Vasculitis Syndromes
Paul J. Allegretti and Keri Robertson

KEY POINTS

- A patient’s combined genetic predisposition and regulatory mechanisms control expression of the immune response to antigens.
- Negative test results for antineutrophil cytoplasmic antibodies do not exclude disease, nor do positive results indicate a specific syndrome.
- The combination of clinical, laboratory, biopsy, and radiographic findings usually points to a specific vasculitis syndrome.
- Definitive diagnosis of a vasculitic syndrome depends on demonstration of vascular involvement and may be accomplished by biopsy or angiography.
- Differentiation of primary and secondary vasculitis is essential because their pathophysiologic, prognostic, and therapeutic aspects differ.
- The diagnosis of vasculitis should be considered in any patient with febrile illness and organ ischemia without other explanation.

EPIDEMIOLOGY

In 1994, the Chapel Hill Consensus Conference named and defined the 10 most common forms of vasculitis according to vessel size (Box 110.1). This system is based on the fact that different forms of vasculitis attack different vessels.1,2 These criteria were established to differentiate specific types of vasculitis, but they are often used as diagnostic criteria. The vasculitic syndromes feature a great deal of heterogeneity and overlap, which leads to difficulty with regard to categorization.3 In addition, many patients display incomplete manifestations, thereby adding to the confusion. Emergency physicians should keep in mind the fact that nature does not always follow the patterns and artificial boundaries drawn by classification systems.4

TEMPORAL (GIANT CELL) ARTERITIS

Temporal, or cranial or giant cell, arteritis is a granulomatous large vessel vasculitis that affects the extracranial branches of the carotid artery, particularly the temporal artery. Females are affected two to four times more often than males, and the disorder usually occurs in patients older than 55 years. Its incidence is estimated to be 1 per 3000 individuals older than 50. Up to 59% of the time it is associated with polymyalgia rheumatica, which is characterized by pain and stiffness in the shoulders, neck, and pelvis, along with an elevated erythrocyte sedimentation rate (ESR).

TAKAYASU ARTERITIS

Takayasu arteritis (also referred to as aortic arch syndrome) is a granulomatous large vessel vasculitis that primarily affects the aorta, its branches, and the pulmonary and coronary arteries.1 This rare disease predominantly affects women in the 20- to 30-year-old age group and is more common in Asian and South American women. Mortality ranges from 10% to 75%.

POLYARTERITIS NODOSA

Polyarteritis nodosa is a multisystem necrotizing vasculitis of small- and medium-sized muscular arteries. Visceral and renal artery involvement is characteristic.3 The mean age at onset is 50 years, although it can occur at any age. Men, women, and racial groups are all affected equally. This rare disease affects fewer than 10 per 1 million persons worldwide.

KAWASAKI DISEASE

Kawasaki disease, also referred to as mucocutaneous lymph node syndrome, primarily affects children younger than 5 years. This acute systemic vasculitis is a febrile multisystem disease that is the leading cause of acquired heart disease in children in the United States.1 The disease occurs worldwide but predominates in Japan, Asia, and the United States.

WEGENER GRANULOMATOSIS

Wegener granulomatosis is a vasculitis of the upper and lower respiratory tract and kidneys. A systemic small vessel vasculitis is also involved. It may occur at any age but has a mean onset at 40 years of age. Wegener granulomatosis affects men and women equally and involves whites more commonly than blacks.

CHURG-STRAUSS SYNDROME

Churg-Strauss syndrome is a rare small vessel vasculitis manifested by fever, asthma, and hypereosinophilia.1 This disease is also referred to as allergic angiitis and granulomatosis,
Vasculitis, also known as the vasculitides or the vasculitis syndromes, is a clinicopathologic process that results in inflammation and damage to blood vessels. Cell infiltration with inflammatory modulators causes swelling and changes in function of the vessel walls. This compromises vessel patency and integrity and leads to tissue ischemia, necrosis, and bleeding. Because most forms of vasculitis are not restricted to a certain vessel type or organ, the syndromes are broad and heterogeneous. Vasculitis is a systemic multiorgan disease, so the findings may be dominated by a single or a few clinical organ manifestations.

Vasculitis can be separated into two broad categories. It may develop de novo as a primary manifestation of vessel inflammation without a known cause. Alternatively, it may be a secondary manifestation of an underlying disease or exposure to a drug. Distinction between primary and secondary vasculitis is essential because their pathophysiologic, prognostic, and therapeutic aspects differ.

Management of patients with the secondary forms of vasculitis needs to be directed toward the underlying disease process. The primary vasculitides, once thought to be uncommon, have proved to be much less rare than previously estimated, and awareness of the incidence and prevalence of all forms of vasculitis has recently increased.

This chapter focuses on the primary or de novo vasculitides. The pathophysiology of the vasculitis syndromes remains poorly understood, with variation between disease states contributing to the difficulty. It is also not clear why vasculitis develops in certain patients in response to antigenic stimuli and not in others; however, in each disease state, immunologic mechanisms play an active role in mediating blood vessel inflammation.

Blood vessels can be damaged by three potential mechanisms (Box 110.2). Particularly when it affects the lungs. It is estimated that about 3 million people are affected worldwide, with an equal incidence between sexes. It is seen at all ages with a mean onset at 44 years of age.

**HENOCH-SCHÖNLEIN PURPURA**
Henoch-Schönlein purpura (anaphylactoid purpura) is a small vessel vasculitis that predominantly affects children and is characterized by palpable purpura, arthralgia, glomerulonephritis, and gastrointestinal symptoms. Though also seen in adults, 75% of cases occur in children younger than 8 years. It is more common than other vasculitides and affects males more frequently than females in a 2:1 ratio. It has a peak incidence in winter and spring and usually follows an upper respiratory tract infection.

**CUTANEOUS LEUKOCYTOCLASTIC VASCULITIS**
This disorder, also called hypersensitivity vasculitis or predominantly cutaneous vasculitis, involves small vessels of the skin and is the most common vasculitic manifestation seen in clinical practice. It has an incidence of 15 per million. In about 70% of cases, cutaneous vasculitis occurs along with an underlying process such as infection, malignancy, medication exposure, and connective tissue disease or as a secondary manifestation of a primary systemic vasculitis.

**BEHÇET SYNDROME**
Behçet syndrome is a multisystem inflammatory disease that affects vessels of all size. It is manifested as recurrent aphthous oral and genital ulcerations along with ocular involvement. Behçet syndrome is most prevalent at ages 20 to 35 years, with males suffering more severe disease.

**PATHOPHYSIOLOGY**

**BOX 110.1 Chapel Hill Consensus Conference Classification of Primary Vasculitides**

<table>
<thead>
<tr>
<th>Large Vessel</th>
<th>Medium Vessel</th>
<th>Small Vessel</th>
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<tr>
<td>Giant cell (temporal) arteritis</td>
<td>Polyarteritis nodosa</td>
<td>Wegener granulomatosis</td>
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<tr>
<td>Takayasu arteritis</td>
<td>Kawasaki disease</td>
<td>Churg-Strauss syndrome</td>
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**BOX 110.2 Three Potential Mechanisms of Blood Vessel Damage in Vasculitis with Corresponding Diseases**

<table>
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<th>Pathogenic Immune Complex Formation</th>
<th>Pathogenic T-Lymphocyte Responses and Granuloma Formation</th>
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<td>Temporal arteritis</td>
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<tr>
<td>Vasculitis associated with collagen vascular diseases</td>
<td>Takayasu arteritis</td>
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<td>Cutaneous vasculitic syndromes</td>
<td>Churg-Strauss syndrome</td>
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<tr>
<td>Hepatitis C, cryoglobulinemia</td>
<td>Microscopic polyangiitis</td>
</tr>
<tr>
<td>Hepatitis B, polyarteritis nodosa</td>
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</tbody>
</table>

| Antineutrophilic Cytoplasmic Antibodies | |
| Wegener granulomatosis | |
| Churg-Strauss syndrome | |
| Microscopic polyangiitis | |


Immune complex deposition in vessel walls is the most well-known pathogenic mechanism of vasculitis and results in tissue damage from such deposition. Complement components are then activated and infiltrate the vessel walls. The immune complexes are phagocytosed and release damaging enzymes. As the condition progresses and becomes subacute, the vessel lumen may become compromised with subsequent tissue ischemia.

Antineutrophil cytoplasmic antibodies (ANCAs) develop in a large number of patients with systemic vasculitis, especially Wegener granulomatosis. These antibodies attack proteins in the cytoplasm of neutrophils. Two main types of ANCA are differentiated by the different targets of the antibodies: perinuclear ANCA (p-ANCA) attacks the enzyme myeloperoxidase, whereas cytoplasmic ANCA (c-ANCA) attacks the proteinase-3 enzyme.

The exact role of ANCAs in the pathogenesis of vasculitis is unclear. Although a number of mechanisms have been proposed, confusion remains because vasculitis develops in many patients without ANCAs, there is a lack of correlation with the quantitative value of ANCAs and disease activity, and many patients in remission continue to exhibit high ANCA titers.

Pathogenic T-lymphocyte responses and granuloma formation may also be involved in damaging blood vessels. Delayed hypersensitivity and cell-mediated immune injury are the most common mechanisms in this category. Direct cellular toxicity or antibody-dependent cellular toxicity may also occur.

Two main factors are involved in the expression of a vasculitic syndrome: genetic predisposition and regulatory mechanisms associated with the immune response to antigens. Only certain types of immune complexes cause vasculitis, and the process may be selective for only certain vessel types. Other factors are also involved—for example, the reticulonendothelial system’s ability to clear the immune complex, the size and properties of the complex, blood flow turbulence, intravascular hydrostatic pressure, and the preexisting integrity of the vessel endothelium.  

**TEMPORAL (GIANT CELL) ARTERITIS**

Giant cell arteritis is a panarteritis characterized by inflammatory mononuclear cell infiltration and giant cell formation in vessel walls. The intima proliferates and the internal elastic lamina fragments. Organ pathology results from ischemia related to the involved vessel derangement.

**TAKAYASU ARTERITIS**

The inflammation in Takayasu arteritis involves all vessel wall layers of medium- and large-sized vessels, especially the aorta and its branches. Panarteritis with inflammatory mononuclear cell infiltration and giant cells predominates. This results in scarring and fibrosis with disruption and degeneration of the elastic lamina. Narrowing of the vessel lumen (Fig. 110.1) follows with frequent thrombosis. Vessel dilation and the formation of aneurysms may also occur. Organ pathology results from ischemia.

**POLYARTERITIS NODOSA**

The inflammatory lesions associated with polyarteritis nodosa are segmental and involve the bifurcations and branches of arteries. Polymorphonuclear neutrophils infiltrate all layers of the vessel wall. The resultant intimal proliferation and degeneration of the vessel wall lead to vascular necrosis, which in turn results in thrombosis, compromised blood flow, and infarction of the involved tissues and organs. Characteristic aneurysmal dilations of up to 1 cm are common. Multiple organ systems are involved.

**KAWASAKI DISEASE**

The etiology of Kawasaki disease is unknown, but increasing evidence supports an infectious cause; however, whether the inflammatory response results from a conventional antigen or a superantigen continues to be debated. Although a strong predilection for the coronary arteries is seen, this vasculitis is systemic and may involve medium-sized arteries with corresponding manifestations. Initially, neutrophils are present in great numbers, but the infiltrate rapidly switches to mononuclear cells, T lymphocytes, and immunoglobulin A (IgA)-producing plasma cells. Inflammation involves all three layers of vessels. As in other vasculitides, there is typical intimal proliferation and infiltration of the vessel wall with mononuclear cells, which leads to beadlike aneurysms and thrombosis. Cardiomegaly, pericarditis, myocarditis, myocardial ischemia, and infarction may result.

**WEGENER GRANULOMATOSIS**

The pathology of Wegener granulomatosis involves a necrotizing vasculitis of small vessels with granuloma formation. The typical necrotizing granulomatous vasculitis in the lungs commonly leads to scarring, atelectasis, and obstruction. The upper airways also become inflamed, with necrosis and granuloma formation. Renal involvement takes the form of a focal and segmental glomerulonephritis that may become rapidly progressive. Few or no immune complexes are found on biopsy; the involvement of immunopathology is unclear. c-ANCAs develop in a large number of these patients, but this correlation is not clear. Besides the typical sinus, lung, and kidney involvement, other organs may be affected because Wegener granulomatosis is a systemic small vessel vasculitis.

**CHURG-STRAUSS SYNDROME**

The characteristic histopathologic features of Churg-Strauss syndrome include tissue infiltration by eosinophils, necrotizing small vessel vasculitis, and extravascular “allergic”
granulomas. The process can occur in any organ, but lung involvement predominates, and its association with asthma is strong. The combination of asthma, eosinophilia, granulomas, and vasculitis strongly suggests a hypersensitivity reaction as the triggering factor.

HENOCH-SCHÖNLEIN PURPURA
Henoch-Schönlein purpura is an immune complex disease characterized by deposition of IgA-containing complexes. Suggested but unproved inciting antigens include upper respiratory infections, foods, drugs, insect bites, and vaccinations.

All aspects of the disease are more serious when an adult is affected.

CUTANEOUS LEUKOCYTOCLASTIC VASCULITIS
The pathology predominantly involves small vessels, especially postcapillary venules. Acutely, neutrophils infiltrate the vessels, cause destruction, and result in nuclear debris—thus the term leukocytoclastic. As the process becomes more chronic, mononuclear cells and eosinophils become involved. Erythrocytes frequently extravasate and cause a classic palpable purpura, which is a hallmark of the disease.

BEHÇET SYNDROME
The main pathology in Behçet syndrome is vasculitis with a tendency to form venous thrombi.

PRESENTING SIGNS AND SYMPTOMS
The diagnosis of many vasculitic syndromes is based more on the clinical findings than on laboratory results; therefore, a detailed history plus physical examination is an essential first step in the diagnosis. A high index of suspicion is necessary. The diagnosis should be considered in any patient with systemic febrile illness and signs of organ ischemia without a direct explanation. Nonspecific symptoms such as weight loss, night sweats, and malaise are common. The vessels involved may correlate with the specific symptoms displayed.

TEMPORAL (GIANT CELL) ARTERITIS
Patients with temporal arteritis have local symptoms related to the arteries involved. Headache, scalp tenderness associated with the inflamed temporal artery (Fig. 110.2), jaw claudication, and visual disturbances are typical. Symptoms associated with polymyalgia rheumatica are frequently displayed. Constitutional symptoms such as fever, malaise, fatigue, anorexia, weight loss, arthralgias, and night sweats are also common. The most serious complication is ocular involvement as a result of ischemic optic neuropathy, which may lead to blindness; however, loss of vision is usually avoided with proper treatment. A later complication may be an aortic aneurysm.

TAKAYASU ARTERITIS
Patients with Takayasu arteritis have ischemic symptoms of the involved vessels; such symptoms include visual problems, faint or absent pulses in the upper extremities, and myocardial, abdominal, and lower extremity ischemia. Differences in extremity blood pressure and bruits may also be present. Up to 40% of patients may experience systemic symptoms such as fever, malaise, night sweats, arthralgias, myalgias, weight loss, and anorexia. Death usually occurs from congestive heart failure or stoke. The course may be progressive and unremitting and become fulminant or may stabilize into remission.

POLYARTERITIS NODOSA
The most common symptoms of polyarteritis nodosa are fever, hypertension, myalgias, arthralgias, weight loss, malaise, and headache. Renal involvement evolves as flank pain, hematuria, renovascular hypertension, and renal failure. Skin lesions range from subcutaneous nodules to distal ischemia. Gastrointestinal manifestations include pain, malabsorption, bleeding, and perforation. Congestive heart failure secondary to coronary artery vasculitis may occur. A classic symptom is orchitis, which may occur in one third of male patients.

KAWASAKI DISEASE
The characteristic clinical features of Kawasaki disease are fever for at least 5 days, conjunctivitis, changes in the oral mucosa, a generalized rash, red palms and soles, indurative edema with subsequent skin desquamation, and cervical lymphadenopathy. The presence of five of these symptoms confirms the diagnosis. Of course, atypical cases with fewer symptoms occur.

WEGENER GRANULOMATOSIS
The characteristic manifestation of Wegener granulomatosis involves symptoms in the upper or lower airways (or both) for a prolonged period before the disease becomes systemic. Up to 90% of patients have sought medical attention for sinus or pulmonary problems earlier. Upper respiratory symptoms
include pain, purulent or bloody drainage, ulcerations, hoarseness, stridor, and deafness. Pulmonary findings are manifested as cough, dyspnea, chest pain, and hemoptysis, which may become severe. Pulmonary nodules, infiltrates, or cavitations may be seen on chest radiographs. Hypoxemia ensues when the lungs become affected.

Other manifestations include ocular inflammation ranging from conjunctivitis, episcleritis, and scleritis to retinal vasculitis and retroorbital masses. Skin lesions may appear as ulcerations, subcutaneous nodules, or purpura with necrosis. Central nervous system symptoms stem from infarction, cranial nerve neuropathy, and mononeuritis multiplex. Bowel perforation and bleeding may be symptoms of gastrointestinal involvement; pericarditis, coronary ischemia, and cardiomyopathy may signal cardiac involvement. Vague symptoms such as malaise, weakness, arthralgia, fever, and anorexia are common.

Glomerulonephritis is present in 20% of patients at the time of diagnosis and develops in 80% at some point as the disease progresses. If not treated properly, renal involvement accounts for most mortality.

**CHURG-STRAUSS SYNDROME**

Symptoms such as fever, anorexia, malaise, and weight loss suggest a multisystem disease. Churg-Strauss syndrome has three identifiable phases. It begins with a prodrome of allergic rhinitis, nasal polyps, and asthma. The next phase includes peripheral eosinophilia and eosinophilic tissue infiltrates, especially in the lungs. The third phase is marked by a systemic vasculitis involving the lungs, heart, kidneys, central nervous system, and gastrointestinal tract. These phases may not occur in sequence and may not be seen in all patients.

The disease is best known for its severe and frequent exacerbations of asthma and relapsing vasculitis. The asthma associated with Churg-Strauss syndrome is not a classic allergic asthma that begins early in life; rather, it begins later in life around 35 years of age. It is severe, and patients frequently become steroid dependent.

**HENOCH-SCHÖNLEIN PURPURA**

The classic clinical picture of Henoch-Schönlein purpura includes four cardinal manifestations—palpable purpura, arthralgias, gastrointestinal involvement, and glomerulonephritis. The palpable purpura develops in nearly all cases and occurs most commonly over the buttocks and legs (Fig. 110.3). Polyarthralgia also develops in most patients. Gastrointestinal symptoms include abdominal pain with nausea, vomiting, diarrhea, constipation, and occasional gastrointestinal bleeding.

Renal disease is characterized by a mild glomerulonephritis with hematuria and proteinuria. Glomerulonephritis is seen in 20% to 50% of patients, with 2% to 5% progressing to end-stage renal disease.

**CUTANEOUS LEUKOCYTOCLASTIC VASCUITIS**

Clinically, besides purpura, patients may exhibit macules, papules, vesicles, bullae, subcutaneous nodules, or urticaria. The skin usually becomes pruritic and painful, and the lesions may progress to ulcers. Although the skin is predominantly involved, patients may exhibit systemic symptoms such as myalgias, fever, anorexia, and malaise. The course of the disease ranges from a brief single episode to multiple prolonged recurrences with infrequent progression to systemic vasculitis.

**BEHÇET SYNDROME**

Patients with Behçet syndrome have painful ulcers that occur as one ulcer or multiple ulcers; the ulcers last for 1 to 2 weeks and resolve without scarring. Besides oral ulcers, patients with Behçet syndrome may exhibit two or more of the following signs or symptoms: recurrent genital ulcers, skin lesions, eye lesions, and a positive pathergy test.

The genital ulcers resemble the oral ulcers. Skin lesions range from erythema nodosum and folliculitis to a general inflammatory exanthem. The ocular manifestations usually arise at onset of the disease but may develop later in the first few years. Iritis, posterior uveitis, retinal artery and vein occlusion, and optic neuritis may be seen. Hypopyon uveitis is rare but is pathognomonic of the disease. The ocular involvement may lead to blindness.

Other symptoms include mild arthritis of the lower extremity joints, gastrointestinal inflammation, and ulcerations. Central nervous system manifestations include meningoencephalitis, benign intracranial hypertension, multiple sclerosis–like symptoms, and psychiatric disturbances. Large venous or arterial thrombi or occlusions occur in 25% to 38% of patients. Pulmonary emboli are possible.

**DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING**

**LABORATORY TESTS**

The complete blood count may reveal leukocytosis, normocytic normochromic anemia, and thrombocytosis. C-reactive protein (CRP) levels and the ESR may be elevated. Complement levels may be low. Because of renal involvement, urinalysis may reveal proteinuria or active sediment. Cerebrospinal fluid findings in patients with central nervous system vasculitis reveal elevated protein.

The ANCA associated with Wegener granulomatosis, first reported in 1985, is now an established entity in the evaluation of patients with suspected vasculitis. As with any diagnostic test, the predictive value of ANCA depends on the pretest probability of the disease. A negative test result does not exclude the disease, nor should the diagnosis of a vasculitic
syndrome be made or treatment initiated based on a positive ANCA titer alone. There have been reports of positive ANCA titers in patients with chronic infections and clinical features similar to systemic vasculitis. Therefore, caution is advised and testing for c-ANCA should not replace tissue biopsy.

**BIOPSY AND ANGIOGRAPHY**

Definitive diagnosis is dependent on demonstration of vascular involvement and may be accomplished by biopsy or angiography. Biopsy is preferred and should be directed toward tissue showing evidence of clinical involvement. Biopsy provides the distinct advantage of differentiating active from chronic disease. Such differentiation allows appropriate treatment.

Angiography is an excellent diagnostic modality when medium and large vessels are involved and visceral organ involvement is likely. This modality is the “gold standard” in the work-up of Takayasu arteritis, for which a full evaluation of the aorta is recommended. Angiography demonstrates luminal patency but provides no information about cellular or tissue status. Early vessel inflammation may still be present in a fully patent vessel. Conversely, vessel narrowing may also be due to fibrosis, not active disease. Therefore, clinical correlation is advised with each angiographic finding.

**NONINVASIVE IMAGING**

Noninvasive imaging modalities are useful in evaluating changes in the vessel wall not evident on angiography. They are associated with less morbidity than angiography and biopsy and have recently gained popularity in the serial evaluation and detection of early disease in patients with vasculitis.

High-resolution ultrasonography is an efficient, noninvasive, and inexpensive method of monitoring known cases of vasculitis. An example of clinical application is the evaluation of stenotic segments of the carotid arteries. Progression—and hopefully resolution—with treatment of this pathology can also be monitored with ultrasonography. The fact that it cannot detect disease in all vessels, particularly the pulmonary, thoracic, and abdominal visceral vessels, limits this modality.

Computed tomography (CT) can be useful to detect vessel wall thickening, especially in early Takayasu arteritis. CT angiography, high-resolution CT, and electron beam CT have all improved diagnostic outcomes. CT may also be used to evaluate sinus pathology or pulmonary lesions in patients with Wegener granulomatosis. To exclude infection, sarcoidosis, and malignancy, biopsy should follow CT when evaluating these lesions.

Magnetic resonance imaging (MRI) can be used to assess vessel wall thickening and has the advantage of axial, sagittal, and coronal plane views. Magnetic resonance angiography (MRA) correlates well with findings on CT angiography when evaluating the aorta or renal arteries. Further studies are needed before MRI or MRA can be considered first-choice diagnostic tools.

Positron emission tomography measures glucose metabolism in tissues. Increased glycolysis is seen in inactivated leukocytes and macrophages and is a hallmark of inflammation in certain vasculitides, especially giant cell arteritis.

Single-photon emission computed tomography (SPECT) uses multplanar nuclear imaging to investigate abnormalities in perfusion, especially when evaluating central nervous system vasculitis. Clinical correlation is necessary because perfusion defects may not distinguish vasculitis from entities such as vasospasm, thromboembolism, atherosclerosis, and malignant hypertension. SPECT may also be useful in evaluating the coronary arteries in patients with Kawasaki disease.

**DIAGNOSIS OF SPECIFIC VASCULITIC SYNDROMES**

**Temporal (Giant Cell) Arteritis**

Classic laboratory manifestations include an elevated ESR and CRP. Normochromic anemia and thrombocytosis secondary to the chronic inflammation are common. Liver function abnormalities, particularly an elevated alkaline phosphatase level, are common.

The diagnosis can be determined clinically because of the classic scenario of headache, fever, anemia, and an elevated ESR. Temporal artery biopsy is confirmatory. Because involvement of the vessel may not be contiguous, several separate biopsies may be needed. Color duplex ultrasonography, angiography, or MRI may play a role in making the diagnosis. A rapid clinical response to treatment also confirms the diagnosis.

**Takayasu Arteritis**

Laboratory findings during active disease include an elevated ESR and increased CRP levels. Angiography demonstrates stenosis, occlusion, dilation, and aneurysms of the aorta and its branches. The entire aorta should be visualized to fully appreciate the spectrum of this disease. Spiral CT angiography and MRA have been shown to be useful.

The diagnosis should be suspected in any young woman with the systemic signs and symptoms previously described and with any blood pressure or pulse discrepancies or bruits. Establishment of the diagnosis must then be achieved by radiologic procedures.

**Polyarteritis Nodosa**

No diagnostic serologic tests are available for polyarteritis nodosa, and laboratory findings are nonspecific; the ESR, CRP, and leukocytes are elevated. Normochromic anemia is present and is indicative of chronic disease. The diagnosis may be achieved by biopsy demonstrating histologic necrotizing inflammation in the arteries. If biopsy is not possible, angiography demonstrating microaneurysms, stenosis, or sequential narrowing and dilation suggests the diagnosis.

**Kawasaki Disease**

Echocardiography and angiography confirm the cardiac complications and vasculitis. Laboratory findings include elevated leukocytes, platelets, ESR, and CRP.

Although the disease is generally benign and self-limited, coronary artery aneurysms occur in 20% to 30% of patients, usually during the third or fourth week as convalescence ensues. The presence of four symptoms along with coronary artery aneurysms is diagnostic. The case fatality rate secondary to coronary artery aneurysm is 0.5% to 2.8%.

**Wegener Granulomatosis**

Laboratory findings include an elevated ESR and CRP, anemia with leukocytosis, thrombocytosis, and positive tests for ANCA, which is seen especially when the kidneys are affected.
The diagnosis is made by biopsy demonstrating necrotizing granulomatous vasculitis with an aggregation of neutrophils in nonrenal tissue. Renal biopsy reveals focal, segmental, necrotizing, crescentic glomerulonephritis. Biopsy findings coincide with the characteristic clinical findings of sinus, pulmonary, and renal symptoms. Although the use of ANCA testing is only adjunctive, its specificity is 90% for Wegener granulomatosis if active glomerulonephritis is present.

**Churg-Strauss Syndrome**

Classic laboratory findings include leukocytosis with notable eosinophilia, anemia, and elevated ESR and CRP. The diagnosis is confirmed via biopsy in a patient with the characteristic clinical manifestations.

**Henoch-Schönlein Purpura**

Laboratory studies are nonspecific and may reveal a mild leukocytosis and occasional eosinophilia. Serum IgA levels are elevated in 50% of patients. The diagnosis remains a clinical diagnosis based on the characteristic findings. A skin biopsy is occasionally necessary for confirmation and reveals leukocytoclastic vasculitis with IgA immune deposition. Renal biopsy better serves as a prognostic indicator.

**Cutaneous Leukocytoclastic Vasculitis**

Laboratory values are usually within normal limits, including ESR and CRP levels. Mild leukocytosis and eosinophilia may be present. Laboratory studies should be used primarily to rule out the presence of systemic vasculitis. Minimal to no signs of inflammation should be found. The diagnosis is made by skin biopsy and by carefully ruling out systemic disease or exogenous reasons for the vasculitis.

The clinical and histopathologic appearance of the lesions is indistinguishable from the cutaneous manifestations of the systemic vasculitides; therefore, the diagnosis should be one of exclusion after other causes have been ruled out. Only then can the disorder be called true cutaneous leukocytoclastic vasculitis or idiopathic cutaneous vasculitis.

**Behçet Syndrome**

Laboratory findings indicate nonspecific inflammation such as leukocytosis and elevated ESR and CRP levels. Half of patients are found to have autoantibodies to human oral mucous membranes. The diagnosis is based on the clinical findings of recurrent aphthous oral ulcers.

**TREATMENT**

The combination of clinical, laboratory, biopsy, and radiographic findings usually points to a specific syndrome (Table 110.1). Therapy should then be initiated as appropriate. If the vasculitis is associated with a specific disease such as nephropathy, infection, or connective tissue disease, the underlying disease should be treated. If the syndrome resolves, no further treatment is needed. If the syndrome persists, treatment of vasculitis should be initiated. Likewise, if an offending antigen is recognized, it should be removed if possible. No further treatment is needed if the syndrome resolves; however, if the syndrome continues, treatment must be initiated. Treatment initiated for a primary vasculitis syndrome should focus on using the most effective and least toxic options based on published experience.

**TEMPORAL (GIANT CELL) ARTERITIS**

Treatment should commence immediately and not be delayed by diagnostic procedures. Administration of 40 to 60 mg of prednisone daily for 1 month is followed by a taper to 7.5 to 10 mg daily. This should be continued for 1 to 2 years to prevent relapse. Aspirin, 81 mg daily, has been shown to reduce cranial ischemic complications and should be given to patients without contraindications. Clinical symptoms and the ESR are used to monitor disease activity.

**TAKAYASU ARTERITIS**

Treatment consists of the combination of 40 to 60 mg/day of prednisone and aggressive surgical or angiographic procedures directed toward stenotic vessels. This approach corrects hypertension caused by renal artery stenosis, improves blood flow in ischemic vessels, and decreases risk for stroke, thereby resulting in decreased morbidity and improved survival.

**POLYARTERITIS NODOSA**

Combination therapy consisting of prednisone (1 mg/kg/day) and cyclophosphamide (2 mg/kg/day) has resulted in a long-term remission rate of 90% after therapy has been discontinued. Glucocorticoids may be used alone in mild cases.

**KAWASAKI DISEASE**

Treatment consists of high-dose intravenous gamma globulin (2 g/kg infused over a 10-hour period) administered concomitantly with aspirin (80 to 100 mg/kg/day for 2 weeks followed by 3 to 5 mg/kg/day for several more weeks). Early therapy has proved beneficial in reducing coronary artery abnormalities.

**WEGENER GRANULOMATOSIS**

Administration of cyclophosphamide (2 mg/kg/day) combined with prednisone (1 mg/kg/day) has proved to be the most successful therapy. Reported results are complete remission in 75%, a survival rate of 80%, and marked improvement in 91%. Though very effective, cyclophosphamide may be associated with severe bone marrow toxicity. Leukocytes must be monitored closely and kept at a level above 3000 mcg.

Full-dose cyclophosphamide therapy should be continued for 1 year after remission and then tapered off. Prednisone therapy may be changed to alternate-day administration after 1 month and then tapered off by 6 months. Methotrexate has shown some success in patients who cannot tolerate cyclophosphamide.

**CHURG-STRAUSS SYNDROME**

The most effective therapy is prednisone (1 mg/kg/day). The vasculitis usually remits more readily than the asthma, which may remain moderate to severe and thus make discontinuation of prednisone therapy difficult. Cyclophosphamide at 2 mg/kg/day may be added to the prednisone in patients not responsive to prednisone alone.

**HENOCH-SCHÖNLEIN PURPURA**

Although renal failure is the most common cause of death, Henoch-Schönlein purpura usually resolves without therapy. In general, the disease is self-limited with an excellent prognosis for full recovery in as little as a few weeks.
Table 110.1 Comparing the Vasculitides

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<td>Angiography</td>
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<td>formation</td>
<td>differences in extremity blood pressure and pulses</td>
<td></td>
<td>Surgical or</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>angiographic</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>intervention</td>
</tr>
<tr>
<td>Polyarteritis nodosa</td>
<td>Polymorphonuclear infiltration</td>
<td>Fever, hypertension, myalgias, abdominal pain,</td>
<td>ESR, CRP, Biopsy</td>
<td>Prednisone plus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hemorrhia, CHF, GI bleeding, orchitis</td>
<td></td>
<td>cyclophosphamide</td>
</tr>
<tr>
<td>Kawasaki disease</td>
<td>Polymorphonuclear infiltration</td>
<td>5-day fever, conjunctivitis, oral lesions, rash,</td>
<td></td>
<td>Aspirin plus IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>red palms and soles, edema, cervical lymphadenopathy</td>
<td></td>
<td>gamma globulin</td>
</tr>
<tr>
<td>Wegener granulomatosis</td>
<td>Granuloma formation secondary to aggregating</td>
<td>Upper and lower respiratory symptoms, renal</td>
<td>ESR, CRP</td>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td></td>
<td>neutrophils</td>
<td>insufficiency, skin lesions, visual disturbance</td>
<td>c-ANCA</td>
<td>plus prednisone</td>
</tr>
<tr>
<td>Churg-Strauss syndrome</td>
<td>Eosinophilic infiltration</td>
<td>Allergic rhinitis, Nasal polyps, Asthma</td>
<td></td>
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<tr>
<td></td>
<td>Allergic granulomas</td>
<td></td>
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</tr>
<tr>
<td>Henoch-Schönlein purpura</td>
<td>IgA complex deposition</td>
<td>Palpable purpura, arthralgias, GI disturbances,</td>
<td></td>
<td>Usually self-limited</td>
</tr>
<tr>
<td></td>
<td></td>
<td>glomerulonephritis</td>
<td></td>
<td>Prednisone if</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>necessary</td>
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<tr>
<td>Cryoglobulinemic</td>
<td>Cold precipitable monoclonal or polyclonal</td>
<td>Palpable purpura, glomerulonephritis, myalgias,</td>
<td>Low complement</td>
<td>Interferon alfa</td>
</tr>
<tr>
<td>vasculitis</td>
<td>immunoglobulins</td>
<td>weakness, peripheral neuropathy</td>
<td>levels</td>
<td>plus ribavirin</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>Neutrophilic infiltration</td>
<td>Palpable purpura, macules, vesicles, bullae,</td>
<td>Skin biopsy</td>
<td>Prednisone</td>
</tr>
<tr>
<td>leukocytoclastic</td>
<td>Mononuclear and eosinophilic infiltration</td>
<td>urticaria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vasculitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Behçet syndrome</td>
<td>Polymorphonuclear infiltration</td>
<td>Recurrent oral aphthous ulcers, genital ulcers,</td>
<td>ESR, CRP</td>
<td>Topical glucocorticoids</td>
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<tr>
<td></td>
<td></td>
<td>skin lesions, visual disturbance</td>
<td>Leukocytosis</td>
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<td></td>
<td></td>
<td></td>
<td>Oral mucosa</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>autoantibodies</td>
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</table>

c-ANCA, Cytoplasmic antineutrophil cytoplasmic antibody; CHF, congestive heart failure; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GI, gastrointestinal; IgA, immunoglobulin A; IV, intravenous.

However, when required, prednisone at 1 mg/kg/day is effective in lessening tissue edema, arthralgias, and abdominal pain. The dose should be tapered as the symptoms abate. Glucocorticoids have no proven benefit on skin and renal involvement and have not been shown to shorten the course of the disease or prevent relapse.

**CUTANEOUS LEUKOCYTOCLASTIC VASCULITIS**

If an underlying process is discovered to be the cause of the cutaneous symptoms, treatment should be aimed at the underlying process. If an exogenous agent is the culprit, removal of it usually results in remission of the skin process. If true cutaneous leukocytoclastic vasculitis is determined to be the etiology, glucocorticoids administered at a dosage of 1 mg/kg/day have proved effective.

Frequently, the disease is self-limited; otherwise, it generally responds very rapidly to steroid therapy. Some symptomatic agents may be used on occasion, such as antihistamines, nonsteroidal antiinflammatory drugs, and colchicine. In the rare scenario in which glucocorticoids are not effective, cytotoxic agents such as methotrexate, azathioprine, and...
cyclophosphamide may be used, but these drugs should be reserved for severe cases.

**BEHÇET SYNDROME**
Treatment is based on disease manifestations. Oral and skin lesions respond well to topical glucocorticoids, dapsone, or colchicine. Thrombophlebitis is treated with aspirin. Ocular and central nervous system manifestations require aggressive treatment with immunosuppressive agents such as glucocorticoids, azathioprine, or cyclosporine.\(^1\)

**HENOCH-SCHÖNLEIN PURPURA**
Patients with Henoch-Schönlein purpura who have severe abdominal pain, significant gastrointestinal bleeding, or marked renal insufficiency may require hospitalization.

**CUTANEOUS LEUKOCYTOCLASTIC VASCULITIS**
This disorder may be managed on an outpatient basis.

**BEHÇET SYNDROME**
Treatment may be managed on an outpatient basis unless ocular or central nervous system manifestations are evident.

**FOLLOW-UP, NEXT STEPS IN CARE, AND PATIENT EDUCATION**

**TEMPORAL (GIANT CELL) ARTERITIS**
The prognosis is good; the majority of patients go into remission and remain in remission after discontinuation of steroids. Patients with severe disease or impending vision loss should be hospitalized and given high-dose intravenous steroids.

**TAKAYASU ARTERITIS**
Hospital admission for diagnostic testing and treatment should be considered for suspected cases. It is the best practice but not always possible to control the vascular inflammation with prednisone before any surgical procedures.

**POLYARTERITIS NODOSA**
Discharge home with follow-up is appropriate except in patients with evidence of end-organ failure.

**KAWASAKI DISEASE**
Except for rare fatal cardiac complications, the prognosis is good, typically with full recovery.\(^3\) Children in whom aneurysms develop require close follow-up after discharge, and some patients with severe disease may need long-term anticoagulation.

**WEGENER GRANULOMATOSIS**
Outpatient management is appropriate except in patients with advanced end-organ involvement. On achievement of remission, long-term follow-up is essential. Up to 50% of patients have one or more relapses. With close follow-up and immediate reinstitution of therapy, induction of remission is almost always a success. In many patients, especially those with multiple relapses, some degree of long-term morbidity develops, such as renal insufficiency, tracheal stenosis, hearing loss, or sinus impairment.\(^3\) Aggressive prompt therapy during the initial manifestation of the disease, as well as during relapses, helps diminish the degree of chronic morbidity.\(^3\)

**CHURG-STRAUSS SYNDROME**
Outpatient management is appropriate except in patients with advanced end-organ involvement. The prognosis of untreated patients is a 25% 5-year survival rate, which improves to 50% with proper treatment.\(^1\)

**HENOCH-SCHÖNLEIN PURPURA**
Patients with Henoch-Schönlein purpura who have severe abdominal pain, significant gastrointestinal bleeding, or marked renal insufficiency may require hospitalization.

**REFERENCES**

References can be found on Expert Consult @ www.expertconsult.com.
REFERENCES