Sarcoidosis

Non-caseating granulomas in search of a diagnosis of exclusion · treat the organ dysfunction, not the chest radiograph

Not every case *needs steroids*

DIAGNOSIS *three requirements, and the third is the one people skip*

1. COMPATIBLE PICTURE

Clinical and radiological features that fit. **Bilateral hilar lymphadenopathy** is the classic finding, often incidental on a chest radiograph in an asymptomatic patient.

2. NON-CASEATING GRANULOMAS

Tissue from the most accessible site. **EBUS-guided sampling of mediastinal nodes** has largely replaced mediastinoscopy. Biopsy skin lesions or a lacrimal gland when present, since they are far easier.

3. EXCLUDE THE MIMICS

This is a diagnosis of exclusion and the step most often skipped. Rule out **tuberculosis and fungal infection** with stains and culture on every specimen, plus **lymphoma**, berylliosis (occupational history), hypersensitivity pneumonitis and IgG4-related disease.

SCADDING STAGES *a radiographic description, not a treatment ladder*

Stage	Chest radiograph	Behavior
0	Normal	Extrapulmonary disease only
I	**Bilateral hilar lymphadenopathy alone**	**Most remit spontaneously**, frequently within 2 years
II	Hilar lymphadenopathy **plus** parenchymal infiltrates	Many still remit, though less reliably
III	**Parenchymal infiltrates without** lymphadenopathy	Lower rate of spontaneous remission
IV	**Fibrosis**, with volume loss and traction bronchiectasis	**Irreversible.** Immunosuppression does not reverse established fibrosis, so the aim shifts to preventing progression and managing complications

The stage does not tell you to treat. It describes the radiograph and gives a rough prognosis, and it is not sequential: patients do not march from I to IV. **The decision to treat rests on symptoms and organ dysfunction**, so an asymptomatic Stage II patient with normal physiology is observed while a Stage I patient with cardiac involvement is treated urgently.

WHEN TO TREAT *and when confidently not to*

Situation	Approach
Asymptomatic with preserved organ function	**Observe.** Serial symptoms, pulmonary function tests and imaging. Spontaneous remission is common, and treating an asymptomatic radiograph exposes the patient to steroid harm for no benefit
⚠ **Lofgren syndrome**	**Erythema nodosum, bilateral hilar lymphadenopathy, ankle arthritis and fever.** Roughly **90% remit spontaneously within 3 to 6 months**, so **steroids are not indicated**: treat with NSAIDs and reassurance. Recognizing it prevents unnecessary immunosuppression, and it carries an excellent prognosis
Treat when...	**Symptoms significantly impair quality of life, or there is significant organ dysfunction.** That is the threshold, in place of any radiographic rule
Treat urgently regardless of symptoms	**Cardiac, neurologic, ocular**, severe hypercalcemia, and progressive renal or hepatic involvement. These organs are treated because the cost of waiting is irreversible damage or sudden death
How to treat	**Prednisone** is first-line, typically starting around **0.5 mg/kg/day** for significant disease and tapering slowly over months. **Consider a steroid-sparing agent early**, usually methotrexate, given the morbidity of prolonged steroids. Refractory disease escalates to **TNF inhibitors such as infliximab**

THE ORGANS THAT CHANGE THE PLAN *screen for these in everyone*

Organ	Why it matters	How to look
Heart can kill first	**Conduction block, ventricular arrhythmia and sudden death**, sometimes as the presenting event, and often with minimal pulmonary disease	**Symptom check, ECG and echocardiogram in every patient.** If any are abnormal, or symptoms suggest it, proceed to **cardiac MRI or FDG-PET**. Unexplained heart block in a young or middle-aged adult should raise it
Eye	**Uveitis** can be asymptomatic and cause permanent visual loss	**Baseline ophthalmology assessment in everyone**, including slit lamp, then periodically
Calcium	Granulomas make **1,25-dihydroxyvitamin D**, causing hypercalcemia, hypercalciuria, stones and nephrocalcinosis	Serum calcium and a **24-hour urine calcium**, which is abnormal more often than the serum. **Avoid vitamin D and sun-exposure-driven supplementation**; steroids treat it
Nervous system	**Cranial neuropathy, most classically facial nerve palsy**, plus meningitis, hypothalamic and pituitary involvement	MRI with contrast and lumbar puncture when suspected. **Bilateral facial palsy should always prompt consideration of sarcoidosis**
Lungs	Determines most long-term morbidity	**Pulmonary function with DLCO**, which is the most sensitive early marker, and high-resolution CT

PEARLS & PITFALLS

- **Serum ACE is not a diagnostic test and should not be used as one.** It is neither sensitive nor specific, is falsely lowered by ACE inhibitors, and is unreliable for tracking activity. **Do not order it to rule sarcoidosis in or out.**
- **Always culture the biopsy.** Granulomas look similar across causes, and starting steroids in undiagnosed **tuberculosis or endemic fungal disease** is the serious error this diagnosis invites. Send mycobacterial and fungal stains and cultures on every specimen.
- **Fatigue is common, disabling and does not track disease activity.** It frequently persists after inflammation is controlled, so escalating immunosuppression for fatigue alone is usually wrong. Consider small fiber neuropathy, sleep apnea, depression and steroid myopathy instead.
- **Cover the steroid course properly:** bone protection, glucose monitoring, and **PJP prophylaxis** when high-dose steroids are combined with another immunosuppressant. Screen for **latent tuberculosis before any TNF inhibitor**.

References: ATS clinical practice guideline on the diagnosis and detection of sarcoidosis · ERS clinical practice guidelines on the treatment of sarcoidosis (2021) · expert consensus on cardiac sarcoidosis screening and management.

Educational aid; verify against current guidance, local formulary and patient factors.