

Target Audience: Rheumatology, GP, Rural Health

Data Source: Med2Date Clinical Guidelines

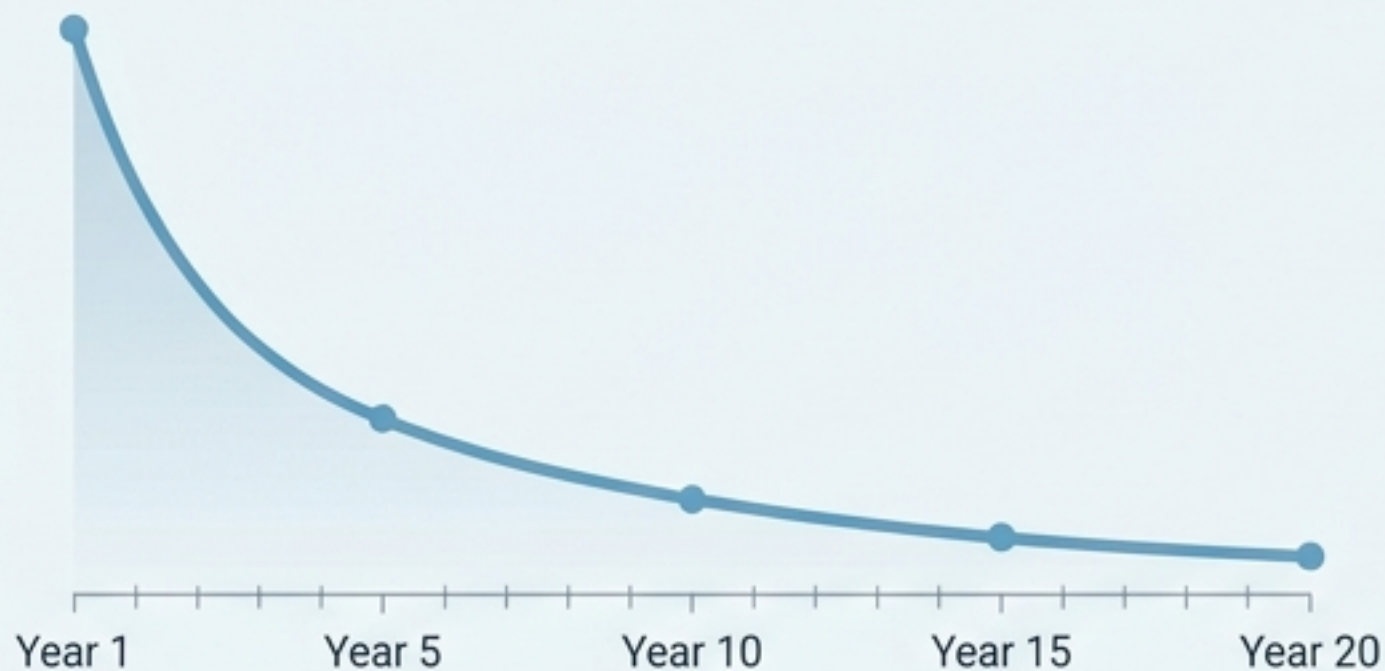
⚠ Status: High Acuity



Rheumatoid Vasculitis: A Clinical Blueprint

Rapid-reference diagnostic and management protocols for a declining but deadly RA complication.

| CLINICAL CONTEXT | DIAGNOSTIC FOCUS | MANAGEMENT PROTOCOL OVERVIEW |
|--|---|--|
| <ul style="list-style-type: none">• Systemic inflammation affecting blood vessels.• Associated with long-standing, seropositive RA.• Affects small to medium-sized arteries. | <ul style="list-style-type: none">• Cutaneous Manifestations: Purpura, ulcers, gangrene.• Neurologic Involvement: Mononeuritis multiplex.• Systemic Symptoms: Fever, weight loss, fatigue. | <ul style="list-style-type: none">• Immediate Recognition & Stabilization.• High-Dose Corticosteroids & Cyclophosphamide. (severe emergency)• Biologic Therapies (e.g., Rituximab, TNFi).• Long-Term Disease-Modifying Agents. |



<0.5% Incidence

The prevalence of RV has plummeted in the biologic and early aggressive DMARD era.

It is no longer an expected outcome of RA.



30–50% 5-Year Mortality

For those who do develop severe, multisystem RV, the mortality rate rivals aggressive malignancies.

Delayed diagnosis is the single greatest modifiable risk factor.

Management requires immediate specialist escalation to a multidisciplinary vasculitis or combined rheumatology–immunology center.

The High-Risk Avatar

Secondary Amplifiers: Demographics & Lifestyle

- **Male sex** (RV ratio is 1.5–2:1 M:F, contrasting RA's female dominance).
- **Smoking** (current or ex-smoker doubles risk, dose-dependent).

Disease Duration:
>10 years established
erosive RA
(median 15–20 years).

Seropositivity:
High-titre
Rheumatoid
Factor (>3x ULN)
± Anti-CCP.

Nodulosis:
Subcutaneous
nodules present
in 80–90% of
RV patients.

Secondary Amplifiers: Clinical Clues

- Previous **extra-articular features** (episcleritis, pleuritis, Felty syndrome).
- **HLA-DRB1** shared epitope homozygosity.



Clinical Pearl: New skin lesions or neuropathy in a long-standing, seropositive, nodular RA patient = URGENT vasculitis assessment.

Skin as the Sentinel Sign

Visible Sentinel Signs

- **Nailfold Infarcts:** Distal digital arteriolar occlusion (splinter hemorrhages).
- **Digital Ulceration:** Punched-out ulcers on pulps/periungual areas; deep extension risks gangrene.

- **Palpable Purpura:** Leucocytoclastic vasculitis; most common histological finding.
- **Livedo Reticularis:** Violaceous mottling indicating medium-vessel involvement.

waterline

In 50% of patients, cutaneous lesions precede or coincide with nerve, eye, or visceral involvement.

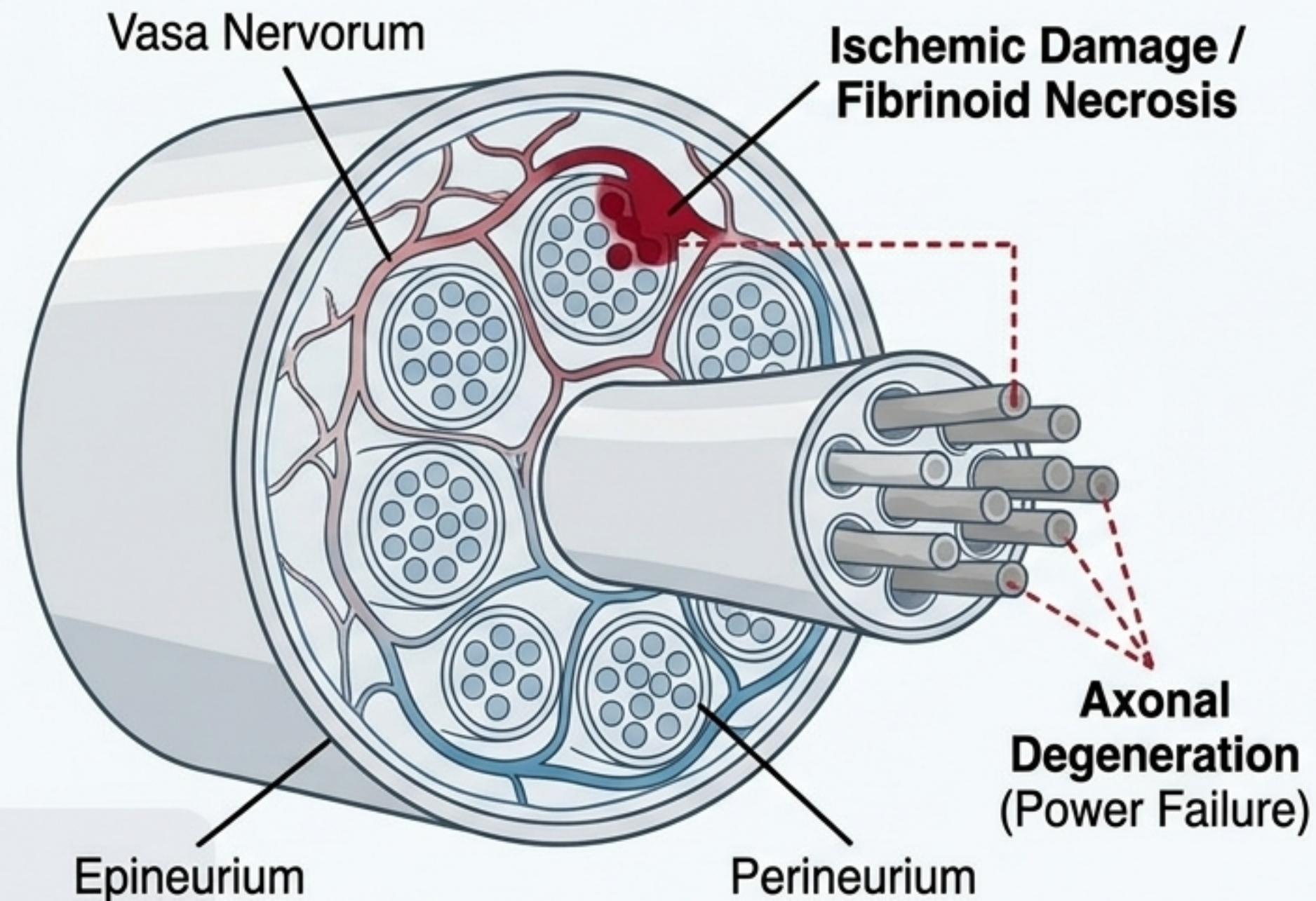


**Visceral
Ischemia**

**Mononeuritis
Multiplex**

**Necrotizing
Glomerulonephritis**

Neurological Complications: Mononeuritis Multiplex



Clinical Presentation

- Acute onset (hours to days) of asymmetric motor/sensory deficits in ≥ 2 named nerves.
- Preceded by severe neuropathic pain.

Hallmark Deficits

- Foot-drop (common peroneal nerve)
- Wrist-drop (radial nerve)
- Sensory loss (sural/superficial peroneal nerve)

Neurological Emergency: Requires immediate high-dose immunosuppression (pulse methylprednisolone + rituximab) to prevent permanent axonal loss.

Systemic Threat: Visceral Manifestations Map

Ocular (10-15%)

- Necrotizing scleritis, peripheral ulcerative keratitis (PUK).
- Requires urgent slit-lamp exam.

Pulmonary (5-10%)

- Hemorrhage, parenchymal vasculitis, cavitating nodules.
- Check HRCT/BAL.

Coronary & CNS (<5%)

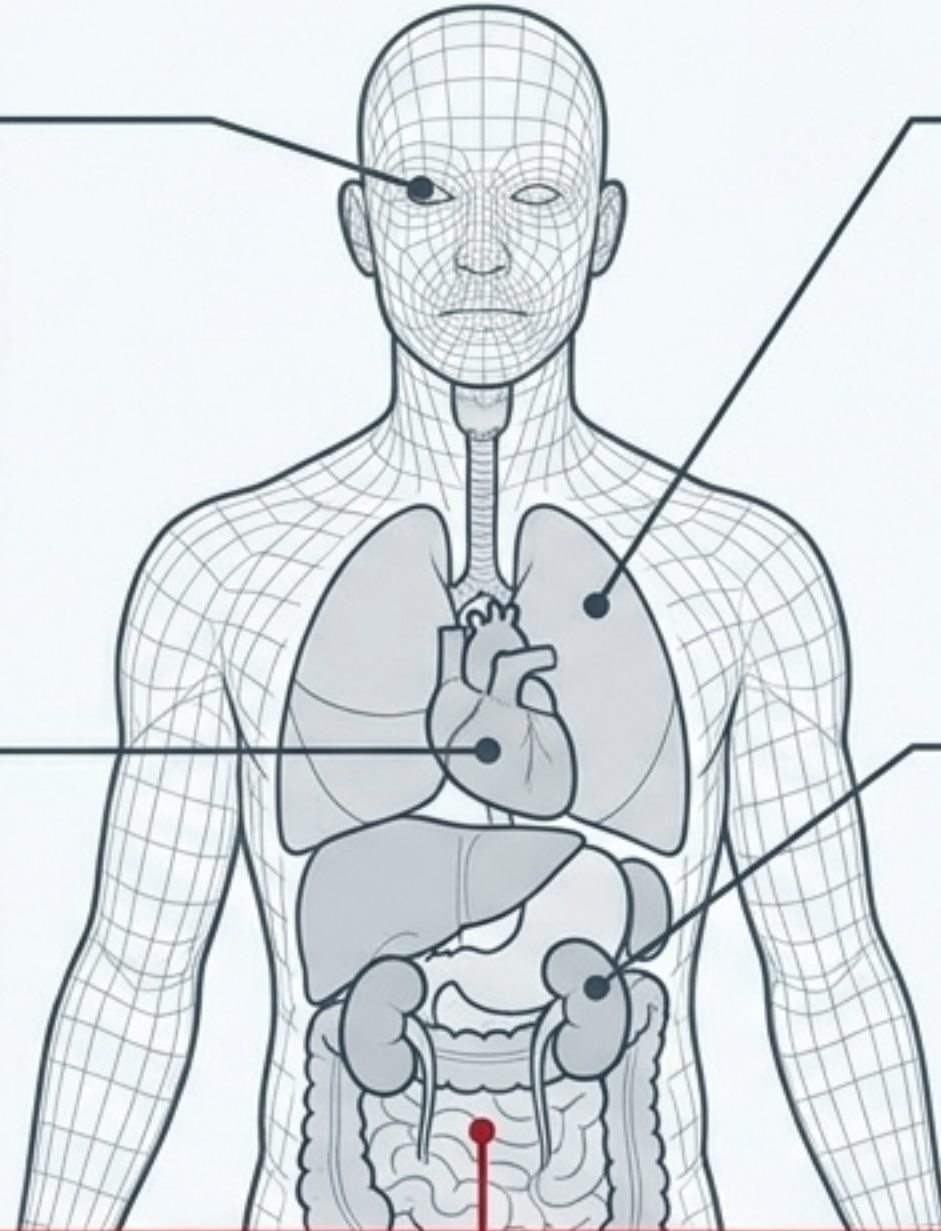
- Vasculitic MI or Stroke.
- Rare but catastrophic.

Renal (5-15%)

- Pauci-immune necrotizing glomerulonephritis.
- Check urinalysis/creatinine.

Mesenteric / GI (5-10%)

- **Acute Abdomen:** Bowel ischemia/perforation. Requires urgent CT angio.
 - Dual Surgical + Rheumatological emergency.



Step-by-Step Diagnostic Approach

Step 1: Clinical Suspicion

- New skin lesions, mononeuritis multiplex, scleritis, or visceral ischemia in seropositive RA.

Step 2: Exclude Mimics

- Check ANCA (c-ANCA/PR3, p-ANCA/MPO) to exclude ANCA-vasculitis (~15% of RV patients have positive ANCA).
- Rule out endocarditis, cholesterol emboli, PAN, and drug-induced vasculitis.

Step 3: Tissue Biopsy

- Skin punch biopsy (active lesion + subQ fat) is first-line.
- Sural nerve biopsy if neuropathy present and skin is non-diagnostic.

Step 4: Systemic Workup

- Assess full extent of organ involvement to determine Limited vs. Severe disease trajectory.

Laboratory & Histopathology Dashboard

Lab Panel (Essential Baseline)

- FBC, ESR, CRP, Renal/Urinalysis, LFTs.

- High-titre RF (>3x ULN) & Anti-CCP.

- Hepatitis B/C Serology (Crucial pre-immunosuppression).

- Complement levels (C3/C4 may be consumed).

- Blood cultures (Rule out infective endocarditis).

Histopathology Panel (Yield & Findings)

Skin (60-80% yield): Leucocytoclastic vasculitis of dermal vessels, fibrinoid necrosis, nuclear dust. Palpable purpura has highest diagnostic yield.

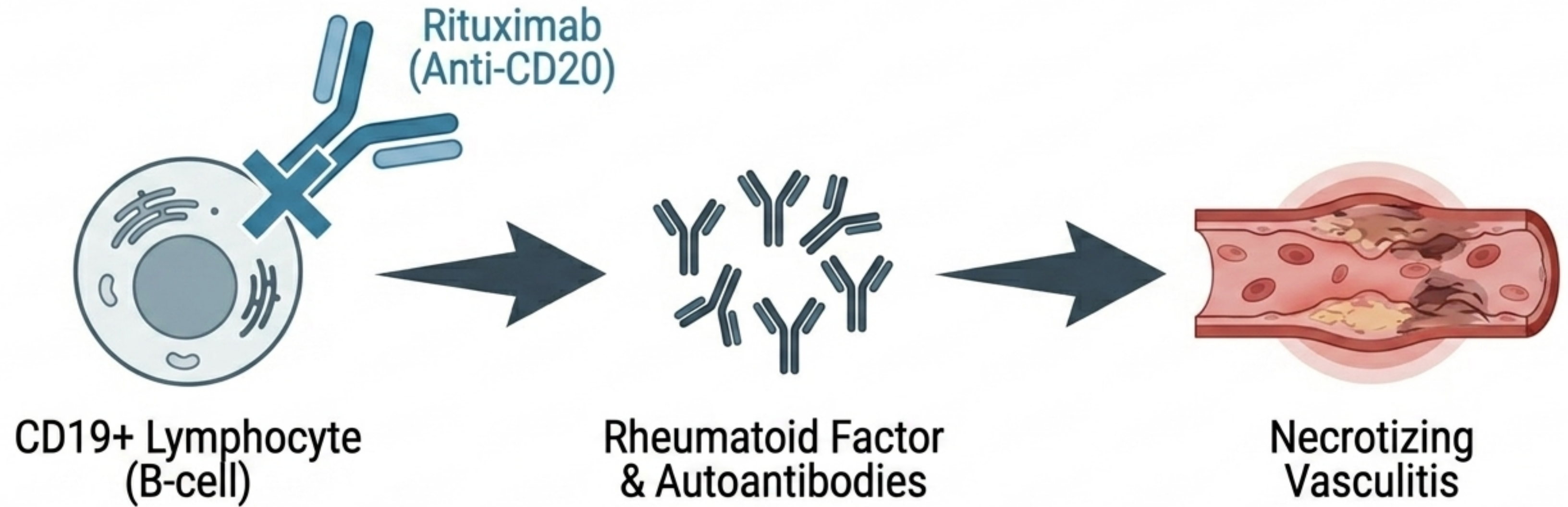
Sural Nerve (80-90% yield if MNM): Necrotizing arteritis of epineural vessels, axonal degeneration.

Kidney: Pauci-immune necrotizing crescentic glomerulonephritis.

Severity Stratification & Treatment Matrix

| Limited RV | Moderate RV | Severe RV |
|--|--|---|
| <ul style="list-style-type: none">Cutaneous-only (nailfold infarcts, palpable purpura, superficial ulcers). No deep tissue/nerve/visceral disease. | <ul style="list-style-type: none">Cutaneous + Mononeuritis Multiplex (limited nerve) or Scleritis/PUK. No immediate life threat. | <ul style="list-style-type: none">Visceral/Life-threatening (Mesenteric ischemia, rapidly progressive GN, severe polyneuropathy, digital gangrene). |
| Outpatient Rheumatology. | Inpatient or Day-Infusion; Ophthalmology co-management. | ICU / HDU; Multidisciplinary team. |
| Prednisolone 0.5 mg/kg + DMARD optimization. | IV Methylprednisolone pulse + Rituximab (Induction). | Intensive IV Methylprednisolone + Rituximab or Cyclophosphamide. |

Targeted Mechanism: Breaking the Vasculitis Cycle



Extrapolated from RAVE and RITUXVAS trials in ANCA-vasculitis, Rituximab is the preferred B-cell depleting agent because it directly addresses the pathophysiology of RV—halting the production of RF and autoantibodies driving the vascular inflammation.

Induction Pharmacology (Moderate/Severe Disease)

Methylprednisolone

Dose: 500 mg–1 g IV daily x 3 days, then oral taper (1 mg/kg/day over 3-6 months).

Notes: Monitor electrolytes/glucose. ⚠️

Status: PBS General Benefit (inpatient). ✅

Rituximab (1st-Line Induction)

Dose: 1000 mg IV on Day 1 and Day 15 (2-dose induction).

Pre-medication: Paracetamol 1g + Chlorphenamine 10mg + Methylpred 100mg.

Notes: Requires Hep B screen, IgG check. ⚠️

Status: PBS Authority Required. ✅

Cyclophosphamide

Dose: 15 mg/kg IV every 2-3 weeks x 6 pulses OR 2 mg/kg/day PO.

Notes: Mesna 20% prophylaxis required. Reduce dose 25% if eGFR <30. ⚠️

Status: PBS General Benefit. ✅

Limited Disease & Maintenance Pharmacology

Prednisolone (For Limited Skin-Only)

Dose: 0.5 mg/kg/day PO (typically 25-40 mg). Taper over 4-8 weeks to ≤ 7.5 mg/day.

Notes: Concurrently optimize background DMARDs (MTX, Leflunomide). Consider HCQ 200mg BD.

Rituximab Maintenance



Dose: 500–1000 mg IV every 6 months (min 2 years).

Notes: Guided by relapse risk. Monitor CD19+ B-cells and immunoglobulins.

Azathioprine Alternative

Dose: 2 mg/kg/day PO.

⚠ TPMT/NUDT15 Screening Mandatory. Homozygous deficiency = severe myelosuppression risk. Intermediate metabolizers need 50-75% reduction.

Adjunctive Rescue & Mandatory Prophylaxis

IVIg (Intravenous Immunoglobulin)

- **Dose:** 2 g/kg total, divided over 2-5 days. Repeat monthly if needed.
- **Indication:** Used as an adjunct when severe infection precludes further immunosuppression, for refractory skin disease, or cryoglobulinemic overlap.

Mandatory PJP Prophylaxis



- **Requirement:** Mandatory for all patients on Rituximab + high-dose steroids, or Cyclophosphamide.
- **Primary Regimen:** Trimethoprim/Sulfamethoxazole (Bactrim DS) 160/800 mg PO three times weekly. Continue for 6 months post-Rituximab.
- **Sulfa-Allergy Alternatives:** Dapsone 100mg daily, Atovaquone 1500mg daily, or Inhaled Pentamidine 300mg monthly.

Special Populations: Pregnancy & Pediatrics



Pregnancy Profiles

⚠️ Cyclophosphamide

- Absolutely contraindicated. Teratogenic. Require contraception for 3 months post-therapy.

⚠️ Rituximab

- Contraindicated (Category C).
- Causes neonatal B-cell depletion if given in 2nd/3rd trimester. Washout 6-12 months before conception.

Safe Options

- Azathioprine (maintenance).
- Hydroxychloroquine (protective against heart block).
- Prednisolone (doses >20mg risk GDM/pre-eclampsia).



Pediatric Considerations

- RV is exceptionally rare. Usually a distinct entity within Juvenile Idiopathic Arthritis (JIA).

- Mandatory referral to tertiary pediatric rheumatology.

- **Rituximab dosing adapted:** 375 mg/m² weekly x 4 or 750 mg/m² x 2.

Impaired Populations: Adjustments & Vulnerabilities



Elderly Vulnerabilities

- High risk of steroid complications (**osteoporosis, cataracts**).
- Must start **bone protection** (alendronate + Ca/Vit D).
- High risk of **hypogammaglobulinemia** with repeated **Rituximab** cycles.



Renal Impairment

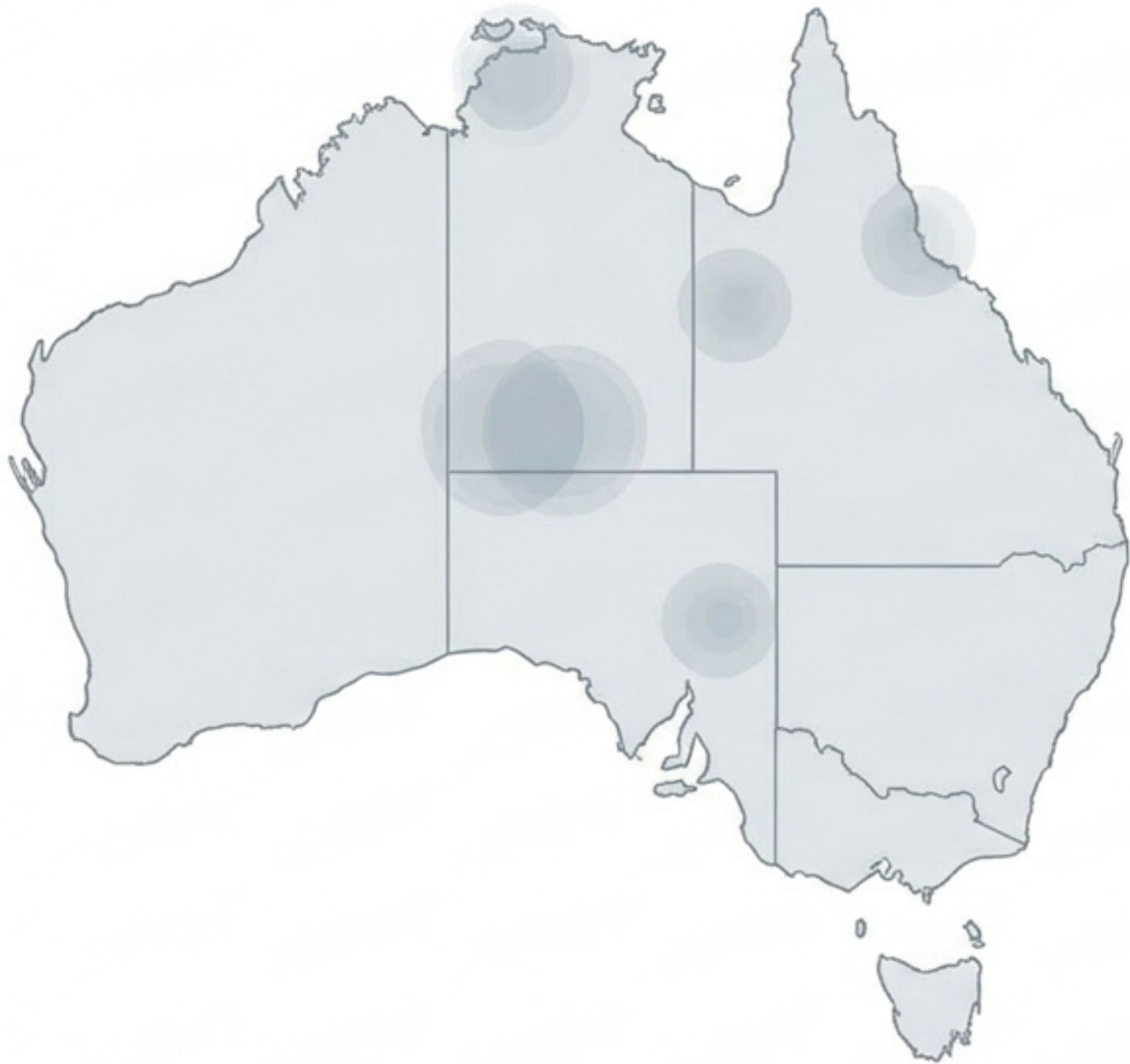
- Rituximab: **Safe** in dialysis. No dose adjustment.
- Cyclophosphamide: **Reduce 25%** (eGFR 15-30) or **50%** (eGFR <15).
- Methotrexate: **Contraindicated** if eGFR <30.



Hepatic Impairment

- Hep B Positive: **Antiviral prophylaxis** (entecavir/tenofovir) required ≥ 2 weeks before Rituximab and 12 months after.
- Methotrexate: **Contraindicated** in Child-Pugh B/C.

Indigenous Health: Epidemiology & Access Gaps



Epidemiology

- Higher prevalence, earlier onset of RA, and more severe extra-articular manifestations. AIHW data shows higher hospitalization rates.

⚠ The Access Gap

- Barriers to specialist rheumatology in remote communities lead to late presentation. RV often presents at an advanced stage (established nerve damage, deep ulceration).

Systems Solutions

- Utilize **Telehealth** for early specialist review.
- RFDS retrieval for severe disease requiring tertiary pulse immunosuppression.
- Integrate vasculitis screening into Closing the Gap PBS chronic disease programs.

Indigenous Health: Clinical Protocols & Cultural Safety



Endemic Infection Risk Protocol

- High background rates of TB, Hepatitis B, and Strongyloidiasis.
- Protocol: **Strongyloides serology mandatory** for patients from endemic areas (Northern Australia, Torres Strait) prior to immunosuppression.
- Action: If positive, **treat with Ivermectin** to prevent **lethal hyperinfection syndrome** triggered by steroids/rituximab.



Cultural Safety

- Engage **Aboriginal Health Workers** and **Liaison Officers**.
- Ensure informed consent for invasive procedures (e.g., nerve/skin biopsies) allows adequate time for family and community consultation.

Patient Lifecycle Roadmap

Weeks 0–2
(Acute & Induction)

Baseline labs, Hep B/C, Ig levels.
Biopsy. Initiate **IV pulse steroids + Rituximab** Day 1 & 15.
Start PJP prophylaxis.

Weeks 2–6
(Toxicity Check)

FBC monitoring (fortnightly for RTX).
Assess ulcer healing / nerve pain.
Check CD19-19+ depletion at 4 weeks.

Months 3–6
(Consolidation)

Repeat NCS if MNM present.
Check IgG levels (if <4 g/L, consider IVIg).
Perform DEXA scan if on prolonged steroids.

Months 6–12+
(Maintenance)

Transition to RTX 6-monthly or Azathioprine.
Killed vaccines safe 6 months post-RTX.
Live vaccines strictly contraindicated.

Rheumatoid Vasculitis is a life-long trajectory requiring vigilance. Survive the acute ischemia, manage the profound immunosuppression, and monitor the long-term systemic damage.