Laboratory Testing for Thrombophilia

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Scope

The aim of guidelines on thrombophilia testing is to assist clinicians in identifying patients in whom results of thrombophilia testing would be expected to change clinical management. These guidelines apply to adult, non-pregnant patients only.

Key recommendations

There is a limited role for thrombophilia testing in the management of patients with venous and arterial thrombosis.

Clinical factors, such as the personal and family history of venous thrombosis, are more useful than thrombophilia test results in determining the duration of anticoagulation and risk of recurrence in the majority of patients with venous thrombosis.

Screening of unselected patients is not recommended.

Epidemiology

Venous thrombosis has an incidence of approximately 1/1000 of the general population. Clinical risk factors for venous thrombosis include immobility, surgery, oestrogen containing medications or pregnancy, older age, active cancer, some cancer medicines, central venous catheters, obesity, cigarette smoking, long-haul travel, active IV drug use and medical conditions such as HIV, nephrotic syndrome, inflammatory bowel disease and myeloproliferative disorders.

Testing

Indications for testing and for NOT testing:

Testing for Antithrombin or Protein C or Protein S **is recommended** in the following clinical circumstances:

- Asymptomatic relatives with a family history of Antithrombin, Protein C or Protein S deficiency **AND** a family history of thrombosis,
- Neonates and children with purpura fulminans (severe Protein C or Protein S deficiency).

Thrombophilia testing is **not recommended** in the following clinical circumstances:
- Unselected patients after a first venous thrombosis event,
- Asymptomatic relatives of patients with the Factor V Leiden or Prothrombin gene mutations,
- Asymptomatic relatives of patients with venous thrombosis prior to hormonal treatment,
- Upper limb thrombosis,
- Catheter related thrombosis,
- Retinal vein occlusion,
- Patients prior to assisted conception or patients with ovarian hyperstimulation,
- Hospitalised patients as part of risk assessment for thrombosis,
- Arterial thrombosis.

Thrombophilia testing **may be considered** in the following clinical circumstances:
- First venous thrombosis in a patient with a family history of unprovoked or recurrent venous thrombosis in one or more first degree relatives,
- Asymptomatic relatives of venous thrombosis patients with a known heritable thrombophilia prior to hormonal treatment,
- Cerebral venous sinus thrombosis,
- Splanchnic vein thrombosis,
- Skin necrosis secondary to Vitamin K antagonists.

Antiphospholipid antibody testing (Lupus anticoagulant, antiphospholipid antibodies, anti beta 2 glycoprotein 1 antibodies) **is recommended** in the following clinical circumstances:
- History of recurrent first trimester miscarriage (>/= 3 consecutive miscarriages),
- >/=1 unexplained deaths of a morphologically normal foetus at or beyond 10/40,
- >/=1 premature birth of a morphologically normal neonate before 34/40 because of eclampsia / severe pre-eclampsia or placental insufficiency,
- Young adults (<50 years) with ischaemic stroke,
- Patients with an unprovoked PE or proximal DVT if anticoagulation is discontinued (note that these patients generally warrant long-term anticoagulation and if it has already been decided to continue long-term anticoagulation, then testing is not indicated).

Antiphospholipid testing **may be considered** in the following clinical circumstances:
- History of immune disorders and venous or arterial thrombosis,
- Unusual or extensive venous or arterial thrombosis.

Where testing is done and who does testing

Primary care / Hospital.

Thrombophilia Testing includes any or all of the following laboratory assays:
- Antithrombin,
- Protein C,
- Protein S,
- Factor VIII,
- Fibrinogen,
- Activated protein C resistance,
- Genetic test for the Factor V Leiden gene mutation,
- Genetic test for the Prothrombin gene mutation,
- Lupus anticoagulant,
- Antiphospholipid antibodies,
- Beta 2 glycoprotein 1 antibodies.

Interpretation of tests

The results of thrombophilia tests should be interpreted in the light of the clinical and family history of thrombosis. Advice is available from the Consultant Haematologist locally or from the Consultant Haematologists at the National Centre for Hereditary Coagulation Disorders.

Information required on the referral form

A completed standard laboratory test request form must be sent with all samples (6 Trisodium Citrate samples and 1 EDTA sample) to the Coagulation Laboratory for Thrombophilia Testing. A serum sample should be sent to the Immunology Laboratory for Antiphospholipid antibody / Beta 2 glycoprotein 1 antibody testing. The request form must include detailed patient and clinical information including:

- **Patient demographics**
  - Patient's Name,
  - Patient's Date of Birth,
  - Medical Record Number,
  - Name of Referring Clinician,
  - Name of Referring Hospital,
  - Order number / external laboratory number (if applicable to external agencies only).

- **Request details**
  - Clinical indication for testing,
  - Number of months post partum or pregnancy loss if appropriate,
  - Anticoagulant therapy,
  - Specific tests requested.

Full clinical information should accompany all requests for thrombophilia testing. In the event a request is received which does not have the required data (above) or does not have adequate clinical details the laboratory could:

- Issue a letter to the requesting doctor, requesting additional clinical details and / or advise that the case is discussed with the local Consultant Haematologist,
- Store the sample for up to eight weeks awaiting further communication from the referring clinician,
- Samples can be discarded after eight weeks if the referring clinician has not provided the required details or if it is determined that testing is not indicated.

Samples should not be sent for laboratory thrombophilia testing if patients are being treated with heparin or low molecular weight heparin or with any oral anticoagulants. In specific cases, the patient anticoagulant therapy may be discussed with the local Consultant Haematologist.

References

Baglin, T., Gray, E., Greaves, M., Hunt, B. J., Keeling, D., Machin, S., Mackie, I., Makris, M., Nokes, T., Perry, D., Tait, R. C., Walker, I. and Watson, H. Clinical guidelines for testing for heritable thrombophilia. British Journal of Haematology, 2010; 149:209–220. doi: 10.1111/j.1365-2141.2009.08022.x.