

Table IV. Thrombophilia testing: tests, timing and artifacts

Thrombophilia	Diagnostic testing	Timing	Causes for erroneous results
Antithrombin (AT) deficiency	Antithrombin activity (measure AT antigen if abnormal)	Prior to anticoagulation or after discontinuation	Acute thrombosis, DIC, surgery, warfarin, vitamin K deficiency, heparin (anti-Xa) level > 1.0 units/mL, liver disease, nephrotic syndrome, L-asparaginase, pregnancy, oral contraceptives
Protein C (PC) activity	Protein C activity (PC antigen if abnormal)	Prior to anticoagulation or after discontinuation	Acute thrombosis, DIC, surgery, warfarin, vitamin K deficiency, heparin (anti-Xa) level > 1.0 units/mL, direct thrombin inhibitors, lupus anticoagulant, elevated factor VIII concentrations, liver disease, L-asparaginase
Protein S (PS) deficiency	Protein S activity (if abnormal total and free PS antigen)	Prior to anticoagulation or after discontinuation	Acute thrombosis, DIC, surgery, warfarin, vitamin K deficiency, estrogen therapy, pregnancy/post-partum, heparin (anti-Xa) level > 1.0 units/mL, lupus anticoagulant, elevated factor VIII concentrations, liver disease
Factor V Leiden	Activated protein C resistance assay (if abnormal DNA-based testing)	Anytime	Heparin (anti-Xa) level > 1.0 units/mL, DNA contamination-for factor V Leiden
Prothrombin gene G20210A mutation	DNA-based testing	Anytime	DNA contamination
Dysfibrinogenemia	Fibrinogen activity (that is, standard Clauss fibrinogen assay), thrombin time, fibrinogen antigen, reptilase time	Prior to anticoagulation with heparin or direct thrombin inhibitors	Heparin (thrombin time is very sensitive to heparin, fibrinogen less sensitive, reptilase time and fibrinogen antigen insensitive), direct thrombin inhibitors affect thrombin time and fibrinogen activity, myeloma proteins, liver disease
Hyperhomocysteinemia	Homocysteine level (consider MTHFR and CBS mutation analysis if abnormal)	Fasting specimen	Affected by vitamin deficiencies (folate, vitamin B12, pyridoxine), renal failure, smoking, older age
Factor VIII activity	Factor VIII activity	At least 6 months after thrombotic event and in the absence of inflammation,	Inflammation, acute thrombosis, stress, pregnancy, heparin, direct thrombin inhibitors, exercise, estrogens

		acute thrombosis	
Factor IX antigen	Factor IX antigen	At least 6 months after thrombotic event and after warfarin discontinued	Vitamin K deficiency, warfarin
Factor XI antigen	Factor XI antigen	At least 6 months after thrombotic event and after warfarin discontinued	N/A
Antiphospholipid antibodies	Low phospholipid reagent activated partial thromboplastin time or kaolin clotting time	Positive results must be confirmed on separate tests done at least 12 weeks apart	Heparin (anti-Xa) level > 1.0 units/mL, direct thrombin inhibitors, low molecular weight heparin, fondaparinux, factor inhibitors
	Dilute Russell viper venom time with confirmation procedure	Positive results must be confirmed on separate tests done at least 12 weeks apart	Warfarin, vitamin K deficiency, Heparin (anti-Xa) level > 1.0 units/mL, direct thrombin inhibitors, low molecular weight heparin, fondaparinux, factor X, V and II inhibitors
	Anticardiolipin antibody ELISA	Positive results must be confirmed on separate tests done at least 12 weeks apart	Rheumatoid factor, syphilis and HIV can result in positive test and must be ruled out
	Beta2-Glycoprotein I ELISA	Positive results must be confirmed on separate tests done at least 12 weeks apart	Rheumatoid factor can produce false positive results

Abbreviations:

ELISA - Enzyme-linked immunosorbent assay, DIC - Disseminated intravascular coagulation, DNA - Deoxyribonucleic acid

Compiled from:

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