INTRODUCTION
A procoagulant, or hypercoagulable, state is one where there is increased risk of thrombus formation, particularly when the other aspects of Virchow's triad (blood stasis and endothelial injury) are present. Diagnosis of a hypercoagulable state can be complex, with recognition of the possibility an important first step. There are many disease processes associated with procoagulant states in our patients, but sometimes these are not diagnosed prior to the presentation of a patient with clinical signs secondary to thrombus formation.

DIAGNOSIS OF HYPERCOAGULABILITY
There are generally two reasons why testing for a procoagulant state is undertaken. The first is that a patient presents with evidence of thrombus formation and the second is that the patient has a disease process commonly associated with hypercoagulability. In both cases, testing is often performed to aid guidance of antithrombotic therapy. However, as the diagnosis of hypercoagulability is not straightforward, with access to, and interpretation of, tests often being difficult, it is not inappropriate to start empirical antithrombotic therapy in many cases such as in dogs with immune-mediated haemolytic anaemia (IMHA) and cats with aortic thromboembolism (ATE) or patients with evidence of thrombus formation, without full diagnosis of hypercoagulability.

Simple surrogate tests for hypercoagulability
D-dimer levels, antithrombin activity and fibrinogen concentration are all tests which are readily available to practitioners which may help in the diagnosis of a procoagulant state. D-dimers would be expected to be elevated due to increased thrombus break down (fibrin degradation products are less useful as it cannot be determined whether they were ever in a thrombus), antithrombin is decreased due to consumption and fibrinogen is increased in the hypercoagulable patient. Although not perfect, in conjunction with clinical signs of thrombosis, or in a patient with a disease associated with hypercoagulability, these tests can be very useful.

It was thought that PT and PTT results were not helpful in the diagnosis of hypercoagulability, however a retrospective study found increased clinical evidence of thrombus formation in patients with decreased PT and PTT times compared to a control population with normal times, although there was no evidence of increased hypercoagulability when comparing TEG parameters between the populations (Song et al, 2016). The use of shortened PT and PTT times for the diagnosis of hypercoagulability is not definitive though and a prospective study would be beneficial. It is also clear that it cannot be stated that if PT and PTT are within normal limits, the patient is not hypercoagulable.

Viscoelastic testing
Thromboelastography (TEG) and thromboelastometry are both methods of viscoelastic testing. This method aims to replicate clot formation in vitro, with the use of whole blood and calcium, with or without an activator and mechanical analysis of clot production, thereby allowing the clinician to determine whether a patient is hyper- or hypo-coagulable, or indeed if their clotting function is normal. These tests can be very useful for the detection of hypercoagulability, but they are not perfect. Patients with a lower haematocrit have more hypercoagulable tracings, and high fibrinogen levels (associated with hypercoagulability but also with inflammatory disease) can also lead to similar results. Results can be harder to interpret in cats as there can be greater inter-individual variability (Döderlein and Mischke, 2017).
IMMUNE MEDIATED HAEMOLYTIC ANAEMIA
IMHA is a fairly common immune mediated condition of dogs which can also be seen, albeit less frequently, in cats. The anaemia is often severe and life threatening and can require aggressive treatment with immunsuppressive therapy and blood products. Dogs appear to be hypercoaguable at the time of diagnosis and then therapy with corticosteroids and/or cyclosporine is thought to exacerbate this tendency. There are many reasons for hypercoagulability in the IMHA patient with postulated causes including increased tissue factor expression by monocytic and endothelial cells, phosphatidylserine exposure on damaged erythrocytes interacting with the tenase and prothrombinase complexes, prothombotic microparticles and damaged erythrocytes leading to direct occlusion of vessels and decreased anticoagulant levels (Kidd and Mackman, 2013) as well as increased neutrophil extracellular traps (Lawson et al, 2018). Several studies report evidence of thrombosis in IMHA dogs (particularly pulmonary venous thrombosis) with TEG changes consistent with hypercoaguability (deLaforcade and others, 2019).

There are studies looking at the use of anti-thrombotic medication in IMHA dogs but they are small. The recommendations of the CURATIVE collaborative are that IMHA patients should be treated with antithrombotic medication but there is no clear evidence as to the best protocol. Given most thrombi are reported to be venous (and erythrocyte rich) rather than arterial (and platelet rich) and are therefore associated with low shear, rather than high shear conditions, theoretically anticoagulants should be superior to anti-platelet agents in decreasing the risk of thrombus formation in these patients. However, this is probably a simplistic understanding of the pathogenesis of thrombus formation and also arterial thrombi can occur in these patients. Therefore, although the major recommendation is that anticoagulants, such as low molecular weight heparin (LMWH), should be used in IMHA dogs, anti-platelet agents can also be recommended (Goggs et al, 2019). Unfractionated heparin is substantially cheaper than LMWH, but the use of LMWH is associated with a decreased risk of bleeding. Rivaroxaban is a newer drug which appears to be safe in dogs and may be useful in IMHA patients, but further studies are required to compare its efficacy to LMWH and unfractionated heparin.

FELINE CARDIOMYOPATHY
Cardiomyopathies, particularly hypertrophic cardiomyopathy (HCM), are very common in cats, with a prevalence of 14.7% reported in a large study of apparently healthy cats in re-homing centres (Payne, Brodbelt et al, 2015). In a population referred for HCM, within 2 years 9% had died with aortic thromboembolism (Payne, Borget et al, 2015). Thromboembolism is associated with spontaneous echocontrast and an enlarged left atrium on echocardiography, suggesting that part of the pathogenesis of thrombus formation is blood stasis, but hypercoaguability has also been reported (Stokol et al, 2008). Interestingly, there is very little evidence to support an association between cardiac disease and venous or aortic thrombosis in dogs (deLaforcade et al, 2019).

Given the predominance of arterial thromboembolism in these patients, anti-platelet therapy is recommended, with evidence that clopidogrel is superior to aspirin (Googs et al, 2019). Abciximab may be a useful drug in these patients but, in the author's opinion, further study is required. Dual therapy with clopidogrel and LMWH could be considered for these cats, but there is no evidence to support this approach (Goggs et al, 2019).

OTHER DISEASE PROCESSES
Dogs with protein-losing nephropathy are also recommended to be treated with anti-thrombotic drugs due to the well reported association between the disease and both arterial and venous thrombus formation and documented hypercoaguability (deLaforcade et al, 2019). Other disease processes which are associated with thrombosis risk include pancreatitis, sepsis, hyperadrenocorticism and neoplasia. Due to much lower risks of thrombus formation in these groups, routine thrombophylaxis is not recommended (deLaforcade et al, 2019). However, if a thrombus has occured then therapy is recommended. In dogs and cats which present with venous or arterial thrombosis, dual therapy with anti-platelet and anticoagulant therapy should be considered although increased risk of bleeding is reported with dual therapy in humans (Googs et al, 2019).
REFERENCES


7. Payne JR, Brodbelt DC, Luis Fuentes V. Cardiomyopathy prevalence in 780 apparently healthy cats in rehoming centres (the CatScan study). J Vet Cardiol. 2015;17 Suppl 1:S244-57
