younger than 17 years of age, the annual incidence of HSP is approximately 20 per 100,000. Males are more commonly affected than females (approximately 2:1), and HSP occurs more frequently during the winter and spring months.

Medium Vessel Vasculitis

Polyarteritis nodosa (PAN) is a medium vessel vasculitis that is characterized by arterial aneurysmal and stenotic lesions of muscular arteries, often located at segmental and branch points. In contrast to small vessel vasculitis, renal involvement in PAN is not characterized by glomerulonephritis but rather by aneurysms and stenoses of renal arteries that may result in hypertension or renal dysfunction or both. PAN may occur either as a primary vasculitis or secondary to viral infections, mainly hepatitis B or C, or human immunodeficiency virus (HIV). Determining the incidence of this vasculitis is difficult, because PAN and MPA were not differentiated until 1994.

Kawasaki disease is a medium vessel vasculitis most often seen in boys younger than 5 years of age. It is the second most common vasculitis in childhood after HSP, accounting for about 23% of all childhood vasculitis cases. In the United States, the annual incidence in children younger than 5 years old is 20 per 100,000.

Large Vessel Vasculitis

Giant cell arteritis (GCA), also known as temporal arteritis, is the most common form of vasculitis in adults. It is a large vessel vasculitis that typically affects patients of Eastern European descent, with a mean age at onset of 70 to 75 years. It affects women more commonly than men (3:1). About 40% of patients with GCA have the related condition, polymyalgia rheumatica (PMR), which is characterized by subacute onset of aching and stiffness in the muscles of the neck, shoulder girdle, and hip girdle. However, only 10% to 25% of patients with PMR have or will develop GCA.

Takayasu's arteritis (TAK), or "pulseless disease," is a rare large vessel vasculitis that was initially identified in young women from East Asia in the 1800s but is now described worldwide. In adults, the female-to-male ratio is about 8:1, with an average age at diagnosis in the mid-20s.

PATHOLOGY

For most of the systemic vasculitides, the etiology and pathogenesis of disease are largely unknown. It has been proposed that a number of diverse mechanisms contribute to the development of vascular inflammation and subsequent injury on the background of genetic susceptibility (Fig. 81-2). Proposed triggers of disease include infection and environmental exposures (e.g., chemicals, pollutants). For most vasculitides, these associations remain speculative.

Humoral and cellular immune responses, cytokine release, chemokine activation, and immune complex deposition are important in disease pathogenesis. Normal protective and repair processes in the vessel can also contribute to injury and ischemia. For example, after injury, cellular migration and proliferation occurring as part of vessel repair can result in intimal hyperplasia, and the procoagulant milieu that is protective against hemorrhage may lead to thrombosis and vessel occlusion. Impairment of blood flow in injured vessels results in tissue ischemia and

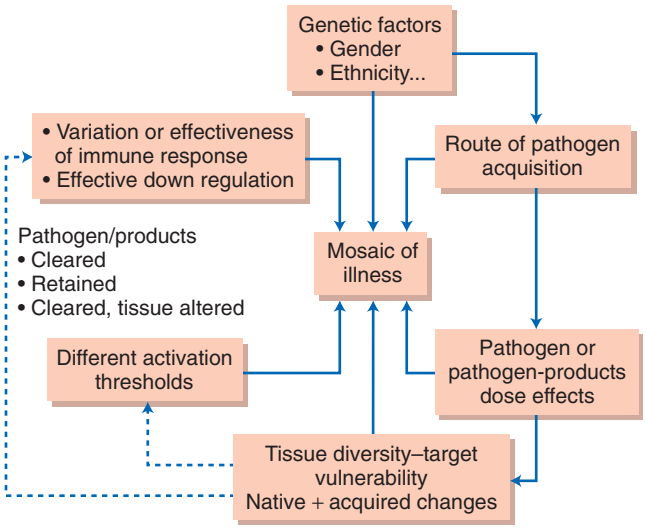

FIGURE 81-2 Factors affecting disease vulnerability and expression.

damage. The degree of blood flow impairment varies along a broad spectrum of severity and may depend on the type of vasculitis as well as the size and location of the vessels involved.

Among the AAVs, the pathology of GPA is typically characterized by necrotizing granulomatous inflammation of small blood vessels supplying the upper and lower respiratory tract. In both GPA and MPA, renal pathology shows a pauci-immune necrotizing crescentic glomerulonephritis. In EGPA, there is a strong association with allergic and atopic disorders, including allergic rhinitis, nasal polyposis, and asthma. Approximately 70% of patients with EGPA have elevated levels of immunoglobulin E (IgE) and eosinophilia of peripheral blood and tissue. Small vessel histopathology typically reveals transmural eosinophilic infiltrates with scattered plasma cells and lymphocytes and extravascular granulomas.

The pathology of HSP is characterized by a leukocytoclastic vasculitis of small vessels with IgA deposition seen on immunofluorescence. Various infectious agents, including bacteria and viruses, have been reported as triggers for HSP.

The pathology of GCA and TAK are very similar histologically. In both, large vessels demonstrate a lymphoplasmacytic inflammatory infiltrate. Giant cells and granulomas may be seen in the media, and lumen-occlusive arteritis may occur from exuberant intimal hyperplasia. Additional pathologic features include proliferation of vascular smooth muscle cells and fragmentation of the internal elastic lamina.

CLINICAL PRESENTATION AND DIAGNOSIS

Clinical manifestations of the systemic vasculitides are diverse and differ not only among disorders but also among patients. Typical clinical manifestations associated with the size of the affected vessel are detailed in Table 81-1.

Small Vessel Vasculitis

ANCA-Associated Vasculitides

GPA most commonly affects the sinuses and upper airway, the lungs, and the kidneys, although almost any organ system may be affected. Chronic refractory sinusitis, nasal crusting and ulcers,