Haemostasis is the delicate balance between the naturally occurring procoagulant and anticoagulant mechanisms found in the body. Any shift in this balance or interference in the control mechanisms results in either a bleeding or a thrombotic tendency.

Both conditions are potentially life-threatening and in many instances may be debilitating to such a degree that the patient is unable to have a normal life.

Management of the disorders, once diagnosed, is specific and largely successful. These tests should preferably be performed after consultation with a haematologist as their relevance, as well as the clinical history of the patient, will determine which tests should be performed.

If possible, all medication should be discontinued for 14 days prior to the testing. Ideally, testing should be performed at least 14 days after active thrombosis, blood transfusion or a bleed. There is often confusion as to what tests should be requested.

This communication serves to clarify some of the questions and advise what tests are available and offered by Ampath.

Full bleeding tendency screen
Any patient with a bleeding disorder, however mild, presents the clinician with a complex diagnostic problem.

Clinical features: Any account of unusual and/or excessive bleeding, easy bruising in the absence of trauma, prolonged bleeding from wounds after minor procedures, nosebleeds, excessive menstrual bleeding, gastro-intestinal bleeding and spontaneous bleeds into joints or tissues. The site of the observed bleeding could assist in the diagnosis of the disorder.

Prior to testing any patient for a bleeding tendency, clinical evaluation should be done, as suggested in the British guidelines. Five questions should be asked, which also directs the clinician in deciding which role player may be the culprit, e.g.: Is there really a bleeding tendency, is there any family history, is it a platelet type dysfunction (epistaxis, petechiae) or a clotting factor issue (muscle/joint bleed), what medication is the patient taking and are there renal, hepatic or hematological disease present. Only after this a full screen, including vWF, platelet function testing and the standard testing is suggested.

Laboratory testing: A profile of tests is done to detect a possible disorder of any of the haemostatic mechanisms, namely vascular, platelets, coagulation and fibrinolysis. No single test exists to detect a general abnormality.
1. Full blood count and platelets, including morphology.
2. Bleeding time to assess the vascular system and platelet function.
3. PT/INR, aPTT and TT to evaluate the coagulation factors and, if prolonged, further investigation follows specific routes to identify the deficient factors or factors (e.g. Haemophilia A and B, Von Willebrand disease) or demonstrate the presence of an inhibitor.
4. Platelet aggregation studies with ADP, collagen, arachidonic acid and ristocetin as agonists to detect qualitative platelet function defects (including drug-induced).
5. Factor VIII assay, Von Willebrand antigen and activity assays to detect Von Willebrand disease. If a Von Willebrand defect is detected, multimer analysis at UFS is recommended for typing of the disorder.
6. Factor XIII screening test to check for fibrin stability.
7. Plasmin inhibitor and tissue plasminogen activator (tPA) to test for fibrinolytic efficiency.
8. A possible diagnosis will be made based on the results of all the above tests in conjunction with the clinical history by a haematologist.

**Required samples:** 1x EDTA, 4x citrate tubes and the bleeding time is performed on the patient at the time of venesection.

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**ENDOTHELIAL INJURY**

**Thrombosis**

**Abnormal blood flow**

**Hypercoagulability**

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**Full thrombotic screen**

This profile of tests is recommended in patients presenting with symptoms of DVT, pulmonary embolism and/or a stroke, particularly at an early age and with a positive family history of thrombotic disease. The testing is also indicated in patients with thrombosis occurring at unusual sites (e.g. mesenteric vein), recurrent thrombosis without a precipitating factor, recurrent thrombosis while on oral anticoagulant therapy and warfarin skin necrosis.

We recommend that the whole profile be included in the testing as the incidence of more than one disorder is common and predisposes more severely to a thrombotic disorder, even in the absence of environmental factors such as obesity, diabetes and immobilisation.

A possible diagnosis will be made based on the results of all the above tests in conjunction with the clinical history by a haematologist. Heparin therapy must have been discontinued for at least 10 days prior to testing and clinicians must be aware that Protein C and S are vitamin K-dependent factors that are reduced during warfarin therapy. All other tests can be accurately performed if the patient is on warfarin.

Once anticoagulation has been initialized, even with the new oral anticoagulant drugs, assays for hypercoagulability will be compromised. It is therefore suggested that these tests be done after all anticoagulation has been stopped post treatment period, or prior to starting, keeping in mind that the acute thrombotic event may influence some results as well.

**Recent developments:** Elevated levels of factor VIII and Von Willebrand factor have been described to be associated with an increased risk of arterial thrombosis; and some suggestion that low levels of ADAMTS13 are associated with an increased risk of ischemic stroke has also been described.

**Required samples:** 1x EDTA, 4x citrate tubes. If second-level testing is being done, then, 1x citrate post stasis and 1x CTAD for the PAI-1.

**References**