THROMBOEMBOLIC DISEASE

LABORATORY EVALUATION

AT-III (Functional assay)
Protein C Activity
Protein S Activity
Factor V Leiden mutation (PCR)
Prothrombin 20210 gene mutation (PCR)
Lupus anticoagulant (Functional Assay)
Antiphospholipid antibodies (ELISA)
Includes antiphosphitylserine, anticardiolipin, and antibeta-2 glycoprotein IgG and IgM
Homocysteine levels

Consider Factor VIII, IX, XI levels or fibrinolytic enzymes if above evaluation negative and high index of suspicion remains

Consider evaluation for paroxysmal nocturnal hemoglobinuria (PNH) with CD 55/59 studies, myeloproliferative diseases with JAK-2 mutation, and heparin-induced thrombocytopenia (HIT) with ELISA for PF4-heparin complex or serotonin release assay if thrombosis in unusual location or clinical situation suggestive of these alternate disorders

In acute thrombosis it is not useful to obtain:
AT-III, Protein C, Protein S levels

For patients on warfarin it is not useful to obtain:
Protein C, Protein S

For patients on heparin it is not useful to obtain:
AT-III, Lupus anticoagulant, Protein C, Protein S

TREATMENT OF VENOUS THROMBOEMBOLIC DISEASE

GUIDELINES FOR ANTICOAGULATION

For a complete listing of prophylaxis and treatment recommendations, refer to the Eighth ACCP Conference on Antithrombotic and Thrombolytic Therapy *Chest*. 133(6) Supplement 2008.

Current unfractionated heparin protocols are based on anti-Xa levels and doses are adjusted per protocol. Four heparin protocols exist at Shands at the University of Florida. Therapeutic levels are listed below

UNFRACTIONATED HEPARIN PROTOCOLS	
PROTOCOL	**THERAPEUTIC ANTI-Xa LEVEL**
Full Intensity (Standard DVT/PE)	0.3 – 0.7 U/mL
Low Intensity (for Patients Considered at High Risk for Bleeding)	0.25 – 0.35 U/mL
Acute Coronary Syndrome	0.3 – 0.6 U/mL
Ventricular Assist Device	0.25 – 0.35 U/mL

Low molecular weight heparins and pentasaccharides are also reasonable first line treatment of venous thromboembolic disease with careful consideration for age, weight, renal function, bleeding risk, and upcoming invasive procedures or surgeries. Please note these drugs are cleared renally, have a longer half life than unfractionated heparin, and are not fully reversible. See drug monographs or package insert for specific dosing recommendations.

OVER-ANTICOAGULATION WITH WARFARIN

MANAGING PATIENTS WITH HIGH INR VALUES

CONDITION	DESCRIPTION (LEVEL OF EVIDENCE)
INR that is above the therapeutic range but less than 5; no clinically significant bleeding	Lower the dose or omit the next dose; Monitor frequently; Resume warfarin therapy at a lower dose when the INR approaches desired range; If only minimally above the therapeutic range, no dose reduction may be required (All Grade 1C)
INR 5 or greater but less than 9; no clinically significant bleeding	Omit next 1 – 2 doses; Monitor INR more frequently; Resume warfarin therapy at a lower dose when the INR is in therapeutic range. (All Grade 1C) Alternatively, omit dose and give vitamin K (1–2.5 mg PO), particularly if at increased risk of bleeding. (Grade 2A) If more rapid reversal is required because the patient needs urgent surgery, vitamin K ($\leq$5 mg PO) can be given with the expectation that a reduction in the INR will occur in 24 hours; If the INR is still high, additional vitamin K (1–2 mg PO) can be given (Grade 2C)
INR greater than 9, no clinically significant bleeding	Hold warfarin therapy; Give higher doses of vitamin K (2.5–5mg PO) with the expectation that the INR will be reduced substantially in 24 to 48 hours; (Grade 1B) Monitor frequently; Use additional vitamin K if necessary; Resume therapy at lower dose when INR therapeutic.
Serious bleeding at any elevation of INR	Hold warfarin therapy; Give vitamin K (10 mg by slow IV infusion), supplemented with fresh frozen plasma or prothrombin complex concentrate or recombinant FVIIa, depending on the urgency of the situation; Vitamin K can be repeated every 12 hours for persistently ↑ INR. (All Grade 1C)
Life-threatening bleeding (eg. intracranial) + any ↑ INR	Hold warfarin therapy; Give prothrombin complex concentrate or FVIIa supplemented with vitamin K (10 mg by slow IV infusion); Repeat if necessary, depending on INR (Grade 1C)

Reference: Ansell J, et al. *Chest* 2008:133;160S-198S.

Note: In patients with mild-moderate ↑ INR without major bleeding, Vitamin K PO rather than SQ (Grade 1A)