# "Hey... Clot It Out!"

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#### **Rob's Case**

A 44-year-old male presents to the ED complaining of pain (4/10 intensity) and swelling of his right leg, localized to the right calf region. The pain has worsened over the past two days, and has not been improving with conservative care at home (oral acetaminophen, massage, and warm compress). The patient denies any history of trauma or deep vein thrombosis. There is no personal or family history of thrombophilia. He denies recent travel, or infectious symptoms. Upon examination, the patient is in stable condition with no signs of respiratory distress. His vital signs, including temperature and oxygen saturation, are normal. Examination of the right leg demonstrates calf swelling, use prohibited pitting edema of the lower leg, and tenderness to wand print palpation in the calf and thigh.

Read on for more on Rob.

Questions and Answers

#### What is going on?

All patients who present with unilateral limb swelling or pain should be considered for possible deep vein thrombosis (DVT). Unilateral leg swelling can result from numerous possible causes; the differential diagnosis should include (but is not limited to): DVT, cellulitis, necrotizing fasciitis, trauma, venous insufficiency, lymphedema and a ruptured popliteal cyst. History and physical examination will help fine-tune the diagnosis; however, confirmation of the diagnosis with these alone is challenging. Objective clinical investigations play an important role in differentiating these conditions.

DVT occurs when the coagulation cascade is activated in an area of reduced blood flow,

resulting in the formation of a blood clot. These clots typically occur in the deep veins of the leg, and put the patient at an increased risk of pulmonary embolism. Virchow's triad of venous stasis, endothelial cell injury, and hypercoagulable state are considered the primary mechanisms responsible for DVT (Figure 1). Within each element of the triad, are various features that have been recognized as risk factors for DVT.USe

The significance of each of these risk factors Authoris a single in an individual patient is unclear; however, it is generally accorted the tive in nature. Studies have shown a correlation between the number of risk factors present and the prevalence of DVT in the ED. In patients with suspected DVT but no identified risk factors, DVT was confirmed in only 11%, compared to 50% of patients with three risk factors.





Table 1	
Well's Score	
Clinical Parameter	Score
Active Cancer (recent treatment or palliative)	1
Paralysis or Plaster Immobilization	1
Bedridden > 3 days or Major Surgery > 4 weeks	1
Localized Tenderness Along Distribution of	
Deep Venous System	1
Entire Leg Swelling	1
Calf Swelling > 3 cm vs. Asymptomatic Leg	1
Pitting Edema	1
Previous DVT	1
Collateral Superficial Veins	1
Alternative Diagnosis (as likely or greater than DVT)	-2
Well's Score calculated by summing all noted findings. Total score < 2: DVT "unlikely"	

Total score  $\geq$  2: DVT "likely"

## **2.** Clinical Presentation and Diagnostic Criteria

The classic symptoms of DVT include pain, swelling and redness in the affected limb. The Well's clinical decision instrument with validated scoring (Table 1) can be used to assess the probability of DVT in individual patients. The score allows clinicians to risk stratify patients as DVT 'likely' (score  $\geq 2$ ) or DVT 'unlikely' (score < 2). Further testing can follow a simple decision algorithm (Figure 2). The Well's clinical prediction guide incorporates risk factors, clinical signs, and the presence or absence of alternative diagnoses to predict the probability that a patient has DVT.

For patients deemed 'unlikely' to have DVT, the D-dimer test is used as a sensitive screening tool. D-dimer is a fibrin degradation product, present when a blood clot is broken down, and typically elevated in cases of acute thromboembolism. The D-dimer has excellent negative predictive value, with a negative result effectively ruling out DVT in a patient that is felt to be low risk. However, if the D-dimer is positive, the low risk patient requires further testing with ultrasound to confirm the presence of clot.

The predictive value of the D-dimer is less compelling for the DVT 'likely' or high risk group, and as such it should not be used for these cases. Instead, ultrasonography should be the first test. Ultrasound is highly sensitive and specific, particularly for proximal vein DVTs. The negative predictive value of ultrasound is very good, approaching 99% for proximal DVTs.

### **3.** What do we need to remember about D-dimer?

The D-dimer level can be elevated in many medical conditions; it is not limited to diseases with thrombosis. Possible causes of false positive D-dimer results are: trauma, hemorrhage, recent surgery, cancer, congestive heart failure and sepsis. D-dimer has a low specificity, and should therefore only be used to rule out DVT. Confirmation with ultrasound is required for patients with positive D-dimer tests, or in the DVT 'likely' patient group.

### What should be done for patients • with a DVT?

The primary objective in treating DVT is preventing the extension of the thrombus, thereby reducing the likelihood of embolization and pulmonary embolism. Other goals of therapy include reducing morbidity, minimizing the risk of post-thrombotic syndrome and reducing the risk of recurrent DVT. In the absence of significant comorbid illness, the treatment of acute DVT can be done safely as an outpatient. The mainstay of therapy is anticoagulation, and a 5-day course of low molecular weight heparin (LMWH) and a six month course of warfarin should be initiated on the first treatment day. The LMWH regimen should be extended until warfarin, an oral vitamin K antagonist, has reached a therapeutic level (INR between target values 2.0 and 3.0). In patients where anticoagulation is ineffective or contraindicated, a vena cava filter can be inserted.

Adjunctive therapies include analgesia, ambulation and compression stockings. Compression stockings have been useful in reducing the incidence of post-thrombotic syndrome by aiding circulation and reducing leg edema. Patients should be encouraged to ambulate as tolerated. Analgesia with NSAIDs or acetaminophen is recommended. Patients taking both anticoagulation and NSAIDs should be advised to monitor for signs and symptoms of gastrointestinal hemorrhage.

DVT diagnosis and treatment has many nuances. Some variations in clinical presentation are detailed in Table 2.  $D_k$ 

#### **Back To Rob**

Rob has a Well's Score of 3 (localized tenderness along distribution of deep venous system, pitting edema, and calf swelling greater than 3 cm compared to asymptomatic leg). DVT is considered 'likely' using the Wells score, thus D-dimer is not performed (poor utility in DVT 'likely' patients). A doppler ultrasound reveals a thrombus in the deep veins of his thigh.

Anticoagulation therapy is initiated in the ED. Rob is started on a five day course of subcutaneous LMWH and oral vitamin K antagonist (warfarin) for the next six months. He is counselled on indications to return promptly to the ED (signs of gastrointestinal bleeding, chest pain or symptomatic shortness of breath). He is instructed to follow up with his primary care practitioner for routine anticoagulation monitoring. Rob is also instructed to use analgesia as required for pain therapy, and he is told to use compression stockings for edema care.



Figure 2: Decision-making algorithm to diagnose suspected DVT

Table 2 DVT Special Scenarios		
Pulmonary Embolism (PE)	<ul> <li>Complication of underlying venous thrombosis</li> <li>Occurs when venous thrombosis migrates to pulmonary vasculature</li> <li>Significant morbidity/mortality</li> <li>Consider pulmonary involvement for patients with tachycardia and shortness of breath or chest pain</li> </ul>	
Distal DVT	<ul> <li>Treatment of DVT found on ultrasound to be below the knee is controversial</li> <li>Anticoagulation may be full dose Coumadin or simply anti-platelet therapy (ASA 325 mg p.o. daily); evidence-based guidelines are lacking</li> <li>NSAIDs and compression stockings should be used for symptom control</li> <li>Follow-up ultrasound after one week can be used to assess for propagation of clot</li> </ul>	
Phlegmasia Cerulea Dolens	<ul> <li>Described as "painful blue leg"</li> <li>Occurs with massive proximal thrombosis obstructing venous return</li> <li>Venous ischemia produces the painful cyanotic leg</li> <li>Emergency vascular surgery or thrombolytic therapy may save limbs</li> </ul>	
Upper Limb DVT	<ul> <li>Thrombosis may occur in upper limb</li> <li>Embolization to pulmonary system is possible</li> <li>Can be precipitated by occlusive force in thorax (pacemaker, PICC line, central venous catheter, malignancy)</li> <li>Treatment includes anticoagulation and removal of offending agent</li> </ul>	
Hypercoagulable State	<ul> <li>Various hematologic disorders may cause thrombophilia</li> <li>Protein C, Protein S, and Antithrombin III deficiency, Factor V Leiden, Anti-Phospholipid Antibodies</li> <li>Unprovoked DVT or PE should be investigated for hypercoagulable states</li> </ul>	
Malignancy	<ul> <li>In the appropriate clinical scenario, malignancy screening should be done for patients with unexplained DVT/PE</li> <li>Approximately 10% of patients with idiopathic DVT are diagnosed with a malignancy within five years</li> </ul>	
Pregnancy	<ul> <li>Mechanical and hormonal changes of pregnancy are pro-thrombotic</li> <li>D-dimer increases throughout the gravid period</li> <li>Negative predictive value of D-dimer is unknown in pregnancy</li> <li>Use of D-dimer is highly controversial and should be used judiciously in pregnancy</li> <li>Proceeding directly to ultrasound should be considered</li> <li>Anticoagulation should avoid use of vitamin K antagonists</li> </ul>	

Resources

1. Marx J, Hockberger R, Walls R. 2010. Rosen's Emergency Medicine: Concepts and Clinical Practice. 7th ed. St. Louis: Mosby.

 Schreiber D. Deep Vein Thrombosis and Thrombophlebitis [Internet]. Emedicine; [updated 2010 Jun 10; cited 2010 December 21]. Available from: <a href="http://emedicine.medscape.com/article/758140-overview">http://emedicine.medscape.com/article/758140-overview</a>

 Wells P, Owen C, Doucette S, et al. Does This Patient Have Deep Vein Thrombosis? JAMA 2006;295(2):199-207. **Mr. Heath** is a Medical Student at the University of Calgary, in Calgary, Alberta.

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