BACTERIAL-ASSOCIATED DIARRHOEA IN DOGS AND CATS
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Infectious diarrhoea in dogs and cats is one of the most common maladies facing small animal veterinarians today, but the role of enteropathogenic bacteria is poorly understood. *Clostridium perfringens*, *C. difficile*, *Campylobacter* spp., and *Salmonella* spp. are four of the most commonly incriminated enteropathogenic bacteria in canine and feline diarrhoea; however, the clinical documentation of these bacteria in dogs and cats is clouded by their presence as normal constituents of the indigenous intestinal microflora in many animals. The indications for performing faecal enteric panels on diarrhoeic dogs and cats are poorly defined, resulting in indiscriminate testing, and misinterpretation of results.

**Clostridium Perfringens**

*Clostridium perfringens* is an anaerobic, spore-forming, gram-positive bacillus that has been associated with outbreaks of acute, often severe diarrhoea in humans, horses, dogs, and cats. The elaboration of four major toxins (α, β, ι, and ε) is the basis for typing the organism into five toxigenic phenotypes, A-E. Each type may also express a subset of at least 10 other established toxins, including *C. perfringens* enterotoxin (CPE), a well-characterized virulence factor whose production is co-regulated with sporulation. A recently published study evaluating 843 *C. perfringens* isolates collected from 103 dogs revealed that all isolates tested were type A, with 15% harboring the enterotoxin gene. The role of CPE in the development of diarrhoea is clouded because CPE is detected in up to 34% of diarrhoeic dogs, and in 5 to 14% of nondiarrhoeic dogs.

**Diagnosis**

There is currently no gold standard for the diagnosis of canine *C. perfringens*-associated diarrhoea. The optimal diagnostic approach utilizes a combination of faecal CPE immunodetection and PCR for detection of the enterotoxin gene (*cpe*).

**Clinical Signs**

There are no pathognomonic clinical sign indicative of *C. perfringens*-associated diarrhoea in the dog, and the spectrum of disease attributed to this organism varies greatly, and can involve both the small and large intestine. *C. perfringens*-associated diarrhoea can also cause an acute hemorrhagic diarrhoea in dogs.

**Culture**

Because *C. perfringens* is a normal commensal of the intestinal microflora, the mere culture of an isolate from the stool is of little clinical significance. In addition, isolation rates for *C. perfringens* are similar in diarrhoeic and nondiarrhoeic dogs.
Faecal Endospores
Several studies have reported no association between faecal endospore counts and the presence of diarrhoea, or between spore counts and the detection of CPE in faecal specimens. The diagnostic value of finding increased endospores in a faecal smear from a diarrhoeic dog is virtually zero.

Faecal Enterotoxin Immunodetection
Detection of CPE via ELISA in faecal specimens is the most widely used diagnostic tool for C. perfringens in humans and animals; however, the performance characteristics of this human-based assay have not been validated in dogs or cats.

Molecular Techniques
PCR performed on faecal specimens or isolates collected via culture is of diagnostic value. A recently published study showed that nondiarrhoeic dogs were far less likely to be positive for both CPE and the enterotoxin gene (cpe) (4%), compared to diarrhoeic dogs (28%).

Therapy
Optimal antibiotics for the treatment of canine C. perfringens-associated diarrhoea include ampicillin, metronidazole, and tylosin. Recent evidence has shown a high rate (21%) of in vitro resistance to tetracycline, and its routine use in dogs should be discouraged.

Clostridium Difficile

Clostridium difficile is a gram-positive, anaerobic spore-forming bacillus, and is the major cause of antibiotic-associated pseudomembranous colitis in human patients. Clostridium difficile-associated diarrhoea is less common in cats, and a recent study by the author documented an incidence of 5% in diarrhoeic cats. To date, three toxins produced by C. difficile have been described: toxin A (an enterotoxin), toxin B (a cytotoxin), and CDT (an ADP-riboseyltransferase). There are increasing reports of variant strains isolated from human, canine, and equine clinical cases of C. difficile-associated disease (CDAD) that produce only toxin A or toxin B. Antibiotic administration, especially in hospital environments, is the most commonly reported predisposing factor for the development of CDAD in people. In contrast, administration of antibiotics does not appear to predispose dogs to CDAD.

Diagnosis

Clinical signs
Clinical signs that have been associated with canine C. difficile infection range from asymptomatic carriage to a potentially fatal acute haemorrhagic diarrhoeal syndrome. There does not appear to be a specific anatomic intestinal localization of clinical signs.

Culture
Isolation of *C. difficile* from diarrhoeic specimens is of little diagnostic value, as isolation rates are similar between nondiarrhoeic and diarrhoeic dogs (0 to 40%); however, a negative culture result in a diarrhoeic animal virtually excludes *C. difficile* as a causative enteropathogen.

**Faecal toxin detection**

The current gold standard assay is the cell culture cytotoxicity assay, which detects toxin B activity; however, this assay is expensive and requires up to 48 hours for conformation of a negative result. Routine diagnosis of *C. difficile*-associated diarrhoea has been made based on positive faecal ELISA assays for toxins A or B; however, the performance characteristics of the human-based immunoassays is unacceptably low in dogs.

**Molecular Techniques**

The detection rates of toxigenic *C. difficile* strains following culture is similar in diarrhoeic and nondiarrhoeic dogs reducing the diagnostic value of PCR studies.

**Therapy**

Metronidazole is the drug of choice for dogs with suspected *C. difficile*-associated diarrhoea. The second drug of choice is vancomycin; however, it is used only in cases of nonresponsive CDAD or when metronidazole-resistant strains have been demonstrated.

**Campylobacter SPP.**

*Campylobacter* spp. are small (0.2 to 0.5 μm x 0.5 to 5 μm), microaerophilic, gram-negative, curved rod-shaped bacteria. *Campylobacter* species that have been implicated in canine enteric disease include *C. jejuni*, *C. coli*, *C. helveticus*, and *C. upsaliensis*. Faecal shedding of *C. jejuni* is significantly greater in dogs < 6 months old and during the summer and autumn. The higher prevalence of infection in pups versus adult dogs may reflect increased exposure of young animals to faecal excrement and confinement to a limited space. In addition, the unexposed immune system of the pups may increase the susceptibility to intestinal colonization by *C. jejuni*. Several authors have concluded that Campylobacters are not a primary pathogen in dogs because of similar isolation rates between nondiarrhoeic (0 to 49%) and diarrhoeic animals (0 to 74%). *Campylobacter jejuni* secretes a cytotoxin which destroys the mucosal epithelium, and a heat-labile-like toxin which is thought to deregulate the adenyl cyclase system, similar to that described for *E. coli*.

**Diagnosis**

**Clinical signs**

Clinical signs include mucus-laden or watery diarrhoea, with or without blood and leukocytes, partial anorexia, occasional vomiting, and slight fever of 3 to 7 days duration.

**Stained faecal smears**
Campylobacter-like organisms (CLO’s) can be identified by examining stained smears (Gram stain or Romanovsky-type stain) of fresh feces from the patient. The organism’s characteristic morphology (slender, curved rods with an “S” shape or sea gull-shaped appearance) allows it to be identified relatively easily. The major limitation of direct examinations is that the procedure fails to differentiate between Campylobacter spp., and the mere identification of CLO’s is not sufficient to warrant a diagnosis of Campylobacter-associated diarrhoea, as many healthy dogs and cats can harbor CLO’s in their intestinal tract.

Faecal culture
For optimal recovery of Campylobacter spp., feces or faecal swabs should be fresh or placed immediately into anaerobic transport medium before refrigeration at 4 C. For isolation, the use of a formulated selective medium containing antimicrobial agents (e.g., Campy-CVA containing cefoperazone, vancomycin, and amphotericin B) gives better recovery than other direct-plating selective media. Microaerophilic incubation conditions should be maintained, and the plates should be incubated at 37 C or at 42 C. Biochemical tests complimented with multiplex PCR assays are used to speciate Campylobacter-like organisms isolated.

Therapy
Although diarrhoea produced by Campylobacter organisms is usually self-limiting, the zoonotic potential of the organism often necessitates medical therapy. The drugs of choice are the macrolides (erythromycin at 10 to 15 mg/kg TID) or quinolones (enrofloxacin at 5 mg/kg BID), although the macrolides are preferred due to the high rate of mutational resistance the campylobacters have to the quinolones. The duration of excretion in infected dogs and cats can be as long as 4 months and restriction of high risk contact should be implemented with appropriate hand hygiene.

Salmonella SPP.
Salmonellae are primarily motile, non-spore-forming, gram negative aerobic bacilli. Salmonella spp. are one of the most common causes of human food-borne disease, with an estimated 1.4 million cases occurring annually in the United States. Clinical salmonellosis in dogs and cats is rare, although prevalences are higher in puppies and kennel populations. Isolation of Salmonella spp. from adult dogs and cats ranges from 0 to 2% in non-diarrhoeic animals, and from 0 to 1% in diarrhoeic animals. The prevalence of Salmonella is much higher among dogs fed raw food diets. Faecal shedding of Salmonella in naturally occurring infections can continue for a period of at least 6 weeks, but may persist for longer due to the harboring of the organism in the lymph nodes.

Diagnosis
The traditional diagnosis of salmonellosis is made based on isolation of the organism in conjunction with clinical signs and assessment of potential risk factors such as hospitalization, age, environmental exposure, and antibiotic administration. However, isolation of Salmonella is not necessarily indicative
of involvement in disease, as similar isolation rates can be detected in healthy non-diarrhoeic animals. Haematological abnormalities are variable, and include a non-regenerative anemia, lymphopaenia, thrombocytopenia, and neutropaenia with a left shift.

Clinical signs
Signs of clinical salmonellosis in dogs include fever, anorexia, diarrhoea (which may be bloody), vomiting, weight loss, nasal discharge, pelvic limb paresis, and abortion. Most salmonella-infected dogs and cats are asymptomatic, although some animals may manifest clinical signs of systemic sepsis.

Faecal culture
There are a number of different protocols for the isolation of *Salmonella* spp. Fresh faecal specimens are typically placed onto one or more selective media, including MacConkey agar, XLD agar, and brilliant green agar. For enrichment, selenite F, tetrathionate, or gram negative broth (GN) is recommended.

Therapy
The treatment of Salmonella in diarrhoeic dogs and cats is a controversial topic, with many microbiologists and infectious disease specialists arguing that antibiotics are not advocated for treating animals with uncomplicated *Salmonella* gastroenteritis. Instead, antibiotics should be reserved for animals with concurrent signs of systemic infection or a history of immunosuppression. Faecal shedding can be prolonged with the injudicious administration of antibiotics, and infecting organisms may acquire transferable (plasmid-mediated) resistance. For septic dogs and cats, antibiotics reported to be effective against *Salmonella* include fluoroquinolones, chloramphenicol, trimethoprim-sulfonamide, and amoxicillin. Determination of a susceptibility profile is recommended for selection of optimal antimicrobials.

Public Health Considerations
*Salmonella* spp., *Campylobacter* spp., and *C. difficile* have zoonotic implications, and the importance of documenting infections in diarrhoeic dogs and cats allows one to minimize risk of transmission to people by implementing appropriate strategies in the household. These strategies include the restriction of high risk contact, the prompt cleaning and disinfection of “accidents” in the house, and the rigorous practice of hand hygiene. Infected animals should not be walked in public places for at least one month beyond the clinical resolution of diarrhoea.

References