leukemias are not FeLV-associated disorders. Megakaryocytic leukemia is an uncommon disease manifested by an increase in megakaryocyte and platelet numbers. Myelofibrosis is a terminal state of myeloproliferative disease manifested by marrow hypoplasia and fibrosis.

Figure 13. At necropsy, the thymic tumor filled the cranial thoracic cavity and had invaded the pericardium. (From *Virus Infections of Carnivores*, Elsevier Science Publishing)

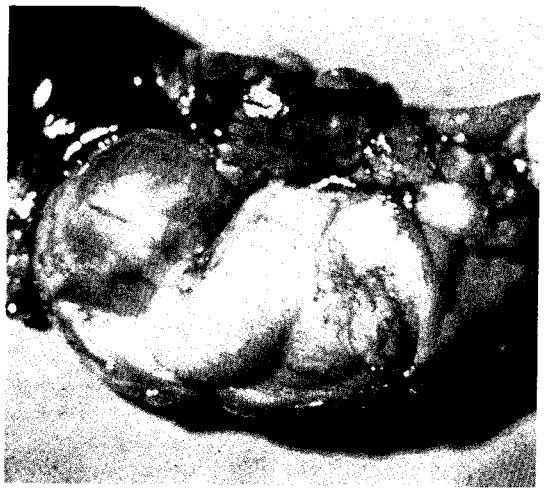
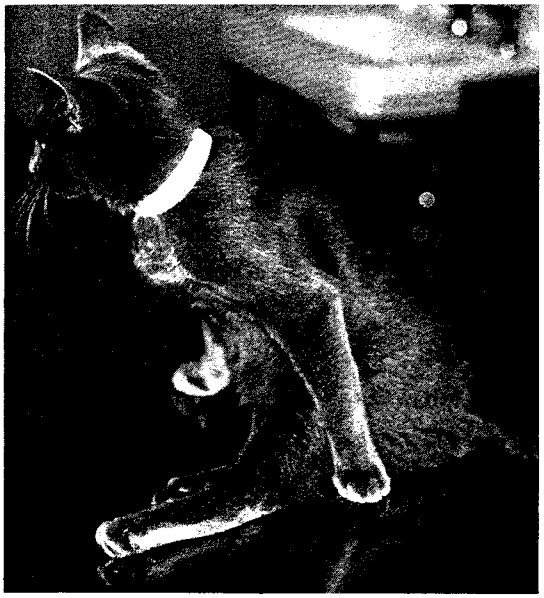


Figure 14. Acute hind limb paralysis in an FeLV-infected cat. Necropsy revealed focal lymphosarcoma of the spinal cord dura mater. (From *Virus Infections of Carnivores*, Elsevier Science Publishing)



There are several miscellaneous quasi-neoplastic or neoplastic syndromes associated with the FeLV carrier state. Though uncommon, they are very flamboyant in clinical expression. Multiple cartilaginous exostoses are seen in younger FeLV-infected cats.[55] Multiple firm pea- to egg-sized growths occur on flat bones of the skull, ribs, scapula, spine and long bones of the limbs. The growths are basically chondromas. Affected cats slowly waste away and die. Benign cutaneous keratin horns on the footpads have also been associated with chronic FeLV infection.[4] They probably represent overgrowth of keratinocytes, similar to the hyperplasia of chondrocytes seen in multiple cartilaginous exostoses. Multicentric rapidly growing fibrosarcomas almost always occur in FeLV-infected cats.[19] A cell-free extract of these tumors induces the same type of tumors when inoculated into susceptible cats. The tumor extract contains two types of viruses, an intact replication-competent FeLV and a replication-incompetent mutant FeLV. This mutant FeLV, called feline sarcoma virus (FeSV), arises within a very small proportion of FeLV-infected cats as a result of genetic recombination between FeLV and normal cat genes. These normal cat genes, called oncogenes, are important for differentiation of cells during embryogenesis. When these genes are incorporated into FeLV, however, they become activated and cause uncontrolled cell differentiation and a fibrosarcoma. Olfactory neuroblastoma, a rare tumor of the brain and nasal cavity of cats, also appears to be an FeLV-related disorder.

Figure 15. Iridal lymphosarcoma in an FeLV-infected cat. (Courtesy of Dr. Ned Buyukumihci, University of California)

Aplastic and hypoplastic anemias are common in chronic FeLV carriers and account for about one-fourth of all FeLV-related deaths. Aplastic anemia is characterized by progressive anemia and subsequent death. More commonly, the anemia is hypoplastic rather than aplastic and the RBC count hovers at a low level for weeks or months, or may also rise or fall in increments. If anemic cats live long enough, many develop myeloproliferative disease. In fact, anemia almost always precedes clinical expression of tumor cells by weeks or months.[53] Anemia is not always the sole abnormality in cats with hypoplastic or aplastic bone marrow. Thrombocytopenia and granulocytopenia are frequent accompanying features. Cats with hypoplastic or aplastic anemia do not usually show clinical signs until the anemia becomes severe. Listlessness, pallor of the mucous membranes and occasionally jaundice are the signs most noticeable to the owner. Hepatomegaly and

splenomegaly are usually detected on physical examination.

Neuropathies are infrequent but important features of chronic FeLV infection. Cats with neuropathies may have no histopathologic abnormalities or may have sparse focal lymphocytic infiltrates into peripheral nerves or the spinal cord. Persistent unilateral mydriasis (anisocoria) in the absence of blindness or intraocular disease is the most common neuropathy seen in FeLV-infected cats (Fig 16). The anisocoria is due to involvement of the short ciliary nerve innervating the muscles of the iris. Urinary incontinence may be another manifestation of neuropathy in infected cats. Of 11 cats with urinary incontinence, 9 were FeLV infected.[2] The cats responded poorly to conventional therapy for urinary incontinence and no lesions were seen on histologic examination of 4 cats necropsied. Some cats with neuropathies show vague pain or hyperesthesia over the spine, or posterior paresis. Acute demyelinating myelopathies have also been seen in FeLV-infected cats.[18]

All of the aforementioned disorders are caused by the direct effect of the virus on certain cells of the body. In contrast, the remaining disorders are indirectly related to FeLV infection and occur because of more complex interactions of the virus and host tissues. Disorders that are indirectly related to the infection are either infectious disease potentiated by FeLV-induced immunosuppression or immune-mediated diseases. Viral diseases potentiated by FeLV include feline infectious peritonitis (FIP) and upper respiratory infection. In the past, about 40% of cats suffering from FIP had concurrent FeLV viremia.[5,47] This relationship is not nearly as common as it used to be, due mainly to a great reduction in the incidence of FeLV infection in catteries and other multiple-cat households. The precise mode of FeLV-induced enhancement of FIP virus infection is unknown, but it appears to be very selective.[49] Severe and intractable rhinotracheitis virus infections have been seen in some FeLV-infected cats, especially debilitated or bone marrow-suppressed animals (Fig 17). FeLV-infected cats also have a higher incidence of viral upper respiratory disease than uninfected cats.[2]

Figure 16. Anisocoria in an FeLV-infected cat. The right pupil did not constrict upon exposure to light.

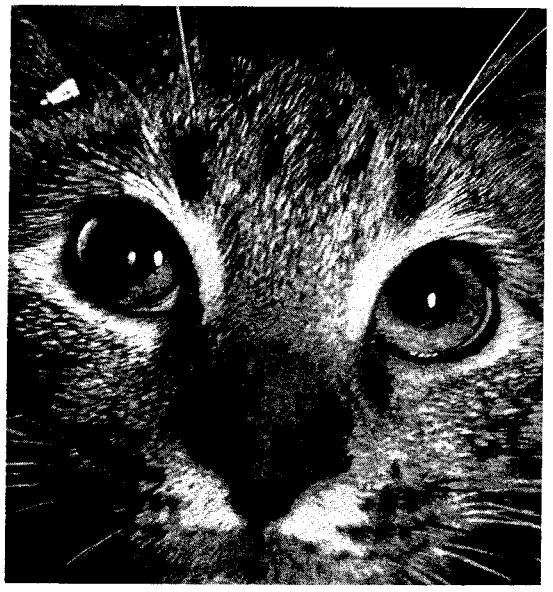
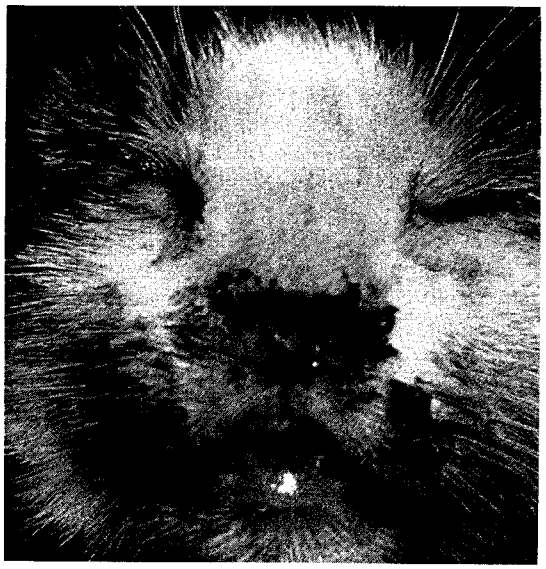


Figure 17. Intractable herpesvirus type-1 infection in an FeLV-infected cat. Squinting is from painful keratoconjunctivitis. The nares are occluded by exudate from herpesvirus-induced rhinitis.



Cats infected with both FeLV and FIV in nature appear to have more severe illnesses than cats naturally infected with either virus alone.[73] FeLV infection was a potentiating cofactor for experimentally induced FIV infection.[74]

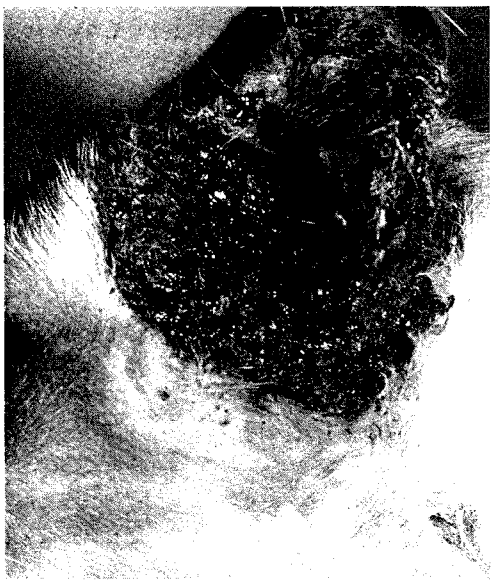
Protozoal diseases enhanced by chronic FeLV infection include toxoplasmosis and hemobartonellosis. Toxoplasmosis is usually not associated with disease in healthy cats

over 8-12 weeks of age, and when it occurs in older animals underlying immunosuppression should be considered (see section on toxoplasmosis).[7] *Hemobartonella felis*, the causative agent of feline infectious anemia (FIA), exists as a subclinical infection in many normal cats. About 50-70% of cats clinically diagnosed with FIA are FeLV infected.[45] Many of these cats have preexisting hypoplastic anemia, or lymphoproliferative or myeloproliferative disorders, so *Hemobartonella* treatment does not always correct the anemia.[57]

FeLV-infected cats have an increased frequency of acute and chronic bacterial diseases.[20,59] Depending on the study, 30-50% of atypical bacterial infections of cats are FeLV associated. Most bacterial diseases occur in cats with subnormal peripheral WBC counts and, as such, a deficiency of phagocytes may be an important underlying cause. However, some FeLV-infected cats also have diminished antibody responses to bacterial antigens.[48] This may contribute to secondary infections. Low-grade proliferative gingivitis is seen in some FeLV-infected cats. Isolated tooth root abscesses and purulent otitis externa are also frequently related to FeLV infection (Fig 18). Peracute enterocolitis (panleukopenia-like syndrome) can be the ultimate cause of death in FeLV-infected cats with myeloproliferative diseases and low WBC counts, or in cats with suppressed cellular and humoral immunity.[58,59] Recurrent abscesses or abscesses that fail to heal normally are frequently associated with chronic FeLV infection. A peculiar necrotizing pneumonia caused by a saprophytic Gram-negative bacterium called EF4 occurs mainly in FeLV-infected cats.

Many immune-mediated diseases are associated with chronic FeLV viremia. Immune-mediated diseases in FeLV-infected cats have 2 major causes: high levels of antigen-antibody complexes circulating in the blood; and interference with normal immunoregulation and autoantibody formation. Immune-complex diseases in FeLV-infected cats are manifested in a number of ways. Many FeLV-infected cats have such vague signs as unthriftiness, episodic depression and minor neurologic problems associated with fine muscle tremors. These signs usually have no histopathologic basis but often subside with continuous use of small doses of corticosteroids. Severe polyneuropathy and myopathy are infrequently associated with FeLV infection. Affected cats develop severe muscle atrophy and myasthenia. This polyneuropathy/myopathy may be due to immune-complex disease.

Figure 18. Severe bacterial infection of the external ear and pinna in an FeLV-infected cat.



About one-third to one-half of cats with autoimmune hemolytic anemia and thrombocytopenia are chronically infected with FeLV. FeLV-related hemolytic anemia in cats is often a prelude to lymphosarcoma or myeloproliferative disease.

Chronic progressive polyarthritis is another disorder potentiated by FeLV infection; about 20% of cats with this disease are FeLV carriers.[52] Chronic progressive polyarthritis is an acute, febrile polyarthritis resembling Reiter's disease in people or a low-grade destructive joint disease resembling human rheumatoid arthritis. The disease is partially responsive to immunosuppressive drug therapy. The precise role of FeLV in chronic progressive polyarthritis is unknown. The disease occurs only in male cats, and all of these cats tested were also infected with feline syncytium-forming virus.

Pathologic Features

Pathologic and histopathologic changes in FeLV-infected cats are as numerous and

diverse as FeLV-related diseases themselves. For this reason, only the salient pathologic features of FeLV-related diseases will be discussed, such as bone marrow dyscrasias, lymphoid and myeloid neoplasms, lymphadenopathy and glomerulonephritis.

Bone marrow abnormalities are seen during the primary phase of the disease, when the host and virus interact for the first time, and in the secondary phase of the illness that occurs months or years later in chronically viremic cats.[53] Anemia, thrombocytopenia and leukopenia in the primary phase of the illness are associated with bone marrow hypoplasia and dysplasia. Anemia later in the course of the disease can have numerous causes.

Lymphoid neoplasms in FeLV-infected cats are comprised of solid masses of cells ranging in maturity from immature lymphoblasts to mature lymphocytes.

Myeloid neoplasms usually originate in the bone marrow and invade the spleen, liver and other tissues to a lesser extent. Myeloid tumors are usually preceded by bone marrow dysplasia or hypoplasia.[53] This suggests that neoplasia is secondary to problems associated with bone marrow maturation. Malignant cells are usually present in the marrow for weeks or months before they appear in the blood. In terminal stages, abnormal cells are released into the marrow in large numbers. The terminal appearance of abnormal cells in the blood of cats with myeloproliferative disorders is reminiscent of the acute blast-cell crisis in leukemic people.

Generalized lymphadenopathy is common in FeLV-infected cats. It is particularly pronounced in the primary phase of infection in younger cats.[53] Lymph nodes may become 0.5-2 cm or so in diameter during this phase, and the increase is due to a reactive lymphoid hyperplasia. Lymphadenopathy in the later stages of infection is frequently due to lymphoid neoplasia.

Clinicopathologic Features

Feline leukemia virus infection is diagnosed by assaying for viral antigens in the blood, by IFA or ELISA tests, or by more laborious tissue-culture isolation procedures from plasma or blood leukocytes. Viremic cats have high levels of viral proteins in their plasma and within the cytoplasm of peripheral blood leukocytes and platelets.

If properly conducted, the IFA test has a high degree of accuracy. False positives are relatively infrequent. However, the IFA procedure is cumbersome to run. It also suffers from a low percentage of false negatives caused by blood smears with inadequate numbers of infected platelets and leukocytes, or by absence of virus in blood cells.

The ELISA is currently the most widely used test for FeLV detection.[36,41,42] The ELISA is simple to run and requires a very small amount of serum or plasma. It has been also adapted for use with tears and saliva.[25,40] Tear or saliva tests detect only about 90% of serum-positive animals and should be used only for rapid or mass screening purposes. ELISA is very sensitive and specific if run properly. However, if the washing steps are not carefully and properly done, or if badly hemolyzed serum or whole blood is used, false positives can occur. This is probably the greatest single weakness of the procedure, but it can be virtually eliminated by proper wash techniques and avoidance of whole blood and hemolyzed serum.[42]

Latent FeLV infection cannot be detected by either ELISA or IFA staining.[51] To detect a latent infection, bone marrow cells must be cultured *in vitro* for up to 6 weeks.[43,51,65] Latent FeLV infections are very uncommon in the cat population, are not associated with illness, and only last for several weeks or months after recovery from initial infection. Therefore, there are no good clinical reasons for testing for latent infections.

Treatment and Prevention

Treatment for FeLV infection is directed at the viral infection itself, and the specific and varied FeLV-related diseases that occur as a result of infection. Treatment of the infection itself has been difficult. Ultimately, control of the infection is totally dependent on the host's ability to mount and sustain an effective immune response. Once the infection becomes persistent, however, the likelihood for eventual self cure is very low. Various immunostimulants, megadoses of multivitamins or vitamin C, and a great number of strange concoctions and proce-

dures have been claimed as cures for FeLV infection; however, none has proven effective. Interferon preparations inhibit the virus in cell cultures, but do not seem to affect the disease in the animal.[70,72] Staphylococcal protein A reportedly cured FeLV infection and/or FeLV-induced tumors in some cats.[6,35,38,70] Anecdotal reports on this treatment were made between 1980 and 1985, but no reconfirmation has appeared since that time and large-scale clinical trials were never conducted. Antiretroviral drugs, such as azidothymidine (AZT), have been used to treat FeLV infection.[29] These drugs inhibit virus replication in the body, but are only effective while they are given, and their toxicity can be severe with chronic use. Many new antiretroviral drugs are under development and testing for treating human AIDS, and some of these drugs may be someday applied to treatment of FeLV-infected cats.

The course of infection in healthy, persistently viremic cats can be influenced by a number of stressful situations. Infected cats living in high-stress, multiple-cat households are more apt to develop complicating disease than cats in single-animal households. Surgical procedures, such as ovariohysterectomy, castration or declawing, can sometimes precipitate crises in otherwise healthy carrier cats, so such procedures should be done with as little stress as possible. Boarding, changes in home environments and other such activities may also shorten the lives of some infected animals. Therefore, it is important to maintain infected cats in environments as free from stress and disease exposure as possible.

Treatments for specific FeLV-related diseases are as varied as the diseases themselves. Lymphoid cancers can be treated with chemotherapy with a reasonable chance for remission but not a cure. However, myeloid cancers respond poorly to treatment. Some secondary infectious diseases, such as hemobartonellosis, tooth infections, abscesses and ear infections, are treatable; others, such as FIP, are not. Immune-mediated disorders, such as autoimmune hemolytic anemia or thrombocytopenia, can be successfully treated with corticosteroids. Cats with aplastic anemia can be kept alive for weeks or months with blood transfusions.

Many FeLV-infected cats suffer from cycles of vague illness manifested by depression, anorexia, vague nervous twitches and weight loss. Such cats benefit greatly from intermittent small doses of glucocorticoids.

Prevention and control of FeLV have been based on routine testing and elimination of carriers.[17] These procedures have been extremely effective in eliminating FeLV infection from confined cat populations, such as in catteries or other multiple pet-cat households. Though testing and elimination have controlled infection in cattery cats, they have had less impact on the spread of disease in the general cat population. In relatively free-roaming cat populations, FeLV infection still remains an important disease.

Testing and eradication consist of 7 steps: test all cats for FeLV infection; remove all FeLV-infected cats from the household; clean all dishes, litter pans and bedding with hot water and soap, and wait 10 days before introducing any new cats; prevent movement of cats in or out of the cattery; retest all quarantined cats 12 weeks after the first test to detect any cats that might have been incubating the infection; lift the quarantine when all cats in the cattery have tested FeLV negative in 2 tests done 12 weeks apart; and test all new cats for FeLV before introduction into the household.[17] In addition, owners of free-roaming cats must be made aware that many cats in the surrounding environments may also be carriers. In this situation, decontamination of the home environment may be of minor importance as compared to limiting direct-contact exposures. Using widespread test and removal, the Dutch have decreased the incidence of FeLV infection among the general cat population in the Netherlands from 9.0% to 3.4% between 1974 and 1985.[69] The incidence in purebred catteries was decreased from 11.5% to 0% between 1974 and 1984.[69] This same pattern of decreasing FeLV infection has also occurred in the United States. Because FeLV infection is so severe when it is introduced into confined cat populations, vigilance by cattery and multiple-cat household owners will be required for as long as the disease continues to exist as an enzootic infection among outdoor cats.

The first vaccine for FeLV infection was marketed in the United States in 1985 (Leukocell: Norden).[67] Two new inactivated whole FeLV vaccines have also been marketed in the United States (Covenant: Diamond Laboratories, VacSyn: Synbiotics). Several more vaccines are at various stages of development and licensing, and will undoubtedly appear on the market in the next few years. Independent efficacy and immunogenicity tests of vaccines currently on the market by the author and other laboratories have not been as positive as tests reported by the manufacturers.[46,48,50] Manufacturers' efficacy claims for FeLV vaccines range from 80% to 90% or more, while independent tests (using USDA test procedures) by the author showed them to be 17-40% effective.[48] One vaccine, tested under natural exposure conditions, was 62% effective.[75] A second group tested the vaccine in essentially the same manner and found it to be totally ineffective.[76] A proportion of cats vaccinated with these products in the field have subsequently become FeLV infected when exposed to infected cats, but the low natural infection rate for FeLV in household pets and cattery cats makes it very difficult to determine whether these cases were exceptions or the rule.

The reasons for discrepancies between independent and manufacturers' test results are not known. However, it is apparent that further independent testing should be done on current and future products. It is hoped that much better vaccines will be forthcoming from worldwide research on FeLV infection and immunity. Until accurate efficacy figures can be obtained for present and future FeLV vaccines, vaccines should not be considered to give total protection. As such, vaccinated cats should not be knowingly exposed to FeLV-infected animals and vaccination should not replace test and elimination procedures for disease control in multiple-cat environments.

Cats have been successfully vaccinated with live-virus vaccines.[17,54] Relatively avirulent strains are available that produce a high degree of protection when given in small doses to older kittens.[54] However, these same strains induce fatal anemia in very young kittens.[28] Also, cats that have recovered from such live-virus vaccinations may be at a much greater risk of developing virus-negative lymphosarcoma later in life.[11,17,23] Doubts expressed by some people about the possible public health hazards of live FeLV have also made it unlikely that a live-virus vaccine will ever by employed for prevention of FeLV infections.[17]

Infection and Immunity

The ultimate outcome (recovery or persistent viremia) of FeLV infection is largely determined by events that occur within the host during the first 16 weeks of infection.[53] Immunity during this critical period is greatly influenced by the age of the cat, dose and virulence of the virus, and stress. Age resistance develops rapidly after 4-8 weeks of age. Cats exposed at a very young ages usually become persistently viremic; older cats usually become aviremic.[28] Age-acquired resistance can be overcome to some extent by increasing the dose of challenge virus and using more virulent strains. It is most easily overcome, however, by subjecting the animal to artificial stress. A single injection of methylprednisolone given within the first 2 weeks after exposure dramatically increases the proportion of cats that become persistently infected.[63]

Termination of viremia appears to be associated with the appearance of virus-neutralizing antibodies in the blood.[31,66] Disappearance of viremia also corresponds with a cessation of virus production by infected cells.

The latent phase of FeLV infection is a transient phase for most cats, and is terminated in most individuals within 1-6 months.[51] It is merely an extension, therefore, of the recovery process. Latency is followed by complete recovery, at which time the virus is no longer present in a form that can be activated in the body.

The persistently viremic state appears to involve some sort of immunologic tolerance. This tolerance develops rather abruptly. At one stage of infection the cat is actively fighting the virus, as evidenced by the pronounced lymphadenopathy. At the other stage, the lymph nodes become quiescent in the face of the same infection that previously evoked an intense immune response. As with any state of immunologic tolerance, it can sometimes be broken. A small proportion of FeLV-infected cats can terminate the persistent viremia after many months or even years. The tolerant

state can sometimes be abrogated by immunologic manipulations.[6,35,38]

Feline leukemia virus infection has been likened to AIDS of people. While human AIDS and FeLV infection have many dissimilarities, there is little doubt that some FeLV-infected cats are immunodeficient. Unlike the immunodeficiency of human AIDS, which involves specific components of the immune system, FeLV infection causes immunodeficiency in many different ways.[20,37,61] Immunodeficiency is not present in all FeLV-infected cats, and is not usually evident until clinical signs of illness appear.

Animal and Public Health Considerations

Feline leukemia virus is found only in domestic cats and some related wild Felidae. The potential health hazard of FeLV-infected cats to people has been controversial.[39,68] This controversy has been an impetus for many research studies. To date, these studies have not shown FeLV to be infectious to people.

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Feline Immunodeficiency Virus Infection

Cause

Feline immunodeficiency virus (FIV) is one of the most recently discovered infectious agents of cats. Though it is a problem in the general cat population, FIV infection is not a cattery disease.[13,29,35] It is a problem mainly of household cats allowed to roam freely outdoors, farm cat populations, and multiple-cat households that adopt free-roaming feral or homeless cats. The disease is discussed herein because of its interesting epidemiologic contrast with FeLV infection (which can be a major cattery problem), the intense interest in the disease by cat owners, and the potential problem with the disease in households with multiple pet cats.

Feline immunodeficiency virus has several biologic features in common with human and simian immunodeficiency viruses (HIV and SIV), which are the causative agents of acquired immunodeficiency syndrome (AIDS) in people.[21]

Pathogenesis

Feline immunodeficiency virus infection was first recognized in cats in Northern California.[21] The infection has been subsequently recognized throughout the United States and Canada, South Africa, Australia, New Zealand, Europe and Japan.[1,2,8,9,12,13,15,25,29,31,33,36] The infection rate varies greatly, depending on environmental factors. Depending on the area, the incidence of FIV among the general cat population ranges from less than 1% to as high as 12%, similar to that of FeLV.[13,15,35] From 4% to 44% of cats with clinical signs suggestive of immunodeficiency test positive for the virus.[13,35] The highest rates of infection are in areas where there is a high density of freely roaming cats. Japan, where there are many freely roaming animals, has a higher incidence than countries where the cat population is less dense and a greater proportion of cats are kept strictly indoors.[13,35] The infection rate seems to be lower in cities than in suburban areas or smaller towns. Purebred catteries have the lowest rate of infection.[13,35]

In every study, male cats have been infected over twice as frequently as females.[1,2,8,11,13,29,35] Most clinically ill cats have been over 5-6 years of age, though infected kittens as young as 6 months have been identified.[13,35] It is not uncommon to find diseased animals that are over 10-15 years of age. This age incidence contrasts with that for FeLV, which is more common in cats less than 5-6 years of age and rare in aged animals. About one-sixth of clinically ill FIV-infected cats are also infected with FeLV.[13,25,27,35]

Feline immunodeficiency virus appears to be transmitted predominantly by bites.[35,36] The virus is shed in the saliva, and puncture of the skin by a canine tooth of an infected cat is highly efficient in transmitting the infection. Clinically ill cats shed much more virus in their saliva than apparently normal infected individuals.[35] The presence of mouth lesions may also increase the infectivity of an infected animal. Transmission by intimate contact in indoor situations, where biting does not usually occur, is very inefficient;[35,36] this is different from FeLV infection.[22] *In-utero* transmission is either nonexistent or uncommon, again different from FeLV infection.[36] Neonatal transmission from infected queens to their kittens, via milk or maternal grooming, also does not occur to any extent.[36] Infected queens, therefore, usually give birth to healthy kittens that remain uninfected. The transmissibility of the virus by blood-sucking insects, such as fleas, remains to be determined.

Infection occurs in 2 stages. The initial stage of the infection has been experimentally studied in specific-pathogen-free kittens.[36] Experimentally infected kittens develop transient leukopenia and fever beginning about 4 weeks after infection. These signs last from several days to 4 weeks. The leukopenia is mainly due to an absolute, and sometimes profound, neutropenia.[36] Platelet and RBC counts remain normal. Generalized lymphadenopathy appears at about the same time and lasts 2-9 months.[36] The initial stage of fever, leukopenia and lymphadenopathy is reminiscent of the initial stage of FeLV infection.[22] The

leukopenia seen in the primary phase of FeLV infection involves other cell types in addition to neutrophils, and is usually accompanied by thrombocytopenia and varying degrees of anemia. The lymphadenopathy of FeLV infection is usually of shorter duration, rarely lasting more than 12-16 weeks.[22]

Most FIV-infected cats recover from the initial stage of the disease after a brief period of malaise; some kittens, however, may succumb to local or generalized sepsis during this period.[36] Sepsis is probably due to the profound neutropenia and not to a more specific immunodeficiency. The initial stage of FIV infection is not dissimilar to the initial stage of HIV infection in people. People infected with HIV develop a transient mononucleosis-like illness several weeks after infection. They then return to a state of normal or near-normal health that lasts until the secondary, or AIDS stage, of illness appears.

Most FIV-infected cats are seen in the so-called AIDS-like phase of the illness, when secondary and opportunistic infections, neurologic signs and myeloid or lymphoid tumors are seen. The levels of T_4 (helper) lymphocytes slowly decline over months or years.[38] Significant decreases ($\leq 1000/\mu l$) are often reached after 24-36 months after infection. Clinical signs of AIDS-like disease are expected as levels decrease below this point. This feature of FIV infection is identical to that of HIV infection of people and human AIDS. The AIDS phase of HIV infection of people occurs on the average of 6 years after initial infection. As in infected people, FIV-infected cats entering the AIDS-stage of illness become progressively more immunocompromised with time.

Clinical Features

Numerous distinct and intertwined disease syndromes have been observed in FIV-infected cats, and these syndromes are similar to those seen in HIV-infected people. Signs referable to an AIDS-like syndrome occur in one-half or more of sick FIV-infected animals. About one-half again of the cats with AIDS-like disease develop chronic and progressive infections of the mouth, including the gingiva, periodontal tissues, cheeks, oral fauces or tongue (Figs 19, 20).[11,13,14,29,35] Oral lesions may be present for months or years before the diagnosis is made. Though chronic oral cavity infections are a common feature of FIV infection, not every cat with severe mouth disease is FIV infected. Less than one-fourth of the cats with severe mouth infections in the United States are FIV positive. In a study in the United Kingdom, three-fourths of a group of cats with chronic stomatitis were infected.[14]

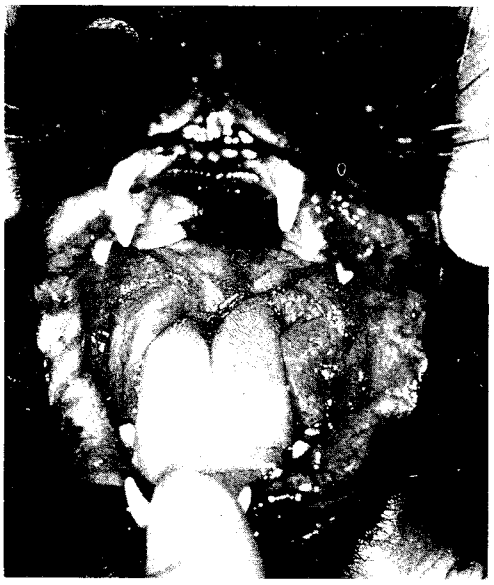
About one-fourth of FIV-infected cats with AIDS-like disease have chronic upper or lower respiratory infections (rhinitis, conjunctivitis, bronchitis, pneumonitis, bronchiolitis) (Fig 20).[2,11,13,21,31,35] Respiratory signs can occur by themselves or in association with infections in other areas of the body. It must be remembered, however, that chronic rhinitis and sinusitis commonly seen in cattery-reared cats is not an FIV-related disease. This condition usually begins as a kittenhood viral respiratory infection that leads to permanent damage to the nasal and sinus membranes and chronic secondary bacterial infections (see section on feline herpesvirus).

One-sixth of FIV-infected cats with AIDS-like disease develop chronic infections of the skin, including the ear canals.[13,21,35] Bacterial skin lesions are usually associated with staphylococcal infections. Chronic abscesses have also been observed in FIV-infected animals.[8,13,29] Generalized mange mite infestations (demodectic and notoedric) tend to be concentrated in FIV-infected cats.[6,13]

Chronic enteritis, usually manifested by diarrhea and weight loss, is the main clinical complaint in about 10% of FIV-infected cats with AIDS-like disease.[1,11-13,21,31,35] Bowel disease in FIV-infected cats is probably more common than indicated; many cat owners do not examine their cat's stools and diarrhea in cats is not as obvious as in other species. Chronic infections of the upper and lower urinary tract are seen in only a small proportion of FIV-infected animals.[8]

Numerous opportunistic infections have been identified in FIV-infected cats with AIDS-like disease. These include feline calicivirus, poxvirus infection, toxoplasmosis, cryptococcosis, candidiasis, mycobacteriosis, demodectic and notoedric mange, and hemobartonellosis.[1,4,8,11-14,31,34]

Figure 19. Severe stomatitis, periodontitis and tooth loss in a cat with chronic FIV infection. (Courtesy of Dr. Takuo Ishida, Nippon Veterinary and Zootechnical College, Tokyo, Japan)



Feline infectious peritonitis, which is often linked with FeLV infection, has yet to be linked with FIV.[13]

One-third of all clinically ill FIV-infected cats show vague signs of illness, such as recurrent fevers, leukopenia, anemia, lymphadenopathy, unthriftiness, inappetence, weight loss or ill-defined behavioral abnormalities.[1,11,13,31,35]

About 5% of all clinically ill FIV-infected cats have neurologic problems as the predominant clinical feature of illness.[29,31,35] An equal or greater proportion of infected animals has neurologic signs as one feature of their illness.[9,21,29] Neurologic signs can be either a direct effect of the virus (most commonly), or due to other opportunistic organisms (less commonly). Most FIV-related lesions are in the cerebral cortex and clinical signs are more behavioral or psychomotor than motor. Dementia, twitching movements of the face and tongue, psychotic behavior (hiding, rage, aggression), loss of toilet training and compulsive roaming have all been observed in FIV-infected cats. Convulsions, nystagmus, intention tremors and ataxia have also been observed in a smaller number of cats.

Chronic progressive renal disease has been a complicating feature of FIV infection in some cats.[1,13] It is uncertain whether this is merely a reflection of old age (both FIV infection and renal disease tend to occur in older animals), or whether there is a cause and effect relationship.

Inflammatory disease of the eye, in particular the anterior uveal tract, has been seen in several FIV-infected cats. There is some indication that some of these animals have active toxoplasmosis.

Immune-mediated diseases may be associated with FIV infection. Some anemic FIV-infected cats are Coombs' test positive. Several cats with FIV infection and thrombocytopenia have also been observed. An inflammatory arthritis has also been seen in FIV-infected cats.[11]

Hematologic abnormalities are common in sick FIV-infected cats.[1,8,11,13,26,29,31,35] The main abnormalities are leukopenia and/or anemia.

Lymphosarcomas have been observed in a number of FeLV-negative, FIV-positive cats.[1,11-13,25,28,29,35] This relationship is more than chance.[27] The relative risks for developing leukemia/lymphoma were 5.6, 62.1 and 77.3 times greater in cats infected with FIV, FeLV or FeLV/FIV, respectively, than in uninfected animals. Lymphoid tumors in FIV-infected cats have often occurred in the

Figure 20. Chronic rhinitis and periodontitis in a cat with chronic FIV infection. (Courtesy of Dr. Takuo Ishida, Nippon Veterinary and Zootechnical College, Tokyo, Japan)

head and neck. Lymphoid tumors of the nasal passages may arise from surrounding chronic plasmacytic-lymphocytic inflammation.

Myeloproliferative disorders have been reported in some FeLV-negative, FIV-positive cats with severe anemia and leukopenias.[1,13,35] A myeloproliferative disorder has been induced in specific-pathogen-free cats infected only with FIV.[21,36] Myeloid neoplasms and myelodysplasias (preleukemias?) are common in cats, and only 70% have been linked with FeLV infection.[3] A portion of the remainder may well be FIV induced.

FIV infection has been diagnosed in some older cats with squamous-cell and mammary-gland carcinomas.[11,13] The rate of FIV infection among cats with squamous-cell carcinomas of the mouth and skin at the School of Veterinary Medicine, University of California, Davis, has been around 10-20%. However, cats with squamous-cell carcinomas tend to be old and mainly outdoor roaming. Both of these are also significant risk factors for FIV infection, so more epidemiologic studies must be done before a real relationship can be determined. A number of other seemingly rare types of tumors have been reported in FIV-infected cats, but again, a cause and effect relationship has yet to be determined.[11-13]

Pathologic Features

The principal lesions seen in the terminal stages of FIV infection are concentrated in the digestive tract. Mild to severe gingivitis, periodontitis and stomatitis are the most common features of FIV infection. Diffuse enterocolitis is common.

Respiratory tract lesions are usually suppurative, with underlying necrosis.

Lymphoid lesions vary greatly, depending on the stage of the disease. In the initial stages of infection, lymphadenopathy is prominent.[36] The secondary or AIDS stage of the disease is characterized by a wider spectrum of lymphoid changes. Thymic lesions are difficult to evaluate in older cats that normally have atrophic thymuses. However, thymic atrophy is profound in younger animals that would normally have considerable amounts of thymic tissue.

Clinicopathologic Features

Any cat with chronic, poorly responsive or refractory infections should be tested for FIV infection. Cats with infectious diseases that are of an opportunistic nature should also be tested. Because FeLV and FIV infections often coexist, it is important to test such animals for both viruses. At the present time, most tests for FIV infection involve antibody detection. Because the presence of serum antibodies is directly related to persistent infection, antibody tests accurately detect almost all infected individuals.

Three basic procedures are used to test for FIV antibodies: enzyme-linked immunosorbent assay (ELISA); indirect immunofluorescent antibody assay (IFA); and Western blotting.[10,21,34,35] Currently available ELISA procedures are highly sensitive in detecting antibodies and are probably over 98% specific when used to test high-risk populations, that is, cats with signs of the disease or cats in contact with known infected individuals. A greater proportion of nonspecific (false) positive test results may occur in low-risk groups, that is, cats kept strictly indoors, cats with no known exposure, or purebred cattery cats. False positives are generally associated with antibodies that react with minor cell culture contaminants in the ELISA antigen. Because many feline vaccines contain these contaminating antigens, heavily vaccinated cats are more likely to have false-positive reactions than cats that are infrequently vaccinated. False-positive reactions are generally weak; some true positives may also be weak, however.

The ELISA is the assay of choice for high-risk animals. When used on such populations, further confirmatory testing is probably not necessary. Confirmatory testing, either by IFA or Western blotting, should be considered for weakly or or suspicious positive samples from cats in low-risk categories. The IFA procedure is slightly less sensitive than ELISA and may give a low percentage of false negatives. If properly conducted, however, it rarely gives a false-positive reaction. The same can be said for Western blotting.

A small proportion of FIV-infected cats may have too little antibody to be detected.[21,22] Such cats may be in an early

stage of infection or in the AIDS phase of illness, in which there is a state of antigen excess with suppression of antibody production. Perhaps tests will be devised to detect such animals.

Hematologic abnormalities are common in both the initial stage of the infection and in the secondary or AIDS stage of illness. Varying degrees of leukopenia, seldom lower than 3000 cells/μl, are seen transiently in the initial stage of infection.[21] This is usually associated with mild to profound neutropenia. The RBC and platelet counts are usually normal.[21] Anemia and leukopenia are seen in about one-third of cats in the terminal AIDS stage of illness. The leukopenia is usually associated with neutropenia and/or lymphopenia.[20] The anemia is usually mild and of the depression type. In some cats with myeloproliferative disorders, the anemia is often profound and may be associated with varying degrees of leukopenia and anemia.

Cats coinfected with both FIV and FeLV tend to be younger than cats infected only with FIV, have more severe disease signs, and die earlier.[7,36] The disease potentiation of dual FeLV/FIV infections has also been experimentally documented.[37] Feline immunodeficiency virus infection is also strongly linked to feline syncytium-forming virus (FeSFV) infection.[20] Three-fourths of a group of FeSFV-infected cats in one study were coinfected with FIV. This high rate of coinfection of cats with FeSFV and FIV probably results from the common modes of transmission of these 2 agents. FeSFV is also spread by bites and the same animals at risk for FIV infection are at risk for FeSFV infection.[20]

Treatment and Prevention

Only cats in the AIDS stage of disease should be treated. Treatment is largely supportive and symptomatic, and directed primarily at secondary or opportunistic infections. Cats in the earlier phases of AIDS-like illness often respond favorably to such treatment. As the disease progresses, however, the response becomes less favorable. The usefulness of human anti-HIV drugs, such as azidothymidine, lymphokines, interferons and immunostimulants, has not yet been adequately explored in cats.

The most successful way to prevent infection is by not allowing cats to run free. Even if a susceptible cat is housed indoors with an infected individual, the likelihood of transmission is small. Strictly indoor cats rarely resort to biting, and biting is the principal mode of infection. Casual transmission, though uncommon, has been described in at least one closed cattery that took in homeless outdoor cats.[12] Contact transmission is much less efficient than with FeLV, and infected and uninfected cats can live together indoors with a lower risk for disease spread than with FeLV.

Infection and Immunity

Whether or not FIV infection of cats is analogous in all aspects to HIV infection in people remains to be determined. However, there are great similarities in progression of disease in HIV-infected people and FIV-infected cats. Both diseases start with a brief, self-limiting illness. Following this initial bout of disease, infected people and cats return to a state of normalcy or near normalcy. With time, usually many months or years, the immune system deteriorates and secondary or opportunistic infections begin to appear.[15] These respond initially to symptomatic treatment, but as the immune system becomes progressively more crippled, treatment becomes less and less effective.

Opportunistic infections seen in human AIDS patients are usually associated with organisms that tend to be intracellular, thus requiring cellular immunity for elimination. Mycobacteria, *Toxoplasma, Cryptococcus, Pneumocystis carinii,* cytomegalovirus, Epstein-Barr virus and hepatitis B virus are just a few. Identical or related types of organisms have been associated with disease in FIV-infected cats.[7]

Cats experimentally infected with FIV begin to make antibodies 2 weeks after infection.[21] The titer of these antibodies rises rapidly and then plateaus. Cats with naturally acquired FIV infection and in the AIDS stage of illness tend to have lower antibody levels than experimentally infected cats in the asymptomatic stage of infection. This observation suggests that FIV antibodies in cats behave similarly to HIV antibodies in people over the course of the respective infections.

Similar to HIV-infected people, FIV-infected cats appear to be infected for life. This is typical of all lentivirus infections; the chance of recovery, even in the face of immunity, is virtually nil. This feature of lentivirus infections makes them resistant to known vaccine strategies. It is difficult to develop a vaccine for an infection against which the host cannot immunize itself, even in a small percentage of cases.

Animal and Public Health Considerations

Feline immunodeficiency virus has a distant genetic relationship to HIV of people.[19,31] It is one member of a large group of lentiviruses that appear to have adapted themselves species by species over eons of time. The adaptation of HIV to people is a very recent event in lentivirus evolution. The current theory is that HIV is a mutant of simian immunodeficiency virus. Though lentiviruses have apparently adapted themselves to a number of species of animals by mutation, once that adaptation occurs, they become very species specific. Lentiviruses of one species of animals do not readily infect a divergent species of animals. This high degree of species specificity obviates FIVs being a public health concern. Preliminary studies have failed to identify FIV antibodies in the blood of people in intimate contact with infected cats, inadvertently bitten by infected cats, or accidently injected with infectious materials.[21]

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Campylobacteriosis

Cause

Campylobacter species are Gram-negative curved bacterial rods.[2] *Campylobacter jejuni* is the main pathogen in this genus. Organisms remain viable at 4 C for 3 weeks in feces and 5 weeks in urine, and for less time at 25 C.[1] Viable organisms were still present in bile kept at 37 C for 2 months.

Pathogenesis

Campylobacter jejuni is found worldwide and carried by many different species of animals, including poultry, wild and caged birds, sheep, goats, dogs, cats, swine, hamsters, primates and people. Infected animals shed the organism in their feces. Canine and feline isolates are identical to human isolates.[13]

The incidence of *C jejuni* infection in dogs and cats is difficult to determine due to variations in isolation rates. The highest recovery rates are from animals that are young or housed in high-density environments. Isolation rates vary from 0.5% to 45% or more in dogs and from 2% to 45% in cats.[7] However, isolation rates in cats in most concurrent studies are usually only a fraction of those in dogs.

The relatively high incidence of *C jejuni* infections in kittens from high-density environments is compatible with what is known about infectious diseases in general. Young animals are most susceptible to infection and continue to shed organisms until good immunity develops, a process that sometimes takes many weeks. Hamsters and ferrets experimentally infected with *C jejuni* shed organisms for several months.[6] Puppies have shed organisms for at least 40 days.[5] Environmental factors favoring serious infection include: overcrowding with increased contact between animals; poor sanitation and increased fecal contamination of the environment; large numbers of kittens and a proportionate increase in carrier individuals; concurrent diseases and lowered resistance; and increased stresses in the population.[6,12]

The role of *C jejuni* in disease has only recently been demonstrated. It causes vibrionic hepatitis in poultry and transient enterocolitis in animals and people.[16] However, epidemiologic studies have had variable success in linking *C jejuni* to disease in dogs and cats. Some studies show the same incidence of infection in dogs or cats with diarrhea and asymptomatic animals.[8,9] In other studies, however, the infection rate is considerably higher in animals with diarrhea than in asymptomatic animals.[7] Cats with acute diarrhea, cats in the postinfection convalescent stage of disease, and chronic asymptomatic carriers are sources of the bacteria. Outbreaks usually occur when susceptible and infected cats commingle.[12]

Infection with *C jejuni* is by the fecal-oral route. The infection is generally limited to the cecum and colon, though bacteremias are sometimes associated with severe primary bowel disease. The incubation period is 3-7 days.

Clinical Features

Clinical signs of *C jejuni* infection are seen mainly in 6- to 12-week-old kittens during the postweaning period. However, whether the infection is clinically apparent is related to a variety of poorly understood factors. The level of infecting organisms, nutritional status, presence of concurrent diseases, and status of passive and active immunities all play some role in the disease outcome. It is not unusual that the disease strikes weanling kittens that have stopped nursing. The kittens suddenly lose the passive local (lactogenic) immunity provided by their mother's milk. Their passive systemic immunity also wanes, their diet is markedly changed, they are exposed to other young animals, and the stress level is high.

Diarrhea, which is sometimes profuse and watery but more often soft and mucoid, is the predominant sign of *C jejuni* infection in kittens.[12] Fever is generally absent and anorexia mild. Vomiting and colic are sometimes observed in the acute stages of illness. Dehydration can be rapid and severe in young kittens with profuse watery diarrhea. Death has been occasionally reported in severely affected kittens.[14] The diarrhea usually subsides within 3-7 days, but the stool may remain somewhat soft for 2-4 weeks. Bloody diarrhea is not a common sign of *C jejuni* enterocolitis in kittens.

Pathologic Features

Lesions in cats have not been described, but changes are identical in most species that have been studied. Gross changes are limited to the distal intestinal tract, particularly the colon, and include mild redness of the mucosa.

Clinicopathologic Features

Highly motile spiral or S-shaped organisms can be seen in fresh fecal suspensions viewed by phase or subdued-light (contrast) microscopy. This can be of some value in tentatively diagnosing *C jejuni* enterocolitis. The organism can be readily isolated on selective *Campylobacter* media. Small, flat, grayish, mucoid colonies appear within 24-48 hours. Typical Gram-negative spiral or S-shaped organisms are seen in stained smears.

Overinterpretation of culture results should be avoided. Many healthy kittens in the same environment also shed organisms, and a number of other enteric pathogens can cause similar disease signs. These other diseases also tend to occur in the postweaning period. A rapid response to specific antibiotic therapy can be helpful in confirming *C jejuni* as the responsible organism.

Treatment and Prevention

Campylobacter jejuni is resistant to penicillin, cephalosporins and trimethoprim.[2,12] Sensitivity to ampicillin, trimethoprim-sulfonamides and metronidazole is intermediate. Almost all *C jejuni* isolates are sensitive to erythromycin, which is considered the drug of choice.[12] Erythromycin is given PO at 20-40 mg/kg divided 3 times daily for 5 days. Tetracycline, aminoglycosides, clindamycin, chloramphenicol and furazolidone are also effective.

Kittens with severe and profuse diarrhea should not be given food or water for 24-72 hours. Fluids and electrolytes should be given parenterally. *Campylobacter jejuni* enterocolitis usually responds well to treatment, and clinical signs resolve within 2-5 days. Cats with milder signs do not necessarily require treatment; signs usually resolve after a few days to a week.

Prevention of *C jejuni* infection in catteries usually requires drastic changes in environment and husbandry. The disease is most severe in situations in which many breeding cats and kittens are crowded into inadequate quarters.

Infection and Immunity

Most *C jejuni* isolates are obtained from animals less than 6 months of age.[7] Bacterial shedding continues for up to 2 months or more after infection, indicating that development of complete immunity is a slow process. This is true of many enteric infections of dogs and cats. Shedding of *Salmonella* also continues for weeks or months after initial infection. Interference with the natural course of salmonellosis with antibiotics can actually prolong the carrier state by removing the stimulation necessary to evoke protective immunity. Animals that have not established immunity immediately become reinfected with *Salmonella* follow-

ing cessation of antibiotic treatment. Experience with human campylobacteriosis suggests that antibiotic therapy does not have a similar effect. Cultures done several weeks to months after treatment are usually negative.[11]

Animal and Public Health Considerations

Campylobacter jejuni is a cause of severe acute enterocolitis in people, especially in children. In underdeveloped areas of the world, person-to-person transmission by the fecal-oral route is common. Human infection in more-developed countries is usually associated with ingestion of contaminated lamb, beef, pork, poultry or unpasteurized milk. Contaminated water is another common source of human infection. Exposure to infected dogs and cats has been estimated to account for no more than 5% of human infections.[17] Dogs are generally more infectious to people than cats, largely due to their higher incidence of infection.[18] Puppies and kittens are more infectious than older animals and diarrheic individuals are more of a health hazard than asymptomatic individuals.[3,10,18,19] Young kittens and puppies are more apt to harbor the infection. Animals with diarrhea shed more organisms and are more likely to contaminate the environment.

People, especially children, who develop acute enterocolitis after contact with a diarrheic kitten should be checked by their physicians for *C jejuni*. If positive cultures are obtained from the patient, fecal cultures from the pets might be warranted. Pets shedding *C jejuni* should not be destroyed without good reason. The infection is self-limiting in both people and animals, and the number of people infected by pets is relatively small. Infected animals can be isolated from people for 40 days or so, and then samples obtained for culture. Alternatively, animals shedding *C jejuni* can be treated with erythromycin for 5 days.

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Streptococcosis

Cause

Streptococci are Gram-positive spherical bacteria that form long chains under optimum growth conditions. Streptococci are commensal organisms that live on mucous membranes of the nasal passages, oropharynx, colon and distal genitourinary tract (urethra, vagina, prepuce). Both pathogenic and nonpathogenic species of streptococci coexist in healthy animals and people. The most common isolate from cats is *S canis*.[1]

Healthy cats are the primary source of streptococci. The level of bacterial growth

in mucous membranes of the mouth, nasal passages and distal genitourinary tissues varies greatly, depending on the age of the animals. Of female cats <2 years of age in the Davis, California, area, 50% carried *S canis* in their vaginal tract.[1] The carrier rate in older cats was lower.

Pathogenesis

Three main forms of streptococcal infections have been recognized in cats: epizootic, neonatal and localized. Each form of the disease will be discussed as a distinct clinical entity, though the various forms often occur together in the same environment. Streptococcal infections are enhanced by a number of unfavorable environmental factors that are most likely to occur in catteries, multiple-cat households and animal facilities (pounds, humane shelters, laboratory animal facilities).

Clinical Features

The epizootic form of streptococcosis has been seen mainly in large experimental cat colonies.[1,4,7-9] This form occurs less frequently in catteries and is virtually nonexistent in normal outdoor/indoor pet cat populations. Outbreaks usually occur among cats kept in close confinement and in free-housed groups of 4 or more animals, rather than in individually caged cats. Animals affected with epizootic streptococcosis were usually fed from common bulk feeders.

Infection rates vary from 2.3% to 28% over several months. The highest incidence of disease is in the postweaning period from 8-10 weeks of age or in new animals introduced into an enzootic environment.

The most common clinical signs associated with this form of infection are acute fever, submandibular edema and lymphadenopathy. The mandibular lymph nodes often spontaneously rupture and drain, or require lancing. Conjunctivitis, sinusitis and abscesses on the feet and legs develop in some animals. Dyspnea, due to a severe suppurative pleuritis and hydrothorax, occurs in a small proportion of affected cats. The epizootic form of the disease has been experimentally recreated.[4] Adolescent and adult cats fed organisms became febrile on day 2, with anorexia, listlessness, and swelling and edema of the mandibular lymph nodes. Draining abscesses often occurred in the area of the enlarged nodes over the following 24 hours. Conjunctivitis, laryngitis and tracheitis were associated signs. Streptococci ingested with food rapidly colonized the tonsils and disseminated via the lymphatics to regional lymph nodes in the head and neck.[7] Purulent inflammation of the lymph nodes was followed by toxemia and fever.

The neonatal form of streptococcal infection occurs more frequently in large breeding catteries.[1,10] Sporadic cases of epizootic disease in weanling and adolescent kittens are often seen in the same environment. The disease has a predilection for kittens born to primiparous queens.[1] Kittens are usually infected during birth from vaginal secretions or when the queen severs the umbilical cord. Umbilical vein infections are more frequent when the umbilical cord is chewed off at the level of the abdominal wall. If the umbilical cord is left long, infection is limited to the dried-up portion and cannot travel up the cord and reach the patent part of the vein. Kittens infected at or shortly after birth often develop a small abscess of the umbilical vein in the inner abdominal wall. Infection at this site is seldom apparent on gross examination. The infection then showers organisms directly into the bloodstream. Infected kittens usually become listless within the first week of life and fade away and die over the next few days. It is not uncommon for entire litters to be affected. Subsequent litters are less likely to succumb from the infection.

Streptococci can be isolated from several localized pyogenic processes, in pure form or as mixed bacterial infections. Abscesses of the skin and subcutis, conjunctivitis, mastitis and uterine, vaginal, oral, ear and wound infections are just a few processes associated with streptococci.[3]

Pathologic Features

Pathologic findings in epizootic streptococcosis are relatively stereotyped. Many affected cats have tonsillitis, with acute inflammation and microabscess formation in the lymph nodes of the head and neck. Acute rhinitis, unilateral or bilateral otitis media, acute splenitis and reactive hyperplasia and histiocytosis of lymphoid tissue throughout the body are associated findings.[8,9]

Pathologic features of neonatal streptococcosis include omphalophlebitis and thrombosing bacteremia.[1] Gross or microscopic abscessation of the abdominal portion of the umbilical vein is common, and bacterial thrombi are observed within vessels in the liver, spleen, lungs and kidneys. Gross and microscopic abscesses are seen in the liver; suppurative meningoencephalitis is common.

Clinicopathologic Features

Epizootic streptococcal lymphadenitis is easily diagnosed on the basis of clinical history (environment, feeding practices) and signs of acute fever and adenitis of the lymph nodes of the head and neck. Pure cultures of beta-hemolytic streptococci are obtained from lymph node exudates.

Neonatal streptococcosis must be differentiated from the myriad diseases that cause mortality in kittens during the first 2 weeks of life. Careful necropsy, histopathologic examination of tissues, and bacterial cultures usually pinpoint the problem. Special attention should be given to examination and culture of the umbilical cord remnant within and outside of the abdomen.

Treatment and Prevention

Streptococci are sensitive to a number of antibiotics, but penicillin is the drug of choice. Antibiotic therapy should be combined with drainage of abscessed lymph nodes and evacuation of pleural exudate in cats that also have streptococcal pleuritis. If neonatal streptococcal infections are a problem, prophylactic treatment of all kittens born to primiparous queens is indicated. A single subcutaneous injection of benzathine penicillin at 35,000 IU/kg at birth often prevents systemic disease and decreases mortality.

An outbreak of streptococcal lymphadenitis in a cat colony was successfully halted by treating all animals in the group with 150,000 IU procaine penicillin and 150,000 IU benzathine penicillin subcutaneously.[9,10] However, such treatment will not eliminate the organism from the premises. Prevention of infection involves changes in husbandry practices to prevent overcrowding and maintain clean feeders. Infected cats should be segregated from uninfected cats. Elimination of communal bulk feeders and use of individual caging also help prevent spread of disease during an outbreak.

Infection and Immunity

Pathogenic strains of streptococci cause similar syndromes in people and many species of animals. Streptococcal diseases of animals are usually related to certain husbandry practices. Overcrowding of animals, infrequently cleaned communal feeders, and premises with a high proportion of younger animals are common predisposing factors. Such conditions favor an increasing level of streptococci in the environment and a higher primary infection rate. The larger the exposure dose of pathogenic streptococci, the higher the incidence and severity of primary infections. An increased incidence of primary infection leads to a higher proportion of cats that carry and shed the organism during the primary phase of illness and in the postconvalescent period.

The severity of pathogenic streptococcal infections in a group of cats is proportional to the percentage of asymptomatic cats that carry the organism in the oropharynx, prepuce and vagina. The reason for higher incidence of streptococcal infections in neonatal kittens born to primiparous queens is not completely understood. Queens less than 2 years of age harbored significant levels of *S canis* in their vaginal canals throughout pregnancy and at parturition.[1]

In contrast, queens greater than 2 years of age had progressively decreasing levels of vaginal streptococci beginning at mid-gestation. Cultures from older queens at parturition were often negative.

The basis of the effect of pregnancy on vaginal populations of streptococci is unknown. Pregnancy, at least in relation to herpesvirus and *Toxocara* infections of cats, is usually immunosuppressive. The immunosuppressive effect of pregnancy is also well recognized in people. Therefore, it is unlikely the pregnancy-associated decrease in streptococcal vaginal populations in older cats is due solely to immunologic mechanisms. Hormonal effects of pregnancy may alter the nature of the membranes and secretions of the vaginal tract and make the local environment less favorable for bacterial growth.

Animal and Public Health Considerations

Pathogenic streptococci vary among animal species. Streptococcal diseases are associated with different groups of streptococci in people more so than in cats. Streptococci isolated from people are usually of human and not animal origin. Occasionally, however, group-G beta-hemolytic streptococci are isolated from infants with neonatal septicemia and from local purulent processes of adult people.

Cats have been implicated as asymptomatic reservoirs for group-A streptococci of people.[2,5] Group-A streptococci are the main cause of pharyngitis in children. It is possible, however, that the cats were infected by the children. Cats shed group-A streptococci for 1, 2 or 3 weeks after being removed from homes where human outbreaks were occurring.[5] *Streptococcus pneumoniae* was isolated from an aged cat with acute fever, septicemia and septic arthritis. An infant in the household had a cold for 3 weeks and was also culture positive. This was almost certainly an incident of person-to-cat transmission.

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Bordetellosis

Cause

Bordetella bronchiseptica is a small, aerobic Gram-negative spherical bacterium. It is a normal inhabitant of the upper respiratory tract of many species of animals and people.

Pathogenesis

Bordetella bronchiseptica is associated with a disease called "kennel cough" in dogs, a condition manifested by tracheobronchitis and a chronic dry cough. In cats, however, it is more often isolated from animals with clinical or subclinical pneumonia.[1,5] The organism can be routinely isolated from oropharyngeal swabs in 3-10% of normal cats.[5,6] Disease appears to be triggered by crowding and stress, and is usually recognized in laboratory cat colonies and catteries.[1,5] The carrier rate increased rapidly from 10% to 48% in a group of randomly obtained cats kept in close confinement for 3 weeks.[5] Disease results from increased colonization of the upper respiratory tract with the bacterium, coupled with other stresses that lower local membrane immunity. The predisposing role of respiratory viruses, such as feline herpesvirus or calicivirus, has not been elucidated. Viral infections can set the stage for *B bronchiseptica*-induced tracheobronchitis in dogs.[7] Of 7 cats with *B bronchiseptica* pneumonia, 3 had concurrent viral rhinotracheitis.[5]

Clinical Features

Pneumonia induced in cats by *B bronchiseptica* can be generalized or focal in nature. Therefore, clinical signs are variable. Manifestations of clinical signs is further obscured by normal feline behavior. Cats with pneumonia often do not show typical pneumonic signs, such as a cough and dyspnea (difficult breathing), even when severely affected. Of 10 cats with fatal *B bronchiseptica* pneumonia, only 7 were noticeably ill before death.[5] Of these 7 cats, 3 had signs of rhinotracheitis, 1 had a cough, and 1 behaved as if it had chronic pneumonia. Of the 7 remaining cats, 2 showed nonspecific signs of listlessness, anorexia, dehydration and emaciation before death. All 10

cats had gross lesions of pneumonia in their lungs at the time of necropsy.

Pathologic Features

Primary lesions of *B bronchiseptica* infection in cats are limited mainly to the lungs. Gross lesions consist of reddish areas of consolidation involving 1 or more lung lobes. Large, firm, grayish nodules 2-5 mm in diameter are occasionally seen in the lungs of some animals. Purulent exudate can be seen on the cut surfaces of affected lungs in about one-third of the cases. Histopathologic findings are compatible with bronchopneumonia. Interstitial disease is less common. The pulmonary parenchyma is congested and edematous, with focal necrotic areas surrounding bronchioli.

Clinicopathologic Features

Recognition of existing pneumonia is the first and most difficult step in diagnosing bordetellosis in cats. In certain catteries where disease is common, the pattern of disease in younger cats is stereotypic. The bronchopneumonia usually is diagnosed by thoracic radiography rather than physical examination. Tracheal aspiration and culture usually confirm the presence of *B bronchiseptica* in large numbers and pure form. Isolation of *B bronchiseptica* from oropharyngeal swabs should be interpreted with more caution; many cats, especially those living in problem environments, are asymptomatic carriers.

Treatment and Prevention

Bordetella bronchiseptica is susceptible to antibiotics, such as chloramphenicol, gentamicin, kanamycin and tetracycline.[2] Therapy should be continued for about 10-14 days. The prognosis is good if the pneumonia is mild, but can be poor in severely affected cats.

Problems with *B bronchiseptica* can be minimized with proper husbandry. Overcrowding of animals, stress on the population and the presence of numerous animals kept in poorly cleaned and ventilated quarters are major factors in the disease. Bordetellosis can be a complication of feline herpesvirus and calicivirus infections; these diseases are also likely to be more severe under poor husbandry conditions.

Avirulent live and inactivated *B bronchiseptica* vaccines are available for prevention of "kennel cough" in dogs.[3,4] The former is given intranasally and the latter by injection. The avirulent live vaccine appears to be much more effective, however. Both of these vaccines have been used by some cat breeders but their safety and efficacy for cats have not been determined.

Infection and Immunity

Bordetellosis is largely an environmentally potentiated disease. A percentage of normal animals carry small numbers of the bacterium in their oropharynx for months and years. In highly stressful, overcrowded, poorly cleaned and improperly ventilated environments, the levels of organisms can increase dramatically. Exposure to small numbers of organisms favors asymptomatic colonization of the oropharynx with no disease, while exposure to large numbers of organisms favors colonization of the upper respiratory tract (trachea and mainstem bronchi) and invasion of the mucous membranes, especially if coupled with stress. Viral infections, which can temporarily damage mucociliary-clearance mechanisms and induce microscopic areas of interstitial pneumonia, may allow *Bordetella* to move from the upper to the lower airways (bronchioles, alveoli) and invade virus-damaged tissues.

Animal and Public Health Considerations

Bordetella bronchiseptica infection is relatively common in many species but clinical disease is uncommon. For this reason, infected cats should not be considered human or animal health hazards.

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Pasteurellosis

Cause

Pasteurella is a small, nonmotile, Gram-negative, ovoid bacterial rod. The organism is a commensal parasite of the oral cavity of many species of animals, including cats.[10] *Pasteurella multocida* has been isolated from 80% of swabs taken from the canine teeth and adjacent gingiva of normal cats. *Pasteurella* was isolated from the oral cavity and upper respiratory tract of 60-75% of normal cats.[5,6] The rate of isolation is higher from animals with dental tartar and gingival disease than from animals with clean teeth.[1]

Pathogenesis

Pasteurella species exist in a number of different serotypes that differ greatly in virulence in mouse-inoculation tests. Of 8 mouth isolates from healthy cats, all were nonpathogenic, while 4 of 10 isolates from wounds and abscesses were pathogenic.[9] Of 6 oropharyngeal isolates from normal cats, 3 were nonpathogenic to mice, 1 was weakly pathogenic and 2 were highly pathogenic.[3]

Clinical Features

Pasteurella is most frequently isolated as a facultative anaerobe along with other anaerobic bacteria from infected wounds and abscesses in cats (see discussion of anaerobic bacteria). It has also been isolated from purulent infections of the external ear canals, conjunctiva, nasal passages and sinuses, tooth root abscesses, periodontal infections and surgical wounds. Omphalophlebitis in kittens can be caused by *Pasteurella.* Similar to *Bordetella, Pasteurella* species are commonly associated with pneumonia in colony- or laboratory-reared cats.[8] *Pasteurella* species are frequent secondary invaders in cats with primary viral pneumonia and are commonly isolated from thoracic exudates in cats with empyema (purulent infections of chest cavity).

Pasteurella organisms enter tissues by licking of wounds or bites. Organisms are frequently isolated from the claws of cats, but cat scratches are less apt to be associated with infections than bites.[1] *Pasteurella multocida* was isolated from 24 of 46 infected cat-fight wounds and abscesses.[9] It has also been isolated from the spinal cord of a cat that developed ascending meningomyelitis after being bitten in the caudal back by another cat.[2]

Pathologic Features

Lesions caused by *P multocida* often exude a great deal of grayish pus. Pasteurella infections in cats tend to remain localized. Local tissue necrosis is usually minimal; when necrosis does occur, it is generally localized to the skin overlying the abscess. There are no specific pathologic features of *Pasteurella* infections in cats. Disease processes associated with these organisms are generally of a purulent nature.

Clinicopathologic Features

Pasteurella infections are easily diagnosed by routine cultures of purulent exudates.

Treatment and Prevention

Fresh wounds should be cleansed. Purulent infections should be opened to allow drainage of the exudate and then cleansed periodically until exudation ceases and the wounds begin to heal. Systemic antibiotics are an important part of treatment and should be given for 5-10 days. Feline isolates of *P multocida* are most sensitive to tetracycline and chloramphenicol, only moderately or relatively sensitive to penicillin, and more or less resistant to sulfas.[1] Trimethoprim-sulfonamides are effective for treatment of *Pasteurella* respiratory infections.[4]

Infection and Immunity

Pasteurella infections in cats are interesting in 2 respects. First, cats seem resistant to the septicemic forms (hemorrhagic fever) of pasteurellosis that are common in

other species. Second, though cats are notorious carriers of pathogenic strains of *Pasteurella*, they seem fairly susceptible to wound infections with the organism.

Animal and Public Health Considerations

Pasteurella species are transmitted from cat to cat almost exclusively by bites. Therefore, affected cats are not a hazard to other cats.

Pasteurellosis is probably the most common zoonotic disease passed from cat to people.[10] Pasteurellosis exists in people in 2 clinical forms: localized infection caused by animal bites, usually from cats; and a systemic form manifested variably as sinusitis, pneumonia, empyema, puerperal sepsis, bacteremia or brain abscess. The origin of *P multocida* in the systemic form is usually unknown, though many affected people have a history of animal exposure.

Cat bites preceded 301 of 1234 (24.3%) human *Pasteurella* infections reported in the British Isles from 1975 to 1979.[3] A high proportion of veterinary students developed *Pasteurella* infections following cat bites.[5] Of human *Pasteurella* infections caused by animal scratches or bites, 60-80% were associated with cats.[10]

Localized pasteurellosis in people occurs at the site of the bite, usually in soft tissues of the hand. Joint infections can be a serious consequence of bites that penetrate into the synovial spaces. The wound becomes painful and inflamed within a few hours.[10] The infection spreads rapidly to surrounding tissues and along lymphatics to the regional lymph nodes. The most common local complications are abscess formation and tenosynovitis.[10] The condition is most severe after the first bite; subsequent bites are less likely to become infected. Cat-bite wounds should be cleansed as soon as possible. If pain, redness and swelling begin to develop at the site after a few hours, medical attention should be sought as soon as possible.

In a study of the role of healthy cats in the spread of *Pasteurella* to turkeys, *P multocida* was readily recovered from the throats of cats on poultry farms, but only some isolates could cause pasteurellosis in chicks.[3] Feline strains were invariably more closely related to the strains isolated from rats on the farms than from those associated with outbreaks of pasteurellosis among turkeys.

Cat bites can also have a devastating effect on small birds. It has been estimated that 60% of wild birds rescued from the jaws of cats die from pasteurellosis.[7] This suggests that prophylactic antibiotic therapy for birds undergoing such trauma is almost mandatory.

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Anaerobic Bacterial Infections

Cause

Anaerobic bacteria grow only under conditions of low oxygen and play a major role in many suppurative infections of people and animals. Most of the species involved are normal inhabitants of the mouth and distal intestinal and genitourinary tracts. The most commonly isolated anaerobic bacteria belong to the genera *Bacteroides* and *Fusobacterium*. *Bacteroides* species are straight or curved rod-shaped bacteria. *Fusobacterium* species are highly pleomorphic, existing in rod and filamentous forms.

Bacteroides species involved in suppurative processes of cats include *B tectum, B fragilis, B asaccharolyticus, B disiens, B bivius, B salivosus, B heparinolyicus, B melaninogenicus/intermedius, B zoogleoformans, B distasonis, B vulgatus, B gingivalis,* pigmented group, and so-called corroding strains.[2,3,6-8,11,13,14] Many unspeciated strains also exist.[7] *Fusobacterium* species include *F russii, F necrophorum, F naviforme and F symbiosum.*[2,8,12-14]

Another common anaerobe isolated from suppurative processes in cats is *Peptostreptococcus anaerobius.*[1,6,9,12,14] Motile *Borrelia*-like organisms have also been occasionally isolated.[4] *Clostridium villosum* is another anaerobe frequently recovered from pyogenic processes in cats.[6,12]

Pathogenesis

Anaerobic organisms are frequently isolated as mixed cultures from pyogenic processes in cats, often in association with facultative anaerobes. Common facultative anaerobes isolated in combination with anaerobic bacteria include *Pasteurella multocida, Corynebacterium pyogenes, Actinomyces meyeri, A viscosus* and *A odontolyticus.*[1,2,4,5,9,12] *Actinomyces*-like organisms are sometimes seen on stained smears of pus but have not been isolated.[9] Streptococci, lactobacilli and *E coli* are facultative anaerobes less frequently isolated from feline pus.[9]

Of 87 bacterial strains isolated from 19 cats with empyema (pyothorax), 80.5% were anaerobes and 19.5% were facultative anaerobes.[12] *Bacteroides* spp comprised 42.5% of anaerobic isolates, followed by *Clostridium villosum* at 16.1% and *Peptostreptococcus anaerobius* at 12.6%. *Clostridium villosum* was the most commonly isolated species of anaerobic bacterium. *Pasteurella multocida* was the most common facultative anaerobe, comprising 64.7% of the isolates. In a second study, *Bacteroides* species were isolated from 19 of 21 pyothoraxes, predominantly *B tectum* and *B heparinolyticus.*[7]

Of 36 cat abscesses cultured, 32 contained 8 species of anaerobes per culture.[8] Species of *Bacteroides, Fusobacterium, Peptostreptococcus, Clostridium* and *Propionibacterium* comprised 95.8% of anaerobic isolates. *Bifidobacterium, Lactobacillus* and *Eubacterium* comprised the remainder. Facultative anaerobes were isolated from about 28% of the samples. *Pasteurella multocida, Actinomyces* and streptococci made up the bulk of facultative anaerobic isolates. Lactobacilli and *E coli* were uncommon isolates.

Gingivitis, periodontal disease, stomatitis, cheilitis and glossitis are common lesions in cats. Anaerobic bacteria play an important primary or opportunistic role in such lesions. It is therefore surprising that *Bacteroides* species were isolated less frequently from diseased gingiva than from normal gingiva.[7] However, *B tectum* is more frequently isolated from diseased oral tissues of cats than from normal mouths, while *B fragilis* is almost absent from oral lesions.[7]

Infections caused by anaerobic and facultative anaerobic bacteria are almost always highly suppurative. They usually involve the nasal passages (chronic rhinitis and sinusitis), oral cavity (chronic gingivitis, periodontitis), subcutaneous tissues (abscesses, cellulitis) or bone (osteomyelitis). They are usually opportunistic and either secondarily invade tissue damaged by other pathologic processes, or are inoculated directly into tissues in which they are not normally found. For instance, accumulation of dental tartar often leads to gingivitis and eventual periodontitis. When the periodontitis becomes severe, tooth root abscessation is common. Herpesvirus infection can damage the nasal passages and sinuses and predispose to chronic bacterial invasion. Cat bites can directly inoculate oral bacteria into the subcutaneous tissues and bone. Immunosuppressive diseases, especially feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) infections, can predispose the nasal, oral, skin and intestinal tissues to infection by resident flora. Foreign bodies, such as pieces of plant material or bone, can also transport infection by normal bacterial flora into deeper sites.

Pyothorax (pus in the chest) in cats occurs by 3 possible routes: cat bites that penetrate the chest cavity; opportunistic bacterial infections of primary pneumonic processes, with spread to the pleura and chest cavity; and migrating foreign bodies. Most cases of pyothorax in the cat begin

with primary sites of pneumonia, with secondary spread of infection to the pleura and into the chest cavity.

Clinical Features

Infections caused by various anaerobic and facultative anaerobic organisms are either acute or chronic. Cat-bite abscesses and pyothorax are usually acute, while nasal and oral cavity diseases are usually chronic. Suppurative peritonitis associated with normal oral flora has been described in 2 cats.[14] In 1 of these cats, the disease was insidious and may have been present for almost 2 years. The second cat had more acute bacterial peritonitis that occurred several weeks after a suppurative cat-bite abscess on the flank was treated. Chronic osteomyelitis of the radius (after a cat bite) and mandible (after a tooth root infection) in 2 cats has also been associated with anaerobic organisms.[5]

The clinical presentation of animals with pyogenic anaerobic bacterial infections depends on the site of involvement. Cats with pyothorax usually show acute dyspnea and fever. Cats with bacterial peritonitis may have a much more chronic course of fever, depression, weight loss and abdominal distension. Cat-bite abscesses or cellulitis usually cause acute depression, fever, focal swelling (edema, hemorrhage, exudation), redness and pain. The most common sites for cat-bite abscesses or cellulitis are the distal limbs, tail and tailhead, and around the face and neck.

Pathologic Features

Pyogenic processes caused by anaerobic and facultative anaerobic bacteria range from highly suppurative and necrotizing to pyogranulomatous in nature, depending on chronicity.

Clinicopathologic Features

Purulent exudates range from yellow to yellow-green or reddish. They are often malodorous and may contain sulfur-like granules if actinomycetes are present. The characteristic putrid odor of anaerobic bacterial infections is due to production of volatile fatty acids.

Most *Bacteroides* and *Fusobacterium* species are Gram negative, while *Clostridium, Actinomyces* and *Peptostreptococcus* species are Gram positive.

Anaerobic bacteria, such as *Bacteroides, Fusobacterium* and *Clostridium* species, require special culture conditions and are often slow to grow. Isolation of anaerobic and facultative anaerobic organisms may be of doubtful significance, depending of the site of isolation. For instance, isolation of anaerobic bacteria from swabs of the mouth or superficial wounds (which cats often lick) may be meaningless. However, isolation of anaerobic organisms from abscesses, peritoneal and pleural exudates, or curetted bone is much more meaningful.

Prevention and Treatment

Most anaerobic organisms are susceptible to penicillin, ampicillin, chloramphenicol, cephalosporins, clindamycin and metronidazole. They tend to be resistant to aminoglycosides, such as gentamicin and amikacin. The response is not always good if underlying reasons for the infection are not also treated. Severe periodontal disease cannot be cured in the face of chronic tooth-root abscesses. If infections are secondary to immunosuppressive disease, therapy is only palliative. In chronic bone infections with sequestrum formation, therapy should include curettage of devitalized bone.[6]

Infection and Immunity

Infections with anaerobic and facultative anaerobic organisms are usually opportunistic. Infection depends on the breakdown of normal local or systemic defense barriers (as in chronic oral and nasal cavity disease) or inoculation of organisms into tissues where they do not normally exist (as in pyothorax, osteomyelitis, peritonitis, subcutaneous abscesses).

The additive or synergistic role of individual bacterial species in mixed anaerobic infections (the rule rather than the exception) needs further study. A *Borrelia*-like organism and *Corynebacterium pyogenes* were isolated from the thoracic exudate of a cat with pyothorax.[4] Isolates were not particularly pathogenic by themselves but were very pathogenic when inoculated in combination into cats. Facultative anaerobes are hardly ever the sole isolate from pyogenic processes of this type and are always accompanied by a type of anaerobic bacteria.

It may be possible that most aerobic organisms obtain some sort of nutritional supplementation from the coinfecting anaerobes or vice versa. Indeed, *B melaninogenicus* growth is greatly facilitated by vitamin K, a substance produced by some strains of bacteria. One strain of organism might also elaborate toxins that cause necrosis and local tissue hypoxia, thus favoring anaerobic conditions. Other anaerobic bacteria may produce penicillinase that lessens the effectiveness of antibiotic therapy.

Animal and Public Health Considerations

Anaerobic infections, being largely opportunistic in nature, are a minimal animal and public health hazard. Anaerobic strains of bacteria may also be fairly species specific.[8]

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Salmonellosis

Cause

Salmonella species are motile, Gram-negative bacterial rods that inhabit the intestinal tracts of a wide range of mammals, birds, amphibians and reptiles. *Salmonella choleraesuis, S arizonae, S typhimurium* and *S enteritidis* are the most important species in veterinary medicine. *Salmonella enteritidis* occurs in hundreds of different serotypes that are often named after localities in which they were identified, such as Dublin, Khartoum, Minnesota, Chester, Manhattan and Newport. *Salmonella typhimurium* is the most important pathogen of the genus.

Many *Salmonella* species have been isolated from the feces of normal cats. However, isolation rates have varied from virtually 0% to 44%, depending on the source and locality. Isolation rates from normal free-roaming cats are generally 5% or less.[1,2,10,15,19] Isolation rates are high among random-source cats purchased for experimental use. One-third of the shipments of cats sent to research institutions contained infected cats; overall, 10.6% of such cats were carrying *Salmonella*.[5]

Pathogenesis

Salmonella organisms are passed from animal to animal by the fecal-oral route. *Salmonella* can also grow in pet foods; this can be another source of infection. Organisms can survive for some time on objects in the environment. Environmental and fecal contamination are considered synonymous. An outbreak of *Salmonella* infection in cats has been linked to an epidemic of salmonellosis in migratory song birds in the northeastern United States.[13] Cats apparently contracted the infection by preying on diseased birds or by hunting in areas where birds congregated.

Salmonella replicates initially in the GI tract. However, GI tract colonization following ingestion requires quite large doses of organisms.[16] This is probably why salmonellosis is more apt to be seen in dense populations of cats and in conditions of close confinement and poor sanitation. If enough organisms escape the acidic environment of the stomach, they attach to the ileal villi. They then invade and multiply within the villi and reach the mesenteric lymph nodes. Bacteremia is infrequent in asymptomatic infections but is common in clinically affected animals.

Clinical Features

Infection with *Salmonella* is usually inapparent. In high-stress situations and environments that favor massive exposure, infection can be clinically apparent. Kittens are also more likely to be clinically affected than adult cats.[3] Therefore, clinical outbreaks of salmonellosis have largely been limited to hospitalized populations of cats or cats in high-density colony-type environments.[5,18] Spontaneous outbreaks of salmonellosis in individual pet animals are uncommon.[6-8,11,12]

The most common clinical form of salmonellosis in cats is acute gastroenteritis, resembling feline panleukopenia, usually manifested by sudden onset of vomiting, diarrhea, fever and depression 2-5 days after exposure.[4,13] The clinical course lasts 2-7 days in most cases.[13] However, clinical signs in some infected cats are subacute to chronic, with nonspecific signs (fever, anorexia, depression).[4] Acute salmonellosis is more apt to be primary and uncomplicated, while subacute and chronic infections more often occur for some underlying reason (nosocomial or opportunistic infections). In severely affected cats, the disease is rapidly terminated by bacteremia and endotoxic shock.[11,17] Neurologic signs have been associated with intestinal signs in at least 1 kitten.[11] One kitten had intestinal signs and hemolytic anemia. Recovery following milder disease occurs in 3-5 days.[12,13]

Miscellaneous forms of salmonellosis have been also observed in cats. Purulent conjunctivitis associated with salmonellosis has been seen in a cat and experimentally recreated in kittens.[5,6] Acute peritonitis associated with *S typhimurium* has been observed in a kitten.[8] *Salmonella choleraesuis* has been associated with abortion in a queen.[7] Salmonellosis was a complicating bacterial infection in two cats following fracture repair and colonic resection.[4]

Pathologic Features

Cats with *Salmonella* gastroenteritis demonstrate reddening of the intestinal mucosa, as well as congestion and reddening of the mesenteric lymph nodes. In septicemic cats, petechial and ecchymotic hemorrhages, vascular thrombosis, and focal necrosis are seen in the liver, spleen, heart, lungs and brain.[4,11,17]

Clinicopathologic Features

Cats with acute salmonellosis are often leukopenic.[4,13,17] The clinical signs, coupled with leukopenia, resemble those of panleukopenia virus infection. The organism is readily isolated from affected organs and rectal swabs. Bacteremia is present in many cats with salmonellosis; therefore, blood cultures are warranted in any cat with specific or vague GI signs and/or leukopenia.

Treatment and Prevention

Outbreaks of salmonellosis in hospitals and similar settings are often associated with antibiotic-resistant strains. Chloramphenicol and trimethoprim-sulfonamides are the drugs of choice.[4] However, there is some controversy about use of antibiotics to treat uncomplicated cases of *Salmonella* gastroenteritis. Antibiotics can actually favor the growth of antibiotic-resistant *Salmonella* and depress the normal inhibitory flora. Antibiotic therapy also delays establishment of immunity and prolongs fecal shedding in many cats. Such cats should be treated supportively by withholding food or water during the period of vomiting and diarrhea, administering parenteral fluids and enforcing rest. Unfortunately, clinical salmonellosis in cats is often acute and severe, and a decision to treat is often made before a diagnosis is confirmed by culture. Mortality was 61% among affected cats in one outbreak.[18] Therefore, acute salmonellosis in cats should not be viewed lightly.

Infection and Immunity

Clinical salmonellosis is difficult to recreate experimentally. Cats can be experimentally infected by oral inoculation with virulent *Salmonella,* but they shed the organisms without becoming ill.[18] This suggests that factors in addition to the dose of organisms are important in causing disease. Cats experimentally infected with *Salmonella* shed organisms for only about 10 days, though an occasional cat sheds for 4 weeks or more.[17]

Immunity to *Salmonella* infection appears to be mainly cell mediated. Organisms often persist following establishment of immunity in intestinal epithelial cells and mononuclear cells within mesenteric lymph nodes. Stress factors can delay development of cellular immunity, thus increasing the duration and severity of infection and likelihood of bacteremia. Severe stress or use of corticosteroids can also transiently depress immunity and allow reactivation of bacterial shedding in latent carriers. Persistent feline leukemia virus (FeLV) infection and noninfectious immunosuppressive diseases, such as diabetes mellitus, can also lower resistance in some cats and predispose them to fatal salmonellosis.[4] The possible relationship between FIV infection and salmonellosis must be determined, especially in cats with more chronic and atypical forms of the disease.

Animal and Public Health Considerations

There is little doubt that cats can carry and shed *Salmonella* in their stool. Serotypes found in cats are often identical to those that are pathogenic to people and other animals.[9,10,12,14] Considering the number of cats that are carriers of *Salmonella,* however, there are relatively few reports of people infected by exposure to cats. People are more often infected by other types of animals, and cats and people in the same household may both become infected at the same time from a common source.[9,12]

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Colibacillosis

Cause

Escherichia coli is the only important member of the genus. It is a variably motile, Gram-negative bacterial rod that inhabits the distal digestive tract. Similar to *Salmonella, E coli* resists environmental destruction and can survive outside the animal for long periods.

Pathogenesis

Escherichia coli, a natural inhabitant of intestinal tract of all animals, is pathogenic only under certain conditions. Massive initial colonization of the gut with enterotoxigenic strains, especially in young suscepti-

ble animals, can lead to severe and acute gastroenteritis. *Escherichia coli* can secondarily complicate other diseases (wounds, colonization of damaged heart valves, etc). Septicemic *E coli* infections also occur in immunocompromised hosts or following severe damage to the bowel mucosa.

The pathogenesis of neonatal *E coli* infections is unknown. The high frequency of bacterial pyelonephritis and/or pneumonia in kittens with *E coli* septicemia suggests that the infection either ascends the urinary tract or enters through the upper respiratory tract.[5] Alternatively, the pyelonephritis and pneumonia may be secondary to a primary blood-borne infection. Hematogenous spread of *E coli* may also be associated with a primary umbilical vein infection. Carrier cats serve as a ready source of infection for susceptible cats brought into the cattery. Conversely, new cats may introduce different pathogenic strains of *E coli*.

Clinical Features

Escherichia coli infections of cats are generally of 4 types: bacteremia in neonatal kittens; transient gastroenteritis in weanling kittens; bacteremia in older immunocompromised hosts; and localized infection.

Neonatal colibacillosis is common in kittens. From 10-20% of the neonatal kitten deaths in 2 specific-pathogen-free breeding colonies were due to *E coli* septicemia.[4,14] Hemolytic strains of *E coli* were the most consistent bacterial isolates from kittens that died during the first weeks of life.[13] This form of disease can affect all or part of a litter. One queen had a history of entire litters of fading kittens, and one of the kittens that was necropsied had *E coli* septicemia.[5]

Transient gastroenteritis associated with pathogenic strains of *E coli* has been infrequently described in young cats,[8,11] but is probably common. Following ingestion, enteropathogenic strains of *E coli* attach to intestinal mucosal cells and secrete enterotoxins. The toxin causes transient osmotic diarrhea. Infection is terminated when local immunity is established and bacteria-coated intestinal epithelial cells slough, usually after 3-7 days. Very young animals, which are more sensitive to acute fluid and electrolyte imbalances, are more apt to be clinically affected than older animals. Prerequisites for coliform enteritis include exposure to very large numbers of toxin-producing *E coli* and exposure to strains against which the animal has little or no previous immunity. Therefore, disease is more likely in high-density populations where sanitation is poor and fecal contamination is high, and in environments with a frequent influx of animals from different sources. Each environment may have a different strain of enteropathogenic *E coli* to which it is resistant. If a cat carrying one strain is introduced into a cattery that has never experienced infection with that strain, a brief epizootic of enteritis may follow. The same is true of the susceptible newcomer that is exposed to a resident population of cats carrying their uniquely different strains of *E coli*. For these reasons, cattery environments are much more apt to have transient outbreaks of *E coli* gastroenteritis than households.

Fulminating bacterial septicemia, often due to *E coli*, is common in immunocompromised cats. Predisposing conditions include antibody deficiency in neonates that have not received colostrum, feline panleukopenia and various forms of feline leukemia virus (FeLV) infection. Feline panleukopenia is associated with profound depletion of WBCs and severe intestinal damage. Both situations favor rapid movement of bacteria from the intestine to the bloodstream. Cats with myeloproliferative disease, aplastic anemia and various preleukemic (myelodysplastic) disorders often have profound leukopenia and diminished immunoresponsiveness. Such animals may develop severe enterocolitis and bacteremia.

Escherichia coli have been associated with a number of localized infectious processes in cats. Acute and chronic pyelonephritis in mature cats, though uncommon, is often associated with *E coli*. *Escherichia coli* has also been isolated from cat-bite abscesses and wound infections. Septic endometritis has been associated with *E coli*.[8,13] *Escherichia coli* has also been commonly associated with pyometra in cats.[2,6] Though *E coli* is frequently associated with cystitis in dogs, it is rarely associated with cystitis in cats.[12] *Escherichia coli* has occasionally been isolated from cats with gallbladder infections. Several weanling kittens with *E coli* pneumonia and septicemia have been observed. Fulminating

necrotic colitis has been attributed to *E coli*, though definitive proof is lacking.[3]

Pathologic Features

Lesions caused by *E coli* infection are highly variable, consistent with the numerous clinical forms. Kittens with pyelonephritis have pronounced kidney enlargement and suppurative parenchymal disease. Septicemic forms are also frequently associated with thrombotic phenomena and necrosis. Intestinal disease associated with enterotoxigenic strains usually causes mild or inapparent tissue changes.

Clinicopathologic Features

Escherichia coli is readily isolated from affected tissues, and frequently from the blood in fulminating cases of colibacillosis in kittens or immunocompromised adults.

Treatment and Prevention

In a study of the pattern of antibiotic resistance of *E coli* isolated from rectal swabs taken from 93 cats in the Brisbane area, *E coli* strains resistant to common antibacterials (tetracycline, streptomycin, ampicillin, sulfanilamides) were obtained from 26% of the cats sampled.[10] Cephalosporins, aminoglycosides and chloramphenicol were usually effective against most isolates. An aminoglycoside antibiotic, such as amikacin or gentamicin, combined with a penicillin, such as ampicillin, is a particularly effective treatment for coliform septicemia in young kittens.

Infection and Immunity

Similar to the pattern of infection caused by normal commensal bacteria, *E coli* is only pathogenic under conditions that increase the degree of exposure, or damage local and systemic immune defenses. There is some indication, but no definitive proof, that kittens succumbing to coliform septicemias in the first 1-2 weeks of life may be deficient in passive maternal immunity.

Animal and Public Health Considerations

Escherichia coli is ubiquitous and pathogenic strains are widespread. Affected or healthy cats carrying potentially pathogenic serotypes are not considered a public or animal health hazard.

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Cat Scratch Disease (Cat Scratch Fever)

Cat scratch disease is a condition mainly of people rather than of cats. It is mentioned here because it is one of the most important zoonotic (animal to person) diseases of cats. Cats are implicated in most cases of the disease, and veterinarians are often called upon to advise clients on the disorder. Recent studies indicate that the cat scratch bacillus may also cause idiopathic lymphadenopathy in cats.[4,5]

Cause

The causative agent of cat scratch disease is a small Gram-negative bacterial rod that has only been recently cultured *in*

vitro.[4,12] It is often observed within capillary walls in involved regional lymph nodes and, on occasion, in tissues at the primary inoculation site.[9,12] About 90% of human infections result from a scratch, lick or bite from a cat, usually a kitten.[10,11] The disease has been observed less commonly following dog bites, or from puncture wounds associated with thorns, wood splinters or fish bones. Epidemiologic studies indicate that cats may be mechanical vectors and not hosts of the organism for the following reasons: cats implicated as the source of human infection fail to react to cat scratch antigen when skin-tested; involved cats appear to only transmit the causative agent for a brief period, usually 2-3 weeks; and attempts to isolate the causative agent from cat saliva or claws have been unsuccessful.[10] It is also possible that the agent is a part of the normal oral flora of some cats.[5] The organism would then be transmitted to the claws during grooming and from cat-to-cat or cat-to-person by scratching or biting.

Pathogenesis

Cat scratch disease of people occurs throughout the world, more commonly in children than adults, and more frequently in males than females.[10,11] Most cases occur in fall and winter in cooler climates, while seasonal variation is minimal in the tropics. About 2000 cases are reported annually in the United States but the true incidence is unknown. Positive skin tests for the infection are seen in 12-29% of veterinarians and less than 5% of healthy people in other occupations, indicating that subclinical or mild infections are common.

The organism can apparently enter the body through broken skin or by mucous membrane contact. About 90% of patients have primary skin infections, 7% have primary conjunctival infections, and 2% have primary infections of other mucous membranes.[10,11]

The disease begins at the site of initial contact.[10,11] The earliest skin lesion is a single small papule or pustule, or a number of erythematous macules. Conjunctivitis is common in individuals exposed by the conjunctival route, while small mucosal granulomas are associated with primary infection of the mucous membranes. Infection spreads via lymphatics to the regional lymph nodes. However, lymphangitis is not a feature of the disease. Regional lymphadenitis occurs 3-50 days after exposure.[10,11]

Cat scratch disease is usually limited to the site of infection and the regional lymph node(s). Systemic spread has been observed in less than 5% of individuals.[10,11] Systemic manifestations usually result from involvement of the CNS, lungs, liver or bone.[3,10]

Clinical Features

Most patients are not seen until regional lymphadenopathy becomes prominent. An erythematous papular or pustular lesion at the site of infection is detectable in 54-96% of affected people after careful examination.[10,11] Fever, malaise and influenza-like symptoms lasting 1-3 weeks are seen at onset of lymphadenopathy in less than 50% of affected individuals. More widespread skin disorders, characterized by maculopapules, petechiae, erythema nodosum or erythema multiforme exanthema, are associated with the disease in less than 5% of patients. Splenomegaly is detected in about 16% of affected people.[10]

The involved lymph nodes are usually in the axilla, neck or groin, variably tender on palpation and 1-8 cm in diameter. Lymph node enlargement usually persists for 2-4 months and rarely for up to 2 years. Suppuration, detected by needle aspiration, occurs later in the course of the disease in 13% of patients.[10] Spontaneous rupture and drainage of a suppurative node occurs in less than 6% of patients.

In people with primary conjunctival lesions, infection often spreads to the lymph nodes of the head and neck and results in a condition called the oculoglandular syndrome of Parinaud. The parotid area is often swollen due to periauricular lymph node enlargement.[2]

When central nervous system involvement occurs, it appears within 1-6 weeks of the adenopathy. The encephalitic form of the disease may be manifested (in order of frequency) by coma, convulsions, encephalopathy, meningitis, radiculitis, polyneuritis, myelitis with paraplegia, and lethargy and/or confusion.[10] Neurologic manifestations progress over 1-2 weeks and then gradually resolve over the next 1-6 months.

Atypical pneumonia and localized osteomyelitis are uncommon systemic manifestations of the disease.[3,10] Osteomyelitis can result from hematogenous spread or extension from adjacent affected lymph nodes.[3] Hepatic abscesses have also been associated with the cat scratch agent.

The full spectrum of cat scratch disease in cats has not yet been defined. A syndrome of idiopathic generalized lymphadenopathy has been the only disease condition linked to the agent.[4,5]

Pathologic Features

Characteristic lesions of cat scratch disease are seen mainly in affected lymph nodes. Multiple microabscesses appear in the nodes later in the course of disease, only to be replaced by frank abscess formation. Differential diagnoses in the latter stages include tularemia, brucellosis, tuberculosis or sarcoidosis.[4,10]

Hodgkins' disease is the main differential diagnosis in the earlier stages of infection.[7] Cat scratch disease has also mimicked malignant lymphoma in some individuals.[8]

Clinicopathologic Features

Cat scratch disease should be strongly considered in any child or adolescent with persistent localized lymphadenopathy lasting longer than 3 weeks.[10,11] The diagnosis is strengthened by the presence of dermal or conjunctival lesions and history of exposure to a cat within the previous 2 weeks. The diagnosis is less readily made in patients with atypical forms of the disease. Diagnosis of cat scratch disease is usually confirmed when 3 of the following 4 findings are present: history of contact with an animal, usually a cat, and presence of a primary dermal or eye lesion; aspiration of sterile pus from an involved lymph node or laboratory tests that exclude other causes of adenopathy; a positive delayed-hypersensitivity reaction in the skin to cat scratch antigen; and a node biopsy revealing characteristic histopathologic changes, especially if organisms can be identified with Warthin-Starry silver stain.[10]

The cat scratch skin test is positive in about 90% of affected individuals, providing that the duration of illness has been at least 3-4 weeks. The antigen for the test is made from pus collected from patients. A positive reaction consists of a wheal or papule occurring 48-72 hours after intradermal inoculation.

There is no known way to identify whether a cat is harboring the causative agent. Cats invariably react negatively to cat scratch antigen, and the causative agent has not been identified in saliva or on the claws of potentially infectious cats.

Treatment and Prevention

The course of cat scratch disease is usually benign and the disease spontaneously resolves within 2-3 months. Aspiration of pus from suppurated nodes may be necessary to relieve pain and discomfort.

With the isolation of the organism in culture, it has been possible to conduct antibiotic sensitivities on the cat scratch bacillus. It is sensitive *in vitro* to cefoxitin sodium, gentamicin sulfate, amikacin sulfate, tobramycin sulfate, netilmicin sulfate and mezlocilin sodium.[4] *In-vivo* studies appear to confirm the sensitivity of the agent to these antibiotics.[1] Therefore, antibiotic therapy will probably become the treatment of choice for cat scratch disease in people.

Infection and Immunity

Cat scratch disease is typical of a number of bacterial and fungal infections that enter the body through skin abrasions or mucous membranes and spread slowly to regional lymph nodes. Immunity remains strong for many years following recovery.[10]

Animal and Public Health Considerations

Though cat scratch disease can be reproduced with pus in people, monkeys, baboons and the Hartley strain of guinea pigs, there is no evidence of natural person-to-person transmission. It remains to be determined whether diseased cats are any greater risk to other cats or people than asymptomatic animals.

Veterinarians are often called upon to pass judgment on cats associated with human exposure. This is probably best left to people who are considered experts in the disease. Cats only appear to transmit the organism for 2- to 3-week periods or less.[10]

If this is the case, implicated cats can be loosely quarantined from children and adolescents for 2-3 weeks and then allowed to live a normal life. The disease is also very sporadic, and only an infinitesimally small portion of cat bites, scratches or licks lead to the disease. It has also been noted that 12-29% of veterinarians test positive with the cat scratch antigen, as compared to less than 5% of other healthy people and family contacts.[10] Therefore, many veterinarians have been unknowingly infected with the organism at some stage in their careers. Given this information, it is wise not to overreact to the disease or condemn the cat.

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Chlamydiosis

Cause

Chlamydia psittaci variety *felis* parasitizes living cells like a virus, but the organism is more closely related to bacteria. The feline organism can be differentiated from the more virulent avian strains.[1,6] Unlike bacteria, *Chlamydia* depends on host cells for energy. Like bacteria, it is inhibited by certain antibiotics.

Chlamydia psittaci of cats is primarily an inhabitant of mucosal cells of the conjunctiva and genital tract. Yet unclassified *Chlamydia* species inhabit the gastric mucosa of many normal cats.[9] Though gastric isolates cause mild upper respiratory diseasae and gastritis in highly immunocompromised cats, its role in classic feline chlamydiosis has not been determined.[7] In all likelihood, chlamydial isolates from the stomach are either identical or closely related to those found in the conjunctiva and genital tract.

Chlamydia psittaci has been isolated from diseased cats in the United States, Canada, Australia, England and Iran.[3,8,11, 15,18,19] It is found in most cattery populations and is widespread among groups of free-roaming domestic and feral cats.[3,8,18,20]

The organism is carried by clinically ill as well as asymptomatic cats within the epithelial cells of the conjunctiva and gastrointestinal and distal genital tracts. These carrier cats shed low levels of organisms in secretions and feces, but shedding may be greatly increased in situations of heavy stress.[15] Transmission is horizontal from clinical, subclinical or asymptomatic carriers to susceptible animals, and occurs at birth or in the postweaning period when maternal immunity has waned. Some chlamydial vaccines have also been linked to outbreaks of chlamydiosis in cats.

Pathogenesis

Infection requires intimate exposure; fleeting contacts or aerosol exposure over a distance are not usually sufficient. Spread via contaminated objects is also unlikely. *Chlamydia* attach themselves to mucosal cells following contact and are taken into the cell. The organisms infect adjacent epithelial cells and the cycle of replication and infection continues until it is suppressed by host immunity.

Clinical Features

There has been some confusion on the precise types of diseases caused by *C psittaci* in cats. The organism was first isolated from cats with so-called "pneumonitis."[2] This term was used to describe what is now called upper respiratory infection (conjunctivitis, rhinitis, sneezing) or "URI."

Pneumonitis, in its strictest meaning, is a pathologic term that means "inflammation of the lungs." After its discovery, *C psittaci* was thought to be the cause of most upper respiratory disease in cats. With the subsequent discovery of respiratory viruses, it was realized that respiratory disease of cats was in truth multifactorial. In many cases, especially in kittens, multiple agents could be isolated simultaneously from the same animals. When *Chlamydia* was inoculated into susceptible cats by itself, it produced a relatively mild disease manifested mainly by conjunctivitis. With these discoveries, the importance of *Chlamydia* in feline respiratory disease was deemphasized in favor of viruses. This was unfortunate, because chlamydiosis is still an extremely troublesome infection of cats kept in high-density, high-stress multiple-cat environments.

Chlamydia psittaci variety *felis* has been associated with 2 major and several minor disease syndromes of cats. The 2 major disease syndromes include ophthalmitis neonatorum (neonatal conjunctivitis) in neonates (0-2 weeks of age) and conjunctivitis in postweanling (6-12 weeks) kittens. Minor syndromes include fatal neonatal pneumonia, abortion, stillbirths and possibly infertility. All of these syndromes are analogous to forms of human chlamydiosis.

Neonatal conjunctivitis can affect entire litters of kittens, and may be particularly troublesome and recurrent in certain younger queens. The neonates are thought to be infected by the passage of contaminated birthing fluids up the nostrils and nasolacrimal ducts. Conjunctivitis then develops behind the closed eyelids and is usually exudative in nature. The first noticeable sign of the disease is a delay in opening one or both of the eyelids at the normal age of 7-10 days (Fig 21). Bulging of the closed eyelids is often seen, and is due to accumulation of exudate. There is frequently a crusting of honey-like exudate along the closed or partially opened lid margins. When the eyelids are forced open, a copious amount of whitish to grayish mucoid material is exuded. The underlying conjunctivitis is noticeable when the exudate is carefully cleaned away (Fig 21). Failure to open the eyelids and drain the exudates can result in corneal ulcers, some of which may perforate. Aside from the ocular disease, affected kittens appear otherwise normal and grow at a normal rate. The conjunctivitis persists for as long as 2-4 weeks if untreated.

Conjunctivitis in 6- to 12-week old kittens is the most common clinical manifestation of chlamydiosis in cats.[3,10] This form of the disease has been experimentally recreated on several occasions.[4,10,15] Conjunctivitis appears 5-10 days after aerosol exposure.[10] This is followed by a low-grade fever on days 11-15, which lasts for 3-8 days. The fever is likely to go unnoticed, especially because most kittens continue to eat and act otherwise normal. The conjunctivitis is often unilateral in both natural and experimentally induced infections (Fig 22). Even when the disease is bilateral, one eye is often more seriously affected. Rhinitis is usually mild or inapparent, and sneezing is therefore infrequent. The course of primary disease is 2-6 weeks in kittens and 2 weeks or less in older cats.

Chronic chlamydial conjunctivitis sometimes occurs in cats with abnormal ocular conformation. One adult Persian with severe facial foreshortening, exophthalmos, lagophthalmos and chronic tearing had associated bacterial and chlamydial infections (Fig 23).

Recurrent bouts of chlamydial conjunctivitis have been observed in some older cats. Recurrent disease can be due to reactiva-

Figure 21. Kitten with ophthalmitis neonatorum. The first signs are failure of the eyes to open at the normal time, bulging of the closed eyelids, and a honey-colored exudate along the lid margins. If the eyelids are forced open, a typical mucinous, cloudy exudate is evident behind the eyelids. The underlying conjunctivitis is apparent when the exudate is wiped away.

tion of a low-grade asymptomatic infection in a carrier cat, or from reinfection during waning immunity. Recurrent attacks of chlamydial conjunctivitis are seldom as severe as primary attacks, and usually last no longer than 5-10 days.

Chlamydia is a common cause of severe systemic diseases (pneumonia, arthritis) in young livestock, such as foals, calves, lambs, kids and poults. Systemic disease is associated with hematogenous spread of the organism from localized sites of infection in the mucous membranes. Paradoxically, kittens often have severe localized infections but systemic spread is very uncommon. Nevertheless, *Chlamydia* has been isolated from the lungs of 3 kittens from a litter of 6 that died within the first few days of life.[15] The lungs appeared to be grossly consolidated. This condition may be analogous to chlamydial neonatal pneumonitis in human infants.

Chlamydia is emerging as an important cause of abortion and infertility (chronic infection of Fallopian tubes) in people and certain livestock species. However, the role of *Chlamydia* in such diseases of cats is presently unknown. A high incidence of abortion has been associated with outbreaks of chlamydial conjunctivitis in a cattery.[15]

Figure 22. Typical chlamydial conjunctivitis in an 8-week-old kitten. The conjunctivitis is usually unilateral in the early stages, with pronounced epiphora and conjunctival swelling.

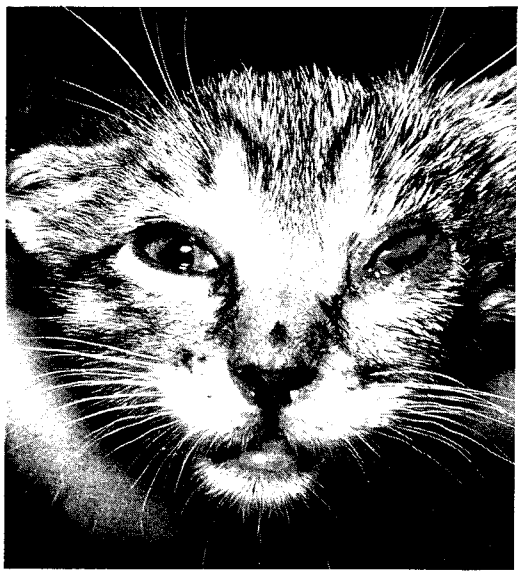

Figure 23. Adult Persian cat with long-standing bilateral conjunctivitis. *Chlamydia psittaci* was seen in conjunctival scrapings. The conjunctivitis cleared with use of tetracycline ophthalmic ointment. However, reinfection is common after therapy is discontinued. Cats with compressed faces may be predisposed to chronic bacterial, mycoplasmal and chlamydial infections because of the relative dryness of their central cornea (lagophthalmos) and excessive tear spillage from abnormal lacrimal apparatus anatomy.

More research is needed in this area of feline reproduction.

Pathologic Features

Conjunctival inflammation changes to prominent lymphoid nodules late in the disease and before recovery begins.

Lung lesions are not significant, but small foci of pneumonia are seen in some animals.[10]

Clinicopathologic Features

Conjunctivitis that usually starts in one eye is presumptive evidence for chlamydial infection, especially if it occurs in weanling kittens from a cattery environment or in older cats under recent stress. The main differential diagnosis in kittens is mycoplasmal conjunctivitis, which can appear in an identical form. In fact, mycoplasmal and chlamydial diseases are often concurrent.[4] Older cats with acute unilateral conjunctivitis should be examined closely for foreign bodies.

Definitive diagnosis of chlamydiosis is by identification of the organism in epithelial cells or by isolation in culture. Conjunctival

scrapings can be stained by conventional or immunofluorescent antibody techniques, the latter being more sensitive.[4]

Treatment and Prevention

Tetracycline is the drug of choice for treatment of cats with *C psittaci* infection. Cats should be treated mainly with topical tetracycline ophthalmic ointments 3-5 times daily for 2 weeks. Response is prompt but recurrences are sometimes seen when the medication is withdrawn. Tetracycline and related antibiotics inhibit growth of the organism, but ultimate recovery depends on development of host immunity, a process that can take 6 weeks or more. Withdrawal of the medication before immunity is established can allow the organisms to proliferate. Systemic therapy is questionable in cats with localized disease. Systemic tetracycline can discolor the erupting permanent teeth if given to kittens. Systemic tetracycline also can cause fever and anorexia as a side effect. The infection is usually superficial, and the potential side effects of systemic therapy are not compensated for by any added therapeutic benefits. However, systemic therapy is warranted in cases where systemic disease or infertility are suspected.[11]

Several vaccines are available for prevention of *C psittaci* infection in cats. Chlamydial vaccines usually contain attenuated living organisms and are generally given in combination with other feline vaccines.[12,13] Despite considerable favorable advertising claims, chlamydial vaccines should be considered poor at best.[5,16,22] This relatively poor efficacy is not a factor of the vaccine itself, but is due to the nature of chlamydial immunity. Natural infection evokes weak and often transient immunity. A chronic carrier state in the face of immunity is the rule rather than the exception. Given these circumstances, it should not be surprising that artificially induced immunity would be more effective.

Chlamydial vaccines decrease the severity of the primary infection but do not prevent colonization of the conjunctiva, gastrointestinal or genital tracts with virulent organisms and the chronic carrier state.[14,20] Even their efficacy against primary disease is lessened if the exposure is high and stress factors are unfavorable. As such, chlamydial vaccines appear to perform much better in environments and under conditions in which disease is not severe anyway. They perform poorly in high-density situations where disease is most severe. This is supported by experimental evidence; cats vaccinated with live chlamydial vaccines developed incomplete resistance to challenge-exposure.[16,22] Though clinical signs of primary infection were diminished, two-thirds of vaccinated cats shed virulent organisms for 21-35 days after challenge and one-third for 61 days or longer.[16]

Control of chlamydiosis in problem catteries must rely heavily on environmental control. Properly managed catteries with low stress levels have very few problems with chlamydiosis even though the infection may be enzootic (see chapter on cattery design and management).

Infection and Immunity

Chlamydial infection stimulates both humoral and cellular immunity.[17] In spite of such immunity, recovery from clinical infection is slow, and persistence of the organism in epithelial cells is common. Once immunity develops, it is generally weak and of relatively short duration. Protective immunity is easily overcome by severe challenge-exposure and is rapidly suppressed by stress. Therefore, recurrent disease is common in the same environments where primary disease is frequent and severe. Recurrent disease results from reinfection in the face of weak immunity and high exposure, or from reactivation of subclinical infections. Recurrent infections are more likely within the first 1-2 years following primary disease. Cats older than 2 years are much more resistant to recurrent disease. Cellular immunity is often slow to develop and takes many months or even years to become solid enough to overcome severe exposure or stress-induced immunosuppression.

The effects of stress on chlamydiosis can be mimicked by corticosteroid administration. Corticosteroids given 40-44 days after infection increased the severity of chlamydial conjunctivitis in cats, an effect that lasted for 4-5 days. Corticosteroids also increase shedding of *Chlamydia* by carrier cats.[15] Therefore, stressful environments are not only more conducive to spread of the organism but are also more apt to produce clinically apparent disease.

Animal and Public Health Considerations

Feline strains of *C psittaci* cause disease in cats and people. However, their role in other species has not been determined.[8] People exposed to cats with active *C psittaci* conjunctivitis have developed conjunctivitis themselves.[14] Human cases of conjunctivitis due to feline chlamydia resemble the feline disease in most respects, except that the duration is usually shorter. It often involves only one eye, the conjunctiva is reddened and edematous, and there is a considerable amount of tearing and irritation. Untreated, the disease lasts 1-2 weeks.

It is doubtful whether *C psittaci* of feline origin is associated with any other chlamydial disease of people. Trachoma, neonatal chlamydiosis, genital infections and ornithosis are all caused by different strains or species of *Chlamydia* than those found in cats.

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Mycoplasmosis

Cause

Mycoplasma and *Mycoplasma*-like organisms belong to 3 groups: *Mycoplasma*; *Ureaplasma* or *T-mycoplasma*; and *Acholeplasma* species. *Mycoplasma*, *Ureaplasma* (*T-mycoplasma*) and *Acholeplasma* species are all commonly isolated from domestic cats. *Mycoplasma felis* and *M gatea* are the most prevalent mycoplasmas in cats.[1,2,12,29]

Pathogenesis

The pathogenicity of mycoplasmal strains varies greatly in cats. *Mycoplasma felis* has been isolated 7-8 times more frequently from cats with respiratory disorders than from normal animals. *Mycoplasma arginini* was isolated at about the same rate in sick and normal animals.[30] The lack of pathogenicity of *M arginini* for cats was reconfirmed.[26] Likewise, *A laidlawii* appears to be nonpathogenic for cats and probably exists as a saprophyte in many species of animals.[30] *Mycoplasma gatea* was isolated more often from normal than sick cats.[26] However, *M gatea* has been isolated from an older animal with widespread arthritis

and tenosynovitis. This appeared to have been an opportunistic infection in an immunocompromised animal.[19]

Mycoplasmal infections are probably acquired at a relatively young age. Many older animals harbor the organisms in the mucous linings of the conjunctival sac, oropharynx and genital tracts (prepuce and vagina). Infection of kittens may occur at birth or shortly thereafter through exposure to vaginal or oropharyngeal secretions from the queen. If kittens are not infected at birth or within the first few weeks of life, they almost certainly are exposed to the organisms as they contact carrier animals after weaning. Following infection, the subsequent course of disease is probably influenced by the animal's immunologic status. Animals most susceptible to disease include fetuses that are not immunologically competent, neonates that have immature immune systems and low levels of maternal antibodies, and postweaning kittens that are partially immunologically competent but have lost their maternal immunity. Older cats that have become immunocompromised through some other primary illness may also be at risk.

Clinical Features

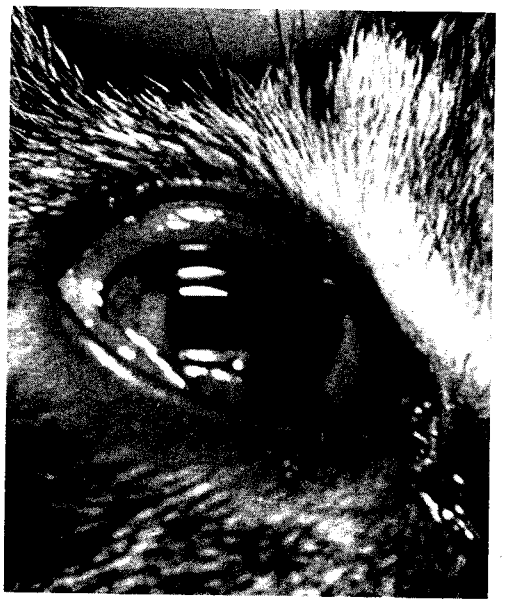
Mycoplasma and *Mycoplasma*-like organisms are important pathogens in lambs, kids, calves, foals and poults. Infections in these species are initially localized but frequently disseminate hematogenously to the lungs and joints. The disease-causing potential of mycoplasmal organisms in cats appears to be much less. Initial infections remain localized and disseminated disease is uncommon in immunocompetent individuals. Conjunctivitis is the most common clinical manifestation of mycoplasmosis in cats.

Mycoplasma isolated from naturally diseased animals did not cause conjunctivitis in normal cats but readily did so in animals that had first received an intrapalpebral inoculation of corticosteroids.[5] Subsequent studies linked *Mycoplasma* to conjunctivitis merely because it was isolated more frequently from inflamed eyes than normal eyes.[10,17,27,32] However, those studies did not consider primary infection and coinfection with other agents, such as herpesvirus or *Chlamydia*.[2,20]

It was not until 1974 that conclusive evidence was obtained for the role of *Mycoplasma* in conjunctivitis.[24] These latter experiments involved kittens, which are more sensitive to infection than adults.

Mycoplasmal conjunctivitis is most frequently caused by *M felis*.[29] It is predominantly a cattery disease and is seldom seen in kittens from single-cat homes. It usually develops shortly after kittens are weaned, around 8-12 weeks of age. The earliest signs are acute swelling and reddening of the conjunctiva in 1 or both eyes (Fig 24). Conjunctivitis may be associated with some squinting and photophobia. Inflammation of the conjunctiva varies greatly; conjunctival membranes may be only slightly reddened or may be so swollen that the globe is barely visible. Early in the disease, the exudate is usually serous but it may become somewhat purulent with time. A diphtheritic or fibrinous coating may sometimes be seen on the inflamed conjunctiva and is highly conducive to formation of conjunctival-corneal adhesions. Sneezing is either mild or not seen and, if present, is more apt to be due to excessive nasolacrimal drainage from the inflamed conjunctiva than from rhinitis. Severe concurrent sneezing and nasal discharge in kittens with unilateral

Figure 24. Mycoplasmal conjunctivitis in a cat. The conjunctiva is swollen and glistening, and the hair around the lower eyelid is wet from the serous discharge.



conjunctivitis usually indicate a complicating herpesvirus infection.

Mycoplasma organisms tend to disappear from the conjunctival sac upon recovery but may persist in the oropharynx. Conjunctivitis may recur in older cats, especially following stress or major disease outbreaks among younger animals. Recurrent disease resembles the primary infection but is usually milder and seldom lasts longer than 7-10 days.

Corneal-conjunctival adhesions may be important sequelae in cats with diphtheritic inflammation. Secondary infections of the conjunctiva with staphylococci or *Pseudomonas* can sometimes occur and, if improperly treated, can lead to corneal ulceration and even perforation.

Mycoplasmal conjunctivitis in cats is often associated with chlamydial conjunctivitis.[6,7] Chlamydial conjunctivitis has virtually the same pathogenesis as mycoplasmal conjunctivitis. Therefore, it is not surprising that *Mycoplasma* and *Chlamydia* infections often occur together.

Pneumonia is an important systemic complication of localized mycoplasmosis in many species of animals but is surprisingly uncommon in cats. The author observed an outbreak of mycoplasmal pneumonia and conjunctivitis in 6 adult cats that had received an injection of long-acting methylprednisolone 2 weeks earlier and in a litter of 4-week-old kittens.

Arthritis and tenosynovitis, though common in other domestic species, are uncommon manifestations of mycoplasmosis in cats. This again indicates the marked resistance that cats have to systemic spread of *Mycoplasma*. *Mycoplasma gatea* was isolated from the synovium of an 8-year-old cat with chronic fibrinopurulent tenosynovitis.[19] This infection appeared to be opportunistic because the cat also had a chronic nasal infection and hypogammaglobulinemia. Though the cat was feline leukemia virus (FeLV) negative, the possibility of some other concurrent virus-induced immunosuppression (feline immunodeficiency virus infection) or nonviral immunocompromising disease was not established. Mycoplasmal polyarthritis has been observed in a second severely immunocompromised cat.[15] Mycoplasmal polyarthritis has also been observed in 2 aged cats seen at the Veterinary Medical Teaching Hospital, University of California, Davis. Both cats had advanced cancer and were undergoing extensive therapy when arthritis occurred.

Urethritis and cystitis have been associated with *Mycoplasma* and *Ureaplasma* in people. They have also been isolated infrequently from dogs with cystitis. Though they have been frequently isolated from the distal genital tracts of male and female cats, they have not been associated with disease. They have not been isolated from cats with feline urologic syndrome, a disease that is probably of dietary origin.

Mycoplasma has caused fetal death and abortions in people, cattle and sheep. Given the high incidence of mycoplasmal infection in catteries and the established role of the organism in fetal disease in other species (and possibly cats), further studies of the role of these organisms in feline abortions are needed.

Pathologic Features

Mycoplasmal organisms cause purulent and fibrinopurulent inflammatory reactions early in the course of primary or systemic infection.

Clinicopathologic Features

Organisms can be identified in conjunctival scrapings stained with Giemsa or Macchiavello stains. Mycoplasmal organisms can be cultured using specific types of agar and broth enriched with equine serum. Identification of *Mycoplasma*, *Ureaplasma* or *Acholeplasma* is by colony size and morphology on agar, susceptibility to various antibiotics, serologic reactions or responses in selective biochemical media.[9,13]

Treatment and Prevention

Mycoplasmal conjunctivitis is treated topically with appropriate nonsteroidal ophthalmic ointments. For best results, medication should be applied 4 times daily or more frequently. Tetracycline is preferred for initial treatment. They are also active against *Chlamydia*, which often complicates mycoplasmal conjunctivitis in cats. Some mycoplasmal isolates are resistant to tetracycline. Erythromycin or spectinomycin should be used in such cases. *Mycoplasma* is resistant to penicillins, cepha-

losporins and aminoglycosides. Systemic antibiotic treatment is not warranted in kittens with localized disease. It only adds to the stress of the condition and may induce intestinal upset. Therapy should be continued for at least 3-5 days after conjunctivitis has completely resolved. Conjunctivitis, especially in kittens, may recur after therapy is discontinued. Therapy must be reinstituted in such cases. If systemic infections are suspected, oral or parenteral tetracyclines are the drugs of choice. However, they can permanently discolor the permanent teeth when given to kittens.

Mycoplasmosis in catteries can be controlled to a great extent with proper design and management. This includes limiting stress and numbers of kittens, and isolating kittens by litters from other young cats.

Infection and Immunity

Cats appear to have a great deal of natural resistance to systemic spread of mycoplasmal infections from primary disease sites in the upper respiratory tract. Therefore, cats are spared from the most serious manifestations of the disease. The reason for this species resistance is not known but it also extends to chlamydial immunity. *Chlamydia* and *Mycoplasma* are responsible for virtually the same type of localized and systemic diseases in cats and other animals. Therefore, it is not surprising that cats show a similar type of resistance to both organisms.

Opportunistic mycoplasmal infections have been seen in older immunocompromised cats. They mimic systemic forms of infection, such as arthritis and serosal disease, seen in susceptible species of animals. The author has observed severe mycoplasmal pneumonia and conjunctivitis in 6 adult cats that received an injection of repository methylprednisolone 2 weeks previously.

Animal and Public Health Considerations

Cats with mycoplasmal infections are not considered public health hazards. The main pathogenic *Mycoplasma* species is *M felis*, an inhabitant of cats that has not been identified in other species. Therefore, cats are the principal reservoir for their own infections. Though cats apparently spread the infection to each other, the myriad environmental and host-resistance factors that influence disease are probably more important than actual exposure in determining the clinical outcome of mycoplasmosis.

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Dermatomycosis (Ringworm)

Cause

Dermatomycosis (ringworm, tinea or dermatophytosis) is a skin condition caused by a group of fungi known as dermatophytes. Dermatophytes penetrate and parasitize keratinous body tissue, such as skin, hair, feathers, horns or nails. There are presently over 35 species of dermatophytes belonging to 3 genera: *Epidermophyton, Microsporum* and *Trichophyton*. Some species of dermatophytes are zoophilic (live on animals), some are anthrophilic (live on people), and others are geophilic (live in soil) (Table 5).[10,16] Among the 35 or so species, only 6 are of particular interest to cats. These 6 species include *Microsporum canis*, *M distortum*, *M gypseum*, *Trichophyton mentagrophytes*, *T verrucosum* and *T rubrum*.[1,3,4,6,14,19,23,30,34,38,42] *Microsporum cookei* and *M gallinae* have been rarely implicated with dermatomycosis in cats.[10] *Trichophyton terrestre* has been associated with ringworm in a cat from the United States.[45] However, it usually is present on the cat's fur as a contaminant or inapparent infection.[2]

Microsporum canis accounts for 75-98% of ringworm seen in cats in most parts of the world.[1,6,18,20,21,38,43] *Microsporum distortum* is a major cause of feline ringworm in Southern New Zealand but is uncommon elsewhere in the world. *Microsporum gypseum* accounts for 0.5-30% of the cases of feline ringworm.[6,18-20,34] Various species of *Trichophyton* account for less than 1% of the cases of feline ringworm; they are more common in dogs or livestock.

Because *Microsporum* species account for almost all feline ringworm in catteries, and *M canis* is by far the most serious pathogen, the remainder of this discussion will apply mainly to this organism. The pathogenesis of other species of dermatophytes is virtually identical, except for the most common reservoir for spore forms in nature. *Microsporum canis* causes disease in a wide number of animal species and in people. However, despite what its name might suggest, the principal host and victim of *M canis* is the cat.

Pathogenesis

Cats are exposed to dermatophytes from spores shed into the environment by infected animals or by direct animal-to-animal contact. Spores of *M canis* have survived in the environment for as long as 13 months.[22] The degree of environmental contamination is proportional to the numbers of kittens raised in the area, density of cats in the quarters, degree of sanitation (removal of hair, keratinous debris), and level and type of disinfection.

Animal-to-animal contact occurs between clinically affected and susceptible cats or between inapparent carriers and susceptible animals. Though cats with clinical lesions are more apt to shed large numbers of spores, and to be more infectious, up to 40% or more of normal cats in an enzootic environment can also be infected.[3,12,40,48] In a survey of *M canis* infection among 1059 cats seen by veterinarians for various reasons, 5.9% were infected.[23] The infection rate among domestic shorthaired cats was 3.8%, while among purebred cats it was 16.9% in Persians and 38.8% in Siamese.

The greater incidence of dermatophytes in cattery-bred cats as compared to regular household pets underscores the importance of the environment in the spread of ringworm. Age is also an important consideration. The highest isolation rate among random-source cats was in kittens less than 3 months of age (12.6%).[23] The infection rate in this study remained constant at 3-5% in cats up to 4 years of age. The isolation rate drops precipitously to less than 1% in cats older than 4 years of age. This great decrease in infection after 4 years of age is also reflected in a marked drop in the incidence of active lesions in older cats.[32]

Infection usually involves dermal contact with spores in the environment or spores shed from infected animals. *Microsporum canis* spores remain viable on affected hairs for 315-422 days at room temperature.[22] Kittens born in catteries where ringworm is enzootic are usually infected shortly after birth, while kittens born into dermatophyte-free environments do not get infected until they are placed into new homes.

The severity of clinical disease depends on many factors. Kittens that are malnourished, sickly or concurrently infected with viral, bacterial and parasitic agents, kittens that live in stressful conditions, or kittens born in badly contaminated environments develop much more severe disease than kittens born in normal environments. Genetics also appear to play a role. Persian cats have a much higher incidence of clinically apparent infections and the disease course is more severe and protracted in Persians than in other breeds.

Ringworm lesions slowly expand by horizontal and centrifugal growth within the interfollicular keratin layer of the skin and vertical and downward growth along the intrafollicular hair shaft.[41] The actual ringworm lesion only comprises a portion of the infected areas; fluorescent hairs often extend many millimeters around the lesion. Typical ringworm lesions occur because of loss of diseased hairs by early breakage, increased desquamation of keratinized skin, host inflammatory responses, and in some cases, by secondary bacterial infection.

Spread of ringworm infection appears to be halted by immunologic means around day 30 after clinical lesions appear.[41] However, this event can be greatly delayed in sickly, malnourished or heavily stressed kittens with impaired immune responsiveness. Large numbers of infectious spores remain on the hairs after recovery, and these are only lost when the hairs grow out and are shed. This process can take another month or more. Even though recovery is widespread and very dramatic, it is not always complete. Small numbers of chronically infected hair follicles can remain for many more months or years.

Clinical Features

Lesions in naturally infected kittens often begin to appear as early as the second or third week of life. The earliest lesions tend to concentrate on the face and paws, but any area of the body can be affected.[5-7,17,32] Early lesions consist of small plaques that are somewhat erythematous. Eventually hairs in the central part of the lesions are lost, while hairs around the periphery appear discolored and otherwise dead (Fig 25). Lesions slowly expand and coalesce to form large, scaly, grayish-brown areas of

Table 5. Principal environmental reservoirs of common and uncommon dermatophytes of people and animals.

Genus	Animals	People	Soil
Trichophyton	*T equinum* *T mentagrophytes* (several varieties)	*T rubrum*	*T terrestre*
Microsporum	*M canis* *M distortum* *M equinum* *T gallinae*	*M audouinii*	*M gypsum-complex* *M nanum* *M cookei*

hyperkeratosis and alopecia (Fig 25). Over time, hairs in the center part of the lesions begin to regenerate. This central area of hair regrowth, surrounded by a zone of hair loss, which in turn is surrounded by a zone of dead hairs, gives lesions their ring-like appearance.

Involvement of the whiskers and eyelashes is especially severe (Fig 26).[5] The hairs are weakened and shed early in the disease course. Extensive hair involvement around the eyelids can also lead to pronounced depilation and a mild conjunctivitis-like syndrome (Fig 26).

Lesions are frequently found in the skin around the toes and nails. The keratin layer of the nail may be involved and lead to nail deformities.[28] The number of lesions on the body is highly variable. Lesions often remain relatively small and localized; they may not be clinically apparent unless closely inspected. In severe cases, a large proportion of the body can be affected. Such severe cases are least likely to respond to therapy and often persist for months before resolving. Cats with smaller and more localized lesions usually recover spontaneously within a month or so.

Deeper nodular skin lesions called mycetomas have been associated with *M canis* infection in cats.[4,33,46] Persian cats are especially prone to this condition. The lesions were poorly circumscribed, solid or cystic in nature, and granulomatous in appearance on histologic examination. Mycetomas can be particularly extensive and severe in some animals.[33]

Figure 25. Persian kitten with a chronic ringworm lesion behind the ear. The lesion is scaly and pigmented. Hair has been lost from the center of the lesion, while peripheral hairs are thinned and apparently dead. (Courtesy of Dr. Peter Ihrke, University of California, Davis)

Figure 26. Litter of kittens with severe acute dermatomycosis caused by *Microsporum canis*. Note the concentration of lesions around the head, loss of whiskers and eyelashes, and low-grade conjunctivitis. (Courtesy of Dr. Peter Ihrke, University of California, Davis)

Pathologic Features

Dermatophytes are essentially parasites of keratin.[27] Early hair loss is caused by massive invasion and weakening of the hair cuticle. Infection spares the nonkeratinized bulb from which the hair grows, thus ensuring a continued substrate for fungal growth.[27] Involvement of the skin's keratin layer leads to an increased rate of keratin sloughing and formation (hyperkeratosis). Inflammatory reactions in tissues surrounding infected hairs are mild in *M canis* infections.

Clinicopathologic Features

Lesions of many different skin disorders can be mistaken for ringworm. Biopsies are essential when the clinical history, age of the animal, appearance and progression of the lesions, and fluorescence studies do not

clearly indicate a diagnosis of ringworm. When the disease course and history are typical, very little diagnostic testing is needed. A minimum workup should consist of a Wood's lamp fluorescence and examination of hairs by light microscopy.[13]

Fungal elements of *M canis* and *M distortum* within hair shafts fluoresce a whitish to bluish-green when examined closely under a Wood's lamp. Hairs at the periphery of the lesions are most likely to fluoresce. Fluorescence is usually concentrated on the proximal ends of the hairs, but can extend the entire length.

Skin scrapings containing hairs, or hairs pulled from the periphery of lesions, can be examined microscopically for fungi. Visualization of fungi can be aided by partially dissolving the hairs to be examined in 10% KOH. Heating the mixture briefly under a flame hastens the process. Branching hyphae that sometimes invade the hair structure, as well as spores, can be readily identified with some experience.

Treatment and Prevention

Treatment and prevention of ringworm in catteries are directed at individual infected animals, potential carriers, and the environment. Treatment and prevention of ringworm in ordinary household pet cats are directed almost entirely at the affected animal.

Treatment of individual cats with ringworm has consisted of systemic antifungal medications, topical treatments and/or combinations of the 2. All 3 approaches have proven effective in individual animals. However, the efficacy of any particular treatment regimen must be evaluated in context of natural immunity and "self-cures." Many articles on ringworm treatment describe complete cures within 30 days, the same length of time that most lesions take to spontaneously resolve. The true test of any treatment regimen is its ability to cure ringworm in cats with chronic and severe disease.

Griseofulvin has been commonly used for treatment of feline dermatomycosis.[9,17,36] It is usually given orally and is carried systemically to keratinized cells, where it is deposited. An oral dosage of 25 mg/kg, divided twice a day, preferably with a fatty meal, for as long as 8 weeks has been recommended for cats. The efficacy of griseofulvin has been reportedly increased by shaving the animal to remove dead hair and including topical antifungal therapy.[36] Resistance to griseofulvin has been occasionally observed.

Griseofulvin given at the newer recommended dosages has limited toxicity for cats. Toxicity appears to be idiosyncratic and not dose related.[25] It has caused pruritic drug reactions to the skin, angioneurotic edema of the skin, mucous membranes or viscera, fever, lethargy, diarrhea, vomiting, developmental anomalies in kittens born to queens treated during pregnancy, anemia, leukopenia, neurologic problems, weight loss and anorexia.[15,25,44]

Ketoconazole is the newest systemic drug used to treat dermatomycosis in cats.[8,47] The suggested dosage is 10 mg/kg orally once a day for up to 8 weeks. Ketoconazole provided much quicker regression of ringworm lesions than griseofulvin.[39] The drug can irritate the GI tract and suppress the adrenal glands. Toxic signs include anorexia, fever, depression and diarrhea. Newer, safer and more effective imidazole compounds are currently appearing on the market.

Topical treatment is commonly used for localized ringworm, or in combination with systemic drugs in severe generalized disease. In one study, the time for resolution of lesions was reduced by more than one-half in cats that received both topical and systemic treatment, versus that in cats that received systemic therapy alone.[5] Many substances have activity against dermatomycosis, including undecylenic acid, mercaptan, tolnaftate, iodophor, iodochlorhydroxyquin, chlorhexidine, nystatin, thiabendazole, clotrimazole, miconazole and numerous other new topical imidazoles, dilute chlorine solutions, and organic and inorganic iodides. If lesions are extensive, total body clipping of hair facilitates treatment and eliminates a great amount of infectious hairs from the environment. As in systemic therapy, topical treatment is more successful in cats with milder and more acute infections than in cats with severe and chronic disease.

Mycetomas due to *M canis* are very difficult to treat medically and they frequently recur following surgical removal. Ketoconazole and amphotericin B plus griseo-

fulvin have proven unsuccessful in 2 cats, and 3 of 4 cats treated surgically have had recurrences.[4,33,46]

Identification and elimination of carrier cats have been elusive for many veterinarians and cat breeders. Carriers can be identified by using the "brush technique," in which large areas of the body can be sampled.[3,7] Carrier cats, when identified, are usually less than 4 years of age. In many enzootic households, 5-40% or more of younger breeding cats may be carriers.

Many veterinarians and cattery owners have recognized the difficulty and expense of mass culturing, and have attempted to eliminate carrier cats by treating all of the cats in the environment with some systemic antimycotic, such as griseofulvin.[7] Such attempts are usually doomed to failure and may even be deleterious to the health of cats being treated and to the unborn fetus. Systemic antimycotics may temporarily clear the infection but do nothing for bolstering immunity to prevent reinfection when drug therapy is stopped. Topical treatment of all cats in the environment is also likely to fail for the same reasons. Moreover, drug therapy is often done in lieu of environmental control measures, which in the long run may be far more effective.

Environmental factors are of paramount importance in ringworm control programs. Spores of most dermatophytes survive for a year or more in the environment and are very difficult to kill with disinfectants and heat treatment. This is especially true if they are protected by porous surfaces, dust, dirt and other debris. Therefore, the emphasis of spore reduction should be on preventing their accumulation in the first place. When possible, cages should be constructed of impermeable materials that can be easily washed down with soap and hot water. This loosens the spores and allows them to be washed away. Hair, dander and other litter should be swept or vacuumed up as often as possible between washings.

The second important step in ringworm control is to reduce spore shedding by infected animals. This can be done by decreasing the total numbers of cats in the environment (which also reduces stress and hastens recovery), decreasing the numbers of cats less than 4 years of age, decreasing the numbers of kittens, and taking special precautions on reintroducing ringworm into a cattery.

Ultimately, cattery owners must realize that ringworm is enzootic in most environments where large numbers of cats (especially young cats) are kept. However, whether or not the organism causes clinical disease following infection is often more a function of environment and genetics than the disease-causing potential of the organism itself. Cattery owners are often quick to blame outside cats for bringing in the infection, when in truth it is often present continuously in the cattery in a fairly innocuous state. Sudden or gradual changes in the cattery may allow this innocuous infection to increase in severity and eventually become clinically apparent. Catteries with relatively few breeding animals, especially if they are older, have far fewer disease problems with ringworm than catteries with many younger breeding cats. Younger breeding cats may serve as a reservoir for the organism, their kittens being infected at a young age. These infected kittens shed far more spores than their parents and become amplifiers for the organism. New litters that are born shortly thereafter are then exposed to far more fungal spores than the initial litters and as a result of increased exposure they develop even more severe clinical signs. Each subsequent litter further amplifies the infection for those that follow. Segregating litters, maintaining the best sanitation possible, and limiting the number of breeding animals all help to break this amplification process.

The clinical severity of ringworm in a cattery is enhanced by factors that lower young animals' resistance. Upper respiratory and enteric infections, ear mite and flea infestations, genetic predisposition (as seen in the Persian breed), nutritional status, unfavorable temperature and humidity, and overall stress levels associated with overcrowding all contribute to more severe disease. Ultimately, it may not be possible to rid an environment entirely of ringworm. However, it is definitely possible to create an environment in which disease is inapparent or mild and self-limiting.

Vaccines for dermatophyte infections have been widely touted during the last decade and are seeing more and more use. There is no experimental evidence that such

vaccines positively affect the course of ringworm in a cattery. Several vaccinated cats have even developed more severe forms of ringworm. Like many infectious diseases of cats, there is an overreliance on vaccination to cure the problem. This is understandable because vaccination is infinitely easier than the alternative of environmental control.

Infection and Immunity

Dermatophytes are superficial parasites of the keratin layer of skin and hair. They do not invade deeply and are slow to elicit host immunity. Moreover, their location away from living tissues makes it difficult for the host to bring blood-borne immunity into contact with the organism. Nevertheless, some type of immunity develops following infection.

Immunity to dermatophyte infection is not complete when clinical lesions disappear. Infected hair follicles remain for many months, and perhaps years, in some individuals. The numbers of infected hairs are far fewer in "recovered" cats than in animals with active lesions, however. The proportion of infected cats that remain carriers decreases with time. By 4 years of age, hardly any of the cats that were infected as kittens remain carriers.[23] This slow decrease in the carrier rate indicates that total immunity can take many months or years to develop, or that repeated reexposures over a long period of time may be required for complete immunization.

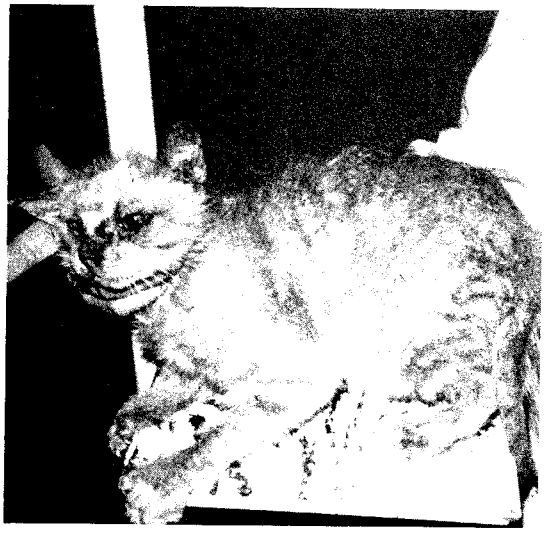
Recurrent infections are seen in both human and feline dermatomycosis. Recurrent disease, unless associated with some immunosuppressive condition, is generally much milder, more localized and more transient than primary disease. Only 1 in 7 recovered kittens is totally resistant to reinfection when exposed 3 months later. Lesions in reinfected kittens also were relatively small, did not tend to spread to secondary sites, and did not last as long as primary lesions.[41]

These findings suggest that immunity to ringworm can be very tenuous in the early stages.

Corticosteroid treatment in the first 1-4 months following recovery may lead to a severe recurrence of disease (Fig 27). Corticosteroid therapy after this time is less apt to cause recurrence. This suggests that a substantial proportion of ultimate ringworm immunity develops in the first few months following infection. Reactivation of disease is particularly severe when long-acting corticosteroids, such as methylprednisolone, are used. Similar to corticosteroids, chronic stress can greatly delay natural recovery from both the initial clinical stage of disease and the subsequent carrier state. It can lead to a higher incidence of clinically apparent infections, more severe disease signs, greater proportion of carriers after recovery, and a longer carrier period. Congenital or acquired diseases can also have a similar effect.

Genetic factors also play a role in ringworm of cats. Individual cats of the Persian breed are especially prone to clinical disease following infection with ringworm spores. Lesions in some Persians tend to be more widespread and to resolve more slowly with or without therapy. Persians are also much more prone to develop more deeply seated lesions (mycetomas) than other breeds.[4,33,46] This predisposition extends even to dermatophytes other than *M canis*.[2] The nature of this increased susceptibility is unknown.

Figure 27. This 8-month-old cat had dermatomycosis (*Microsporum canis*) at 3-4 months of age. The cat was apparently fully recovered until it received an IM injection of repository methylprednisolone at 10 mg/kg. Dermatomycosis reappeared on the face within 2 weeks, and spread rapidly to the remainder of the body. Note the poor haircoat, extensive hair loss on the head, and low-grade conjunctivitis.



Animal and Public Health Considerations

Microsporum canis is the most important cause of ringworm (tinea) in people, and cats are the major reservoir.[10,12,16,18,26,29,32,35,37,43] Cat-to-people transmission of ringworm due to *Trichophyton* is uncommon.[42] Kittens, with or without clinical lesions, are the most common reservoir for *M canis* infection of people, and children are much more commonly affected than adults.[24,26,29,35] The highest infection rate is among children 10 years of age or younger. The incidence declines rapidly in children over 11 years of age. Most adults are resistant to infection or, if infected, lesions are often small, localized and transient. Infected children are not very infectious to other children. The disease course in people, though not as severe as in cats, is surprisingly similar. Lesions in people tend to concentrate on the scalp, forearm, trunk and neck. Recurrent infections throughout life occur in some individuals, while others resist all subsequent exposures. Like cats, some people develop a strong immunity, while in others the it is short-lived and/or tenuous. Secondary infections, similar to those of cats, are more localized, mild and transient than primary infections.

To limit spread of infection from cats with clinical lesions to susceptible people, infected animals should be clipped as close as possible to remove all infected hairs. They should then be dipped periodically over a 2- to 4-week period in some topical antifungal solution to destroy as many remaining surface spores as possible. Infected cats should be handled mainly by adults or older children, who are usually immune or more resistant.

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Coccidiosis

Cause

Coccidiosis is a term used to describe intestinal infections caused by a number of different coccidia. Species of coccidia infecting cats belong to the genera *Isospora, Hammondia, Besnoitia* and *Sarcocystis.*[10] However, classification of these organisms changes rapidly. It has been proposed that *Isospora* species, such as *I felis*, be classified in a new genus called *Cystispora.*[8] Changes in names and classification can be expected as more is learned about individual coccidia.

Various species of intestinal coccidia are found in cats throughout the world. In a survey of cats in the general population in Illinois, Kansas, Missouri, Ohio and Hawaii, 0-1.5% were infected with coccidia that appeared similar to *Toxoplasma* or *Hammondia*, 6-22% with *I felis*, 3-22% with *I rivolta* and 0-0.8% with *Sarcocystis.*[2] However, the precise genera and species of coccidia found within specific groups of cats varies greatly according to their environment and feeding habits. *Isospora* species are the sole or predominant coccidia found within confined cattery cats fed entirely commercial food or cooked meat. *Besnoitia, Hammondia* and *Sarcocystis* are found only in cats allowed to prey on wildlife or that are fed raw or undercooked meat. These differences are due to the life cycles of the various coccidia; only *Isospora* can be spread efficiently from cat to cat (see below). The infection rate of *Isospora* within closely confined groups of cats is also increased because of poor sanitation, overcrowding and stress. Subclinical infection with *I felis* was observed in 49 of 58 cats in a single colony.[15]

Cats are infected with *Isospora* by ingesting sporulated oocysts (shed by other cats) or by eating tissues of prey animals that contain encysted forms of the organism.[2,4,6,9] When oocysts are the source of infection, organisms appear in the feces 12-48 hours later.[4] Infectious forms released from the cysts or oocysts infect intestinal mucosal cells, which later shed unsporulated oocysts. Oocysts sporulate in the environment within a day or less under optimum conditions. Mammalian intermediate hosts

are infected upon ingestion of sporulated oocysts.

Besnoitia and *Hammondia* differ from *Isospora* in their absolute requirement for a nonfeline intermediate host (rodents).[2,6,13,14] Cats can only be infected by eating encysted forms of the organism and not by ingestion of sporulated oocysts. Coccidial replication occurs in the cat following ingestion of infected prey. Unsporulated oocysts appear in the feces 5-9 days after ingestion of cysts and are shed for 1-2 weeks or longer.

Like *Besnoitia* and *Hammondia, Sarcocystis* requires nonfeline intermediate hosts for development (rodents, small and large ruminants).[2,12] Unlike other coccidia, shedding of *Sarcocystis* oocysts is very prolonged, lasting 60 days or longer.[11,12] Infection of intermediate hosts can be particularly widespread and severe.

Pathogenesis

Coccidiosis is probably one of the least understood yet most commonly diagnosed intestinal infections of dogs and cats. Diarrhea is common in cats, and coccidia are commonly found in the stool at the same time, especially in kittens. However, shedding of coccidia is usually totally unrelated to the presenting clinical syndrome.

Clinical coccidiosis has only been observed in very young animals infected with relatively large numbers of cysts.[4] *Isospora* is the only coccidian (in this group) that is also infectious for cats in the oocyst form. Severe coccidial enteritis has been experimentally induced in newborn kittens and immunosuppressed animals.[4,10]

Clinical Features

Experimentally induced coccidiosis in weanling kittens is inapparent or relatively mild.[10] Clinical signs in natural infections consist mainly of diarrhea that lasts for several days. In severely affected animals, the stool is mucus laden and may contain some blood.[15] Rarely, intestinal infection is widespread and severe, and hemorrhagic diarrhea may develop. *In-utero* transmission from the queen to fetus has not been observed with coccidia.[3]

Clinicopathologic Features

Coccidiosis should not be automatically diagnosed in every cat that has diarrhea and organisms in the feces. This is especially true if it is a young purebred cat from a cattery, or young animals from other multiple cat environments (pounds, shelters, pet stores). Every attempt should be made to rule out other causes of diarrhea before diagnosing the condition as coccidiosis.

Coccidia are easily detected in fecal flotations. Some coccidia are of characteristic size or morphology and easily identified.[2] Others are difficult to distinguish from each other and can only be identified by experts or from animal inoculation studies. Coccidia are 10 μ (*H hammondi*) to 35-40 μ (*I felis, H pardalis*) long (Fig 28). Smaller forms of *Besnoitia* and *Hammondia* may be particularly hard to differentiate from oocysts of *Toxoplasma gondii* (Fig 29). Oocysts of *Sarcocystis* are also small like those of *Toxoplasma* (Fig 30).

Treatment and Prevention

The usual treatment for coccidiosis in cats is sulfadiazine, sulfadimidine or sul-

Figure 28. Smear from fecal flotation from a cat infected with *Ancylostoma tubaeformes, Isospora felis* and *Hammondia*-like coccidia. The embryonated ova of *A tubaeformes* (A) are easily distinguished from the smaller oocysts of *I felis* (B). The *Hammondia*-like oocysts (C) are less than half the size (10 μ) of *I felis* oocysts (30-40 μ). (Courtesy of College of Veterinary Medicine, Texas A&M University)

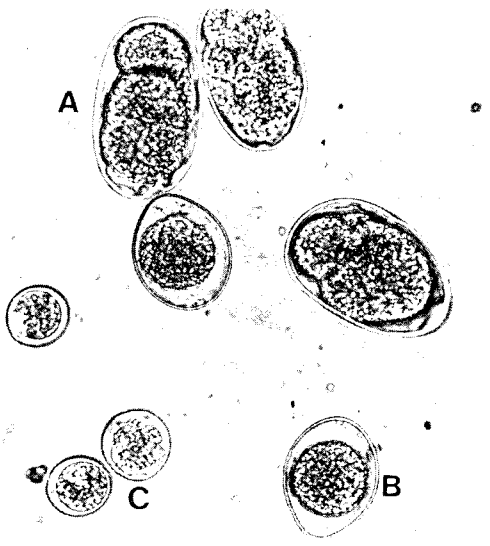
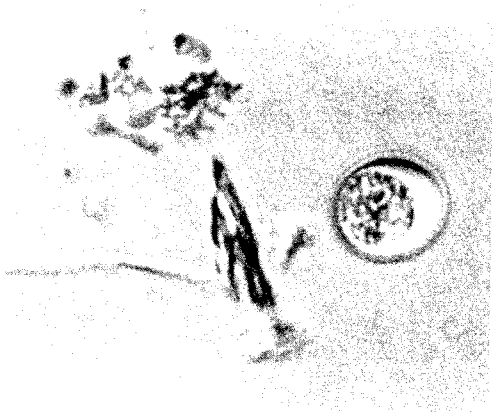


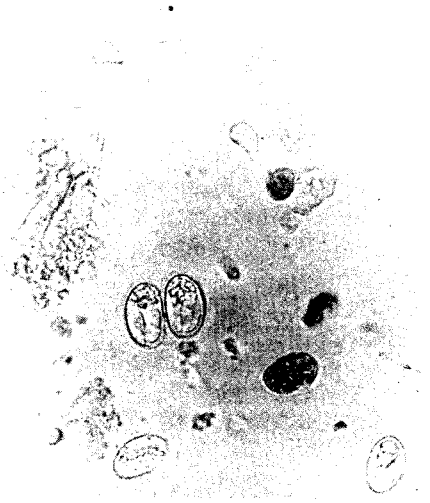
Figure 29. Unsporulated oocyst of *Toxoplasma gondii*. The oocyst is 10-12 μ in diameter and virtually impossible to distinguish from oocysts of *Hammondia* and *Besnoitia*. (Courtesy of Drs. Jerry Theis and Norman Baker, University of California, Davis)



fadimethoxine orally at a dosage of 50 mg/kg daily or divided twice daily for 14 days.[15] Nitrofurazone at 15 mg/kg daily is an alternative treatment. All drugs that show activity against coccidia are coccidiastatic and not coccidiacidal.

Total elimination of coccidia from a closed cattery by improved hygiene and sulfa treatment has been reported by Wilkinson.[15] However, dramatic or long-term successes with such approaches are uncommon.

Figure 30. Oocysts of *Sarcocystis* in cat feces. *Sarcocystis* oocysts are 10-15 μ in diameter and easily distinguished from the oocysts of other coccidia. (Courtesy of Dr. Norman Baker, University of California, Davis)



Infection and Immunity

Immunity to coccidia is the same as described for toxoplasmosis. Immunity appears species specific. Cats infected sequentially with *T gondii, I felis, I rivolta* and *H hammondi* shed oocysts of the respective organism within 11 days postinoculation.[3] Immunity to the intestinal stages is usually acquired within about 2 weeks. Immunity appears tenuous or short-lived because reinfections are common.[2] This differs from toxoplasmal immunity, which is usually more stable.[1]

Sarcocystis appears to elicit little or no immunity in carnivore hosts, which can be infected repeatedly.[12] Immunity to *Besnoitia* spp appears similar.

Animal and Public Health Considerations

Only cats that shed *Isospora* are infectious to other cats. Oocysts of *Hammondia, Besnoitia* and *Sarcocystis* are only infectious for the appropriate intermediate hosts; cats are infected by eating tissues containing encysted organisms. Feline species of these coccidia are not pathogenic to people.[12]

Cats may play an important role in the pathogenesis of *Sarcocystis* infections of livestock.[11,12] Cats frequently defecate in barn litter and feed bunkers, and contaminate livestock forage with oocysts. A small number of *Sarcocystis* oocysts can cause severe systemic disease in calves. Systemic disease in cattle resembles systemic toxoplasmosis to some extent. Disease in older cattle is often less fulminating and frequently goes unnoticed except for the presence of numerous cysts at slaughter.

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Toxoplasmosis

Toxoplasmosis is important to cats and cat owners for 4 reasons: it is one of the most important zoonotic diseases of people; the human disease affects mainly the unborn and newborn child, which impacts strongly on women (the main owners of cats) and human emotions; cats are the sole definitive host for the causative agent and are one source of human infection; and occasional cats suffer from clinical toxoplasmosis. However, the infection is virtually nonexistent in closed cat populations that are not allowed to hunt, or that are not fed raw or undercooked meat.

Cause

Toxoplasma gondii is a complex intracellular parasite. It occurs throughout the world and is responsible for clinical illness in a wide range of animals, both domestic and wild.

Toxoplasma gondii is unique among coccidian parasites of cats and other animals. Though many different animals can serve as intermediate hosts, the entire life cycle can be completed within cats. In this regard, it resembles *Cryptosporidium* and *Isospora.*

Pathogenesis

Cats are the only recognized definitive hosts for *T gondii.* However, literally thousands of species of fish, amphibians, birds and mammals may serve as intermediate hosts. Clinical disease can occur in either definitive or intermediate hosts, making *T gondii* one of the most important pathogenic coccidian parasites of people and animals.

The incidence of toxoplasmal infection in cats varies greatly from country to country and from one subpopulation to another, depending on the incidence of the infection in wildlife and the importance of raw meat (wild-caught or domestic) in their diet. Morbidity also varies with age. Antibodies were found in up to 10% of kittens younger than 10 weeks of age, 16.2% of 11- to 26-week-old domiciled kittens, 37.5% of adult house cats, and 57.9% of adult stray cats.[4] In Washington, the incidence of toxoplasmal antibodies was 31% in cats from animal pounds.[23] Morbidity was higher in house cats that owners relinquished than in strays. Incidences of this magnitude are common among domestic cats throughout the world.

The primary sources of infection for cats are probably small birds, rodents and reptiles containing encysted forms of the organism. Cats can also be infected by ingesting sporulated oocysts shed by other cats. However, a significantly lower percentage of cats will shed oocysts after having been infected with oocysts rather than cysts.

The life cycle of *T gondii* in the definitive host is complex. It usually begins when cats ingest freshly killed prey, or raw or undercooked meat containing encysted forms of the organism. Cats can also be infected with oocysts shed in the feces of other cats. However, this means of transmission is not nearly as efficient.

Encysted forms of *T gondii* are found in highest concentration in the muscle of intermediate hosts. Cysts remain relatively inactive in the muscles until the muscle is ingested by a carnivore or omnivore. Proteolytic enzymes within the digestive tract

of the carnivore or omnivore break down the cyst wall and release the enclosed bradyzoites. Bradyzoites transform into tachyzoites, which infect the intestinal epithelium. Some tachyzoites undergo sexual division intestinal cells and become fertile oocysts. Others spread throughout the body, divide asexually and ultimately become cysts.

Oocysts are passed in the feces at up to 10,000 per day during initial infection. Oocysts generally appear in the feces after 3-10 days when cysts are ingested, or after 20 days or longer when oocysts are the source of infection.

Cats usually shed oocysts for 5-14 days after primary infection. Oocysts passed in the feces of cats are unsporulated. In this form, oocysts of *T gondii* are very difficult to differentiate from those of *Hammondia* and *Besnoitia* (see Figs 28-30). Oocysts are relatively resistant and can survive in soil, especially if warm and moist, for at least 1 year.

Intermediate hosts (usually omnivores or herbivores) are infected by ingestion of sporulated oocysts. Cysts form in the diaphragm, brain, lungs, abdominal muscles and heart. They are found less frequently in the stomach, small and large intestines, mesenteric lymph nodes, spleen and gallbladder.[22] It must be remembered that people, being omnivorous, can be infected either by eating cysts or by ingesting oocysts. Therefore, cats are not the sole source of human toxoplasmosis. Further, because people did not evolve as a natural prey species of cats, they are a "dead-end host" for toxoplasmosis.

Clinical Features

Clinical signs related to *Toxoplasma* infection are infrequently observed in cats. When disease occurs, it is associated with 4 distinct phases of infection: intestinal disease related to intraepithelial replication during primary infection; systemic disease resulting from extraintestinal replication of the organism during primary infection; secondary disease associated with reactivation of encysted organisms; and neonatal disease associated with maternal transmission either in utero or at parturition.

Clinical signs related to primary intestinal replication are uncommon in cats. Though intestinal signs can be experimentally induced in kittens, naturally occurring cases of *Toxoplasma* enteritis have not been recognized.

Signs of systemic toxoplasmosis occurring during or shortly after primary infection are uncommon. The severity of this form of disease is proportional to the extent of extraintestinal proliferation of organisms after initial infection. This is age related. Cysts can be recovered from only about 10% of cats infected after 8 weeks of age but can be isolated from most kittens infected before this time.[10] Of 12 cats with acute toxoplasmosis, most had negative *Toxoplasma* antibody titers.[28] The ages of these cats ranged from 3 months to 15 years, and the most common presenting signs were anorexia, lethargy, fever and dyspnea. Cats with dyspnea had harsh bronchial lung sounds, tachypnea and deep abdominal breathing, but only a mild or inapparent cough. Two cats had signs similar to those of feline panleukopenia, that is, fever, vomiting or diarrhea, anorexia, abdominal pain on palpation, and enlarged mesenteric lymph nodes. Of the 12 cats, 2 had uveitis along with other signs, and 2 were obviously jaundiced. One cat aborted during the course of illness. The clinical course in these cats was 3-19 days (usually 3-8 days) and the disease was fatal in all 12 animals.

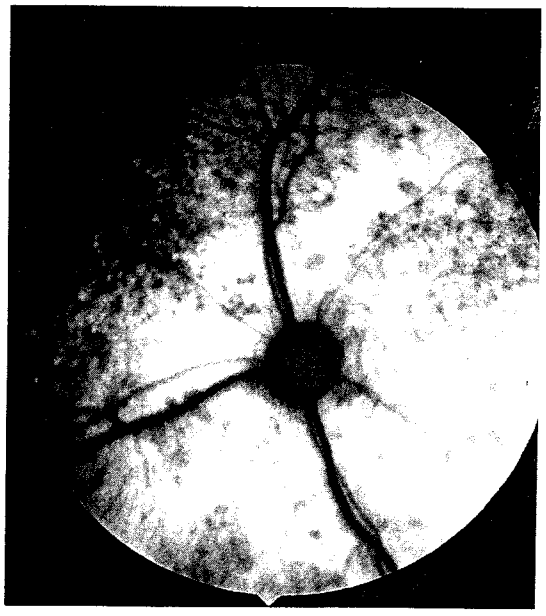
Secondary toxoplasmosis, resulting from reactivation of encysted organisms, is probably the most common clinical form of the disease in cats. Evidence that this type of disease is caused by reactivation of latent organisms rather than primary extraintestinal infections is circumstantial and includes the following: the disease course is more apt to be chronic; toxoplasmal antibody titers are often high when animals are seen; it often occurs in conjunction with other debilitating or immunosuppressive diseases; both encysted and actively replicating forms of the organisms are often seen within the same animal; and many asymptomatic cats have subclinical foci of chronic inflammation associated with cysts in the brain.[8]

The secondary form of toxoplasmosis, referred to as chronic toxoplasmosis, has been reported on numerous occasions.[1,2,20,21,26,28,29,31] This form of toxoplasmosis is often associated with fever, abortion, vomiting, diarrhea, anterior and/or posterior uveitis

(Fig 31), anemia, myocardial disease, CNS signs, lymphadenopathy and respiratory signs of varying durations and intervals (weeks, months and sometimes years). Feline leukemia virus and feline immunodeficiency virus infections may predispose cats to secondary toxoplasmosis by their immunosuppressive effects.

Neonatal toxoplasmosis has been observed on several occasions, but whether the disease is transmitted *in utero* or shortly after birth has not been determined. Fetal infection is common in animals or people in which active intestinal replication of the organism occurs during gestation. In dogs, this can lead to abortion or progressive central nervous system (CNS) and muscle disease manifested shortly after birth.[17] Human infants, depending on the stage of gestation in which they are infected and the dose of organisms, are born: healthy with protective immunity; with severe disease manifested at birth by ocular and CNS abnormalities; healthy but with disease signs developing during the first few weeks of life; or healthy but with low-grade chronic disease that can lead to disease signs as late as the third or fourth decade.[24] More severely affected fetuses are stillborn or aborted.

Figure 31. Chorioretinitis in a cat with systemic toxoplasmosis. (Courtesy of Dr. Ned Buyukmihci, Univ California, Davis)



Queens appear much more resistant to maternal transmission than bitches or human mothers. Queens exposed to *T gondii* during weeks 1-7 of gestation did not have any infected fetuses or newborn kittens.[9] However, 3 kittens born to these queens developed neonatal toxoplasmosis. The route of transmission in this instance was not determined but was postulated to involve transfer from mother to kitten in the milk. Milk-borne transmission of toxoplasmosis is also a serious problem in dairy goat kids. *In-utero* transmission of toxoplasmosis by queens was suggested by an outbreak.[11] Of 7 littermate kittens, 3 developed toxoplasmosis and died at 16-32 days of age with dyspnea, mucopurulent nasal and ocular discharges, and progressive neurologic disease. Pneumonitis, hepatitis, myocarditis, retinitis and encephalitis were evident on microscopic examination of tissue. The presence of encysted organisms in the brain indicated that primary infection occurred before birth. Cell cultures from fetal kittens have occasionally contained *Toxoplasma*, again suggesting that toxoplasmosis can occur as an *in-utero* infection in cats.

Most cases of maternally transmitted toxoplasmosis manifest themselves before weaning. The most common sign of toxoplasmosis in kittens up to 3 weeks of age was sudden death or rapidly developing "sickness."[27] Fever, depression, body tremors, dyspnea, paralysis and diarrhea were more apt to be seen in kittens between 5 and 8 weeks of age.

Pathologic Features

Lesions of active toxoplasmosis are widespread in the body but tend to be most concentrated in the lungs, followed by the liver and CNS.[19,26-28] Involvement of the alimentary tract is less frequent.

Gross lesions are most noticeable in the lungs. Lung lesions consist of edema and diffuse or focal firmness and reddening. Diffuse white and yellow foci are scattered throughout the parenchyma. Subpleural hemorrhages are sometimes seen, along with small amounts of free reddish pleural fluid or blood. The liver is often pale and mottled yellow-brown, or may contain small whitish foci. When involved, the pancreas is edematous and bordered by necrotic fat containing whitish or yellowish foci. Mesen-

teric lymph nodes are occasionally enlarged and edematous. Focal thickening of bowel walls has also been observed in some cats with predominantly GI disease. Likewise, the spleen is often enlarged and meatier than normal.

Clinicopathologic Features

Toxoplasmosis should be suspected in younger cats dying of vague illnesses and in animals with disease involving the lungs, CNS or eyes. Toxoplasmosis should also be considered in cats with acute GI disease, especially if associated with mesenteric lymphadenopathy, pneumonia and hepatitis.

Toxoplasmosis is often suspected before death but almost always diagnosed postmortem necropsy. Cats with acute primary toxoplasmosis may have had insufficient time to produce serum antibodies; antibody titers in cats with chronic or reactivated toxoplasmosis are often high. Cats with primary toxoplasmosis are often shedding oocysts when presented, while cats with recurrent disease are often nonshedders. Further, *T gondii* oocysts are not significantly different in appearance from those of *Hammondia* or *Besnoitia*. Accurate identification by inexperienced investigators is difficult. Definitive identification of oocysts is by mouse inoculation, after allowing time for oocyst sporulation. Oocysts may not be present in the feces of cats with chronic or maternally transmitted toxoplasmosis.

Serum antibodies appear within 7 days after primary infection.[32] These antibodies can be measured by the Sabin-Feldman dye exclusion test, indirect fluorescent antibody (IFA) procedure, indirect hemagglutination test, complement-fixation or enzyme-linked immunosorbent assay (ELISA). The Sabin-Feldman dye exclusion test is considered the most reliable in all species, including cats, though the IFA test is the most widely used and an acceptable alternative. Antibody levels rise rapidly during the course of disease and reach levels somewhat proportional to the severity of extraintestinal replication and cyst formation.

A single antibody titer, regardless of magnitude, is of very little diagnostic value. As many as 60% of normal adult cats have positive antibody titers, some being very high. Therefore, it is important to use serologic test results wisely in making a diagnosis. A 4-fold rise in the IgG antibody titer over a 2-week period has been used by some clinicians to diagnose toxoplasmosis. Measurement of specific IgM antibodies may be an accurate way to diagnose the disease; only active infections induce such antibodies. While this is acceptable in cats with active primary infections, it may not be diagnostic in cats with chronic or reactivated disease.

The radiographic appearance of lung lesions of toxoplasmosis may be quite specific.[1] Radiographic changes mirror the focal alveolar nature of the infection. Ill-defined, coalescent, patchy densities appear throughout the lung parenchyma. Densities tend to adjoin bronchi. Air bronchograms become more noticeable as the disease progresses due to consolidation of parenchyma around air-filled bronchi. This reaction may extend down into the alveoli and lead to the appearance of air alveolograms.

Though variable blood and serum abnormalities are seen in cats with toxoplasmosis, none is specific for the disease. White blood cell numbers vary from low to high, the PCV is usually normal, liver enzymes are elevated with hepatic involvement, and urine and serum bilirubin levels are elevated in a few cats. Platelet counts are normal or decreased.

Cats showing signs compatible with toxoplasmosis should be tested for FeLV and FIV infections. About one-half or more of cats with toxoplasmosis may be FeLV or FIV positive. As in people, toxoplasmosis of cats is mainly an opportunistic disease.

Treatment and Prevention

The disease can be prevented by not allowing cats to eat raw and undercooked meat (especially from swine, goats and sheep) or milk, hunt or contact sporulated oocysts shed by other cats. These steps are seldom practical, so the disease cycle is difficult to break. Freezing meat at -20 C, a temperature not always achieved by home freezers, inactivates the organism, as does cooking meat at temperatures above 60 C.

Treatment of naturally occurring toxoplasmosis has had limited success. This may partly be because many cases occur in immunocompromised hosts, in which treatment is not as effective. Further, many cats are treated for toxoplasmosis because they

have compatible signs and positive antibody titers when, in fact, they actually have other illnesses. The oldest treatment is a combination of pyrimethamine and sulfadiazine.[12] Sulfadiazine is given orally at 100 mg/kg divided 3 or 4 times a day. Pyrimethamine is given in conjunction at 1 mg/kg daily. Treatment is continued for 2 weeks. Folinic acid or bakers' yeast is sometimes given to counteract the side effects of pyrimethamine without interfering with treatment. Trimethoprim-sulfa is similar to the above drug combination and has been used to treat some animals. Clindamycin IM at 5 mg/kg 4 times daily has been used to treat dogs with toxoplasmosis and is probably the treatment of choice.[16,25]

Infections and Immunity

After primary infection, oocysts are shed for 4-16 days.[10] Oocyst production apparently ceases as a result of local immune mechanisms at about the same time that systemic immunity is developing and extraintestinal replication is halted. Systemic immunity causes the rapidly dividing tachyzoites to become slowly dividing bradyzoites and to encyst in muscles.[14]

Even during the active shedding stage, oocyst production appears regulated to some extent by various host factors. Male cats appear to shed more oocysts after ingesting infected mice than females, and cats under 12 months of age shed more than older cats.[10] Even though oocyst production ceases with development of local immunity, some organisms remain inactive in the epithelium.

Immunity to reinfection occurs after initial recovery from oocyst shedding. This immunity is somewhat age dependent. About 60% of cats <13 weeks of age when initially infected subsequently shed oocysts when fed infected mice; immunity in cats initially infected after 13 weeks of age is much better.[6,10] Oocysts are more apt to be shed after ingestion of cysts than sporulated oocysts, and oocysts are shed after a longer latent period and for a briefer duration than in primary infection. Immunity to subsequent bouts of extraintestinal replication appears more solid than local immunity to oocyst shedding.

The nature of immunity to toxoplasmosis is not entirely understood. However, the level of serum antibody at challenge bears no relationship to the degree of immunity.[8,10] Toxoplasmosis in people and cats is usually associated with immunosuppressive diseases, particularly those that profoundly affect cellular immunity. Infections with FeLV and FIV underlie one-half or more of the cases of feline toxoplasmosis.

Reactivation of latent organisms in intestinal and extraintestinal sites, resulting in oocyst reshedding and even clinical disease, has been induced in carrier cats by corticosteroid administration.[8] Such immunosuppression can result from a wide range of stressful and debilitating diseases in cats.

Certain manipulations have activated latent organisms in the intestinal tract. If a cat has not been previously infected with *Isospora,* infection with this organism causes transient shedding of *T gondii* oocysts as well.[5] Primary infection with *Isospora* apparently interferes with established local immunity to *T gondii*.

Animal and Public Health Considerations

Cats are much less infectious to other cats than to other species of animals. Cat-to-cat infection occurs exclusively by ingestion of sporulated oocysts, a relatively inefficient mode of infection. Because cats are the definitive host for the organism, they play an important role in transmitting the disease to many types of animals, particularly herbivores. Carnivorous and omnivorous animals are not only infected by ingesting oocysts from cats, but also by ingestion of encysted forms in the muscles of a multitude of intermediate hosts.

Farm cats are a common source of infection for cattle, sheep, goats and swine.[33] Defecation in feed bunkers, barnyard litter and soil can lead to a large accumulation of oocysts. Transmission of toxoplasmosis from cats to other animals may be particularly severe in goat dairies, where cats are an important source of infection. Maternal transmission to newborn goats via milk is an important link in the disease cycle in this species.

People are infected with toxoplasmosis by ingesting sporulated oocysts from cats, raw milk (especially from goats), or uncooked or poorly cooked meat, especially lamb, pork and goat meat. In fact, in North

America and western Europe, where cats are kept more closely confined and fed largely processed foods, consumption of infected meat by people is probably of greater public health importance than contact with cats.[24,30]

The frequency of infection in the human population in the United States varies greatly according to sociologic, economic and environmental factors. Morbidity and seropositivity increase with age. Less than 1% of infants are congenitally infected. The infection rate is low in young children, but rises abruptly in teenagers. Morbidity rises about 1% each year from the ages of 15 to 50.[24]

The most important form of human toxoplasmosis is associated with transplacental transmission. Such infection results from extraintestinal replication of organisms in the mother during pregnancy. About 0.5-1% of women in the US and Europe show rising titers during pregnancy. This indicates active infection, but only about 40% of these infections are transmitted to the fetus.[24] Moreover, only a small proportion of the infected fetuses have significant clinical disease.

Veterinarians are frequently called upon to give advice to pregnant women with cats or to clients contemplating pregnancy. Medical advice to clients should be limited to steps needed to prevent cat-to-person transmission. Prenatal exposure advice is better left to experts on the human disease, and not to general medical practitioners or obstetricians. The last 2 groups often view the disease and the cat in an overly and unduly negative light. Most important, clients can be comforted that cats are only one of many reservoirs for toxoplasmosis, that only a small fraction of infants are ultimately infected, and that even a much smaller percentage of infants are clinically affected.

Human exposure by cats to toxoplasmosis can be minimized by reducing the chances of infection in cats.[13,17,18] This can be done by confining cats to prevent hunting, feeding cats only processed meats, and changing litter boxes daily to prevent sporulation of oocysts. Oocysts must sporulate before becoming infectious, a process that takes several days. Litter should be discarded in a sealed plastic bag (not buried in the garden). People should eat only thoroughly cooked or processed meat, wash hands thoroughly after handling raw meat and uncooked home-raised vegetables, wear gloves when working in yards likely to be contaminated with cat feces, prevent cats from defecating in children's sand boxes, have someone other than the expectant mother change the litter box daily, and avoid raw milk (especially from goats).

Oocyst shedding by cats has been suppressed by feeding cats 0.02% monensin with their dried food.[15] Kittens appear to tolerate the medicated food well. However, use of such treatment to prevent oocyst shedding has not been widely applied in the field. Immunization of cats against toxoplasmal shedding has been attempted.[14]

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Cryptosporidiosis

Cause

Cryptosporidium is a protozoan that is similar to coccidia. Cryptosporidial infections are apparently common and widespread among animals and people throughout the world.[1,5,16]

Infection occurs by ingestion of thick-walled oocysts. Oocyst shedding in the feces in normal immunocompetent hosts begins as early as 5 days after infection and continues for a 2- to 3-week period.[10] Unlike other coccidia, many species of animals act as definitive hosts and cross-infection between species is common.[3,8,9,12-15]

Pathogenesis

Infections are often limited to the ileum but can involve virtually the entire bowel in massive exposures in neonates and immunocompromised individuals. Clinical signs are seen only when a substantial part of the bowel is affected.

Clinical Features

The importance of *Cryptosporidium* in enteric diseases of cats is uncertain. Many cats shed organisms in the feces, kittens more so than adults. However, oocyst shedding is often unrelated to concurrent intestinal disease. Adult cats fed large numbers of *Cryptosporidium* showed no signs of illness.[6]

Severe cryptosporidiosis has been described in an adult cat with chronic diarrhea, anorexia, weight loss and bowel thickening.[13] The disease in this cat was clinically and histopathologically similar to plasmacytic-lymphocytic enteritis, a disease of allergic or pre-lymphomatous origin. Feline immunodeficiency virus (FIV) infection of cats produces a similar intestinal disorder.

Pathologic Features

Most of what is known about cryptosporidiosis has come from experimental transmission studies in lambs or swine.[8,12,14] However, disease in these species is considerably more severe than naturally occurring infections of carnivores, which are usually inapparent.

Clinicopathologic Features

As in coccidiosis, every attempt should be made to eliminate other causes of enteritis before diagnosing cryptosporidiosis in cats with positive fecal examinations. This includes use of hypoallergenic diets to rule out food allergy, which is the most common cause of diarrhea in cats. Older cats with chronic diarrhea and cryptosporidia in their stool should also be tested for FeLV and FIV infections.

The Sheather's sugar flotation method has been used to concentrate oocysts from fecal specimens.[5] Oocysts are very small and difficult to see without phase microscopy or special contrast staining. They resemble miniature coccidia in morphology.

Treatment and Prevention

Standard anticoccidial drugs have no effect on *Cryptosporidium*. In fact, no single treatment has proven uniformly effective. Infection in healthy cats is usually subclinical or mild, and is self-limiting. For this reason, treatment is not generally recommended except in cats with particularly severe infections and there is a high likelihood that cryptosporidia are the cause of the enteritis.

Spiramycin has proven effective in some people with congenital or acquired immunodeficiency and severe cryptosporidiosis.[15] However, spiramycin is not available in the United States, and its efficacy against animal cases of cryptosporidiosis is unknown. Oral clindamycin and quinine have proven less effective in people and are associated with many more side effects.

Oocysts of *Cryptosporidium* are relatively resistant to disinfectants.[2] Cresylic acid (3%), hypochlorite (2-5%), benzalkonium chloride (5%), sodium hydroxide (0.02 M) and isophore (1-4%) failed to inactivate oocysts after 18 hours. However, oocysts are sensitive to ammonia (5-10%) and formaldehyde (10%).

Infection and Immunity

Immunity to *Cryptosporidium* appears within 1-2 weeks in normal individuals but is tenuous and short-lived. The poor post-infection immunity to cryptosporidiosis may be due to the superficial nature of infection in the bowel. Debilitating diseases and excessive stress can lower resistance and further increase the incidence of recurrent infections.

Animals that are debilitated or immunocompromised by other diseases often shed greater numbers of oocysts for a more prolonged period. If the infection is particularly severe and persistent, it can contribute to clinical signs. An FeLV-infected cat had acute signs apparently due to chronic cryptosporidiosis.[7] Another cat appeared to be suffering from concurrent cryptosporidiosis and lymphocytic-plasmacytic enteritis of unknown origin.[11]

Animal and Public Health Considerations

Infected cats are hazards to human and animal health only in that they serve as one of hundreds of different mammalian, avian and human hosts. Cryptosporidiosis as a clinical entity is seen mainly in neonatal ruminants and immunocompromised people. Mild to moderately severe enteritis has been induced in neonatal lambs and there seems little doubt that cryptosporidiosis is an important natural cause of diarrhea in very young calves.[10,12] Cryptosporidiosis in calves is considered an important source of human infection.

Cryptosporidiosis in normal people is characterized by acute diarrhea and abdominal cramps lasting 1-10 days.[4] Clinical signs usually begin within 5 days or sooner after exposure. A severe and potentially fatal form of intestinal cryptosporidiosis has been seen in people with acquired or congenital immunodeficiency syndromes.[4] Opportunistic cryptosporidiosis appears particularly prevalent and severe among people with AIDS.[15]

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Giardiasis

Cause

Giardia species are droplet-shaped protozoan parasites that are found throughout the world. They are found most consistently in the duodenum and jejunum of most species of animals. However, they are more common in the distal jejunum and proximal ileum in cats.[12,13] They do not invade mucosal cell surfaces, and obtain nutrients directly from intestinal contents.

Encysted and non-encysted forms of the organism are passed in the stool. Encysted forms are quite resistant to environmental degradation and can survive for weeks or months under cool and moist conditions. Non-encysted forms die rapidly after being passed in the stool.

Pathogenesis

Surveys in different countries show an infection rate of 1-11% in cats.[11] Younger cats and kittens are more likely to be clinically infected than older cats.[11,15,22] Giardiasis is most prevalent in high-density and closely confined populations. Infection occurs by direct animal-to-animal transmission (fecal-oral) or contamination of drinking water with cyst forms. Fecal-oral transmission is probably the most important route in cats, while water-borne transmission is the most common route in people.[7,9,10] Ingested cysts are partially dissolved by stomach acids and cysts appear in the feces within 5-16 days.[11]

Large numbers of organisms in the small intestine damage underlying epithelial cells. The mechanism of this effect is not understood but may include mechanical interference, elaboration of a yet-unidentified soluble toxin, competition between parasites and epithelial cells for essential nutrients, direct damage of epithelial cells by adherent organisms, changes in the microenvironment favoring bacterial overgrowth, and secondary damage to the epithelium caused by host immunity against the parasites.[1,8,24,25] Intestinal disease caused by *Giardia* is of a malabsorption type.[25]

Clinical Features

Giardial infections of cats are usually subclinical. Clinical signs are most often seen in younger animals from multiple-cat households and catteries. Outbreaks of disease are often associated with introduction of new animals into the environment. The introduced cat develops signs from exposure to the household cats, or is the vehicle for infecting the resident population. In its most severe form, infection is characterized by loose, mucoid and frequently foul-smelling stools, steatorrhea, flatulence, abdominal distension and poor haircoat.[6,9,11,13,15,18,22,23,28]

The course of the disease in untreated individuals varies from less than a week to several months.

Pathologic Features

Pathologic changes are limited to the intestinal tract, mainly the jejunum. Gross anomalies are not seen and histopathologic changes vary from nonexistent to marked.

Clinicopathologic Features

Giardiasis is diagnosed by demonstrating cysts in the stool. However, organisms are often shed sporadically and are not always easy to identify. Direct examination of fresh fecal smears is the simplest procedure. A small amount of feces is diluted with saline, mixed with a drop of Lugol's iodine solution and examined by conventional light microscopy. Cysts can be concentrated from feces by zinc sulfate centrifugal flotation but not with flotation procedures using sugar or other salts. Diagnosis of giardiasis is complicated by the cyclic nature of cyst shed-

ding.[13] Therefore, at least 3 collections must be examined before declaring a fecal sample negative.

Treatment and Prevention

A favorable response to treatment is often the most accurate way to diagnose clinical giardiasis in animals and people. This is because some animals with giardiasis do not have demonstrable numbers of organisms in their stool, while others have demonstrable organisms but suffer from totally unrelated problems. Quinacrine hydrochloride, orally at 1.5 mg/kg 3 times daily for 10 days, is the treatment of choice for people. In cats, a dosage of 11 mg/kg daily for 12 days eliminated clinical signs but not shedding of cysts.[6] Metronidazole orally at 8 mg/kg twice daily for 10 days eliminated both clinical signs and fecal organisms in 2 cats.[18] Similar success was reported in a cat given metronidazole at 25 mg/kg BID for 5 days.[28] Experimental studies in cats showed good results with metronidazole at 10 mg/kg twice daily for 5 days or furazolidone given orally at 4 mg/kg twice daily for 5 days.[13]

Infection and Immunity

Immunity to *Giardia* is probably similar to that of *Cryptosporidium*. Both cellular and humoral immunity appear involved in resistance,[2,21,24,26] as further supported by the high incidence of infection in people with combined or specific IgA immunodeficiencies.[24]

Immunity in mice appears to be highly controlled by genetics.[4,20,21] Under normal circumstances, immunity to infection develops in several weeks. Infection can be greatly prolonged by stress and debilitating diseases. Glucocorticoid treatment has prolonged the course of primary infection and triggered reactivation of low-grade or latent infection in mice.[17]

Shedding of cysts increased more than 100-fold 2 days after an injection of glucocorticoids in 1 cat; other cats given lower daily oral dosages of prednisolone for 5 days did not shed more organisms until after therapy was stopped.[13] Once established, immunity is probably tenuous and short-lived. Therefore, reinfection with episodic shedding of organisms is probably common.

Animal and Public Health Considerations

Though cats apparently carry many strains of *Giardia* that antigenically resemble those found in other species, feline strains are probably more pathogenic for cats than for other animals.[7,27] Therefore, cats are the greatest health hazard to other cats. Human isolates of *Giardia* appear to be minimally infectious or noninfectious for cats.[14] The converse situation has not been studied, so the exact public health significance of infected cats is not known. Only 2 instances of concurrent human and feline giardiasis in the same households have been reported.[7] Until more information is obtained, infected cats should be considered as potential, but probably not important, reservoirs for human giardiasis.

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Toxocariasis (Roundworm Infection)

Ascarids, or roundworms, are the most common helminth parasites of cats. They are one of the few helminths that persist in closed catteries; most other such parasites require several species of vertebrate or invertebrate animals as intermediate hosts and are usually ingested by cats during hunting. Roundworms, such as *Toxocara cati*, can complete their entire life cycle in cats, and though rodent intermediate hosts can be involved, they are not essential.[8] As with many other infectious diseases involving cat-to-cat transmission, ascarid infections are most severe in high-density environments where fecal contamination is high, where conditions are favorable for survival of ascarid eggs, and where many susceptible (young) cats are present.

Cause

Toxocara cati is the principal ascarid that infects cats and is found throughout the world. It is found as an adult in the small intestine of domestic and wild Felidae.[8] Adult male worms are 3-6 cm long, while females are 4-10 cm long. Eggs laid by female worms are shed in the feces in relatively large numbers. Ascarid eggs can survive several months or longer in the environment.

In Iowa, the proportion of infected cats was 0% in newborns, 4.3% in 0.5- to 2-week-old kittens, 5.8% in 2- to 6-week-old kittens, 1.9-2.1% in 0.5- to 4-year-old cats, and 0.8-1.3% in 4- to 15-year-old cats.[5] No infections were seen in cats over 15 years of age. These percentages are considerably lower than those reported in other studies. In Missouri, the rate of infection was 24.4%.[10] Australian studies reported 20.3% infection among urban cats in western Australia, 24.5% infection in Brisbane and 21.9% infection in New South Wales.[6,7,12] In southwest England, 63% of farm cats were infected.[3]

Pathogenesis

Cats are infected when they inadvertently consume ascarid eggs that are shed into the environment by other cats, or by ingestion of encysted larvae in the tissues of rodent prey. Eggs passed in the feces of infected cats contain fully developed second-stage larvae. Following ingestion by other cats, the second-stage larvae are released from the egg and enter the stomach wall, where they remain for 1-2 days. Larvae migrate to the liver in the mesenteric veins, and then enter the bloodstream and are carried to the lungs. They exit the pulmonary vasculature and enter the alveoli, bronchioli and trachea, where they form third-stage larvae. Then they are coughed up and swallowed, and reenter the stomach wall. Following further maturation, they migrate to the lumen of the small intestine, where egg laying occurs. This entire migration can take place in as short a time as 10 days.

Transmission of *T cati* through ingestion of intermediate hosts is important for hunt-

ing cats. Eggs passed by the cat are ingested by rodents, and second-stage infectious larvae are released in the intestinal tract and migrate to various tissues, particularly the liver. Because rodents are not the definitive host, larval development is arrested and encystation occurs. Rodents are referred to as paratenic hosts because no essential developmental stages occur in them. Encysted second-stage larvae can remain alive for months in rodent tissues. When a cat eats the rodent, second-stage larvae are released from the cysts by digestive enzymes and enter the stomach wall, where they develop to third-stage larvae over a 6-day period. They then reenter the stomach, where they become fourth-stage larvae. These make their way to the small intestine, where they become adults. Following ingestion of paratenic hosts, the entire cycle takes about 3 weeks. Larval migration through the liver and lungs does not occur in cats infected with encysted worms.

In addition to being infected by eggs or encysted second-stage larvae, kittens can be infected through nursing. Larval forms may be encysted in the tissues of the queen as a result of an earlier primary infection. For reasons that are not completely understood, pregnancy causes some of the encysted worms to excyst and enter the bloodstream. They then find their way to the mammary glands and are secreted in the milk. Transmammary infection is a continuous phenomenon; larval ascarids are present in the milk throughout lactation, not just in colostrum.[9] Larvae ingested by the kittens while nursing develop in the same manner as larvae acquired by eating infected rodents.

Clinical Features

Clinical signs of *T cati* infections are mainly caused by visceral migration. Pulmonary changes occur over a 2-month period or longer following exposure.[11] Irritation to gastric and intestinal walls, aberrant migrations into such sites as the bile ducts, and mechanical obstruction of the bowel can also cause clinical signs.

Clinical signs associated with *T cati* infections are limited mainly to kittens and to cats in environments in which exposures and worm egg numbers are high. The most prominent feature of severe infections is generalized unthriftiness manifested by delayed growth, a poor haircoat, and a pot-bellied appearance due to generalized muscle thinning caused by malnutrition. Acute colic, peritonitis and death have been associated with intestinal blockage by masses of adult worms. In kittens, this can be associated with perforation of the proximal small intestine. Pulmonary changes due to visceral larval migrans, though severe at times, usually are not clinically apparent.

Pathologic Features

Lesions within the intestinal tract are absent or mild. Reddening of the gastric and small intestinal walls is the predominant gross change. Likewise, changes in the liver are usually not grossly apparent or consist only of subcapsular scarring. Pulmonary changes can be severe in some animals and occur within 2 weeks of infection.[10] Multiple tan lesions 1-2 mm in diameter may be observed throughout the lung parenchyma, particularly on the pleural surfaces. Some foci may be hemorrhagic.

Clinicopathologic Features

Ascarid infections are diagnosed by examination of feces for typical eggs. In kittens with visceral larval migrans, eosinophilia may be pronounced.

Treatment and Prevention

Prevention of environmental egg contamination is an essential part of disease control. To minimize egg accumulation, cattery surfaces should be as impervious as possible to allow for thorough cleaning with soap and water.

Numerous drugs are effective against adult and immature intestinal stages of the worm. The most popular are various piperazine salts. A single oral treatment with piperazine adipate at 200 mg/kg removes both immature and adult forms from the intestine. Dichlorvos is also highly effective but has been associated with severe diarrhea and, occasionally, rectal prolapse in some kittens. Fenbendazole, orally at 10 mg/kg twice daily for 2 days or at 100 mg/kg orally as a single treatment, and pyrantel pamoate at 5 mg/kg orally as a single treatment, are also effective. Fenbendazole may also reduce the number of larvae in tissues of bitches with *T canis*

infections.[2] The efficacy of fenbendazole against tissue stages in cats is unknown. Ivermectin, given once subcutaneously at 200 g/kg, has also eliminated all egg shedding in infected cats.[4] Its effect against the larval stages is unknown, but may be substantial. If this is so, ivermectin may ultimately be the drug of choice.

Infection and Immunity

Immunity to ascarid infection develops over time. The infection rate was 39.9% in 6- to 8-week-old kittens, 41.2% in 5- to 8-month-old kittens, 21.1% in 10- to 15-month-old cats and 4.6% in cats over 2 years of age.[12] This immunity is directed against both tissue-migrating forms and stages confined to the intestinal tract.

Immunity may explain why ascarids are much more common in cats younger than 6 months of age than in older animals. Neutered cats also appear to have about half the ascarid load of intact cats, perhaps because of some hormonal influence on immunity.[10]

Animal and Public Health Considerations

Cats that shed *Toxocara* eggs are the principal reservoir for infection of other cats. However, when cats hunt freely, paratenic hosts (rodents) also constitute an important reservoir.

Visceral larval migrans is a potentially serious disease that occurs mainly in children. *Toxocara canis* is a far more common cause of this disease than *T cati*.[8] Nevertheless, a wide range of roundworms has been incriminated at times with the human syndrome. These include *Toxascaris leonina* and *Toxocara cati*. Visceral larval migrans in children is similar to the somatic infection seen in rodents infected with *T cati*. Larval forms are apt to migrate to the liver, lungs, brain and eyes. Encysted or dying organisms in human tissues provoke an eosinophilic granulomatous response and, if sufficiently severe, clinical signs. Clinical signs include fever, coughing, asthma-like wheezing, malaise, weight loss, hepatomegaly, central nervous system disturbances, and eye disease ranging from retinal granulomas to severe exudative enophthalmitis.[1] Eosinophilia is very pronounced. The ocular lesions can be particularly severe in people and lead to blindness or enucleation because of misdiagnosis as an ocular tumor.

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Stomach Worm Infection

Like other helminth infections of cats, only certain types of stomach worms are a problem for catteries. The troublesome species are those that can complete their entire life cycles within cats. Those that involve other animal hosts in their life cycles are usually only a problem with cats allowed to hunt.

At least 8 nematodes parasitize the stomach of domestic cats. These include the trichostrongyloid worm *Ollulanus tricuspis*, the spiruroid worms *Cyathospirura dasyuridis* and *Cylicospirura felineus,* the physaloptерid worms *Physaloptera praeputialis, P felidis, P pseudopraeputialis* and *P canis,* and *Gnathostoma spinigerum*.[17] Only one of these worms, Ollulanus tricuspis, is likely to be a problem among cattery-confined

cats. The others occur sporadically among free-roaming cats that are more likely to prey upon the reservoir species (arthropods, insects, fish, reptiles, amphibians).[17,18] For these reasons, the remainder of the discussion will be concerned with *Ollulanus tricuspis*.

Cause

Ollulanus tricuspis has been recognized in Europe, North America, Australia and Chile.[14] Male worms are 0.7-0.8 mm and females are 0.8-1.0 mm long (Fig 32). In addition to domestic cats, they also infect wild Felidae, foxes and pigs. The incidence of infection has been reported as 6.1% in indoor pet cats and about 40% in free-roaming outdoor cats in Germany, 42.8% in feral cats in Australia, 30% in outdoor cats in Greece, 18.3% in Turkey, and 27% in cats in the United States.[1,4,10,13-16] The overall infection rate is reportedly higher in catteryhoused cats than among individual pet and free-roaming animals.[2,12,16] However, the clinical importance of stomach worm infection in cattery populations has yet to be determined.

Figure 32. Adult male and female *Ollulanus tricuspis*. The male worm (left) has a well-formed bursa, while the female has a tricuspid tail (arrow). (Courtesy of Dr. A. Hargis and *Veterinary Pathology*)

Pathogenesis

Adult worms are found in the stomach, and do not penetrate or firmly attach to the mucosa.[3] In severe infections, worms may also be found in the most proximal part of the duodenum. The female worm is viviparous. Large eggs formed in the single uterus hatch within the reproductive tract and develop through first and second stages before release as third-stage larvae into the gastric lumen. Third- and fourth-stage larvae develop free in the stomach. Sexual differentiation is complete in fourth-stage larvae, which rapidly mature to adults within the stomach. Third- and fourth-stage larvae that pass into the intestinal tract are rapidly destroyed by digestive processes and intact worms are not seen in the feces except when transit time is decreased. However, infectious third- and fourth-stage larvae are present in vomitus. Susceptible animals are apparently infected when they ingest infectious larvae that have been expelled in this manner into the environment.

The exact pathogenic effect of *Ollulanus* infection of cats is debatable. It is probably related to the degree of infection and chronicity. Even with large worm burdens, infection is often asymptomatic. When clinical signs occur, they are usually associated with chronic irritation, inflammation, increased mucus secretion and vomiting associated with the presence of worms adjacent to the mucosa and in gastric glands.

Clinical Features

Infection with *O tricuspis* is widespread and often asymptomatic.[10,12] Periodic vomiting is the most frequent clinical sign.[2,3,5,12,19] Vomiting is first seen within 4 months of infection and correlates within a week or so to detection of worms in gastric contents.[18] Vomiting is usually intermittent, occurring every 1-93 days (mean of 12 days).[19] Vomiting usually occurs 10-15 minutes after eating. A mild intermittent diarrhea has been seen in several cases, though whether the infection was the cause was not determined.[2,9]

A more severe fibrosing or sclerosing gastritis has been associated with *O tricuspis* infection in both wild and domestic Felidae.[7,11,14] Clinical signs include vomiting, chronic weight loss, poor coat condition and, in some instances, death.

Pathologic Features

Gross and microscopic lesions of *O tricuspis* infection have been well documented.[2,7,10,12,14] Gross lesions are seen in less than 5% of infected cats. The gastric wall in such cases appears thickened and the rugal folds much more prominent. Mucosal fibrosis that progresses at times to sclerosis may be evident in severe cases. More mildly affected cats may show some mucosal reddening, with excessive mucus production.

Clinicopathologic Features

Diagnosis of *Ollulanus tricuspis* infection requires a high index of suspicion. Larvae of the parasite are destroyed by digestive enzymes in the intestines and do not usually appear in the feces. An exception is when transit time decreases, such as in diarrhea.[9] Adult female worms are about 1 mm long and have 3 major cusps or projections on their caudal end. Males are slightly smaller and have a caudal bursa. Larvae can be very small and difficult to visualize. Larvae can only be observed in the gastric mucosa, gastric contents or vomitus.[6,14]

Cats are usually induced to vomit 1-2 hours after feeding using xylazine at 2.2 mg/kg IM. If vomiting cannot be induced, a stomach wash is obtained with a large tube. Gastric contents are strained through coarse gauze or a kitchen strainer to remove particulate debris and examined under a dissecting microscope.

Treatment and Prevention

Ollulanus infection has reportedly responded to a single dose of tetramisole at 5 mg/kg orally or dichlorvos at 11 mg/kg.[5,14]

Prevention of *Ollulanus* infection in catteries and closely confined groups of cats can be attempted in enzootic environments. Thorough deworming of all animals, coupled with increased cleanliness and reduced population density, greatly reduces the problem. Special attention should be paid to cats that vomit more frequently than expected; such animals are the main source of environmental contamination with infectious larvae.

Infection and Immunity

Nothing is directly known about immunity to *O tricuspis* infections. However, immunity to *Ollulanus* appears quite minimal. Some groups of cats develop many chronic infections, and average worm burdens are often very large.

Animal and Public Health Considerations

Cats infected with *O tricuspis* are health hazards only to other cats.

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Tapeworm Infection

Tapeworms have ribbon-like bodies and lack an alimentary canal.[9] They are composed of tens to thousands of connected segments. The head segment, or scolex, attaches to the mucosa of the small intestine. The adjacent neck segment serves as the germinative center for subsequent reproductive segments, called proglottids. As new proglottids are formed from the neck segment, older proglottids move caudally. Terminal proglottids break off and are shed in the feces.

Tapeworms are hermaphroditic; each proglottid has both testes and ovaries. Mature proglottids contain from 10 to several thousand elongated eggs. In some cases, all of the eggs are released through the lateral pores of the proglottids during passage down the intestine and intact proglottids are not seen in the feces. In other cases, only part of the eggs are released and eggs appear both free and within motile proglottids in the stool.

Tapeworms can live 2-3 years and reach 50 cm to several meters in length, depending on the species. Though some species of tapeworms have cats as their definitive hosts, only 9 have been commonly described in the literature.[9] Several other species of tapeworms can have cats as aberrant intermediate hosts. The life cycles, geographic distribution and incidence of infection for tapeworms of domestic cats are quite variable.[9]

Dipylidium caninum is the most common tapeworm of cats and dogs found throughout the world. It is one of the few feline tapeworms found more commonly in urban areas than among rural populations.[1,5,7] It is the only tapeworm that occurs among closely confined cattery-reared cats. This is because the cat flea is the intermediate host, and fleas abound within many catteries. The 8 other species of tapeworms are seen only among cats allowed to hunt small reptiles and rodents, which are essential intermediate hosts. For these reasons, the remainder of the discussion will be on *D caninum*. However, the same basic principles apply to all species of tapeworms.

Cause

Adult *Dipylidium caninum* are up to 50 cm long and attach to the wall of the small intestine. The average worm burden in heavily infected cats is 46-256.[5] A dozen or more proglottids, each containing 30 or more eggs, are passed in the feces each day.

Eggs are released during passage of proglottids down the intestine or from desiccated proglottids on the ground. Eggs are ingested by the larvae of several species of fleas (*Ctenocephalides canis, C felis, Pulex irritans*) or lice (*Trichodectes canis*).[9] The infectious form develops within fleas and lice.

Pathogenesis

The infection rate for *Dipylidium caninum* is intimately related to the type of environment. The more fleas, dogs and cats in a closed area, the more likely that tapeworm-infected fleas will be present, and the more infected fleas that will be ingested. One study found one-third of the urban cats in Australia to be infected, while the infection in feral cats in Australia was only 2-11.6%.[1,5,16]

Cats are usually infected with *Dipylidium caninum* when they ingest adult fleas during grooming. Infectious forms are released in the digestive tract, attach themselves to the small intestinal mucosa by their scolex and develop to adults in several weeks. Tapeworms obtain nutrients by diffusion from intestinal contents. They do not usually cause clinical signs in the host. If infection is massive, there may be some competition for nutrients between the host and worms. Irritation and inflammation in the intestinal wall may be seen with heavy infestations.

Clinical Features

Adult tapeworms in the intestinal tract of cats usually do not cause clinical signs. However, diarrhea attributable to tapeworm infection has been described. Owners usually notice motile or desiccated proglottids around the anus of the cat and in the stools, which is aesthetically displeasing. Massive infections may cause cats to be nutritionally deprived and somewhat thin and rough in appearance.[9]

Clinicopathologic Features

Intestinal tapeworm infections are usually diagnosed by grossly visualizing proglottids around the anus or on the feces, or by visualizing microscopic eggs or egg-packets in fecal flotations. Freshly passed *Dipylidium* segments resemble small pumpkin seeds that move slowly in inchworm fashion. However, they rapidly become desiccated and immobile. Dried proglottids look more like small brownish kernels of rice. Tapeworm eggs are also present in the feces, having been released from proglottids during their passage down the digestive tract.

Treatment and Prevention

Prevention of tapeworm infection involves eliminating intermediate hosts from feline habitats or preventing cats from entering environments where intermediate hosts are found. In the case of *Dipylidium caninum*, this involves flea control.

Several drugs are effective against intestinal tapeworms. Perhaps the safest and most effective is praziquantel.[6,8] Oral or subcutaneous dosages of 4.2-12.7 mg/kg given once are safe and effective; 5 mg/kg is the recommended dosage. Alternative drugs commonly used to treat intestinal tapeworm infections include a single treatment of niclosamide orally at 100-150 mg/kg or dichlorophene orally at 0.1-0.2 mg/kg. Mebendazole is also used orally at 100-200 mg twice daily for 5 days.

Infection and Immunity

Cats mount very little immunity to adult tapeworms in the intestine, and worms appear to die within 1-3 years from natural aging.[10] No or only minimal immunity to reinfection develops after natural or drug-induced death of worms.[10] However, it appears that some mechanism prevents massive accumulations of organisms associated with continuous reexposure. Numbers of tapeworms found in intestines of cats remain fairly constant even though animals in certain environments are continuously reexposed to infected intermediate hosts.[5] A similar phenomenon may explain why animals cannot be superinfected. Immunity may vary greatly from one cat to another, similar to strain variations that have been recognized in rodents.[4] Acquired immunity has been recognized in dogs and appears to interfere with development during the parasite's rapid growth stage. It has less effect on the more stable adults.[2]

Animal and Public Health Considerations

Cats infected with *Dipylidium caninum* are not directly infectious for other cats. Eggs shed by cats must first be ingested by appropriate intermediate hosts, in which essential developmental stages occur.

Some tapeworms of cats are infectious to people, including *Dipylidium caninum*, and adult tapeworms are found infrequently in the alimentary tract of people, particularly children.[11] Infection is by eating infected intermediate hosts and not eggs, so the flea rather than the cat is the source of infection.

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Ear Mite Infestation

Cause

Otodectes cynotis commonly infests the external ear canals of dogs, cats, foxes, rac-

coons, ferrets and other carnivores.[5] The mite is found throughout the world and is particularly prevalent among cats kept in cattery-type environments.

Adult mites live mainly in the middle to proximal portion of the external ear canals and inner pinnae, where they feed on epidermal debris and inflammatory exudate. Eggs are laid singly and hatch in 1-3 days.[5] Larval mites molt at least twice during a 5- to 7-day period and become sexually competent young adults. Mating occurs shortly after the second molt. Gravid young female mites molt a third time 2 days after mating and begin to lay eggs 1 day later. Therefore, the period from hatching to egg laying is as short as 9 days. Adult mites live for a month or more and lay 2-3 eggs per day.

Pathogenesis

Ear mite infestations are very common among cats, especially those housed in catteries or cattery-like environments. The extent and severity of infestation within a closely confined group of cats are usually directly proportional to incidence of other common cattery problems, such as flea infestation, ringworm and viral upper respiratory diseases. Stress, environmental contamination and husbandry practices that favor infectious diseases in general also appear to favor large mite accumulations.

The route of transmission from cat to cat has not been precisely determined. Infestation is much more severe when multiple animals are closely confined. This indicates that transmission is direct and by close contact. Mites may then transport themselves from host to host, or from environment to host, and migrate to the external ear canals. Mites feed on inflammatory products stimulated by the mites themselves.[3] Inflammation of feline ear canals, regardless of cause, also causes eventual exhaustion of sebaceous glands, hypersecretions of apocrine glands, and increased secretions of acidic lipids, acid mucopolysaccharides, protein-bound lipids and carbohydrates.[2] Such inflammatory products are probably more desirable for mite nutrition than normal sebaceous-gland secretions (cerumen).

Mite infestations are first noticed in 2- to 6-week-old kittens. Infestation is usually less severe in adult cats than in kittens and adolescent animals. It is also less severe in females than males. The severity of infestations also varies greatly from animal to animal within the same environment. Certain animals have severe infestations, while others have light infestations or are completely free of mites.

Ear mites occasionally cause pruritic miliary lesions distant from the ears. In a study of cats with miliary dermatitis, 4 of 133 had ear mite infestations.[4]

Clinical Features

Cats with ear mite infestations may show no outward signs or may scratch at their ears. Close examination of the proximal part of the external ear canals and inner pinnae often demonstrates darkening and thickening of the epidermis and greatly increased amounts of blackish, flaky or granular sebaceous exudate. Scratch marks and small sores may be seen on the more sparsely haired region in front of the ears and on the inner pinnae. If secondary bacterial infection occurs, the exudate may be purulent and the ear canals are much more inflamed.

Clinicopathologic Features

A presumptive diagnosis of ear mite infestation can be made on the basis of the characteristic appearance of involved tissues of the ear and associated exudate. Ear mites are often seen grossly within the exudate, appearing as small whitish specks that move slowly under bright light and low magnification with a hand lens. Exudate can also be smeared onto a slide and examined microscopically under low power. Eggs and adult, nymphal and larval mites are readily observed in most cases (Fig 33).

Treatment and Prevention

Infested ears should be cleansed of exudates by instilling a few drops of warm mineral oil or ceruminolytic ear drops into each ear canal and gently massaging the base of each ear. This loosens the exudate, which can then be gently removed with cotton swabs. Following exudate removal, the ears are treated daily for 10-14 days with mineral oil, commercial oil-based acaricidal preparations, or a 20% suspension of benzyl benzoate. A short repeat treatment is often done 9-10 days later. Organophosphate-im-

pregnated flea and tick collars are not effective against ear mites.[6]

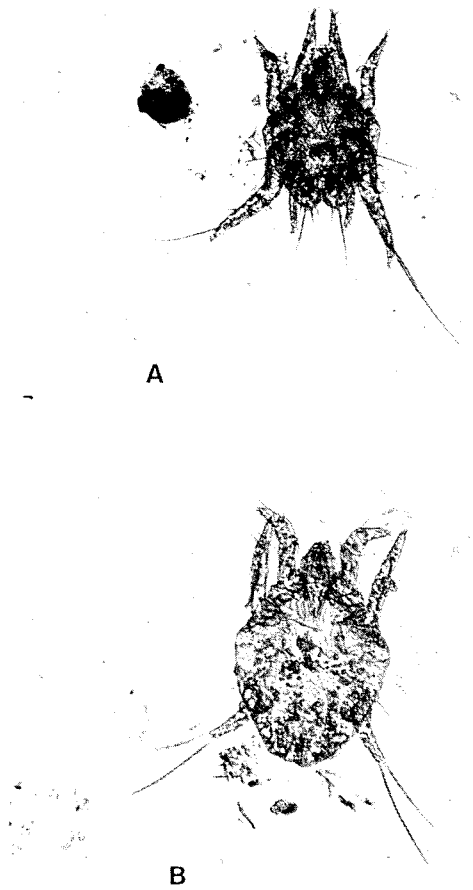
Ivermectin is effective in treatment of ear mites in dogs and cats and is probably the treatment of choice.[1,7] A single subcutaneous dose of ivermectin at 200-1330 μg/kg (400 μg/kg preferred) has been highly effective.

Topical antibacterial medications are sometimes required for ear infestations with a secondary bacterial component.

With repeated use, topical ear medications can elicit hypersensitivity reactions that may mimic the original mite infestation. With ear mite infestations that appear refractory to treatment or recur despite continuous therapy, such reactions should be suspected. If the true cause of the otitis is doubtful, therapy should be discontinued for several weeks. Otitis externa rapidly resolves following discontinuation of treatment if drug hypersensitivity is causing the problem.

Elimination of ear mites from catteries is difficult with topical medications. The mites persist on normal untreated parts of the body and in the environment. Use of ivermectin has facilitated eradication. All cats should be treated as described for individual infestations, with treatment repeated in 2 weeks. The cats are then monitored at monthly intervals and treated again if new mite infestations are detected.

Figure 33. Adult male (A) and female (B) *Otodectes cynotis* in exudate from the ear of a cat. (Courtesy of Dr. Norman Baker, University of California, Davis)



Infection and Immunity

Cats vary greatly in their resistance to ear mite infestations. However, the nature of this resistance is not clearly understood. Ear mite infestations are more common among younger cats and declines as they become older.[3]

Animal and Public Health Considerations

Otodectes cynotis can be transmitted between dogs and cats. However, people cannot become infested.

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Flea Infestation

Cause

Fleas are wingless insects 1.5-4 mm long, with a chitinous covering. Their long strong legs are well adapted to jumping and for

continuous movement between their hosts and the environment.

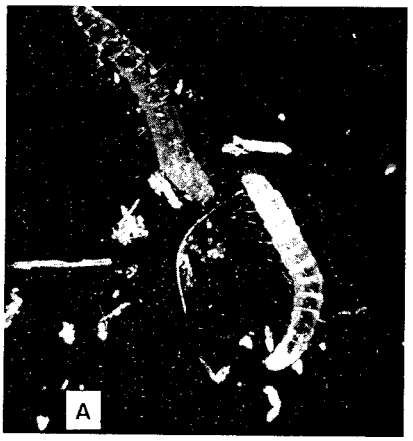
Ctenocephalides felis is the principal flea of cats.[17] Cats may also be infested with the dog flea (*C canis*) and human flea (*Pulex irritans*).

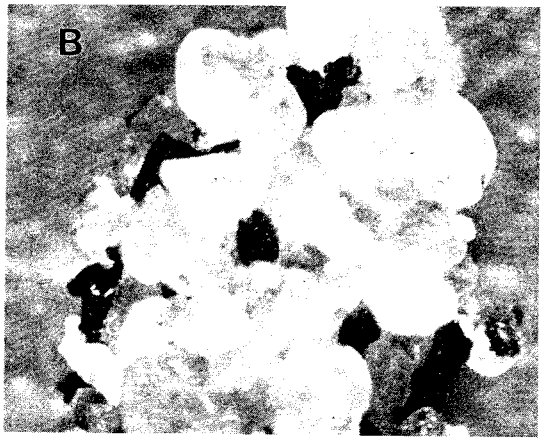
Adult fleas live on the skin of the cat and obtain nutrients by sucking blood. Most of the adult flea's life is spent on the animal.[2] After mating, female fleas lay 400-500 eggs during their lifetime. Eggs are laid in clutches of 20 or more while the females are off the host. After egg laying, fleas return to the cat for feeding until the next egg-laying cycle. Adult fleas live 58 days off the host if fed, and 234 days if unfed.[17] Eggs are usually laid in the dust and dirt in carpeting, bedding or yards. Larvae hatch in 2-16 days, depending on temperature and humidity. Larval fleas are maggot-like and feed on organic matter (Fig 34A). Flea feces, which are rich in nutrients and continually shed from the coat of infested animals, may be a particularly good source of nutrition. Within about 10 days, mature maggots spin a cocoon that quickly becomes camouflaged by dust and debris adhering to its sticky surface (Fig 34B). The pupal stage lasts 10 days to several months, depending on temperature and humidity. Young fleas then emerge and jump onto a cat, where they feed and complete their life cycle (Fig 34C). The remainder of their lives is spent on and off the cat.

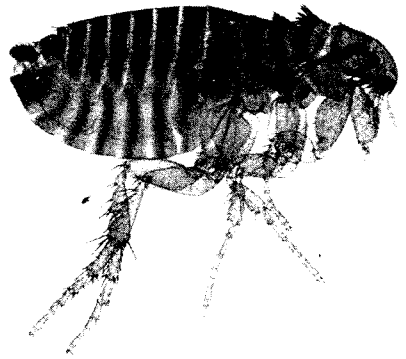
Pathogenesis

Fleas are found throughout the world but are particularly prevalent in warmer and more humid climates. Extremely cold or hot and dry climates limit accumulations of fleas by killing or impeding development of both adult and immature forms. Fleas have adapted for survival and reproduction both within dwellings and in the environment. Seasonality may be less evident when animals are continuously kept in air-conditioned environments. Extremely large flea accumulations can occur when climate, humidity and host numbers are favorable. Therefore, fleas are more apt to be a problem within catteries, multiple-cat households, or urban and suburban environments where climate and humidity are favorable and the feline population is dense.

Figure 34. Various stages in the life cycle of the cat flea, *Ctenocephalides felis*. Maggot-like larvae (A) are found free in the cat's environment. The pupa (B) is very sticky and accumulates a coating of debris, which makes it difficult to distinguish from house dust. The adult (C) is the most likely form to be found on an infested cat. (Courtesy of Dr. Lorry Dunning, University of California, Davis)







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Clinical Signs

Clinical signs associated with flea infestations vary greatly, depending on numbers of fleas and whether the animal becomes hypersensitized (allergic) to flea saliva. Severe anemia and death have been associated with massive flea infestations in kittens. Such infestations are more apt to be seen among confined cat populations. The anemia in such infestations is of the blood-loss type and associated with feeding by adult fleas.

Most healthy cats infested with fleas maintain a small and relatively stable resident population and do not show marked clinical signs. The natural grooming behavior of cats usually keeps numbers of fleas at a minimum, providing that the flea population in the environment is not overwhelming. However, if cats become sick for any reason and stop grooming, flea numbers on the cat can greatly increase. Excessive numbers of feeding fleas can further drain an ill cat of energy and contribute to the overall disease.

Cats that become allergic to flea bites show considerably more clinical signs, the severity of which depends on the degree of hypersensitivity and numbers of feeding fleas. Flea allergies usually develop in cats after 3 years of age.[14] Initial lesions consist of small erythematous papules on the skin at the site of flea bites. These are most prevalent around the tailhead, inner thighs, abdomen, and head and neck. Lesions are usually pruritic. Lesions resemble those described for miliary dermatitis; 55% of cats presented with miliary dermatitis in one study were suffering from flea-bite hypersensitivity.[14] Appearance of the lesion can be greatly altered by self-excoriation and secondary bacterial infection due to chewing, biting and scratching. In severe and chronic infestations on sensitized animals, the involved skin becomes thickened, crusty, scabby, darkened and alopecic (Fig 35). Peripheral lymphadenopathy is common in such animals.[14]

Clinicopathologic Features

Flea infestations are easily diagnosed by close examination of the skin and coat for adult fleas or flea feces. In mild infestations, fleas and flea feces may be hard to visualize. Diagnosis can be facilitated by vigorously rubbing the coat while the animal is standing over a moistened white paper towel. After 20-30 seconds, the paper towel is examined for small black specks, which are flea feces. Within a minute or longer, reddish discoloration emanates from the specks due to dissolution of the blood in the flea feces.

Cats with severe flea allergic dermatitis often have mild to severe eosinophilia that is proportional to the chronicity and severity of the skin lesions.[14]

Intradermal skin testing appears to have more value for diagnosing flea allergies in cats than it does for desensitization.

Treatment and Prevention

Treatment and prevention of flea infestations require patience, persistence and expense. Control of fleas on premises should be directed to 4 areas: controlling flea populations by environmental manipulation; killing adult fleas on all host animals; destroying adult and larval flea populations within the home; and killing adult fleas in surrounding yards.

Figure 35. Back of a cat with severe, chronic flea-bite hypersensitivity dermatitis. The skin is thickened, darkly pigmented, scabby and depilated. Secondary bacterial infection may be manifested as pustules.

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Several studies have dealt with survival of adult and immature fleas in the environment and how environmental factors apply to flea control. Temperature and relative humidity are the 2 most important environmental variables for flea growth and survival. Adults and immature forms survive best in warm, but not exceptionally hot, environments with high relative humidity. Survival of cat fleas at ambient temperatures of 21-32 C (70-89 F) and 80% relative humidity was 90-99%.[5] Adult emergence from pupae was almost totally inhibited when relative humidity fell below 45% and ambient temperatures were greater than 32.2 C (89 F). The lower and upper ambient temperature limits for optimal flea development were 13 C (55 F) and 32 C (89 F), respectively.[16] Relative humidities from 50% to 92% within this temperature range resulted in greater than 80% flea egg hatch, 100% larval development and 90% pupal survival.

Studies on optimum temperature and humidity do not explain flea survival in semi-arid climates. Pupae survived outdoors most of the year in semi-arid southern California, except for July and August, when ambient temperatures often exceeded 35 C (96 F) and relative humidities were low.[15] Pupal survival decreased dramatically at ambient temperatures as low as 27 C (81 F) when relative humidities fell below 33%. At 27 C (81 F), relative humidities of 12% and 33% killed 97% and 100% of pupae, respectively, over a period as short as 16 hours. However, larval survival at warmer ambient temperatures was greatly increased when humidity of the air or microenvironment rose above 50%. Larvae could also survive in the ground at high temperatures and low relative humidity if soil moisture was 1-10%. However, soil moistures from 20% to 50% were deleterious. Exposure to ambient temperatures from -1 C (30 F) to 3 C (37 F) killed all immature stages of the flea within 5-10 days, respectively.

In another study of flea populations in southern California, more fleas were found in living rooms and bedrooms, and in carpeted rooms than in uncarpeted rooms.[12] Fleas were found in the yards of only 8 of 50 infested residences. Flea control should be concentrated in areas where most fleas are found.

Knowledge of the optimum ambient temperatures and relative humidity for flea development can be used in some areas for environmental flea control. For instance, in semi-arid and arid regions, catteries should be kept dry. Yards around the catteries should be planted with vegetation requiring as little irrigation as possible. Lawns should not be planted around the cattery, and swamp water coolers should not be used for air-conditioning. Cats should be kept outdoors in open catteries rather than indoors. Indoor environments are often cooler and more humid because of air conditioning and other factors (running water, washing, cooking, toilets, baths, poor ventilation, respiration).

In cooler regions, the ambient temperature in the cattery should be maintained as low as possible. Cats easily acclimate to ambient temperatures as low as 55 F, which inhibit flea growth. However, flea control by environmental manipulation is virtually impossible if cats are maintained in homes. People usually maintain the home environment at a temperature and humidity that is comfortable to them and ideal for flea development, thus negating any beneficial effect of outside temperature and humidity.

Fleas on animals can usually be killed with appropriate insecticidal powders, sprays or shampoos. Active ingredients within these preparations vary greatly. New insecticides are also continuously being developed and incorporated into flea-control products. Preparation changes are mandated mainly by safety to cats and developing drug resistance of fleas. Drug resistance occurs commonly, necessitating incorporation of new insecticides.

Insecticides are generally active against adult fleas (adulticides) or larvae (larvicides). Adulticides currently used belong to 1 of 4 groups of drugs: carbamates, organophosphates, chlorinated hydrocarbons and botanical compounds.[9] Carbamates are cholinesterase inhibitors, which fortunately are more toxic to fleas than to host animals. The 2 most commonly used carbamates in cats are carbaryl and propoxur. Carbaryl is a common insecticide in garden powders. It has a relatively low toxicity for cats but tends to stain fur, furniture and rugs. Propoxur is popular in many commercial flea preparations and has good residual action.

Organophosphates are also cholinesterase inhibitors. Organophosphates used in cats include dichlorvos (a component of many flea collars), dioxathion, malathion, naled, phosmet, ronnel, temephos and tetrachlorovinphos. Organophosphates tend to be much more toxic to cats than carbamates, even though their mode of action is similar. Though they are used routinely in cats, careful attention must be given to concentration of the compounds used, total amount applied, and amount of residual insecticide on the fur. Toxic signs include vomiting, diarrhea, sweating, dyspnea, miosis and, in severe cases, death. Atropine sulfate at 0.2 mg/kg IM is considered the best of readily available antidotes for organophosphate or carbamate poisoning. Poisoned cats should be thoroughly washed to remove residual insecticide on the fur.

Fenthion (20%) is being increasingly used for flea control in cats. About 0.3 ml is applied to the top of the head, behind the ears, or in the ears. This is repeated every 1-2 weeks initially, then every 4-6 weeks as needed to keep the cats flea free. Use of such a potent organophosphate in cats is questionable. Signs of organophosphate poisoning are subtle at this dosage but nevertheless common. Deaths have been reported in catteries using fenthion in this manner. These may have resulted, however, from incorrect dosage of the drug. Chronic neurotoxicity has been reported in people exposed to fenthion, as well as other potent organophosphates. Dogs may develop a similar syndrome after brief or prolonged use of fenthion. Use of such compounds as fenthion in this manner is reminiscent of the military tactic of directing artillery on your own position when it is being overrun by the enemy. It is a desperation measure that is no replacement for more conservative regimens.

Chlorinated hydrocarbons are selectively more neurotoxic to fleas than to host animals. Many forms of chlorinated hydrocarbons, such as DDT or chlordane, are no longer permitted in many countries because of environmental hazards. Lindane and methoxychlor are 2 chlorinated hydrocarbons that are still used for flea control in cats. Other environmentally acceptable chlorinated hydrocarbons are considered too toxic for animals. Similar to organophosphates, chlorinated hydrocarbons have a lower safety margin for cats than other species. Serious toxicities have even been seen in some cats following use of approved products. Toxic signs include hyperexcitability, inappetence, muscle weakness, tremors, convulsions, paralysis and death. Mildly toxic animals should be treated with diazepam; more severely affected animals should be treated with phenobarbital. The fur should also be thoroughly washed to eliminate drug residues.

Botanical compounds are of plant origin and include rotenone, d-limonene and pyrethrin. D-limonene has not proven nearly as effective as pyrethrins.[14] Synthetic pyrethrin-like compounds include allethrin, d-trans allethrin, fenvalerate, d-phenothrin, resmethrin and tetramethrin. Both natural and synthetic compounds in this class have a high margin of safety. Potency and residual effect of natural pyrethrins can be "potentiated" by addition of piperonyl butoxide. Some synthetic pyrethrins are naturally potentiated.[9]

The effectiveness of many adulticides has been limited by emergence of drug-resistant strains of fleas. This is especially true for carbamates and chlorinated hydrocarbons. Pyrethrins and pyrethrin-like compounds are much less likely to evoke drug resistance. Resistant strains of fleas are usually found in areas where flea populations accumulate all year and use of insecticides is heavy. Due to problems with low drug resistance of and toxicity to cats, natural and synthetic pyrethrins are preferred. Their organic or "natural" composition also makes them much more acceptable to people concerned with environmental accumulation of toxic chemicals. A potentiated or long-acting pyrethrin compound should be applied to infested cats every 3-7 days during the flea season in temperate climates and throughout the year in more tropical areas.

Flea collars impregnated with organophosphate adulticides are very popular with cat owners but are becoming less and less effective as resistant fleas appear. Fresh flea collars can cause mild signs of poisoning when used in kittens. Severe contact allergies of the skin have been occasionally

described; the allergy appears to be due to resins in the plastic.

Adult and larval fleas living in the environment, usually in carpeting, bedding and dusty areas, should also be eliminated with appropriate insecticides. If possible, this should be done by experienced pest exterminators. Nevertheless, various compounds incorporating both adulticides and larvicides are available as over-the-counter preparations for home use. These various preparations are administered as powders, sprays or aerosol "bombs" that can be set off after the house is temporarily vacated of people and animals.

Adulticides used indoors usually kill fleas quickly but have a short residual action. However, the larvicide portion of such preparations usually has a very long residual effect. The most popular larvicide is a synthetic hormone called methoprene.[4] This compound has a residual effect of 75-90 days and prevents pupation of fourth-stage larvae. Methoprene is virtually nontoxic for other living organisms, including adult fleas and flea eggs. Home environments should be retreated with adulticide-larvicide combinations every 75 days during the flea season in seasonal areas and all year in more tropical climates. Methoprene combined with pyrethrins has proven completely effective in controlling fleas within homes.[12]

Fleas in surrounding yards can be killed with chlorpyrifos or diazinon. Both have relatively long residual effects. Diazinon is also available in microencapsulated form. Malathion is also effective against fleas but has a very short residual effect. Yards should be treated 3 times at 10- to 14-day intervals during the height of flea season or all year in more tropical climates.

Flea repellents have emerged again as a popular means to control fleas. Early preparations were not highly effective and quite messy to use. Recently, however, more effective and aesthetically pleasing preparations, such as N,N-diethyl-m-toluamide (Deet), have been developed and sold commercially. Repellents are usually combined with an adulticide. Though relatively safe when used separately, combinations of Deet and fenvalerate can sometimes cause toxicity and death when used heavily on kittens and adult cats.[18]

Contrary to common myths, fleas are not repelled by feeding brewers' yeast or thiamin.[1,7] Likewise, special collars that use ultrasonic sound waves to repel fleas have proven totally ineffective on cats.[6] Use of flea repellents in a good flea-control program in a cattery is questionable. The object of flea control is to lower numbers, not merely redistribute fleas from one animal to another. It is also highly unlikely that any flea repellent will be 100% effective, especially in areas with large flea numbers. Repellents may be most helpful in limiting the numbers of fleas that cats bring into the home from outside.

Persistent treatment of fleas on the animals and in the home and environment can greatly reduce flea problems. In more temperate climates, such methods may effectively eliminate the problem. In more tropical areas, where fleas are rampant and drug resistance is high, control is less successful even when rigorously applied. Moreover, many people are not prepared to spend the time and money required to continuously control fleas in highly enzootic areas. In these areas, it is important to prevent fleas from initially entering the environment. Cat owners moving into flea-free homes and environments should maintain flea control at all times and not wait until infestation occurs. This is especially true in tropical climates where flea problems can sometimes be overwhelming. The importance of designing cattery quarters to prevent flea infestations cannot be overemphasized (see chapter on cattery design and management). Proper cattery design can mean the difference between success and failure in flea control. The problem of flea control in these areas is compounded by cats roaming outside and large flea-infested feral cat populations.

When it is impossible to eliminate fleas from the environment of animals suffering from flea-bite allergies, the skin itself may require direct treatment. This has been approached in 2 ways: treatment of the allergy with drugs, usually glucocorticoids; and desensitization of the animal with injections of flea proteins. Drug treatment usually consists of prednisolone or prednisone at an initial dosage of 2-4 mg/kg daily for 7-14 days, then 2 mg/kg every other day. Once

the condition is under control, the lowest possible dosage of glucocorticoid should be used to maintain remission. Cats are reportedly much easier to desensitize with flea-antigen extracts than dogs.[11,13] However, such optimism has not been borne out by well-controlled hyposensitization trials in cats.[8,14] Therefore, desensitization should still be considered as an experimental approach to control of flea allergic dermatitis in cats.

Infection and Immunity

The absolute number of fleas on any given animal often remains constant; however, flea numbers differ greatly from cat to cat. This implies that some cats are naturally more resistant to fleas than others; the nature of this immunity is not known. Flea numbers on cats increase dramatically when they become ill and stop grooming. Whether fleas are ingested during grooming or inhibited by proteinaceous products in saliva has not been determined.

Factors that cause some animals, and not others, to become sensitized to fleas have not been determined.

Animal and Public Health Considerations

Cat fleas can be a major problem to dogs that live in the same environment. Dogs appear much more susceptible to flea-bite allergies than cats. Therefore, it is common to have households of animals in which the cats serve as reservoirs, while the dogs suffer most with clinical disease. Cat fleas are also the principal intermediate host of the dog and cat tapeworm, *Dipylidium caninum*. Repeated infection with this tapeworm is inevitable as long as fleas exist in the same environment.

Cat fleas attack people when other suitable hosts are not available. Human bites most often occur when a flea-infested house has been left vacated of people and animals for several weeks or more. People returning from a vacation or moving into such a home or apartment may be greeted by a hungry population of fleas. Bites occur around the ankles and lower legs. People can also become sensitized to flea bites, and repeated exposure may elicit large and highly pruritic lesions.

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