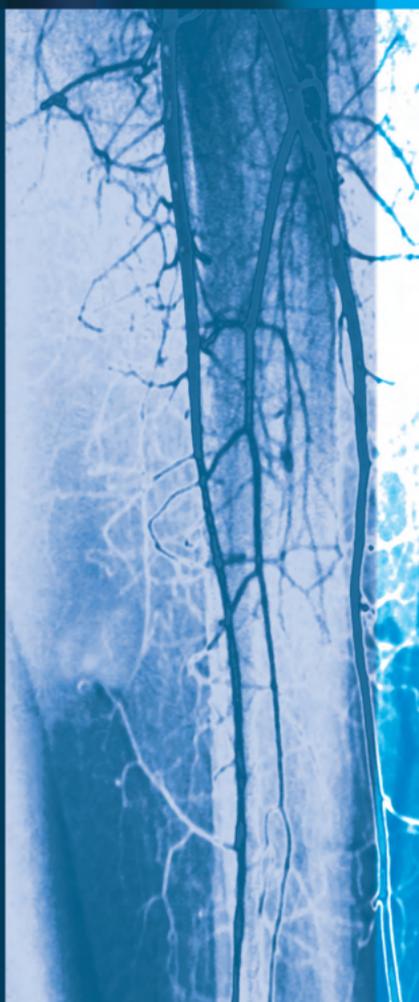
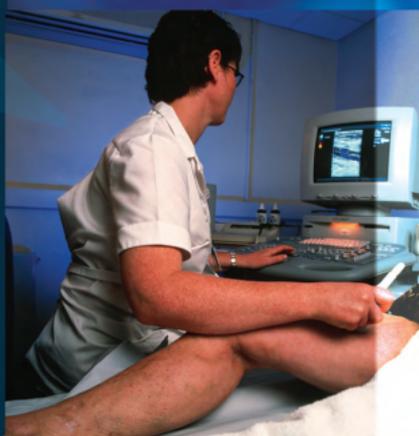


A CME/CE CERTIFIED EDUCATIONAL PAMPHLET

# VTE PREVENTION and TREATMENT: A Practical "How To"

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## **PROGRAM STATEMENT OF NEEDS**

A recent multinational survey based on acute care hospital chart reviews utilized American College of Chest Physicians (ACCP) guidelines to assess the risk of developing venous thromboembolism (VTE). Survey results showed that less than half of at-risk medical patients received ACCP-recommended VTE prophylaxis, highlighting the important need for proactive identification of at-risk medical patients in acute care through stratification and institution of guideline-recommended preventive measures. In addition to inconsistent recognition and underutilization of appropriate preventive strategies, there are also important clinical needs concerning the treatment of VTE. For instance, the transition from the hospital environment to the home or other outpatient setting is a time when suboptimal management or gaps in communication can adversely impact outcomes. Recognizing these clinical gaps in patient care, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) has established prophylaxis and treatment of VTE as a safety priority in their currently published National Patient Safety Goals (NPSGs).

This Educational Pamphlet will address methods to assess risk for deep-vein thrombosis (DVT), duration of VTE prophylaxis and treatment, and other important issues relevant to the contemporary treatment of VTE.

### *Agenda*

- Front Matter: 5 minutes
- Pamphlet Presentation: 45 minutes
- Evaluation Forms: 5 minutes
- Posttest: 5 minutes
- Total Estimated Time to Complete This Activity: 1 hour

## **CME INFORMATION**

### *Educational Objectives*

- Identify hospitalized patients who are at risk for venous thromboembolic events
- Describe appropriate VTE prophylaxis and treatment based on current evidence-based recommendations
- Review JCAHO standards concerning VTE management and assess their clinical applications

### *Audience*

This activity is intended for hospitalists, orthopedic surgeons, hematologists, intensivists, general internal medicine and family physicians, and nurses who treat patients with or at risk for DVT.

## **CREDIT DESIGNATION STATEMENT**

### *Physicians*

SCEPTER designates this educational activity for a maximum of 1.0 *AMA PRA Category 1 Credit*<sup>™</sup>. Physicians should only claim credit commensurate with the extent of their participation in the activity.

This activity, VTE Prevention and Treatment: A Practical ‘How To’, has been reviewed and is acceptable for up to 1 Prescribed credits(s) by the American Academy of Family Physicians. AAFP accreditation begins July 6, 2010. Terms of approval is for one year(s) from this date, with option for yearly renewal.

### *Nurses*

This educational activity for 1.0 contact hour is provided by Global Education Group.

For information about the nursing accreditation of this program, please contact Global at 303-395-1782 or [inquire@globaleducationgroup.com](mailto:inquire@globaleducationgroup.com).

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This activity has been reviewed for relevance, accuracy of content, and fair balance by CME Peer Review, LLC.

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Participants should read the educational objectives and review the pamphlet in its entirety. After reviewing the pamphlet, complete the posttest and evaluation in the back of the pamphlet and fax to 866-463-1693. You can also visit [www.sceptercme.com/VTEHowTo](http://www.sceptercme.com/VTEHowTo) to complete the posttest and evaluation online.

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Amanda Glazer, PhD, has no significant financial relationships to disclose.

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Dr. Moll may discuss unlabeled/unapproved uses of dabigatran and rivaroxaban.

#### *AAFP Reviewer Disclosure*

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# VENOUS THROMBOEMBOLISM: 30 Clinical Highlights and Management Aids

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## A. VTE PREVENTION

1. *VTE prophylaxis*: Upon admission to the hospital, individualized VTE risk assessment of each patient is necessary. VTE prophylaxis should be given based on VTE risk, unless absolute or relative contraindications exist. Hospital-wide VTE prophylaxis guidelines should be in place at each institution.<sup>1-2</sup> Detailed, evidence-based recommendations of VTE prophylaxis are discussed in the American College of Chest Physicians (ACCP) 2008 guidelines.<sup>2</sup> Discrepant recommendations for VTE prophylaxis for patients undergoing hip and knee arthroplasty exist between the ACCP and American Academy of Orthopedic Surgeons (AAOS).<sup>3</sup> VTE risk categories are as follows:
  - Highest risk (These patients should receive pharmacologic VTE prophylaxis PLUS sequential compression device):
    - Hip and knee arthroplasties
    - Hip and pelvic/acetabular fractures
    - Acute spinal injury with paresis
    - Major trauma
    - High risk neurosurgery
  - Moderate to high risk (These patients should receive pharmacologic VTE prophylaxis; sequential compression device is optional):
    - Medical and surgical patients, not low or highest risk
  - Low risk (These patients do not require pharmacologic VTE prophylaxis or sequential compression device. Early ambulation is sufficient):
    - Medical patients, fully mobile
    - Minor surgery, fully mobile patients, no risk factors
    - Pregnancy, no other risk factors
    - Arthroscopy, no risk factors
2. *Reassessment of VTE risk*: The risk of VTE and the indication for VTE prophylaxis should be re-assessed daily in hospitalized patients.
3. *Length of VTE prophylaxis*: Extended VTE prophylaxis for up to 4-5 weeks should be considered in high risk orthopedic and surgical patients, such as those undergoing total hip and knee replacement,

hip fracture surgery, general and gynecologic cancer surgery, or those with a previous history of VTE.

## B. DIAGNOSIS

4. *VTE risk factors*: Recognition of a patient's VTE risk factors is important when assessing the etiology of a patient's extremity or respiratory symptoms. The Well's score can be used for outpatients.<sup>4-5</sup> If the pretest probability for DVT or PE based on the Well's criteria is low, a D-dimer can be obtained. A negative D-dimer in patients with low pretest probability of VTE rules out VTE. A positive D-dimer needs to be followed up with an imaging study. A D-dimer or guide imaging work-up should not be obtained in the patient with an intermediate or high pretest probability for VTE.
5. *Computed Tomography Angiography*: CTA findings may be false positive or false negative<sup>6</sup>: a negative CTA in a patient with a high pretest probability for PE does not rule out PE and should be followed by another imaging study, such as a ventilation-perfusion (VQ) scan. And, vice versa, a positive CTA in a patient with a low pretest probability for PE does not necessarily mean that the patient has a PE. Another imaging study, such as a VQ scan, should be obtained.
6. *VQ scan*: A VQ scan can not differentiate between acute or chronic PE because both present as a perfusion-ventilation mismatch. VQ scan abnormalities frequently persist for at least several months.<sup>7</sup> Thus, in a patient with previous PE and new respiratory symptoms, an abnormal VQ scan is not diagnostic for recurrent PE unless an old VQ scan is available for comparison.

## C. TREATMENT

7. *ACCP Guidelines*: The 2008 American College of Chest Physicians Practice Guidelines on Antithrombotic and Thrombolytic Therapy offer detailed, evidence-based recommendations on a multitude of anticoagulation issues regarding venous thromboembolism prevention and treatment. They are collectively available as a PDF file on the web.<sup>8</sup> They are an extremely valuable tool.

### a) Acute Management:

8. *Outpatient management*: A subcutaneous drug such as LMWH or fondaparinux is the preferred treatment for patients with acute DVT. If the patient needs to be admitted, LMWH is the preferred choice over unfractionated heparin (UFH).<sup>9</sup> Alternatively, fondaparinux can be used. If UFH is used, a *heparin nomogram* should be administered: a bolus of 80 U/kg should be followed by a continuous infusion of 18 U/kg/hour.<sup>9</sup> For outpatient treatment of PE, LMWH, fondaparinux or UFH are good options, but, for inpatients LMWH is preferred over UFH.<sup>9</sup>

9. **HIT:** In any patient on heparin, UFH or LMWH, heparin-induced thrombocytopenia (HIT) should be considered in the differential diagnosis if thrombocytopenia or new thrombosis develops. The “4T score” is a clinically useful tool for a pretest probability assessment of whether HIT is present or not (**figure 1**).<sup>10</sup>

**Figure 1:** The 4T score to assess pre-test probability of HIT

4T's	2 Points	1 Point	0 Points
Thrombocytopenia	Platelet count fall > 50% and platelet nadir $\geq 20 \times 10^9/L$	Platelet count fall 30-50% or platelet nadir $10-19 \times 10^9/L$	Platelet count fall < 30% or platelet nadir < $10 \times 10^9/L$
Timing of platelet count fall	Clear onset between days 5-14 or platelet fall $\leq 1$ day (prior heparin exposure within 30 days)	Consistent with days 5-14 fall, but not clear (e.g. missing platelet counts) or onset after day 14 or fall $\leq 1$ day (prior heparin exposure 30-100 days ago)	Platelet count fall $\leq 4$ days without recent exposure
Thrombosis or other sequelae	New thrombosis (confirmed); skin necrosis at heparin injection sites; anaphylactoid reaction after IV heparin bolus	Progressive or recurrent thrombosis; Non-necrotizing (erythematous) skin lesions; Suspected thrombosis (not confirmed)	None
Other causes of thrombocytopenia	None apparent	Possible	Definite

High probability: 6-8 points; intermediate probability: 4-5 points; low probability:  $\leq 3$  points.

- The 4Ts of the score are: (a) Thrombocytopenia degree, (b) Timing of platelet decrease, (c) new Thrombosis on heparin, and (d) oTher causes of thrombocytopenia. 0-2 points are given for each of these 4 criteria. A score of 0-3 is considered a low, 4-5 an intermediate, and 6-8 a high pretest probability for HIT. The 4T model may be used as a guide for clinicians, but should not replace clinical judgment. In clinical studies, the 4T model has demonstrated excellent sensitivity (low probability score indicates low probability of HIT), but limited specificity (intermediate or high probability score may or may not indicate the presence of HIT). A clinically helpful and easy to use HIT Pocket Guide with an algorithm for diagnosis and initial treatment is available on the web by the American Society of Hematology.<sup>11</sup> In the case of a low pretest probability, heparin may be continued and alternative reason for the thrombocytopenia considered.<sup>11</sup> In the case of intermediate or high pretest probability, heparin should be discontinued and immunologic testing (HIT-PF4 ELISA) performed.<sup>11</sup>
10. **IVC filters:** The only clear indication for an IVC filter is the presence of an acute DVT in a patient who can not be fully anticoagulated due to a high risk for bleeding.<sup>9</sup> In this situation, a retrievable filter should typically be placed and then removed once the patient can be safely anticoagulated. The ACCP 2008 guidelines do not recommend IVC filters for primary VTE prophylaxis, not even in patients at high risk for VTE.<sup>2</sup> Whether an IVC filter should be placed in the patient with recurrent VTE in spite of therapeutic anticoagulation is controversial.

11. *Thrombolytic therapy ± mechanical thrombectomy*: The role of thrombolytic therapy and mechanical thrombectomy in the treatment of DVT and in preventing PTS has not yet been appropriately studied. Thus, their effectiveness and safety in different types of patients is not yet clear. However, this is presently being studied in the ATTRACT trial and patients with DVT symptoms of  $\leq 2$  weeks should be encouraged to find an ATTRACT trial site for consideration of enrollment.<sup>12</sup> Thrombolytic therapy in PE is indicated in the patient with hemodynamic compromise. It can be considered in selected patients without hypotension, but at high risk for adverse clinical outcomes, i.e. patients with right ventricular dysfunction. Its benefits in this situation have not yet been appropriately studied, but results of an ongoing trial (PEITHO) are expected in 2011-2012.
12. *Genotyping for warfarin sensitivity*: Certain polymorphisms in the CYP2C9 enzyme metabolizing warfarin and in the VKOR enzyme metabolizing vitamin K help predict what warfarin dose a patient may need to prolong the INR into the therapeutic range.<sup>13-14</sup> However, this method has not yet been shown to improve clinical outcomes or to be cost-effective.<sup>13-14</sup> Accordingly, genotyping should not be considered for routine clinical use at this time.
13. *Warfarin nomogram*: A nomogram should be used when initiating warfarin therapy (**figure 2**).<sup>15</sup> The starting dose should be decreased if indicators of a lower warfarin dose are present, for example age  $>75$  years, malnutrition, serum albumin  $<3.0$  g/dL, recent bowel resection, antibiotic therapy, liver dysfunction, baseline INR elevation, liver disease, alcoholism, congestive heart failure, diarrhea, body weight  $<50$  kg, or drugs known to interfere with warfarin metabolism. A warfarin initiation dose can also be calculated by using the non-profit website [www.warfarindosing.org](http://www.warfarindosing.org).

**Figure 2.** Nomogram for warfarin initiation<sup>15</sup>

Day	INR	Warfarin dosage (mg)
1		5.0
2	<1.5	5.0
	1.5-1.9	2.5
	2.0-2.5	1.0-2.5
	>2.5	0.0
3	<1.5	5.0-10.0
	1.5-1.9	2.5-5.0
	2.0-2.5	0.0-2.5
	2.5-3.0	0.0-2.5
	>3.0	0.0
4	<1.5	10.0
	1.5-1.9	5.0-7.5
	2.0-3.0	0.0-0.5
	>3.0	0.0
5	<1.5	10.0
	1.5-1.9	5.0-7.5
	2.0-3.0	0.0-5.0
	>3.0	0.0
6	<1.5	7.5-12.5
	1.5-1.9	5.0-10.0
	2.0-3.0	0.0-7.5
	>3.0	0.0

14. *Overlapping warfarin with parenteral anticoagulant:* The patient with acute VTE who is initiated on warfarin needs to receive a parenteral anticoagulant overlapping with warfarin for at least 5 days and until the INR is above 2.0 in order to minimize risk of progression of thrombosis and of warfarin skin necrosis.<sup>9</sup>
15. *Thrombophilia work-up:* No consensus exists as to what patients should be tested for thrombophilia, as finding a thrombophilia often has unclear implications for treatment. A recently published guideline, therefore, recommends only very selected testing.<sup>16</sup> However, acknowledging the lack of data on the impact of thrombophilia on an individual patient and on the patient's family members who have not yet had a VTE, tests to detect a strong thrombophilia (homozygous factor V Leiden, double heterozygous factor V Leiden plus II20210 mutation, deficiency of antithrombin, protein C or protein S, or antiphospholipid antibody syndrome) in a patient with unprovoked VTE are recommended. Finding of a strong thrombophilia has the following consequences:
- Decreases threshold to recommend long-term anticoagulation in a patient who has had an episode of spontaneous VTE.
  - Leads to discussion with the patient about an unexplained arterial, non-arteriosclerotic thromboembolic event and whether anticoagulant or antiplatelet therapy might be the preferred treatment for secondary prevention.
  - Prompts recommendation for testing of the identified thrombophilia(s) in asymptomatic family members (**figure 3**) and, if strong thrombophilia is found, (a) advice against the use of estrogen birth control methods and for anticoagulation prophylaxis during the postpartum, and possibly the antepartum period, and (b) consideration of pharmacologic VTE prophylaxis during long airline travel or procedures (immobilization cast), where normally no such therapy is given.

**Figure 3. Thrombophilia work-up – in what family members to consider testing**

Proband's thrombophilia	Male Family Member		Female Family Member	
	Sons	Brothers	Daughters	Sisters
Hetero FVL or hetero prothrombin 20210	no	no	no	no
Homo FVL or homo prothrombin 20210	no	reasonable	no	yes
Double hetero	reasonable	reasonable	yes	yes
C, S, AT	reasonable	reasonable	yes	yes

**"reasonable"** consider LMWH with airline travel, cast, non-major surgery; prolonged after major surgeries.

**"yes"** advise against estrogen contraceptives/hormone therapy; give ante- and postpartum anticoagulation.

**Figure 4** lists the thrombophilia tests to use when deciding on a thrombophilia work-up, and **figure 5** lists the type of patients whom physicians may consider testing. Multiple factors such as acute thrombosis, heparin and warfarin therapy, liver

synthetic function, estrogen therapy and pregnancy influence the results of thrombophilia tests, particularly protein C, S and antithrombin. These caveats need to be kept in mind when interpreting the results.<sup>17</sup>

**Figure 4. Thrombophilia work-up – what to test**

**Venous Thromboembolism**

- Factor V Leiden
  - Prothrombin 20210
  - Protein C activity
  - Protein S activity, free protein S antigen
  - Antithrombin activity
  - Antiphospholipid antibodies  
ACA, LA, anti- $\beta_2$ -glycoprotein-I antibodies
  - CBC
- Do not obtain MTHFR genetic tests

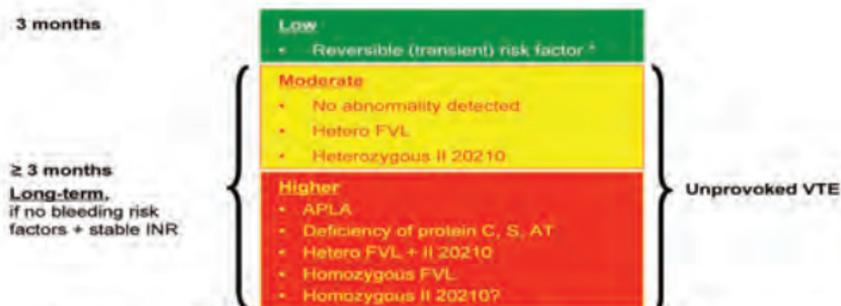
**Figure 5. Thrombophilia work-up – in whom to consider testing**

- In whom to consider thrombophilia w/u**
1. "Young" patient with unexplained, unprovoked VTE
  2. VTE in unusual location (incl. CBC, JAK-2, PNH)
  3. Very extensive VTE (evidence-based? No)
  4. Strong family history of VTE
  5. Unexplained arterial thrombosis with no arteriosclerosis on imaging studies and without arteriosclerosis risk factors

**b) Longer-Term Management**

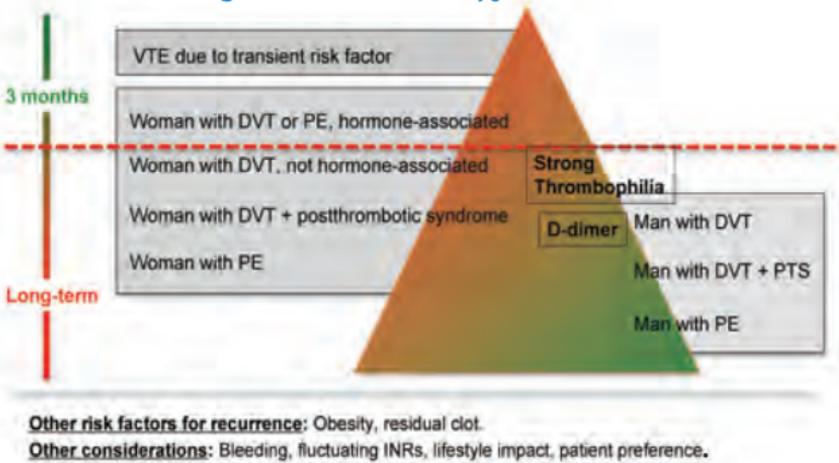
16. **Length of warfarin therapy (figures 6, 7, 8):** The length of anticipated warfarin therapy should be clearly defined based on the risk factors associated with the VTE event, the risk for recurrent VTE, and the risk for major and life-threatening bleed.

**Figure 6. Venous thromboembolism and length of warfarin therapy**



\* major: surgery; hospitalization, plaster cast immobilization  
 minor: estrogens, pregnancy, travel > 8 hrs. above risk factors: 1-3 months before diagnosis

**Figure 7. Unprovoked (idiopathic) venous thromboembolism and length of warfarin therapy**



**Figure 8. Unprovoked (idiopathic) VTE - Length of Warfarin Decision Aides<sup>15</sup>**

**REASONS THAT MAY ARGUE FOR LONG-TERM WARFARIN**

- Recurrent VTE
- Strong thrombophilia present (i.e. antiphospholipid syndrome, antithrombin deficiency, protein C or S deficiency, homozygous factor V Leiden, double heterozygous for factor V Leiden and prothrombin 20210 mutation)
- Male gender
- Patient had a PE = DVT, not "just" a DVT
- D-dimer result on warfarin positive at 3 or 6 months
- D-dimer positive after having been off warfarin for 4 weeks
- Warfarin well tolerated with good control of INR and no bleeding complications
- Little or no impact of anticoagulant therapy on patient's lifestyle (profession, hobbies)
- Patient's preference is to stay on warfarin

**REASONS THAT MAY ARGUE AGAINST LONG-TERM WARFARIN**

- VTE was associated with estrogen excess (estrogen contraceptives, hormone replacement therapy, pregnancy)
- Female gender
- Distal DVT only
- D-dimer result on warfarin therapy negative at 3 or 6 months
- D-dimer negative after having been off VKA for 4 weeks
- Warfarin poorly tolerated with widely fluctuating INRs
- Occurrence of bleeding complications or significant risk for bleeding
- Significant impact of anticoagulant therapy on patient's lifestyle
- Patient's preference is to come off warfarin

- Reversible VTE risk factor: Patients whose first VTE event was associated with a transient, i.e. reversible, VTE risk factor that was major (major surgery, hospitalization or cast immobilization), or minor (estrogen therapy, pregnancy, travel >8 hrs) within 3 months prior to the diagnosis of VTE, should be treated with 3 months of anticoagulation.<sup>9</sup>
- Unprovoked (also called "idiopathic") VTE: Patients should be treated with at least 3 months of anticoagulation. The ACCP guidelines recommend long-term anticoagulation in these patients if they have no bleeding problems or risk factors and tolerate warfarin well.<sup>9</sup> Patient preference should also be taken into consideration. In clinical practice, this is a complex issue. Several parameters can be used in the discussion with the patient about that individual's risk of recurrence and can help in the decision process to stop or to continue warfarin therapy (**figure 8**). Presence of a mild thrombophilia (for example heterozygous factor V Leiden, heterozygous II20210 mutation) does not typically influence the decision on length of warfarin therapy.

- Cancer and DVT or PE: LMWH for 3-6 months, thereafter LMWH or warfarin, INR 2-3 indefinitely or until the cancer has resolved.<sup>9</sup>
  - Distal DVT, symptomatic: Anticoagulation for 3 months, then stop.
  - Superficial thrombophlebitis: Spontaneous, i.e. not related to phlebotomy or IV catheter: at least 4 weeks of anticoagulation, such as intermediate dose LMWH or UFH, or warfarin (target INR 2-3) overlapped with LMWH or UFH for 5 days.<sup>9</sup>
17. *Anatomy/Terminology*: Confusion as to which veins are superficial and which are deep can lead to misclassification of superficial thrombophlebitis and DVT and, thus, to incorrect treatment decisions. The key terminology:
- *Arm*: Basilic and cephalic veins are superficial veins; brachial vein is a deep vein.
  - *Leg*: Greater and lesser saphenous veins are superficial veins; popliteal vein and anything proximal to it are proximal veins; gastrocnemius and soleal veins are intramuscular calf veins and part of the deep venous system, and, together with the peroneal and tibial veins, make up the deep veins of the distal leg. The superficial femoral vein has been renamed femoral vein; it is a deep vein.
  - Doppler ultrasound of the legs can only visualize the veins distal to the inguinal ligament and therefore can not assess DVT in the iliac veins. CT or MRI venogram is needed to examine the iliac veins for DVT.
18. *Anticoagulation clinics*: Patients on warfarin need to be followed in a systematic way to optimize safety and efficacy.<sup>18</sup> While smaller volume physician practices may well have these criteria in place, structured anticoagulation clinics often have the expertise and resources for optimal warfarin management. Information about the location of anticoagulation clinics can be found at [www.acforum.org](http://www.acforum.org), the website of the non-profit Anticoagulation Forum.
19. *INR patient self-testing*: In appropriately selected patients on warfarin, self-testing is reliable, safe and effective.<sup>19</sup> It is reimbursable for the patient by Medicare, Medicaid and many other insurance carriers. Instructions on how patients and physicians can obtain a device are given in detail in a newsletter from the non-profit patient organization NBCA.<sup>20</sup>
20. *Managing elevated INRs and bleeding on warfarin*: **Figure 9** summarizes management as recommended by the ACCP 2008 guidelines.<sup>14</sup>
21. *Surgical procedures on warfarin*: If anticoagulation needs to be discontinued in a patient because of a surgical procedure, the decision of whether pre- and post-procedural anticoagulation bridging with a parenteral anticoagulant (LMWH, UFH, or fondaparinux) is needed

**Figure 9. Management of elevated INRs or bleeding on warfarin**

INR	Bleeding?	Risk factor for bleeding?	Intervention
<5.0	No	No/yes	Omit next warfarin dose and reduce dose
5.0–9.0	No	No	Omit next 2 warfarin doses and reduce dose
5.0–9.0	No	Yes	Vitamin K 1–2 mg PO
>9.0	No		Vitamin K 2.5–5 mg PO
Serious bleed at any INR			Vitamin K 10 mg IV + FFP or PCCs (Bebulin®, Profilline®) or rVIIa

FFP = fresh frozen plasma; PCCs = plasma prothrombin complexes; rVIIa = recombinant factor VIIa

depends on a patient's thrombotic risk when not on anticoagulants, as well as the bleeding risk when on the bridging anticoagulant. The ACCP 2008 guidelines give guidance as to whom to bridge and what anticoagulant dose to use (prophylactic or therapeutic dose), summarized in **figure 10**.<sup>21-22</sup>

**Figure 10. Perisurgical anticoagulation management in patients on warfarin (= Bridging therapy)**<sup>21-22</sup>

Risk of thrombosis	Bridging before and after procedure?	How?
Low	None	Does not apply
Intermediate	Suggested	Therapeutic or prophylactic LMWH or UFH
High	Recommended	Therapeutic LMWH or UFH

<b>Low risk for thrombosis</b> <ul style="list-style-type: none"> <li>• AFib: CHADS<sub>2</sub> score 0–2</li> <li>• VTE &gt; 12 months ago</li> <li>• Bi-leaflet aortic valve replacement</li> </ul>	<b>High risk for thrombosis</b> <ul style="list-style-type: none"> <li>• AFib: CHADS<sub>2</sub> score 5–6</li> <li>• VTE &lt; 3 months ago</li> <li>• Any mitral valves, old aortic valves</li> </ul>
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<ul style="list-style-type: none"> <li>• Stop warfarin 5 days before surgery / procedure</li> <li>• Restart 12–24 hr afterwards</li> </ul>	<ul style="list-style-type: none"> <li>• Discuss with surgeon</li> </ul>
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- Dental procedures on warfarin:** Many dental procedures can be done while on warfarin with therapeutic INRs (**figure 11**).<sup>23</sup> More extensive procedures may require warfarin dose reduction or interruption.<sup>23</sup> Dentists can also use local measures (extra stitches, gauze packing, use of topical hemostatic agents) to minimize bleeding risk.
- Safe birth control options:** The risk of VTE with contraceptives is determined by the estrogen component, but also the type of progestin in combination pills. Limited data are available on the risk for VTE with progestins taken alone for contraceptive purposes.

Figure 11. Dental procedures in patients on warfarin<sup>23</sup>

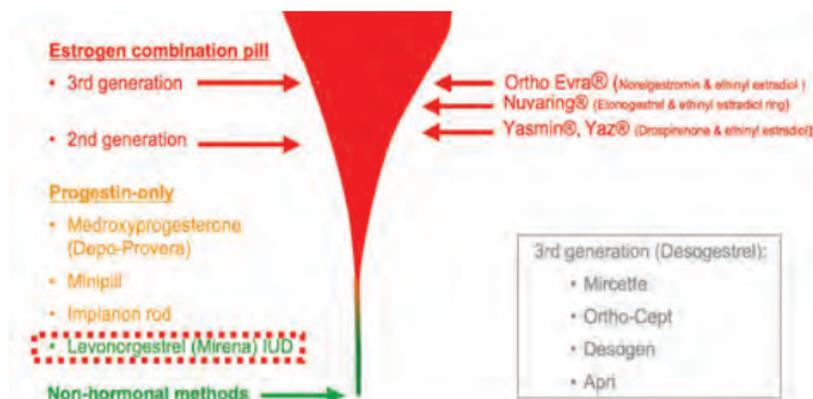
Dental Treatment	Suboptimal INR range		Target INR Range			Out of Range
	< 1.5	1.5 to < 2.0	Other Conditions / Mech Heart Valve 2.0 to < 2.5	2.5 to < 3.0	3.0 to < 3.5	
Exam, X-ray, study models						
Simple Restorations, supragingival prophylaxis						
Complex restorations, SCR/P, RCT					Caution: probably safe	
Simple extraction, curettage, gingivoplasty				Caution: local measures	Caution: local measures	
Multiple extractions, single bony impaction			Caution: local measures	Caution: local measures	Caution: local measures	
Gingivectomy, apicoectomy, minor perio flap surgery, single implant placement	Caution: probably safe	Caution: probably safe	Caution: probably safe			
Full mouth/ full arch extractions	Caution: probably safe	Caution: local measures				
Extensive flap surgery, multiple bony impactions, multiple implant placement	Caution: probably safe					
Open fracture reduction, orthognathic surgery	hospital procedure	hospital procedure	hospital procedure	hospital procedure	hospital procedure	hospital procedure

\* RP = root planing  
Permission requested.

■ Safe  
■ Use caution  
■ Not advised at current INR

It appears that they may increase the risk for VTE if given orally or as depot subcutaneous or intramuscular applications, but appear to be without VTE risk if released at low doses from intrauterine devices. The thrombotic risks are summarized in **figure 12**.<sup>24-28</sup>

Figure 12. Contraceptives and risk for thrombosis<sup>24-28</sup>



The decision on the type of contraceptive used should be based on a woman's individual VTE risk factors, including degree of overweight, smoking, family history of VTE, and presence of a thrombophilia. In this situation, considering the absolute risk of VTE rather than relative risks is helpful in clinical practice. Women with a history of VTE who are no longer on anticoagulants should avoid estrogen-containing contraceptives, and possibly also progestin-only oral or injectable progestins. Progestin-releasing IUDs appear to be a good choice for these women if hormonal contraception is desired.

24. *Whom to refer to a thrombosis center?* This decision depends on the local health care structures, and availability of and access to health care providers with special expertise in thrombosis and/or a comprehensive thrombosis center. **Figure 13** provides one way a referral triage can be viewed.

**Figure 13. Which patients to consider referring to a thrombosis clinic**

<b>a) Yes:</b> <ul style="list-style-type: none"><li>• &lt; 50 years, unprovoked (idiopathic) DVT or PE</li><li>• Unusual thrombosis (e.g. portal, mesenteric, sinus vein thrombosis, etc.)</li><li>• Arterial clot in patient &lt; 50 years of age without arteriosclerosis</li><li>• Known strong thrombophilia</li><li>• Family history of strong thrombophilia</li></ul>
<b>b) Maybe:</b> <ul style="list-style-type: none"><li>• Any patient with unprovoked (idiopathic) DVT or PE</li></ul>
<b>c) Probably not:</b> <ul style="list-style-type: none"><li>• Any patient with VTE with transient risk factor</li></ul>
<b>d) Definitely not:</b> <ul style="list-style-type: none"><li>• Any patient with unexplained pregnancy loss</li></ul>

#### D. Long-Term Complications

25. *Postthrombotic syndrome (PTS)*: Prevention is key. Individually fitted, graduated compression stockings are indicated in the patient with DVT.<sup>9</sup> Their tightness is referred to as “grade 2”, meaning a compression pressure of 35 mm Hg at the ankle and 25 mm Hg at the mid-calf. In the patient with pronounced established PTS, pelvic MRV (magnetic resonance venography) or CTV (computer tomographic venography) should be considered to evaluate for possible pelvic vein stenosis or occlusion, which might be amenable to angioplasty or venous stenting. Use of a home compression pump worn on the extremity for 30-60 minutes once or twice daily may be of benefit for the patient.
26. *Pulmonary hypertension*: The current hemodynamic definition is a mean pulmonary artery pressure of greater than 25 mm Hg by right heart catheterization, with normal pulmonary capillary wedge pressure, left atrial pressure, or left ventricular end-diastolic pressure. It typically occurs within the first 2 years after a PE, affecting 3.8% of PE patients. For a patient with a history of large PE or significant residual shortness of breath, the following screening for pulmonary hypertension is appropriate:
- Pulse oximetry at rest and after climbing stairs (or formal 6 min walk test in a pulmonary function laboratory).
  - Cardiac echo with focus on right heart and estimation of pulmonary artery pressure.
  - VQ scan to look for chronic PE – CTA of the chest is NOT sensitive for chronic PE.
  - Right heart catheterization with pulmonary artery pressure measurements and pulmonary arteriography if any of the aforementioned screening tests raise the suspicion for presence of pulmonary hypertension.

## E. Education of Patients and Health Care Providers

27. *Education of patients* with thrombosis<sup>29</sup>, thrombophilia, and/or on anticoagulation is important.<sup>1</sup> Health care providers can find downloadable, peer-reviewed education materials for their patients from various sources, including:

- [www.stoptheclot.org](http://www.stoptheclot.org), the website of the non-profit patient organization NBCA (National Blood Clot Alliance).
- [www.fvleiden.org](http://www.fvleiden.org).

28. *An education resource for health care providers* involved in anticoagulation management is

- [www.acforum.org](http://www.acforum.org), the website of the non-profit organization Anticoagulation Forum.

## F. Joint Commission Activities on Anticoagulation and VTE

29. *National Safety Goals*<sup>28</sup>: In 2008, the Joint Commission established national patient safety goals on anticoagulation for inpatient services to reduce the likelihood of patient harm associated with the use of anticoagulation therapy. The key elements, as they relate to individual patient care, are:

- Use of protocols (i.e. nomograms) for the initiation and maintenance of anticoagulation drugs including warfarin, heparin, and LMWH.
- Appropriate anticoagulation drug monitoring, including having obtained a baseline INR prior to warfarin initiation, an aPTT before unfractionated heparin, and a creatinine before starting LMWH.
- Dietary counseling for the patient on warfarin and education about anticoagulant therapy for any patient on anticoagulants.

30. *VTE Measures*<sup>1</sup>: In 2009, the Joint Commission created and published VTE core measures for hospitals with the goal to improve VTE prevention and treatment. The measures are:

- VTE-1 and VTE-2: to encourage VTE prevention in surgical and intensive care unit patients.
- VTE-3: to encourage patients initiated on warfarin to receive overlapping parenteral anticoagulation therapy for at least 5 days and until the INR is in the therapeutic range.
- VTE-4: to encourage the use of a nomogram when giving unfractionated heparin and monitoring platelets on a defined basis to discover heparin-induced thrombocytopenia.
- VTE-5: to encourage education of the patient being discharged on warfarin from the hospital on compliance, dietary issues, follow-up INR monitoring, and potential adverse drug reactions and interactions.
- VTE-6: to encourage hospital-wide DVT prophylaxis in at-risk patients.

## ABBREVIATIONS

AAOS	= American Academy of Orthopedic Surgeons
ACA	= anticardiolipin antibody
ACCP	= American College of Chest Physicians
AFib	= atrial fibrillation
AT	= antithrombin
APLA	= antiphospholipid antibodies
aPTT	= activated partial thromboplastin time
CBC	= complete blood count
CHADS <sub>2</sub>	= congestive heart failure–hypertension–age– diabetes–stroke
CT	= computed tomography
CTA	= computer tomographic angiography
CTV	= computer tomographic venography
DVT	= deep vein thrombosis
FVL	= Factor V Leiden
Hg	= mercury
HIT	= heparin-induced thrombocytopenia
INR	= international normalized ratio
IUD	= intrauterine device
IVC	= inferior vena cava
LA	= lupus anticoagulant
LMWH	= low molecular weight heparin
MTHFR	= methylene tetrahydrofolate reductase
MRI	= magnetic resonance imaging
MRV	= magnetic resonance venography
NBCA	= National Blood Clot Alliance
PE	= pulmonary embolism
PNH	= paroxysmal nocturnal hemoglobinuria
PTS	= postthrombotic syndrome
UFH	= unfractionated heparin
VKA	= vitamin K antagonists
VKOR	= vitamin k epoxide reductase
VQ	= ventilation-perfusion
VTE	= venous thromboembolism

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## **POSTTEST AND EVALUATION**

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