Vasculitis

Edward Dwyer, M.D.

Division of Rheumatology

- VASCULITIS is a primary inflammatory disease process of the vasculature

Determinants of the Clinical Manifestations of Vasculitis:

- Target organ involved
- Size of vessel involved
- Pathobiology of the inflammatory process of involved vasculature

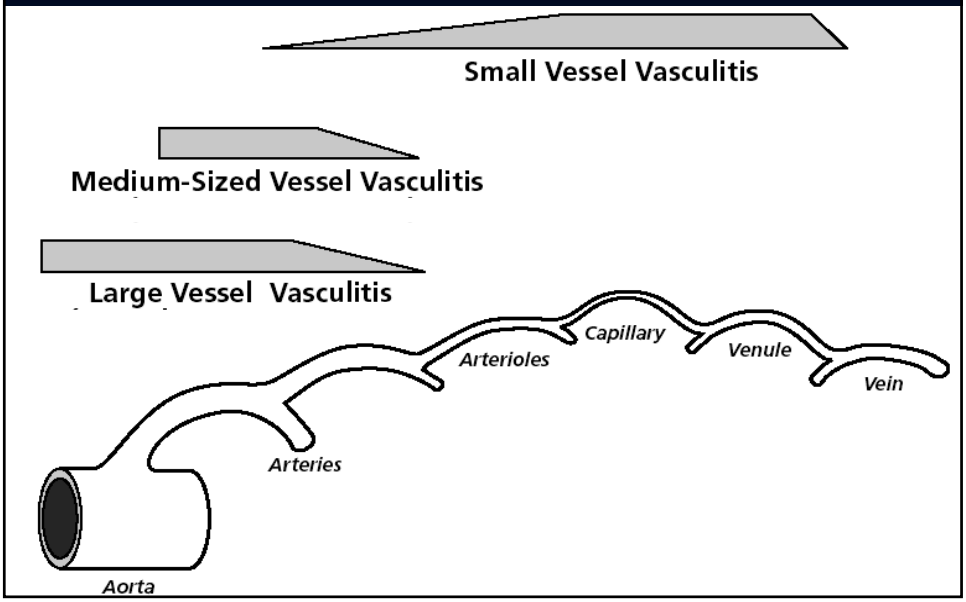
Classification of Vasculitis

- Large-sized Vessels
  - Giant Cell Arteritis
  - Takayasu's Arteritis
- Medium-sized Vessels
  - Polyarteritis Nodosa
  - Kawasaki's Disease
- Small-sized Vessels
  - Anti-Neutrophil Cytoplasmic Ab (ANCA) Associated
    - Wegener's Granulomatosis
    - Microscopic Polyangiitis
    - Churg-Strauss Syndrome

Classification of Vasculitis

- Small-sized Vessels(cont.)
  - Immune-Complex mediated:
    - Henoch-Schonlein purpura
    - Cryoglobulinemia
    - Hypocomplementemic Urticarial Vasculitis
    - Vasculitis associated with SLE, Rhuematoid arthritis, or other autoimmune diseases
    - Serum-sickness or drug-induced vasculitis

Classification of Vasculitis



Sequelae of Vasculitis

- Stenosis and/or occlusion of involved vasculature resulting in organ ischemia or infarction
- Necrosis of vessel walls resulting in aneursymal dilatation and/or thrombosis causing organ ischemia, infarction, or hemorrhage.

Diagnostic Approaches

- Biopsy of involved organs
- Radiographic evaluation of involved vessels
  - Conventional Angiography
  - CT Angiography
  - MR Angiography
- Serology (e.g., autoantibodies)

Giant Cell Arteritis
(Temporal Arteritis)

Non-necrotizing vasculitis resulting intimal proliferation causing luminal stenosis or occlusion

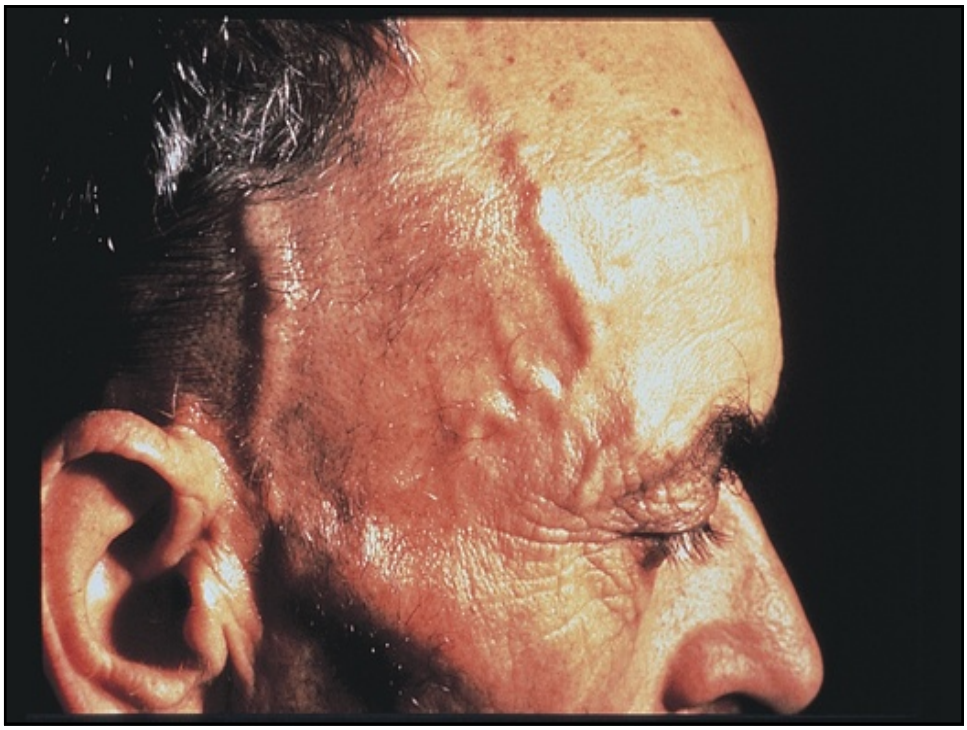
Epidemiology of Giant Cell Arteritis

- Age: > 50 years-old
- Racial/Ethnic Background (annual Incidence)
  - 20/100,000 Northern European
  - 2/100,000 African Americans and Hispanics
  - <1/1,000,000 Asians

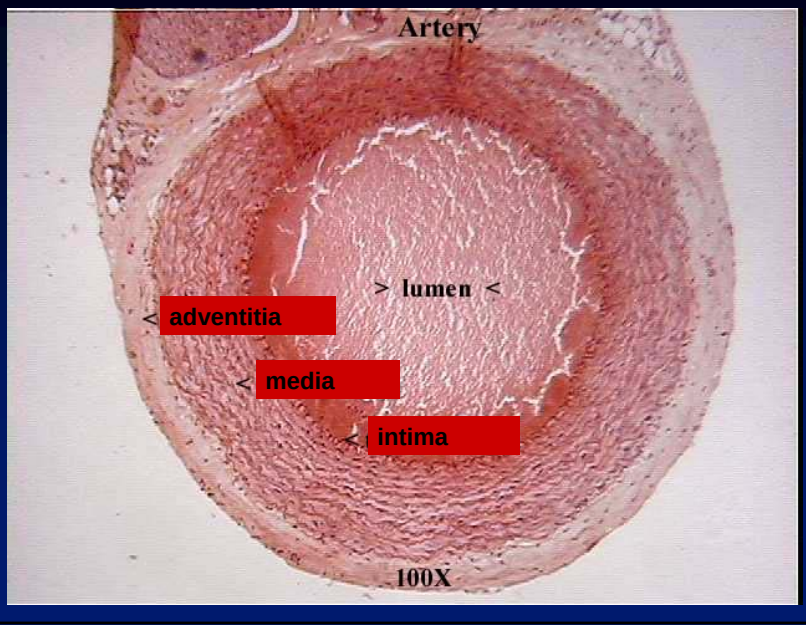
Vasculature involved

Thoracic aorta and major branches:

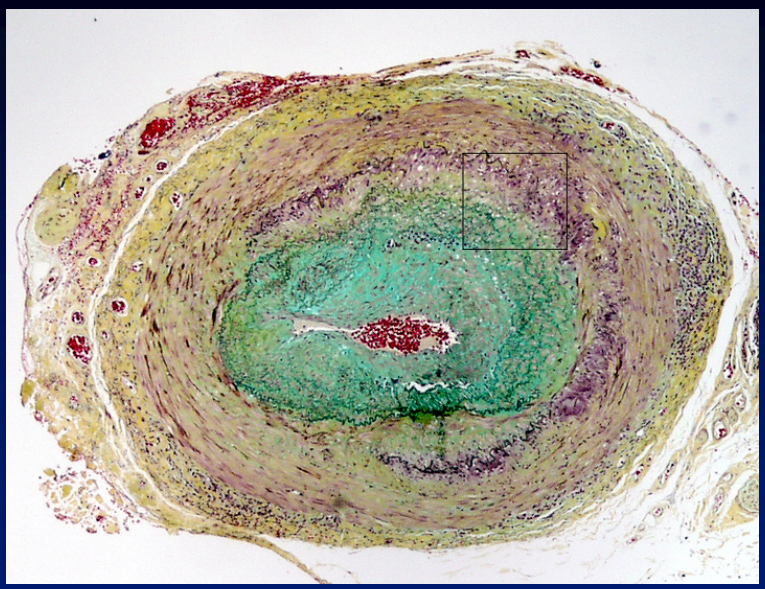
- Carotid artery extra-cranial branches
  - Temporal artery
  - Occipital artery
  - Ophthalmic artery
  - Posterior ciliary artery
- Subclavian/axillary artery



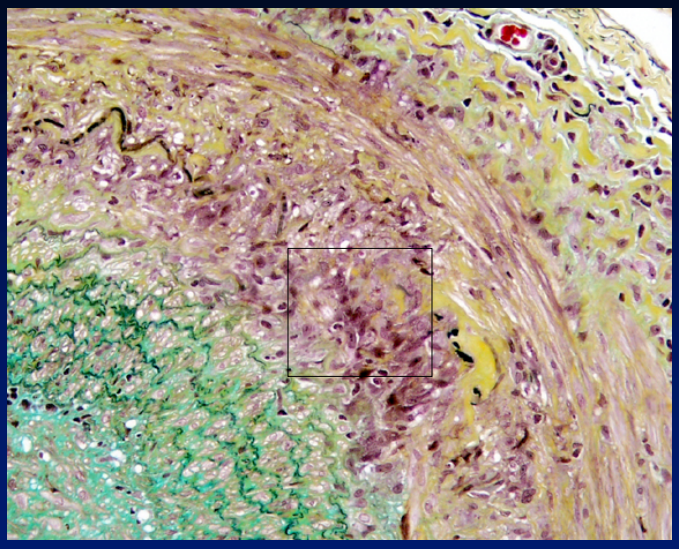
Muscular Artery



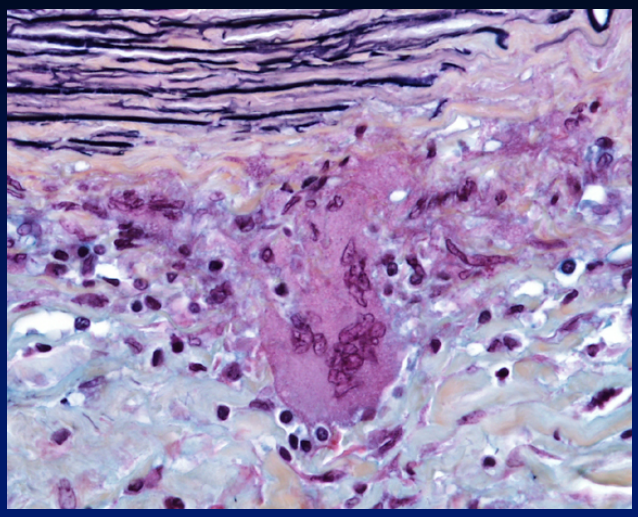
Temporal Artery Biopsy



Temporal Artery Biopsy



Giant Cell



Clinical Manifestations

- Constitutional
  - Fatigue
  - Weight loss
  - Fever
- Headache
  - 66% of patients
  - Most commonly temporal, but frontal or occipital pain also common
- Jaw pain(claudication)
  - 30% of patients

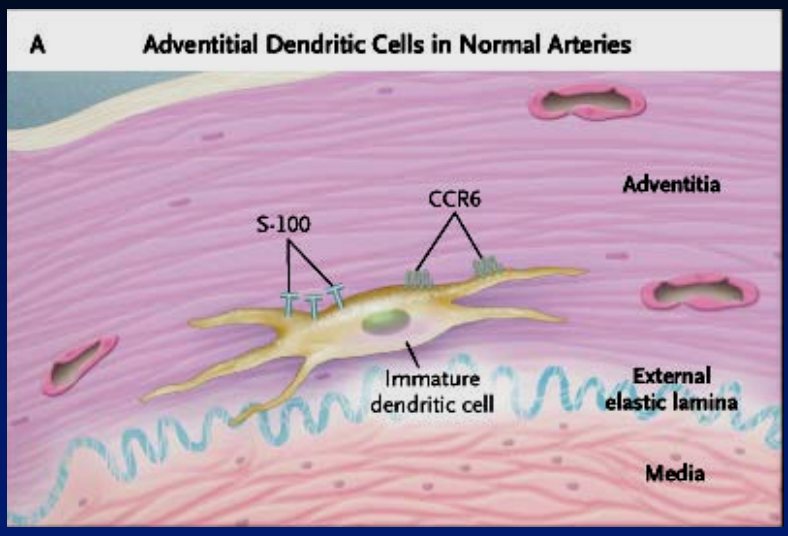
Clinical Manifestations

- Visual loss
  - Acute onset partial or complete visual field loss in 15% of patients
- Arm claudication
  - 5% of patients

Laboratory Abnormalities

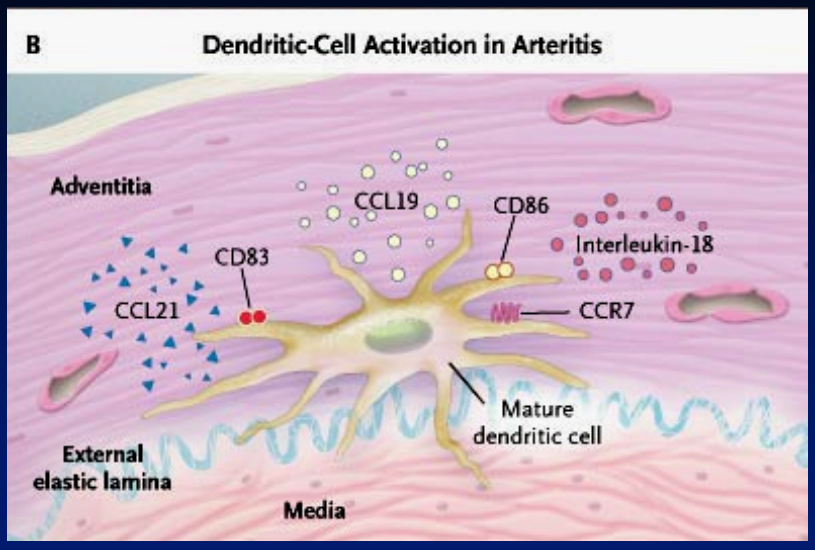
- Elevated Acute Phase Reactants
  - Erythrocyte sedimentation rate (ESR)
  - C-reactive protein
  - Elevated IL-6 levels

Giant Cell Arteritis Pathogenesis



Weyand, C. M. et al. N Engl J Med 2003;349:160-169

Giant Cell Arteritis Pathogenesis



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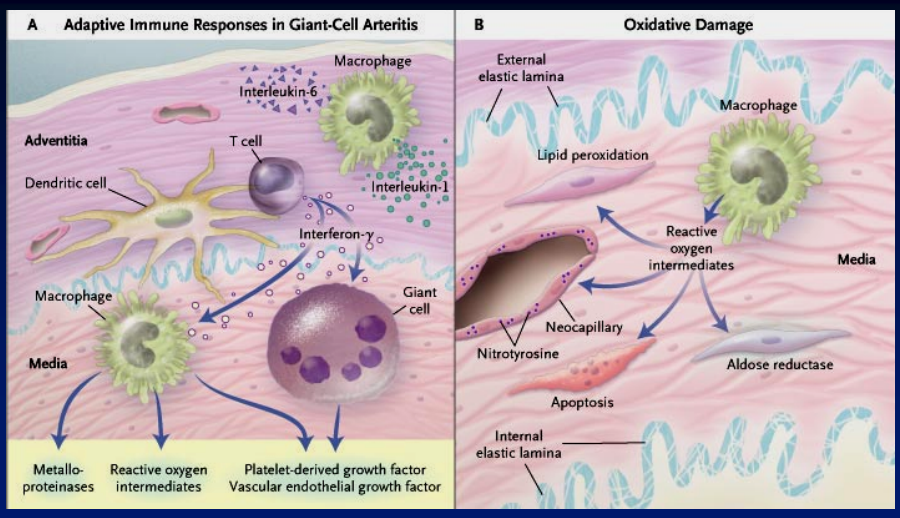
Giant Cell Arteritis Pathogenesis



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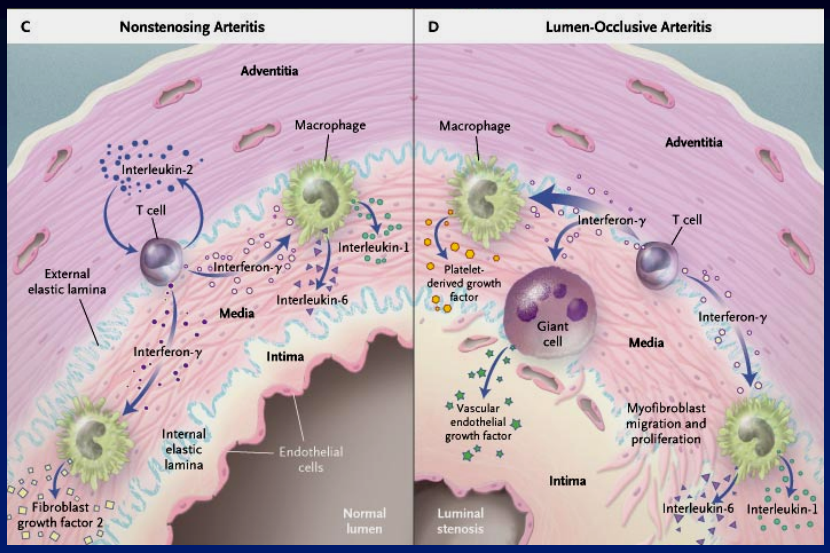
Giant Cell Arteritis Pathogenesis



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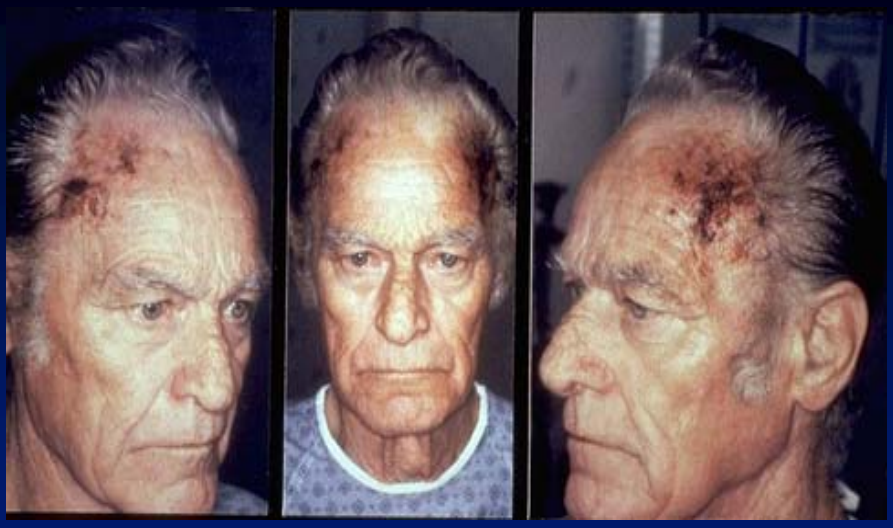
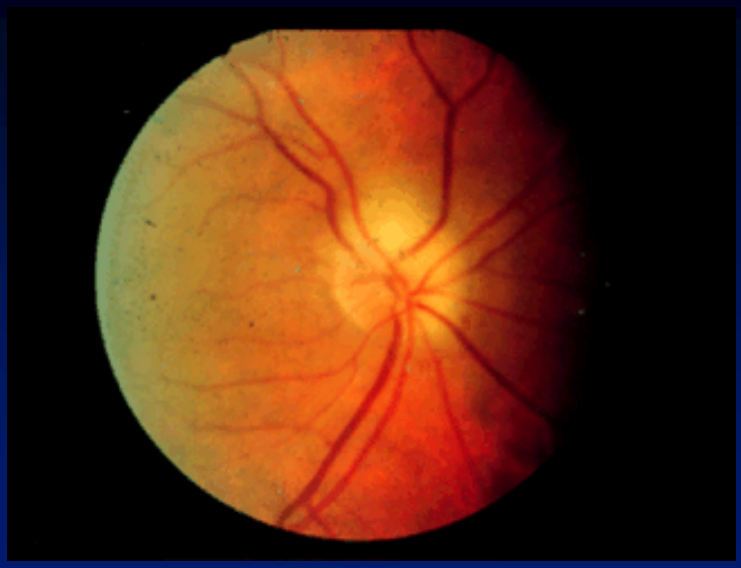
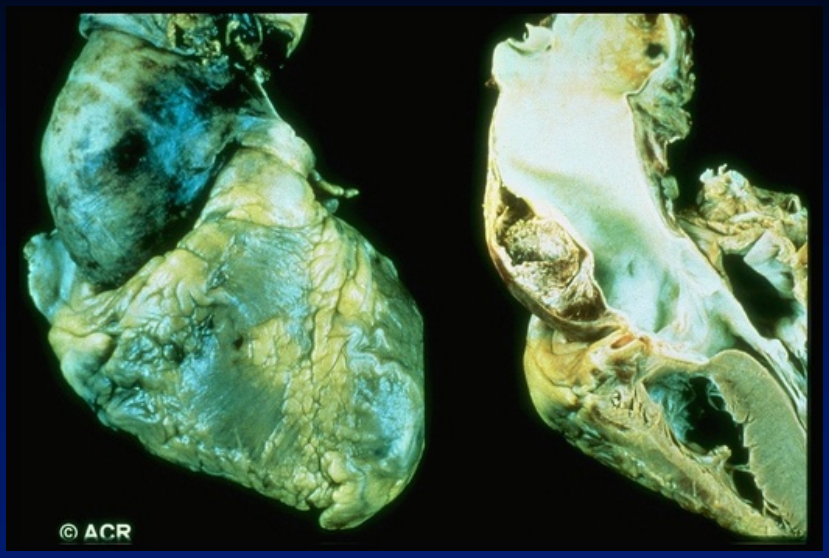


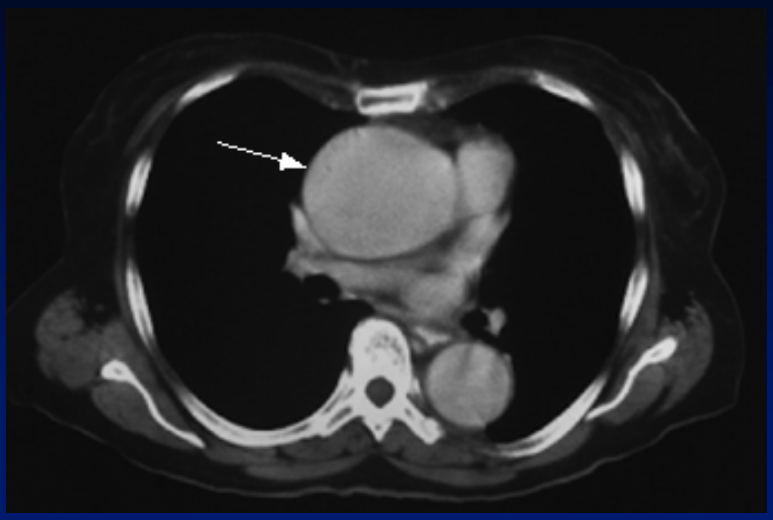
Optic Nerve Ischemia



Thoracic Aortic Aneurysm



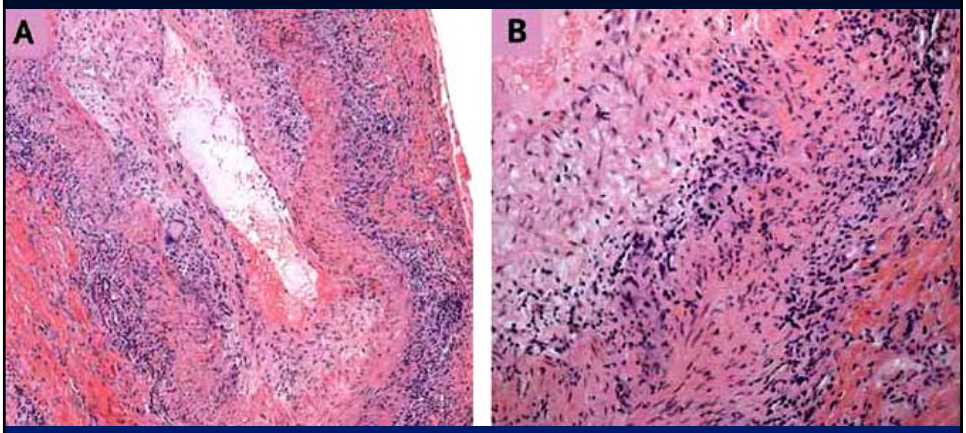
Thoracic Aortic Aneurysm



Diagnosis

- Elevated Acute Phase Reactants
  - Erythrocyte sedimentation rate (ESR)
  - C-reactive protein
- Temporal Artery biopsy

Giant Cell Arteritis of Temporal Artery



Weyand C and Goronzy J. N Engl J Med 2003;349:160-169

Treatment

- Glucocorticoids
  - Prednisone 1 mg/kg q d with tapering regimen over 4-6 months

Polyarteritis Nodosa

- Necrotizing arteritis of medium-sized muscular arteries
  - Pathology: “fibrinoid necrosis”

Vasculature involved

- Superior mesenteric artery
- Celiac and hepatic arteries
- Renal artery
- Muscular arteries of the extremities

Epidemiology of Polyarteritis Nodosa

- Age: 20-70 years-old
- No racial or ethnic predilection
- Incidence
  - 2-4/1,000,000 annual incidence
  - 70-80/1,000,000/ in regions which are endemic for Hepatitis B

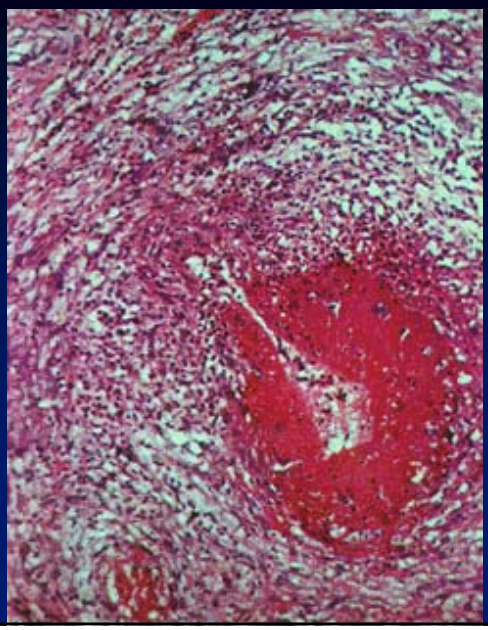
Hepatitis B Virus Association

- Usually occurs during the first 6 months after infection
- Usually positive for $HBAg_s$ and e antigen

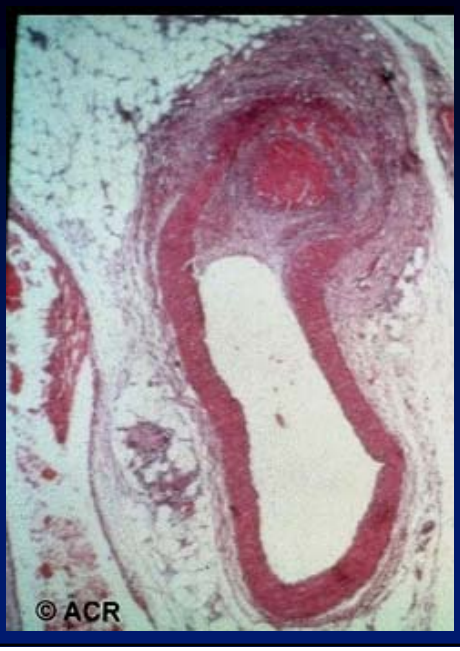
Prognosis of Polyarteritis Nodosa

- Untreated: 13% 5-year survival
- Treated: >70% 5-year survival

Polyarteritis Nodosa with Fibrinoid Necrosis



Polyarteritis Nodosa



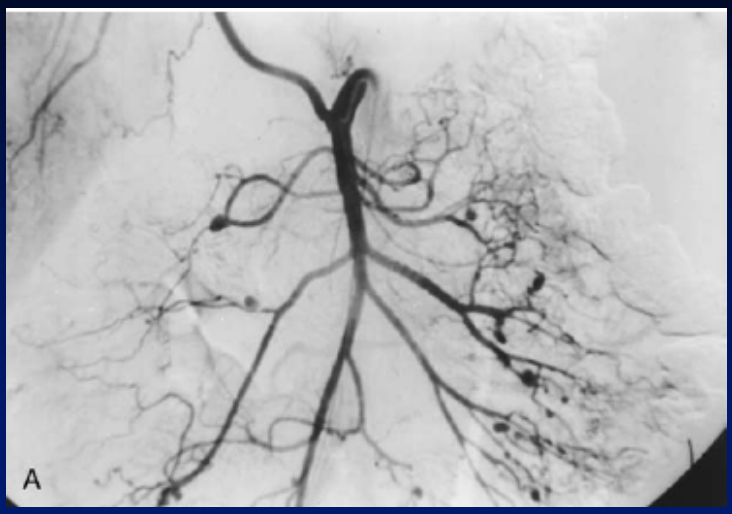
Clinical Manifestations

- Constitutional symptoms
  - Fatigue
  - Weight loss
  - Fever
- Gastrointestinal
  - Abdominal pain
  - Abdominal catastrophes
    - Shock secondary to aneurysmal rupture and resultant hemorrhage
    - Shock secondary to sepsis from intestinal ischemia or infarction

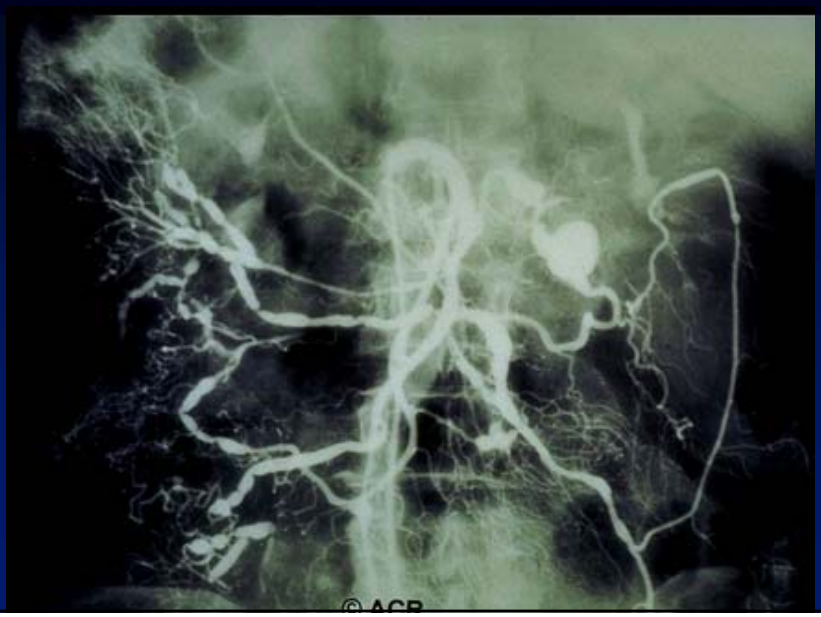
Clinical Manifestations

- Kidney
  - Hypertension
  - Renal Insufficiency
- Peripheral Nervous System
  - Mononeuritis multiplex (e.g. wrist drop, foot drop)
- Skin
  - Nodules or ulcers
  - Purpura
- Digital gangrene

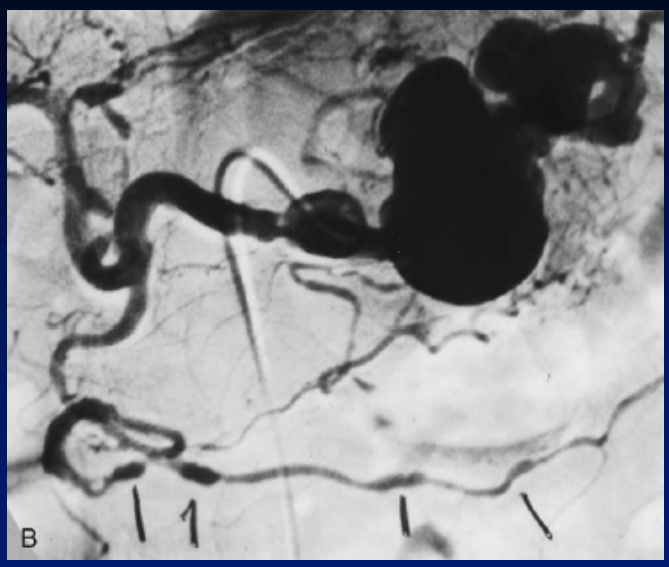
Angiogram of Superior Mesenteric Artery



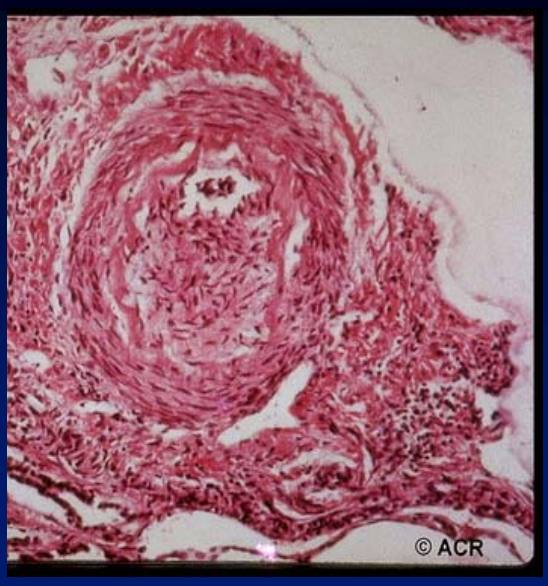
Angiogram of Superior Mesenteric Artery



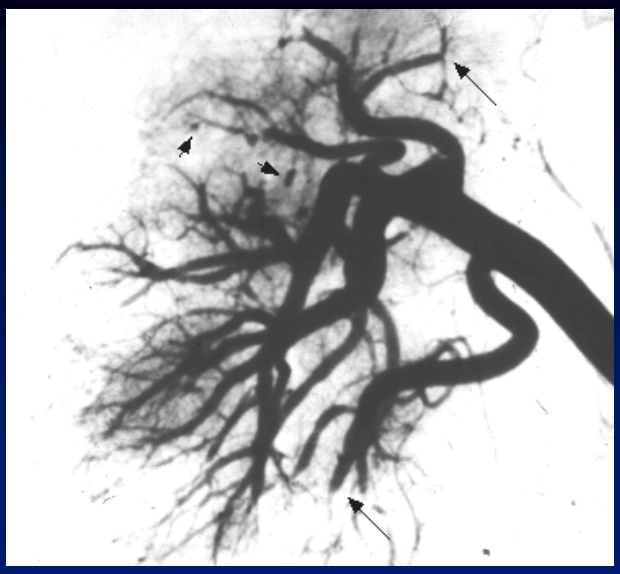
Angiogram Splenic Artery

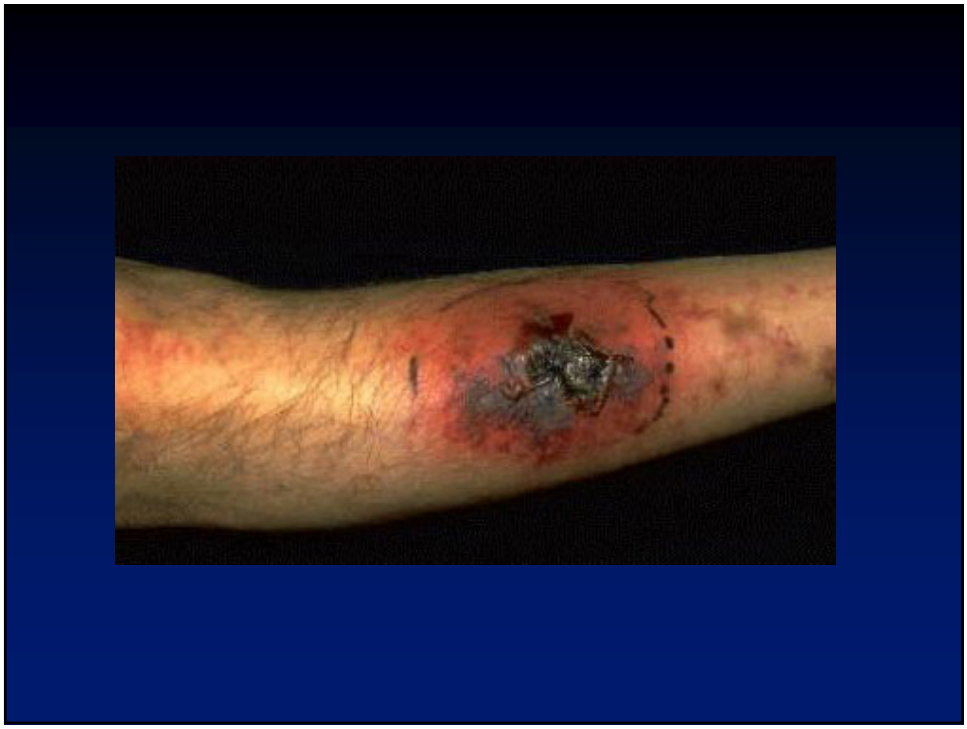


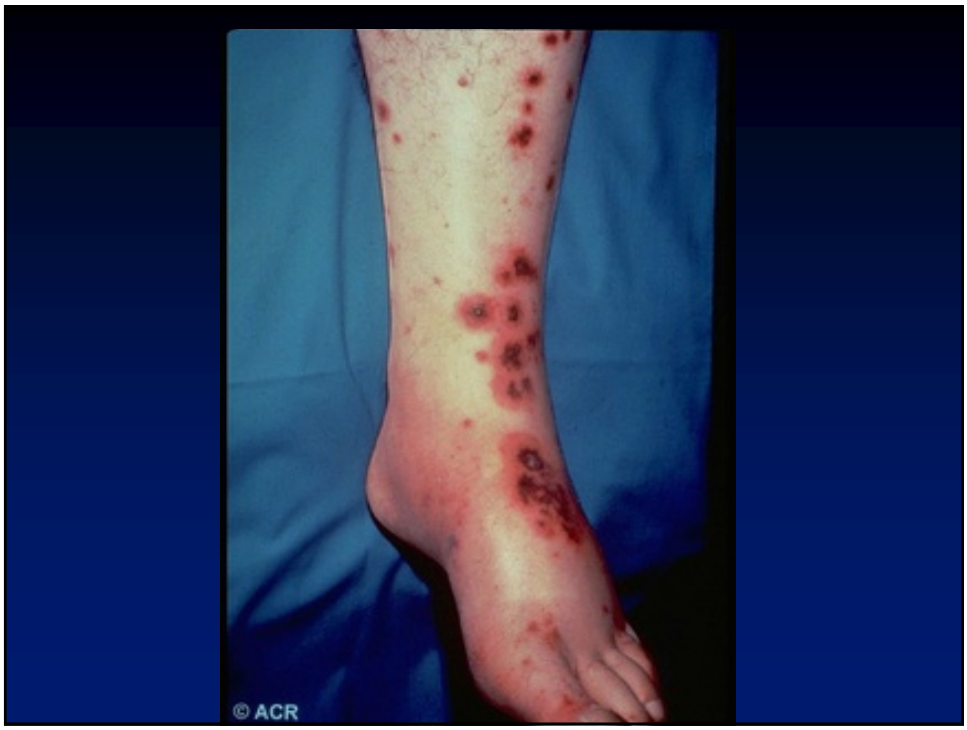
Vasculitis of Interlobar Artery of the Kidney



Renal Arteriogram



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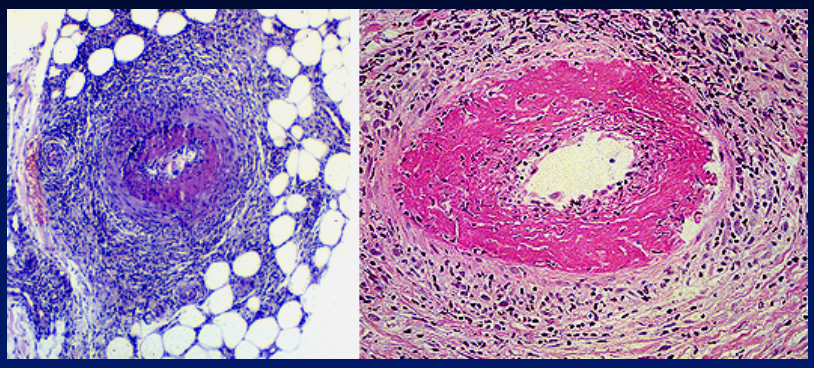
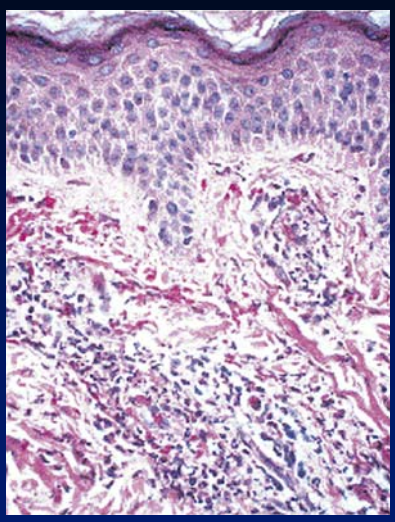
Dermal Vasculitis



Dermal Vasculitis



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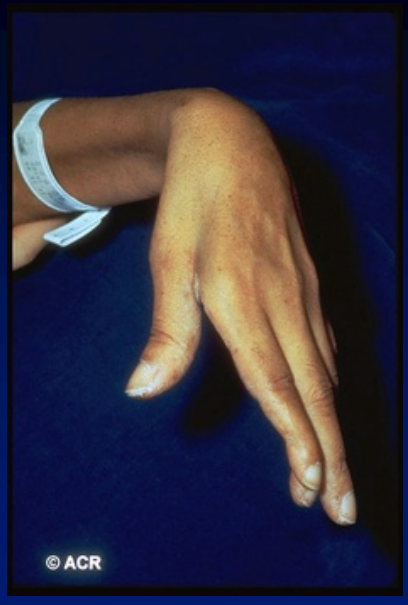
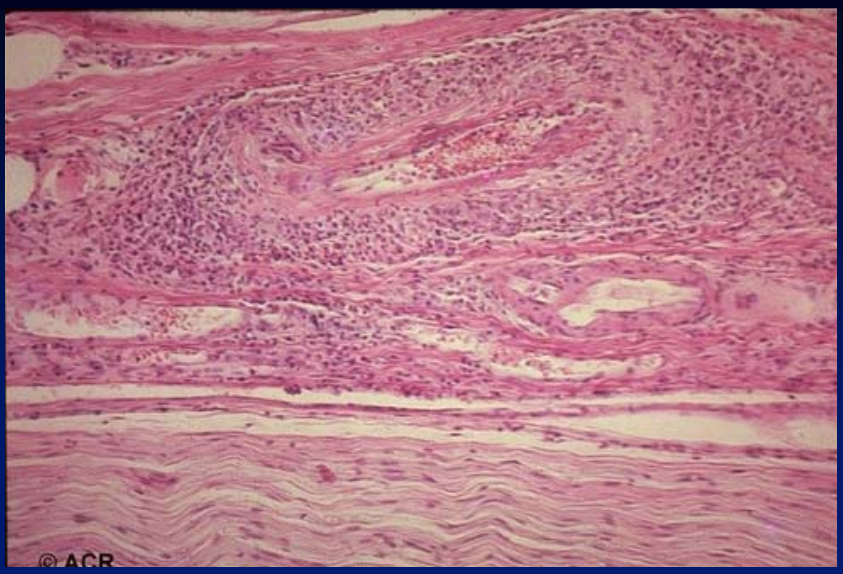
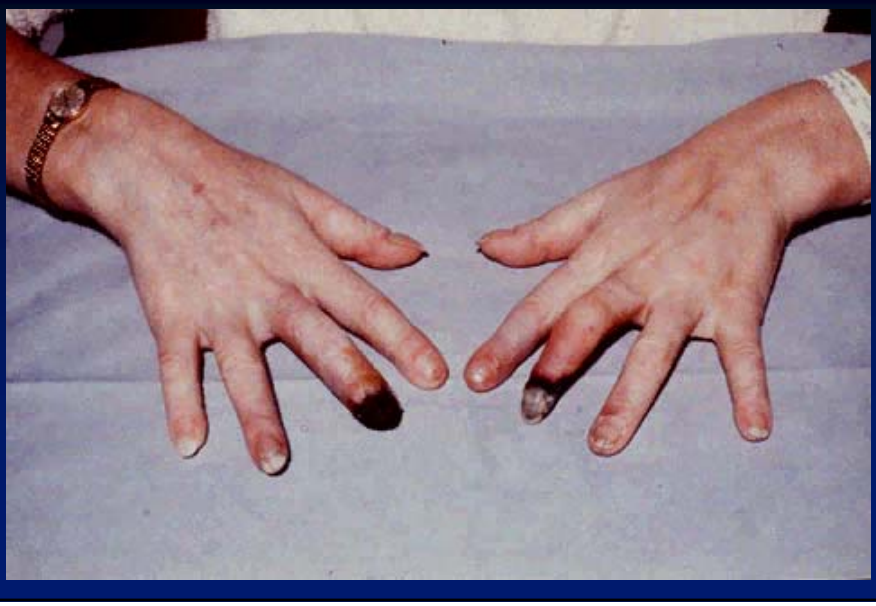
Mononeuritis Multiplex



Nerve Biopsy



Digital Gangrene



Treatment

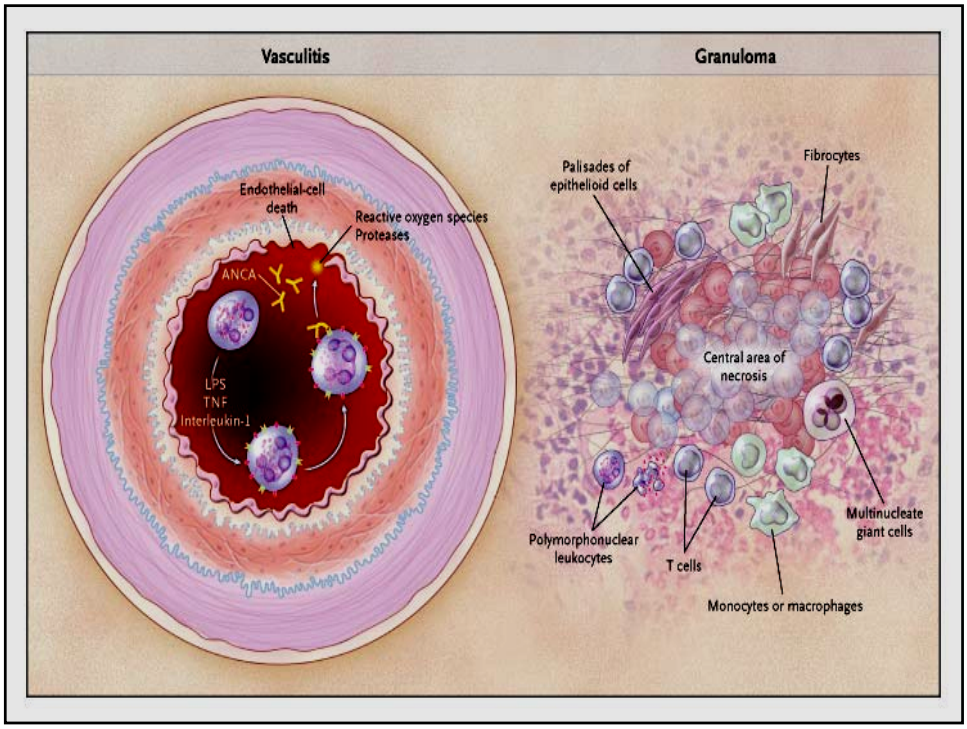
- 5 yr survival untreated: 13%
- Disease onset
  - Prednisone 1 mg/kg q d
  - Oral cyclophosphamide 2 mg/kg q d
- Duration of treatment
  - At least one year
- +HBV PAN
  - Interferon-α
  - Lamivudine

Wegener's Granulomatosis

- Necrotizing vasculitis of arterioles, capillaries, and postcapillary venules
- Associated with anti-neutrophil cytoplasmic antibodies (ANCA)

Granuloma

- Nodular aggregate of macrophages or cells derived from the monocyte-lineage, which is typically surrounded by a "rim" of lymphocytes, and commonly associated with the presence of multinucleated giant-cells



Vasculature involved

- Upper respiratory tract arterioles and capillaries
- Lung arterioles and capillaries
  - Pulmonary “capillaritis”
- Kidney
  - Glomerulonephritis (“pauci immune”)
    - No immune deposits
- Skin
- Peripheral Nervous system

Epidemiology of Wegener's Granulomatosis

- Age: 25-60 years-old
- No racial or ethnic predilection
- Prevalence: 5-7/100,000

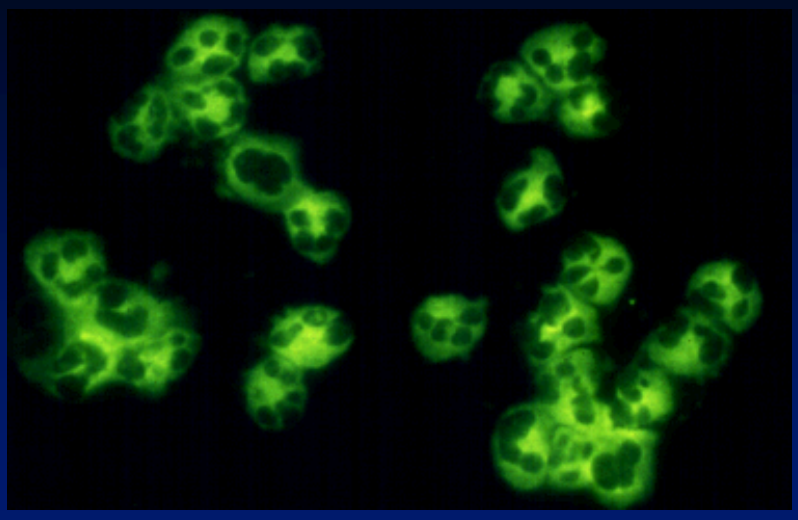
Clinical Manifestations

- Upper Respiratory Tract
  - Chronic Sinusitis
  - Chronic Otitis
- Lower Respiratory Tract
  - Pulmonary nodules
  - Alveolar hemorrhage(hemoptysis)
- Kidney
  - Glomerulonephritis(crescentic)
- Peripheral Nervous System
  - Mononeuritis multiplex
- Skin
  - Purpura

ANCA associated

- > 90% have elevated titers of anti-neutrophil cytoplasmic antibodies

Anti-Neutrophil Cytoplasmic Ab (ANCA)



ANCA in Wegener's Granulomatosis

- Cytoplasmic reactivity (C-ANCA)
  - Antigenic target = Proteinase 3
    - Serine proteinase of lysosomal granules of monocytes and azurophilic granules of neutrophils
- Assay: Anti-proteinase 3 Ab titers (ELISA)

Morbidity of Wegener's Granulomatosis

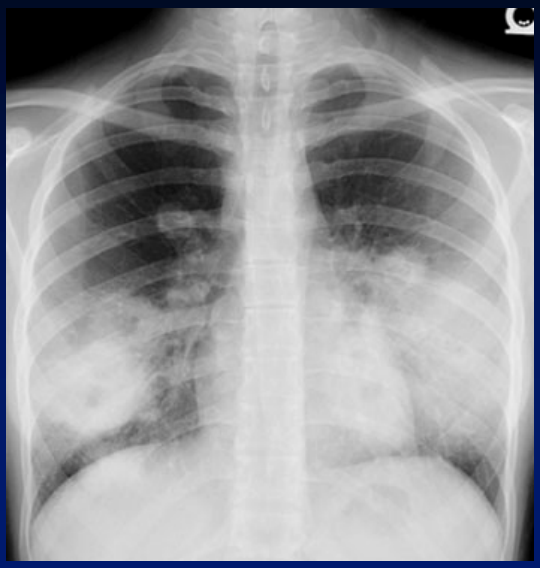
- Permanent renal insufficiency- 42%
- End-stage renal disease- 11%
- Hearing loss- 35%
- Nasal deformities- 28%
- Tracheal stenosis- 13%

Mortality of Wegener's Granulomatosis

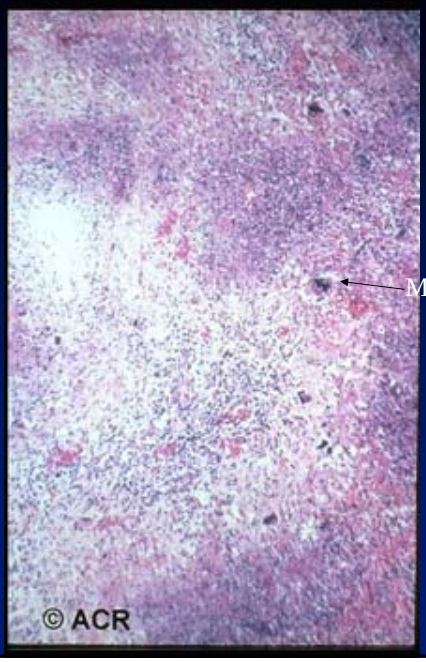
- Untreated: 10% survival at 2 years
- Treated: 80% survival at 10 years

Saddle Nose Deformity

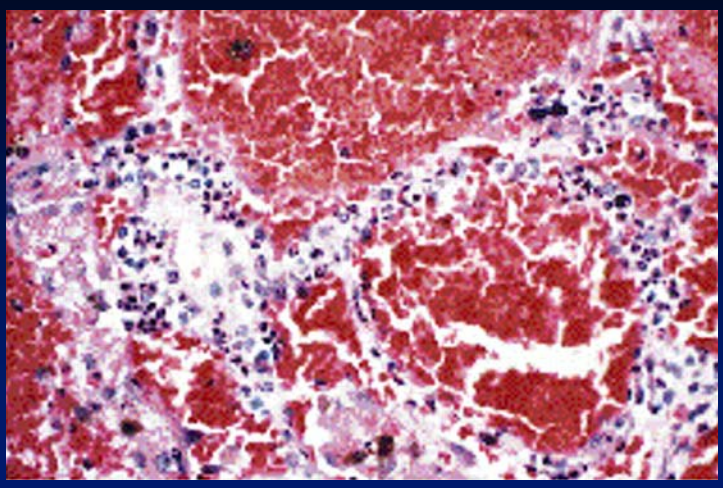
Pulmonary Nodules



Granulomatous Inflammation



Pulmonary Hemorrhage



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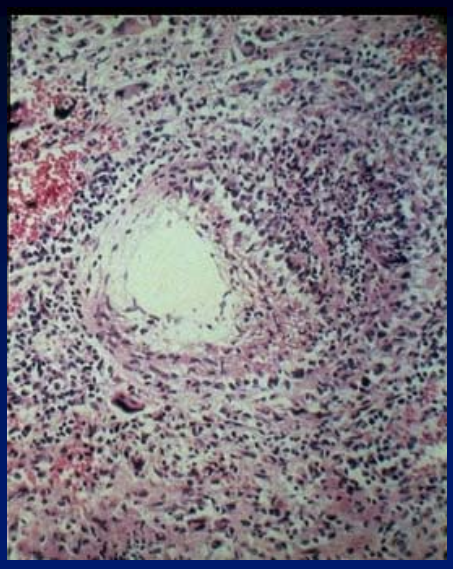
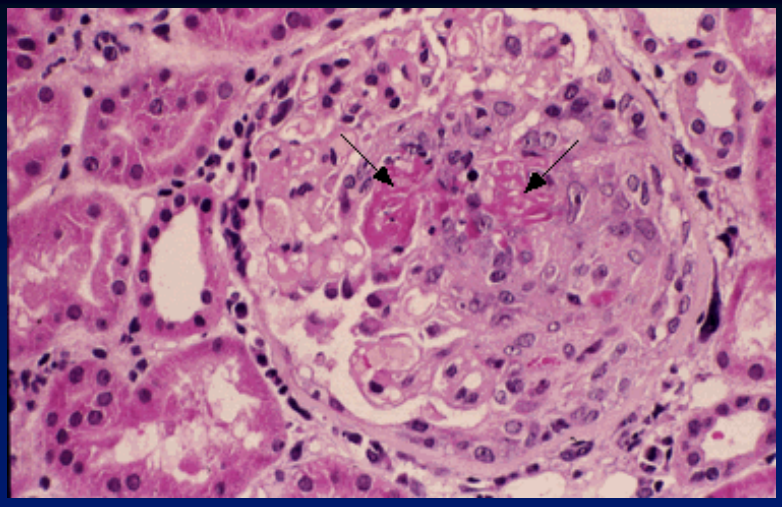
Pulmonary Arteriolar Vasculitis

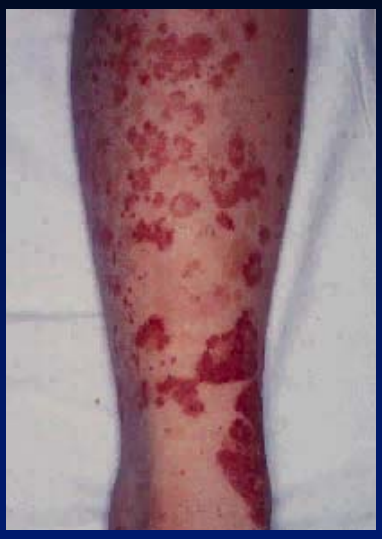


Necrotizing Glomerulonephritis*

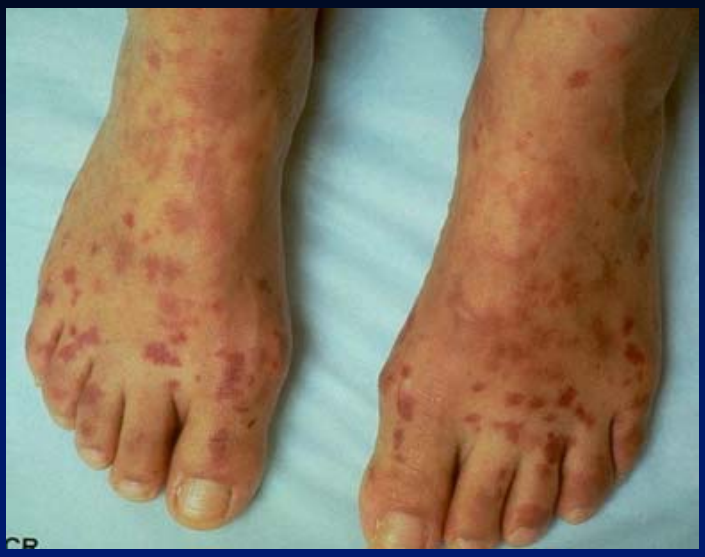


* “Pauci-immune” Glomerulonephritis

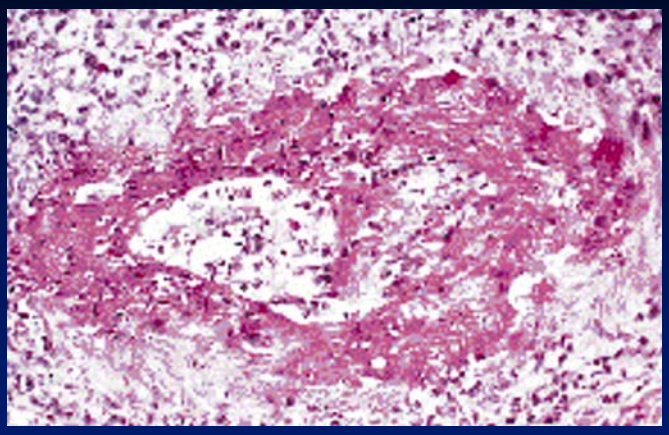
Palpable Purpura



Palpable Purpura



Necrotizing Arteritis in a Small Epineural Artery



Jennette J and Falk R. N Engl J Med 1997;337:1512-1523

Treatment Regimen

- Prednisone 0.5-1 mg/kg q d (tapered) plus cyclophosphamide 2 mg/kg q d for approximately one year
  - 85-90% response rate
  - 75% complete remission
  - 30-50% at least one relapse

Henoch Schonlein Purpura

- Immune-complex mediated small vessel vasculitis

Henoch Schonlein Purpura

- Age: 5-7 years old (range: 5-15)
  - Children: 20/100,000
    - 50% preceded by upper respiratory tract infection
  - Adults: <1/100,000
- Gender: male/female : 1.8/1

Vasculature involved

- Gastrointestinal tract
  - Submucosal arterioles/venules
- Kidney
  - Glomerulonephritis(mesangial)
- Skin
  - Dermal arterioles, capillaries, and postcapillary venules

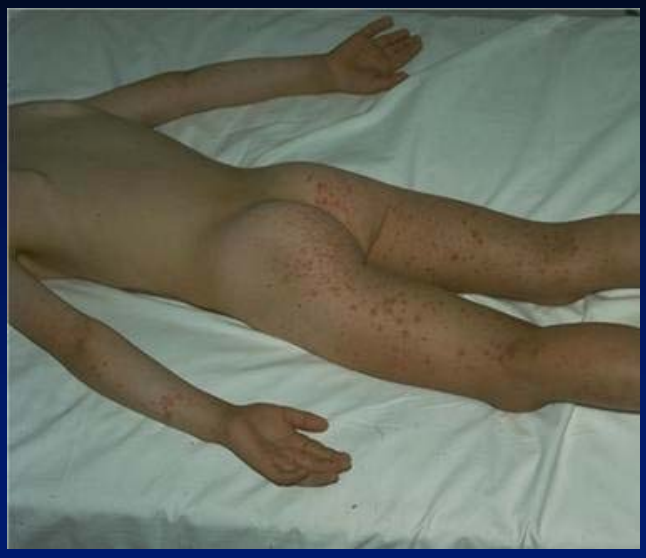
Clinical Manifestations

- Abdominal pain ("purpura" of the small bowel, i.e., submucosal hemorrhage)
  - Intussusception
- Hematuria/proteinuria
  - Renal insufficiency infrequent
- Purpura
- Arthralgia/arthritis

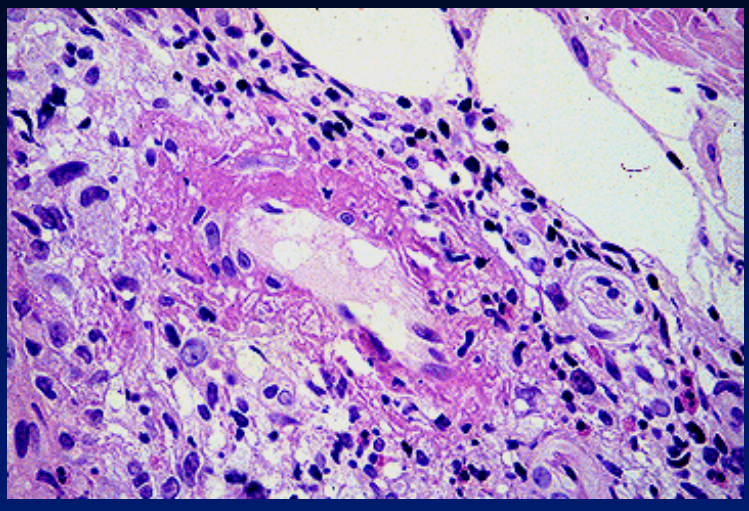
Pathogenesis

- Activation of the mucosal humoral immune compartment resulting in tissue (vascular) deposition of IgA-containing immune complexes

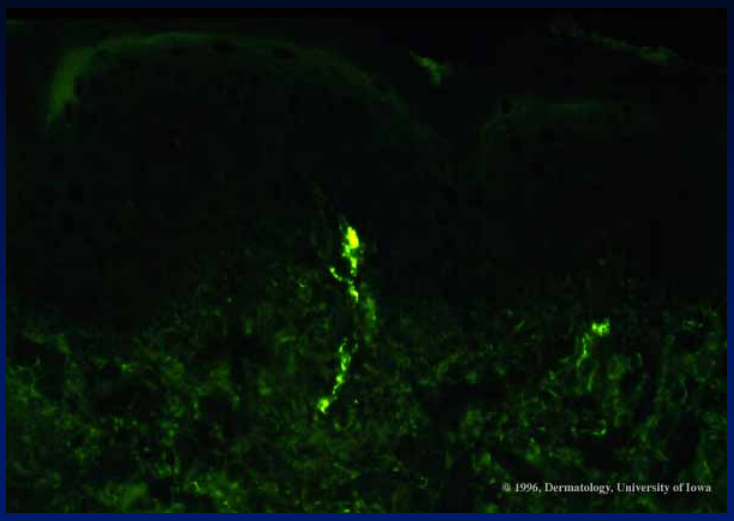
Purpura of the Buttocks



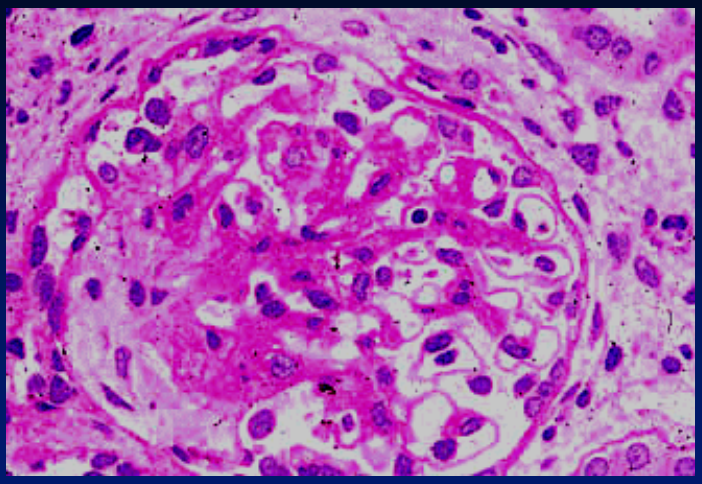
Small Vessel Dermal Vasculitis



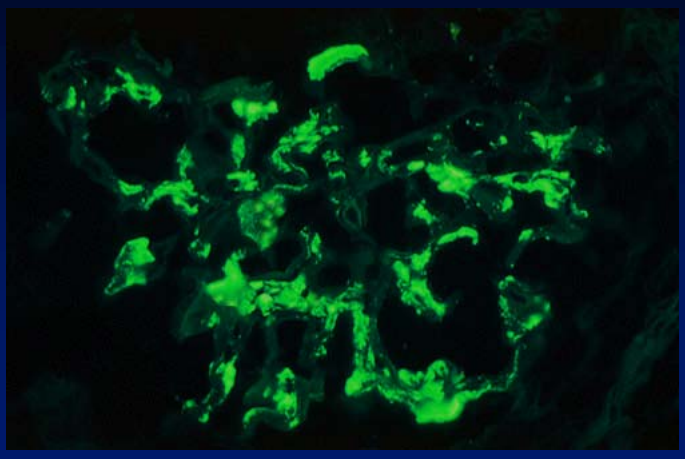
IgA Deposition in Dermal Vasculature



HSP Glomerulonephritis



IgA Deposition in the Mesangium



Prognosis of Henoch Schonlein Purpura

- 90-95% of patients exhibit spontaneous remission after 3-4 weeks, with 20-30% experiencing short-term relapses within the following 6-12 months

Treatment

- Supportive
  - Hydration
  - Bed rest
  - Analgesia
    - Non-steroidal antiinflammatory agents

Vasculitis

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