Chapter 11

Food Safety

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"Do not eat any detestable thing . . .
Do not eat anything you find already dead."
Deuteronomy 14: 3, 21

INTRODUCTION

Each year more than 24 million Americans are affected by foodborne illnesses such as salmonellosis, botulism and staphylococcal food poisoning (Ensminger et al, 1995). In people, both identified and undocumented pathogens likely cause 76 million cases of foodborne illness, 323,000 hospitalizations and 5,200 deaths annually (Mead et al, 1999). Luckily, the typically affected person often improves in 24 hours and has little more than an upset stomach. Likewise, domesticated pets can become ill from ingesting contaminated food. Most animal feedstuffs including spoiled foods such as garbage and carrion are rich in the nutrients needed to support rapid microbial colonization (Coppock and Mostrom, 1986). This phenomenon occurs quickly because most bacteria have the ability to double their number every 30 minutes under favorable moisture and temperature conditions.

Microbes of all shapes and sizes are everywhere in our environment. Foods can be contaminated at any stage of production, starting in the field and ending with storage in the home. The time between the harvesting of pet food ingredients, food handling and preparation in the home and consumption of the final product provides multiple opportunities for microbial populations to proliferate. Microbial growth can result in either food spoilage or risk of foodborne illness. The current methods of food processing and preservation simply forestall the final outcome: spoilage. The earlier in the food production cycle the contamination occurs, the more widespread the outbreak.

Foodborne diseases (**Figure 11-1**) can be divided into two types: 1) food infections (usually bacterial) and 2) food intoxication (microbial toxicoses) (Ensminger et al, 1995). Food infections such as salmonellosis and salmon disease (*Neorickettsia helminthoeca*) result from ingestion of infectious microbial cells that invade the host's tissues, and after an appropriate incubation period, produce the disease. Because it takes time for these cells to replicate to pathogenic numbers, clinical disease in food infections does not become evident until at least 12 to 24 hours after ingestion.

Food intoxications do not depend on the ingestion of viable cells, but result from ingestion of a food that already contains a microbial toxin. Because cell replication is not required, the signs of food poisoning appear rapidly, sometimes in less than one hour after ingestion. The term "food poisoning" is often incorrectly used as a synonym for foodborne illness or any illness thought to be food related.

CLINICAL IMPORTANCE

When a pet exhibits signs of gastrointestinal (GI) disease, the owner often concludes that food must be the culprit. In the past, when pets relied on table foods, carrion, garbage and improperly cooked pet foods for sustenance, this conclusion would have been credible (Galton, 1955; Thornton, 1972).

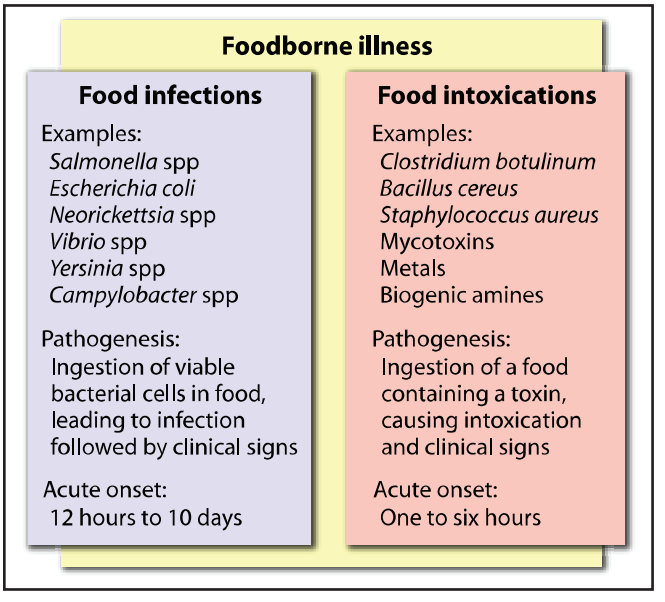

Figure 11-1. Classification of foodborne illnesses.

Table 11-1. Causes of poisonings in dogs and cats.*

Substance	Total cases (%)
Drugs	25.0
Insecticides	19.6
Plants	12.1
Miscellaneous/unknown	8.9
Rodenticides	8.4
Cleaning products	5.9
Cosmetics	2.9
Hydrocarbons	2.9
Foreign bodies	2.8
Chemicals	2.7
Fertilizers	2.2
Food	1.7
Herbicides	1.6
Paints	1.6
Bites/stings	1.2
Heavy metals	0.5

*Adapted from Hornfeldt CS, Murphy MJ. 1990 Report of the American Association of Poison Control Centers: Poisonings in Animals. Journal of the American Veterinary Medical Association 1992; 200: 1077-1080.

Today, foodborne disease in household pets is rare (Dillon, 1986). The 1993-1994 report of the American Association of Poison Control Centers (AAPCC) indicated that of the 116,432 dog and 19,489 cat poisoning cases reported, foodborne illnesses accounted for only 0.11 and 0.13%, respectively (**Table 11-1**) (Hornfeldt and Murphy, 1998). However, foodborne illness is still a common disease in the United States racing greyhound industry (Fenwick, 1996).

The low incidence of foodborne illnesses in domestic pets can be attributed to two primary changes in feeding practices. First, most pets in developed countries depend totally on commercial pet foods to meet their nutritional needs. More than 90% of the pet owners in the United States purchase commercial pet foods for their pets (Lund et al, 1996). Although these figures are lower for the United Kingdom and Europe, the majority of pet owners in those geographic regions also feed commercial pet foods (Pet Food Manufacturers Association, 1994).

Second, present-day commercial pet foods are much safer than in the past. Modern pet foods are not composed of a single ingredient, but are formulated from multiple ingredients including grains, meats, meat by-products, vegetables, eggs, dairy products, fish and other added nutrients. The use of many and varied ingredients tends to dilute any contamination that might occur in a particular commodity or ingredient. Commercial pet food manufacturers commonly use manufacturing techniques such as extrusion and retorting to produce heat levels sufficient to destroy many pathogens and heat-labile toxins (Dziezak, 1989; Lopez, 1987). Improved packaging materials and a better knowledge of proper warehousing also help to protect raw materials and finished products from moist conditions and possible contamination during storage. Furthermore, manufacturers use sensitive analytical techniques to verify that ingredients and final products are high quality and free of contaminants. The value of these efforts is supported by a study in which researchers analyzed 35 dog and 17 cat foods and found that most were remarkably free of toxic contaminants (Mumma et al, 1986).

REGULATION OF COMMERCIAL PET FOOD

To ensure safety, pet foods and individual pet food ingredients are regulated by several governmental agencies in addition to meeting manufacturer's quality control and storage standards. In the United States, the Food and Drug Administration (FDA) regulates foods and ingredients that are shipped across state or international boundaries under the authority of the Federal Food, Drug and Cosmetic Act (FFDCA) (Superintendent of Documents, 2004; Van Houweling et al, 1977; Price et al, 1993). Section 402 of the FFDCA states that foods, including pet foods, shall be considered adulterated when they contain an added substance that may render the food injurious to health. Section 406 of the FFDCA empowers the Secretary of Health and Human Services to promulgate regulations and tolerances that limit the quantity of contaminants, such as mycotoxins. Additionally, sections 501, 505 and 512 of the FFDCA authorize the FDA control over the use of veterinary drugs. As part of the drug approval process, the FDA can set the conditions of drug use in animal feeds. The use levels established for veterinary drugs prevent excessive drug residues in meat, milk and other by-products from food-producing animals that may be used as ingredients in pet foods. The FDA and the Association of American Feed Control Officials (AAFCO) publish annually the approved animal drug levels in feeds along with the species for which the drug is approved (Superintendent of Documents, 2005; AAFCO, 2007).

The threat of terrorism to the nation's food supply has also prompted expansion of the federal role. The Federal

Government has the authority under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (i.e., the Bioterrorism Act) to administratively detain food items that may present a threat of serious adverse health consequences or death to people or animals. The Act also authorizes enforcement actions that may be taken against perishable foods subject to a detention order.

A tolerance is a codified legal regulation whereas action and advisory levels constitute nonbinding FDA guidelines that the agency uses in exercising its enforcement discretion. Instead of a tolerance, the FDA may choose to issue either an action or an advisory level for some unnatural additives. All three are considered maximum allowable levels, but an action level is generally supported by more definitive safety data than is an advisory level. Therefore, some circumstances may elicit enforcement action at levels below an action or advisory level whereas others may not, even when an action or advisory level has been exceeded.

The FDA does not set tolerances for pesticides; instead these fall under the jurisdiction of the United States Environmental Protection Agency (EPA) by the authority of the FFDCA and the Federal Insecticide, Fungicide and Rodenticide Act (Superintendent of Documents, 1995). The EPA establishes and publishes pesticide tolerances for the various plant and animal commodities in 40 CFR 180. These tolerances are developed by combining the results of field trials and laboratory animal toxicity testing (NRC, 1993). The United States Department of Agriculture (USDA) and FDA are then jointly responsible for enforcing the pesticide tolerances.

For contaminants not covered by a tolerance, an action level or advisory level, the limit remains theoretically at zero. However, present day analytical methods have become so sensitive that minuscule amounts can be detected. Fortunately, the FDA has discretionary power when a contaminant is detected at a low level not considered to be a safety concern.

In Europe, the regulation of intentional additives (e.g., vitamins and minerals) and unintentional additives (e.g., pesticides, drug residues and metals) falls under the authority of the European Union (EU) (Ministry of Agriculture, Fisheries and Food, 1995). Control measures are implemented on a national basis and can be stricter but never more permissive than the EU legislation. Non-EU foreign countries regulate pet food safety with a variety of internal regulations and policies.

Most regulatory agencies, both domestic and international, use monitoring programs to maintain surveillance over pet food products. Specifically, in the United States, the FDA monitors pet food and individual pet food ingredients for pesticides, mycotoxins and heavy metals as part of its Feed Contaminants Program (Van Houweling et al, 1977).

Intrastate pet foods are under less federal scrutiny, with primary regulation left to state and local officials. This relationship has created concern that unsuitable food components, most notably mycotoxin-contaminated grains, may be used inadvertently (Nicholson, 1986). In addition, such products are often pelleted instead of extruded; therefore, processing temperatures may not be sufficient to kill bacteria and inactivate heat-labile toxins. Both factors tend to increase the risk of foodborne disease in locally produced foods.

The risk of litigation also encourages pet food manufacturers to be diligent in maintaining high product quality standards. Under tort claims law, all products offered for sale to the public contain an implied warranty (The American Law Institute, 1965). The law specifically provides "that a person who sells a product in a defective condition unreasonably dangerous to the user or consumer or his property is liable for the physical harm the product causes . . ." News programs frequently report large verdicts against manufacturers of human food products because of the harm allegedly caused by their products (Taylor, 1996). Animal feed and pet food manufacturers have also been caught up in this trend. Procedural breakdowns or oversights during production or storage can have a catastrophic effect on profits or even company viability. Mycotoxin litigation alone cost the pet food industry an estimated $7 million in the early 1990s (McCoy, 1996). Recent problems with mycotoxin contamination had financial repercussions and severely damaged the reputation of companies involved (Industry News, 1995; Anonymous. FDA Recall, 2005). Such experiences have made it necessary for manufacturers to devote extensive resources to documenting product quality.

HOME-PREPARED FOODS

The use of home-prepared pet foods also has clinical relevance to foodborne disease. Meat and eggs produced for human consumption and used to prepare homemade pet foods are contaminated with microbes (Notermans et al, 1995; Fenlon et al, 1996; Remillard, 2005). Research indicates that many people are careless about cross-contamination during food preparation at home (Patil et al, 2005). If breeders and pet owners use grocery store ingredients that have been stored properly, heat foods to temperatures sufficient to destroy pathogens and prepare amounts that are readily consumed, the potential for foodborne illness in the pet is expected to be similar to that for people in the same household. Some health-conscious pet owners forgo commercial foods and, instead, prepare foods for their pets daily. These owners must be fastidious and very careful about preparing and storing their pets' food, and truly be committed to the long-term maintenance of proper hygiene and preparation methods. Otherwise, the best method to lessen the risk of foodborne illness is to feed the pet a high-quality commercial pet food manufactured by a company that uses state of the art quality control procedures. There are no such requirements or regulations for pet food manufacturers to do so and most do not; however, there are a few world-wide manufacturers that maintain self-imposed rigorous product quality control procedures.

RAW INGREDIENT DIETS

Feeding raw ingredient diets (commercially available or homemade) to household pets has become increasingly popular.

Some advocates of raw food claim that dogs should be fed raw meat because their wild canine ancestors survived and present day relatives survive on uncooked food. There is no evidence to support dogs evolved from jackals, foxes or coyotes (Wayne, 1993). Comparisons of mitochondrial DNA indicate that dogs most likely descended from wolves. However, the mitochondrial DNA patterns of modern dogs and wolves are distinctly different, and there is no single wolf ancestor that is common to all dogs (Semyenova et al, 2002). No compelling scientific evidence based on evolution supports statements that dogs should eat uncooked food as did wild canids. Claims that dogs are carnivores, rather than omnivores, are likely due to confusion of taxonomy (*Carnivora*) with feeding behavior (carnivore). Dogs belong to the order *Carnivora*, but their eating habits are those of an omnivore (Chapter 12). Panda bears, for example, are herbivores in their feeding behavior, but are included in the order *Carnivora* taxonomically.

Advocates of raw food emphasize the importance of ingredients (Billinghurst, 1993; Schultze, 1998; Volhard and Brown, 2000) with less emphasis on nutrient balance. Advocates claim the nutrients from commercial moist or extruded pet foods are less or not available or even absent (Pottenger, 1939; Billinghurst, 1993; Schultze, 1998; Volhard and Brown, 2000) when compared with feeding raw ingredients. Although no digestibility studies of a complete raw diet have been published to date, average apparent digestibilities of nutrients in commercial pet food have been published. Opponents to feeding raw food point out that some nutrients actually are more readily available from cooked ingredients (Zia-ur-Rehman and Salariya, 2005), and that overall nutrient availability and balance are more significant than for certain individual ingredients.[a]

Advocates of feeding raw food report coat and/or dental benefits (Pottenger and Simonson, 1939; Billinghurst, 1993; Schultze, 1998; Volhard and Brown, 2000) based upon empirical and anecdotal evidence (Billinghurst, 1993; Schultze, 1998; Volhard and Brown, 2000); however, some who recommend raw meat recognize the limits of using such evidence (Silver, 2004). The high fat content (>50%) of raw food diets compared to that found in most dry kibble (<30%) often can account for owners' reports of improvement in the appearance of their pet's coat (Dunn, 1999). The incidence of periodontitis and fractured teeth, however, increased with age in 67 dogs eating raw animal carcasses with bones in a dental health study (Robinson and Gorrel, 1997). None of the homemade and commercially available raw food diets analyzed were appropriate for long-term feeding (Freeman and Michel, 2001, 2001a), which is consistent with the clinical experience of one editor of this textbook (RLR). To date, no scientific evidence exists that demonstrates raw food diets provide additional or exceptionally unique nutrients that cannot be obtained from cooked food.

Professionals at zoos and racing greyhound kennels, who have historically fed raw meat, recognize the potential for contamination and attempt to decrease risks of foodborne illness. Raw meat may make up 50 to 75% of the food consumed by racing greyhounds in the United States (Chengappa et al, 1993). Sporadic fatalities and contamination of the environment with *Salmonella enterica* have occurred in greyhound facilities in which raw meat was fed (Morley et al, 2006). Unlike raw food advocates in the dog-racing industry, pet owners share their household and food-preparation area with their pet. The FDA "does not believe raw meat foods for animals are consistent with the goal of protecting the public from significant health risks, particularly when such products are brought into the home and/or used to feed domestic pets." Thus, the FDA has drafted guidelines for companies selling raw meat diets to pet owners (2000).

Often, pet owners will refer to the quality of their raw homemade diet ingredients as "all natural," "whole food" "or organic," none of which decreases the potential for microbial contamination. Numerous studies have demonstrated the presence of bacterial pathogens in retail meat for human consumption (Sinell H-J et al, 1984; Fenlon et al, 1996; Tamplin et al, 2001; Duffy et al, 2001; Whyte et al, 2001; Zhao et al, 2001; White et al, 2001; Villani et al, 2005; O'Keefe, 2005). Raw meat diets prepared by pet owners fed to dogs and cats have been documented to contain pathogenic *Yersinia enterocolitica* 4/O:3, *Salmonella* spp. and *Escherichia coli* O157:H7 (Fredriksson-Ahoma et al, 2001; Joffe and Schlesinger, 2002; Freeman and Michel, 2001; Chengappa et al, 1993). Commercially available raw meat diets (beef, lamb, chicken and turkey), sampled over a two-month period, cultured positive for non-type specific *E.coli* and *S. enterica* (Strohmeyer et al, 2006). Of 25 commercial raw meat diets (beef, lamb, quail, chicken and ostrich), 64% were positive for *E. coli* and 20% were positive for *Salmonella* spp. In addition, 20% were contaminated with *Clostridium perfringens* and a toxigenic strain of *C. difficile* was isolated from one food (Weese et al, 2005). Any claims that a finished pet food is "human grade," or any connotation that a pet food is derived from raw ingredients "like, or similar to, what your own human family members eat" is considered false and misleading under current AAFCO rules and regulations.[a]

Advocates of feeding raw meat, bone and eggs claim that pathogenic organisms in raw meat do not affect dogs and cats due to the lower stomach pH and shorter GI transit times in these species. Stomach pH and GI transit times are in fact similar among people, dogs and cats and do not lower the risk to pets. Dogs and cats succumb to foodborne pathogens and exhibit clinical signs similar to those in people (Fredriksson-Ahomaa et al, 2001; Gayle, 2003; Remillard and Wynn, 2005). Neither freezing raw meat before feeding nor purchasing freeze-dried commercial foods eliminates pathogens; freezing and freeze-drying are ineffective means for killing bacteria. In fact, both methods are used for long-term preservation of valuable stock bacterial cultures in laboratories. Grape seed extract itself does not kill microorganisms and does not render meat safer. The antimicrobial activity attributed to grapefruit seed extract is merely due to the synthetic preservative agents added to the product. Natural grape seed appears not to have antimicrobial activity (von Woedtke et al, 1999).

Opponents to feeding raw food point out that meat and egg supplies for people are contaminated with microorganisms and that feeding raw meat increases the likelihood of exposure of

owners and pets to foodborne bacterial diseases (LeJeune and Hancock, 2001). Advocates of raw food do not deny its potential health risks to pets (Volhard and Brown, 2000; Hofve and Smith, 2001; Silver, 2004). Pet owners may not realize that infected dogs shed bacteria capable of infecting people. Dogs may be excreting *Salmonella* spp., *Campylobacter* spp. or *Y. enterocolitica* in their feces, yet remain clinically normal (LeJeune and Hancock, 2001). Pets fed homemade raw meat diets shed viable organisms in their feces. In one study, *Salmonella* spp. were isolated from 80% of the raw meat and bone diets sampled and in 30% of the stool samples from dogs consuming those diets (Joffe and Schlesinger, 2002). Greyhounds fed raw meats diets shed the same subspecies of *Salmonella* in their feces as that found in their diets (Stone et al, 1993). Sled dogs were subclinical shedders of *Salmonella* spp. when fed a contaminated diet (Cantor et al, 1997). Dogs infected with *Campylobacter* spp. excrete organisms in their feces, but may remain clinically normal (Hald and Madsen, 1997). However, serovars of *Campylobacter* isolated from diarrheic dogs were the same as those isolated from poultry carcasses fed to the dogs (Varga et al, 1990). Therefore, pets fed contaminated raw meat diets are a source of contamination to people and other pets in the same household. Transmission of *Salmonella* infection from pets to people in the same household has been documented (Morse et al, 1976; Sato et al, 2000; Tauni and Osterlund, 2000). Pet owners feeding raw chicken necks and backs or other raw meat are putting themselves, their family and their pet at increased risk for exposure to *Salmonella* spp. Household transmission of foodborne *Y. entercolitica* from dogs to people has been documented (Gutman et al, 1973). Exposure may occur either by direct contact with food/utensils, or by contact with the contaminated environment shared between people and pets (Sanchez et al, 2002).

A recent meta-analysis demonstrated that consumers engage in risky behaviors regarding food handling. High-income individuals were less knowledgeable about food hygiene and performed higher risk, cross-contamination practices more often than other groups studied (Patil et al, 2005). Exposure to foodborne illness due to ingestion of pathogens from undercooked hamburger or eggs, raw chicken and work surfaces used to slice raw vegetables is a continuous threat to people who prepare raw foods for their pets (Hedberg, 2001). Safe handling of food and feeding containers is of paramount importance for pet owners who feed raw meat. Some people are unaware of any food safety issues because the raw meat used to feed their pet is sometimes derived from the same source as meats they use for their own consumption. However, USDA product labels on meat sold in grocery stores give clear warnings and cooking instructions to reduce the risk of foodborne illnesses. Foodborne pathogenic organisms may infect people handling contaminated meat and egg products and products intended for pets (bones, pig ears and treats) (Grimsrud, 1999).

Even advocates of feeding raw foods or ingredients admit that people "extremely susceptible to infectious disease" should not feed raw meat (Hofve and Smith, 2001). Individuals who clean the cat's litter box or pick up their dog's stool should consider the feces contaminated with viable pathogenic microbes. Households with elderly persons who may be immunocompromised should avoid raw food and soiled environments. Extra precautions should be taken when persons (or other pets) in the household have immunosuppressive (human immunodeficiency virus, feline leukemia virus or feline immunodeficiency virus) infections, are undergoing chemotherapy or being treated with antiinflammatory medications. Additional caution should be emphasized when young children are in the household and pet food-oral or fecal-oral contamination is possible. Because children are more susceptible than healthy adults, families with children who crawl and those with children who play with the family pet may decide to feed commercially prepared moist or extruded foods to prevent foodborne illness in the child (Trevejo et al, 2003). Veterinarians recommending commercial or homemade foods containing raw meat or eggs have an ethical responsibility to fully inform pet owners of the increased potential risk of foodborne pathogens not only to the pet but the entire household (LeJeune and Hancock, 2001; Remillard, 2005).

PATIENT ASSESSMENT

The most important goal in dealing with a case of suspected foodborne illness is to obtain an accurate diagnosis. However, this may be difficult because many factors, including the pet owner, can mislead the veterinarian. One must adhere stubbornly to the principles of a proper toxicologic investigation, including the careful evaluation of information supplied by: 1) the history, 2) clinical signs, 3) postmortem findings, 4) chemical analyses and 5) laboratory animal tests (Osweiler et al, 1985). For live patients, an accurate diagnosis will aid in the initiation of specific treatments and preventive measures. The veterinarian should also use preliminary information and clinical signs to guide the history-taking process.

History

Although an adequate history is important in all clinical cases, it is especially important when foodborne illness is suspected because some of the critical facts in the case may be lacking. For example, it may not be possible to obtain a sample of garbage or a carrion source. Pet owners who often express the opinion that food is to blame also complicate the history-taking process. In such cases, veterinarians must be methodical if they are to reach an unbiased and accurate diagnosis.

The natural starting place is the discussion with the pet owner. First, ascertain when and what clinical signs first appeared. From here, veterinarians can annotate the sequence and relevant facts about the events that transpired before the patient's presentation. Aspects of the history that seem vague or incomplete should be probed further. Facts that seem unrelated should be noted for later consideration. For example, it is important to know what day the neighborhood trash is left out for pickup, especially if it was the day before the illness occurred. The recent application of a pesticide to the premises or yard, coupled with signs typical of pesticide toxicity, would

Table 11-2. Clinical signs of selected foodborne illnesses.

Clinical signs	Agents causing the foodborne illness
Vomiting/diarrhea	*S. aureus, Salmonella* spp., *Neorickettsia* spp., *E. coli, B. cereus, Yersinia* spp., *Campylobacter* spp., biogenic amines, aflatoxins, vomitoxin, cyclopiazonic acid, lead, arsenic, zinc, cadmium
Liver disorders, jaundice	Aflatoxins, fumonisins, lead, arsenic, rubratoxin, *Yersinia* spp.
Blood disorders, e.g., anemia, hemorrhages	Aflatoxins, *Neorickettsia* spp., lead, onions, garlic, rubratoxin, cyclopiazonic acid, mycotoxins
CNS/nervous disturbances	*C. botulinum*, fumonisins, penitrem A, lead, arsenic, mercury, chocolate
Kidney pathology	Ochratoxin, cyclopiazonic acid, *E. coli*, lead, arsenic, mercury, cadmium, chocolate, grapes/raisins
Skin lesions	*E. coli*, garlic, arsenic, cyclopiazonic acid

be important, particularly if the pet owner, instead of a professional exterminator, had applied the pesticide. Exposure to other toxicants in the pet's environment, such as recent use of certain cleaning chemicals, is always a distinct possibility and should be thoroughly investigated. A run or hike in the woods may allow the pet access to contaminated material containing bacteria or mycotoxins that induce foodborne illness. The AAPCC reported that home exposures are responsible for 91.6% of canine and 93.3% of feline poisonings (Hornfeldt and Murphy, 1998). If pets are allowed to roam freely outdoors, the scope of investigation must be expanded. Free-roaming animals have access to pesticides, other toxic chemicals, poisoned bait, trash, garbage and spoiled foods. Pets on farms and ranches have an increased exposure to pesticides and agricultural chemicals. They also have the freedom to ingest animal feeds intended for other species that may contain feed additives such as ionophores and organic arsenicals, which are toxic to pets.

These examples lend credence to the fact that one cannot achieve an adequate history by allowing the pet owner to simply describe the events that preceded the illness. Instead, it is imperative that the veterinarian take the initiative to tactfully probe and query the pet owner for every piece of key information. Most pet owners feel that such facts are irrelevant, and others may refuse to admit that their pet would scavenge garbage cans. Still others may even give incorrect information to conceal their own negligence. All family members should be included in these discussions if possible. This is a good time to request that the pet owner bring the food in its container to the hospital for testing. It is important that the entire food container be brought, not just a sample selected by the pet owner (to be discussed later in the chapter).

Contamination of a commercial pet food will usually produce an epizootic of sick pets within a wide geographic area, as exemplified by events in Europe and recently in the United States. A popular brand of cat food was inadvertently contaminated with the food animal drug salinomycin, causing paralysis and death in several hundred cats (Spillers Petfoods, 1996). Toxic levels of aflatoxin in a commercial food led to numerous reports of affected dogs (Derezynski et al, 2006; Stenske et al, 2006). Therefore, knowledge of this information can be used in the diagnostic process. If other animals in the same household are eating food from the same bag or container and remain asymptomatic, then implication of the food is diminished, and other possible causes should be investigated. Date codes on bags or cans of food may be used by the manufacturer to link illness of multiple pets in widely separated geographic areas. The food is not a likely suspect if pets consuming food with the same date code are not experiencing similar clinical signs.

However, even if it appears that the commercial food has been exonerated in a wide geographic area, one should not end the commercial food investigation because the pet owner may have compromised the product's integrity by improper storage or usage. The veterinarian should contact the manufacturer to determine if similar cases have been reported. Company technical personnel can also help the differential diagnostic process by supplying key information about product testing, additional areas of investigation and beneficial laboratory tests. Major pet food companies frequently check raw ingredients for mycotoxins, mineral levels, heavy metals, pesticides, spoilage indicators, peroxides and other substances as part of their quality control and specifications for incoming raw materials.

Physical Examination

The physical examination of patients suspected to have a foodborne illness should be thorough, just as for other diseases. Although signs of GI disease may be obvious, one should also be alert for other clinical signs such as cutaneous lesions or signs that might signify central nervous system or hepatic disease (**Table 11-2**). If possible, samples of vomitus and feces should be obtained for laboratory testing. Veterinarians should also use their own olfactory senses. Many toxicities impart unique odors to the patient. For example, fishy breath emanating from a dog known to be consuming a cereal-based dry dog food with no added fish oil or fish meal would be noteworthy. Likewise, a pesticide odor on a cat's coat would be a significant observation. Again, one cannot overemphasize the investigative prowess that must be exercised in foodborne illness cases.

Another important reason for conducting a routine physical examination is to evaluate the need for symptomatic treatment. Patients may have signs such as dehydration, seizures or high fever that require symptomatic or supportive treatment before a final diagnosis is made. This determination is best made during the physical examination. If emergency treatment is warranted, consultation with a local veterinary school, state veterinary diagnostic laboratory, hospital poison control center or the American Society for Prevention of Cruelty to Animals may be useful. The National Animal Poison Control Center (888-426-4435) may also prove helpful.

Clinical Laboratory Testing

Clinical laboratory testing should be performed routinely in all suspected foodborne illness cases. Many such illnesses are short-lived so hematologic and serum biochemistry values may

be within normal limits. However, clinical biochemistry values may be invaluable in establishing the diagnosis and prognosis in serious illnesses such as mycotoxicosis.

Vomitus, feces and urine should be collected, labeled, frozen and tested for bacteria, viruses, biotoxins, metals, pesticides or chemicals as deemed appropriate by discussions between the veterinarian and laboratory testing personnel. The collection and analysis of a urine sample is also important because many toxic compounds are concentrated in urine. In fatal cases, organ tissue samples, bile, urine and stomach and intestinal contents should be collected during the postmortem examination.

Risk Factors

Individual factors such as age, species and state of health influence susceptibility to foodborne illness. Young and old animals are most susceptible. Debilitated and immunocompromised animals are more prone to foodborne illness. Dogs are at higher risk than cats because they are more likely to forage spoiled foods (e.g., trash, garbage and carrion). The AAPCC reported that dogs account for 75% of all animal poisonings (Hornfeldt and Murphy, 1998). Historically, the risk of foodborne illnesses in pets is increased when raw ingredient diets are fed, during warm weather, during hunting seasons, and around two holidays: Thanksgiving and Christmas (Coppock and Mostrom, 1986).

Cats tend to be more discerning and fastidious in their eating habits. Cats may vomit because of subtle variations between different batches of the same food. Slight changes in moisture content or application of palatability enhancers can lead to vomiting in cats. If a cat vomits after eating a recently opened can or bag of a commercial product, but is otherwise healthy, you may choose to try a food with a different date code before concluding that the food is adulterated. If the cat is truly ill, and you suspect the food, call the company to check for other reports of illness in cats eating that product or a product with the same date code. Reputable companies will want to know about any problems.

The most important factors to consider in establishing risk are the food source and the environment. Knowledge of these factors will help quantify the patient's exposure to other sources of toxicants and microbial agents. If the pet owner feeds a commercial pet food and follows label directions and proper storage recommendations, the likelihood of foodborne illness is low. However, if the same pet is allowed to roam freely outdoors, then the risk of exposure to foodborne disease agents is increased greatly. Home-prepared foods are riskier if owners do not follow proper preparation and storage procedures. Animals fed foods containing uncooked meat, eggs or offal are at much greater risk for foodborne agents. In general, the risk of contracting foodborne illness from various food sources increases as follows (from least to greatest risk):

- Federally regulated canned pet foods
- Federally regulated dry pet foods
- Federally regulated semi-moist pet foods
- Individual homemade fresh foods
- Locally prepared commercial dry pet foods
- Mass-produced kennel foods
- Free access to garbage, trash and carrion.

The risk of contracting a foodborne agent from any of these food sources can be markedly increased by improper storage of the food. All of the effort that goes into selection of raw ingredients, product manufacturing and choice of food or home preparation is wasted if the pet owner fails to properly store the food. Proper storage depends on control of three factors: 1) temperature, 2) moisture and 3) availability of oxygen (Ensminger et al, 1995). If these factors are controlled, commercial canned products will have a shelf life of well over a year and dry foods of at least six months. Therefore, risk is also influenced by proper food storage.

Consumers should store dry food in the closed bag, at room temperature if possible, and away from moisture (Chapter 8). If the consumer puts the food in a plastic container, the bag itself should be placed in the container to retain integrity of the product and preserve the date code (Chapter 8). Opened cans of food should be covered and immediately refrigerated for no longer than specified by the manufacturer, usually three to five days.

Etiopathogenesis

The bacteria of major concern as potential causes of foodborne illnesses in people include: *C. perfringens, C. botulinum, Staphylococcus aureus, Bacillus cereus, Salmonella* spp., *Listeria* spp., *Yersinia* spp., *Aeromonas* spp., *C. jejuni, E. coli, Vibrio* spp., *Enterococcus faecalis, E. cloacae* and *Klebsiella ozaenae* (Potter, 1992; Council for Agricultural Science and Technology, 1994). These organisms also have the potential to cause disease in pets. However, as stated previously, the prevalence of foodborne disease is low in dogs and cats. The following discussion involves the etiopathogenesis of bacteria and other agents that can cause foodborne disease in pets.

Bacteria and Rickettsia

SALMONELLA SPECIES

Salmonellae are gram-negative, aerobic bacilli that are normally present in the intestinal tracts of many mammals, birds and reptiles. Healthy adult dogs and cats are fairly resistant to the pathogenic effects of salmonellae but serve as important sources of infection for people and weak, debilitated animals. It has been estimated that 36% of healthy dogs and 17% of healthy cats harbor these organisms in their GI tracts (Green, 1995; Morse and Duncan, 1975).

The most common route of exposure is through ingestion of fecal-contaminated food and water. The presence of salmonellae in food or water indicates inadequate hygiene and improper cooking. Racing greyhounds are frequently infected when they consume foods largely composed of contaminated raw meat and offal from rendering plants. Researchers who sampled and cultured raw meat used in greyhound foods found that 45% of the meat samples were contaminated with salmonellae. *S. typhimurium* was the most commonly isolated serotype (Chengappa et al, 1993). When racing greyhounds ingest raw meat containing large numbers of cells, a clinical enteritis syndrome termed "kennel sickness" or "blowout"

results (Fenwick, 1996).

Salmonellae produce a heat-labile endotoxin, which is responsible for their pathologic effects. Clinical syndromes can be divided into gastroenteritis, bacteremia/toxemia and organ localization. Infections can usually be treated successfully with a combination of appropriate antibacterial drugs and supportive treatment. Persistent carriers are common and can be a source of human exposure. Proper cooking of foods and boiling water will kill vegetative bacterial cells and inactivate the endotoxin.

CLOSTRIDIUM BOTULINUM

The heat-labile toxin of the gram-positive, anaerobic, spore-forming bacterium *C. botulinum* causes botulism. These saprophytic bacilli are commonly found in soil and as contaminants in raw meat, carrion and vegetables. They are not considered dangerous to man or animals unless allowed to grow under anaerobic conditions in uncooked meats, improperly canned foods and the carcasses of dead animals. Under anaerobic conditions, *C. botulinum* produces the most potent biotoxin known (Klassen and Eaton, 1993). This powerful exotoxin blocks the release of the neurotransmitter acetylcholine. Dogs are less susceptible to the effects of the toxin than people, but naturally occurring botulism has occurred in dogs (Green, 1995; Barsanti, 1984; Barsanti et al, 1978). Cats, previously thought to be resistant to botulinum toxin, have also been found to be susceptible. Eight cats fed pelican carrion contracted the disease, and four died during the course of the illness. Toxigenic *C. botulinum* type C bacteria were found in the stomach of one cat and in the pelican muscle (Elad et al, 2004). Clinical signs can occur as early as 12 hours or as late as five to six days after the exotoxin is ingested. The primary clinical sign is generalized paralysis that starts in the posterior limbs and progresses to quadriplegia.

Primary care consists of supportive treatment. Spontaneous recovery will occur provided the dose of toxin ingested was insufficient to severely affect vital functions, such as respiration. Prevention can be achieved by heating foods before consumption to either 80°C (176°F) for 30 minutes or 100°C (212°F) for 10 minutes (Ensminger et al, 1995). These heating protocols are sufficient to destroy the heat-labile toxin of *C. botulinum*; however, any bacterial spores present will survive this procedure.

STAPHYLOCOCCUS AUREUS

The ubiquitous staphylococci are common inhabitants of the skin and mucous membranes of man and other animals (Jawetz et al, 1980). *S. aureus* is the most common cause of foodborne illness in people. The typical GI signs result from a potent *S. aureus* enterotoxin. Although *S. aureus* organisms are easily killed by heat, their enterotoxin can withstand typical cooking temperatures and even the canning process (Tatini, 1976). Ingestion of about 25 µg of enterotoxin will produce nausea and vomiting within two to four hours in people. Spontaneous recovery occurs in 24 to 48 hours. Dogs and cats are reported to be tolerant to staphylococcal enterotoxin and have remained asymptomatic after administration of oral doses as high as 100 µg/kg body weight (Freer and Arbuthnott, 1986).[b]

ESCHERICHIA COLI

E. coli is a well-known pathogen of people. However, the role of *E. coli* as a pathogen of dogs and cats has been unclear (Burrows et al, 1995; Olson et al, 1985). *E. coli*, strain O157:H7 has been involved in a number of outbreaks of foodborne illnesses stemming from improperly cooked meat purchased from fast-food restaurants (Potter, 1992). The same strain has been incriminated in an unusual clinical syndrome in racing greyhounds termed "Alabama rot" or "Greenetrack disease" (Fenwick et al, 1995). This disease is characterized by erythema, ulceration of the extremities and renal glomerular pathology (Fenwick, 1996; Fenwick et al, 1995; Hertzke et al, 1995). No particular treatment has proved effective, but many animals will recover with symptomatic treatment and good nursing care.

BACILLUS CEREUS

B. cereus causes vomiting and diarrhea in people, but it is not thought to pose a significant danger for foodborne illness in animals (Turnbull and Kramer, 1991). At room temperature, *B. cereus* flourishes, producing a potent endotoxin. The organism is a ubiquitous, spore-forming aerobic saprophyte found in soil, grains, cereal products and other foods (van Netten and Kramer, 1992). As an example, it is commonly found in uncooked rice (Ensminger et al, 1995). *B. cereus* has been found as a common isolate in samples of dry pet food.[c] It has also been isolated from food packaging paper and materials (Vaisanen et al, 1992).

The standard heat used to manufacture pet foods is not likely to destroy the spores of this organism. However, the number of organisms isolated from pet food samples ($<10^5$ cells/g of food) is unlikely to cause foodborne disease in pets unless the food is exposed to moisture and heat conditions conducive to bacterial proliferation (van Netten and Kramer, 1992; Claus and Berkeley, 1986; Drobniewski, 1993). Therefore, pet owners should be warned not to add water to dry pet foods and leave them exposed to high ambient temperatures for prolonged periods.

NEORICKETTSIA SPECIES

In dogs, *Neorickettsia helminthoeca* and *N. elokominica,* cause a serious systemic infection known as salmon poisoning (Breitschwerdt, 1995; Gorham and Foreyt, 1984). The disease is transmitted by ingestion of raw salmon containing the vector, a fluke named *Nanophyetus salmincola*. The fluke matures in five to seven days and then attaches to the intestinal mucosa of the host animal. The rickettsiae leave the fluke, invade the intestinal mucosa and enter the bloodstream to produce an acute systemic infection.

Clinical signs include vomiting, hemorrhagic diarrhea, high fever, dehydration and peripheral lymphadenopathy. Tetracycline therapy is the treatment of choice. Supportive treatment with parenteral fluids is also indicated. The anthelmintic preferred for elimination of the fluke is fenbendazole. If timely treatment is not instituted, mortality can reach 50 to 90% (Burrows et al, 1995).

Mycotoxins

Estimates suggest that one-quarter of the world's annual food crop is affected by mold metabolites called mycotoxins (Mannon and Johnson, 1985). Produced by a wide variety of saprophytic and pathologic fungi, they can be highly toxic (Council for Agricultural Science and Technology, 1989). Toxic syndromes range from mild GI discomfort and vomiting to an acute fulminating episode with death. Long-term, low-level exposure can produce vague signs such as chronic organ damage (e.g., hepatic cirrhosis), immunosuppression and decreased production or performance. Mycotoxins interfere with absorption of antioxidant compounds from food, and modulate activity of antioxidant enzyme systems in cells. Combinations of mycotoxins may be more toxic than single mycotoxins (Surai and Dvorska, 2005). Although cereal grains are most commonly associated with mycotoxins, a wide variety of foodstuffs including cheeses, nuts, forages, fruits and even beer can be contaminated (Council for Agricultural Science and Technology, 1989).

Mycotoxin production occurs in the field and during harvesting, processing, transportation and storage. Stressors, such as drought and insect damage, predispose crops to infestation and mycotoxin production. Warm ambient temperatures and high humidity also favor mycotoxin production. Some molds thrive in cooler, wet conditions. Presence of mold, however, does not necessarily mean mycotoxin production. The conditions under which mycotoxins are formed are relatively narrow when compared to conditions favorable to mold growth (Pitt, 2001). Some degree of mycotoxin production is unavoidable. Mycotoxin content may be controlled through identification, quantification and regulation. The genera of the three major mycotoxin-producing fungi are *Aspergillus, Fusarium* and *Penicillium*. Dietary supplementation with antioxidants proved protective against the toxic effects of mycotoxins in various animal species (Surai and Dvorska, 2005).

AFLATOXINS

Aflatoxin, a mycotoxin produced by *Aspergillus flavus* or *A. parasiticus*, can produce varying degrees of toxicity in birds and mammals. Corn, peanuts, cottonseed and grains are potential sources of aflatoxins in pet foods. Dogs and cats are among the species most sensitive to the effects of aflatoxin, with LD_{50} values ranging from 0.5 to 1.0 mg/kg (Newberne and Butler, 1969; Edds, 1973). Aflatoxin B_1 is metabolized in the liver to highly reactive intermediates that bind to DNA, disrupt transcription and lead to abnormal cell proliferation, mutagenesis and carcinogenesis. Aflatoxins also inhibit various enzymes (Hocking, 2001). The net effect is decreased protein synthesis, leading to hypoalbuminemia and a shortage of clotting factors.

The onset and severity of the clinical syndrome depend on the dose and duration of exposure. In 1955, the canine disease known as hepatitis X was successfully reproduced by feeding dogs a brand of dog food previously incriminated in cases of the same disease (Seibold and Bailey, 1952; Newberne et al, 1955). Later, researchers discovered that the identical disease syndrome could be elicited in dogs fed purified aflatoxin B_1 (Newberne et al, 1966). Cases of canine aflatoxicosis resulting from contaminated food have been reported in South America and Africa (Coppock and Mostrom, 1986; Hagiwara et al, 1990). Consumption of an aflatoxin-contaminated commercial pet food was reported to result in the deaths of more than 100 dogs in the United States in 2006 (Stenske et al, 2006).

The principal target organ in all species is the liver. Clinical signs, such as anorexia, severe GI disturbances, jaundice and hemorrhage, with a corresponding increase in hepatic enzyme activities and a decrease in serum protein values, are typical (Newberne and Butler, 1969; Edds, 1973; Neal, 1973; Stenske et al, 2006). The most frequently observed hepatic lesions are centrilobular necrosis, fibrosis and bile duct proliferation (Puschner, 2002). Intravascular coagulation can also be a complication of chronic aflatoxicosis (Green, 1977). Marked cytoplasmic vacuolar degeneration consistent with accumulation of hepatocellular lipids was noted in dogs with confirmed aflatoxicosis. Progression of clinical signs corresponded with increases in alanine aminotransaminase (ALT) and aspartate aminotransaminase activities, hyperbilirubinemia, hypoalbuminemia, hypocholesterolemia and coagulopathy (Stenske et al, 2006). Hematemesis or melena was associated with a grave prognosis. In another report, dogs that died were significantly younger, had lower total protein and higher total bilirubin, ALT and alkaline phosphatase values when compared to the same parameters in survivors. The authors concluded that hypocholesterolemia and reduced protein C values were biomarkers for aflatoxicosis (Dereszynski et al, 2006).

Today, manufacturers and governmental regulatory agencies strive to minimize exposure to aflatoxins by using low-level detection methods. Aflatoxins are heat stable and not destroyed by boiling, autoclaving or food manufacturing methods. The FDA has established an action level of 20 ppb for total aflatoxins in pet food (Office of Enforcement, 1994). Therefore, prevention strategies involve identification of raw materials with unacceptable levels (>20 ppb), maintenance of proper storage conditions and assay of final feeds.

VOMITOXIN

Vomitoxin, chemically known as deoxynivalenol, is a mycotoxin produced by members of the genus *Fusarium* (Council for Agricultural Science and Technology, 1989). Vomitoxin can be found in any grain but most commonly affects wheat and barley. Like most other mycotoxins, it is heat stable and survives extrusion and drying (Hughes et al, 1999).

Dogs and swine, the species most susceptible to the effects of vomitoxin, are affected at relatively low concentrations. The mechanism of action is inhibition of protein synthesis (Bohm and Razzazi-Fazeli, 2005). Experimentally, acute toxicity affects rapidly dividing cells in lymph nodes, spleen, thymus and intestinal mucosa, and may be immunosuppressive (Bondy and Pestka, 2000). Clinical signs include feed refusal, vomiting and diarrhea. Vomiting and feed refusal are apparently due to neurochemical changes in the brain, rather than taste (Riley and Pestka, 2005). In a study using 0 to 10 mg deoxynivalenol/kg pet food, individual dogs and cats were

highly variable in their response to vomitoxin. Some animals vomited immediately after eating, whereas others exhibited food refusal or decreased food intake without vomiting. Compared to dogs, cats tolerate higher levels of deoxynivalenol. Cats consumed small, frequent meals, whereas dogs ate one large meal when the food was presented. Feeding behavior of cats may have influenced their ability to tolerate higher levels of deoxynivalenol (Hughes et al, 1999).

In 1993, the FDA advisory level for deoxynivalenol in grains and grain by-products used in pet foods was 5 ppm with the added recommendation that these ingredients not exceed 40% of the food (i.e., 2 ppm deoxynivalenol in the complete pet food) (Chesemore, 1993). However, feed refusal in dogs has been reported in levels approaching 2 ppm (Maune, 1995). Therefore, a more practical maximum level is 1 ppm. In 1995, vomitoxin levels in winter wheat were reportedly as high as 32 ppm. One major pet food company recalled 16,000 tons of products due to deoxynivalenol contamination at a cost of about $20 million (Industry News, 1995).

FUMONISINS

The fumonisins are a group of recently described mycotoxins produced by *Fusarium moniliforme*, a common field fungus found in grains, beans and fruit (Gelderblom et al, 1988; Haschek and Haliburton, 1986). Although *F. moniliforme* reportedly infects 80 to 100% of all corn harvested in the United States, little information is available about the toxicity of fumonisins in dogs and cats. However, these potent mycotoxins cause leukoencephalomalacia in horses and liver disease in a number of other species. Fumonisin-contaminated pet foods have not been a problem to date.

OTHER MYCOTOXINS

The mycotoxins produced by *Penicillium* can be roughly categorized into those that cause kidney or liver lesions, such as ochratoxin A, and those that are neurotoxins, called tremorgens. The tremorgens are mold metabolites that act as neurotoxins. Mortality resulting from tremorgens is difficult to diagnose postmortem because they cause no visible lesions (Pitt, 2001). The toxic effects of penitrem A have been reported (Arp and Richard, 1979; Hayes et al, 1976). Penetrim A toxicity led to life-threatening tremors in dogs that ingested moldy cream cheese or unidentified materials in a compost pile (Boysen et al, 2002; Young et al, 2003). Affected animals recover with no residual effects if the tremors are addressed with anesthesia and dehydration is prevented (Richard, 2000).

Ochratoxin A primarily affects the kidney, but can affect the liver if levels are high. Toxicity in dogs has been reported (Szczech et al, 1973). The toxin is not rapidly removed from the body and may accumulate. High levels of ochratoxin have been detected in house dust (Richard, 2000).

Canine and feline toxicity data for many of the other foodborne mycotoxins are scant in the scientific literature. The toxic effects of rubratoxin B and cyclopiazonic acid have been described and documented (Hayes and Williams, 1977; Nuehring et al, 1985).

Biogenic Amines

"Cadaveric alkaloids" isolated from putrefied bodies have been known to forensic toxicologists for more than 100 years (Blanke and Poklis, 1993). Modern chemistry has now established that these decomposition products are not alkaloids but instead are "biogenic amines." They are produced when bacteria decarboxylate amino acids in animal tissue. Examples of biogenic amines include histamine, putrescine and cadaverine.

Detection of histamine in the tissues of fish indicates decomposition or spoilage. Normal commercially canned fish contain histamine levels less than 5 to 6 ppm (Dykstra, 1995). As the level of histamine approaches 20 ppm, spoilage becomes organoleptically and physically evident.

Excessive levels of histamine (around 500 ppm) in the flesh of spoiled fish in combination with a toxin called saurine are thought to be involved in the pathogenesis of a human foodborne illness called "scombroid fish poisoning" (Dykstra, 1995; Russell and Dart, 1993; Morrow et al, 1991). This common seafood-related illness is named for its association with consumption of scombroid fishes, such as tuna, wahoo, mackerel and sardines, although other fishes and cheese have been implicated (Morrow et al, 1991; Taylor, 1986). The disease produces clinical signs of an allergic nature, i.e., flushing, sweating, nausea, diarrhea, rash, dizziness, facial swelling, respiratory distress and occasionally vasodilatory shock, but the disease is rarely fatal (Morrow et al, 1991; Taylor, 1986). The FDA has recognized histamine's role in scombroid poisoning by setting a maximum action level of 500 ppm histamine in canned fish (Dykstra, 1995).

Histamine and other biogenic amines such as putrescine and cadaverine have also been detected in pet foods. Their presence has been attributed to the use of poultry, fish and meat by-products as raw ingredients. The levels of histamine in pet foods reported in each of two different studies ranged from 3.8 to 88.8 ppm and 16 to 65.5 ppm, respectively (Guilford et al, 1994; Guraya and Koehler, 1991). Dogs and cats are tolerant to much higher levels of histamine (2,500 ppm), but research is needed to determine whether certain hypersensitive animals may be at risk (Blonz and Olcott, 1978).

Metals

Metals are probably the oldest toxic agents known to man (Goyer, 1993). They are unique in that they are never destroyed nor created, just redistributed in the environment. Food is the most common source of metal toxicity in people and other animals. Pets frequently serve as sentinels for human exposure.

Pet foods can become contaminated in several ways. First, metals tend to accumulate in plant and animal matter, creating the possibility of toxic levels in food ingredients. Foods can also become contaminated during commercial manufacturing and home preparation by the inadvertent addition of metal shavings, grease, oils and other chemicals. Acidic foods can leach paint, soldered joints or plating agents from food containers. Young animals may ingest lead by chewing on painted wood, linoleum, metal toys, golf balls, roofing materials, drapery weights and ornaments (Osweiler et al, 1985).

Most foodborne metal toxicities in dogs and cats involve lead, zinc, cadmium and arsenic. These agents cause a variety of clinical syndromes depending on age, dose ingested and length of exposure. The specifics of metal toxicities are well described in several veterinary toxicology textbooks and are beyond the scope of this chapter.

The tendency of metals to accumulate in plants and animals has ramifications for the manufacture of commercial pet foods. Several studies have been conducted to quantify such accumulations. In one study, researchers analyzed 28 brands of commercial dog food and seven brands of cat food and found that average levels of lead, arsenic and cadmium were 1.26, 0.37 and 0.22 ppm, respectively (Edwards et al, 1979). A later study of 35 dog foods and 13 cat foods found the average levels of lead, cadmium and zinc were 0.88, 0.80 and 122.0 ppm, respectively (Mumma et al, 1986). These studies confirm that nontoxic levels of metals may be present in some pet foods; however, their presence at these levels would not support a diagnosis of metal toxicity. Instead, a definite diagnosis must be based upon finding toxic levels in the food that correspond to elevated levels in the patient's tissues, such as blood, liver and kidney.

Other Sources

SUPPLEMENTS

Many people supplement their own food with vitamins, herbal remedies and other items purchased at health food stores. Well-meaning pet owners likewise think that what is good for them is also good for their pets. Unfortunately, this practice fails to consider species and dose differences. Cats, in particular, may be adversely affected by medications considered safe for people. Certainly, vitamin A and D toxicity is well documented. It is also known that many herbal remedies cause adverse effects in people and animals (Poppenga, 1995; Remillard and Wynn, 2005). Therefore, the safety of other "natural" supplements such as aloe, ginseng root, eucalyptus, ginger and oil of wintergreen has yet to be established for dogs and cats. As the investigation of the clinical case proceeds, the veterinarian should ask the owner how and why the animal's food is being supplemented with these substances.

ONIONS AND GARLIC

Owners may also supplement a pet's food with onions or garlic. Onions derive part of their flavor from n-propyl disulfide, which is toxic to the erythrocytes of several species (Jain, 1993). In 1990, a phenolic compound was extracted from onions that increased methemoglobin concentrations and caused the formation of Heinz bodies in canine erythrocytes (Miyata, 1990).

Onions may injure the lipid membranes of erythrocytes and irreversibly denature hemoglobin (Jain, 1993). These changes result in Heinz body formation, hemolytic anemia and hemoglobinuria. The most common cause of Heinz body hemolysis in dogs is related to ingestion of onions. Although the toxicity has been known for more than 50 years, animal owners still unknowingly feed onions to dogs as part of table food or intentionally as a supplement. The hemolytic episode may be difficult to correlate with onion ingestion because it occurs several days postingestion. Clinical signs related to moderate Heinz body anemia have occurred in dogs consuming relatively small amounts (5 to 10 g of onions/kg body weight) of raw, cooked or dehydrated onions (Harvey and Rackear, 1985; Ogawa et al, 1986). In one study, consumption of approximately 30 g of raw onions/kg body weight for three consecutive days produced severe anemia, erythrocyte Heinz bodies and hemoglobinuria in all dogs fed onions (Ogawa et al, 1986). One animal developed severe icterus and died on Day 5.

Cats are prone to developing erythrocyte Heinz bodies after exposure to many chemicals in food (Jain, 1993; Hickman et al, 1990; Christopher et al, 1989). Likewise, Heinz body anemia has occurred in cats after consumption of onions (Kobayashi, 1981). Baby food or other foods containing similar amounts of onion powder should not be fed to cats because of Heinz body formation and the potential for development of anemia, especially with high food intake. Cats with concurrent oxidative diseases may develop additive hemoglobin damage when fed baby food containing onion powder (Robertson et al, 1998).

Garlic (*Allium sativum*) is also a member of the onion family. Long-term exposure to garlic and garlic extracts caused anemia, contact dermatitis and asthmatic attacks in dogs (Poppenga, 1995). Eccentrocytosis appears to be a major diagnostic feature of garlic-induced hemolysis in dogs. The constituents of garlic have the potential to oxidize erythrocyte membranes and hemoglobin, inducing hemolysis associated with the appearance of eccentrocytes in dogs. Thus, foods containing garlic should not be fed to dogs (Lee et al, 2000).

CHOCOLATE

Pets today are often fed "people" food. One delicacy that has potential to cause toxicity is chocolate. Chocolate products contain variable amounts of theobromine, a potent cardiovascular and central nervous system stimulant (Clark et al, 1981). Although pet owners might believe that chocolate is innocuous, one poison control center documented six cases of chocolate poisoning in dogs during a single year (Hornfeldt, 1987). Signs such as vomiting, diarrhea, panting, nervousness, excitement, tremors, tachycardia, cardiac dysrhythmias, coma, convulsions and sudden death may appear in four to 15 hours after ingestion (Hornfeldt, 1987; Gauberg and Blumenthal, 1983; Hooser, 1984; Sutton, 1981). Renal damage may occur in severe cases.

The toxic dose of theobromine has been reported to be greater than 200 mg/kg body weight (Hornfeldt, 1987). However, a springer spaniel died after ingestion of two lb of milk chocolate, corresponding to a dose of only 92 mg of theobromine/kg body weight (Gauberg and Blumenthal, 1983). Based on this case, consumption of one typical 1.55-oz. milk chocolate bar (93 mg theobromine)/kg body weight could produce clinical signs and possibly death (Hooser, 1984). Unsweetened baking chocolate also contains high levels of theobromine (450 mg/oz.) and has been implicated in cases of toxicity (Hooser, 1984). Finally, dogs have also been poisoned by ingesting cocoa powder (1 to 3% theobromine) (Sutton, 1981).

Theobromine is eliminated very slowly in dogs. This metabolic peculiarity prolongs the clinical syndrome and increases the risk of toxicity from repeated ingestion of small doses of theobromine. Because there is no available antidote for theobromine toxicity, symptomatic treatments such as administration of emetics, activated charcoal, tranquilizers, sedatives and lidocaine should be used in clinical cases of chocolate toxicity.

GRAPES AND RAISINS

Acute renal failure has been associated with ingestion of variable amounts of grapes or raisins by dogs; as little as 0.41 oz./kg in one case (Gwaltney-Brant et al, 2001). Vomiting and azotemia are the most consistent findings, occurring in 100% of the cases in a retrospective review (Eubig et al, 2005). Varying degrees of renal tubular degeneration and proximal necrosis also occur (Morrow et al, 2005). A number of etiologies have been proposed, including heavy metals, mycotoxins and pesticide residues, but given the lack of a dose-response relationship, no clear toxic principle has been identified. Suggested therapy includes gastric decontamination protocols to induce emesis followed by activated charcoal administration and fluid diuresis (Mazzaferro et al, 2004).

FEEDING PLAN

If a diagnosis of foodborne illness seems feasible, then the pet owner should be questioned extensively about the animal's food. First, the veterinarian should identify all possible food sources (including commercial foods, home-prepared foods and table scraps) and determine the feeding amounts and the availability of unintentional food sources. Common questions concerning commercial foods should include: 1) brand name, 2) manufacturer, 3) lot or date code, 4) form of food (i.e., dry, semi-moist, moist), 5) feeding method (i.e., meal fed, free choice), 6) the length of time the pet has been consuming the brand of food, 7) the length of time the pet has been fed from the present container of food (i.e., bag or can), 8) whether water is mixed with the food, 9) how long the food is left in the food bowl, 10) the ambient temperature at feeding, 11) the method of storing the food and 12) whether other pets in the household consume the same food.

Questions about home-prepared foods should include: 1) the source of ingredients, 2) storage methods for the ingredients and the food, 3) method of preparation, 4) preparation temperatures, 5) method of measuring temperatures and 6) feeding method. Any recent change in either the food ingredients or preparation methods should be investigated further.

The amount of food consumed should be compared with the calculated amount typically consumed by an animal of similar size. If the amount consumed is markedly less than the calculated amount, it could mean that the animal does not like the food and may be foraging other food sources or garbage. Decreased intake may also indicate food refusal typical of vomitoxin contamination.

Sampling Procedures

Most veterinary diagnostic laboratories can perform the tests necessary to facilitate a diagnosis of foodborne illness. Many investigative tests and techniques are available to the diagnostic laboratory to help assess the case. In fact, the number is so overwhelming that only a few can be used on a particular sample. It is essential that the veterinarian discuss the likely diagnoses with laboratory personnel before test initiation to ensure the tests most critical to a correct diagnosis are performed. Veterinarians also need to determine the laboratory's preferred specimens and methods of specimen preservation.

Sample/specimen collection should follow the rules of physical evidence even if the possibility of litigation seems remote or nonexistent to ensure results are admissible in court if circumstances change. The admissibility of this information in a trial depends on whether: 1) all specimens and/or samples were properly identified, 2) the "chain of custody" (**Table 11-3**) is documented by a specific and detailed description of all events and changes of possession starting at the time of collection, through transportation and transferal to final sample analysis at the laboratory and 3) the evidence is relevant to the case (Grau, 1993). Therefore, it is also important to inform laboratory personnel if there is any possibility of litigation.

The best sources of samples for assessment of the food for possible etiologic agents are: 1) the actual food source, 2) food ingredients (homemade foods), 3) stomach contents, 4) intestinal contents and 5) feces. The following procedures and methods relate primarily to assessment of the food but also could be used to evaluate any previously described specimens (e.g., urine, blood, tissues, etc.).

The pet owner should bring the entire container of food or containers of food ingredients to the veterinarian to ensure that sample collection follows aseptic technique and the rules of evidence collection (Grau, 1993; Edwards, 1989). Sample collection techniques are described in detail in **Table 11-4**. Label all sample containers as space allows with a sample number and a description of the contents, submitter's name, pet owner's name, date, product label information and lot number. Supporting information and descriptions that cannot be written on the sample label because of space constraints should be numbered identically to the sample and submitted with the sample (Osweiler et al, 1985; Edwards, 1989; Galey, 1992).

Detection Methods

Bacterial Isolation and Identification

Pet food ingredients, like most other foods, contain a diverse microbial flora. Therefore, no single growth medium will satisfy the requirements of all organisms that may be present in a sample. The veterinarian should discuss likely pathogens with laboratory personnel so that the best methods, enrichment techniques and selective media can be used (Galey, 1992; Quinn et al, 1994).

Most laboratories will use a variety of direct examination and culture techniques to attempt a successful identification (Quinn et al, 1994). First, smears of the specimens collected by either the veterinarian or laboratory personnel will be stained and

examined. Then growth and colony characteristics of bacterial isolates will be determined using a variety of media. The presence or absence of certain bacterial biochemical characteristics and atmospheric growth conditions will also be explored. Finally, a variety of other tests and techniques will be used to facilitate the identification process (e.g., API 20E strips and Staph-Trac).[d]

Analytical Chemistry

Metal assays are usually performed using some type of atomic spectroscopy, e.g., atomic absorption spectroscopy and inductively coupled plasma emission spectroscopy (Galey, 1992). Organic compounds such as pesticides and solvents are usually detected by chromatography, e.g., gas chromatography, high-pressure liquid chromatography, thin-layer chromatography. After a compound has been identified preliminarily by chromatography, results are often confirmed using mass spectrometry.

Mycotoxins can be detected by chromatography methods, radioimmunoassay (RIA) and enzyme-linked immunosorbent assay (ELISA) (Quinn et al, 1994). Staphylococcal enterotoxins can be identified using ELISA, RIA, serologic, precipitin and gel diffusion techniques (Freer and Arbuthnott, 1986). ELISA can also be used to detect the exotoxins and endotoxins of other bacterial species. *C. botulinum* exotoxins can be identified by serum neutralization using commercially available antisera followed by assay in laboratory animals (Quinn et al, 1994).

Significant Pathogen Levels in Food

Commercial foods are not sterile and may contain species of organisms associated with foodborne illnesses in people. However, the infective dose of each foodborne pathogen can vary greatly depending on the food substrate, the immunologic status of the host and the resistance of the normal intestinal flora (Council for Agricultural Science and Technology, 1994).

The same factors apply to foodborne illness in animals with the exception that the animal species can also influence the infective or toxic dose. Therefore, the relationship between microbial populations and the quality of foods can only be estimated and must be viewed with caution, especially when one considers that most sampling and microbial counting procedures possess inherent inaccuracies. Also, many organisms have fastidious growth and unique colonization requirements (i.e., medium, temperature and atmosphere). Although laboratory personnel will try various permutations, it is not always possible to find the correct combination given the limitations of sample size. In addition, the specimen may contain a microorganism that produces antimicrobial peptides that inhibit the growth of other species. Finally, the various counting procedures will also kill some of the bacteria present in the sample.

The scientific literature contains few data establishing the relative risk of foodborne illness and the microbial content of pet foods. Measuring the microbial content of pet foods is difficult but interpreting the results with respect to wholesomeness or food safety is even more difficult because risk quantification also depends on other factors, such as storage conditions.

Table 11-3. Procedures for the collection, transfer and preservation of physical evidence.*

- Collect, package and identify all samples according to the procedures listed in **Table 11-4.**
- Maintain a record of every person who had custody of any sample(s) or other evidence from the time that it was collected until presented in court ("chain of custody") by keeping a written log or diary of all relevant facts and sample transfers.
- Write notes documenting the time, place, description and circumstances of all samples entered in the log. Describe in detail how the samples were identified (numbered), processed, packaged, stored and shipped.
- If possible, photograph any apparent pathologic lesions, mold growth, foreign matter in the food, etc. Number the photographs consecutively and describe each photograph in the written notes.
- Write notes about all telephone conversations related to the case in the log, including the date, time and content of the conversation.
- Date all new entries in the log and have the person writing in the log initial the entry.
- Retain and store all relevant product labels in a safe place.
- Use a shipping method that expedites delivery of the samples to the laboratory. Keep copies of all shipping records. Hand carry the samples to the laboratory if possible. Obtain written proof of delivery (e.g., receipt).

*Adapted from Grau JJ. Criminal and Civil Investigation Handbook, 2nd ed., New York, NY: McGraw-Hill, Inc, 1993.

However, measurement of microbial populations may yield valuable information when used to compare one sample of a pet food with another sample of the same product. For example, it would be valuable to know whether bacterial numbers had increased dramatically while the food was in the pet's bowl. This information helps establish the level of hygiene and timeliness of the pet's feeding schedule. In summary, the presence of an organism in a food does not alone establish the diagnosis but must be considered as one piece of the diagnostic "puzzle."

Control and Prevention

Methods for control and prevention of foodborne illness in pets apply to commercial (after purchase) and home-prepared foods. Following the practices described in **Table 11-5** can best prevent foodborne illnesses in pet foods.

Food storage is an important preventive measure. Proper storage depends on control of: 1) temperature, 2) moisture and 3) availability of oxygen. First, high temperatures markedly decrease the shelf life of both canned and dry foods, especially when temperatures exceed 20°C (68°F) (Emsminger et al, 1995; Containers, 1968). Therefore, all commercial pet foods should be stored in the 4.4 to 15.6°C (40 to 60°F) temperature range. Fresh, home-prepared foods should be refrigerated at –1.6 to 15.5°C (29 to 60°F) before feeding. (Most household refrigerators hold foods at 4.4 to 7.2°C [40 to 45°F].) The length of time that a food can be kept refrigerated depends on its type and age. Fresh meats, fish and poultry can be kept for two to 10 days whereas fruits and vegetables will remain wholesome for weeks when refrigerated.

Moist products are sealed and therefore not affected by moisture or air; control of these factors applies only to storage of

Table 11-4. Sampling procedures for foodborne illnesses.

- Collect samples for toxicologic and microbiologic studies as separate samples and label them accordingly.
- Collect several samples from the same source, e.g., different areas of the food bag, stool specimen.
- Treat samples as though they were being prepared for a legal case by following the rules of evidence.
- Collect duplicate samples or split samples so that the veterinarian can retain one sample and the other can be submitted to the laboratory.
- Collect samples for microbiologic testing aseptically using sterile gloves, instruments and containers.
- Use watertight sample containers, preferably with screw-type lids.
- Label all sample containers with an accurate and complete description of the contents, e.g., submitter's name, client's name, date and time collected, product name, etc. Submit other sample information and any supporting descriptions with the samples.

Table 11-5. Prevention of foodborne illness in animals.

Commercial pet foods (moist or dry kibble)
Discard foods from bulging or leaking cans and damaged bags.
Discard all foods with an abnormal color, foreign materials, odor or moldy appearance.
Discard dry foods 30 minutes after adding water.
Avoid frozen raw diets.
Homemade diets
Use raw ingredients appropriate for human consumption.
Cook ground meat thoroughly to the center.
Sear the surface of whole meat cuts.
Cook all eggs: whole, yolks, whites and shells if used as calcium supplement.
Wash all raw fruits and vegetables.
Control food contamination
Use stainless steel utensils, feeding bowls, etc. whenever possible.
Keep food preparation areas, cooking utensils and food bowls spotlessly clean. Wash and disinfect bowls and utensils daily.
Store dry, commercial foods in a cool, dry environment, free from insects and rodents.
Empty the feeding bowl of moist or moistened foods not consumed within two to four hours if the ambient temperature is above 10°C (50°F).
Clean, wash and disinfect food utensils and food bowls after each feeding.
If feeding free choice, check food daily for mold and spoilage.
Control microorganisms in food using physical means
Cook all home-prepared foods at 82°C (180°F) for at least 10 minutes.
Verify cooking temperatures with a cooking thermometer and internal meat temperatures with a meat thermometer.
Validate thermometer accuracy periodically with boiling water.
Cover all perishable foods and opened cans of pet food and store in the refrigerator at 4°C (40°F) when not being prepared, cooked or consumed.
Control the pet's access to unintentional foods
Minimize roaming on trash pick up days.
Monitor closely when off leash.

bulk dry commercial foods. Spoilage bacteria require at least 30% moisture for growth whereas molds require 5 to 15%. Dry pet foods have moisture content in the range of 6 to 9%. Therefore, dry commercial pet foods will have a satisfactory shelf life if stored in a cool dry place with the top of the bag or container closed. These precautions limit the availability of moisture and air needed for oxidative chemical degradation and microbial growth. Placing the food still in its sack in a canister or other closed container will extend the shelf life by further reducing the availability of moisture and oxygen. This method of storage has the added advantage of preventing rodent and insect damage and maintaining palatability. In addition, storing the product in the original bag will preserve the date code information stamped on the bag and enhance investigation of a problem if one occurs.

REASSESSMENT

The type and duration of therapy will be dictated by the diagnosis and the physical condition of the patient. Therapy typically will consist of supportive, symptomatic treatment because most foodborne illnesses are self-limiting. With illnesses such as metal poisoning or mycotoxicoses that produce characteristic blood or biochemical changes, those specific parameters should be monitored routinely for evidence of recovery. In those cases in which the patient does not recover, veterinarians should first reassess the patient to ascertain whether exposure to the foodborne agent has been discontinued. If so, then an inaccurate diagnosis or other pathologic factors may have complicated the case. Continued monitoring of laboratory parameters is warranted. Animals that recover only to suffer another bout of foodborne illness at a later date are obviously being exposed to unsafe foods. Therefore, the veterinarian should counsel the pet owner to prevent further recurrences (**Table 11-5**).

ACKNOWLEDGMENT

The authors and editors acknowledge the contribution of Dr. James Cullor in the previous edition of Small Animal Clinical Nutrition.

ENDNOTES

a. Crane S. Feeding raw diet mythology. Personal communication. 2006.
b. Miller EP. Unpublished data. September 1996.
c. Cullor JS. Unpublished data. May 1995.
d. Analytab Products, Inc, Plainview, NY, USA.

REFERENCES

The references for **Chapter 11** can be found at www.markmorris.org.

CASE 11-1

Ulcerative Dermatitis in a Greyhound

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Patient Assessment

A two-year-old female greyhound that had been in training at a racetrack in Arkansas was examined for depression, swelling of the distal limbs and feet and skin ulceration. Other dogs from the same racing kennel had been affected with similar problems in the past.

Results of physical examination included depression, vomiting, subcutaneous edema involving both rear limbs, primarily distal to the stifle, and skin lesions. The skin lesions were focal, reddened areas that became dark red or black on the surface after a few hours. Several small ulcers were present on the distal extremities (**Figure 1**) and a large, well-demarcated ulcer was present on the left medial thigh (**Figure 2**). A large area of bruising and ecchymoses was evident on the ventral abdomen.

Clinical pathologic abnormalities included leukocytosis with neutrophilia, thrombocytopenia (29,000 platelets/µl; reference range = 200,000 to 500,000/µl), and severe azotemia (urea nitrogen = 240 mg/dl [10 to 20 mg/dl]; serum creatinine = 5.6 mg/dl [0.6 to 1.2 mg/dl]).

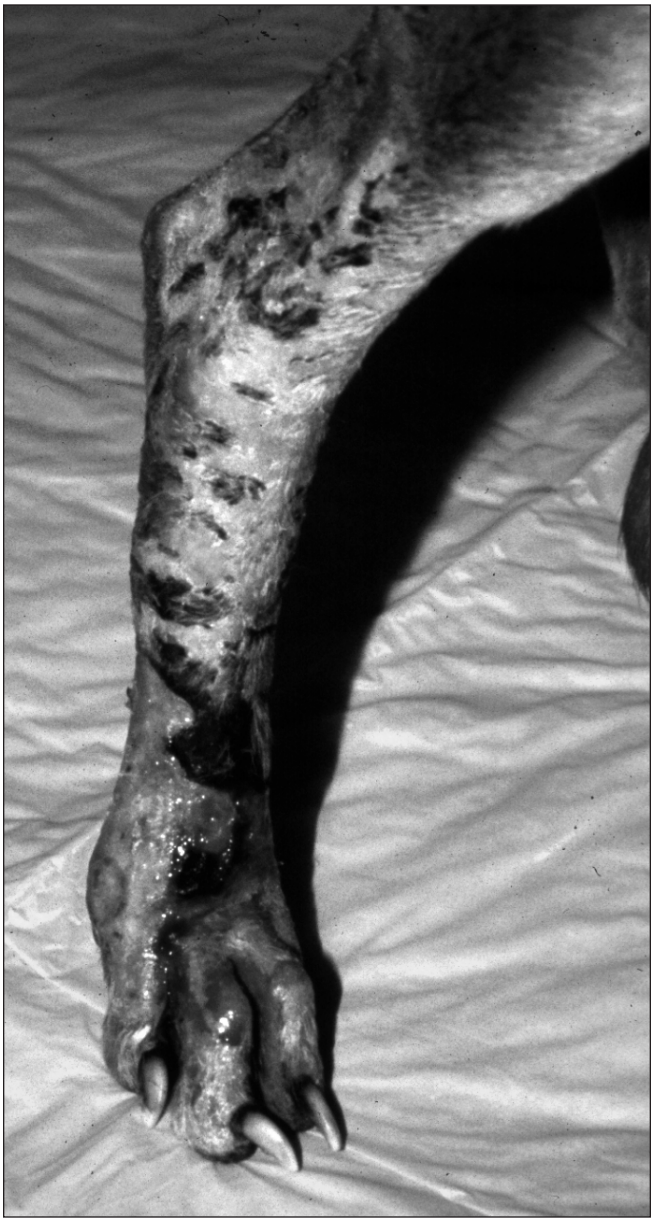

Figure 1. Right distal limb of a two-year-old female greyhound. Note the numerous small, well-demarcated ulcers.

Assess the Food and Feeding Method

All dogs in the kennel were fed a mixture of raw ground beef, dry commercial dog food and a powdered vitamin-mineral supplement. The beef was obtained from a commercial vendor in frozen packages and thawed before it was mixed with the dry food and supplement. The dogs were fed a portion of this mixture once daily.

Questions

1. What foodborne illnesses might be responsible for the clinical signs in this patient?
2. What specific diagnostic tests should be performed to investigate causes of foodborne illness in this patient?
3. What measures should be instituted to prevent outbreaks of foodborne illness in this kennel?

Answers and Discussion

1. Outbreaks of *Salmonella* enteritis ("kennel sickness," "blowout") and systemic salmonellosis are common among greyhounds in kennels. The clinical signs are usually mild to severe diarrhea that typically resolves in a few days. Occasional systemic infections occur with high morbidity rates, especially in puppies and young dogs. Racing greyhounds contract salmonellosis primarily by eating contaminated raw meat. Other foodborne bacterial diseases that result in gastrointestinal or systemic signs include campylobacteriosis, shigellosis and listeriosis.

A syndrome of cutaneous multifocal ulceration, often accompanied by limb edema or acute renal failure, has been recognized in young, adult greyhound dogs. The syndrome has been referred to as "Alabama rot" and described as idiopathic cutaneous

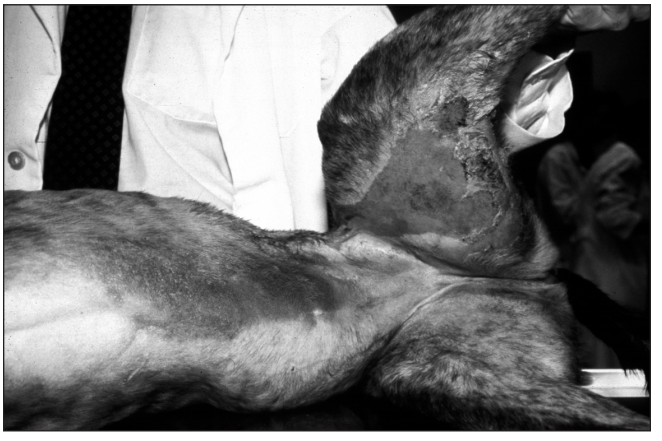

Figure 2. View of the ventral abdomen and left medial thigh of the same dog. Note the extensive contusions on the ventral abdomen and large, well-demarcated ulcer involving a large portion of the medial thigh

and renal glomerular vasculopathy. Reports of this syndrome have been limited to the greyhound breed. Clinical signs include acute erythema and edema progressing rapidly to well-demarcated cutaneous ulcers of the distal extremities, especially the hind limbs. Some dogs develop acute renal failure, which is usually fatal. Significant microscopic lesions are limited to the skin and kidney. Cutaneous lesions are characterized by vascular necrosis of arterioles, with ischemic necrosis and ulceration of the epidermis. Renal lesions are predominantly glomerular, including thrombi in glomerular capillaries and glomerular endothelial necrosis.

This syndrome in greyhound dogs resembles hemolytic uremic syndrome in people and edema disease in swine, which are thought to involve a Shiga-like toxin binding to and damaging vascular endothelium. Platelet aggregation contributes to thrombosis. Shiga-like toxins can be produced by a variety of bacteria, but *Escherichia coli* strain O157:H7 is incriminated most often. Because most racing greyhounds are fed raw meat, there is the potential for them to be exposed to Shiga-like toxin-producing *E. coli*

2. Bacterial organisms can be recovered by culturing the raw meat and commercial dry food and the patient's feces and blood. Large numbers of toxin-producing *E. coli* have been found in meat samples fed to greyhounds and in fecal samples from clinical cases.
3. The occurrence of disease related to contaminated meat is closely related to how the meat is handled on the farm or track before feeding. Preventive measures should include proper cooking and storage of meat whenever possible. Of primary importance is the temperature of the meat once it has thawed. When large blocks of frozen meat are thawed at room temperature, the outermost surface of the meat can reach unacceptably high temperatures before the center has thawed. Thawing meat slowly at refrigerator temperatures or in a camp cooler will markedly reduce surface bacterial growth.

   Many foodborne pathogens persist in the environment for extended periods. In some cases, the occurrence of food poisoning is associated with inadequate hygiene and failure to isolate dogs with diarrhea that are shedding large numbers of organisms. All facilities and equipment should be frequently cleaned with soap and then disinfected with bleach or phenolic compounds.

Progress Notes

The dog was treated with intravenous fluids, parenteral antibiotics and whirlpool baths in dilute povidone-iodine solution. Cimetidine and antiemetics were given to help control vomiting. Despite these efforts, the dog died 48 hours later of acute renal failure.

Necropsy findings included slightly pale, swollen kidneys with prominent, congested glomeruli and capsular petechiae. Mural edema of the stomach and black tarry colonic contents were also evident. Microscopic renal lesions included glomerular thrombotic microangiopathy; hyalin thrombi were present in glomerular capillaries and afferent arterioles. Glomerular capillary walls were thickened.

Bibliography

Chengappa MM, Staats J, Oberst RD, et al. Prevalence of *Salmonella* in raw meat used in diets of racing greyhounds. Journal of Veterinary Diagnostic Investigation 1993; 5: 372-377.

Cowan LA, Hertzke DM, Fenwick BW, et al. Clinical and clinicopathologic abnormalities in greyhounds with cutaneous and renal glomerular vasculopathy; 18 cases (1992-1994). Journal of the American Veterinary Medical Association 1997; 210: 789-793.

Fenwick BW, Hertzke D, Cowan LA. Alabama rot: Almost the complete story. In: Proceedings. Eleventh Annual International Canine Sports Medicine Symposium. Orlando, FL, 1995: 15-21.

Hertzke DM, Cowan LA, Schoning P, et al. Glomerular ultrastructural lesions of idiopathic cutaneous and renal glomerulopathy of greyhounds. Veterinary Pathology 1995; 32: 451-459.

CASE 11-2

Food Poisoning in Two Dogs

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Patient Assessment

A three-month-old male Australian shepherd dog was examined for severe muscle tremors, polypnea, hyperkinesias and ataxia, with intermittent opisthotonos and generalized seizures. The dog was anesthetized with sodium pentobarbital to control motor activity. Intravenous fluids were administered. After recovery from anesthesia, the dog was still atactic but less hyperkinetic.

On the same day, a one-year-old male Irish setter from the same neighborhood was admitted for treatment of muscle tremors and clonic seizures. The dog vomited 30 minutes before clinical signs were observed. It was treated in a similar manner to the first dog. Both dogs were clinically normal 12 hours later except for slight incoordination.

Assess the Food and Feeding Method

The owner of the first dog reported finding a partly eaten package of moldy cream cheese in his yard. The cream cheese had been purchased about one month earlier, had been partially used and then refrigerated until it was found covered with mold. The owner had thrown it out the previous day. Both dogs had access to the cream cheese but were not seen eating it. The cream cheese was covered with a dark blue-green fungal mat. Both dogs were of normal weight for their age and had normal body condition scores (3/5). No other nutritional history was available.

Questions

1. What potential foodborne diseases might cause the clinical signs in these dogs?
2. What diagnostic tests could be performed to confirm a foodborne illness?

Answers and Discussion

1. Members of the genera *Penicillium* and *Aspergillus* produce penitrem A and aflatoxin, respectively, two potent mycotoxins. These fungi are isolated most frequently from refrigerators and moldy foodstuffs in the home. These fungal genera also may be isolated from stored feeds and cereal grains that may eventually enter the pet food chain.

   Penitrem A causes acute muscle tremors, seizures and prostration in several animal species. The severity of clinical and pathologic features is dose dependent. Mildly affected dogs have transitory muscle tremors and ataxia lasting two to four hours, whereas larger doses may cause seizures and death. Normal neurologic function progressively returns after one or two days in animals that recover. Visceral petechiae, hepatic necrosis and hyperthermia may occur in dogs with mycotoxicosis.

   Ingestion or topical exposure to a variety of other compounds may also cause neurologic signs. Examples include various insecticides (pyrethrins, pyrethroids, organophosphates, carbamates), methylxanthines (chocolate), metaldehyde, various ornamental plants (Chinaberry, English ivy, jimson weed, tulip, yellow iris), illicit drugs (marijuana, cocaine, amphetamines), strychnine and lead.
2. The moldy cream cheese could be sent to a laboratory for identification of fungal elements and further toxicologic testing. Establishing a diagnosis of plant or illicit drug poisoning is difficult without specific evidence of ingestion. Whole blood cholinesterase activity will be depressed in organophosphate and carbamate toxicosis.

Progress Notes

Because both dogs recovered rapidly there was no need to change the foods or the feeding methods. The owners were instructed to limit access to spoiled food by proper disposal.

Examination of the moldy cream cheese by light microscopy revealed fungal elements typical of the genus *Penicillium*. The organism was later identified as *P. crustaceum*, a common contaminant of refrigerated foodstuffs. *P. crustaceum* produces large quantities of penitrem A at 4°C.

Three mice were given a moldy cheese emulsion by mouth and developed hyperkinesia, irritability, generalized muscle tremors and tonic-clonic seizures within two hours. Penitrem A was identified by thin-layer chromatography from a sample of the moldy cream cheese; therefore, this mycotoxin was considered the cause of the clinical signs in both dogs.

Bibliography

Arp LH, Richard JL. Intoxication of dogs with the mycotoxin penitrem A. Journal of the American Veterinary Medical Association 1979; 175: 565-566.

CASE 11-3

Vomiting and Diarrhea in a Puppy

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Patient Assessment

A nine-week-old male German shepherd puppy was examined for evaluation of vomiting and diarrhea. There had been no problems until six days earlier when the puppy's feces became liquid and bowel movements more frequent. The puppy vomited twice several hours after the diarrhea was first noticed. The vomitus contained undigested food, but no evidence of foreign material, blood or parasites. The dog was confined to the house or a fenced outdoor enclosure. The puppy was vaccinated a week before the clinical problems began. When examined the puppy was mildly lethargic, about 5% dehydrated, but otherwise healthy.

Assess the Food and Feeding Method

The dog was fed a commercial dry grocery brand food formulated for puppies. Fresh water and the dry food were offered free choice. The food had been purchased from a large retail outlet one week before the onset of clinical signs. The puppy was eating the dry food with no obvious problems. Three days before the onset of clinical signs, the owner began mixing the dry food with water. The moistened food remained at room temperature or outside where temperatures reached 32.2°C (90°F) for several days. The puppy became ill several hours after eating most of the moistened food.

Questions

1. What potential foodborne illnesses could be causing the clinical signs in this dog?
2. What techniques could be used to diagnose whether foodborne illness is causing the vomiting and diarrhea in this patient?

Answers and Discussion

1. A variety of foodborne illnesses can cause vomiting and diarrhea. These include contamination of food with bacterial organisms or their toxins (*Staphylococcus aureus, Salmonella* spp., *Neorickettsia* spp., *Escherichia coli, Bacillus cereus, Yersinia* spp., *Campylobacter* spp.), biogenic amines, aflatoxins, vomitoxin and heavy metals (lead, arsenic, zinc, cadmium). The fact that the dry food was moistened with water and left at high ambient temperatures makes bacterial proliferation a likely cause of clinical signs.
2. Most veterinary diagnostic laboratories can perform the tests necessary to facilitate a diagnosis of foodborne illness. It is important to determine the laboratory's preferred specimens and method of specimen preservation. Bacterial isolation techniques can often be performed on the food, vomitus and feces. Heavy metal, pesticide, biogenic amine and toxin assays can be performed on food, serum, feces and other biological samples.

Progress Notes

There was no history that the puppy had access to illicit drugs, heavy metals, pesticides, toxic ornamental plants and garbage. Results of a hemogram were normal, which made a diagnosis of viral enteritis unlikely. Three samples from the dry commercial puppy food and three from the moistened food were cultured and grown aerobically. Feces were also cultured daily over the next three days. Cultures revealed 1×10^2 colony forming units (cfu) of *Bacillus cereus*/g dry food and 1×10^7 cfu of *B. cereus*/g moistened food. These results confirmed that bacteria had proliferated after the food was moistened and left at warm to hot ambient temperatures. *B. cereus* was also cultured once from diarrheic feces. No other bacterial pathogens were recovered from the food or feces.

The puppy was treated with subcutaneous fluids and was fed a complete, balanced homemade food consisting of boiled lean ground beef and rice, offered in small, frequent meals. The puppy's feces gradually became firmer. After two days of therapy with the homemade food, the original commercial dry puppy food was offered, without added moisture. The puppy was feeling well, eating normal amounts of food and had normal stools by Day 7 after the onset of clinical signs. The pet owner was advised to not add water to dry pet foods and leave them exposed to ambient temperatures for more than a few hours.

A tentative diagnosis of *B. cereus* enterotoxemia was made. *B. cereus* is known to cause vomiting and diarrhea in people; however, it is not thought to pose a significant danger for foodborne illness in animals. *B. cereus* flourishes at room temperature, and certain isolates possess the genetic capability to produce a potent enterotoxin. The organism is a ubiquitous, spore-forming aerobic saprophyte found in soil, grains, cereal grain products and other foods. As an example, it is commonly found in uncooked rice. *B. cereus* has been found as a common isolate in samples of dry pet food. It has also been isolated from food packaging paper and materials.

The standard heat treatments used in pet food manufacturing are not likely to kill the spores of this organism. However, the num-

ber of organisms isolated from the pet food (<10^5 cells/g of food) is unlikely to cause foodborne disease in pets unless the food is exposed to moisture and heat conditions conducive to bacterial proliferation.

Bibliography

Claus D, Berkeley RCW. Genus *Bacillus*. In: Sneath PHA, Mair NS, Sharpe ME, et al, eds. Bergey's Manual of Systematic Bacteriology. Baltimore, MD: Williams and Wilkins, 1986; 1105-1139.
Drobniewski FA. *Bacillus cereus* and related species. Clinical Microbiology Reviews 1993; 6: 324-328.
Turnbull PCB, Kramer JM. *Bacillus*. In: Balows A, Hausler WJ, Herrmann KL, et al, eds. Manual of Clinical Microbiology, 5th ed. Washington, DC: American Society for Microbiology, 1991: 296-303.
Vaisanen OM, Mentu J, Salkinoja-Salnen MS. Bacteria in food packaging paper and board. Journal of Food Microbiology 1992; 71: 130-133.

CASE 11-4

Acute Renal Failure in a Yorkshire Terrier

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Patient Assessment

A 10-year-old, spayed female Yorkshire terrier was presented for evaluation of vomiting after consuming 1/2 to 3/4 cup of raisins (organic flame variety), either in the overnight hours before or in the early morning hours of the day of presentation. The dog vomited a large quantity of raisins in the late morning and also had a bout of diarrhea that contained raisins. The dog vomited foam and bile four to five more times throughout the day. Although the dog wasn't anorectic, it would vomit shortly after eating.

Physical examination revealed an alert patient with a normal body temperature, a heart rate of 140 beats/min. and a normal body condition score (3/5; body weight was 7.2 kg). The patient was minimally dehydrated (5%) and had a full, but non-painful abdomen.

Abnormalities noted on the complete blood count and serum biochemistry profile included hemoconcentration (hematocrit 58% [reference range 37 to 55%]), azotemia (urea nitrogen 49 mg/dl [reference range 8 to 30 mg/dl], creatinine 4.0 mg/dl [reference range 0.5 to 1.4 mg/dl], hyperphosphatemia (8.6 mg/dl [reference range 2.3 to 6.5 mg/dl]), hyperkalemia (6.6 mmol/l [reference range 3.8 to 5.5 mmol/l]), hypercalcemia (15.6 mg/dl [reference range 7.2 to 12.8 mg/dl]) and elevated alanine transaminase (220 U/l [reference range 13 to 79 U/l]) and alkaline phosphatase (913 U/l [reference range 12 to 122 U/l]) activities. The total protein was 6.4 g/dl (reference range 5.6 to 7.9 g/dl) and the albumin was 3.7 g/dl (reference range 3 to 4.5 g/dl). A stress leukogram was also noted. The serum was moderately hemolyzed and moderately lipemic. There was no urine in the urinary bladder.

Problems identified included azotemia with hyperkalemia, hypercalcemia, elevated liver enzymes, vomiting, historical idiopathic hyperlipidemia and unknown urine production.

Assess the Food and Feeding Method

The dog had been diagnosed with idiopathic hyperlipidemia three years earlier and was being fed a low-fat, high-fiber veterinary therapeutic food (Prescription Diet r/d Canine,[a] dry). No additional medications were necessary to control the hyperlipidemia. The dog was meal fed twice daily and fresh water was always available.

Questions

1. What is the likely cause of the azotemia?
2. What is the likely cause of the hyperkalemia and hypercalcemia?
3. What parameters need to be closely monitored?
4. What treatment options need to be considered for this patient?

Answers and Discussion

1. The historical ingestion of raisins makes acute renal failure from raisin toxicity the most likely differential diagnosis for this dog. The clinical course and laboratory abnormalities identified are characteristic of raisin toxicity. (See chapter text.) Without a urine specific gravity, however, the possibility that this dog has pre-renal azotemia cannot be dismissed. The disproportionately high

creatinine to urea nitrogen would be less supportive of prerenal azotemia. Possible differential diagnoses to consider for this constellation of clinical signs and laboratory findings could include: 1) diseases that cause hypercalcemia (neoplasia such as lymphoma, anal sac adenocarcinoma, parathyroid adenoma), however, the chronic nature of these diseases and the lack of previously recognized polydipsia/polyuria would make them seem unlikely, 2) hypoadrenocorticism, although the sodium concentration was normal and the dog had a stress leukogram, 3) acute pancreatitis, however, hypocalcemia is more common than hypercalcemia in this disorder and the dog had a non-painful abdomen when palpated and 4) vitamin D toxicity (e.g., rodenticides, dermatologic creams) would present with all of the changes seen in this dog; however, there was no historical evidence for this toxicity.

2. The hyperkalemia in this patient is caused by a combination of decreased glomerular filtration rate from the intrinsic damage to the renal tubules and dehydration. Aldosterone deficiency (i.e., hypoadrenocorticism) is unlikely given the lack of other supportive evidence for that disease.

   Hypercalcemia is a commonly recognized laboratory abnormality with raisin toxicity. The etiology is unknown. Other differential diagnoses for hypercalcemia include hypercalcemia of malignancy, primary hyperparathyroidism, granulomatous disease, vitamin D toxicosis and hypoadrenocorticism. The serum calcium concentration in this dog decreased to 13.9 mg/dl 12 hours later and to 11.3 mg/dl 36 hours later. The patient's ionized calcium, performed when the serum calcium was 13.9 mg/dl was normal.

3. The most critical parameters to monitor in this dog include urine production and serum potassium concentration. Urine production can be monitored directly with placement of a urinary catheter and closed collection bag. Indirect measures of urine production include frequent weighing of the dog and weighing of the pads in the kennel before and after urination. Placement of a central venous catheter for measurement of central venous pressure is critical if the patient becomes oliguric or anuric to prevent potentially life-threatening overhydration. In anuric and severely oliguric patients, serum potassium values can rise precipitously, resulting in cardiac arrhythmias and death. Avoiding potassium-containing fluids for rehydration is important as an initial step in an attempt to lower the serum potassium concentration. If necessary, emergency measures can be implemented including administration of calcium gluconate, sodium bicarbonate and insulin:dextrose infusions.

4. For this patient, the first steps should be rehydration and establishing whether the dog is anuric, oliguric or polyuric. If the dog is anuric, the best options include hemodialysis and peritoneal dialysis. If the dog is oliguric, furosemide, mannitol and dopamine may increase urine production. Patients in polyuric renal failure are easily managed as long as fluid losses are met with intravenous fluid replacement and electrolytes are monitored to prevent hypokalemia.

Progress Notes

On the night of admission, a catheter was placed in the cephalic vein and the dog was administered 0.9% sodium chloride at 11 ml/kg/hour. The following morning the dog was still alert; however, urine production was minimal; the patient had gained 0.45 kg (6.25%) after receiving approximately 700 ml of fluids. A serum biochemistry profile performed that morning showed that the azotemia had worsened (urea nitrogen 68 mg/dl, creatinine 5.3 mg/dl, phosphorous 9.0 mg/dl), the hypercalcemia had improved (13.4 mg/dl) and the hyperkalemia was essentially unchanged (6.5 mmol/l). A jugular catheter was placed that morning to monitor central venous pressure. The initial pressure was measured at 5 to 6 cmH_2O; however, this value increased to 10 cmH_2O approximately eight hours later. A urinary catheter was also placed that morning; no urine was produced over the next eight hours. The dog became progressively depressed over that time period. A serum chemistry profile was repeated that afternoon: the urea nitrogen was 84 mg/dl, creatinine 6.5 mg/dl, phosphorous 12.4 mg/dl and potassium was 8.6 mmol/l.

Cardiotoxicity from the hyperkalemia was now evident, as the heart rate had decreased from 120 beats/min. to 60 beats/min. The respiratory rate had increased to more than 80 breaths/min. and breathing was becoming more labored. The decision was made to place catheters for peritoneal dialysis. The dog was given butorphanol (1.4 mg IV) as a preanesthetic agent and anesthesia was induced and maintained with sevoflurane inhalation. The dog developed atrial standstill on induction and was given intravenous sodium bicarbonate (3 ml), which temporarily resolved the cardiac dysrhythmia. Three Jackson-Pratt tubes were placed through 2-cm incisions made in the right ventral abdomen, left ventral abdomen and along the ventral midline for use as peritoneal dialysis catheters. No attempt was made to remove the omentum because the dog's critical state necessitated minimal anesthesia time. Atrial standstill developed again during the procedure; the dog was administered sodium bicarbonate (3 ml IV), 50% dextrose (5 ml IV) and two doses of calcium gluconate (10% solution, 1.5 ml IV).

Peritoneal dialysis was initiated immediately after the dog recovered from anesthesia. A dialysate was made by placing 25 ml of 50% dextrose in 500 ml of lactated Ringer's solution. A total of 125 ml of dialysate was infused into the abdomen every hour for 15 exchanges and allowed to remain for 40 minutes, after which it was allowed to drain for 20 minutes. The amount of dialysate was then increased to 210 ml and was allowed a dwell time of 100 minutes. This process was repeated for the next four days, at which time the dwell time was increased to six hours and the volume of dialysate was left at 210 ml.

A constant infusion rate of furosemide (0.1 mg/kg/hour) was started at the time of dialysis to stimulate urine production; however, the dog remained markedly oliguric (<1 ml/kg/hour) for the following three days. Urine production began to increase from Days 4 through 6, although the dog was still considered oliguric (2 to 3 ml/kg/hour). On Day 7, the dog became markedly polyuric, with hourly urine production of approximately 10 ml/kg/hour.

The dog was hospitalized for 20 days. Additional therapies administered included famotidine (0.5 mg/kg IV q12hours) to minimize gastric hyperacidity, cefazolin (22 mg/kg IV q8hours) for prophylaxis to prevent infection from the peritoneal dialysis catheters and total parenteral nutrition, which was administered for seven days, at which time the dog began to eat on its own. A biochemistry profile performed at the time of discharge revealed these values: urea nitrogen 52 mg/dl, creatinine 3.0 mg/dl and phosphorous 11.5 mg/dl.

Because of the previously diagnosed idiopathic hyperlipidemia, a diet change was not initiated in this dog. A chitin-based phosphate binder (Epakitin[b]) was added to the food to control hyperphosphatemia. The higher protein content of the food (vs. foods formulated for renal failure) necessitated three to four times the standard dose of phosphate binder to control hyperphosphatemia. There was also a concern that the increased protein in the food would increase intraglomerular pressure; therefore, the dog was given enalapril (0.25 mg/kg PO q24hours). At four months from discharge, the dog had a stable creatinine at 3.7 mg/dl, phosphorous of 6.0 mg/dl and was reported to be active and eating well.

Endnotes

a. Hill's Pet Nutrition, Inc., Topeka, KS, USA.
b. Vetoquinol, Buena, NJ, USA.

CASE 11-5

Acute Vomiting in a German Shepherd Dog

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Patient Assessment

A nine-year-old, neutered male, German shepherd dog was examined for a three-day history of occasional vomiting and progressive lethargy. The dog was uninterested in food for the past few days and was drinking excessively. Before the onset of these signs, the dog had been healthy and no medications had been administered.

Physical examination revealed a 46-kg dog with a normal body condition score (5/9 [BCS]). Vital signs were within normal limits. The dog was lethargic, but responsive and able to walk around the exam room. The abdomen was not painful and abdominal palpation was normal. The mucous membranes were tacky and faintly icteric, as were the sclera. Thoracic auscultation was normal.

Diagnostic evaluation included a complete blood count, which showed hemoconcentration (hematocrit = 55%), and a serum biochemistry panel, which revealed hyperbilirubinemia and increased liver enzyme activities (**Table 1**). A coagulogram showed that the prothrombin time (PT) and activated partial thromboplastin time (aPTT) were prolonged (**Table 1**). Results of a urinalysis were normal except for bilirubinuria.

Abdominal radiography showed no significant abnormalities. An abdominal ultrasound found the gallbladder to be full, but showed no dilatation of the bile ducts. The liver appeared structurally normal although a small amount of fluid was noted between the liver lobes that could not be sampled due to its location. Because of the prolonged clotting times and concern of bleeding, no liver biopsy or aspirates were taken. The tentative diagnosis was an acute hepatic insult of unknown cause.

Assess the Food and Feeding Method

The dog had been eating the same brand of dry dog food for several years. The exact daily caloric intake was unknown because the dog was fed free choice. Upon further questioning, the owner admitted the dog had been eating a food that was identified as being contaminated with aflatoxin. Based on national recall information, a primary rule out of aflatoxin toxicosis was established.

Questions

1. What method of delivering nutrition to this patient is most appropriate during its hospitalization?
2. How can a diagnosis of aflatoxicosis be confirmed?
3. Is there a specific antidote for this toxin?

Answers and Discussion

1. For patients that are not vomiting, enteral feeding is the method of choice because it increases mucosal blood flow, preserves enterocyte function and decreases bacterial translocation from the intestinal tract. This dog was vomiting; therefore, enteral feeding would likely worsen its nausea. Additionally, placement of a feeding tube (nasoesophageal tube, esophagostomy tube, gastrostomy tube, etc.) carries the risk of hemorrhage because the patient was found to be hypocoagulable. Administration of parenteral nutrition (PN) is the most appropriate method of providing nutrition to this patient.
2. A sample of the contaminated food can be submitted to a diagnostic lab for analysis. Alternatively, a fresh or frozen sample of hepatic tissue may be used to identify the presence of aflatoxin by thin-layer chromatography or high-performance liquid chromatography; however, the toxin may be eliminated from the body in 24 hours; therefore, these tests are often negative. Formalin preserved liver tissue can be submitted for histologic evaluation because the histologic changes (diffuse lipidosis and hepatocellular necrosis) are fairly unique to this toxin in dogs.
3. There is no antidote for aflatoxin toxicosis. Aggressive treatment to support the liver and treat signs of liver failure are recommended.

Progress Notes

The dog was treated in two hospitals for five days. Although the specific treatments at both hospitals differed slightly, the goals were the same: 1) intravenous fluid support, 2) replacement of clotting factors with fresh frozen plasma and supplementation with vitamin K_1, 3) use of gastroprotectants to minimize gastrointestinal ulceration (omeprazole, famotidine), 4) antiemetic therapy (metoclopramide, dolasetron), 5) nutritional support, 6) antioxidants and antioxidant precursors to minimize damage to the liver (N-acetylcysteine, Denosyl,[a] vitamins E and C) and 7) prophylactic antibiotics (ampicillin) to minimize the chance of infection due to intestinal bacterial translocation and incompetent hepatic immune function.

Occasional hematemesis occurred during the first two days of hospitalization. Although the patient was offered several different types of dog food, it refused to eat. Therefore, it was occasionally syringe fed 100 ml of a highly palatable, homogenized veterinary therapeutic food (Prescription Diet a/d Canine/Feline [b]). Although this food is relatively calorie dense (1.4 kcal/ml), the dog's resting energy requirement (RER) was much higher (70 x (46 kg)$^{0.75}$ = RER = 1,236 kcal/day). Furthermore, the dog's vomiting made enteral feeding impractical.

On the third day of hospitalization, PN was started through a peripheral catheter. A central line was not used due to concerns about hemorrhage. The PN was formulated to contain a minimum of amino acids (1.0 g/100 kcal), due to the liver's inability to process ammonia derived from deamination of amino acids.

In several separate infusions, the dog received 1,170 ml of fresh frozen plasma (24 ml/kg) to replace clotting factors. This treatment improved the dog's clotting times. Nonetheless, the patient's clinical condition deteriorated; the dog became weaker, vomited more often and began to have bloody diarrhea. Hepatic encephalopathy was suspected on the fifth day of hospitalization. Within two hours the patient underwent cardiac arrest and died.

Table 1. Biochemistry and clotting values for a nine-year-old German shepherd dog.

Test	Day 1	Day 5	Reference values
ALP (IU/l)	124	221	71-120
AST (IU/l)	ND	502	13-50
ALT (IU/l)	194	885	21-97
Bilirubin (mg/dl)	8.2	23.2	0.1-0.3
Albumin (g/dl)	2.7	2.2	3.1-4.2
PT (seconds)	70	24.5	7.3-11.8
aPTT (seconds)	>100	28.4	10.6-14.8

Key: ALP = alkaline phosphatase, AST = aspartate aminotransferase, ND = not done, ALT = alanine aminotransferase, PT = prothrombin time, aPTT = activated partial thromboplastin time.

Endnotes

a. Nutramax Laboratories, Inc., Edgewood, MD, USA.
b. Hill's Pet Nutrition Inc., Topeka, KS, USA.

Bibliography

Hooser SB, Talcott PA. In: Peterson ME, Talcott PA, eds. Small Animal Toxicology, 2nd ed. St. Louis, MO: Elsevier Inc, 2006; 889-892.

Marik PE, Zaloga GP. Early enteral nutrition in acutely ill patients: A systematic review. Critical Care Medicine 2001; 29: 2264-2270.

Proulx J. Nutrition in critically ill animals. In: Raffe MR, Wingfield WE, eds. The Veterinary ICU Book, 1st ed. Jackson, WY: Teton NewMedia, 2002; 202-217.

CASE 11-6

Azotemia in a Cat

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Patient Assessment

A 10-year-old, castrated male domestic shorthair cat was enrolled in a cohort of blood donor cats. Initial diagnostics at enrollment included testing for feline leukemia virus, feline immunodeficiency virus, heartworm, toxoplasmosis, haemobartonellosis, bartonellosis and ehrlichiosis. Prior medical history included mild periodontal disease, constipation that resolved with lactulose treatment and, recently, forelimb lameness.

The patient was fed a high-protein therapeutic food for more than a year. When the food was listed as a product recalled due to contaminated wheat gluten, the cat was examined for possible adverse effects. Physical examination findings were within normal limits, although the cat was less active than usual. Results from a serum biochemistry profile indicated that the patient was azotemic, with blood urea nitrogen (BUN) and creatinine values of 66 mg/dl and 3.3 mg/dl, respectively. Urine collected by cystocentesis had a specific gravity of 1.018, with many crystals, originally thought to be ammonium urate (**Figure 1**). An abdominal ultrasound was performed; pathologic changes included hydronephrosis of the left kidney, bilateral nephrocalcinosis, fluid surrounding the left kidney and a large amount of gravity-dependent sediment in the urinary bladder. A peripheral intravenous catheter was placed and fluid therapy was initiated. Therapy included intravenous fluids, a histamine receptor antagonist (famotidine[a]) and lactulose.

The patient was transitioned to a therapeutic food targeted for management of renal disease (Prescription Diet k/d Feline[b]). Despite therapy, lethargy, anorexia and the degree of azotemia continued to progress for several days (**Figures 2** and **3**). A central intravenous catheter was placed for delivery of fluids and measurement of central venous pressure. Urine output was monitored by routinely weighing litter box contents. Urine volume was large and dilute; therefore, the patient was classified as polyuric. Following four days of fluid and drug therapy, BUN and creatinine values decreased markedly. Renal panels were repeated daily; the azotemia continued to improve over the following five days. After 10 days of treatment for acute renal failure (ARF), the cat was transitioned to subcutaneous fluids, therapy with famotidine was discontinued; however, the renal therapeutic food was continued. After the acute crisis, azotemia resolved in three weeks.

Assess the Food and Feeding Method

When enrolled in the blood donor program, the cat was fed an adult feline maintenance food. Approximately one year before the pet food recall, the patient and its cohorts were transitioned to a high-protein, low-carbohydrate food (Prescription Diet m/d Feline[b]). Food was administered in measured amounts by kennel staff twice daily. As mentioned above, the cat was fed Prescription Diet k/d Feline when it was affected with ARF.

Questions

1. Could ARF be related to contamination of pet food with a toxic agent?
2. How can ARF be differentiated from chronic renal failure?
3. What treatment plan(s) should be considered for suspected cases of ARF?
4. What are some risks following successful treatment of ARF?

Answers and Discussion

1. In March 2007, a massive recall of pet food was instituted following reports of renal failure in animals following a palatability trial. Over several weeks, many contaminants were considered. Melamine was isolated from pet food ingredients, pet food and renal and urine samples from affected patients. In vitro studies demonstrated that melamine, when combined with a similar moiety (i.e., cyanuric acid), would form crystals in cat or dog urine. ARF was thought to result from severe crystalluria, similar to ARF in ethylene glycol cases.

   In December 2005, a pet food manufacturing company issued a similar recall because aflatoxin was identified as the cause of severe hepatic necrosis and cirrhosis in dogs. Ten years earlier, in 1995, pet food was recalled for excessive levels of vomitoxin in pet food.

   Product contamination should be considered in unexplained acute disease, particularly if the incidence of that disease process increases dramatically and other causes have been ruled out. Reputable pet food manufacturers conduct multiple tests on raw ingredients and finished products and can provide immediate information about calls involving products to their toll-free numbers. When the pet food recall was instituted, renal failure caused by melamine ingestion was undocumented, and the agent was considered relatively nontoxic. In cases of unexplained acute illness, exposures to toxins, whether environmental or in pet food

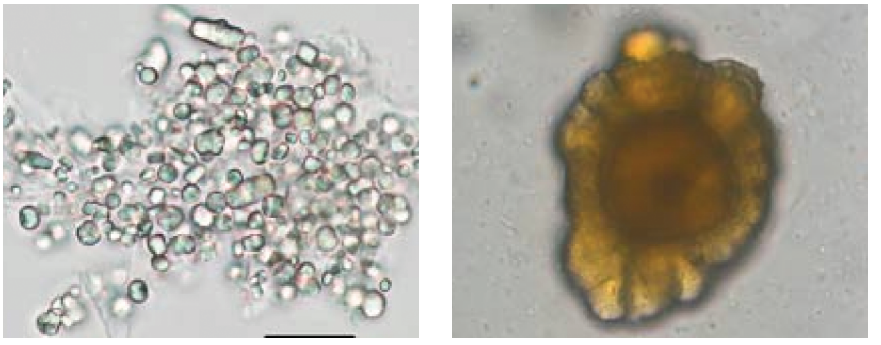

Figure 1. Melamine/cyanuric crystals produced in vitro (left). Crystal from the urine of an affected cat (Magnification 1,000x) (right).

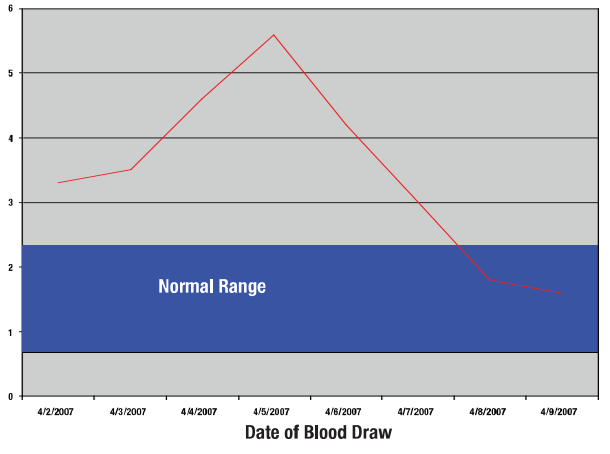

Figure 2. Creatinine changes during ARF.

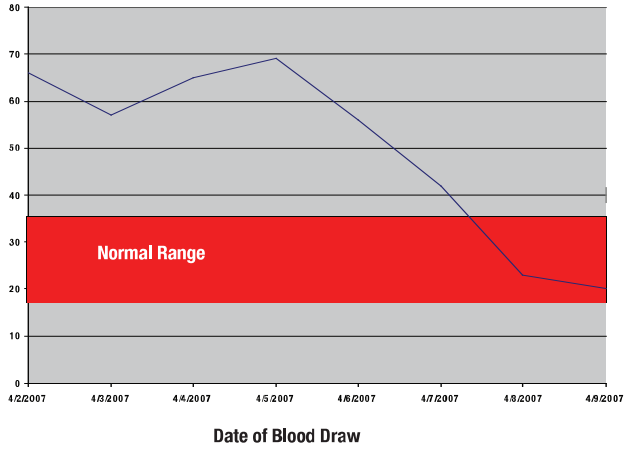

Figure 3. BUN changes during ARF.

should be documented.

2. The most obvious differences between acute and chronic renal failure are the speed of onset and duration of signs. In ARF, signs appear rapidly with illness usually lasting less than one week. ARF patients are oliguric or anuric, whereas animals with chronic renal failure are usually polyuric. However, normal or increased urine production should not be used to rule out ARF. In cases of acute uremia, mucous membranes remain pink, as opposed to pale mucous membranes and anemia often noted in chronic renal failure. Mineral and electrolyte imbalances may also be more apparent in cases of ARF, and may include hypocalcemia and hyperphosphatemia. Patients with chronic renal disease also show outward signs of chronic disease including poor body condition and coat, whereas patients with ARF generally present with good body condition and a normal coat.
3. Management of ARF is multifactorial. Immediate actions should include removing the inciting source, in this case, discontinuing use of the contaminated food. Fluid therapy should be instituted to correct extracellular fluid imbalances and deficits. After replacement fluids have been administered and adequate hydration achieved, fluid therapy should continue with respect to maintenance and continued fluid loss. Diuresis is the optimal method of preventing medullary tubule blockage by crystals. To prevent further acid-base derangements, gastric protectants should be administered, and continued for two to three weeks, until uremic gastritis has been effectively controlled. Caloric intake should be carefully monitored. Uremia and metabolic acidosis can induce protein catabolism, which is compounded by anorexia and vomiting. Patients should be routinely weighed to evaluate weight loss, although this measure can be confounded by changes in hydration status and lean body mass. A low-protein, low-phosphorus food is typically recommended for uremic patients. The protein should be highly digestible, and the food should have increased amounts of fat to increase caloric density. Whenever possible, enteral feeding methods should be employed to promote gastrointestinal health.
4. Risks associated with acute uremia include derangements of fluid balance, electrolyte imbalances and cardiovascular and pulmonary complications. If morphologic changes are not treated and reversed during the recovery phase, acute uremia can progress to chronic renal failure. Overaggressive fluid therapy can potentially result in volume overload, leading to hypertension and pulmonary edema. Care should be taken to continually assess the hydration status of the patient.

Progress Notes

The patient was assessed and diagnostic studies were conducted to detect ARF before the onset of clinical signs. Due to aggressive treatment, the patient recovered fully within three weeks. The patient was discharged from the blood donor program and given to a private owner. At the time of discharge, the cat's BUN and creatinine concentrations had decreased to normal limits, and no signs of renal disease were present. The cat was bright, alert and responsive and fully recovered. Recommendations were made to contin-

ue feeding the therapeutic kidney food, due to the patient's increased risk for developing chronic renal disease at a later date. Lactulose treatment was continued, and considered unrelated to the ARF episode.

Acknowledgement

The author thanks Dr. Amy Tamulevicus of the Veterinary Teaching Hospital, Kansas State University, Manhattan, for providing clinical information about this patient.

Endnotes

a. Pepcid. Merck & Co., West Point, Pennsylvania, USA.
b. Hill's Pet Nutrition, Inc., Topeka, KS, USA.

Bibliography

Cowgill LD, Francey T. Acute uremia. In: Ettinger SJ, Feldman EC. Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat, 6th ed. St. Louis, MO: Elsevier Saunders, 2005; 1731-1751.

Grauer G. Early detection of renal damage and disease in dogs and cats. Veterinary Clinics of North America: Small Animal Practice 2005; 35: 581-596.

Interim melamine and analogues safety/risk assessment. U.S. Food and Drug Administration Center for Food Safety and Applied Nutrition. www.cfsan.fda.gov/~dms/melamra.html.

Lees G. Early diagnosis of renal disease and renal failure. Veterinary Clinics of North America: Small Animal Practice 2004; 34: 867-885.