Vasculitis 🩸

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1. Definition

Vasculitis = inflammation of blood vessel walls.

Major pathogenic mechanisms:

1. Immune-mediated inflammation
2. Direct infectious invasion
3. Physical/chemical injury (radiation, toxins, trauma)

⚠️ Critical: Immune-mediated vasculitis → treated with immunosuppressives;

Infectious vasculitis → immunosuppression can worsen infection.

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2. Classification

Vasculitis can be classified by:

- Vessel size (large, medium, small)
- Immune mechanism (immune complex vs ANCA-mediated)
- Granuloma formation
- Organ involvement
- Demographics

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3. Clinical Features ✨

- Local signs: depend on vascular bed affected → ischemia, infarction, hemorrhage
- Systemic signs: fever, malaise, myalgia, arthralgias

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4. Noninfectious Vasculitis: Immunologic Mechanisms 🧬

I. Immune complex deposition

II.   Antineutrophil cytoplasmic antibodies (ANCA)

III. Anti-endothelial cell antibodies

IV. Autoreactive T cells

4a. Immune Complex-Associated Vasculitis

- Seen in autoimmune disorders (e.g., SLE)
- Vascular lesions resemble Arthus reaction / serum sickness
- May contain antibody + complement deposits

Examples:

I. Drug hypersensitivity vasculitis
- A. Drugs bind host proteins → antibody formation → immune complex deposition
- B. Common drugs: penicillin, streptokinase
- C. Clinical: mild skin lesions → severe/fatal
- D. Management: stop offending drug ✅

II. Infection-associated vasculitis

A. Immune complexes formed against microbial antigens
B. Example: Polyarteritis nodosa (~30% cases related to HBV antigen–antibody complexes)

4b. ANCA-Associated Vasculitis 🔬

ANCAs = autoantibodies against neutrophil cytoplasmic antigens

ANCA Type	Antigen	Disease Association	Notes
PR3-ANCA (c-ANCA)	Proteinase-3 (neutrophil azurophilic granules)	Granulomatosis with polyangiitis (GPA)	Shares homology with microbial peptides
MPO-ANCA (p-ANCA)	Myeloperoxidase	Microscopic polyangiitis, Eosinophilic granulomatosis with polyangiitis (EGPA)	Can be drug-induced (e.g., propylthiouracil)

Key points:

- ANCAs correlate with disease activity
- Cause neutrophil activation → ROS & proteases → endothelial injury
- Lesions are usually pauci-immune (minimal immune complexes)

4c. Pathogenic Sequence: ANCA Vasculitis 🔄

Flowchart:

Immune trigger (drug / microbial antigen)

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Induction of ANCA formation (PR3 or MPO)

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Inflammatory stimulus → cytokines (e.g., TNF) ↑

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PR3/MPO expressed on neutrophil surface

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ANCAs bind → neutrophil activation

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Release of reactive oxygen species & granule enzymes

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Endothelial injury → vasculitis ✅

💡 High-Yield Exam Points

- Immune complex vasculitis → antibody + complement deposition;
- Pauci-immune in ANCA vasculitis (Antibody-mediated neutrophil activation, NOT immune complex deposition in the vessel wall)
- c-ANCA / PR3 → GPA; p-ANCA / MPO → MPA, EGPA
- Drugs & infections are common triggers
- Systemic signs (fever, myalgia, arthralgia) often accompany organ-specific ischemic damage

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S. Other Immunologic Mechanisms 🧬

5a. Anti-Endothelial Cell Antibodies (AECA)

- Target endothelial cells (ECs) directly → EC injury
- Implicated in:
  - Kawasaki disease ✅
  - Some drug-induced or autoimmune vasculitis
- Mechanism: antibody binding → complement activation → inflammation → vessel wall damage

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5b. Autoreactive T Cells

- T cells recognize self-antigens on vascular cells → chronic inflammation
- Often associated with granuloma formation
- Key examples:
  - Giant cell arteritis (granulomatous inflammation of large arteries)
  - Granulomatosis with polyangiitis (GPA)

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6. Key Points 🔑

- Vasculitis may have overlapping features, making classification tricky
- Classic forms exist, but many cases are mixed or atypical
- Understanding pathogenic mechanism helps guide:
    - Diagnosis
    - Laboratory testing (e.g., ANCA, AECA)
    - Therapy (immunosuppressive vs antimicrobial)

Summary: Immunologic Mechanisms of Vasculitis 📝

Mechanism	Examples	Key Features	Notes
Immune Complex Deposition	SLE, Drug-induced, Infection-related	Antibody + complement in vessel wall	Often small vessels; variable severity

ANCA (PR3/MPO)	GPA, MPA, EGPA	Pauci-immune, neutrophil activation	Titers correlate with activity
Anti-Endothelial Cell Antibodies (AECA)	Kawasaki disease	Direct EC injury	Often in children
Autoreactive T Cells	Giant cell arteritis, GPA	Granulomatous inflammation	Chronic vessel wall injury

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💡 High-Yield Tip

- Mechanism → Lab test → Treatment
  - Immune complex → complement/Ab deposition → stop trigger / immunosuppression
  - ANCA → PR3/MPO antibodies → immunosuppression
  - AECA → anti-EC antibody detection → immunosuppression
  - T-cell mediated → biopsy showing granulomas → corticosteroids

-> The End <-