2.7 Vasculitis (Polyarteritis Nodosa, Microscopic Polyangiitis, Wegener’s Granulomatosis, Henoch-Schönlein Purpura)

### APPROXIMATE FREQUENCY OF ORGAN SYSTEM INVOLVEMENT IN SMALL VESSEL VASCULITIS

<table>
<thead>
<tr>
<th>Organ system</th>
<th>Henoch-Schönlein purpura, %</th>
<th>Cryoglobulinemic vasculitis, %</th>
<th>Microscopic polyangiitis, %</th>
<th>Wegener’s granulomatosis, %</th>
<th>Churg-Strauss syndrome, %</th>
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</thead>
<tbody>
<tr>
<td>Renal</td>
<td>50</td>
<td>55</td>
<td>90</td>
<td>80</td>
<td>45</td>
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<td>Pulmonary</td>
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<td>&lt;5</td>
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<td>40</td>
<td>70</td>
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<td>70</td>
</tr>
<tr>
<td>Ear, nose, and throat</td>
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<td>&lt;5</td>
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<td>40</td>
<td>30</td>
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</tr>
</tbody>
</table>

**FIGURE 2-12**

All of the small vessel vasculitides share signs and symptoms of small vessel injury in multiple different tissues; however, the frequency of involvement varies among the different diseases [1]. Combined renal and pulmonary involvement (pulmonary-renal syndrome) is most common in ANCA vasculitis, whereas combined renal and dermal involvement (dermal-renal syndrome) is most common in immune complex vasculitis. The cutaneous involvement in small vessel vasculitides usually manifests as purpura caused by venulitis, but occasionally is more nodular or necrotizing secondary to arteritis or granulomatous inflammation. Nodular cutaneous lesions, as well as neuropathies, abdominal pain, and musculoskeletal symptoms also can be caused by medium sized vessel vasculitis (e.g., polyarteritis nodosa), and thus these clinical manifestations are not specific for a small vessel vasculitis; whereas glomerulonephritis, purpura, or alveolar capillaritis are.

### Henoch-Schönlein Purpura

**FIGURE 2-13**

Cutaneous purpura in a patient with Henoch-Schönlein purpura. This clinical appearance could be caused by any of the small vessel vasculitides, and thus is not specific for Henoch-Schönlein purpura. Henoch-Schönlein purpura is the most common small vessel vasculitis in children [7]. In a young child with purpura, nephritis and abdominal pain, the likelihood of Henoch-Schönlein purpura is approximately 80%; however, in an older adult with the same clinical presentation, the likelihood of Henoch-Schönlein purpura is very low and the patient has an approximately 80% chance of having an ANCA-associated vasculitis.

**FIGURE 2-14**

Skin biopsy from a patient with small vessel vasculitis demonstrating the typical dermal leukocytoclastic angitis pattern of venulitis that results in vasculitic purpura. This histologic lesion is nonspecific and can be a component of any of the small vessel vasculitides. Additional immunohistologic, serologic, and clinical observations are required to determine what is causing the leukocytoclastic angitis (Figs. 2-9 and 2-10). (Hematoxylin and eosin stain.)
FIGURE 2-15
Direct immunofluorescence microscopy demonstrating granular IgA-dominant immune complex deposits in dermal vessels, which is indicative of Henoch-Schönlein purpura. This procedure typically would show vascular IgM, IgG, and C3 cryoglobulinemic vasculitis, and little or no staining for immunoglobulins in a specimen from a patient with an ANCA vasculitis (a paucity of staining for immunoglobulins in vessel walls indicates pauci-immune vasculitis).

FIGURE 2-16
Direct immunofluorescence microscopy demonstrating granular, predominantly mesangial IgA-dominant immune complex deposits in a glomerulus. This is indicative of some form of IgA nephropathy, including the form that occurs as a component of Henoch-Schönlein purpura.

FIGURE 2-17
Electron micrograph showing mesangial dense deposits representative of the pattern of deposition seen in patients with Henoch-Schönlein purpura glomerulonephritis. The dense deposits are immediately beneath the paramesangial basement membrane.

FIGURE 2-18
Severe crescentic proliferative glomerulonephritis in a patient with Henoch-Schönlein purpura and rapidly progressive glomerulonephritis (Masson trichrome stain). Approximately half of patients with Henoch-Schönlein purpura have mild nephritis with hematuria and proteinuria, but less than a quarter develop renal insufficiency, and rapidly progressive glomerulonephritis is rare. Less than 10% of patients have persistent renal disease that progresses to end-stage renal disease.
Vasculitis (Polyarteritis Nodosa, Microscopic Polyangiitis, Wegener’s Granulomatosis, Henoch-Schönlein Purpura)

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**FIGURE 2-19**
Fibrinoid necrosis obliterating the wall of an arteriole in a renal biopsy specimen from a patient with Henoch-Schönlein purpura (hematoxylin and eosin). Involvement of renal vessels other than glomeruli is rare in Henoch-Schönlein purpura.

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**ANCA Small Vessel Vasculitis**

**FIGURE 2-20** (see Color Plate)
C-ANCA staining pattern of ethanol-fixed normal human neutrophils in an indirect immunofluorescence assay of serum. Approximately 90% of C-ANCA are specific for proteinase 3 (PR3-ANCA) in specific immunochemical assays, such as enzyme immunoassay (EIA) [8–10].

**FIGURE 2-21** (see Color Plate)
P-ANCA staining pattern of ethanol-fixed normal human neutrophils in an indirect immunofluorescence assay of serum. Approximately 90% of P-ANCA in patients with nephritis or vasculitis are specific for myeloperoxidase (MPO-ANCA) in specific immunochemical assays, such as EIA. P-ANCA in patients with other types of inflammatory disease, such as inflammatory bowel disease are typically not specific for MPO. Using ethanol-fixed neutrophils as substrate, nuclear staining caused by anti-nuclear antibodies (ANA) cannot be distinguished confidently from nuclear staining caused by P-ANCA. Using formalin-fixed neutrophils as substrate, P-ANCA stain the cytoplasm but ANA do not. The difference in staining pattern between ethanol and formalin fixed cells is due to the artifactual diffusion of solubilized cationic ANCA-antigens to the nucleus during substrate preparation of the ethanol-fixed cells, as opposed to immobilization of the antigens in the cytoplasm by covalent crosslinking during formalin fixation.