notoriously unreliable; hence their absence does not exclude a diagnosis of DVT.

Pulmonary embolism is the most common serious clinical complication of DVT, and is often the first manifestation of thrombophlebitis (Chapter 4). It results from fragmentation or detachment of the venous thrombus. Depending on the size and number of emboli, the outcome can range from no symptoms to death.

Superior and Inferior Vena Cava Syndromes

The *superior vena cava syndrome* is usually caused by neoplasms that compress or invade the superior vena cava, such as bronchogenic carcinoma or mediastinal lymphoma. Less commonly, other space occupying lesions in the mediastinum such as aortic aneurysms can be the cause of compression. The resulting obstruction produces a characteristic clinical complex including marked dilation of the veins of the head, neck, and arms with cyanosis. Pulmonary vessels can also be compressed, inducing respiratory distress.

The *inferior vena cava syndrome* can be caused by neoplasms that compress or invade the inferior vena cava (IVC) or by thrombosis of the hepatic, renal, or lower extremity veins that propagates cephalad. Certain neoplasms—particularly hepatocellular carcinoma and renal cell carcinoma—show a striking tendency to grow within veins, and these can ultimately occlude the IVC. IVC obstruction induces marked lower extremity edema, distention of the superficial collateral veins of the lower abdomen, and—with renal vein involvement—massive proteinuria.

Lymphangitis and Lymphedema

Although primary disorders of lymphatic vessels are extremely uncommon, secondary processes frequently develop in association with inflammation or malignancies.

Lymphangitis represents acute inflammation elicited by the spread of bacterial infections into lymphatics; group A β-hemolytic streptococci are the most common agent, although any microbe can be causal. Affected lymphatics are dilated and filled with an exudate of neutrophils and monocytes; the infiltrates can extend through the vessel wall, and in severe cases, can produce cellulitis or focal abscesses. Lymphangitis is manifested by red, painful subcutaneous streaks (the inflamed lymphatics), and painful enlargement of the draining lymph nodes *(lymphadenitis)*. If bacteria are not successfully contained within the lymph nodes, subsequent escape into the venous circulation can result in bacteremia or sepsis.

Primary lymphedema can occur as an isolated congenital defect (simple congenital lymphedema) or as the familial *Milroy disease (heredofamilial congenital lymphedema)*, which results in lymphatic agenesis or hypoplasia. *Secondary* or *obstructive lymphedema* stems from blockage of a previously normal lymphatic; examples include:

- Malignant tumors obstructing lymphatic channels or the regional lymph nodes
- Surgical procedures that remove regional groups of lymph nodes (e.g., axillary lymph nodes in radical mastectomy)
- Postirradiation fibrosis
- Filariasis
- Postinflammatory thrombosis and scarring

Regardless of the cause, lymphedema increases the hydrostatic pressure in the lymphatics distal to the obstruction and causes increased interstitial fluid accumulation. Persistent edema and subsequent deposition of interstitial connective tissue leads to a *peau d'orange* (orange peel) appearance of the overlying skin, seen typically in skin overlying breast cancers after the draining lymphatics are clogged with tumor cells; ulcers may develop due to inadequate tissue perfusion. Rupture of dilated lymphatics (e.g., secondary to obstruction from a tumor) leads to milky accumulations of lymph designated as *chylous ascites* (abdomen), *chylothorax*, and *chylopericardium*.

Vascular Tumors

Tumors of blood vessels and lymphatics constitute a spectrum from benign hemangiomas to intermediate lesions that are locally aggressive but infrequently metastasize, to rare, highly malignant angiosarcomas (Table 11-4). Congenital or developmental malformations and nonneoplastic reactive vascular proliferations (e.g., *bacillary angiomatosis*) can also present as tumor-like lesions. Because the growth of vascular neoplasms appears to depend on the same signaling pathways that regulate angiogenesis, treatment with inhibitors of blood vessel formation (antiangiogenic therapy) is a rational therapy that is being explored.

Vascular neoplasms can be endothelial-derived (e.g., hemangioma, lymphangioma, angiosarcoma) or can arise from cells that support or surround blood vessels (e.g., glomus tumor, hemangiopericytoma). Primary tumors of large vessels (aorta, pulmonary artery, and vena cava) are mostly connective tissue sarcomas. Although a benign well-differentiated hemangioma can usually be readily discriminated from an anaplastic high-grade angiosarcoma, the distinction between benign and malignant can

Table 11-4 Classification of Vascular Tumors and Tumor-Like Conditions

Benign Neoplasms, Developmental and Acquired Conditions
Hemangioma
Capillary hemangioma
Cavernous hemangioma
Pyogenic granuloma
Lymphangioma
Simple (capillary) lymphangioma
Cavernous lymphangioma (cystic hygroma)
Glomus tumor
Vascular ectasias
Nevus flammeus
Spider telangiectasia (arterial spider)
Hereditary hemorrhagic telangiectasis (Osler-Weber-Rendu disease)
Reactive vascular proliferations
Bacillary angiomatosis
Intermediate-Grade Neoplasms
Kaposi sarcoma
Hemangioendothelioma
Malignant Neoplasm
Angiosarcoma
Hemangiopericytoma