TABLE 301-1 DISEASES OF THE AORTA: ETIOLOGY AND ASSOCIATED FACTORS

- Aortic aneurysm
  - Degenerative
    - Aging
    - Cigarette smoking
    - Hypercholesterolemia
    - Hypertension
    - Atherosclerosis
  - Genetic or developmental
    - Marfan's syndrome
    - Loeys-Dietz syndrome
    - Ehlers-Danlos syndrome type IV
    - Turner's syndrome
    - Familial
    - Bicuspid aortic valve
  - Chronic aortic dissection
  - Aortitis (see below)
  - Infective (see below)
  - Trauma
- Acute aortic syndromes (aortic dissection, acute intramural hematoma, penetrating atherosclerotic ulcer)
  - Degenerative disorders (see above)
  - Genetic/developmental disorders (see above)
  - Hypertension
  - Aortitis (see below)
  - Pregnancy
  - Trauma
- Aortic occlusion
  - Atherosclerosis
  - Thromboembolism
- Aortitis
  - Vasculitis
    - Takayasu's arteritis
    - Giant cell arteritis
  - Rheumatic
    - HLA-B27–associated spondyloarthropathies
    - Behçet's syndrome
    - Cogan's syndrome
    - Idiopathic aortitis
  - Infective
    - Syphilis
    - Tuberculosis
    - Mycotic (*Salmonella,* staphylococcal, streptococcal, fungal)

The most common pathologic condition associated with degenerative aortic aneurysms is *atherosclerosis*. Many patients with aortic aneurysms have coexisting risk factors for atherosclerosis (Chap. 291e), as well as atherosclerosis in other blood vessels.

Medial degeneration, previously designated *cystic medial necrosis,* is the histopathologic term used to describe the degeneration of collagen and elastic fibers in the tunica media of the aorta as well as the loss of medial cells that are replaced by multiple clefts of mucoid material, such as proteoglycans. Medial degeneration characteristically affects the proximal aorta, results in circumferential weakness and dilation, and leads to the development of fusiform aneurysms involving the ascending aorta and the sinuses of Valsalva. This condition is particularly prevalent in patients with Marfan's syndrome, Loeys-Dietz syndrome, Ehlers-Danlos syndrome type IV (Chap. 427), hypertension, congenital bicuspid aortic valves, and familial thoracic aortic aneurysm syndromes; sometimes it appears as an isolated condition in patients without any other apparent disease.

Familial clusterings of aortic aneurysms occur in 20% of patients, suggesting a hereditary basis for the disease. Mutations of the gene that encodes fibrillin-1 are present in patients with Marfan's syndrome. Fibrillin-1 is an important component of extracellular microfibrils, which support the architecture of elastic fibers and other connective tissue. Deficiency of fibrillin-1 in the extracellular matrix leads to excessive signaling by transforming growth factor β (TGF-β). Loeys-Dietz syndrome is caused by mutations in the genes that encode TGF-β receptors 1 (*TGFBR1*) and 2 (*TGFBR2*). Increased signaling by TGF-β and mutations of *TGFBR1* and *TGFBR2* may cause thoracic aortic aneurysms. Mutations of type III procollagen have been implicated in Ehlers-Danlos type IV syndrome. Mutations of *SMAD3*, which encodes a downstream signaling protein involved with TGF binding to its receptors, have been described in a syndrome of thoracic aortic aneurysm; craniofacial, skeletal, and cutaneous anomalies; and osteoarthritis. Mutations of the genes encoding the smooth muscle–specific alpha-actin (*ACTA2*), smooth muscle cell–specific myosin heavy chain 11 (*MHC11*), and myosin light chain kinase (*MYLK*) and mutations of *TGFBR2* and *SMAD3* have been reported in some patients with nonsyndromic familial thoracic aortic aneurysms.

The infectious causes of aortic aneurysms include syphilis, tuberculosis, and other bacterial infections. *Syphilis* (Chap. 206) is a relatively uncommon cause of aortic aneurysm. Syphilitic periaortitis and mesoaortitis damage elastic fibers, resulting in thickening and weakening of the aortic wall. Approximately 90% of syphilitic aneurysms are located in the ascending aorta or aortic arch. *Tuberculous aneurysms* (Chap. 202) typically affect the thoracic aorta and result from direct extension of infection from hilar lymph nodes or contiguous abscesses as well as from bacterial seeding. Loss of aortic wall elasticity results from granulomatous destruction of the medial layer. A *mycotic aneurysm* is a rare condition that develops as a result of staphylococcal, streptococcal, *Salmonella*, or other bacterial or fungal infections of the aorta, usually at an atherosclerotic plaque. These aneurysms are usually saccular. Blood cultures are often positive and reveal the nature of the infective agent.

Vasculitides associated with aortic aneurysm include Takayasu's arteritis and giant cell arteritis, which may cause aneurysms of the aortic arch and descending thoracic aorta. Spondyloarthropathies such as ankylosing spondylitis, rheumatoid arthritis, psoriatic arthritis, relapsing polychondritis, and reactive arthritis (formerly known as Reiter's syndrome) are associated with dilation of the ascending aorta. Aortic aneurysms occur in patients with Behçet's syndrome (Chap. 387), Cogan's syndrome, and IgG4-related systemic disease. Aortic aneurysms also result from idiopathic aortitis. *Traumatic aneurysms* may occur after penetrating or nonpenetrating chest trauma and most commonly affect the descending thoracic aorta just beyond the site of insertion of the ligamentum arteriosum. Chronic aortic dissections are associated with weakening of the aortic wall that may lead to the development of aneurysmal dilatation.

THORACIC AORTIC ANEURYSMS

The clinical manifestations and natural history of thoracic aortic aneurysms depend on their location. Medial degeneration is the most common pathology associated with ascending aortic aneurysms, whereas atherosclerosis is the condition most frequently associated with aneurysms of the descending thoracic aorta. The average growth rate of thoracic aneurysms is 0.1–0.2 cm per year. Thoracic aortic aneurysms associated with Marfan's syndrome or aortic dissection may expand at a greater rate. The risk of rupture is related to the size of the aneurysm and the presence of symptoms, ranging approximately from 2–3% per year for thoracic aortic aneurysms <4.0 cm in diameter to 7% per year for those >6 cm in diameter. Most thoracic aortic aneurysms are asymptomatic; however, compression or erosion of adjacent tissue by aneurysms may cause symptoms such as chest pain, shortness of breath, cough, hoarseness, and dysphagia. Aneurysmal dilation of the ascending aorta may cause congestive heart failure as a consequence of aortic regurgitation, and compression of the superior vena cava may produce congestion of the head, neck, and upper extremities.

A chest x-ray may be the first test that suggests the diagnosis of a thoracic aortic aneurysm (Fig. 301-1). Findings include widening