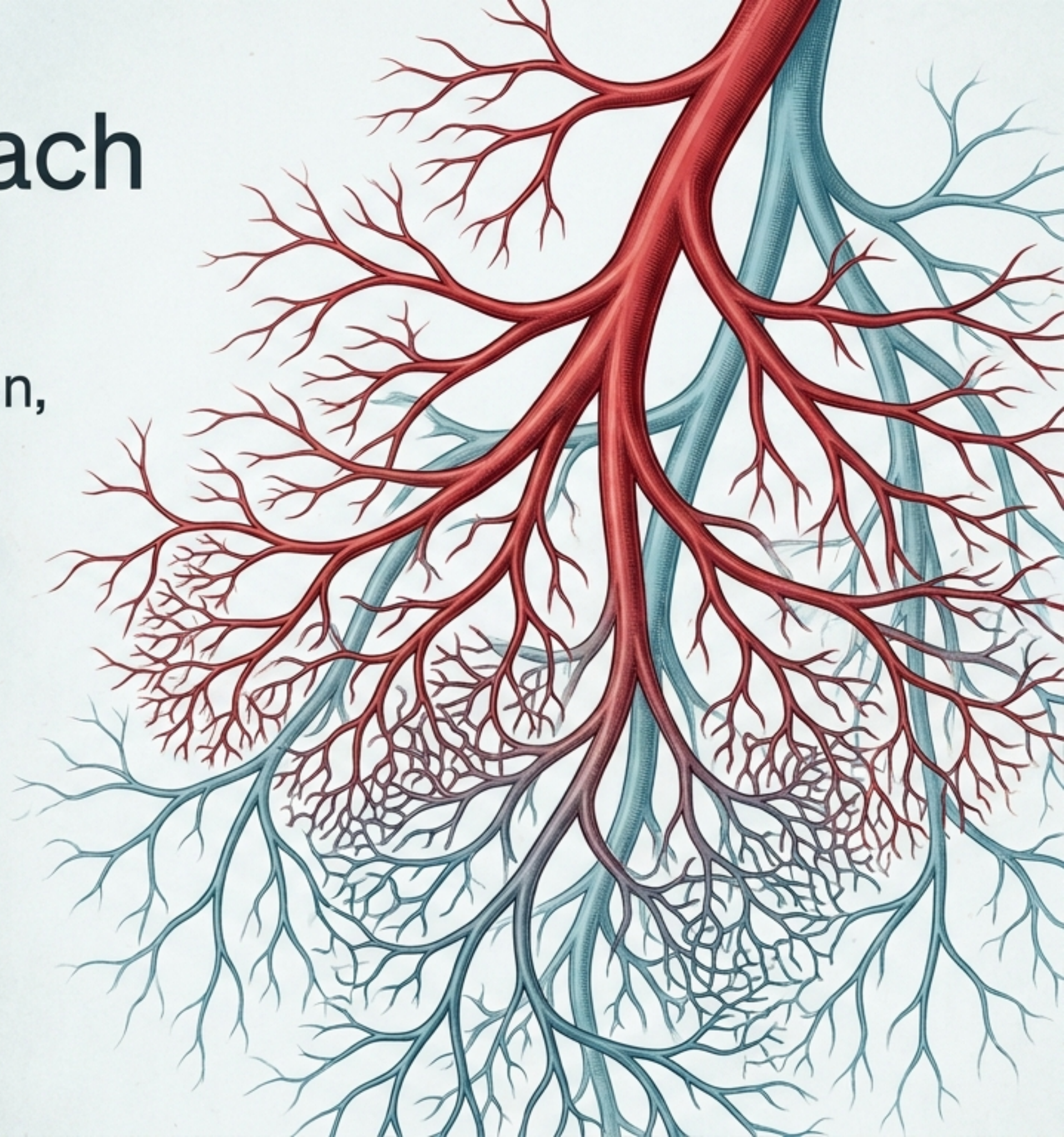


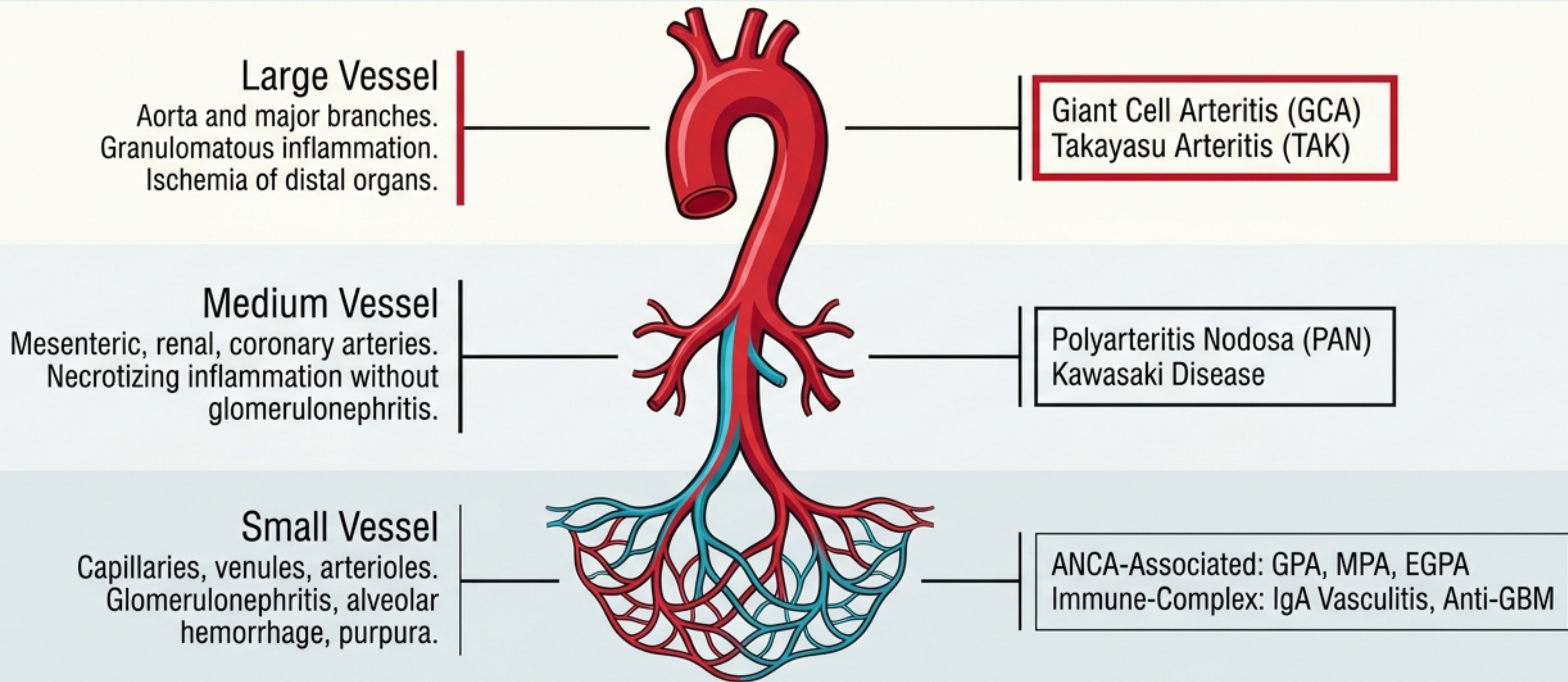
A Systemic Approach to Vasculitis

Clinical diagnosis, risk stratification, and targeted management across the vascular tree.



Based on the International Chapel Hill Consensus Conference (CHCC) Nomenclature and current Australian PBS/TGA guidelines.

The Chapel Hill Calibration Diagram



Diagnostic Pitfall: CHCC 2012 is a nomenclature system, not a diagnostic algorithm. Diagnosis requires integrating history, histopathology, serology, and imaging.

Differentiating Large Vessel Vasculitis

Giant Cell Arteritis (GCA)

Epidemiology

Age >50 (Peak 70-80).
Female:Male 2-3:1.
Australian incidence: 15-25 per 100,000.

Prime Targets

Cranial branches of the aorta (Temporal artery).

Clinical Clues

New-onset headache (~70%)
Jaw claudication (~50%, highly specific)
Polymyalgia Rheumatica coexistence (40-60%)

Takayasu Arteritis (TAK)

Epidemiology

Age <40 (Peak 15-30).
Female:Male 8-9:1.
Higher prevalence in Asian/Middle Eastern descent.

Prime Targets

Aorta and major arch branches.

Clinical Clues

Limb claudication, pulse deficits
Subclavian/carotid bruits
Limb BP discrepancy (>10 mmHg)

Diagnosis: CTA or MRA (MRA preferred for follow-up to avoid radiation).
PET-CT useful for early/occult active disease.

The GCA Emergency Protocol

Hour 0 - Suspicion

Triggers: Visual symptoms (amaurosis fugax, diplopia), jaw claudication, temporal tenderness, ESR >50 mm/hr.



Sudden irreversible vision loss occurs in up to 20% of untreated GCA.

Immediate Action - Before Biopsy

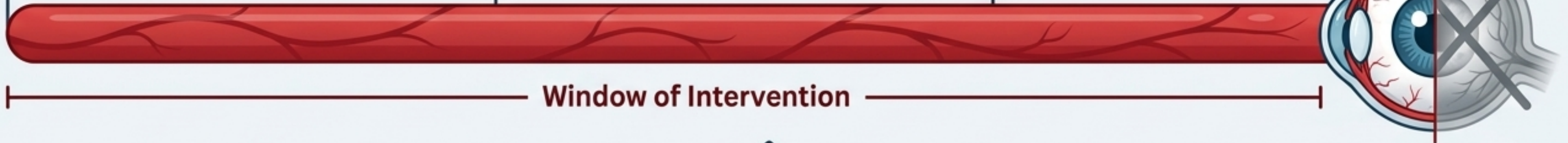
Treatment: High-dose IV **Methylprednisolone** (500 mg–1 g daily for 3 days).

Rule: DO NOT wait for temporal artery biopsy (TAB) or imaging.

Diagnostic Confirmation - Days 1 to 14

Action: **Temporal Artery Biopsy** (Gold standard, unilateral ≥ 1 cm segment to avoid skip lesions) or **CDUS** (looking for Halo/compression signs).

Rule: Biopsy remains diagnostically valid within 2 weeks of starting glucocorticoids.

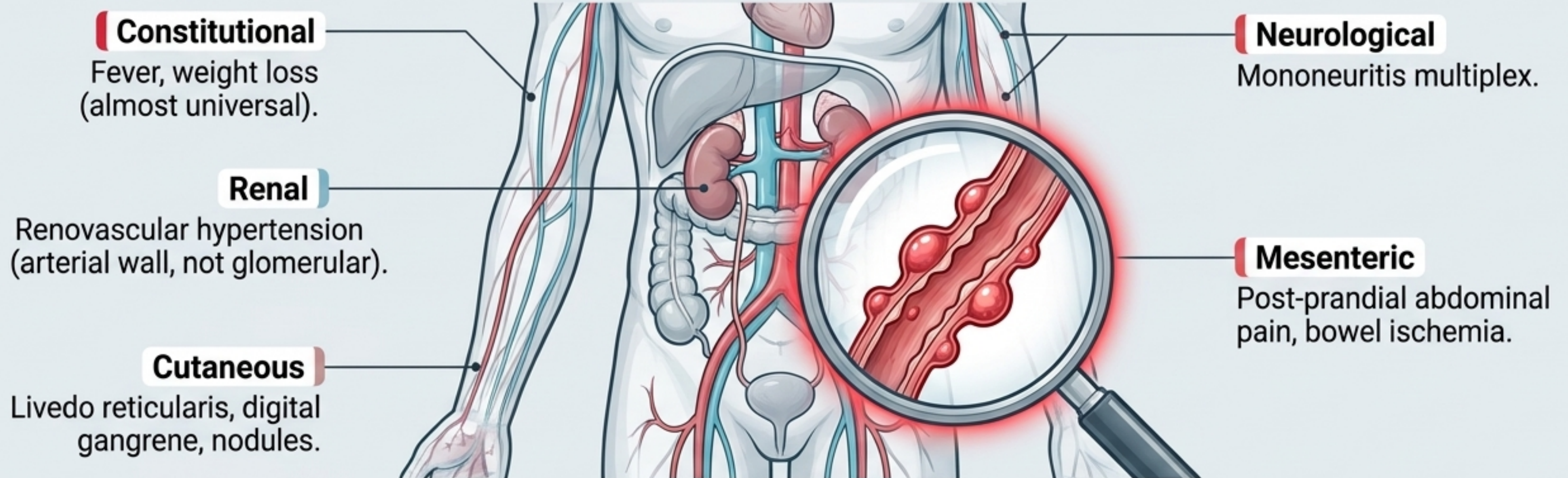


Long-Term Follow-up: Taper to oral prednisolone (1 mg/kg/day).
Tocilizumab (162 mg SC weekly, PBS Authority Required) reduces relapse by ~50%.

Polyarteritis Nodosa (PAN): The Muscular Artery Target

Necrotizing medium-vessel vasculitis. Crucial differentiator: **Sparses the lungs and glomeruli** (ANCA is negative).

Clinical Presentation Map



Diagnostic Pillars

Imaging:
Conventional or CT Angiography
(renal/hepatic/mesenteric microaneurysms).

Biopsy:
Fibrinoid necrosis of medium-vessel
walls with neutrophilic infiltrate.

Serology Mandatory:
Hepatitis B screening must be
performed in every case.

The HBV-PAN Divergence

Confirmed PAN Diagnosis → Mandatory Hepatitis B Serology (HBsAg, anti-HBc, anti-HBs)

HBV-Negative PAN

Mechanism: Primary autoimmune etiology.

Therapy: Standard Immunosuppression. Prednisolone (1 mg/kg/day) + Cyclophosphamide for severe/organ-threatening disease.

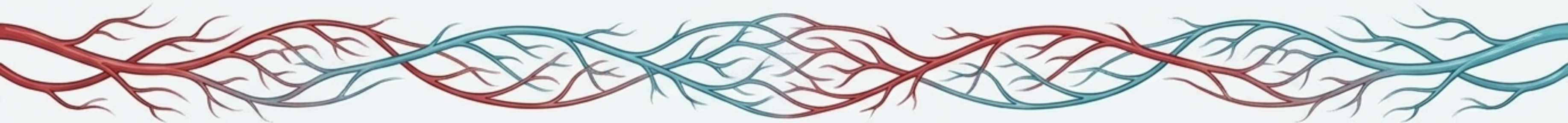
HBV-Associated PAN (~30% worldwide)

! Mechanism Alert: Prolonged immunosuppression causes disastrous viral replication flare and impairs clearance. Do NOT use Rituximab or Cyclophosphamide.

Therapy Phase 1: Short-course corticosteroids only (1–2 weeks) for acute symptom control.

Therapy Phase 2: Antiviral cornerstone (Entecavir 0.5mg or Tenofovir 300mg daily). Consider plasma exchange (PLEX) for severe cases.

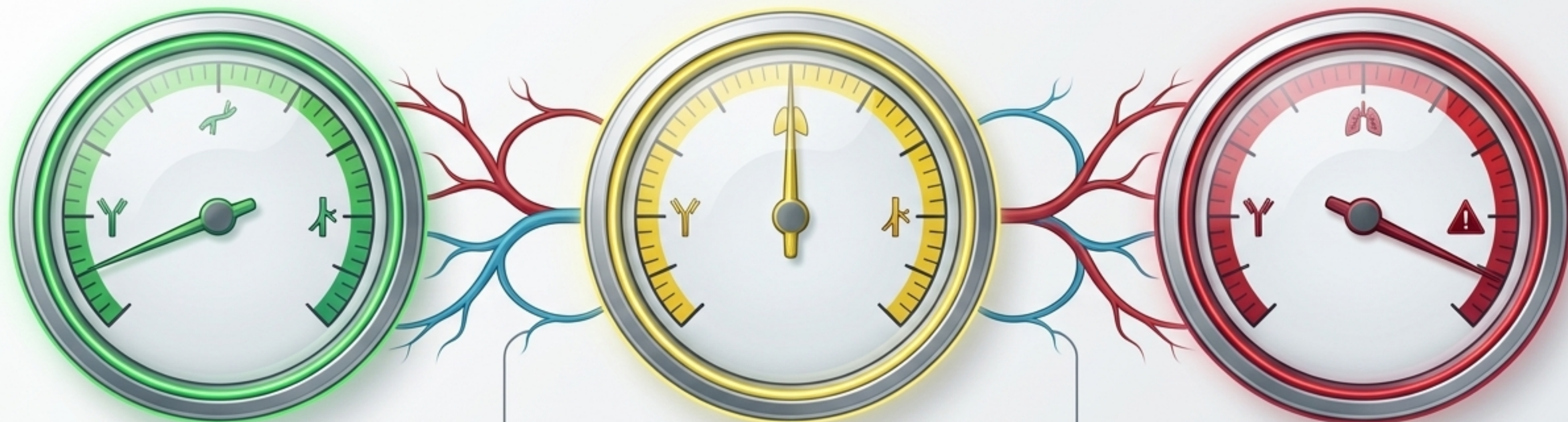
The ANCA-Associated Vasculitis (AAV) Spectrum



The AAV Spectrum Matrix

	GPA	MPA	EGPA
Classic Presentation	The Triad (Upper airway/saddle-nose + lower airway/cavities + pauci-immune glomerulonephritis).	Pulmonary-Renal Syndrome (Rapidly progressive glomerulonephritis + pulmonary capillaritis).	Asthma + Migratory pulmonary infiltrates + Mononeuritis multiplex.
Typical Serology	c-ANCA / anti-PR3 (70-90%).	p-ANCA / anti-MPO (60-80%).	p-ANCA / anti-MPO (~40%).
Histological Hallmarks	Granulomatous inflammation.	No granulomas; necrotizing.	Eosinophilia ($\geq 10\%$ or $\geq 1.0 \times 10^9/L$) + extravascular eosinophilic inflammation.

AAV Severity Stratification



Mild / Limited

- **Threat Level:** Non-organ-threatening. Upper airway disease, arthralgia, minor skin involvement.
- **Setting:** Outpatient rheumatology/immunology.

Moderate / Generalised

- **Threat Level:** Active, not immediately life-threatening. Mild renal impairment (eGFR >30), pulmonary infiltrates (no hemorrhage).
- **Setting:** Specialist-initiated, outpatient-supervised induction.

Severe / Life-Threatening

- **Threat Level:** Organ-threatening. Pulmonary hemorrhage, RPGN (eGFR <30 / dialysis), cerebral vasculitis, motor neuropathy.
- **Setting:** Inpatient / ICU.

Monitoring Note: Use the BVAS (Birmingham Vasculitis Activity Score) tool to assess ongoing disease activity across all severities.

Severe AAV Induction & Maintenance Algorithm

Step 1: Acute Induction (Hospital Admission)

Pulse IV **Methylprednisolone** 500 mg–1 g daily for 3 days.
Transition to: **Oral Prednisolone** 1 mg/kg/day (max 60 mg).

Step 2: Primary Biologic/Cytotoxic Choice

Option A: Rituximab

Preferred for relapsing, PR3-ANCA, first-line alternative.
Screen for Hep B first.

Option B: Cyclophosphamide

IV pulse preferred over oral to reduce cumulative toxicity.
Use MESNA, monitor for cystitis.

Step 3: Glucocorticoid Sparing (Optional Add-on)

Avacopan (C5a receptor inhibitor) 30 mg PO BD. TGA-approved for severe AAV alongside standard induction. Allows rapid steroid taper.

Step 4: Mandatory Adjuncts

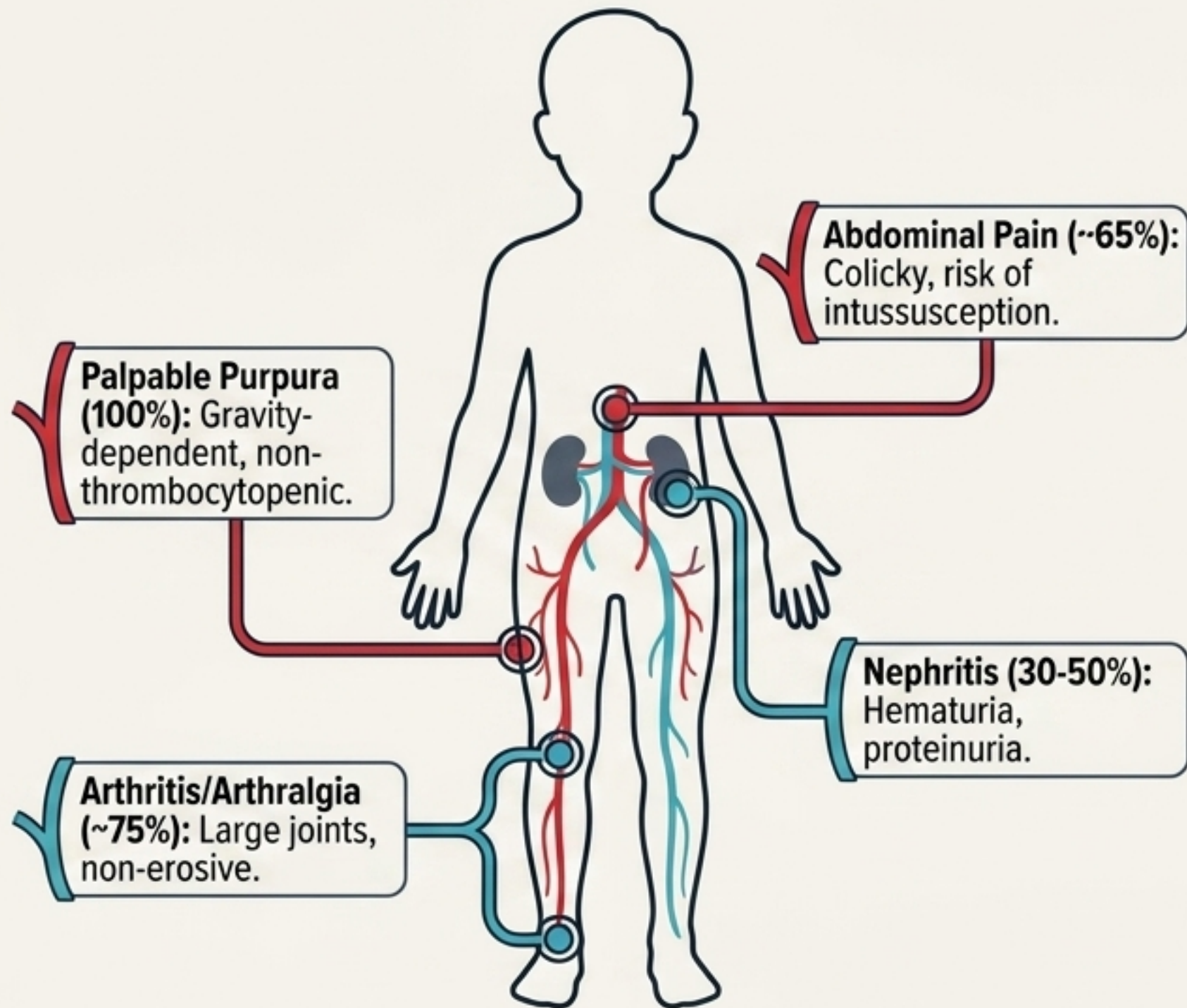
PJP Prophylaxis: Co-trimoxazole daily or 3x/week (avoid if eGFR <15).

Step 5: Maintenance Phase

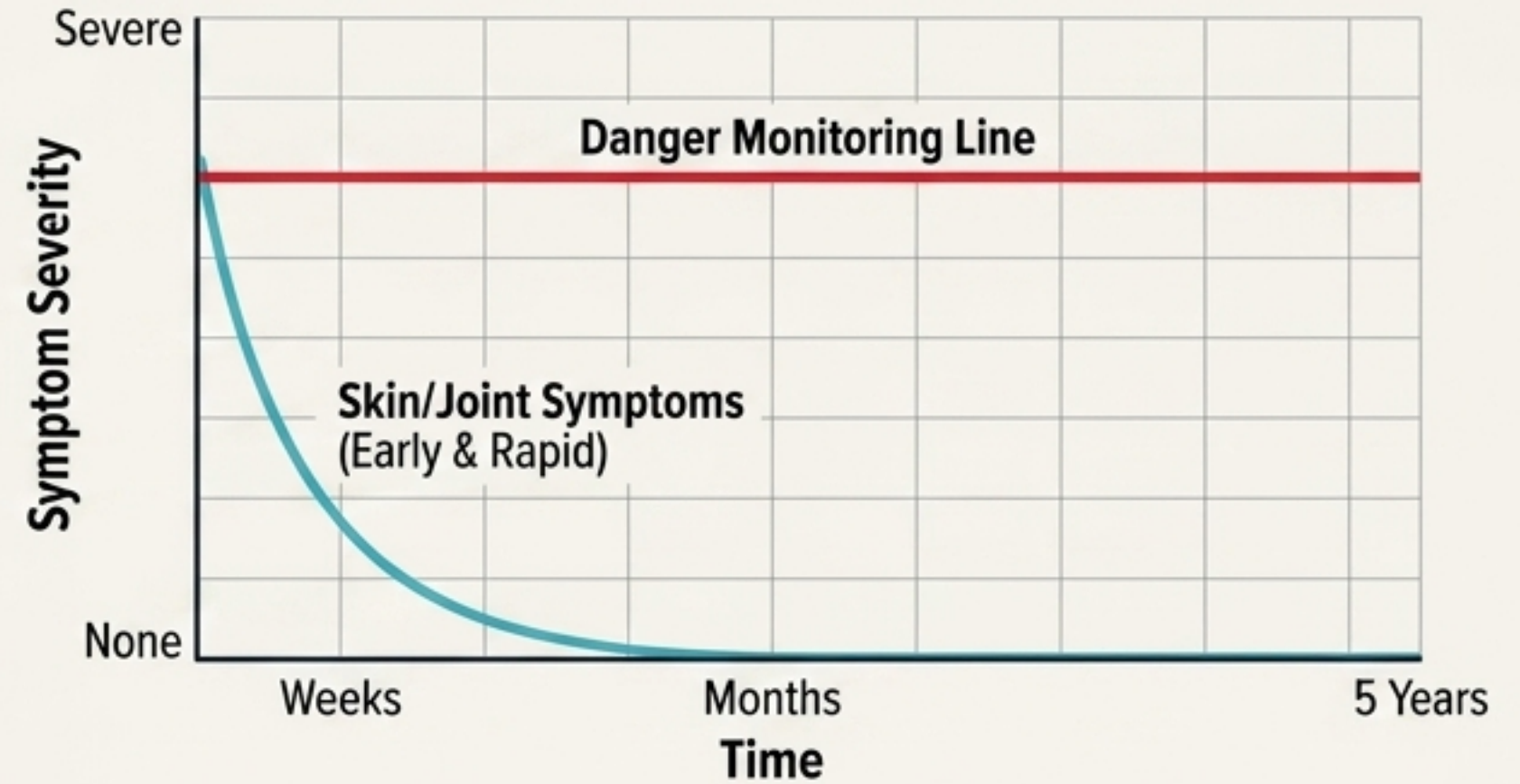
Rituximab 500 mg IV every 6 months **OR** **Azathioprine** 2 mg/kg/day. Minimum duration: 24 months.

IgA Vasculitis: The Pediatric Tetrad & Nephropathy Monitor

The Classic Tetrad



The Nephropathy Monitor



Pediatric vs Adult: 90% of cases are pediatric (peak 3-10 yrs) and self-limiting. Adults face higher risk of severe RPGN, CKD, or ESKD.

Renal Monitoring Protocol: Urinalysis and BP checked at diagnosis → Weekly for 4-6 weeks → Monthly for 6 months → 6-monthly for 5 years.
Action Trigger: Persistent proteinuria/hematuria at 6 months requires nephrology referral and biopsy.

The Immunosuppressive Arsenal

Drug & Mechanism	Role	Key Clinical Warnings
Rituximab (Anti-CD20)	AAV Induction/Maintenance.	Screen for Hep B/C, Latent TB. Time COVID vax ≥ 4 weeks prior. PBS Authority Required.
Cyclophosphamide (Alkylating Agent)	Severe AAV Induction (Alternative to Rituximab), severe PAN.	Cumulative gonadotoxicity , hemorrhagic cystitis. Reduce dose 25-50% if eGFR < 10 .
Avacopan (C5a Receptor Inhibitor)	Glucocorticoid-sparing in severe AAV.	Contraindicated in severe hepatic impairment (Child-Pugh C). TGA-approved, not PBS-listed.
Tocilizumab (IL-6 Inhibitor)	GCA (steroid-sparing), relapsing Takayasu.	PBS listed for GCA. Reduces relapse by $\sim 50\%$.
Azathioprine (Purine Antimetabolite)	Maintenance therapy (AAV). Safe in pregnancy.	Must check TPMT/NUDT15 genotype before commencing. Hepatically metabolized.

Nuances in Special Populations



Pregnancy

Contraindicated: Cyclophosphamide & Methotrexate (Teratogenic/Abortifacient).
Stop MTX 3 months pre-conception.

Preferred: Azathioprine (Safe, category D but standard use).

Prednisolone (Lowest effective dose, low fetal exposure).



Renal Impairment

Cyclophosphamide: IV pulse preferred over oral to reduce cumulative dose;
reduce dose 25-50% if eGFR <10.

Prophylaxis: Avoid Co-trimoxazole if eGFR <15 (use dapsone/atovaquone).



Elderly

Glucocorticoids: High risk of osteoporosis. Initiate bone protection (calcium, Vit D, bisphosphonate) for courses >3 months.

Toxicity: Prefer IV pulse CYC over oral due to myelosuppression risk.



Immunocompromised

Mandate: PJP prophylaxis is mandatory with dual immunosuppression.

Rule: Avoid live vaccines. Consider pre-exposure COVID prophylaxis during B-cell depletion.

Aboriginal & Torres Strait Islander Health Considerations

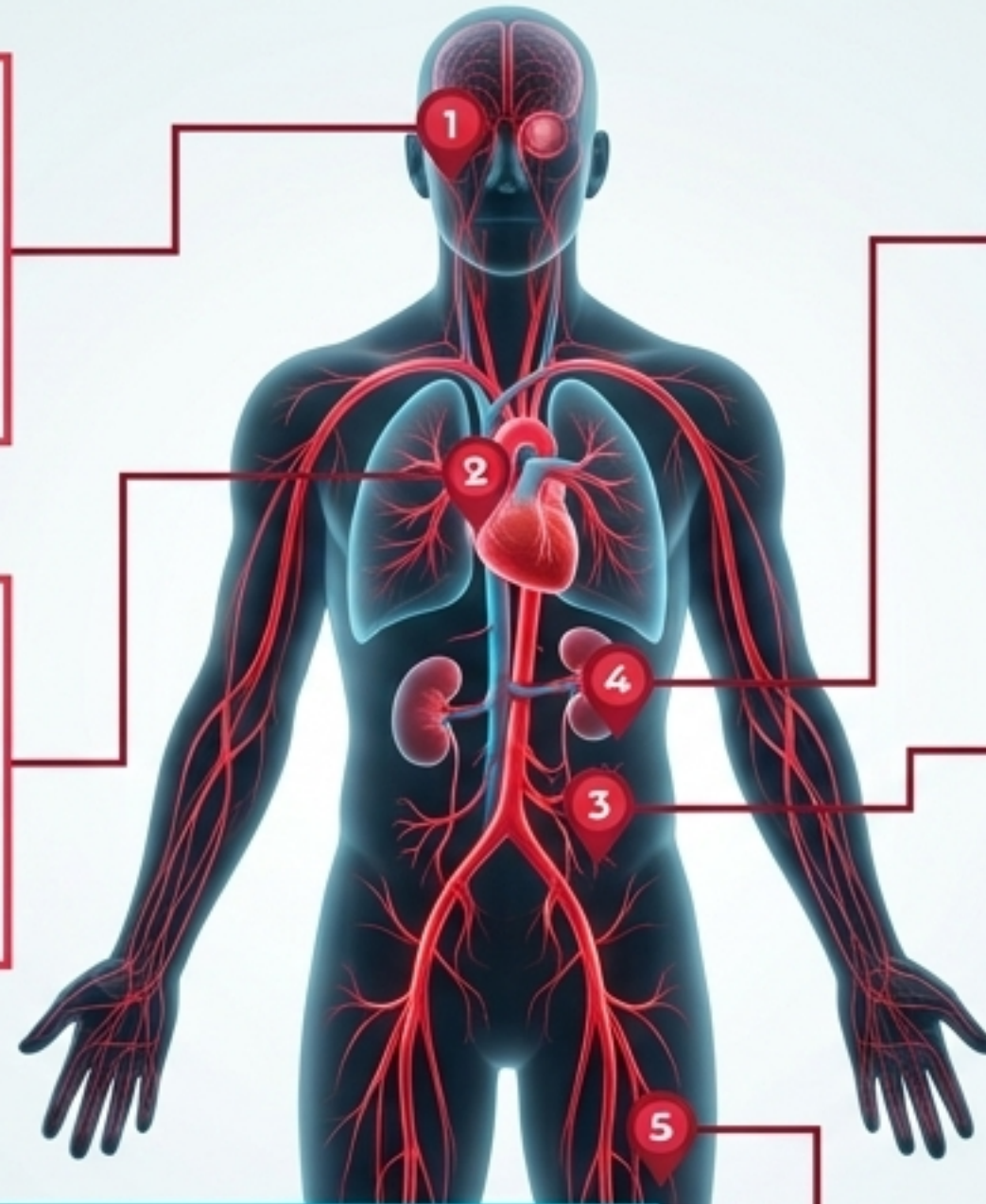
Care Equity Matrix

Clinical Reality	Structural Barrier	Cultural/Logistical Solution
HBV-PAN Prevalence Higher background rates of Chronic Hepatitis B (esp. remote NT/WA).	Prolonged immunosuppression endangers HBV clearance.	Actively consider HBV-PAN in medium-vessel presentations. Prioritize antiviral therapy over prolonged immunosuppression.
Diagnostic & Treatment Delay Advanced vasculitis presentation at baseline.	Geographic isolation limits access to IV infusion centers (Rituximab/CYC) and urgent specialist care.	Utilize MSOAP Telehealth . Facilitate medical retrieval for IV inductions. Leverage S100 provisions via RAAHS for oral meds.
Renal Comorbidity & Monitoring High background CKD compounds vasculitis-related renal damage.	Remote blood monitoring is logistically difficult.	Establish strict baseline eGFR/urinalysis. Use point-of-care iSTAT analyzers via Remote Area Nurses (RANs). Engage Aboriginal Health Workers (AHWs) .

Master Synthesis: Red Flags Across the Vascular Tree

Vessel Size:	Large.
Red Flag:	Sudden amaurosis fugax / irreversible blindness.
Culprit:	Giant Cell Arteritis (GCA).

Vessel Size:	Large.
Red Flag:	Limb BP discrepancy >10 mmHg / Pulse deficits.
Culprit:	Takayasu Arteritis (TAK).



Vessel Size:	Medium.
Red Flag:	Severe post-prandial abdominal pain / bowel ischemia.
Culprit:	Polyarteritis Nodosa (PAN).

Vessel Size:	Small.
Red Flag:	Pulmonary hemorrhage + Rapidly Progressive Glomerulonephritis.
Culprit:	Severe ANCA-Associated Vasculitis (MPA/GPA).

Vessel Size:	Medium to Small.
Red Flag:	Mononeuritis multiplex (sudden asymmetrical nerve pain/weakness)
Culprit:	PAN or EGPA.

Tissue ischemia is dictated by vessel caliber. Recognize the anatomical footprint to accelerate diagnosis and prevent organ loss.