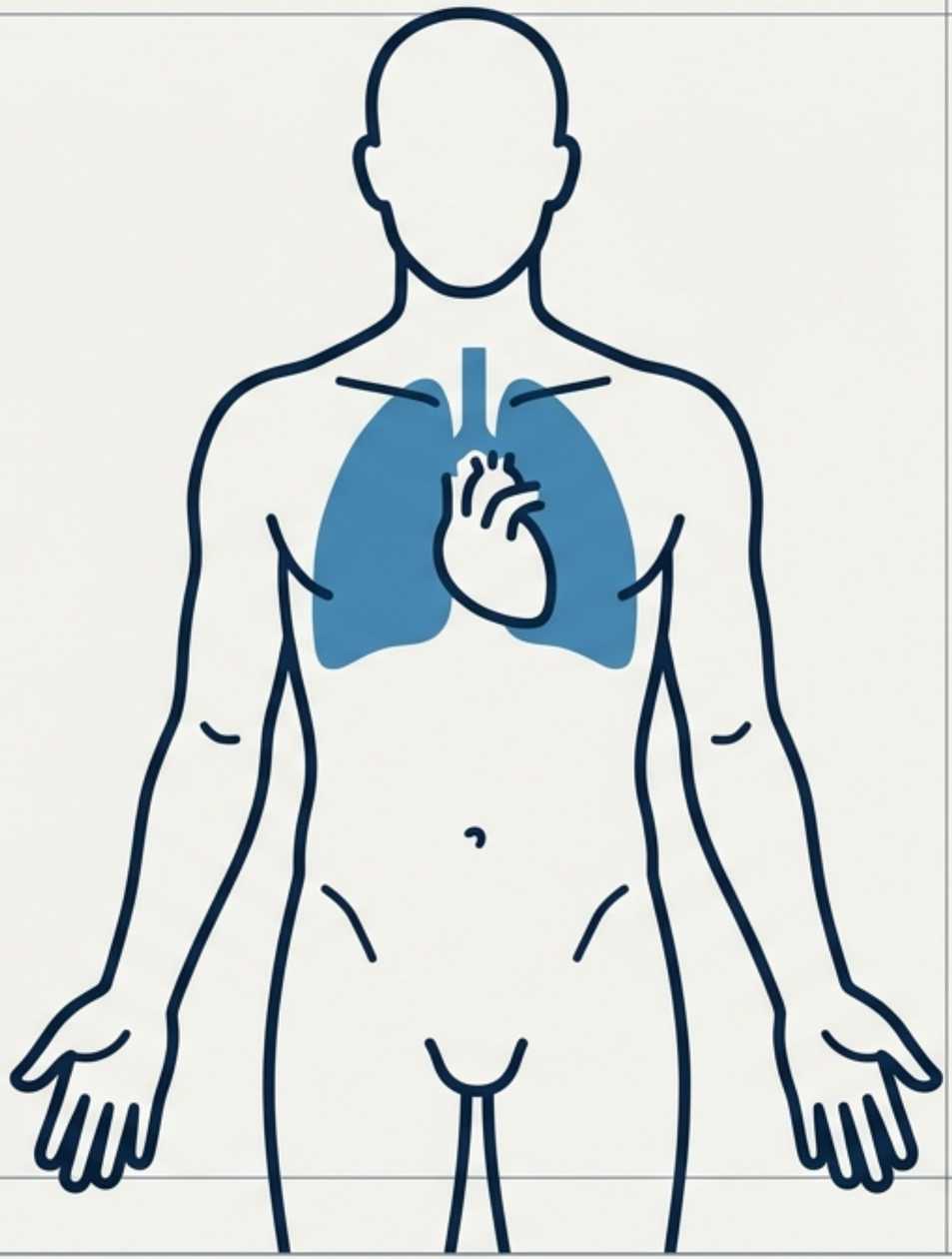
Sarcoidosis Clinical Pathway Blueprint

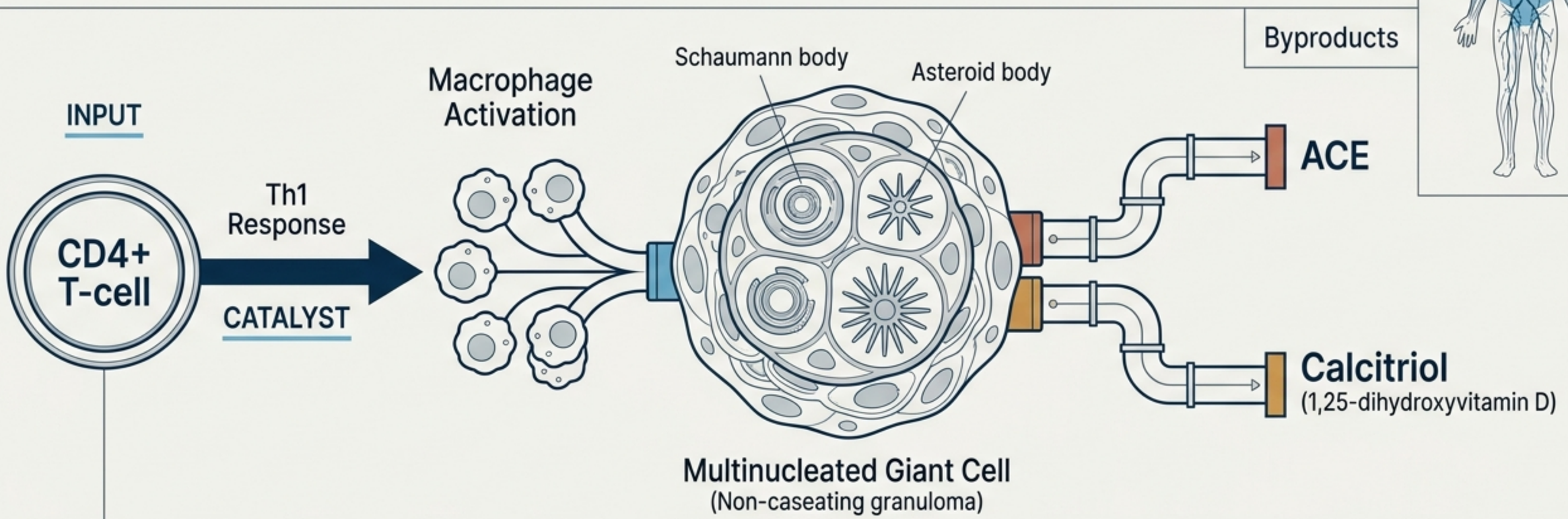
A visual diagnostic and management dashboard for the Australian clinical context.



Med2Date Clinical Guidelines

The Granuloma Factory

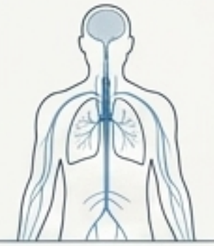
SYSTEMS RADAR



CD4+ T-lymphocyte predominance (BAL CD4/CD8 ratio >3.5 is supportive)

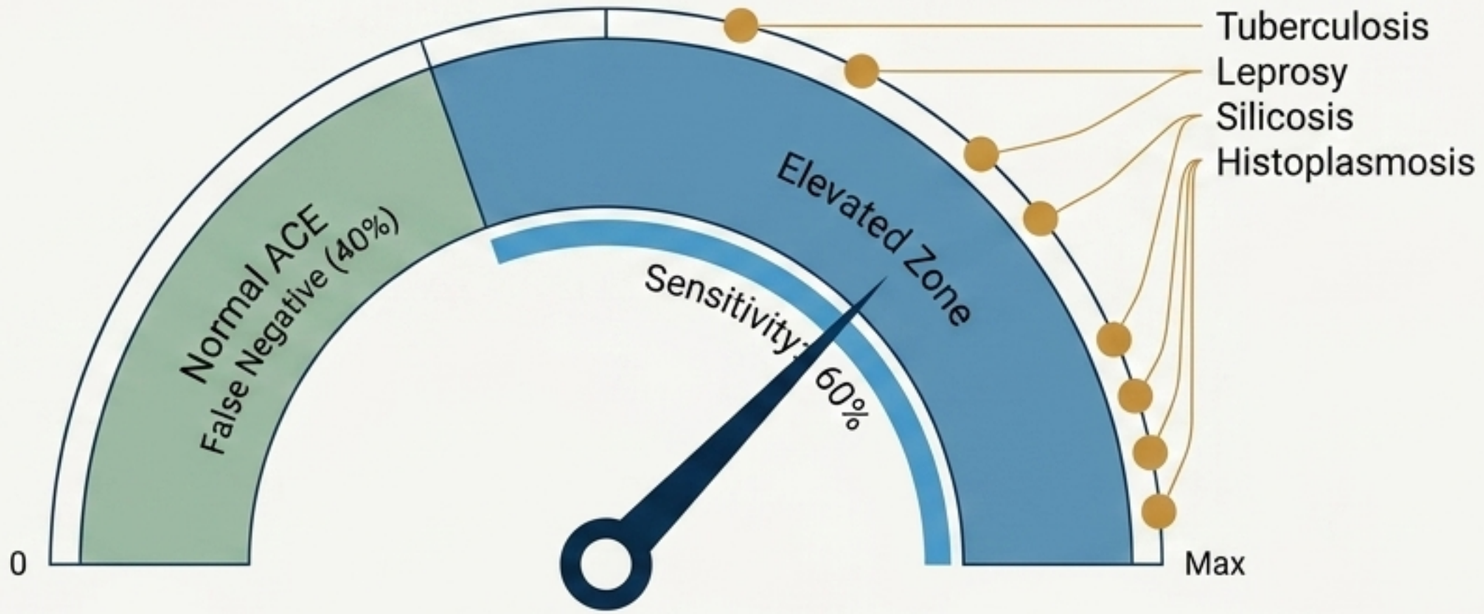
Granulomas produce ACE, reflecting total disease burden

Calcitriol production is independent of PTH, driving hypercalcaemia (10-13%) and hypercalciuria (40%)



The ACE Paradox Gauge

The Maxim: ACE is supportive, not diagnostic.



Normal sACE does NOT exclude active sarcoidosis.

Elevated sACE requires clinical and histological correlation (Specificity ~90% only in the right context).

Clinical Warning

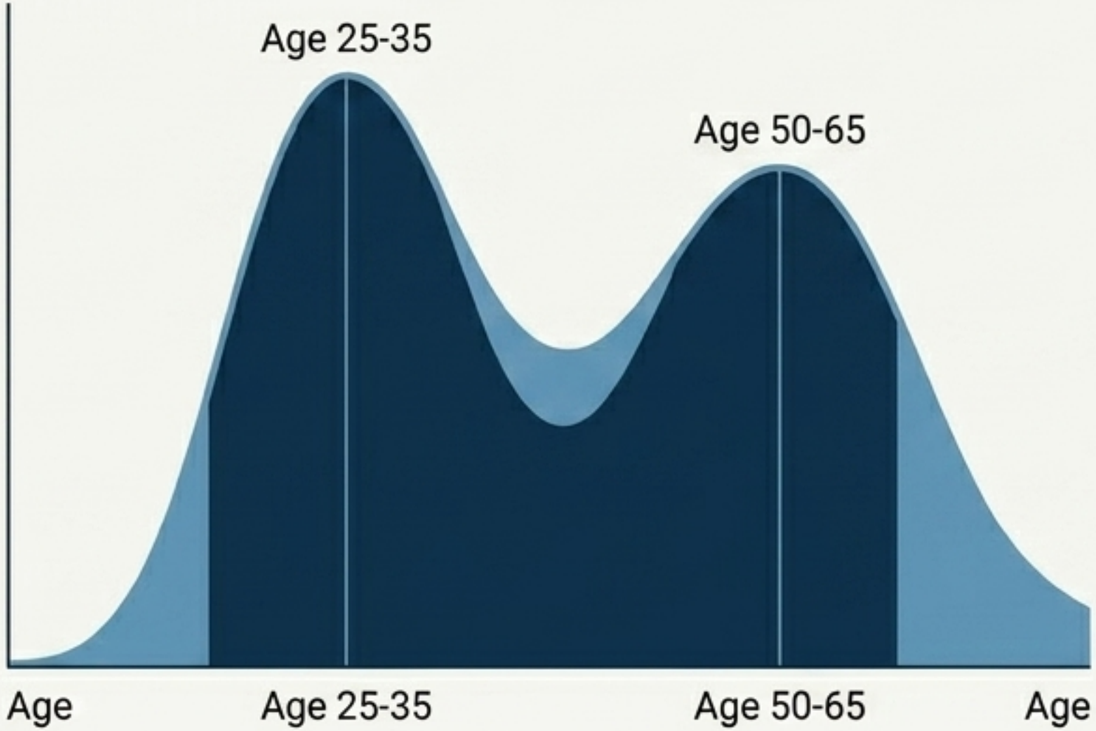
ACE Inhibitor Effect: ACEi medications artificially lower sACE. Interpret with caution; consider temporarily withholding if an accurate measurement is required.

Epidemiology & Trajectory

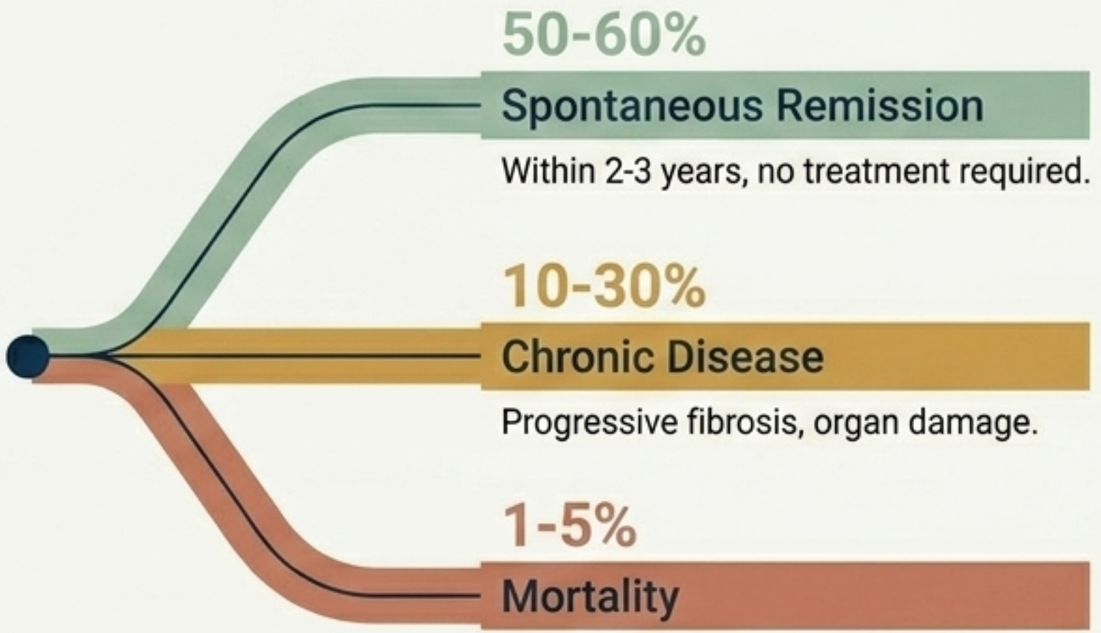
Incidence: 5-10 per 100,000 in Australia

Slight female predominance. Higher rates in Northern European descent.

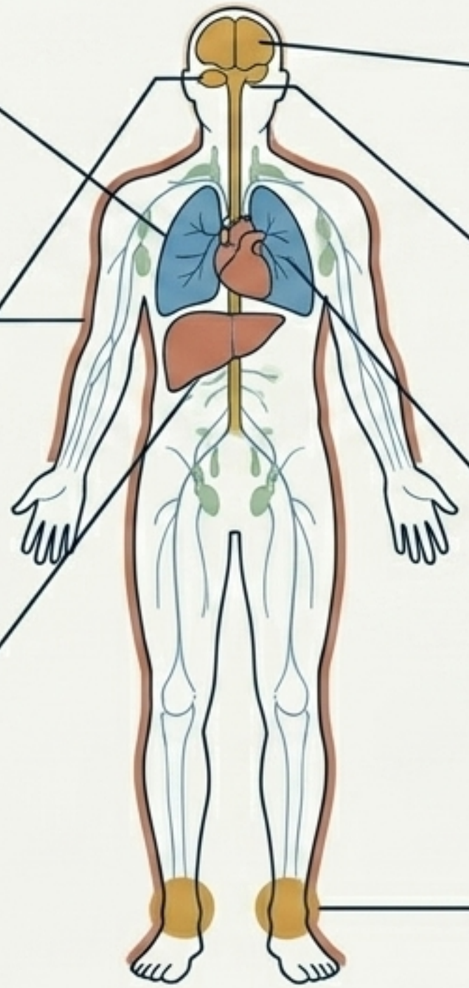
Age Distribution



Prognosis & Disease Trajectory



Systems Radar Overview



Lungs (>90%)
Cough, dyspnoea, BHL.
Key Test: Spirometry (Restrictive pattern).

Skin (25-35%)
Plaques, papules, lupus pernio.
Key Test: Direct visual / Punch biopsy.

Eyes (20-30%)
Anterior/posterior uveitis.
Key Test: Slit-lamp exam.

Lymph Nodes (15-40%)
Hilar, mediastinal, peripheral.
Key Test: EBUS.

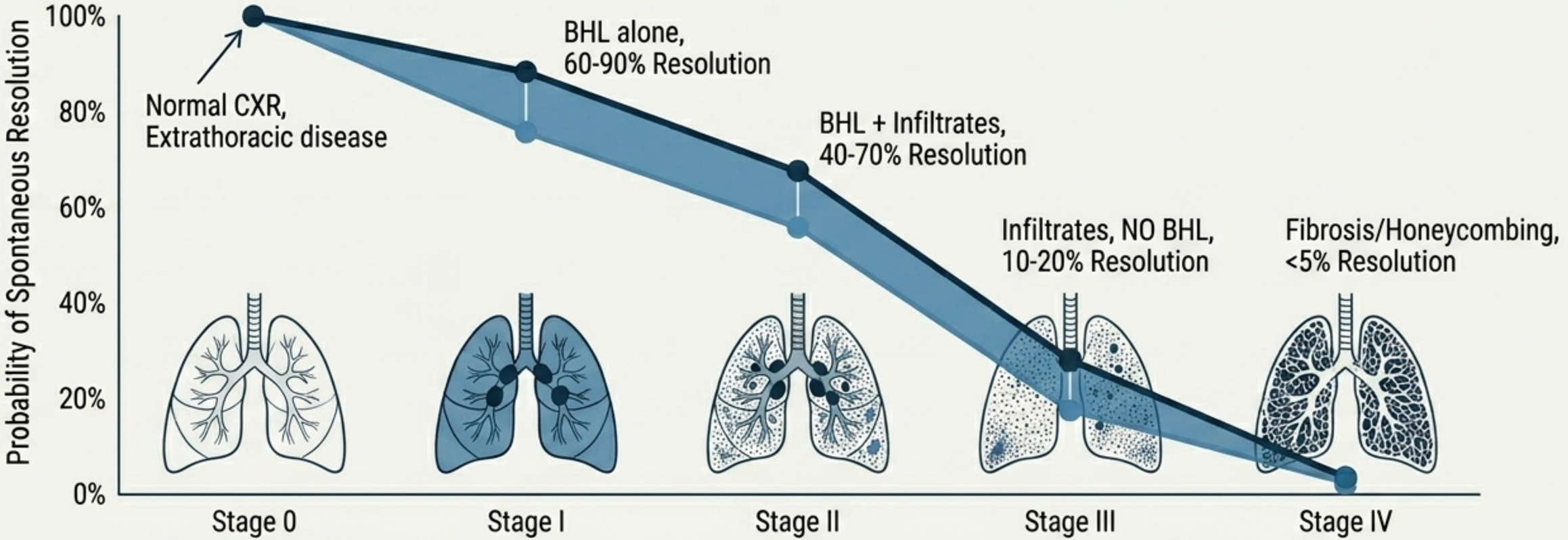
Liver (10-20%)
Hepatomegaly, raised ALP.
Key Test: LFTs.

Nervous System (5-15%)
Facial palsy (CN VII), diabetes insipidus.
Key Test: MRI Brain / LP.

Heart (5% clinical, 25% autopsy)
Heart block, VT, sudden death.
Key Test: ECG, Cardiac MRI (LGE), PET-CT.

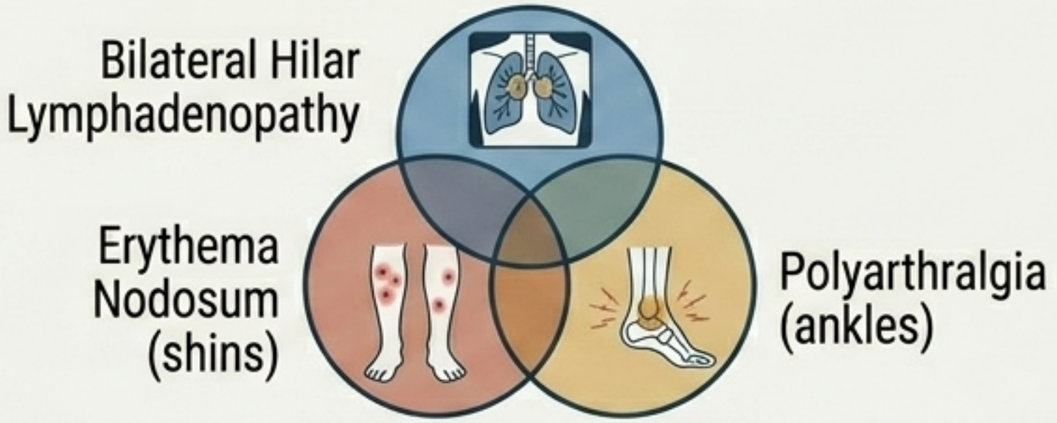
Joints (10-15%)
Ankle arthritis.
Key Test: Clinical evaluation.

Pulmonary Sarcoidosis: Scadding Stage Continuum

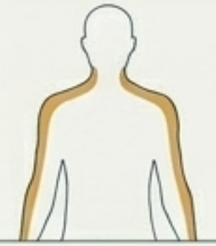


When to Treat Pulmonary Disease: Significant dyspnoea, FVC decline >=10%, progressive infiltrates, or significant airway involvement. Asymptomatic Stage I generally requires ONLY observation.

Systemic Sarcoidosis vs. Lofgren Syndrome

Systemic Sarcoidosis	Lofgren Syndrome (The Acute Triad)
Presentation: Insidious, chronic, highly variable.	
Demographics: Slight female predominance.	**Demographics:** Heavy female predominance (F:M 3:1).
Genetics: Variable (BTNL2).	**Genetics:** Strong HLA-DRB1*03 association.
Prognosis: 50-60% resolution; risk of chronicity.	**Prognosis:** >90% spontaneous resolution.
Management: Often requires systemic immunosuppression.	**Management:** NSAIDs (naproxen/ibuprofen), short-course steroids if refractory. Tissue biopsy often unnecessary.

Cutaneous Manifestations



Specific Lesions (Granuloma Positive)

Plaques: Annular, violaceous (most common in Aus).

Papules: Perioral, perinasal, periocular.

Lupus Pernio: Violaceous plaques on nose/cheeks/digits. Disfiguring, refractory, implies chronic upper respiratory involvement.

Scar Sarcoidosis: Infiltration of old scars (Pathognomonic).

Subcutaneous Nodules: Darier-Roussy variant.

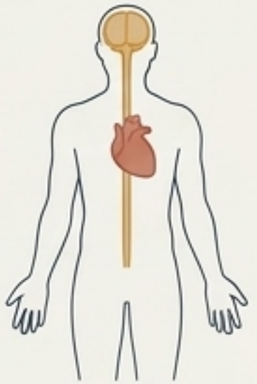
Non-Specific Lesions (Granuloma Negative)

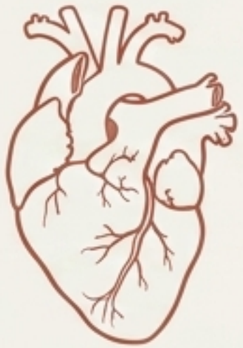
Erythema Nodosum: Tender shin nodules. Represents reactive panniculitis. Most common cutaneous finding overall (Lofgren syndrome).

Treatment Escalation

Topical clobetasol → Intralesional triamcinolone → Systemic (Hydroxychloroquine 200mg BD / Methotrexate) for widespread/disfiguring disease.

High-Risk Phenotypes: Cardiac & Neurosarcoidosis





Cardiac Sarcoidosis (The Silent Killer)

Stats: 20-30% on autopsy, 5% clinical. Accounts for up to 65% of disease-related deaths.

Presentations: AV Block, Ventricular Tachycardia (sudden death risk), Heart Failure.

Diagnostic Pathway: Baseline 12-lead ECG → **Cardiac MRI** (Mid-myocardial/epicardial Late Gadolinium Enhancement) → FDG-PET/CT

Action: Consider ICD if sustained VT or LVEF <=35%.

Neurosarcoidosis

Stats: 5-15% of patients.

Presentations: Cranial Neuropathy (CN VII facial palsy = ~50%), Central Diabetes Insipidus, Chronic Meningitis.

Diagnostic Pathway: MRI Brain with gadolinium (leptomeningeal enhancement) → Lumbar Puncture (lymphocytic pleocytosis, low glucose)

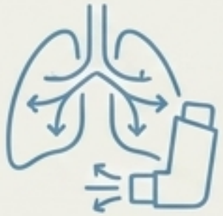
Action: High-dose oral prednisolone (0.5-1 mg/kg/day) + Infliximab for refractory/aggressive cases.

Investigation Dashboard: Baseline Workup

1. CXR (PA)

Scadding staging, BHL.

2. Spirometry + DLCO



Restrictive pattern, serial FVC tracking.

3. Bloods (FBC/UEC/LFT)

Screen for lymphopenia, hepatic/renal granulomas.

4. Serum ACE

Baseline disease activity (MBS item 66817).

5. Corrected Calcium

Screen for hypercalcaemia.

6. 12-Lead ECG

Screen for silent AV block/arrhythmias.

7. Ophthalmological Review

Slit-lamp to screen for anterior uveitis (20-30% incidence).

8. Tuberculosis Exclusion

Mandatory IGRA (QuantiFERON-Gold) or Mantoux before any immunosuppression.

The Biopsy Decision Tree

Is histological confirmation required?

No Biopsy Required

Criteria: Classic Lofgren Syndrome triad OR Asymptomatic Stage I BHL in a young adult.

Action: Clinical diagnosis. Observe.

Biopsy Mandatory

Criteria: Atypical presentation, Stage III/IV disease, Suspected malignancy, or considering systemic treatment.

Action: Proceed to targeted tissue sampling.

Sampling Targets (in order of preference)

1. Skin / Peripheral Lymph Nodes (Most accessible)
2. EBUS-guided mediastinal lymph node sampling (High yield)
3. Bronchoscopy with transbronchial biopsy (Yield ~80%, BAL CD4/CD8 ratio >3.5)

Diagnostic Rule: Diagnosis requires 1. Compatible clinical picture + 2. Non-caseating granulomas + 3. Exclusion of TB/fungal infections.

Severity & Stratification Map

Poor Prognostic Modifiers

African American ethnicity, Lupus pernio, persisting hypercalcaemia, Sarcoid-associated pulmonary hypertension.

Severe (Refractory/Life-Threatening)

Phenotype: Cardiac (arrhythmia), Neuro (palsy/myelopathy), Progressive Fibrosis (Stage IV), Lupus Pernio, Hypercalcaemia.
Action: High-dose immunosuppression +/- Biologics (Infliximab), Multidisciplinary team.

Moderate (Treatment-Indicated)

Phenotype: Symptomatic dyspnoea, FVC decline ≥10%, chronic uveitis, hepatic derangement.

Action: Oral Prednisolone + Steroid-sparing agent.

Mild (Observation-Eligible)

Phenotype: Asymptomatic Stage I-II, Lofgren syndrome, mild cutaneous.

Action: Outpatient review, serial CXR/Spiro every 3-6 months.

Treatment Escalation Staircase

Step 4: Biologics (Refractory)

Infliximab (PBS Authority Required).

Step 3: Steroid-Sparing DM RDs

Methotrexate (Preferred first-line DM ARD
Azathioprine or Mycophenolate.

Step 2: Oral Corticosteroids (First-Line)

Prednisolone 20-40mg daily (taper 6-12 months).
Higher dose (0.5-1mg/kg) for **Cardiac/Neuro**.
Dexa scan if >=3 months.

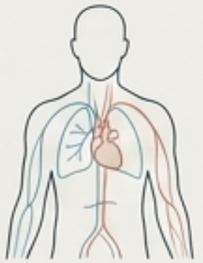
Step 1: Observation

For asymptomatic / Lofgren (NSAIDs).

SAFETY TOLLGATE

STOP: Exclude active TB (IGRA), Hepatitis B/C, and ensure vaccinations (Pneumococcal/Influenza) prior to starting immunosuppression.

Steroid-Sparing DMARD Matrix



Methotrexate (Preferred 1st-line DMARD)	Azathioprine	Mycophenolate Mofetil
Dose: 7.5-15 mg weekly (titrate 2.5mg every 2-4 weeks).	**Dose:** 2-2.5 mg/kg/day (Start 50mg daily).	**Dose:** 1g BD.
Co-prescription: Folic acid 5mg weekly.	**Mandatory Screen:** TPMT/NUDT15 genotype testing mandatory before initiation to avoid severe myelosuppression.	**Role:** Second-line steroid-sparing; often favored in neurosarcoidosis or if MTX/AZA are contraindicated.
Mandatory Limit: Contraindicated if eGFR <30 mL/min. Category X Teratogenic (cease >=3 months before conception).	**Limit:** Dose reduce in CKD/Hepatic impairment.	**Limit:** PBS Authority Required.

Infliximab: Advanced Therapy Profile

Target
(Indications)

Refractory pulmonary sarcoidosis.

Neurosarcoidosis / Cardiac sarcoidosis.

Refractory Lupus Pernio.

Note: PBS Authority Required (conventional therapy must have failed).

Infliximab
(TNF-α inhibitor)

Dose: 5 mg/kg IV at weeks 0, 2, 6, then every 6-8 weeks.

Shield
(Screening & Risks)

Pre-screen: Latent TB (IGRA), Hep B/C, HIV, Varicella.

Risks: Infusion reactions (pre-medicate), TB reactivation, demyelination, exacerbation of heart failure. Live vaccines strictly contraindicated.

Management in Special Populations

Pregnancy

Prednisolone is safe (Cat A).
Methotrexate is highly teratogenic (Cat X).

Azathioprine is widely used (Cat D).
Infliximab crosses placenta (stop by wk 30, no live vaccines for infant x 6 months).

Paediatrics & Elderly

Paeds: Rare <5 years; consider Blau syndrome (NOD2 mutation).

Elderly: High steroid morbidity. Introduce DMARDs earlier. DEXA + bisphosphonate mandatory if steroids ≥3 months.

Renal Impairment

Nephrocalcinosis/nephrolithiasis risk.
Hypercalcaemia exacerbates CKD.
Avoid MTX if eGFR <30.

Immunocompromised

High opportunistic infection risk on biologics/high-dose steroids.
Consider PJP prophylaxis (trimethoprim-sulfamethoxazole) if Prednisolone ≥20 mg/day for ≥4 weeks.

The Access Gap: Indigenous Health Map

Metropolitan Pathway

Immediate access to EBUS, Cardiac MRI, and Rheumatology MDT. Rapid diagnosis.

Remote Indigenous Community Pathway

Hurdle 1: Specialist Absence

EBUS/PET-CT concentrated in cities. Relies on Telehealth and point-of-care testing.

Hurdle 2: The TB Overlap

TB incidence is 6-8x higher. Mandatory requirement to culture for mycobacteria and use IGRA (not Mantoux) Mantoux) before any immunosuppression.

Hurdle 3: Treatment Logistics

Infliximab requires hospital IV infusions -> Requires PATS (Patient Assisted Travel Scheme) or RFDS (Royal Flying Doctor Service).

Hurdle 4: Comorbidities

Higher background DM/CVD/CKD amplifies corticosteroid risks, necessitating earlier DMARD use.

Surveillance & Escalation Schedule

Surveillance Timeline

Every 3-6 Months

Spirometry/DLCO, CXR (first 2 years), Serum ACE (if elevated baseline), Corrected Calcium, Creatinine.

Every 1-3 Months

FBC and LFTs (if on DMARDs).

Annually

12-lead ECG (arrhythmia screen), DEXA scan (at 1-2 years if on steroids).

Escalation Triggers (Red lines for Re-Referral)

- FVC decline >=10% despite treatment.
- New cardiac symptoms (palpitations, syncope).
- New neurological deficits (facial weakness, visual loss).
- Refractory hypercalcaemia.
- DMARD toxicity/intolerance.