MELBOURNE PATHOLOGY
*"We take it personally"*

# THROMBOPHILIA SCREENING
## A GUIDE TO REQUESTING TESTS

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insight

- Many tests are available to screen for hereditary and acquired thrombophilia. Melbourne Pathology is pleased to provide this guide to tests to request.
- Please note that the HIC requires tests to be requested individually. There is no group test that constitutes a "thrombophilia screen."
- Abbreviations in brackets are acceptable at Melbourne Pathology.

### Hereditary Thrombophilia

- Protein C (PC)
- Protein S (PS)
- Antithrombin (AT)
- Activated Protein C Resistance (APCR)[1]
- Factor V Leiden (FVL)[1]
- Prothrombin gene mutation (PGM)
- Factor 8 level[2]
- Homocysteine (fasting)
- Coagulation profile/screen (Provides an APTT, PT & fibrinogen)[3]

### Acquired Thrombophilia

- Lupus anticoagulant (LAC)[4]
- Anti-cardiolipin antibody (ACL)[4]
- Beta 2 glycoprotein-1 antibody (only if high suspicion for antiphospholipid antibodies)[4]
- FBE – to exclude a myeloproliferative disorder.

### Medicare Rebates

A Medicare rebate applies only to the following tests for inherited thrombophilia - PC, PS, AT, APCR, FVL, PGM - if the request states that the patient has a personal or family history (in a 1st degree relative) of a venous thromboembolic event (VTE). Where the VTE occurred in a 1st degree relative, the rebate is limited to testing for the identified marker (either by gene testing or coagulation assays). A rebate also applies to confirmatory testing of PC, PS or AT.

### Which tests are appropriate?

If a patient has had NO venous thrombotic episodes (e.g. DVT/PE) but there is a family history, testing for hereditary thrombophilia may be appropriate. Remember that acquired risk factors (cancer, surgery, age etc.) rather than, or in addition to, hereditary thrombophilia may be implicated in the relative. Random testing in the absence of an established familial abnormality may be misleading as some of these abnormalities are very common in the general community. Appropriate counselling must be given to patients with a positive result.

Melbourne Pathology haematologists can assist you with interpretation.

If a patient has a personal history of a venous thrombotic episode (e.g. DVT/PE), testing for both hereditary and acquired thrombophilia may be appropriate. The circumstances of the episode and patient age should also be considered before testing is undertaken.

**Notes**

1. APCR is the screening test for Factor V Leiden (FVL). APCR can be ordered initially and if results are abnormal, FVL assay can be performed on the current sample which is stored. The APCR result report will prompt you to ring the laboratory to initiate FVL testing.
2. Level must be persistently elevated outside the normal range in the absence of an acute phase response, therefore repeat after 8-12 weeks if abnormally high.
3. Excludes dysfibrinogenemia and assists interpretation of PC, PS, AT and LAC.
4. These three tests screen for antiphospholipid antibodies. A positive result for any of these three antibodies on two separate occasions at least 12 weeks apart is required, together with an appropriate clinical history, for the diagnosis of antiphospholipid syndrome.

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## When to test

Testing during the period of anticoagulant therapy is generally not indicated as the duration of therapy is dictated by the type of event, not by the presence of the abnormality.

Exceptions to this include:

- The patient with an elevated APTT prior to commencement of anticoagulants, which may indicate a lupus anticoagulant.
- When the VTE dictates indefinite anticoagulation (some life threatening or recurrent clots) and the opportunity to test for some abnormalities will not present itself again.

## Warfarin effect

Protein C and S will be low on warfarin.

APCR may be falsely lowered by warfarin but the FV Leiden result will be unaffected.

## Heparin effect

Antithrombin result will be lowered by heparin.

## Other considerations

Lupus anticoagulant results may be unreliable during initial anticoagulation period.

PS, PC and AT may be consumed and falsely reduced in acute thrombosis.

PS is commonly reduced by the OCP and in pregnancy.


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Dr Maxwell is Director of Haematology at Melbourne Pathology. She trained at the Austin and Repatriation Medical Centres and later the Alfred Hospital where she developed her interest in congenital and acquired bleeding disorders, thrombosis and transfusion medicine, particularly through her affiliation with the Alfred Haemophilia Centre and Haemostasis/Thrombosis Unit. Dr Maxwell is a member of the private and rural practice working group for the Better, Safer Transfusion (BeST) program run by the Victorian Department of Human Services.

## ABNORMALITY TABLE

| ABNORMALITY | PREVALENCE (General Population) | RELATIVE RISK OF VENOUS THROMBOSIS (c.f normal population) |
|---|---|---|
| **Hereditary**<br>APC Resistance (Factor V Leiden) | 2-15%<br>(White Caucasian populations)<br>~5% in Australia | 3-8 X (heterozygotes)<br><br>~80 X (homozygotes) |
| Prothrombin gene mutation G20210A | ~2% | ~3 X (heterozygotes) |
| Protein C deficiency | 0.2-0.3% | 10 – 15 X |
| Protein S deficiency | unknown | ?? ~ 2 X |
| Antithrombin deficiency | ~0.02% (Type 1) | 25-50 X (Type 1) |
| **Hereditary or Acquired**<br>Elevated plasma homocysteine (fasting)** | ~2% | 2.5 – 4 X |
| **Acquired**<br>Lupus anticoagulant or anti-cardiolipin antibodies (antiphospholipid syndromes – APS)** | 1-5%<br>(young healthy adults) | Very high risk of thrombosis recurrence (venous or arterial) if detected after an episode of thrombosis |

** Only hyperhomocysteinaemia and anti-phospholipid syndromes are associated with an increased risk of arterial as well as venous thrombosis.

For further information, please contact
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