

# Infective endocarditis in the companion animal

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Infective endocarditis (IE) is an infection of the endocardial structures which can include both the cardiac valves and mural endocardium. IE is uncommon in dogs and rare in cats with estimated prevalence of 0.05-6.6% and 0.007% respectively.<sup>8,19,23</sup> Over-represented breeds noted in canine cases of IE include German Shepherds, Boxers, Golden Retrievers and Labrador Retrievers with males more commonly identified with IE than females.<sup>8,27</sup> In a recent retrospective evaluating cats, no breed or sex predilection was identified.<sup>23</sup> In both species, the mitral and aortic valves are the most commonly affected with rare reports of IE in the tricuspid and pulmonary valves.<sup>2,7,16,20,3,26</sup>

The microorganisms (MO) most commonly cultured include coagulase positive *Staphylococcus*, *Streptococcus*, *Escherichia coli*, *Bartonella*, *Pseudomonas*, *Corynebacterium* and *Erysipelothrix*.<sup>2,7,19,22,26,27</sup> Mitral-valve involvement and polyarthritis were more frequent in dogs with streptococcal endocarditis.<sup>27</sup>

In a retrospective of IE in felines, *Bartonella* was confirmed in four out of five cats tested. Three cats underwent post mortems and *Bartonella* polymerase chain reaction (PCR) was performed on the cardiac tissue, it was negative in all three cats.<sup>23</sup>

## PATHOGENESIS

The pathogenesis of IE is likely multifactorial with many factors involved including immune system function and the integrity of the cardiac valves.<sup>12</sup> It is believed that a healthy vascular endothelium is resistant to bacterial infection.<sup>12</sup> Prior to colonisation to the valves, sterile and thrombotic vegetations must first develop. The vegetation is made up of platelets, fibrin, mononuclear and polymorphonuclear cells, lymphocytes and red blood cells.<sup>12,20</sup> It is on these vegetations that circulating MO can adhere to forming a nidus of infection.

Fibronectin, which is produced by endothelial cells in response to an injury, is likely involved also as many of the causative bacteria carry ligands for this substance.<sup>20,21</sup> The presence of fibrin can encase the bacteria which makes subsequent antimicrobial treatment ineffective.<sup>12</sup> The final process involves multiplication of the MO within the vegetation.

Predisposing valvular conditions known in people include congenital cardiac disease (eg. patent ductus arteriosus, ventricular septal defects) and mitral valve prolapse.<sup>8,12</sup> Sykes et al also found that 11% of dogs with IE evaluated had underlying congenital cardiac disease including subaortic stenosis, pulmonic stenosis or Tetralogy of Fallot.

Typically, the infection is manifested via several different processes. If the MO are released haematogenously, bacteraemia will ensue with the secondary symptoms of sepsis. Other possibilities include: local invasion of the infected valve leaflet leading to dysfunction of the valve; peripheral emboli and secondary septic infarcts; and finally the formation of circulating immune complexes, which can lead to a host of secondary disease processes including arthritis and glomerulonephritis in people.<sup>4,5,9,16</sup>

## COMMON PRESENTATION

One of the difficulties, of rapidly identifying animals with IE, is due to the many ways the disease can present. Typically, they experience vague symptoms of general malaise including depression, weakness, lethargy, anorexia and intermittent lameness. In those who have significant cardiac dysfunction, symptoms of cardiac disease, including dyspnoea and coughing, may be noted.<sup>7,8,27</sup> The presence of a new, previously undiagnosed heart murmur is also believed to be common in these dogs and was found in over 41% of dogs in one cohort.<sup>8</sup> Since the aortic valve is commonly affected in dogs, a diastolic murmur maybe noted. Cats presented with similar symptoms as dogs although a left-sided murmur was more common.<sup>23</sup> In one retrospective, fevers were noted in 38% of dogs.<sup>27</sup> Neurological abnormalities are also common in dogs.<sup>27,9</sup>

## DIAGNOSIS

### ECHOCARDIOGRAPHY, ELECTROCARDIOGRAPHY AND RADIOGRAPHS

Transthoracic echocardiography (TTE) is the most common method of diagnosis. Sensitivity for TTE to detect IE is considered to be over 90% in veterinary medicine.<sup>16</sup> False positives are also possible as the degenerative valvular lesions from endocardiosis can be mistaken for vegetations. Typically, vegetations appear more isolated and echodense when compared to myxomatous lesions. TTE performed in cats revealed lesions on the aortic and mitral valves consistent with IE in eight and five cats respectively.<sup>23</sup> An electrocardiogram (ECG) is an important part of the diagnostic work up for these patients as arrhythmias can occur in a large percentage of these patients with ventricular arrhythmias were most common in one retrospective of canine patients.<sup>17,26,27</sup>

Thoracic radiographs can be helpful to identify secondary congestive heart failure (CHF) and pulmonary oedema but are not specific for IE. Signs of CHF were noted in 9/16 cats on thoracic radiographs.<sup>23</sup>



**CULTURES**

Identification of possible sources of infection is recommended and typically involves cultures (urine, blood, joint effusion). To be performed correctly, blood cultures require sterile collection of three to four blood samples of 5-10ml of blood from different venepuncture sites which may not be feasible in cats and small dogs. Since the actual concentration of bacteria in the blood is low, large volumes of blood are needed to increase sensitivity. Blood-culture negative endocarditis is estimated to occur in 70% of dogs with IE.<sup>17, 26</sup>

**BLOOD WORK**

Common clinicopathologic findings in dogs with IE include anaemia, azotaemia, leucocytosis and thrombocytopenia.<sup>27</sup> As in dogs, hypoalbuminemia and azotaemia were also noted in cats.<sup>23</sup>

**DUKE CRITERIA**

The Duke criteria (DC) were proposed by the Duke University Endocarditis service and has been validated in several studies in human patients with a sensitivity of greater than 80% for detecting IE.<sup>11,14</sup> Although there is limited information in veterinary medicine regarding the use of DC in our patients, modifications to the criteria have been proposed in dogs, see Table 1.<sup>23,27</sup> While the DC do not have 100% sensitivity and specificity for identifying IE, they are useful in guiding clinicians in these difficult cases.

Major criteria	Minor criteria
Identification of a typical organisms (eg. <i>Streptococci</i> , <i>Staphylococci</i> , or <i>E coli</i> )	Predisposing heart condition (ie. SAS)
>2 positive cultures of MO consistent with IE or >3 positive cultures of common skin contaminants	New or worsening heart murmur
	Fever (rectal temperature >103°F/39.4°C)
Positive findings for IE on echocardiogram	Detection of vascular or embolic phenomenon
	Immunologic phenomena: non-degenerate neutrophilic polyarthritis, glomerulonephritis, or immune-mediated haemolytic anaemia
	Microbiologic phenomena: positive MCB not meeting major criteria, serologic evidence of infection with atypical organism or detection of a typical organism by use of PCR technology

**Table 1: Modified DC for diagnosis of IE in dogs by Sykes et al.**

**TREATMENT**

Treatment of IE includes both antimicrobial therapy and management of cardiac dysfunction and/or congestive heart failure. Usually culture results are not available when antibiotics being initiated. Typically, a broad-spectrum combination to target gram positive and gram-negative infections is recommended.<sup>15</sup> Typically, in people,

antibiotics are given intravenously for four to six weeks, which may not be feasible in veterinary patients. In experimental models of IE, fluoroquinolones have been found effective against *Staphylococcal*, *Enterococcus* and gram-negative organisms.

Concurrent treatment of congestive heart failure (CHF) is key to this disease as 31% of canine patients with IE may present in CHF.<sup>27</sup> This involves standard cardiac therapy with diuretics like furosemide and inodilators. Although currently off label, inodilators like pimobendan have shown to be well tolerated and prolong survival in cats with CHF with hypertrophic cardiomyopathy and dilated cardiomyopathy.<sup>13,18, 25,30</sup> Currently, corticosteroids are not recommended to treat IE.<sup>7,8</sup>

### POSSIBLE SEQUELAE

Commonly, large amounts of immune complexes (IC) are formed as the body forms titers of antibodies against the invading MO.<sup>3</sup> These IC can be deposited through the body, most commonly leading to polyarthritis or glomerulonephritis.<sup>4,5,17,29</sup>

Thromboembolic events are also common in these cases, more commonly occurring with mitral valve IE.<sup>1,27</sup> Infarcts have been documented in several organs and in one case series of four dogs, a vascular encephalopathy developed secondary to thrombosis of the middle cerebral artery most commonly.<sup>9</sup>

### PREVENTION

Antibiotic prophylaxis was recommended previously for patients at risk of IE for both dental and non-dental procedures however conclusive benefits for this to prevent IE are lacking in people.<sup>6</sup> More recent guidelines, formulated by the European Society of Cardiology, have formed different categories of a patients' risk with antibiotic prophylaxis recommended for those in the high-risk group.<sup>10</sup> Those believed to carry the highest risk include those with prosthetic valves or prosthetic cardiac materials, patients with historical IE and those with congenital cardiac disease. Although reports exist of IE following dental prophylaxis in dogs with myxomatous valve disease, a definitive association has not been proven so antibiotic prophylaxis in this cohort is likely not required.<sup>24,28</sup>

### PROGNOSIS

The prognosis of IE is still poor. Several studies in dogs have shown a 20% survival rate with dogs with aortic valve IE tending to have a worse prognosis.<sup>7,8,26</sup> More recently, Sykes et al reported a survival rate of approximately 50% although the median survival time was 54 days. Factors negatively associated with survival included thrombocytopenia, azotaemia, renal and thromboembolic complications.<sup>27</sup> Median survival of cats was 31 days.<sup>23</sup>

### CONCLUSION

IE remains a difficult disease to both identify and treat. Survival is poor in both dogs and cats due to concurrent bacteraemia and cardiac dysfunction. Other problems

specific to veterinary medicine which may hinder outcome include the need for both long-term intravenous and oral antibiotics which can prove prohibitively expensive, especially in large breed dogs. Clinicians should be aware of some of the common historical and clinical exam findings in these patients as successful treatment requires prompt recognition of the disease.

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