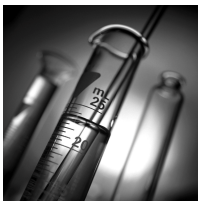

June 2016

Inherited Thrombophilia Testing

SUMMARY OF CHANGES

From 4th July 2016, inherited thrombophilia testing performed at Waikato Hospital, for the Waikato & BOP region, will only be performed in the following clinical situations:

- Idiopathic venous thrombo-embolism in young patients (<45 years)
- Warfarin-induced skin necrosis (Patients should be tested for protein C deficiency and protein S deficiency one month after stopping vitamin K antagonist therapy if this can safely be discontinued.)
- Children presenting with purpura fulminans (Test for protein C and protein S deficiency).
- Siblings of patients with homozygous FVL, homozygous PT20210A or compound heterozygotes for these mutations
- Thrombosis in unusual sites (e.g. cerebral, mesenteric, portal).

In all other situations testing should only be undertaken after consultation with a Haematologist or as part of a clinical trial.

Samples MUST provide clinical details of which criteria for testing the patient meets or the sample will not be tested.

In the absence of meeting one of the testing criteria and testing is still thought to be appropriate, it must be discussed first with a clinical haematologist and their name clearly identified on the request form along with clinical details.

Wherever possible, thrombophilia testing should be avoided in the following settings as one or more of the laboratory tests may give misleading results:

- In people taking hormone replacement therapy (oestrogen)
- Acute thrombosis
- During warfarin or other vitamin K antagonist or DOAC or any heparin therapy
- During pregnancy and for 8 weeks post-partum

Situations where testing is NOT indicated:

- Recurrent VTE
- Recurrent VTE despite adequate therapeutic anticoagulation
- VTE in the context of a family history of unprovoked VTE in a first degree relative
- VTE in association with a history of thrombophlebitis
- Arterial thrombosis (Lupus testing is indicated in this setting)
- Women with a history of miscarriage, pre-eclampsia, abruption or intrauterine growth restriction (Lupus testing is indicated in this setting).
- Prior to use of combined oral contraceptives in patients with a family history of VTE (Current British guidelines recommend avoidance of the combined oral contraceptive pill in women with a history of VTE in a first degree relative regardless of the thrombophilia results)
- In unselected women considering the use of the combined oral contraceptive pill.

Dr Helen Moore
Laboratory Haematologist, Waikato Hospital

See overleaf for more information and background:

CLINICAL UPDATE

Background

The currently recognised conditions resulting in heritable thrombophilia are:-

1. Antithrombin III deficiency
2. Protein C deficiency
3. Protein S deficiency
4. Factor V Leiden (FVL)
5. Prothrombin G20210A mutation (PT20210A)
6. Dysfibrinogenaemia
7. Inherited antiphospholipid syndrome

Patients with deficiencies of the naturally occurring anticoagulants (antithrombin, protein C and protein S) in thrombosis-prone families have a severe thrombophilic tendency with a relative risk for venous thromboembolism (VTE) of approximately 10-20 fold compared to unaffected people. This compares to a relative risk of approximately 3-5 fold for people who are heterozygotes for FVL or PT20210A.

People who are homozygous for FVL or PT20210A or double heterozygotes for these conditions are rarely seen but appear to have a particularly high risk of VTE, with a relative risk rate estimated at approximately 50-80 fold.

The dysfibrinogenaemias and inherited antiphospholipid syndrome are extremely rare and should be discussed with a haematologist prior to ordering any further tests.

Testing for Inherited Thrombophilia

Waikato hospital laboratory recently performed an audit on inherited thrombophilia testing requests performed in a month and bench marked them against international and national standards for performing these tests. (1-3). Results showed that testing for inherited thrombophilia was not being performed wisely or in accordance with these guidelines with only 1/97 tests being performed appropriately.

As a result of this, **from Monday 4th July** testing for inherited thrombophilia will only be permitted in the following situations based on the national NZ laboratory testing guidelines and Waikato DHB laboratory testing guidelines. (3-5)

Testing Indications for inherited thrombophilia:

- Idiopathic venous thrombo-embolism in young patients (<45 years)
- Warfarin-induced skin necrosis (Patients should be tested for protein C deficiency and protein S deficiency one month after stopping vitamin K antagonist therapy if this can safely be discontinued.)
- Children presenting with purpura fulminans (they should be tested for protein C and protein S deficiency).
- Siblings of patients with homozygous FVL, homozygous PT20210A or compound heterozygotes for these mutations (they will be offered testing for FVL and PT20210A as they have at least a 1 in 4 chance of being similarly affected by these severe thrombotic disorders).
- Thrombosis in unusual sites (e.g. cerebral, mesenteric, portal).

In all other situations testing should only be undertaken after consultation with a Haematologist or as part of a clinical trial.

Situations where testing is NOT indicated:

- Recurrent VTE
- Recurrent VTE despite adequate therapeutic anticoagulation
- VTE in the context of a family history of unprovoked VTE in a first degree relative
- VTE in association with a history of thrombophlebitis
- Arterial thrombosis (Lupus testing is indicated in this setting)
- Women with a history of miscarriage, pre-eclampsia, abruption or intrauterine growth restriction (Lupus testing is indicated in this setting).
- Prior to use of combined oral contraceptives in patients with a family history of VTE (Current British guidelines recommend avoidance of the combined oral contraceptive pill in women with a history of VTE in a first degree relative regardless of the thrombophilia results)
- In unselected women considering the use of the combined oral contraceptive pill

CLINICAL UPDATE

Patient counselling
Testing for heritable thrombophilia may reveal the presence of a genetically determined disorder and patients should be counselled appropriately before testing is performed.
Patients should also be advised that testing for heritable thrombophilia may affect their insurance risk and that their access to insurance policies may be changed, regardless of the result of the test result.

Genetic Testing
Index case sequencing (if initial testing has been negative) should only occur at the request of a haematologist.

Requesting an inherited thrombophilia panel from Monday 4th July

The tests comprising an inherited thrombophilia screen are:

- Antithrombin III
- Protein S and C
- Factor V Leiden (FVL); this is a molecular test
- PT20210A (prothrombin gene): this is a molecular test

Testing for antiphospholipid antibodies such as Lupus anticoagulant, IgG anticardiolipin antibodies and beta glycoprotein antibodies is more likely to be informative in cases of arterial thrombosis or in women with pregnancy loss, intrauterine growth restriction, pre-eclampsia and abruption.

Wherever possible, thrombophilia testing should be avoided in the following settings as one or more of the laboratory tests may give misleading results:

- In people taking hormone replacement therapy (oestrogen)
- Acute thrombosis
- During warfarin or other vitamin K antagonist therapy
- During treatment with any form of heparin
- During pregnancy and for 8 weeks post-partum

Testing will only be performed on samples accompanied by appropriate clinical details stating which of the above indications for testing the patient meets.

In the absence of meeting one of the recognised indications, the sample will not be tested unless it has been discussed with a clinical haematologist and this has been clearly documented on the request form.

Samples arriving in the laboratory without appropriate clinical details will not be tested but the sample will be held for 14 days and will be tested if the requesting clinician subsequently provides appropriate clinical details.

Where low levels of antithrombin III, protein C or S are found, a repeat sample will be requested to confirm the abnormal finding.

Patients will only be tested for FVL and prothrombin gene mutation once in their lifetime.

Conclusion

It is hoped by these measures that testing inappropriately for inherited thrombophilia where the result of testing does not alter subsequent management of many patients will be significantly reduced and will bring the Waikato region in line with other areas of New Zealand that have already adopted these practices.

Please contact the haematology laboratory at Waikato Hospital on 07 8398606 for more information if required.

Dr Helen Moore
Laboratory Haematologist, Waikato Hospital

References and useful websites

1) Baglin T el at. Clinical Guidelines for testing for heritable thrombophilia. British Journal of Haematology 2010;149:209-220.
2) http://www.bpac.org.nz/Series/schedule-guidelines.aspx
3) http://centraltas.co.nz/planning-and-collaboration/planning-and-improvement-2/national-programmes/
4) http://lab.waikatodhb.health.nz/news/

CLINICAL UPDATE