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ST JAMES'S HOSPITAL

St. James's Hospital National Coagulation Centre (NCC) and the National Coagulation Laboratory (NCL), LabMed

Thrombophilia Testing Guidelines

SJH: LabMed 005

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This guideline replaces all exiting guidelines from March 2026 onwards and is due for routine review in March 2028. It will be reviewed during this time as necessary to reflect any changes in best practice, law, and organisational, professional or academic changes.

Posted SJH Connect:
PPPGs St James's Hospital
https://www.stjames.ie/services/laboratorymedicinelabmed/coagulationlaboratory/(Public website)
https://stjamesie.sharepoint.com/sites/nationalcoaglab (SJH only)

Distributed to:
Medical, nursing and laboratory staff of the National Coagulation Centre, medical staff of St. James's Hospital, HOPe Directorate management team, LabMed Directorate management team.

1.0 Introduction

Thrombophilia generally refers to conditions associated with an increased risk of thrombosis. Thrombophilias may be inherited (heritable thrombophilias) or acquired, e.g., cancer, inflammatory conditions, obesity.

Heritable thrombophilia are due to genetic disorders leading to altered coagulation proteins, such as deficiencies in the natural anticoagulants (antithrombin, Protein C and Protein S), altered coagulation proteins (e.g., Factor V Leiden) or variants resulting in elevations of coagulation factors (e.g., the Prothrombin gene mutation).

Certain acquired thrombophilias may be detected on laboratory testing, e.g., antiphospholipid antibodies, myeloproliferative conditions and paroxysmal nocturnal haemoglobinuria.

This guideline is limited to conditions for which there is a laboratory assay available, and excludes other disorders associated with an increased risk of thrombosis, such as cancer and inflammatory conditions.

It should be noted that in the majority of cases, the results of thrombophilia testing have not been shown to alter management recommendations. Decisions on choice and duration of anticoagulant therapy are based on clinical grounds, such as the presence of provoking risk factors, the strength of those risk factors, and family history. As a general rule, thrombophilia testing should only be performed in cases where the results are likely to impact on clinical decisions or improve outcomes for patients or their families.

2.0 Abbreviations

APCR	Activated Protein C resistance
APLA	Antiphospholipid antibodies
APTT	Activated partial thromboplastin time
APLS	Antiphospholipid syndrome
AT	Antithrombin
CAPS	Catastrophic antiphospholipid syndrome
EDTA	Ethylenediaminetetraacetic acid
FBC	Full blood count
FVL	Factor V Leiden
MPD	Myeloproliferative disorders
NCL	National Coagulation Laboratory
PC	Protein C
PFO	Patent foramen ovale
PNH	Paroxysmal nocturnal haemoglobinuria
PS	Protein S
PT	Prothrombin time
PTGM	Prothrombin gene mutation
RVO	Retinal vein occlusion
SJH	St. James's Hospital
VTE	Venous thromboembolism

3 Aim:

3.1. To assist healthcare professionals in:

3.1.1. Determining appropriate clinical indications for thrombophilia testing.

3.1.2. The appropriate preparation of samples, labels and request forms sent for thrombophilia testing

4. Definitions:

4.1. Heritable thrombophilia testing:

Antithrombin Protein C Protein S Activated Protein C Resistance Molecular Diagnostic testing for Factor V Leiden Molecular Diagnostic testing for the Prothrombin gene variant	Testing performed in NCL

4.2. Acquired thrombophilia testing:

Lupus anticoagulant	Testing performed in NCL
Anticardiolipin antibodies (IgG and IgM) Anti-β2-Glycoprotein 1 antibodies (IgG and IgM) Molecular testing for myeloproliferative disorders Testing for paroxysmal nocturnal haemoglobinuria	Testing performed outside NCL

4.3. Antiphospholipid antibody testing:

4.3.1. Testing for antiphospholipid antibodies includes testing for the lupus anticoagulant, IgG and IgM anticardiolipin antibodies and IgG and IgM anti-β2-Glycoprotein 1 antibodies.

4.3.2. To improve diagnostic utility, the same venipuncture should be used for all antiphospholipid tests.

4.3.3. If positive, testing for antiphospholipid antibodies should be repeated after a minimum of 12 weeks to determine persistence

4.4. Activated Protein C Resistance:

4.4.1. The APCR test is a screening test for the presence of the FVL polymorphism. A normal APCR ratio excludes the presence of FVL, and so molecular diagnostic testing is not required.

4.5. Myeloproliferative Disease testing:

4.5.1. Molecular testing for MPDs includes testing for the *JAK2* V617F variant, *JAK2* exon 12 variants, *CALR* variants and *MPL* variants.

5. Laboratory Sample Preparation:

5.1. Sample request form:

5.1.1. A completed Thrombophilia Test Request form must be sent with all samples sent to the laboratory for thrombophilia testing.
https://www.stjames.ie/services/laboratorymedicinelabmed/coagulationlaboratory/ (internet)
https://stjamesie.sharepoint.com/sites/nationalcoaglab (intranet)

5.1.2. The request form must include patient details including:

Patient demographics
Patient's date of birth
Patient's medical record number
Name of referring clinician
Name of referring hospital
Specific tests requested
Order number (internal requests only)
External laboratory number (external agencies only)

5.1.3. Full clinical details **must** be provided on the request form. Requests without adequate clinical information will not be tested. Such samples will be held in the laboratory for a period of 6 weeks. The referral source will be informed in writing if this is the case. If clinical details are provided, testing can then be performed if appropriate. If appropriate clinical details are not provided, these samples will be discarded after 6 weeks.

5.1.4. Information on anticoagulation therapy **must** be provided.

5.1.5. Requests not conforming to these clinical guidelines will not be tested. The referral source will be informed in writing if this is the case. These samples will be held in the NCL for a period of 6 weeks. If appropriate clinical details are provided within this 6-week time period, testing can then be performed if indicated. If appropriate clinical details are not provided, these samples will be discarded after 6 weeks.

5.1.6. For additional advice, or to discuss cases which fall outside the indications in this guideline, please discuss with the clinical haemostasis and thrombosis haematology team in SJH (please contact the coagulation registrar via switch at 01 – 410 3000).

5.2 Samples:

5.2.1. For testing within the NCL, 6 Trisodium Citrate (Coagulation) samples and 1 EDTA (FBC) sample should be sent the NCL.

5.2.2. Please refer to individual laboratories for sample requirements for tests performed outside the NCL.

5.3. Timing of testing:

5.3.1. Antithrombin, Protein C and Protein S should not be checked within 3 months of acute thrombosis.

5.3.2. Protein S should not be checked during pregnancy or within 6 weeks after the end of pregnancy.

5.3.3. Lupus anticoagulant testing should not be performed during an acute phase (e.g., in the setting of an acute thrombotic event, acute illness), or within 3 months of an acute thrombotic event.

5.3.4. APLA testing ideally should be performed at least 6 weeks after the end of pregnancy. Results of testing performed during pregnancy should be interpreted with caution.

5.4. Use of anticoagulant therapy:

5.4.1.Testing for antithrombin, Protein C, APCR cannot be performed on anticoagulation.

5.4.2.Lupus anticoagulant testing is affected by heparin at concentrations higher than 1.0 IU/ml as measured by anti-Xa activity.

5.4.3.See table below for individual tests availability on anticoagulation.

	Antithrombin	Protein C	Protein S	APCR	Lupus anticoagulant	Molecular testing for FVL or PTGM
Vitamin K Antagonist, e.g., warfarin	X (levels may be increased)	X	X	X	X	✓
Heparin (Unfractionated or Low Molecular Weight)	X (levels may be reduced)	X (levels may be increased)	✓	X (affected by anti-Xa levels > 1.0 IU/ml)	✓ (if anti-Xa level < 1.0 IU/ml)	✓
Xa-Inhibitors (e.g., apixaban, edoxaban, rivaroxaban)	X (levels may be increased)	X (levels may be increased	✓	X	X	✓
Dabigatran	X (levels may be increased)	X (levels may be increased)	✓	X	X	✓

6. Indications for thrombophilia testing:

6.1. General guidelines on thrombophilia testing:

6.1.1. Testing is not recommended where clinical utility is unclear or results will not alter management.
6.1.2. Patients should be counselled prior to decision to proceed with thrombophilia testing.
6.1.3. Written informed consent is required prior to genetic testing for germline mutations (i.e., APCR ratio, and molecular diagnostic testing for Factor V Leiden and the prothrombin gene mutation).
6.1.4. Testing outside the indications in this guideline must be discussed with the clinical haemostasis and thrombosis haematology team prior to testing.

6.2. Venous thrombosis with a clear provoking factor:

6.2.1. Thrombophilia testing is not recommended in unselected patients.

6.3. Unprovoked or minimally provoked venous thrombosis:

6.3.1. Antiphospholipid antibody testing (lupus anticoagulant, IgG and IgM anticardiolipin antibodies, IgG and IgM anti-β2-Glycoprotein 1 antibodies) may be considered.
6.3.2. Testing for heritable thrombophilia is not recommended.

6.4. Thrombosis at unusual sites:

6.4.1. Thrombosis at unusual sites includes splanchnic vein thrombosis (portal vein thrombosis, mesenteric vein thrombosis, splenic vein thrombosis and Budd-Chiari syndrome) and cerebral venous sinus thrombosis.
6.4.2. Routine testing for heritable thrombophilia is not recommended.
6.4.3. PNH screen is recommended in setting of abnormal haematological parameters suggestive of PNH, e.g., cytopenias, abnormal red cell indices or evidence of haemolysis (e.g., raised LDH, raised bilirubin or raised reticulocyte count).
6.4.4. A full myeloproliferative disorder molecular diagnostic panel (*JAK2* V617F, *JAK2* exon 12, *CALR* and *MPL* mutational analysis) is recommended if abnormal FBC parameters are present suggestive of an MPD.
6.4.5. A *JAK2* mutational analysis (V617F and exon 12) is recommended in cases where no clear provoking factor is identified and FBC parameters are normal.
6.4.6. Antiphospholipid antibody testing (lupus anticoagulant, IgG and IgM anticardiolipin antibodies, IgG and IgM anti-β2-Glycoprotein 1 antibodies) is recommended if no clear provoking factor identified.

6.5. Retinal vein occlusion.

6.5.1. Testing for heritable thrombophilia is not recommended.

6.5.2 Antiphospholipid antibody testing (lupus anticoagulant, IgG and IgM anticardiolipin antibodies, IgG and IgM anti-β2-Glycoprotein 1 antibodies) may be considered if no local risk factors for RVO are identified.

6.6. Arterial thrombosis except stroke (i.e., myocardial infarction, cardiac thrombosis and peripheral vascular thrombosis):

6.6.1. Testing for heritable thrombophilia is not recommended.

6.6.2. Testing for APLAs should be considered in the absence of other vascular risk factors or significant atherosclerosis.

6.6.3. Testing for PNH and MPDs should be considered in patients with abnormal FBC parameters.

6.7. Stroke/Transient Ischaemic Attack.

6.7.1. Testing for heritable thrombophilia is not recommended.

6.7.2. Testing for APLAs should be considered in young patients (<50 years) in the absence of identifiable risk factors for cardiovascular disease.

6.7.3 Testing for PNH and MPDs should be considered in patients with abnormal FBC parameters.

6.7.4. Additional testing is not recommended in patients with a PFO and stroke.

6.7.5 Testing in the setting of Cerebral Venous Sinus Thrombosis is covered under section headed Thrombosis at unusual sites (6.4).

6.8.Testing for antiphospholipid antibodies.

6.8.1.Testing for antiphospholipid antibodies is indicated in the following situations:

6.8.1.1 History of systemic lupus erythematosus.

6.8.1.2. History of other autoimmune disorder **AND** either a history of thrombosis or of a pregnancy complication associated with APLS.

6.8.1.3. Presence of livedo reticularis or livedoid vasculopathy.

6.8.1.4. Unexplained prolonged PT or APTT, particularly prior to commencement of anticoagulation.

6.8.1.5. Recurrent thrombosis despite therapeutic anticoagulation not explained by non-adherence or other clear risk factors.

6.8.1.6. Thrombocytopenia.

6.8.1.7. Cardiac valve abnormalities in the absence of other explanation.

6.9 Suspected Catastrophic Antiphospholipid syndrome:

6.9.1. CAPS may be suspected in patients with acute multiple thrombotic events and evidence of multiorgan failure.

6.9.2. Antiphospholipid antibody testing is recommended.

6.10.1. Family history of thrombosis.

6.10.1 Routine thrombophilia testing of first-degree family relatives of people with a history of VTE is not recommended.

6.11. Family history of thrombophilia.

6.11.1. Selective testing of asymptomatic first-degree relatives of patients with PC, PS or AT deficiency should be performed where this may influence management.

6.11.2. Testing of asymptomatic relatives of patients with FVL or the PTGM is not recommended.

6.12. Pregnancy:

6.12.1.Heritable thrombophilia testing is not recommended in women with a prior history of an unprovoked or oestrogen-provoked venous thrombosis.

6.12.2. Screening of asymptomatic women with a family history of VTE in the absence of a known heritable thrombophilia is not recommended.

6.12.3. Antithrombin testing may be considered in pregnant women with a known family history of antithrombin deficiency or with evidence of heparin resistance.

6.12.4. APLA testing can be considered in women with a history of arterial thrombosis.

6.13. Pregnancy morbidity:

6.13.1. Routine testing for heritable thrombophilia is not recommended.

6.13.2. Women with recurrent early miscarriage (2 or more pregnancy losses before 10 weeks gestation) should be considered for APLA testing.

6.13.3. Women with 1 or more late pregnancy losses (after 10 weeks gestation) should be considered for APLA testing.

6.13.4. Women with a history of delivery at < 34/40 gestation due to eclampsia/pre-eclampsia or placental insufficiency should be considered for APLA testing.

6.13.5. Antiphospholipid antibody testing should be avoided in pregnancy as results may not be reliable. Ideally, testing should be performed a minimum of 6 weeks after the end of pregnancy.

7. References:

Thrombophilia testing: A British Society for Haematology guideline.
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Guidelines on the investigation and management of antiphospholipid syndrome.
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Document Log			
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Document Status i.e. New or Revision etc.	**Version Number**	**Revision Date**	**Description of changes**
Revision	2	Dec. 2012	Section 4.1.4.4 and 4.1.4.5 removed from section 4.1.4 and changed to section 4.1.5.1 and 4.1.5.2. New additions to section 4.1.4.4 and 4.1.4.5 in version 2 Section 4.1.6 added describing guidelines for thrombophilia testing in pregnancy Layout of 4.3.3 amended to split into 2 groups (demographics and request details). New requirement added as: Number of months post-partum or pregnancy loss if appropriate.
Revision	3	March 2016	Section 4.1.4 detailing antiphospholipid testing to include anticardiolipin antibodies. 4.1.5: Antiphospholipid testing considered in work up for SLE by rheumatology and dermatology 4.1.6 amended to take into account guidelines issued by the Royal College of Obstetricians and Gynaecologists 4.3 updated to inform users of occasions when thrombophilia testing is limited to Lupus Anticoagulant testing following review by consultant
Revision	4	July 2016	Section 4.1.6.2 detailing thrombophilia testing in women with second trimester miscarriage as per RCOG greentop guideline No. 17 Section 4.3.1 updated to include details on sample requirements for testing and the requirement to send ACA and anti-Beta 2 Glycoprotein 1 tests separately to Immunology Section 4.3.3 updated to include the requirement for clinical information regarding the number and timing of pregnancy when thrombophilia testing is requested Updated the name of the NCHCD to NCC, updated the name of the coagulation laboratory to NCL Updated the web address for both internet and intranet hosting of thrombophilia testing guidelines
Revision	5	Jan 2019	New SJH Document Number assigned to reflect updated SJH PPG Register. Ownership of document changed from Dr N O'Connell to Dr K Ryan, as per change in Laboratory Consultant for NCL. Document reviewed by Dr K Ryan, Jan 2019, no changes to practice required.
Revision	6	March 2021	Section 4.3.2 stating that a local laboratory Thrombophilia Request Form or the NCL Thrombophilia Request Form can be used for samples from external agencies. Reference 4 added Updated link to guidelines for the intranet and the SJH website
Revision	7	March 2026	These guidelines have been significantly amended to reflect the introduction and publication of new guidelines since revision 6. See section 7 for reference.