

## Deep Vein Thrombosis (DVT) / Thrombophlebitis: Assessment & Urgent Referral

*This condition requires urgent referral. Untreated proximal DVT can lead to pulmonary emboli in up to 50% of patients. 95% of all pulmonary emboli are from DVT and have a 30% mortality rate. There is currently no consensus as to whether the empirical judgment of the practitioner or utilization of one of the published decision-making tools is more accurate in deciding which patients should be referred for diagnostic testing. Information on both approaches is contained in this document.*

### Background

Approximately 2 million people a year develop deep vein thrombosis (DVT). In about half of these patients, the DVT is asymptomatic until a pulmonary embolism occurs. (Caprini 2005) In rare cases, the embolism will travel through a patent foramen ovale in the heart wall and result in a stroke.

The formation of venous thrombosis usually begins when platelets aggregate at the site of endothelial damage. Stasis encourages thrombus formation, followed by the deposition of fibrin, leukocytes and erythrocytes. The process begins in the cusps of venous valves. The resulting thrombus may move along the vessel as a free-floating clot and the organized thrombus then adheres in a venous sinus in about 7-10 days. The vessel may become occluded. The thrombus may eventually extend all the way up the leg and into the pelvis.

In the case of venous *thrombophlebitis*, secondary inflammatory changes occur once the thrombus adheres to the vessel wall. Thrombo-phlebitis ultimately destroys the venous valves in the area. "Central recanalization" may eventually restore blood flow through the area.

Complications of thrombophlebitis/DVT include chronic vein insufficiency (partially obstructed veins with faulty valves),

pulmonary embolism (PE), and post-thrombotic syndrome.

Proximal deep vein thrombosis involves the popliteal vein or more proximal veins. 80% of symptomatic patients with confirmed DVT have proximal thrombosis. Proximal DVT leads to a much higher incidence of pulmonary embolism than does distal.

Distal deep vein thrombosis involves the posterior tibial vein in the calf and leads to a much lower incidence of pulmonary embolism.

**Note:** Although distal DVT by itself rarely causes pulmonary emboli, in about 30% of cases, the distal thrombosis expands upward to the proximal veins and causes proximal DVT. When this occurs, it usually occurs within a week of initial presentation (Kearon 2005).

### Assessment

Clinical suspicion is based on a combination of clinical signs and symptoms, as well as on the assessment of risk factors. *The classic presentation is a patient with a leg that is painful, warm, red, swollen and tender.* But DVT may not present in this way, and this classic presentation is not always caused by DVT. The clinical signs and symptoms tend to be neither sensitive nor specific (Goodacre 2005, Tapson 2005).

The practitioner may simply consider the combination of clinical risks, signs and symptoms, and arrive at an empirical decision to refer for further testing, or using a decision-making tool. Wells has a 9-point standardized scoring system, commonly used to assign the patient to a low, moderate or high risk group (see *Appendix 1*).

The accuracy of Well's scoring system is controversial. A 2005 meta-analysis of 54 studies suggested that this point system appeared to be useful in clinics or emergency departments. A low score had a 0.25 negative likelihood ratio and a high score carried a 5.2 positive likelihood ratio (Goodacre 2005). However, in a cross-sectional study of 1295 primary care patients in the Netherlands (Oudega 2005), the low risk categorization missed 12% of patients with DVT as opposed to the 3-5% reported in Goodacre's meta-analysis. Further, Oudega calculated a 0.45 negative likelihood ratio—considerably higher than the 0.18 reported in Wells' original study or the 0.25 reported by Goodacre.

Oudega's meta-analysis contained four studies revealing that physician judgment of a low risk patient had a negative likelihood ratio of 0.25—the same accuracy reported when using the Wells instrument. *Based on current information, either empirical judgment or Wells tool appear to be viable options.* Further, even if a standardized scoring system is used, the practitioner must still use his/her empirical judgment.

Wells also has a revised 10-point tool that divides patients more simply into high and low risk. This tool may be more effective, although it has not been as extensively studied (see *Appendix 2*). Also contained in this document is a third decision-making tool (see *Appendix 3*) used in a hospital setting to determine the need for prophylactic anti-coagulation therapy, which could also be used to help guide referral decisions in a chiropractic setting (Caprini 2005).

## Major Risks<sup>\*</sup>

Clinical suspicion of DVT is based partly on assessing risks. Major risks include the following:

- **Active cancer.** This includes treatment within the last 6 months or currently receiving palliative treatment.
- **Paralysis, paresis, or recent immobilization casting of the lower extremity (< 1 month).** 59% of DVT cases are attributable to a current hospitalization or a recent nursing home stay. (Heit 2002)
- **Recently bedridden.** 3 days or more.
- **Major surgery within the previous 12 weeks requiring general or regional anesthesia.** Leg or pelvic surgery or prostatectomy is of special concern.
- **Previous DVT.** Increases risk 2-3X. About one third of patients with an initial episode of deep vein thrombosis will present during the following year with signs and symptoms that suggest a recurrence (whereas only one in three of these patients actually *have* a recurrence). (Lensing 1993)
- **Age over 75 years.**
- **History of pulmonary embolism.**
- **Family history of thrombosis.** One of the most frequently missed risk factors. (Caprini 2005)
- **Patients with laboratory or genetic risk factors for coagulation:** positive Factor V Leiden, Prothrombin 20210A, or lupus anticoagulant; elevated serum homocysteine or anticardiolipin antibodies.
- **Heparin-induced thrombocytopenia (HIT).**

## Additional Risks

- **Family history of thromboembolism or blood clotting disorders.** Presents a risk if at least one first-degree relative was diagnosed with DVT.
- **After CVA.** 1/2 will develop DVT.

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<sup>\*</sup> The author of this document designated risks as "major" based on the weightings given in the decision-making tools in the appendices.

- **After MI.** 1/3 will develop DVT.
- **Obesity.**
- **Varicose veins.**
- **Oral contraceptive/HRT.** Risk increases 2X. Concomitant progestin use increases the risk over estrogen alone. (Smith 2004)
- **Older age.** Risk increases over the age of 40 years; exponential increase over 50.
- **Pregnancy.** Risk increases up to 4 weeks post-partum (Miron 2000).
- **Past history of difficult pregnancy.** History of stillborn, miscarriage, premature birth with toxemia may be signs of thrombophilia in the mother (Caprini 2005).
- **Long air flights.** The risk is highest within the first 2 weeks. In one Australian study, the annual risk of thromboembolism was increased by 12% in those experiencing one long flight per year. The degree of risk versus the exact length of flight was not calculated (Kelman 2003). However, flights longer than 6 hours have been identified as a risk (Miron 2000). Another study found that flights of 8 hours or longer doubled the risk for isolated calf thrombosis and also increased the risk for DVT (Schwarz 2003). Long flights serve as a risk factor alone, but may also increase pre-existing risk factors, increasing the risk of patients with thrombophilia 16X and oral contraceptive use 14X. (Eklorf 2005, Martinelli 2003)
- **Tissue trauma.**
- **Systemic lupus erythematosus.**
- **Lower limb arteriography.**

## Physical Exam Findings

### Observation

- **Entire leg swollen.** Thigh swelling has a reported 2.5 positive LR.
- **Calf swelling** at least 3 cm larger than that of the asymptomatic leg (measured 10 cm below tibial tuberosity.)
- **Pitting edema** (greater in symptomatic leg). Ankle swelling in general is present in about 80% of DVT patients. (Lohr 2005)
- **Dilated collateral superficial veins** (nonvaricose).

### Palpation

- **Local tenderness along course of deep venous system** (present in about 50% of cases). (Lohr 2005)
- **Erythema of the area.**
- **A palpable “hard cord”** over the popliteal, femoral or iliac veins. (Waterhouse 2001)
- **Temperature change.** Increased local heat in the case of thrombophlebitis or decreased in deep vein thrombosis.

**Caution: The practitioner should avoid sustained, forceful palpatory pressure if there is a high index of suspicion for DVT. This caution is due to the risk of triggering a pulmonary embolism.**

**Homan’s sign.** This classic test should no longer be performed because it is not considered to be diagnostic. It is present in only about 8% of cases, is non-specific, and there is also concern about triggering an embolism. (Lohr 2005, Waterhouse 2002)

### Additional physical exam procedures

The practitioner should also check oral temperature and pulses in lower leg.

*Physical Findings	Sensitivity	Specificity	Positive LR	Negative LR
<b>Inspection:</b>				
Any Calf or Ankle Swelling	41-90%	8-74%	---	--
Asymmetric Calf Swelling	61%	71%	2.1	0.6
Thigh Swelling	50%	80%	2.5	0.6
Superficial Venous Dilation	29-33%	82-85%	cal	cal
Erythema	16-48%	61-87%	---	---
Superficial Thrombophlebitis	5%	95%	cal	cal
<b>Palpation:</b>				
Tenderness	17-85%	10-65%	---	---
Asymmetric Skin Coolness	42%	63%	cal	cal
Asymmetric Skin Warmth	29-71%	51-77%	---	---
A Palpable “Cord”	15-30%	73-85%	---	---

\* If the reported sensitivity or specificity varied more than 10 percent, then likelihood ratios were not calculated. For “Positive LR” - the **larger** the number, the stronger the predictive power of a positive test. For “Negative LR” - the **smaller** the number, the stronger the predictive power of a negative test. Adapted from Anand 1998, McGee 1998, and Orient 2000.

## Urgent Referral

**It is important to refer suspected DVT within 24 hours, preferably the same day.**

It is also critical to ask the patient about chest symptoms, shortness of breath, transient episodes of syncope and fever. The presence of these additional symptoms may signal a pulmonary embolism (Kopansky-Giles 1995).

***In such circumstances, the referral becomes emergent.***

About 75% of patients who present with signs and symptoms of DVT will turn out NOT to have the condition. (Wells 1995) This is because no matter what decision-making criteria are used, the clinical diagnosis of venous thrombosis has poor accuracy. However, because of the potentially serious consequences, referrals should still be made on the basis of strong suspicion.

### Note these important details:

- The patient should be asked to sign appropriate release forms for medical records and to permit the clinical supervisors to contact the patient or family members for follow-up purposes.
- In the case of urgent referrals, the patient's primary care physician can be contacted by phone, or the patient should be sent to an emergency department in a hospital or an acute care facility, if properly equipped.
- In the case of emergent referrals, *911 should be called for an ambulance.*
- An appropriate PARQ should be performed and charted. A patient's willingness or refusal should also be charted.
- All follow-up contacts and attempts at contact must be recorded in the patient chart in the correspondence section.
- Incidents involving emergent referral should be reported to the Dean of Clinics immediately. Emergent, urgent and semi-urgent referrals must be duly reported at staff meetings.

- The supervising clinician should follow up on all time-sensitive referrals within 24 hours.

## Common Differentials for the Acutely Painful & Swollen Calf

A number of conditions can mimic DVT. For example, strong clinical evidence of one of the following conditions would constitute subtracting 2 points from the Wells system. (See Appendices 1 and 2.)

### Baker's cysts

Baker's cysts are distended gastrocnemio-semimembranosus bursae. Any type of knee arthritis can cause the bursae to become enlarged, allowing for possible rupture or swelling by compressing the popliteal vein. The resulting pain and acute swelling may be indistinguishable from DVT.

In studies of acute calf swelling using both venograms and arthrogram, Baker's cysts were found in about 30% of cases, and DVT was found in about 25% of cases. Both Baker's cysts and acute DVT were found in about 10% of cases. Neither was found in about 35% of cases. (McGee 1998)

### Acute Cellulitis

This is a diffuse spreading infection of the skin and subcutaneous tissues, usually caused by Group A *Streptococcus* or *Staphylococcus aureus*. Portal of entry is usually a break in the skin, but the break may not be apparent. The area involved is usually hot and red, mimicking DVT. **An urgent referral is recommended.**

### Muscle Strains / Hematomas

Calf or thigh muscle tears following trauma or excessive exercise may also cause pain and swelling.

## Ancillary studies

A combination of ultrasound, D-dimer testing, and venography are used to make the diagnosis. These procedures are performed by the staff at the referral site.

## **Ultrasound**

Duplex US and color Doppler compression ultrasound are the diagnostic tests of choice in most circumstances. (Anand 1998, Lohr 2005)



Ultrasound evaluation

Pooled analyses showed that compression ultrasonography had sensitivity of 96% for proximal-vein thrombosis with a specificity of 98%. (Kearon 1998, Lensing 1993)

Ultrasonographic diagnosis of deep vein thrombosis of calf veins is less accurate than that for proximal veins (Lensing 1999). Distal (calf) deep vein thrombosis poses a low risk for embolization, in contrast to the high risk with proximal (thigh) thrombi (Moser 1981).

### **D-dimer**

D-dimer testing can be used to identify patients who require a doppler study. It has a sensitivity of 96% (LR- 0.12) and is good for ruling out DVT. It has low specificity and therefore requires follow-up testing. (Stein 2004)

D-dimer is one of the fibrin degradation products generated during fibrinolysis. D-dimer concentrations are raised in the setting of acute deep vein thrombosis (Kearon 1998), and normal concentrations are expected in the absence of acute venous thrombosis unless other, coexistent conditions that activate the coagulation system are present. (Anderson 2000, Frost 2003, Gouin-Thibault 1999, Hellgren 2003)

Newer, less sensitive, whole blood, qualitative agglutination assays, particularly the

SimpliRED D-dimer test (Agen Biomedical, Brisbane, Australia), and the more sensitive, quantitative, enzyme-linked immunosorbent assays (ELISAs) are sufficiently rapid for use in outpatients. (Keeling 2004, Schutgens 2003)

Among outpatients classified as possessing low clinical probability of having deep vein thrombosis by using the original Wells criteria, strong evidence shows that a normal SimpliRED D-dimer assay safely excludes the presence of acute DVT—although a 2005 study of primary care practitioners suggested as many as 3% of cases may still be missed. (Oudega 2005) In the light of this controversy, once again practitioners will have to use their own clinical judgment.

In the evaluation of the patient with leg swelling or pain, the use of ultrasound may identify alternative causes of symptoms (such as Baker's cyst, calf hematoma, or partial muscle rupture). (Bradley 1993, Elias 1987, Mitchell 1991, Vayssairat 2004, White 1989) Thus, ultrasound testing may still be useful among patients with calf swelling who have a normal D-dimer test and who do not have high clinical probability of having venous thrombosis.

### **Venography**

Contrast venography is the best way of confirming DVT. However, it is invasive, expensive, technically inadequate in about 10% of cases, and induces DVT in about 3% of the patients on whom it is used.

Hospital practice trends over the last two decades show that compression ultrasonography has replaced ascending contrast venography (Stein 2003).

### **A combined strategy**

A number of evidence-based combinations are currently being used to safely diagnose DVT with the least inconvenience for the patient. (Hull 2005)

It has been suggested that a strategy requiring one visit using some combination of ultrasonography, D-dimer testing, and venography offers a relatively safe outcome.

This strategy avoids the need for venography in up to 75% of patients by using it *only* after a negative result on initial ultrasonography and a positive D-dimer test result. (Kearon 2005)

When a sensitive D-dimer assay result (Stein 2004), such as a quantitative rapid ELISA, is negative and the patient has a low or moderate pretest probability, ultrasonography is usually not needed at all. Alternatively, with an initial normal result on ultrasonography, a negative D-dimer result (Kearon 2005, Stein 2004) will avoid the need for repeated ultrasonography (which is the usual procedure), allowing definitive single-visit testing in many patients. Kearon and colleagues' study (2005) used the D-dimer assay to limit patient exposure to venography to less than 25% of patients with a negative result on initial ultrasonography.

If distal DVT is going to extend into the proximal veins, this usually occurs within 1 week of presentation. (Kearon 1998)

## **Management**

Anticoagulant therapy is highly effective in preventing the extension, embolization and recurrence of DVT. Unfortunately, it is associated with increased risk of major bleeding ( $\approx 5\%$ ) and heparin-induced thrombocytopenia ( $\approx 1\%$ ). Therefore, when possible, anticoagulation should be restricted to only those with confirmed DVT.

Recent research suggests that keeping patients mobile while on anticoagulant therapy along with good quality compression stockings may be preferable to confining them to bed. (Parsch 2005)

Prospective studies also demonstrate a 50% net risk reduction of developing post-thrombotic syndrome in patients with DVT who wear elastic compression stockings. (Brandjes 1997, Prandoni 2004)

## **Post-Thrombotic Syndrome (PTS)**

This syndrome is the result of long-term sequela of DVT. Symptoms include pain, swelling, varicosity, pigmentation, and skin changes (Puggiono 2005). Prospective studies have demonstrated a PTS prevalence of 17% of affected limbs at 1 year, 23% at 2 years, and 28% at 5 years. (Prandoni 1996) Symptoms can usually be controlled by leg elevation, graduated compression stockings (30-40mm Hg) and local wound care for ulceration. Surgery is sometimes necessary.

## **Preventing air-travel-related venous thromboembolism (ATVT)**

Risk factors associated with sitting for hours on a plane may be remedied by the following steps (Eklof 2005):

- Stay hydrated (plenty of non-alcoholic liquids).
- Move feet/legs and take deep breaths every hour.
- Passengers with a tendency for significant swelling of legs or with multiple risk factors for DVT may benefit from wearing graduated compression stockings.
- A dietary supplement, Flite Tabs, significantly reduced the incidence of DVT and superficial vein thrombosis during 7-8 hour plane flights in a randomized, controlled study. The supplement contains a proprietary blend of pycnogenol (pine bark extract) and nattokinase (a byproduct of soybean fermentation). 300 mg were taken two hours before takeoff and again six hours later. (Cesarone 2003)
- Patients with severe risk factors may wish to consult a medical physician about whether prophylaxis with low molecular weight heparin is advisable.

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## Appendix 1: Wells' 9-Item Decision-Making Tool

Deep Vein Thrombosis: Simplified Clinical Prediction Guide for Determining DVT Probability (Wells 1995)

<b>History</b>	<b>Score</b>
Active cancer (treatment within the last 6 months)	1
Paralysis, paresis or recent immobilization casting of the lower extremity	1
Recently bedridden (> 3 days) or major surgery within 1 month or less	1
<b>Physical</b>	
Local tenderness along course of deep venous system	1
Entire leg swelling	1
Calf swelling > 3 cm compared to asymptomatic leg	1
Pitting edema (greater in symptomatic leg)	1
Dilated collateral superficial veins (nonvaricose) (Anand 1998)	1
Alternative diagnosis at least as likely as deep vein thrombosis	- 2
<b>TOTAL</b>	

**Each item present is worth 1 point.**

*High probability = 3 or more points*

*Moderate probability = 1-2 points (81% sensitivity)*

*Low probability = 0 (97% sensitivity)*

## **Appendix 2. Wells' Revised 10-Item Decision-Making Tool\***

<b>Clinical Characteristic</b>	<b>Score</b>
Active cancer (patient receiving treatment for cancer within the previous 6 months or currently receiving palliative treatment)	1
Paralysis, paresis, or recent immobilization casting of the lower extremities	1
Recently bedridden for 3 days or more, or major surgery within the previous 12 weeks requiring general or regional anesthesia	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than that on the asymptomatic leg (measured 10 cm below tibial tuberosity)	1
Pitting edema confined to the symptomatic leg	1
Dilated collateral superficial veins (nonvaricose)	1
Previously documented deep vein thrombosis	1
Alternative diagnosis at least as likely as deep vein thrombosis	- 2
<b>TOTAL</b>	

\* A score of two or higher indicates that the probability of deep vein thrombosis is likely; a score of less than two indicates that the probability of deep vein thrombosis is unlikely. In patients with symptoms in both legs, the more symptomatic leg is used as an indicator.

**Note:** Risk factors such as recent trauma, family history, erythema and age were not included because of weak association with DVT based on stepwise logistic regression analysis from earlier studies by Wells. (Wells 1997)

This decision-making tool performed similarly to a method using a longer checklist in conjunction with the empirical judgment of the practitioner. (Miron 2000)

### **Reference:**

Wells PS, Anderson DR, Rodger M, et al. Evaluation of D-dimer in the diagnosis of suspected deep vein thrombosis. N Engl J Med 2003;349(13):1227-35.

## **Appendix 3. Planning for Management: A Post-Surgical Decision-Making Tool**

FROM: THROMBOSIS RISK FACTOR ASSESSMENT (Evanston Northwestern Healthcare) (Caprini 2005)

This instrument is designed to assess patients who are undergoing surgery. In a non-surgical, walk-in clinical setting, it may be most valuable illustrating the relative risk of various factors (e.g., risks rated at 5 points v s 1 point). The total risk factor score is also based on patients currently undergoing surgery.

### **CHECK ALL THAT APPLY**

#### **Each Risk Factor Represents 1 Point**

- Age 41-60 years
- Minor surgery planned
- History of prior major surgery (< 1 month)
- Varicose veins
- History of inflammatory bowel disease
- Swollen legs (current)
- Overweight/Obesity (BMI > 25)
- Acute myocardial infarction
- Congestive heart failure (< 1 month)
- Sepsis (<1 month)
- Serious lung disease incl. pneumonia (<1 month)
- Abnormal pulmonary function (COPD)
- Medical patient currently at bed rest
- Other risk factors: \_\_\_\_\_

#### **Each Risk Factor Represents 3 Points**

- Age over 75 years
- History of DVT/PE
- Family history of thrombosis\***
- Positive Factor V Leiden
- Positive Prothrombin 20210A
- Elevated serum homocysteine
- Positive lupus anticoagulant
- Elevated anticardiolipin antibodies
- Heparin-induced thrombocytopenia (HIT)
- Other congenital or acquired thrombophilia  
If yes, type \_\_\_\_\_

\*most frequently missed risk factor

#### **Each Risk Factor Represents 2 Points**

- Age 60-74 years
- Arthroscopic surgery
- Malignancy (present or previous)
- Major surgery (> 45 minutes)
- Laparoscopic surgery (> 45 minutes)
- Patient confined to bed (> 72 hours)
- Immobilizing plaster cast (< 1 month)
- Central venous access

#### **Each Risk Factor Represents 5 Points**

- Elective major lower extremity arthroplasty
- Hip, pelvis or leg fracture (< 1 month)
- Stroke (< 1 month)
- Multiple trauma (< 1 month)
- Acute spinal cord injury (paralysis)(< 1 month)

#### **For Women Only (Each Represents 1 Point)**

- Oral contraceptives or hormone replacement therapy
- Pregnancy or postpartum (< 1 month)
- History of unexplained stillborn infant, recurrent spontaneous abortion ( $\geq 3$ ), premature birth with toxemia or growth-restricted infant

<b>Total Risk Factor Score</b>	<b>Incidence of DVT</b>	<b>Risk Level</b>
0-1	< 10%	low risk
2	10-20%	moderate risk
3-4	20-40%	high risk
5 or more	40-80% 1-5% mortality	highest risk

**Total Risk Factor Score**

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