angiography, and assessment of the lower extremities for deep vein thrombosis DVT by CT or ultrasound. The Christopher study showed that the frequency of a subsequent venous thromboembolism diagnosis in the 3 months after a negative CT angiogram is low (level 1 evidence).

However, for pregnant women or individuals with renal insufficiency or iodinated contrast dye allergy, the $\dot{V}/\dot{Q}$ scan provides an alternative approach. The $\dot{V}/\dot{Q}$ scan compares lung ventilation by radiolabeled tracer gas with lung perfusion by radiolabeled micro-occlusive particles. The usefulness of the $\dot{V}/\dot{Q}$ scan depends greatly on the pretest probability of the disease, which depends on the expertise of the clinician and his or her level of certainty. A *high-probability* $\dot{V}/\dot{Q}$ scan is characterized by lobar or multilobar perfusion defects that coincide with areas of normal or relatively normal ventilation, and it is more than 90% accurate in diagnosing pulmonary embolism. A *normal* $\dot{V}/\dot{Q}$ scan shows no perfusion or ventilation defects and excludes pulmonary embolism in essentially all cases. However, the test is less reliable when interpreted as *low, intermediate,* or *indeterminate* probability. In these circumstances, pulmonary embolism is likely in 4% to 66% of patients, and further testing is necessary for an accurate diagnosis of pulmonary embolism.

Pulmonary arteriography may be considered in patients without contraindications to the procedure when other tests are inconclusive and a high likelihood of pulmonary embolism exists. Although the rate of complications of pulmonary angiography is low with experienced operators, the complications can be significant, ranging from pulmonary hypertension and sudden death to idiosyncratic hypersensitivity reactions to the dye. Pulmonary angiography is now performed infrequently, and operator experience may be limited in certain care settings.

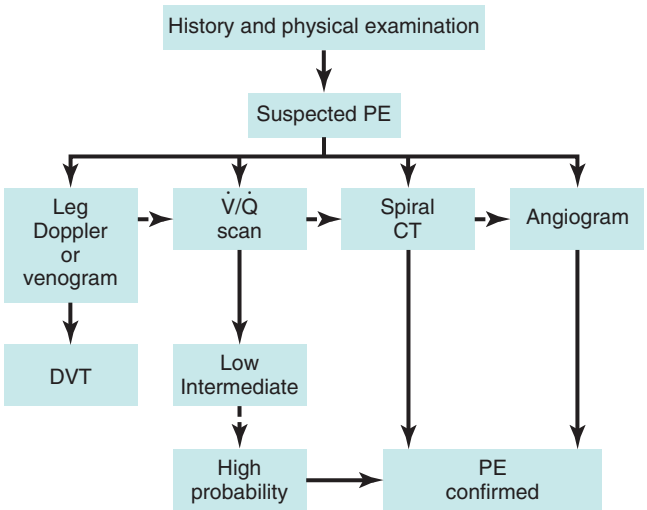

FIGURE 18-1 Tests commonly used in the evaluation of patients who may have pulmonary embolism (PE). Doppler ultrasound or venogram of the leg is useful to evaluate deep vein thrombosis (DVT). Ventilation-perfusion ($\dot{V}/\dot{Q}$) scans are most useful when they are normal or show lesions that suggest an intravascular clot. Unfortunately, these findings are lacking for many patients, who require further investigation. Spiral computed tomography (CT) has high sensitivity and specificity and allows for evaluation of thoracic structures and the vasculature. Angiography is considered the gold standard, but it often is not needed if other noninvasive tests are used alone or in combination.

Treatment

Pulmonary embolism is treated with supportive measures directed at sustaining organ function, such as fluid replacement for hypotension and mechanical ventilation for respiratory failure. Mechanical dislodgement of a pulmonary artery clot, such as by surgical thromboembolectomy, a procedure with a high mortality rate, requires a high level of expertise. Thromboembolectomy is used only for long-standing proximal clots that are complicated by chronic pulmonary hypertension (e.g., group 4 pulmonary hypertension, chronic thromboembolism syndrome) (level 1 evidence).

For acute pulmonary embolism, medical treatments are preferred, and they are used to prevent further clotting or to dissolve an existing clot. Anticoagulation with regular (intravenous) or low-molecular-weight (subcutaneous) heparin (LMWH) is recommended in the acute setting for patients without major contraindications to anticoagulation (e.g., upper gastrointestinal bleeding, hemorrhagic stroke) (level 1 evidence).

For patients with a contraindication to anticoagulation, an inferior vena cava filter should be placed. These filters have been shown to reduce pulmonary embolism occurrence in the setting of proximal deep vein thrombosis in patients also receiving anticoagulation (level 1 evidence). However, the devices carry a long-term risk of increased rates of deep vein thrombosis (level 1), and they do not clearly affect mortality if anticoagulation is also used. The use of thrombolytic medications (e.g., tissue plasminogen activator) is usually reserved for patients at increased risk for death as a result of circulatory collapse caused by obstruction to the flow in large or multiple pulmonary vessels (level 2-2).

Oral anticoagulation therapy with vitamin K antagonists such as warfarin is initiated, overlapping initially with acute heparin or LMWH treatment, and it is continued for at least 3 months to allow resolution of venous clot and to prevent recurrence (level 1 evidence). However, for venous thromboembolism occurring in the setting of active malignancy, LMWH treatment is superior to warfarin in preventing recurrent events (level 1).

Novel oral anticoagulants (i.e., factor Xa inhibitors) have been shown to be noninferior to the combination of heparin and warfarin therapy and to require less testing for safety (level 1 evidence). Patients who have had an unprovoked pulmonary embolism (i.e., pulmonary embolism not associated with a known temporary risk factor such as surgery) have a high rate of recurrence. For these patients, whether therapy should be routinely extended beyond 3 months is unclear, as is the optimal method of anticoagulation, and decisions regarding extended anticoagulation in this setting may be based on clinical factors such as bleeding risk or risk stratification with D-dimer testing.

PROSPECTUS FOR THE FUTURE

Translational research has markedly enhanced understanding of the pathogenesis of pulmonary hypertensive disorders, and this has resulted in the development of therapies that increase quality of life and improve mortality. There is heightened appreciation of the role of increased vascular cell proliferation in pulmonary vascular remodeling. In particular, abnormal proliferation of pulmonary endothelial cells and development of plexiform lesions have suggested that PAH may be a disease of hyperproliferative pulmonary endothelium.