

Hypercoagulability: When, Who, and How To Investigate

Venous thromboembolism is a common clinical problem, with over two million individuals developing the condition each year in the U.S. alone. Dr. Grewal discusses when, who, and how to investigate for this potentially heart-stopping condition.

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Andrea's case

Andrea, 24, presents to the emergency department with a painful left leg. A Duplex ultrasound shows a deep vein thrombosis (DVT) in the femoral vessels.

She started the birth control pill one month ago for control of heavy menses.

Andrea has no chronic medical problems, has never been pregnant, or had a previous DVT. Her family history is significant for a 30-year-old sister who also had a spontaneous DVT. Her parents are alive and well.

Should Andrea be screened for a hypercoagulable state?

When should the screening tests be performed?

What tests should be performed?

What is the most likely genetic defect?



Venous thromboembolism (VTE) is a common clinical problem. Over two million individuals develop VTE each year in the U.S. alone; 60,000 of those die annually from pulmonary emboli.¹

The incidence of VTE increases with age, from 1.8/1,000 for those between 65 to 69 years to 3.1/100 for those aged 85 to 99.² There are also major marked differences between ethnic groups, with Asians having significantly lower rates of VTE than Caucasians or African Americans.

All thrombi have both a genetic and an acquired basis. Thrombophilia is defined as a spontaneous unprovoked VTE, or a VTE which has a severity out of proportion to a recognized stimulus. In terms of hereditary causes, 5% to 15% of thrombophilia cases prior to 1993 had an identified cause, compared to 50% today.³

Prevalence rates of the different hypercoagulable conditions are quite variable and will depend on who is screened (Table 1). For example, one is much more likely to find a hematologic abnormality in an individual with a strong family history and a spontaneous VTE at a young age.

Hypercoagulable states carry varying degrees of risk for VTE (Table 2).

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Table 1

Prevalence of defects

Factor V Leiden	12-40% (Caucasian)
G20210A prothrombin gene mutation	6-18% (Caucasian)
Antithrombin III deficiency	1-3%
Protein C deficiency	3-5%
Protein S deficiency	3-5%
Antiphospholipid antibodies	5-10%
Hyperhomocystinemia	10-20%

Table 2

Degrees of risk for VTE

Hypercoagulable state	Relative risk
Normal	1
Obesity	1-3
Birth control pill	5
Hormone replacement	2
Hyperhomocystinemia	2.5
G20210A prothrombin gene	2.8
Factor V heterozygous	7
Factor V homozygous	80
Antithrombin III deficiency	10-25
Protein C deficiency	10
Protein S deficiency	10

When should I screen?

Screening tests for hypercoagulable states can be affected by many conditions (e.g., medications, pregnancy, infections, active thrombosis). Because it is unlikely the detection of a hematologic abnormality will alter the intensity of anticoagulant therapy, I suggest screening for a hypercoagulable state one to two months after the anticoagulant therapy has been stopped.

Who should be screened?

Individuals with VTE should be screened in the presence of any of the following conditions:

- under 50 years of age,
- recurrent VTE,
- positive family history in first-degree relative,
- recurrent fetal loss,
- while on the birth control pill or hormone replacement, or
- while pregnant/post-partum.

How do I screen for hypercoagulability?

Testing should involve assays for:

- activated protein C resistance or Factor V Leiden,
- genetic test for prothrombin allele,
- functional assay for antithrombin III,
- functional assays for proteins C and S,
- clotting tests for lupus anticoagulant,
- enzyme-linked immunosorbent assay for anticardiolipin antibodies, and
- measure fasting total homocysteine.

Other issues will need to be addressed once a hypercoagulable condition has been detected, including:

- family screening,
- duration of anticoagulant therapy, and
- prophylactic anticoagulants during operating room pregnancies.

About the author...

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Table 3

Duration of treatment

3 months	If VTE is due to a transient or provoked event
6 months (minimum)	If unprovoked VTE
Lifelong	If VTE and: <ul style="list-style-type: none">• Uncontrolled cancer• Homozygous Factor V Leiden• Antiphospholipid syndrome• Antithrombin III deficiency• ≥ 2 hereditary abnormalities• Multiple VTEs• Life-threatening VTE

VTE: Venous thromboembolism

When and how long should treatment last?

Individuals who develop VTE and have a hypercoagulable state do not usually need lifelong anticoagulation. If there is no VTE, and the hypercoagulable state was picked up by screening, the patient does not need treatment, but may benefit from prophylaxis during high-risk periods (e.g., surgery and pregnancy). Table 3 outlines the indicated duration of anticoagulation therapy.

Major advances have been made in our understanding of the conditions that induce thrombosis and, with further research, new therapeutic options and more specific guidelines will hopefully be available to treat patients with these common conditions.



Take-home message

- The incidence of VTE increases with age and displays major marked differences between ethnic groups.
- Because screening tests can be affected by many conditions, testing for hypercoagulability should be done one to two months after the anticoagulant therapy has been stopped.
- Those who develop VTE and have a hypercoagulable state do not usually need lifelong anticoagulation.

References

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