During the last two decades, considerable progress in technology and clinical research methods have led to advances in the approach to the diagnosis, prevention, and treatment of acute venous thromboembolism (VTE). Despite this, however, the diagnosis is often delayed and preventive methods are often ignored. Thus, the morbidity and mortality associated with VTE remain high. The therapeutic approach to acute VTE is discussed, with a particular focus on the intensive care unit (ICU) setting.

The primary goal of treatment of deep vein thrombosis (DVT) is the prevention of thrombus extension and pulmonary embolism (PE). Anticoagulation is the standard of care in patients with acute VTE, but other options in the treatment of PE include thrombolytic therapy, IVC filter placement, and surgical embolectomy. Each approach has specific indications as well as advantages and disadvantages. This article focuses on pharmacologic therapy. Table 1 lists evidence-based recommendations for VTE management as they apply to critical care. While recommendations include low molecular weight heparin (LMWH), these anticoagulants are less commonly used in the ICU because they are longer acting and less easily reversed, both of which are disadvantages in critically ill patients with acute VTE.

**ANTICOAGULATION**

The anticoagulation regimens for the treatment of DVT and uncomplicated PE are generally similar. Although anticoagulants do not directly dissolve preexisting clot, they prevent thrombus extension and indirectly decrease clot burden by allowing the
natural fibrinolytic system to proceed unopposed. When there is a strong clinical suspicion of PE, anticoagulation should be instituted immediately and before diagnostic confirmation, unless the risk of bleeding is deemed excessive.

**Unfractionated Heparin**

Therapy with unfractionated heparin (UFH) reduces the extension and recurrence of symptomatic proximal DVT as well as mortality in acute PE.1,2 UFH is usually delivered by continuous intravenous infusion and therapy is monitored by measurement of the activated partial thromboplastin time (aPTT).3 “Traditional” or physician-directed dosing of heparin often leads to subtherapeutic aPTT results, and validated dosing nomograms are generally favored.4,5 Nomogram dosing reduces the time to achieve therapeutic anticoagulation that may be important in reducing the risk of recurrent VTE.6 UFH should be administered as an intravenous bolus of 5000 U followed by a continuous infusion maintenance dose of 30,000 to 40,000 U every 24 hours (the lower dose being used if the patient is considered at risk for bleeding).7 Two alternative dosing regimens include a 5000-U bolus followed by 1280 U per hour, or a bolus of 80 U/kg followed by 18 U/kg per hour.4,5 After initiation, the aPTT should be measured at 6-hour intervals until it is consistently in the therapeutic range of 1.5 to 2.0 times control values, which corresponds to a heparin level of 0.2 to 0.4 U/mL as measured by protamine sulfate titration.3 Further adjustment of the UFH dose should be weight based. In patients deemed to have heparin resistance (requiring >35,000 U of UFH per day to achieve a therapeutic aPTT), antifactor Xa levels may be used to guide effective therapy.8

Upper extremity thrombosis is common in the critically ill patient and is most often related to a central venous catheter (CVC). These clots should generally be treated with anticoagulation, as with uncomplicated DVT, but with an additional emphasis on prompt catheter removal once the diagnosis is established. The risk of clot embolization that accompanies CVC extraction appears to be outweighed by the risk for chronic thrombotic complications and potential infection.

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**Table 1**

**Initial management of venous thromboembolism**

1. For patients with objectively confirmed PE, we recommend short-term treatment with SC LMWH (Grade 1A), IV UFH (Grade 1A), monitored SC UFH (Grade 1A), fixed-dose SC UFH (Grade 1A), or SC fondaparinux (Grade 1A).

2. Patients with acute PE should also be routinely assessed for treatment with thrombolytic therapy.

3. For patients in whom there is a high clinical suspicion of PE, we recommend treatment with anticoagulants while awaiting the outcome of diagnostic tests (Grade 1C).

4. In patients with acute PE, we recommend initial treatment with LMWH, UFH or fondaparinux for at least 5 days and until the INR is ≥2.0 for at least 24 hours (Grade 1C).

5. In patients with DVT or PE, thrombolytic treatment (Grade 2B) and mechanical (Grade 2C) or surgical embolectomy (Grade 2C) should be reserved for selected, highly compromised patients on a case-by-case basis and not performed routinely.

6. In the absence of contraindications, systemic thrombolytic therapy may be appropriate in selected patients with massive or submassive PE (Grade 2B).

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4 In general, standard UFH is favored in critically ill patients with acute VTE, based upon its shorter half-life and complete reversibility with protamine.
Multiple clinical trials have demonstrated that LMWH is at least as safe and effective as UFH for the treatment of acute VTE.\textsuperscript{9–11} LMWH preparations offer certain advantages over UFH, including greater bioavailability, longer half-life, lack of need for an intravenous infusion, and a more predictable anticoagulant response to weight-based dosing. LMWH can be administered subcutaneously once or twice per day and does not require monitoring of the aPTT. Monitoring antifactor Xa levels (typically 4 hours after injection) may be reasonable in certain settings such as morbid obesity, very small patients (<40 kg), pregnancy, renal insufficiency, or with unanticipated bleeding or recurrent VTE despite appropriate weight-based dosing.\textsuperscript{11–13} LMWH is often suitable for the outpatient treatment of DVT. However, because the anticoagulant effect of UFH is short acting and can be rapidly reversed, it is generally preferred over LMWH in the ICU, where patients are at increased risk for bleeding and may be undergoing fibrinolysis or need frequent procedures.

Fondaparinux is a highly bioavailable synthetic polysaccharide derived from heparin that is effective in the initial treatment and prophylaxis for VTE.\textsuperscript{14} Despite a more limited therapeutic niche, fondaparinux does have some advantages over LMWH. Fondaparinux does not appear to interact with platelet factor 4, so that heparin-induced thrombocytopenia (HIT), although possible, appears to be an exceedingly unlikely event. Its specificity for antifactor Xa allows for very predictable anticoagulant dosing. The anticoagulant effect of fondaparinux is not reversible. Again, in the ICU, UFH is more practical.

Warfarin

For the same reasons as LMWH and fondaparinux, warfarin therapy is less frequently used as therapeutic anticoagulation for ICU patients. Also, oral warfarin therapy must take into account many drug and food interactions, as well as genetic variations in drug metabolism. When warfarin is employed, administration should generally overlap with therapeutic heparin anticoagulation. In patients with thrombophilia (Protein C or S deficiency), warfarin may cause a transient hypercoagulable state due to the abrupt decline in vitamin K–dependent coagulation inhibitors. With warfarin therapy, it is recommended that a heparin preparation be employed for at least 5 days and maintained at a therapeutic level until two consecutive international normalized ratio (INR) values of 2.0 to 3.0 have been documented at least 24 hours apart.\textsuperscript{15} Warfarin may ultimately be appropriate for stable ICU patients with VTE once they are on heparin or LMWH therapy.

New Oral Anticoagulants

Advances in the understanding of thrombosis have led to the development of new anticoagulant therapies.\textsuperscript{16} Among these are dabigatran, a direct thrombin inhibitor, approved for use in the United States for prevention of stroke in atrial fibrillation, and rivaroxaban, a factor Xa inhibitor approved in the United States in mid-2011 for use in prevention of DVT in hip and knee replacement surgery.\textsuperscript{17} A number of other similar agents are being studied and may ultimately gain approval; apixaban, another Xa inhibitor, is included among these. A disadvantage of these newer agents includes lack of reversibility. In the ICU, careful control of anticoagulation generally mandates parenteral therapy. However, clinicians will increasingly encounter patients admitted to the ICU treated with these agents.
COMPLICATIONS OF ANTICOAGULATION

Hemorrhage and HIT are the major complications of anticoagulation. A pooled analysis of 11 clinical trials involving approximately 15,000 patients treated with either UFH or LMWH reported the frequency of major bleeding at 1.9% and a fatal hemorrhage rate of 0.2%. Protamine may rapidly neutralize the anticoagulant effect of UFH, although allergy, hypotension, and bradycardia are possible adverse reactions to its administration. The anticoagulant effect of LMWH is partly but not completely reversed by protamine.

Although anticoagulants clearly increase the risk of bleeding, a number of factors in the ICU also increase the risk. Placement and replacement of arterial and venous catheters, and sepsis with coagulopathy and thrombocytopenia are frequent in the ICU. Renal failure affects platelet function, and hepatic failure is associated with thrombocytopenia and clotting factor deficiency. Intracranial hemorrhage may occur due to trauma, status after procedures, or spontaneously. Retroperitoneal hemorrhage may occur due to femoral line placement and may remain undiagnosed until there is a significant drop in hematocrit.

HIT is an antibody-mediated adverse drug reaction that may lead to venous and arterial thrombosis. The principal clinical feature of HIT syndrome is the development of an otherwise unexplained drop in platelet count (absolute thrombocytopenia or >50% decrease if the platelet nadir remains in the normal range) after exposure to heparin. HIT generally develops 5 to 10 days after the initiation of heparin, but may occur earlier in the setting of prior heparin exposure. The frequency of HIT among patients treated with heparin is variable, and depends both on the preparation (bovine UFH > porcine UFH > LMWH) and the patient population (after surgery > medical > pregnancy). Although relatively infrequent, HIT is one of the most serious causes of thrombocytopenia in the ICU, and careful evaluation and consideration is warranted in this setting. Lepirudin (recombinant hirudin) and argatroban are direct thrombin inhibitors that make them unique in their ability to inactivate fibrin clot–bound thrombin. They are Food and Drug Administration (FDA)-approved parenteral drugs used for the treatment of heparin-induced thrombocytopenia (HIT). This topic is addressed in a separate article.

THROMBOLYTIC THERAPY

Thrombolytic agents may accelerate thrombus resolution by activating plasminogen to form plasmin, resulting in fibrinolysis as well as fibrinogenolysis. Given the paucity of data from randomized controlled trials, there remains considerable controversy regarding the indications for thrombolytic therapy because defining the patients in whom the benefit of a rapid reduction in clot burden outweighs the increased hemorrhagic risk may be difficult. The case for thrombolysis is the strongest in patients with massive PE complicated by shock, where the mortality rate may be more than 30%. Without question, thrombolytic therapy has been shown to accelerate clot lysis in PE and lead to a more rapid resolution of abnormal right ventricular (RV) dysfunction. Evidence of a survival benefit, however, has been generally lacking and would appear to depend on identifying a cohort of patients with a very high risk of dying if lysis is not accelerated. Accepting the limitations of registry data, a recent analysis of the International Cooperative Pulmonary Embolism Registry (ICOPER) nonetheless showed that thrombolysis for massive PE did not reduce mortality or the rate of recurrent PE at 90 days. Thrombolytic treatment in patients with acute submassive PE (echocardiographic evidence of RV dysfunction without hypotension) may offer no survival benefit but may prevent clinical deterioration and
the need for escalation of care. The decision for thrombolysis should be made on a case-by-case basis. Even in the setting of a relative contraindication, thrombolytic therapy may be reasonable when a patient is extremely unstable from life-threatening PE. It is likely that with submassive PE (ie, RV dysfunction without associated hypotension), more severe RV dysfunction, a positive troponin, severe hypoxemia, or more extensive residual DVT might be more important to study and to consider in predicting improved outcome with thrombolytics.

No clear data indicate that one thrombolytic agent is superior to another, and each of the FDA-approved thrombolytic agents is administered at a fixed dose, making measurements of coagulation unnecessary during infusion (Table 2). Tissue-type plasminogen activator (tPA) (2-hour infusion) is most commonly used. Shorter regimens and even bolus dosing may be favored in cases of unstable patients with massive PE. After infusion of thrombolytics, the aPTT should be measured and repeated at 4-hour intervals until the aPTT is less than twice the upper limit of normal, after which continuous intravenous UFH should be administered without a loading bolus dose. Some clinicians elect to simply continue heparin through the thrombolytic infusion. Although thrombolytics have been administered as local intrapulmonary arterial infusions, standard systemic intravenous therapy appears adequate in most cases.

Thrombolytic therapy is contraindicated in patients at high risk for bleeding (Table 3). Intracranial hemorrhage is the most devastating (and often fatal) complication of

### Table 2
FDA-approved thrombolytic therapy regimens for acute PE

<table>
<thead>
<tr>
<th>Drug</th>
<th>Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptokinase</td>
<td>250,000 U IV (loading dose during 30 minutes); then 100,000 U/h for 24 hours</td>
</tr>
<tr>
<td>Urokinase</td>
<td>2000 U/lb IV (loading dose during 10 minutes); then 2,000 U/lb/h for 12–24 hours</td>
</tr>
<tr>
<td>tPA</td>
<td>100 mg IV during 2 hours</td>
</tr>
</tbody>
</table>

* Not currently available in United States (since October 2010).
* The American College of Chest Physicians recommends shorter infusion regimens.

### Table 3
Contraindications to thrombolytic therapy in PE

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous hemorrhagic stroke</td>
<td>Bleeding diathesis/thrombocytopenia</td>
</tr>
<tr>
<td>Intracranial surgery or pathology, including trauma</td>
<td>Recent major trauma, internal bleeding, or nonhemorrhagic stroke</td>
</tr>
<tr>
<td>Active internal bleeding</td>
<td>Uncontrolled severe hypertension</td>
</tr>
<tr>
<td></td>
<td>Cardiopulmonary resuscitation</td>
</tr>
<tr>
<td></td>
<td>Recent major surgery</td>
</tr>
<tr>
<td></td>
<td>Pregnancy</td>
</tr>
</tbody>
</table>

Contraindications must be individualized based upon the minimal clinical trial data examining use in these settings. Less data are available with regard to risk involved with lower doses of thrombolytics delivered by catheter-based methods.

* This time frame may depend on the type of surgery, associated bleeding risk, and the level of critical illness.
thrombolytic therapy and occurs in 1% to 3% of patients. Invasive procedures should be minimized around the time of therapy to decrease the risk of bleeding. A vascular puncture above the inguinal ligament can lead to retroperitoneal hemorrhage that is often initially silent but may be life threatening. Recent data from a randomized trial by Wang and colleagues from China suggest that a lower dose of tPA (50 mg intravenously over 2 hours) is as effective but results in less bleeding. Thus, this may be considered, particularly in smaller patients.

Although there is some rationale for systemic thrombolytic therapy in DVT, such use is controversial and current guidelines are generally not supportive.

CATHETER-DIRECTED THERAPY FOR ACUTE PE

Background and Indications

Catheter-directed thrombolysis is increasingly common, and appears to be a safer alternative for the management of extensive, symptomatic DVT. A multicenter, prospective, randomized trial is currently in progress examining the efficacy of catheter-directed thrombolysis for acute DVT. The focus here is on catheter intervention for acute PE. As with systemic thrombolysis and surgical embolectomy, clinical trial data for percutaneous catheter intervention for acute PE are insufficient for formulating strong recommendations. The potential for an aggressive approach with perhaps a lower bleeding risk than with systemic thrombolysis, and the avoidance of cardiopulmonary bypass, makes these interventional approaches attractive to consider in patients who are compromised enough to meet criteria for thrombolysis or embolectomy. It was demonstrated more than two decades ago that simple infusion of a thrombolytic agent directly into the pulmonary artery offered no benefit over systemic delivery. A number of investigators have, however, found that directed mechanical techniques such as suctioning or fragmentation of large proximal emboli or the combined “pharmacomechanical” approach with intraembolic infusion of thrombolytics into such clots might be more beneficial and potentially safer than simply infusing thrombolytics via a peripherally vein or dripping them in the pulmonary artery. The 2008 ACCP recommendations did not discuss the various techniques, but suggested the use of interventional catheterization techniques if appropriate expertise is available, in selected highly compromised patients, unable to receive thrombolytic therapy because of bleeding risk, or whose critical status does not allow sufficient time for systemic thrombolytic therapy to be effective (Grade 2C). The European Society of Cardiology Task Force indicated that catheter embolectomy or fragmentation of proximal pulmonary arterial clots may be considered as an alternative to surgical treatment in high-risk PE patients when thrombolysis is absolutely contraindicated or has failed.

The presence of a contraindication to systemic thrombolytics increases the practicality of a catheter-directed approach. Of 304 patients from the ICOPER who received PE systemic thrombolysis, 66 (22%) experienced major bleeding and 9 (3%) experienced intracranial bleeding. No randomized controlled clinical trials have compared surgical embolectomy with catheter embolectomy.

The General Approach to Catheter-directed Embolectomy

Acute PE should be proven before the procedure; alternatively, pulmonary arteriography can be performed in the interventional radiology laboratory in a patient with a high clinical suspicion for PE who is compromised enough to prompt consideration of aggressive treatment. In patients with massive PE, the amount of contrast material should be reduced. Because most compromised patients have large proximal emboli, manual injection of 10 to 15 mL of contrast agent is generally sufficient to document
emboli. Power injection of larger volumes is generally not necessary and may be dangerous in the setting of RV failure.

Specific Catheter-directed Techniques

Regardless of which approach is utilized, expertise is required. In most hospitals, the interventional radiologist performs catheter-directed embolectomy, and the level of interest and clinical expertise is variable. The optimal embolectomy catheter should be easily maneuverable; effective at suctioning, fragmenting, or infusing a thrombolytic agent; and safe, so as to avoid pulmonary arterial/cardiac perforation and mechanical hemolysis. Catheter-based techniques that have been clinically reported are listed in Table 4.

Aspiration embolectomy with the Greenfield suction embolectomy catheter (Boston Scientific/Meditech; Watertown, MA, USA) was introduced in 1969 and it remains the only device with FDA approval specifically for acute PE. This 10 French steerable catheter has a 5 to 7 mm plastic suction cup at its tip. Major disadvantages are that it requires insertion by venotomy via the femoral or jugular vein without a guidewire and the device and embolus must be removed as a unit through the surgical venotomy. This device has been utilized effectively in extracting pulmonary emboli in up to 83% of patients, with significant improvement in hemodynamics and a 30-day mortality rate of 30%. Other techniques have been studied including catheter-directed embolus fragmentation, and catheter-based rheolysis (each of which can be done with or without thrombolytic therapy), as well as simple catheter-directed thrombolysis.

The latter simply requires an infusion catheter and involves intrapulmonary administration of a relatively low dose of a thrombolytic agent without the addition of a mechanical device. This has been reported in a number of small studies and case reports. As described, simply infusing thrombolytics directly into the pulmonary

<table>
<thead>
<tr>
<th>Technique</th>
<th>Examples</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration</td>
<td>Greenfield embolectomy device</td>
<td>Boston Scientific, Watertown, MA, USA</td>
</tr>
<tr>
<td>Fragmentation</td>
<td>Rotatable pigtail catheter</td>
<td>Cook Europe, The Netherlands</td>
</tr>
<tr>
<td>Mechanical rheolysis</td>
<td>Amplatz device</td>
<td>Bard-Microvena, White Bear Lake, MN, USA</td>
</tr>
<tr>
<td></td>
<td>Aspirex device</td>
<td>Straub Medical, Wangs, Switzerland</td>
</tr>
<tr>
<td></td>
<td>Hydrolyser</td>
<td>Cordis, Warren, NJ, USA</td>
</tr>
<tr>
<td></td>
<td>AngioJet</td>
<td>Possis, Minneapolis, MN, USA</td>
</tr>
<tr>
<td></td>
<td>Oasis device</td>
<td>Boston Scientific, Watertown, MA, USA</td>
</tr>
<tr>
<td>Local thrombolysisa</td>
<td>tPA (alteplase)</td>
<td>Genentech (Roche), Switzerland</td>
</tr>
<tr>
<td></td>
<td>Urokinase (Abbokinase)</td>
<td>Abbott Laboratories, Abbott Park, IL, USA</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>Ultrasoundb</td>
<td>EKOS Corporation, Bothell, WA, USA</td>
</tr>
<tr>
<td>Angioplasty/stenting</td>
<td>Wallstent</td>
<td>Schneider Europe AG, Bülach, Switzerland;</td>
</tr>
<tr>
<td></td>
<td>Gianturco Z stents</td>
<td>Cook Europe, Bjaerskov, Denmark</td>
</tr>
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Table 4: Catheter-based embolectomy techniques that can be considered in acute PE

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<td>Gianturco Z stents</td>
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There are no large, randomized trials favoring one technique over another.

a More than 100 cases reported.
b More than 20 cases reported.
artery appears to offer no benefit over infusion via a peripheral vein. The technique necessitates the positioning of an infusion catheter within the embolus, with injection of a bolus of thrombolytic drug followed by a continuous infusion. The dose of intrapulmonary thrombolytic agents has generally been approximately 10% to 20% of the systemic dose. Short-acting, newer generation fibrinolytic drugs such as reteplase (2.5–5 U) or tenecteplase (5–10 mg) may be considered. A pulmonary arteriogram showing extensive proximal PE with a guide catheter and infusion catheter in place is shown in Fig. 1.

The mechanism for ultrasound-accelerated thrombolysis involves microstreaming and acoustic dispersion, which generates streams of high flow, consequently enhancing lytic drug infusion.

There are no large, randomized controlled studies favoring one of these catheter-directed techniques over another.

Balloon Angioplasty and Stenting Procedures

Successful balloon angioplasty of obstructing acute emboli has been reported. Too few data are available to speculate on efficacy and safety, and based on other available catheterization techniques, it is rarely undertaken. Pulmonary artery stents have been used successfully in the experimental animal model setting as well as in isolated patient cases. Self-expanding stents have been utilized in the setting of massive PE and failed thrombolysis or failed thrombus fragmentation. It would appear that this approach, if used, should be reserved only in cases of acute PE in which other aggressive measures have failed.

Complications of Catheter-directed Embolectomy

Complications include those resulting from anticoagulation and contrast dye, including bleeding, contrast-induced nephropathy, and anaphylactic reactions to iodine contrast. Potential vascular access complications include bleeding, hematoma,
arteriovenous fistula, and pseudoaneurysm. Major bleeding rates range from 0% to 17%. Arrhythmias may occur when the catheter is advanced through the right heart. The most serious complication resulting from these catheter-directed procedures is perforation or dissection of a pulmonary artery, causing massive pulmonary hemorrhage and immediate death. The risk of perforation increases with smaller vessels. Other serious complications include pericardial tamponade. To minimize the risk of perforation or dissection, embolectomy procedures should be performed only in the main and lobar pulmonary artery branches and not attempted in smaller vessels.

Device-related complications include hemorrhage and mechanical hemolysis. Acute pancreatitis due to mechanical hemolysis has been reported.

**Summary: Catheter-directed Embolectomy**

There are no randomized, controlled data supporting catheter-based techniques but they have been used clinically with some success. Overall success rates range from 67% to 100% but these rates suffer from significant potential reporting bias. Catheter-based embolectomy can be considered when systemic thrombolysis and surgical embolectomy cannot be performed. It is impossible to determine superiority of a particular catheter technique owing to the lack of comparative and randomized trial data. Many of the patients treated with fragmentation techniques have also received thrombolytic agents, making results and comparisons more difficult. At present, local expertise and familiarity with a particular device should guide the clinician when a catheter-based procedure appears indicated.

**PULMONARY EMBOLECTOMY**

Given the high morbidity and mortality associated with it, surgical embolectomy has traditionally been a treatment of last resort, often reserved for patients with documented central PE and refractory cardiogenic shock despite maximal therapy. Contemporary studies show improved outcomes and suggest that emergency surgical pulmonary embolectomy may be feasible in carefully selected patients and with an experienced surgical team. Percutaneous embolectomy is a less well studied method of improving hemodynamics by reducing the burden of central pulmonary artery thromboembolism.

**SPECIAL THERAPEUTIC CONSIDERATIONS: MASSIVE PE**

In cases of massive PE, therapy should progress as directed by clinical likelihood and the diagnostic results. The mere suspicion of massive PE warrants immediate supportive therapy. Cautious infusion of intravenous saline may augment preload and improve impaired right ventricular function. Dopamine or norepinephrine are favored if hypotension remains, and combination therapy with dobutamine may boost right ventricular output, although it may exacerbate hypotension. Supplemental oxygen and mechanical ventilation may be instituted as needed to support respiratory failure. Anticoagulation, thrombolytic therapy, and pulmonary embolectomy should be considered and employed as previously described.

**VTE IN PREGNANCY**

VTE is a leading cause of death in pregnant women, in whom the age-adjusted risk of VTE is at least five times higher compared to nonpregnant women. DVT is more common during the antepartum period, and occurs with almost equal frequency in each of the three trimesters. In contrast, the incidence of PE is highest immediately post partum.
Therapy for VTE in pregnancy is generally similar to that in nonpregnant women, except that warfarin should be avoided because it is teratogenic and can cross the placental barrier. LMWH has been shown to be safe in pregnancy and is often preferred as long-term therapy; warfarin may be employed post partum. Because of the risk of maternal hemorrhage and fetal demise, pregnancy is a relative contraindication for thrombolytic therapy. That being considered, controlled trials are lacking in this area, and thrombolysis may rarely be appropriate in cases of massive PE with hemodynamic instability.

NONTHROMBOTIC PULMONARY EMBOLI

While thrombotic PE is the most common and important syndrome in which embolic material reach the pulmonary circulation, nonthrombotic pulmonary emboli may rarely occur in several clinical settings. Fat embolism syndrome most commonly occurs after blunt trauma complicated by long-bone fractures. The characteristic findings of dyspnea, axillary and subconjunctival petechiae, and alterations in mental status generally occur between 12 and 48 hours after the primary event. Cardiopulmonary derangement is likely due to venous obstruction by neutral fat and to a vasculitis and capillary leak syndrome caused by free fatty acids. The diagnosis of fat embolization syndrome is clinical; however, the identification of fat droplets within cells recovered by bronchoalveolar lavage may be helpful. Therapy is generally prophylactic and supportive as more specific treatments have shown limited benefit. The syndrome is usually mild and the prognosis good.

Amniotic fluid embolism is uncommon but it represents one of the leading causes of maternal death in the United States. The condition may occur during or shortly after either spontaneous or cesarean delivery and there exist no consistent identifiable risk factors. Clinical hallmarks include hypoxemia, cardiogenic shock, altered mental status, and disseminated intravascular coagulation. The diagnosis is clinical and the therapy is primarily supportive. Amniotic fluid embolism is frequently fatal and permanent neurologic deficits are found in 85% of survivors. Septic emboli generally present as multiple bilateral peripheral nodules that are often poorly marginated and may have cavitary changes. Right-sided endocarditis and septic thrombophlebitis are the most common sources of septic pulmonary emboli. Fever, chills, and pleuritic chest pain may be more impressive in septic PE as compared with bland PE. Treatment centers on appropriate antibiotic therapy, but anticoagulation and surgical management may be appropriate in certain circumstances. Intensive care is generally not necessary unless there is significant associated cardiopulmonary dysfunction.

Air embolism requires communication between the air and the venous circulation when venous blood pressure is below atmospheric pressure. Predisposing settings include invasive procedures, barotrauma, and the use of indwelling catheters. Air may gain entry into the arterial system by incomplete filtering of a large air embolus by the pulmonary capillaries or via paradoxical embolization through a patent foramen ovale. The clinical picture is critical in raising the suspicion of disease because the signs and symptoms are generally nonspecific. Immediate Trendelenburg and left lateral decubitus positioning may open an obstructed RV outflow tract, and air aspiration should be attempted if there is a central venous catheter in the right atrium. Administration of 100% oxygen aids in bubble reabsorption via nitrogen washout, and hyperbaric oxygen therapy may also be beneficial.

Other miscellaneous nonthrombotic causes of pulmonary vascular obstruction include cancer cells, schistosomal disease, and inorganic injected material such as talc crystals or various fibers.
REFERENCES


