Venous Thromboembolism
Blood Clots in Veins and Lungs

FACULTY
Leslie L Davis, PhD, RN, ANP-BC, FPCNA, FAHA, FAANP
Associate Professor of Nursing
University of North Carolina Greensboro

Eva Kline-Rogers MS, NP
Cardiovascular Nurse Practitioner
Co-Director, MCORRP
University of Michigan Cardiovascular Center

STAFF
Michele McKay, MSN, APRN, FNP-C
Nurse Practitioner Education Specialist
American Association of Nurse Practitioners

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Healthcare Provider: Please use this table of contents to determine which sections of this educational tool to share with your patient.

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**What Is Venous Thromboembolism (VTE)?**

- **VTE** stands for venous thromboembolism
  - **VENOUS** = veins in the body
  - **THROMBUS** = blood clot
  - **EMBOLISM** = blood clot that is formed in one part of the body that travels to another part

- VTE is when blood clots form in the “deep” veins and get pushed against a blood vessel
- VTE is also when these clots break free and travel to the heart and lungs
  - *This is a life-threatening situation, which requires immediate medical attention.*
  - However, this condition is preventable and treatable

**Points to Emphasize:**

- Emphasize that VTE is common and affects men and women of all ages
- The incidence of VTE rises with age, so VTE is likely to be seen more frequently in clinical practice based solely on demographics alone
- Convey that patients may be asymptomatic or only realize, in retrospect, that they have experienced symptoms
- Reassure that VTE is treatable
  - Explain that there are newer medications, direct acting oral anticoagulants (DOACs), that are easy to use and work well
  - Relate that most patients, even those with pulmonary embolism (PE), can be treated on an outpatient basis

**Additional Information for Healthcare Provider:**

- VTE is a multifactorial disease that can result from a variety of conditions or scenarios
- VTE typically reflects the complex interplay of a patient’s risk for thrombosis based on inherited and acquired factors
  - Examples of acquired factors include: age, obesity, use of contraceptive hormones, etc.
- A complete medical history, including recent surgeries or procedures, is vital
- As VTE can arise from inherited conditions, it’s also important to obtain a complete family history
- Patients should be asked about lifestyle, including daily activities and recent travel
- Guidelines recommend DOACs over vitamin K antagonists or low molecular weight heparin (LMWH) for most patients

Types of VTE

- VTE has 2 main types
  - **Deep Vein Thrombosis (DVT)**
    When a blood clot forms in a large “deep” vein in the leg, pelvis, and sometimes arm
  - **Pulmonary Embolism (PE)**
    When a blood clot breaks off and travels in the blood to the lungs, causing a blockage there

Who Gets VTE?

- Up to 30% die within the first month of being diagnosed
- VTE is more common for women of child-bearing age than for men
- The risk of getting VTE increases with age for both men and women
- Having VTE increases the risk that VTE will occur again
  - Getting treatment (and following treatment instructions) for VTE reduces the risk that VTE will happen again

Points to Emphasize:

- Explain that VTE is common: 1 out of 1,000 Americans have VTE
- Point out that VTE, particularly DVT, is often undiagnosed
  - DVT accounts for ~2/3 of VTE
- Explain that, untreated, VTE has serious consequences, including pulmonary hypertension and death
  - 10%-30% of people die within the first month of diagnosis
  - Sudden death happens in about 25% of patients with PE
  - Half of patients with DVT develop post-thrombotic syndrome
- Emphasize that it’s critical that patients take VTE treatment as directed to reduce the risk of VTE recurrence
  - Half of patients with DVT with get PE
  - About one-third of patients with VTE will have recurrence within 10 years

Additional Information for Healthcare Provider:

- People of all races and ages can get VTE:
  - However, African-Americans and Caucasians are more likely to get VTE than Asian-Americans and Native Americans
  - Women are more likely to have VTE than men until age 45
  - After the age of 45, both men and women are more likely to have PE versus DVT

What Is Deep Vein Thrombosis (DVT)?
- DVT is when a blood clot (thrombus) forms in a large "deep" vein in the body
- DVT usually happens in the leg or thigh but it can happen in other places like the pelvis or arm

Why Do Blood Clots Form?
- Blood clots can form for different reasons:
  — Injury to the inside of a vein resulting from surgery or a serious accident
  — Sluggish blood flow due to lack of movement (sitting or lying down too long)
  — The body's response to inflammation
  — A blood disorder that runs in the family

What Are the Symptoms of DVT?
These symptoms can occur in the affected area of the body:
- Swelling
- Warmth or heat in the swollen area
- Tenderness or pain
- Redness or discoloration (bluish, purplish) of the skin

Points to Emphasize:
- Review the most common reasons for a blood clot to form:
  — Recent surgery, bone fracture, or serious accident often leads to DVT because of:
  — Injury to a deep vein’s inner lining
- Explain that lack of movement is a common cause of DVT for patients who:
  — Have had a surgery
  — Are medically ill or hospitalized
  — Have had a knee or hip replacement
  — Have had long flights or travel
- Relate that 5%-8% of Americans have hereditary factors that heighten their risk for thrombosis
  — Inform that testing for genetic factors is not recommended during the first 3 months of DVT treatment

Additional Information for Healthcare Provider:
- 50% of patients with symptomatic proximal DVT will develop PE
- Approximately half of patients with DVT are asymptomatic
- Often patients don’t realize that they have experienced lower extremity symptoms
- Symptoms should be correlated with potential precipitating factors, such as a long car ride, to assess the likelihood of DVT
- Inflammatory pathways are indicated in DVT, however, the precise interplay remains unclear
  — Symptoms of DVT are also classic symptoms of inflammation

Are There Risk Factors for DVT?

Almost anyone can get DVT but there are risk factors that make it more likely to happen:

- Serious injury to a vein
  - From a broken bone or muscle injury
- Slow blood flow
  - From limited movement when traveling
  - Being on prolonged bedrest
- Increased hormones in the blood
  - Taking hormone therapy
  - Pregnancy or recently given birth
- Some medical conditions
  - Heart or lung disease
  - Current or past cancer
  - Inflammatory bowel disease
- Other things related to the individual
  - Previous DVTs
  - Increased age
  - Excess body weight
  - Smoking
  - Having a central venous catheter in a large vein
  - Family history of blood-clotting disorders

Points to Emphasize:

- Review the most common risk factors for provoked DVT: Surgery, broken bone, long travel, and hormone therapy
- Explain that some DVTs are considered unprovoked because there is no clear cause
- Discuss that the duration of travel can affect VTE risk:
  - Flights lasting 4-8 hours double the incidence of VTE
  - Flights lasting 12-16+ hours have a VTE incidence of 5.3%-5.7%
  - VTE risk remains elevated for ~4 weeks after travel
- If applicable, advise that hormone therapy increases the relative risk of VTE by 2x-4x depending on estrogen dose, progestin type, and other factors
- Be mindful that active cancer increases VTE risk by 4x-6x
  - 10% of patients with unprovoked DVT have an undiagnosed malignancy

Additional Information for Healthcare Provider:

- In rare cases, pregnancy can lead to DVT
  - DVT risk is higher early in post-partum and continues through 12 weeks
- Inflammatory bowel disease raises the relative risk for recurrent VTE by 2.5x
- Obesity increases the relative risk for recurrent VTE by 1.6x
  - Where appropriate, weight loss should be included in overall treatment plans
- Factor V Leiden gene mutation is the most common inherited thrombophilia, accounting for 40% to 50% of cases

Diagnosing DVT
Healthcare providers (HCPs) use a combination of tests to determine whether someone has DVT:
- Physical exam
- Blood test (D-dimer blood test)
- Ultrasound
  - Ultrasound uses sound waves to create images of the flow of blood in the veins
  - Ultrasound is non-invasive, which means that imaging devices remain outside the body
- Other imaging tests with or without contrast dye
  - Computed tomography (CT) scan and magnetic resonance imaging (MRI) may be used to see veins and clots
  - Venography, which uses X-rays to take pictures of veins, is more invasive since it requires a continuous injection of contrast dye

Points to Emphasize:
- Complete a medical history and exam
- Perform a pre-test probability for DVT:
  - The Wells clinical prediction algorithm is the best known pre-test probability model
- Explain that a test for D-dimer in blood may be used in DVT diagnosis:
  - A low pre-test probability of DVT and a negative D-dimer test reliably excludes DVT
- Discuss that compression ultrasound is the first-line imaging test for intermediate or high pre-test probability for DVT
  - High sensitivity (89%-96%) and specificity (94%-99%)

Additional Information for Healthcare Provider:
- CT also has high sensitivity and specificity for DVT but is not typically used because of radiation exposure to patient
- Magnetic resonance imaging (MRI) is used infrequently because of the expense
- Venography is reserved for cases with high suspicion of DVT but other tests have not confirmed DVT or presented discordant results

### Wells Prediction Rule for DVT

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active cancer (or within 6 months of treatment)</td>
<td>1</td>
</tr>
<tr>
<td>Paralysis, paresis, or recent cast of lower limb</td>
<td>1</td>
</tr>
<tr>
<td>Recently bedridden for ≥ 3 days or major surgery within previous 12 weeks</td>
<td>1</td>
</tr>
<tr>
<td>Localized tenderness along deep venous system</td>
<td>1</td>
</tr>
<tr>
<td>Swollen leg</td>
<td>1</td>
</tr>
<tr>
<td>Calf swelling at least 3 cm larger than asymptomatic Side (measured 10 cm below tibial tuberosity)</td>
<td>1</td>
</tr>
<tr>
<td>Pitting edema confined to symptomatic leg</td>
<td>1</td>
</tr>
<tr>
<td>Collateral superficial veins (non-varicose)</td>
<td>1</td>
</tr>
<tr>
<td>Previously documented DVT</td>
<td>1</td>
</tr>
<tr>
<td>Alternative diagnosis as least as likely as DVT</td>
<td>-2</td>
</tr>
</tbody>
</table>

### Pre-Test Probability of DVT

<table>
<thead>
<tr>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
</tr>
<tr>
<td>Intermediate</td>
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<tr>
<td>High</td>
</tr>
</tbody>
</table>

DVT Treatment

- Most patients take an anticoagulant to treat DVT
- An anticoagulant is commonly called a “blood thinner”
  - Anticoagulants don’t actually thin the blood; they stop a blood clot from getting bigger and prevent future clots
- There are different types of anticoagulants to treat DVT
  - Some can be taken by mouth (a pill or tablet)
  - Some are injections (shots) into the skin or through an IV
- The type of anticoagulant prescribed depends on several things:
  - Size and location of the blood clot
  - Other medications that you are taking
  - How well your kidneys are working
  - Whether you are receiving treatment for cancer
- Your healthcare provider will work with you to decide which type of anticoagulant is best for you

Points to Emphasize:

- Discuss that most patients with DVT can be treated on an outpatient basis with an oral anticoagulant (OAC)
- Patients may ask why they need to take medication for their DVT; reiterate that 50% of patients with symptomatic proximal DVT will develop PE
  - If applicable, explain that acute extensive proximal DVT sometimes needs to be treated with inpatient parenteral anticoagulation
  - If parenteral anticoagulation is the initial treatment, inform that an overlap with OAC is needed for some OACs
- Emphasize that treatment duration depends on whether DVT is provoked or unprovoked

<table>
<thead>
<tr>
<th>OAC Duration</th>
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</thead>
<tbody>
<tr>
<td>DVT Type</td>
</tr>
<tr>
<td>Provoked</td>
</tr>
<tr>
<td>Unprovoked</td>
</tr>
<tr>
<td>Unprovoked</td>
</tr>
</tbody>
</table>

Additional Information for Healthcare Provider:

- For cancer-associated DVT, low molecular weight heparin is recommended
- If OAC is stopped in unprovoked DVT, aspirin is recommended

Is it treatment for acute DVT or prevention of recurrent VTE?
Is DVT provoked or unprovoked?
How is the patient’s kidney function?
What other medications is the patient taking?
Is cost an issue?
Would diet changes be an issue?
Can patient manage frequent blood draws?
Once daily or twice daily dosing?

Treatment should be personalized
Review these with your patient as you work together to develop a treatment plan

Sources:
**Oral Anticoagulants for DVT Treatment**

- There are several types of anticoagulants, which target different parts of the blood-clotting process (vitamin K, factor Xa, or direct thrombin).
- Medicines that block vitamin K have been used to treat DVT for many years
  - Routine blood tests are needed to make sure you have the right amount of medication in your blood
  - Their ability to work can be affected by what you eat
- Medicines that block factor Xa or directly block thrombin are newer treatments for DVT (Direct Oral Anticoagulant—DOAC)
- These new anticoagulants work as well as vitamin K treatments
  - Fewer blood tests are usually needed for these new anticoagulants compared to those focused on vitamin K
  - Their ability to work well does not depend on dietary restrictions
- Medical guidelines recommend patients take the new anticoagulants, when possible, instead of medicines that focus on vitamin K to treat DVT

**Points to Emphasize:**

- Explain that medical guidelines recommend a direct-acting oral anticoagulant (DOAC) over warfarin for most patients
- DOACs have been studied for VTE in many clinical trials:
  - They are just as effective as warfarin but have a lower risk of bleeding in the brain
  - Kidney function must be assessed prior to starting a DOAC
- Inform that dose adjustments are needed for some DOACs based on kidney function or other medications
- If applicable, explain that patients with certain conditions cannot take DOACs: Severe kidney disease, pregnancy, breastfeeding, and mechanical heart valve
- Ability to pay for, or insurance that permits, a DOAC is a consideration in treatment planning

**DOAC Dosing for VTE Treatment**

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing</strong></td>
<td>150 mg BID after ≥5 days parenteral anticoagulation</td>
<td>15 mg BID with food x 3 weeks then 20 mg QD with food</td>
<td>10 mg BID for 7 days, then 5 mg BID (with or without food)</td>
<td>60 mg QD after 5-10 days parenteral anticoagulation</td>
</tr>
<tr>
<td></td>
<td>DVT prevention after hip replacement surgery: 110 mg QD first day, 220 mg QD thereafter (May be taken with or without food)</td>
<td>DVT prevention after hip or knee replacement surgery: 10 mg QD with or without food</td>
<td>For secondary prevention, reduce dose to 2.5 mg BID after 6 months DVT prevention after hip or knee replacement surgery: 2.5 mg BID</td>
<td></td>
</tr>
<tr>
<td><strong>Kidney Function</strong></td>
<td>Do not use if CrCl &lt;30 mL/min</td>
<td>Do not use if CrCl &lt;30 mL/min</td>
<td>No dose adjustment/restriction</td>
<td>Use 30 mg QD for CrCl 15-50 mL/min Do not use if CrCl &lt;15 mL/min</td>
</tr>
<tr>
<td><strong>Drug-Drug Interactions and Dose Adjustments</strong></td>
<td>• Do not use with any P-gp inducer • Do not use with any P-gp inhibitor when CrCl&lt;50 mL/min</td>
<td>• Do not use with combined P-gp and strong CYP3A4 inhibitors or inducers</td>
<td>• Do not use with dual strong CYP3A4 and P-gp inducers • For dual strong CYP3A4 and P-gp inhibitors, decrease dose by 50% if dose ≥2.5mg BID • If dose is 2.5mg BID, avoid use with dual strong CYP3A4 and P-gp inhibitors</td>
<td>• Use 30 mg QD with use of certain P-gp inhibitors</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Must be kept in original container (can’t use pill box) Take with full glass of water Swallow whole, do not cut or crush</td>
<td>15 mg &amp; 20 mg must be taken with food (largest meal of day – typically the evening meal)</td>
<td></td>
<td>Use 30 mg QD if weight &lt; 60 kg</td>
</tr>
</tbody>
</table>


Other DVT Treatments

- In rare cases, a procedure may be needed to treat DVT:
  - When anticoagulants cannot be used
  - When anticoagulants don't work well enough to treat the clot
  - When someone has repeat DVTs
- These procedures may include:
  - Inserting a special filter inside the big vein that brings blood into the heart; the filter traps clots before they get to the lungs
  - Having surgery to remove the DVT
- Your healthcare provider will talk to you if a procedure is needed

Points to Emphasize:

- Explain that procedures are rarely performed to treat DVT
- Discuss that procedures are reserved for patients with acute DVT who cannot have anticoagulant therapy or for whom anticoagulants aren’t sufficient
- Review the rationale for a procedure:
  - Prevent development of PE
  - Stop clot extension
  - Reduce risk of late complications (e.g., post-thrombotic syndrome, chronic venous insufficiency, chronic thromboembolic pulmonary hypertension)

Additional Information for Healthcare Provider:

- If patients can take anticoagulants, inferior vena cava (IVC) filters are not recommended
  - If IVC filters are indicated, retrievable filters are preferred over permanent IVC filters
- Catheter-directed or intravenous (IV) thrombolysis, with or without mechanical clot removal, is typically reserved for acute DVT and imminent venous gangrene
Points to Emphasize:
- Reinforce that if they experience an adverse reaction to contact their healthcare provider before stopping OAC:
  —To address the adverse reaction or make changes to medication(s)
- Reinforce that not taking medication increases the risk DVT will recur
- Remind them that minor bleeding is normal and suggest ways to minimize minor bleeding:
  — Use a soft bristle toothbrush and gently “massage” gums
  — Use an electric razor
  — Avoid activities that could result in injury
- Reinforce that it’s OK to exercise and suggest:
  — Walking, swimming, and bike riding are safe (preferred)

Additional Information for Healthcare Provider:
- Patients who are taking aspirin or an antiplatelet in addition to an OAC should take a proton pump inhibitor (PPI) for prevention of GI bleeding

<table>
<thead>
<tr>
<th>Potential Treatment Adverse Reactions</th>
<th>Points to Emphasize:</th>
</tr>
</thead>
<tbody>
<tr>
<td>The most common type of adverse reaction of any anticoagulant is bleeding</td>
<td></td>
</tr>
<tr>
<td>Minor bleeding is common like nose bleeds or prolonged bleeding from a scrape or a cut</td>
<td></td>
</tr>
<tr>
<td>All medications have possible adverse reactions:</td>
<td></td>
</tr>
<tr>
<td>If you experience an adverse reaction, contact your healthcare provider</td>
<td></td>
</tr>
<tr>
<td>Your healthcare provider will let you know what changes, if any, you should make with your anticoagulant</td>
<td></td>
</tr>
<tr>
<td>You can minimize certain types of bleeding by:</td>
<td></td>
</tr>
<tr>
<td>Using a soft bristle toothbrush</td>
<td></td>
</tr>
<tr>
<td>Shaving with an electric razor rather than a blade</td>
<td></td>
</tr>
<tr>
<td>Avoid activities and sports that may cause injury (walking, swimming, and bike riding are safe activities)</td>
<td></td>
</tr>
<tr>
<td>Less common adverse reactions include nausea, diarrhea or constipation, headaches, dizziness, and rashes or itchy skin</td>
<td></td>
</tr>
</tbody>
</table>

Potential Adverse Reactions

<table>
<thead>
<tr>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI bleeding</td>
<td>GI bleeding</td>
<td>Hematuria</td>
<td>GI bleeding</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>Dyspepsia</td>
<td>Subconjunctival hemorrhage</td>
<td>Rash</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Back pain</td>
<td>Urinary tract infection</td>
<td>Abnormal liver tests</td>
</tr>
<tr>
<td>Epidural or spinal hematomas for patients undergoing neuraxial anesthesia or spinal puncture</td>
<td>Epidural or spinal hematomas for patients undergoing neuraxial anesthesia or spinal puncture</td>
<td>Epidural or spinal hematomas for patients undergoing neuraxial anesthesia or spinal puncture</td>
<td>Anemia</td>
</tr>
</tbody>
</table>

*Non-major bleeding.
Sources: Prescribing information package inserts.
Points to Emphasize:
- Reiterate that minor bleeding is common
  — 1 out of 4 patients will have a minor bleed
  — In most cases, not a cause for alarm
- Distinguish between “nuisance” bleeding and serious bleeding
- Patients can manage minor bleeding at home:
  — Demonstrate applying pressure to a wound
  — Demonstrate how to stop a nose bleed

Additional Information for Healthcare Providers:
- Most patients benefit from being given, or directed to, resources for managing minor bleeding
- Additional resources can be found at:
  — http://www.anticoagulationtoolkit.org/patients
  — http://www.clotconnect.org/patients/resources/brochures

Questions to ask if the patient reports bleeding:
- When was the last dose of anticoagulant?
- Are you or did you take any other medications such as aspirin or an NSAID?
- Which OAC are you taking?
- How long have you been bleeding?
  Has it stopped?
- What were you doing when you started bleeding?
- How severe is the bleeding?
Points to Emphasize:

- Discuss that not taking the prescribed medication increases the risk of VTE recurrence
  - Ease and convenience of DOACs may improve adherence
  - Explain that DOACs have rapid onset and offset, which increases the importance of adherence
- Assist patients with suggestions to improve adherence:
  - Take medication at the same time(s) every day
  - Set a calendar reminder on computer or alarm on mobile phone
- Reinforce that aspirin, ibuprofen, and other OTC pain relief medication can make the blood "more thin" and lead to bleeding
  - Acetaminophen can be taken for pain relief as long as there is no known liver disease
- Advise patients taking warfarin:
  - Avoid fluctuations in the amount of food high in vitamin K
  - Consistency is important to maintaining appropriate medication level
- Inform patients taking a DOAC
  - Apixaban and rivaroxaban require dose adjustments at 7 and 21 days, respectively
  - Avoid taking OTC medications and supplements, including vitamins, as they may make the anticoagulant less effective or may increase the risk of bleeding

Additional Information for Healthcare Provider:

- Many DOACs require dose adjustment for change in kidney function
  - Check baseline kidney function and every 6 months thereafter

Points to Emphasize:

- Emphasize that bleeding in the brain is rare with DOACs
  — Clinical trials have demonstrated that DOACs have significantly less intracranial hemorrhage (ICH) compared to warfarin
  — Since there are no head-to-head trials for DOACs in VTE, it’s unknown if 1 DOAC is superior to others on overall incidence of ICH
- Mention that when going to the ED, it’s important to tell medical staff which OAC they are taking
  — They should keep a card in their wallet that indicates which OAC
- Suggest they wear medical alert jewelry/tag with the name of their OAC in case of an emergency and they are unable to communicate
- Emphasize that symptoms of PE are a medical emergency and they should call 9-1-1

Additional Information for Healthcare Provider:

- ICH occurs in ~0.1% of cases with DOACs
- There is an approved reversal agent for dabigatran (idarucizumab) for use in emergency major bleeding
  — Other reversal agents for DOACs are in development
  — Fresh frozen plasma and prothrombin complex concentrate also can be used to treat major bleeds associated with DOACs
Points to Emphasize:

- Emphasize that the risk for recurrent DVT is highest in the first 3 months
- Obesity, combined with other risk factors, significantly increases DVT risk
  - Eating more fish and vegetables, and less red meat, can reduce VTE incidence by 30%-45%
- Reinforce that sluggish blood flow is a DVT risk factor, so frequent movement helps prevent DVT
  - Avoid sitting for long periods of time (>4 hours)
  - Stand and walk around every hour or so (if possible)
  - Flex muscles, do toe-to-heel exercises, and circle ankles if seated for long periods (travel)
- Regular exercise may reduce the risk of DVT
  - Take a brisk walk every day
- Compression stockings can reduce symptoms and improve blood flow although not recommended in acute DVT patients
  - Explain that it may reduce the risk of post-thrombotic syndrome
  - Offer tips to help the patient be compliant (compliance is often suboptimal)
  - Some patients don’t tolerate graduated compression

Additional Information for Healthcare Provider:

- DVT is high following hospitalization and surgery (particularly orthopedic and pelvic)
  - Up to 40% of general surgery patients, 40%-60% of orthopedic surgery patients

Points to Emphasize:

- Reiterate that PE can be life-threatening so it’s important to get treatment as soon as possible
  - 10%-30% of people die within the first month of diagnosis
- Perform risk assessment for acute massive PE
  - Criteria = Hypotension or heart rate <40 bpm
- If applicable, explain that low risk patients can be treated on outpatient basis

Additional Information for Healthcare Provider:

- Up to 25% of patients do not have sudden onset of symptoms
  - Symptoms may precede diagnosis by ≥2 weeks and get progressively worse (e.g., increasing fatigue)

### Pulmonary Embolism Overview

Pulmonary embolism (PE) occurs when a blood clot that has developed in the body breaks free, travels through the blood stream to the lungs, and blocks an artery in lungs

### Why Do Blood Clots Form?

- Blood clots can form for different reasons:
  - Injury to the inside of a vein resulting from surgery or a serious accident
  - Sluggish blood flow due to lack of movement (sitting or lying down too long)
  - The body’s response to inflammation
  - A blood disorder that runs in the family

### What Are the Symptoms of PE?

- Difficulty breathing that occurs suddenly
- Chest pain or discomfort, especially when taking a deep breath or coughing
- Irregular or faster-than-normal heart beat
- Sudden, severe back pain
- Unexplained dizziness or fainting
- Vomiting or coughing blood

### PE Severity Index (PESI) Score

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Age, in years</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>+60</td>
</tr>
<tr>
<td>Systolic BP &lt;100 mmHg</td>
<td>+30</td>
</tr>
<tr>
<td>History of cancer</td>
<td>+30</td>
</tr>
<tr>
<td>Arterial oxygen sat. &lt;90%</td>
<td>+20</td>
</tr>
<tr>
<td>Temp &lt; 36°C</td>
<td>+20</td>
</tr>
<tr>
<td>Respiratory rate ≥ 30/min</td>
<td>+20</td>
</tr>
<tr>
<td>Pulse ≥ 110/min</td>
<td>+20</td>
</tr>
<tr>
<td>Male sex</td>
<td>+10</td>
</tr>
<tr>
<td>Heart failure</td>
<td>+10</td>
</tr>
<tr>
<td>COPD</td>
<td>+10</td>
</tr>
</tbody>
</table>

#### HOW TO ARRIVE AT PESI SCORE:

Add points for each predictor that the patient has to the patient’s age

<table>
<thead>
<tr>
<th>Risk</th>
<th>PESI Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low:</td>
<td>≤65</td>
</tr>
<tr>
<td>Low:</td>
<td>65-85</td>
</tr>
<tr>
<td>Intermediate:</td>
<td>86-105</td>
</tr>
<tr>
<td>High:</td>
<td>106-125</td>
</tr>
<tr>
<td>Very high:</td>
<td>&gt;125</td>
</tr>
</tbody>
</table>

### Sources:

Are There Risk Factors for PE?
Almost anyone can get PE but there are risk factors that make it more likely to happen:

- Serious injury to a vein
  — From a broken bone, muscle injury, or surgery
- Some medical conditions
  — Uncontrolled high blood pressure or heart disease
  — Certain cancers (lung, ovarian, pancreatic)
  — Cancers that have spread to other parts of the body
- Lack of movement
  — Traveling more than 4 hours by car, plane, or bus
  — Prolonged bed rest
- Other things related to the individual
  — Previous DVTs or PE
  — Increased age
  — Excess body weight
  — Smoking
  — Woman with breast cancer who have taken certain chemotherapies (tamoxifen and raloxifene)
  — Family history of blood-clotting disorders

Points to Emphasize:
- Explain that ~95% of PE is from proximal DVT
- Ask about recent events that should raise suspicion of PE in symptomatic patients:
  — Surgery
  — Broken bone
  — Hip/knee replacement
  — Serious accident
  — Hospitalization
  — Myocardial infarction (MI)
  — Onset of heart failure (HF)
  — Air travel of ≥ 12 hours
- If applicable, discuss that cancer type, stage, and treatment affect PE risk
  — More aggressive cancers typically hold greater risk for PE
  — VTE likely in first 3 months of cancer diagnosis
  — VTE also more likely with Stage 3 and 4 cancers
  — Surgery and some chemotherapies increase the risk of PE

Additional Information for Healthcare Provider:
- Age increases the risk of PE for both men and women
- Inherited thrombophilia should be considered for patients with unprovoked PE
  — Factor V Leiden accounts for 40%-50% of inherited thrombophilia
  — Others include deficiencies in protein C or S or antithrombin
  — Testing for genetic factors is not recommended during the first 3 months of treatment

Diagnosing PE
Healthcare providers use a combination of tests to determine whether someone has PE:

- Physical exam
- Blood tests
- Pulse oximetry, which measures the percentage of oxygen in blood by inserting a finger in a special clip
- Your healthcare provider may order special non-invasive imaging tests:
  - Chest x-ray
  - Computed tomography (CT) scan
  - Magnetic resonance imaging (MRI) of the chest
- Some invasive imaging tests may be ordered to determine whether you have PE:
  - A special CT scan, called CT angiography, that takes pictures of the arteries in the lungs
  - An advanced test, called a ventilation-perfusion (V/Q) scan, which involves the injection of special materials to assess breathing as well as the circulation of blood in the lungs

### Wells Prediction Rule for PE

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active cancer (or within 6 months of treatment)</td>
<td>1</td>
</tr>
<tr>
<td>Recently bedridden for ≥ 3 days or major surgery within previous 12 weeks</td>
<td>1.5</td>
</tr>
<tr>
<td>Prior DVT or PE</td>
<td>1.5</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1</td>
</tr>
<tr>
<td>Heart rate ≥ 100 beats/min</td>
<td>1.5</td>
</tr>
<tr>
<td>PE assessed to be most likely diagnosis</td>
<td>3</td>
</tr>
<tr>
<td>Signs &amp; symptoms of DVT</td>
<td>3</td>
</tr>
</tbody>
</table>

### Pre-Test Probability of PE

<table>
<thead>
<tr>
<th>Risk</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low:</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Intermediate:</td>
<td>2-6</td>
</tr>
<tr>
<td>High:</td>
<td>&gt;6</td>
</tr>
</tbody>
</table>

Points to Emphasize:

- Perform a pre-test probability for PE
  - The Wells clinical prediction algorithm is frequently used
- Review the most commonly used imaging tests used in PE diagnosis
  - A CT scan is usually the first-line imaging tool used when PE is suspected
  - CT angiography uses a CT scanner to take pictures of the arteries in the lungs to detect PE
  - A ventilation-perfusion (V/Q) scan uses radioactive material to take images of blood flow in the lungs and measure breathing capacity
- Explain that a chest x-ray may be used to rule out other causes of symptoms, such as pneumonia

Additional Information for Healthcare Provider:

- If patient has a high pre-test probability for PE, it’s appropriate to skip D-dimer testing and proceed to imaging tests
- Pulmonary angiography is rarely used because of expense and right heart catheterization
- Use of magnetic resonance angiography (MRA) depends on facility protocols

Points to Emphasize:

- Discuss that treatment type depends on PE severity and the patient’s hemodynamic stability
- Explain that those with high PESI scores are typically treated in the hospital
  — If parenteral/IV therapy is used initially, there may be overlap with OAC treatment
- Reiterate that most patients can be treated on an outpatient basis with an anticoagulant, either an injectable or OAC
  — If applicable, explain that low molecular weight heparin is recommended for cancer-associated PE
- Inform that treatment duration depends on whether PE is provoked or unprovoked
  — For most patients with provoked PE, treatment duration is 3 months

Sources:
Points to Emphasize:
- Discuss that medical guidelines recommend a direct-acting oral anticoagulant (DOAC) over warfarin for most patients
  — DOACs are just as effective as warfarin but have a lower risk of bleeding in the brain
- Explain that kidney function must be tested prior to starting a DOAC
  — Dose adjustments of a DOAC may be needed based on kidney function or other medications
- If applicable, advise that patients with certain conditions can’t take DOACs: Severe kidney disease, pregnancy, breastfeeding, and mechanical heart valve
- Ability to pay for, or insurance that permits, a DOAC is a consideration in treatment planning


### DOAC Dosing for VTE Treatment

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing</strong></td>
<td>150 mg BID after ≥5 days parenteral anticoagulation</td>
<td>15 mg BID with food x 3 weeks then 20 mg QD with food</td>
<td>10 mg BID for 7 days, then 5 mg BID (with or without food)</td>
<td>60 mg QD after 5-10 days parenteral anticoagulation</td>
</tr>
<tr>
<td><strong>Kidney Function</strong></td>
<td>Do not use if CrCl &lt;30 mL/min</td>
<td>Do not use if CrCl &lt;30 mL/min</td>
<td>No dose adjustment/restriction</td>
<td>Use 30 mg QD for CrCl 15-50 mL/min</td>
</tr>
<tr>
<td><strong>Drug-Drug Interactions and Dose Adjustments</strong></td>
<td>• Do not use with any P-gp inducer</td>
<td>• Do not use with combined P-gp and strong CYP3A4 inhibitors or inducers</td>
<td>• Do not use with dual strong CYP3A4 and P-gp inducers</td>
<td>• Use 30 mg QD with use of certain P-gp inhibitors</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Must be kept in original container (can’t use pill box)</td>
<td>15 mg &amp; 20 mg must be taken with food (largest meal of day – typically the evening meal)</td>
<td>15 mg &amp; 20 mg must be taken with food (largest meal of day – typically the evening meal)</td>
<td>Use 30 mg QD if weight &lt; 60 kg</td>
</tr>
<tr>
<td></td>
<td>Take with full glass of water</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Swallow whole, do not cut or crush</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Points to Emphasize:

- Explain that procedures are usually reserved for massive PE
- Thrombolytics ("clot busters") quickly dissolve blood clots
  - Usually administered via IV in the emergency department
  - Some facilities perform catheter-directed thrombolytics
  - Excessive bleeding is a risk with thrombolytics
- Embolectomy (removal of clot) can be performed surgically or with a catheter

Additional Information for Healthcare Provider:

- ACCP guidelines suggest IV administration of thrombolytics be reserved for:
  - High-risk PE: Systemic hypotension and RV impairment
  - Some intermediate-risk PE: Normotensive, RV impairment
- Patients with intermediate-risk PE that are initially placed on OAC, not IV thrombolytics, should be monitored for deterioration
  - IV thrombolytics may be indicated

Potential Treatment Adverse Reactions

- The most common type of adverse reaction of any anticoagulant is bleeding
- All medications have possible adverse reactions
  - If you experience an adverse reaction, contact your healthcare provider
  - Your healthcare provider will let you know what changes, if any, you should make with your anticoagulant
- You can minimize certain types of bleeding by:
  - Using a soft bristle toothbrush
  - Shaving with an electric razor rather than a blade
  - Avoid activities and sports that may cause injury (walking, swimming and bike riding are safe activities)
- Less common adverse reactions include nausea, diarrhea or constipation, headaches, dizziness, and rashes or itchy skin

Points to Emphasize:
- Reinforce that if they experience any adverse reaction to contact their healthcare provider before stopping OAC:
  - To address the adverse reaction or make changes to medication(s)
- Reinforce that not taking medication increases the risk that PE will recur
- Remind them that minor bleeding is normal and suggest ways to minimize minor bleeding:
  - Use a soft bristle toothbrush and gently “massage” gums
  - Avoid activities that could result in falls, bumps, or bangs
- Reinforce that it’s OK to exercise and suggest:
  - Walking, swimming, and bike riding are safe (preferred)

Additional Information for Healthcare Provider:
- Patients who are taking aspirin or an antiplatelet in addition to an OAC should take a proton pump inhibitor (PPI) for prevention of GI bleeding

Potential Adverse Reactions*

<table>
<thead>
<tr>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI bleeding</td>
<td>GI bleeding</td>
<td>Hematuria</td>
<td>GI bleeding</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>Dyspepsia</td>
<td>Subconjunctival hemorrhage</td>
<td>Rash</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Back pain</td>
<td>Anemia</td>
<td>Abnormal liver tests</td>
</tr>
<tr>
<td></td>
<td>Urinary tract infection</td>
<td></td>
<td>Anemia</td>
</tr>
<tr>
<td>Epidural or spinal hematomas for</td>
<td>Epidural or spinal hematomas for</td>
<td>Epidural or spinal hematomas for</td>
<td>Epidural or spinal hematomas for</td>
</tr>
<tr>
<td>patients undergoing neuraxial</td>
<td>patients undergoing neuraxial</td>
<td>patients undergoing neuraxial</td>
<td>patients undergoing neuraxial</td>
</tr>
<tr>
<td>anesthesia or spinal puncture</td>
<td>anesthesia or spinal puncture</td>
<td>anesthesia or spinal puncture</td>
<td>anesthesia or spinal puncture</td>
</tr>
</tbody>
</table>

*Non-major bleeding.
Sources: Prescribing information package inserts.
Points to Emphasize:

- Reiterate that minor bleeding is common
  — 1 out of 4 patients will have a minor bleed
  — In most cases, not a cause for alarm
- Distinguish between “nuisance” bleeding and serious bleeding
- Patients can manage minor bleeding at home:
  — Demonstrate applying pressure to a wound
  — Demonstrate how to stop a nose bleed

Additional Information for Healthcare Provider:

- Most patients benefit from being given, or directed to, resources for managing minor bleeding
- Additional resources can be found at:
  — http://www.anticoagulationtoolkit.org/patients
  — http://www.clotconnect.org/patients/resources/brochures

Questions to ask if the patient reports bleeding:

- Which OAC are you taking?
- When was the last dose of anticoagulant?
- Are you or did you take any other medications such as aspirin or an NSAID?
- How long have you been bleeding? Has it stopped?
- What were you doing when you started bleeding?
- How severe is the bleeding?
Points to Emphasize:
- Discuss that not taking the prescribed medication increases the risk of VTE recurrence
  — Ease and convenience of DOACs may improve adherence
  — Explain that DOACs have rapid onset and offset, which increases the importance of adherence
- Assist patients with suggestions to improve adherence:
  — Take medication at the same time(s) every day
  — Set a calendar reminder on computer or alarm on mobile phone
- Reinforce that aspirin, ibuprofen, and other OTC pain relief medication can make the blood “more thin” and lead to bleeding
  — Acetaminophen can be taken for pain relief as long as there is no known liver disease
- Advise patients taking warfarin:
  — Avoid fluctuations in the amount of food high in vitamin K
  — Consistency is important to maintaining appropriate medication level
- Inform patients taking a DOAC
  — Apixaban and rivaroxaban require dose adjustments at 7 and 21 days, respectively
  — Avoid taking OTC medications and supplements, including vitamins, as they may make the anticoagulant less effective or may increase the risk of bleeding

Additional Information for Healthcare Provider:
- Many DOACs require dose adjustment for change in kidney function
  — Check baseline kidney function and every 6 months thereafter

Points to Emphasize:

- **Emphasize that bleeding in the brain is rare with DOACs**
  - Clinical trials have demonstrated that DOACs have significantly less intracranial hemorrhage (ICH) compared to warfarin
- **Mention that when going to the ED, it’s important to tell medical staff which OAC they are taking**
  - They should keep a card in their wallet that indicates which OAC
- **Suggest they wear medical alert jewelry/ tag with the name of their OAC in case of an emergency and they are unable to communicate**
- **Emphasize that symptoms of PE are a medical emergency and they should call 9-1-1**

Additional Information for Healthcare Provider:

- **ICH occurs in ~0.1% of cases with DOACs**
  - Since there are no head-to-head trials for DOACs in VTE, it’s unknown if one DOAC is superior to another with regard to ICH incidence
- **There is an approved reversal agent for dabigatran (idarucizumab) for use in emergency major bleeding**
  - Other reversal agents for DOACs are in development
  - Fresh frozen plasma and prothrombin complex concentrate also can be used to treat major bleeds associated with DOACs for major bleeding in patients taking DOACS

---

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Provider Resources

- Anticoagulationtoolkit.org (http://www.anticoagulationtoolkit.org/providers)
  — Provider resource on anticoagulation

  — Guidelines for pulmonary vascular

- Clot Connect (http://www.clotconnect.org/healthcare-professionals/hospital-associated-venous-thromboembolism-vte)
  — Resources and clinical care guidelines for VTE

Patient Resources

- American Heart Association (www.heart.org)
  — Patient information sheets and videos

- National Blood Clot Alliance (www.stoptheclot.org)
  — Patient information, stories, and discussion community

- Centers for Disease Control and Prevention (www.cdc.gov)
  — Venous Thromboembolism: Know the Risks, Signs & Symptoms of Blood Clots

- North American Thrombosis Forum (www.natfonline.org)
  — Patient information, support groups, and patient advocacy groups

anticoagulationtoolkit.org
  — Patient and provider resource on anticoagulation in English and Spanish