Hypercoagulable State Practice Guidelines

Washington State Clinical Laboratory Advisory Council
Originally Published November 2005 Reviewed/Revised: Sept. 2007/ May 2008/July 2010

FOR EDUCATIONAL PURPOSES ONLY

The individual clinician is in the best position to determine which tests are most appropriate for a particular patient

Definition: Hypercoagulable state: balance of the coagulation system is tipped toward thrombosis, due to either acquired or inherited increase in pro-coagulant elements (e.g. cancer pro coagulant) or decrease in anti-coagulant elements (e.g. Protein C deficiency).

Hypercoaguable states are suspected in patients who have:

1)" Spontaneous" thrombosis without obvious associated risk factors
2) Thrombosis, even with a concomitant risk factor, at an early age (e.g. less than 40)
3) Recurrent thrombosis, especially in different sites
4) Family history of recurrent venous thrombosis at an early age.
5) Thrombosis in unusual locations (for example: visceral thrombosis or upper extremity thrombosis)

Acquired Disorders and applicable laboratory test

Initial testing for all patients: PT, aPTT, TT, Platelet, Fibrinogen
(Refer to Coagulation Guideline for Unexplained Bleeding Disorders on the reverse side)

1) Antiphospholipid antibody (aPL) Syndrome (Lupus anticoagulant)
Tests: 1:1 mix showing inhibitor
Hexagonal phase lupus inhibitor assay or dilute Russell viper venom time (dRVVT)
Anticardiolipin or anti-beta-2-GPI antibodies by ELISA (with titers)

2) Heparin induced thrombocytopenia (HIT) in appropriate clinical setting. Two types:
HIT Type I - usually clinically mild and non-progressive
HIT TYPE II - acute, severe, progressive, immuno-mediated and may develop life threating paradoxical thrombosis.
Test: Platelet Factor 4 Antibody (PF4)

3) Cancer
Test: Use what is general practice for cancer diagnosis based on the clinical presentation

Inherited Disorders and applicable laboratory test

Initial testing for all patients: PT, aPTT, TT, Platelet, Fibrinogen
(Refer to Coagulation Guideline for Unexplained Bleeding Disorders on the reverse side)

1) Factor V Leiden/aPC resistance (most common)
Test: aPC (activated Protein C) resistance assay **OR** DNA analysis for factor V Leiden - both can determine if patient is heterozygote or homozygote

2) Factor II (Prothrombin G20210) polymorphism
Test: Factor II DNA Analysis

3) Protein C Deficiency, Protein S Deficiency, or Antithrombin ~~III~~ Deficiency
Test together with: Protein C activity, Protein S free antigen assay, Antithrombin activity assay

4) Persistent elevation of factor VIII with normal CRP
Test: Factor VIII activity and CRP

Notes:

Factor V Leiden/Activated Protein C Resistance, Factor II DNA analysis, antiphospholipid antibody and HIT testing can be done at any time.

<u>At time of acute thrombosis:</u>

1) Protein C, Protein S, antithrombin may be falsely low due to ongoing thrombosis. If normal, deficiency is ruled out, if abnormal they should be repeated when the patient is asymptomatic and off antithrombotic medications for 2 weeks.
2) May identify reactive (not causative) antiphospholipid antibodies.
3) Factor VIII is an acute-phase reactant.

<u>When on heparin/ coumadin:</u>

1) Antithrombin is decreased 20-30% during heparin therapy.
2) Protein C and S are decreased during warfarin therapy.

References:

1. CAP Consensus Conference XXXVI, Diagnosis Issues in Thrombophilia, Nov.2001
2. Hayes, T; Dysfibrinogenemia and Thrombosis. Nov 2002 Arch Pathol Lab Med, Vol 126:1387-1390.
3. Key, NS, McGlennen RC, Hyperhomocyst(e)inemia and Thrombosis. Nov 2002, Arch Pathol Lab Med Vol 126: 1367-1373.
4. Tsai AW; Cushman M; Rosamond WD; Heckbert SR; Tracy RP; Aleksic N; Folsom AR. Coagulation factors, inflammation markers, and venous thromboembolism: the longitudinal investigation of thromboembolism etiology (LITE). Am J Med 2002 Dec 1;113(8):636-42.

PUB #681-NonDOH

(Coagulation Guideline for Unexplained Bleeding Disorders on reverse side)

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Originally published: May, 1999 Reviewed: Oct. 2001/Dec. 2004/July 2006/Sept. 2007/May 2008/July 2010

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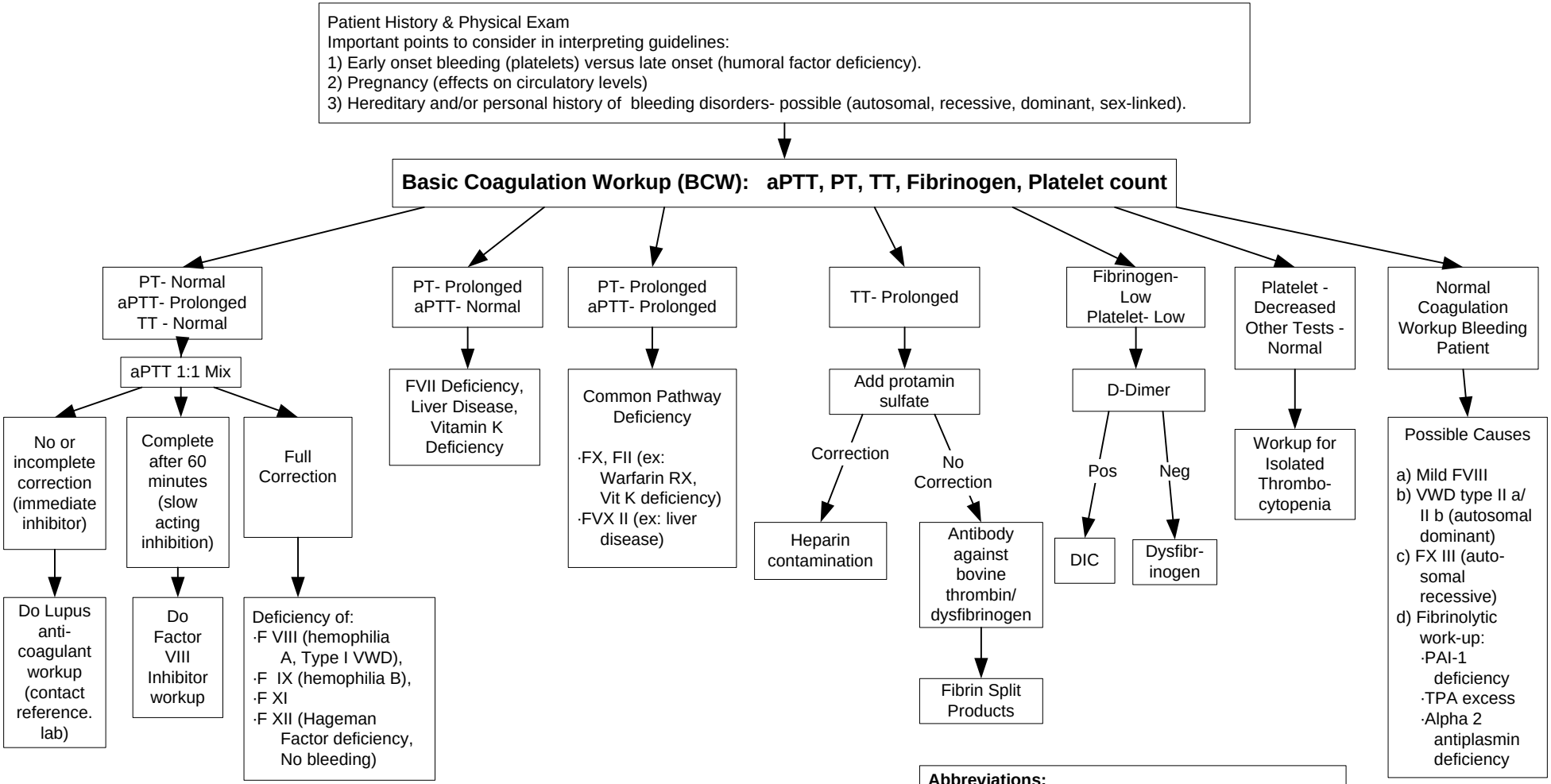

NOTE: Bleeding time or platelet function assay maybe useful as an additional diagnostic tool for familial or acquired platelet disorders such as Von Willebrand's disease or Ticlopidine medication. In general, it is not a predictor of bleeding for surgical procedures.

REFERENCES: Work up extracted from literature and modified by University of Washington Department of Laboratory Medicine.

Abbreviations:
aPTT: Activated Partial Thromboplastin Time
CRP: C-Reactive Protein
DIC: Dessiminated Intravascular Coagulation
F: Factor
PAI: Plasminogen Activator Inhibitor
PT: Prothrombin Time
TPA: Tissue Plasminogen Activator
TT: Thrombin Time
VWD: Von Willebrand's Disease

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