new symptoms should be evaluated. Of these, some 10% will eventually manifest an underlying disorder.

Myocardial Vessel Vasospasm

Excessive constriction of coronary arteries or myocardial arterioles may cause ischemia, and persistent vasospasm can even cause myocardial infarction. In addition to intrinsic hyper-reactivity of medial smooth muscle cells, as described earlier for primary Raynaud disease, high levels of vasoactive mediators can precipitate prolonged myocardial vessel contraction. Such agents can be endogenous (e.g., epinephrine released by pheochromocytomas) or exogenous (cocaine or phenylephrine). Elevated thyroid hormone causes a similar effect by increasing the sensitivity of vessels to circulating catecholamines, while autoantibodies and T cells in scleroderma (Chapter 6) can cause vascular instability and vasospasm. In some individuals, extreme psychological stress and the attendant release of catecholamines can lead to pathologic vasospasm.

When vasospasm of cardiac arterial or arteriolar beds (so-called *cardiac Raynaud*) is of sufficient duration (20 to 30 minutes), myocardial infarction occurs. Elevated levels of catechols also increase heart rate and myocardial contractility, exacerbating ischemia caused by the vasospasm. The outcome may be sudden cardiac death (likely caused by a fatal arrhythmia) or an ischemic dilated cardiomyopathy, so-called *Takotsubo cardiomyopathy* (also called "broken heart syndrome" because of the association with emotional duress; Chapter 12). Histologically, acute cases may show microscopic areas of necrosis characterized by myocyte hypercontraction (*contraction band necrosis*); subacute and chronic cases may exhibit microscopic foci of granulation tissue and/or scar.

Veins and Lymphatics

Varicose veins and phlebothrombosis/thrombophlebitis together account for at least 90% of clinical venous disease.

Varicose Veins

Varicose veins are abnormally dilated, tortuous veins produced by prolonged, increased intraluminal pressure leading to vessel dilation and incompetence of the venous valves. The *superficial veins* of the upper and lower leg are commonly involved because venous pressures in these sites can be markedly elevated (up to 10 times normal) by prolonged dependent posture. Roughly 10% to 30% of adults develop lower extremity varicosities; obesity and pregnancy increase risk by creating mass effects that impede venous drainage. A familial predilection to varicose veins reflects defective venous wall development.

Clinical Features. Incompetence of the venous valves leads to stasis, congestion, edema, pain, and thrombosis. Secondary tissue ischemia results from chronic venous congestion and poor vessel drainage leading to *stasis dermatitis* (also called "brawny induration"; the brawny color comes from the hemolysis of extravasated red cells) and ulcerations; poor wound healing and superimposed infections are common additional complications. *Notably, embolism from these superficial veins is very rare, in contrast to the relatively frequent thromboembolism that arises from thrombosed deep veins* (see later and Chapter 4).

Varicosities in two other sites also deserve mention:

- *Esophageal varices.* Liver cirrhosis (less frequently, portal vein obstruction or hepatic vein thrombosis) causes portal vein hypertension (Chapter 18). Portal hypertension leads to the opening of portosystemic shunts that increase blood flow into veins at the gastroesophageal junction (forming *esophageal varices*), the rectum (forming *hemorrhoids*), and periumbilical veins of the abdominal wall (forming a *caput medusa*). Esophageal varices are the most important since their rupture can lead to massive (even fatal) upper gastrointestinal hemorrhage.
- *Hemorrhoids* can also result from primary varicose dilation of the venous plexus at the anorectal junction (e.g., through prolonged pelvic vascular congestion due to pregnancy or straining to defecate). Hemorrhoids are uncomfortable and may be a source of bleeding; they can also thrombose and are prone to painful ulceration.

Thrombophlebitis and Phlebothrombosis

Thrombophlebitis and phlebothrombosis are largely interchangeable designations for venous thrombosis and inflammation; involvement of deep leg veins accounts for more than 90% of cases. The periprostatic venous plexus in males and the pelvic venous plexus in females are additional sites, as are the large veins in the skull and the dural sinuses (especially in the setting of infection or inflammation). Portal vein thrombosis may occur with peritoneal infections (peritonitis, appendicitis, salpingitis, and pelvic abscesses), as well as certain thrombophilic conditions associated with platelet hyperactivity (e.g., polycythemia vera, Chapter 13).

Prolonged immobilization resulting in venous stasis is the most important risk factor for deep venous thrombosis (DVT) in the lower extremities. This can occur with extended bedrest or even sitting during lengthy trips in an airplane or automobile; postoperative patients are also at risk, in part, due to immobilization. Clearly, DVT can develop in the setting of any other mechanical factor that slows venous return; these include congestive heart failure, pregnancy, and obesity.

Systemic hypercoagulability, including genetic hypercoagulability syndromes (Chapter 4), *often also plays a role in potentiating thrombophlebitis.* In patients with cancer, particularly adenocarcinomas, hypercoagulability occurs as a paraneoplastic syndrome related to elaboration of procoagulant factors by tumor cells (Chapter 7). In this setting, venous thromboses classically appear in one location, disappear, and then occur in another site, so-called *migratory thrombophlebitis (Trousseau sign).*

Thrombi in the legs tend to produce few, if any, reliable signs or symptoms. Indeed, local manifestations, including vein dilation, edema, cyanosis, heat, erythema, or pain may be entirely absent, especially in bedridden patients. In some cases, pain can be elicited by pressure over affected veins, squeezing the calf muscles, or forced dorsiflexion of the foot (*Homan sign*). However, these findings are