Sarcoidosis

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Conflict of Interest Disclosure

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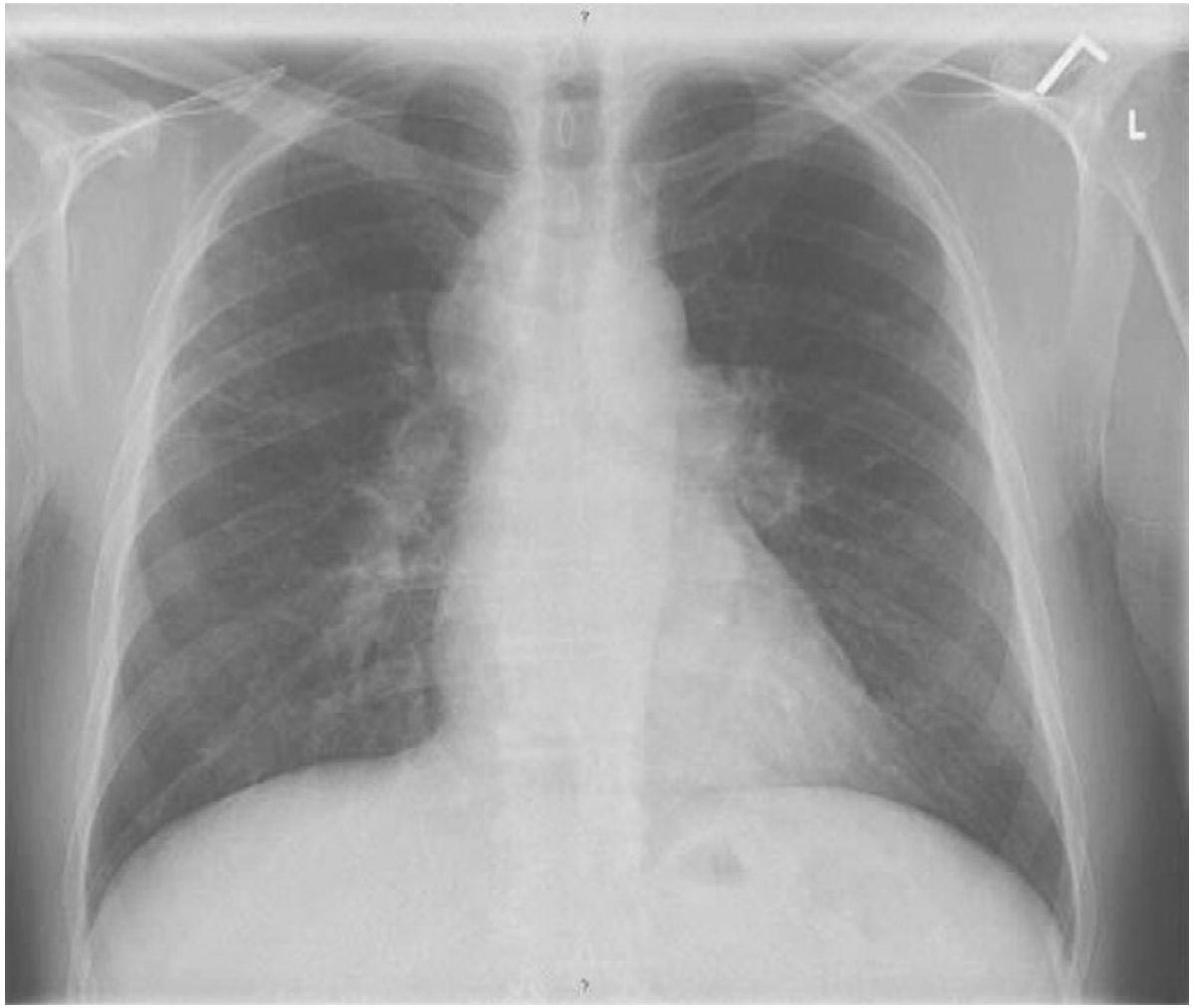
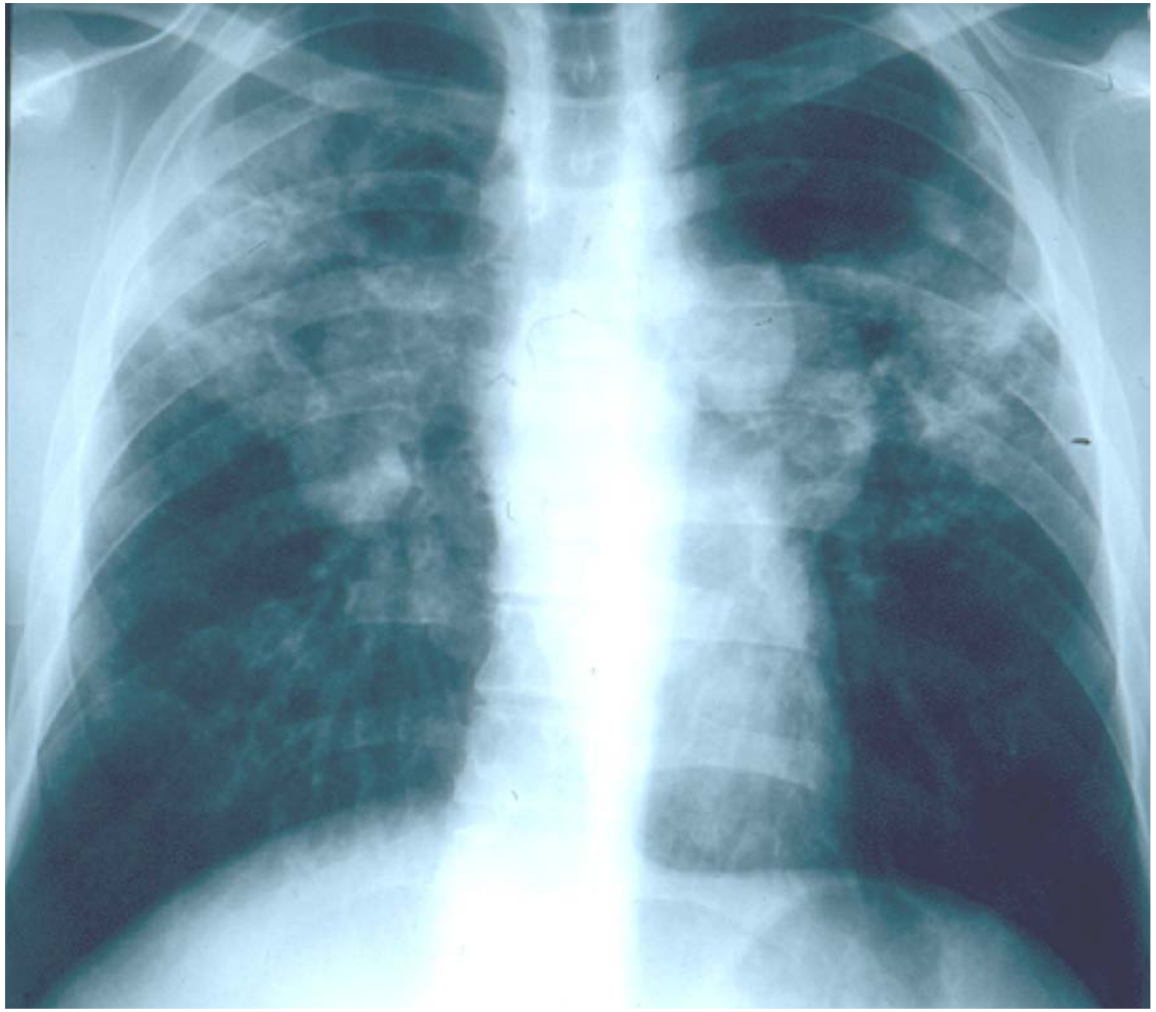
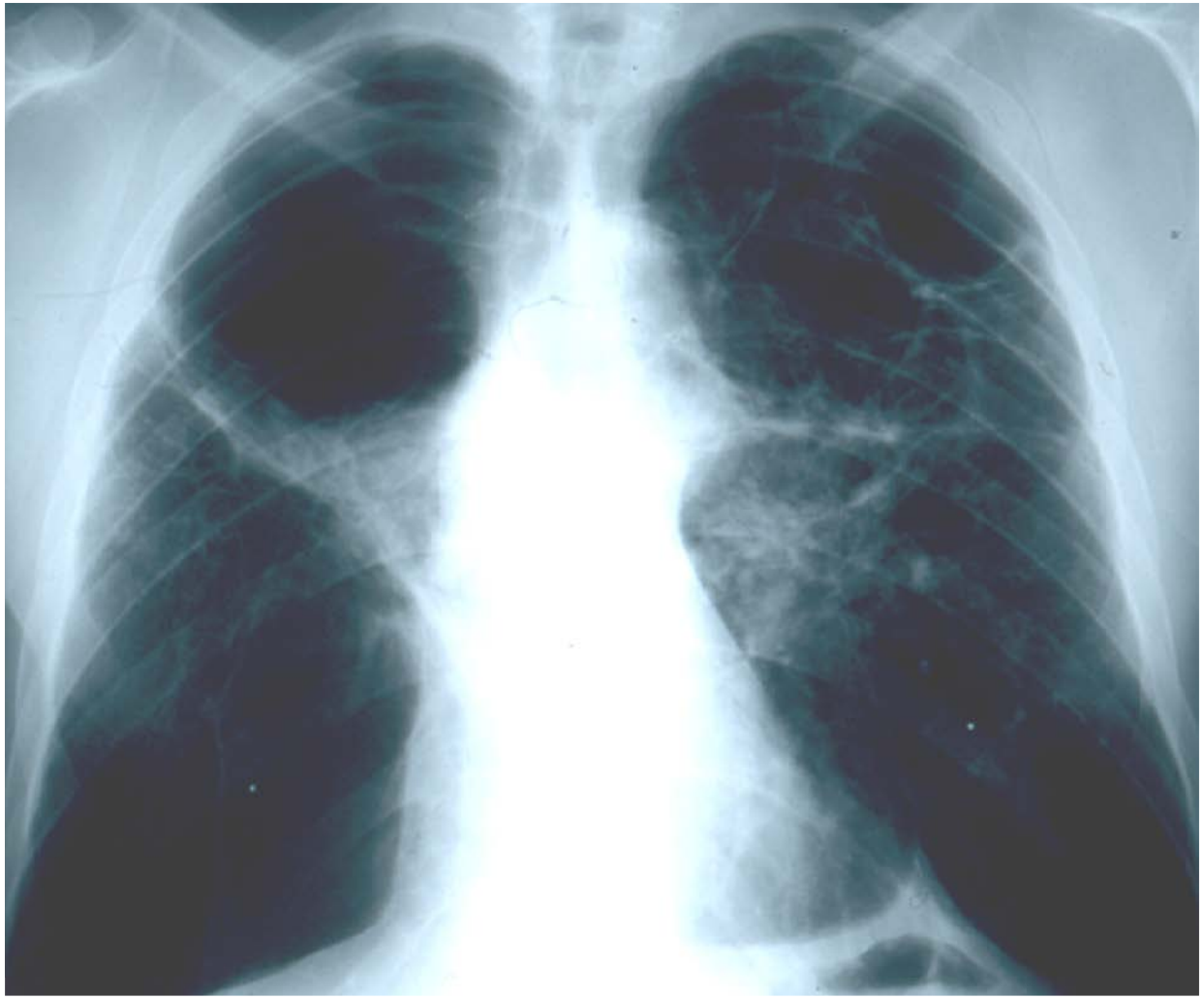
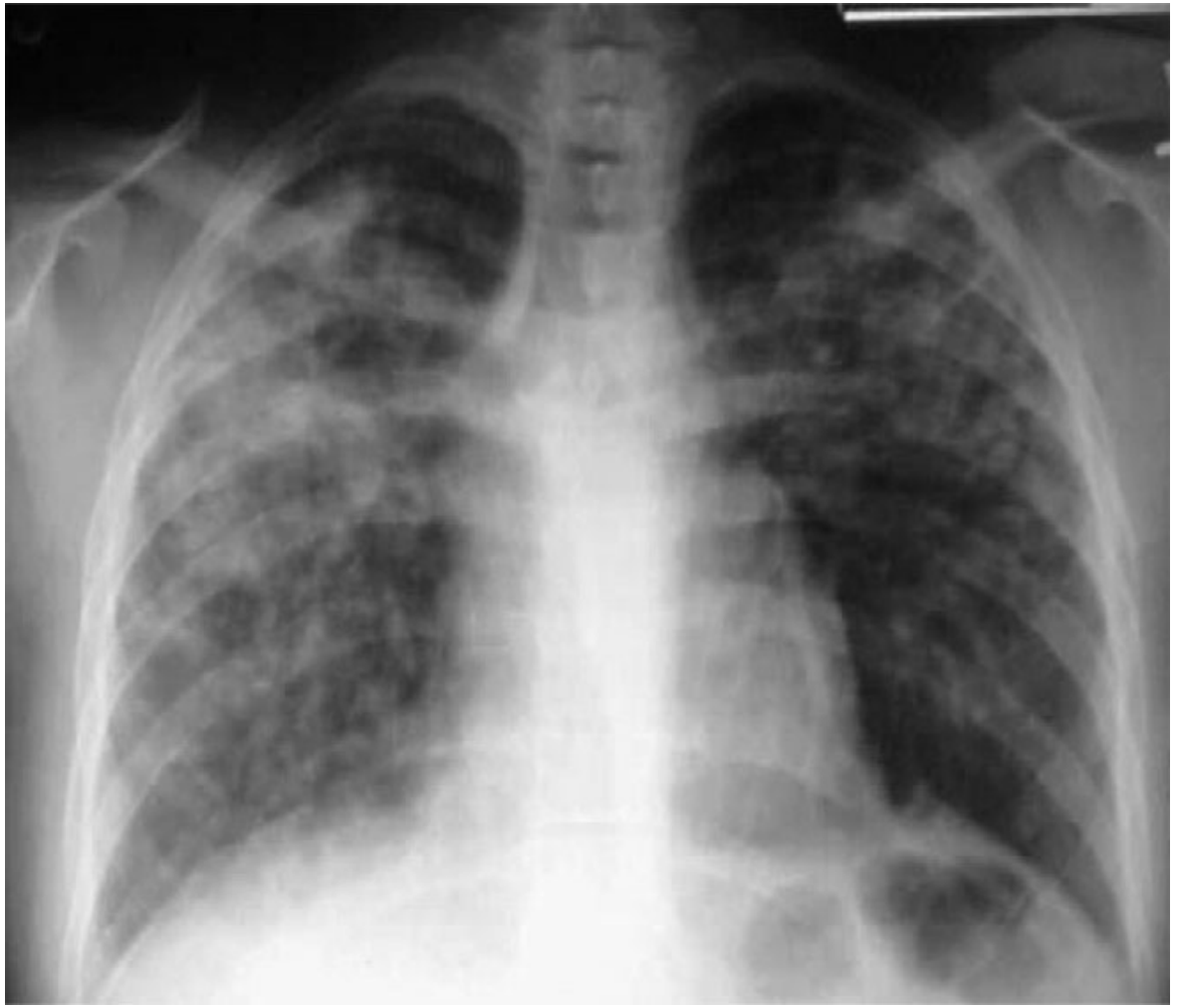




Heinle R, Autoimmunity Reviews 13 (2014) 383–387





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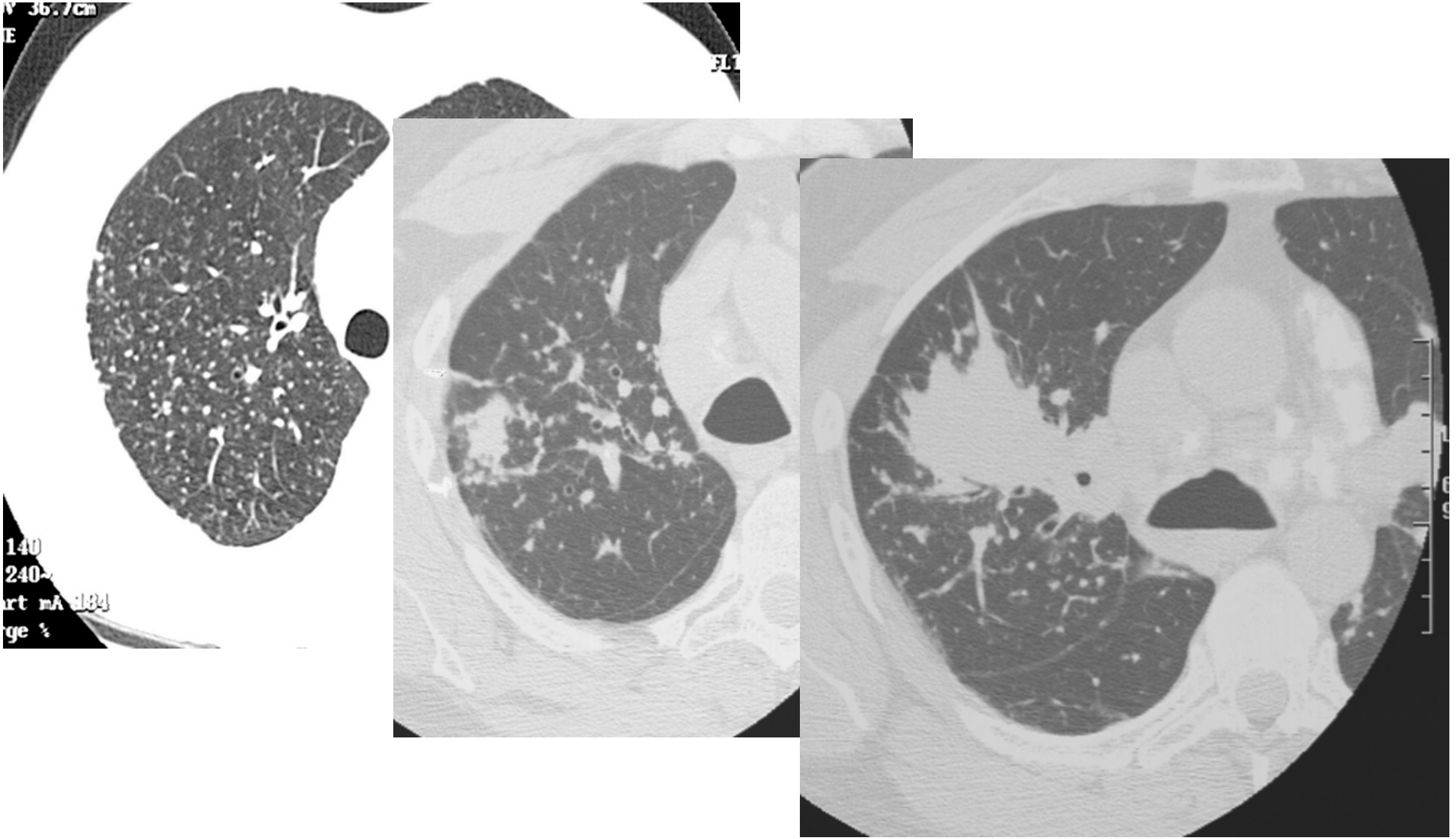


Sarcoidosis

- Sarcoidosisis a systemic granulomatous disease of unknown etiology
- It is pathologically characterized by the presence of noncaseating granulomas in more than one organ
- As an idiopathic disorder, other causes of granulomas must be excluded

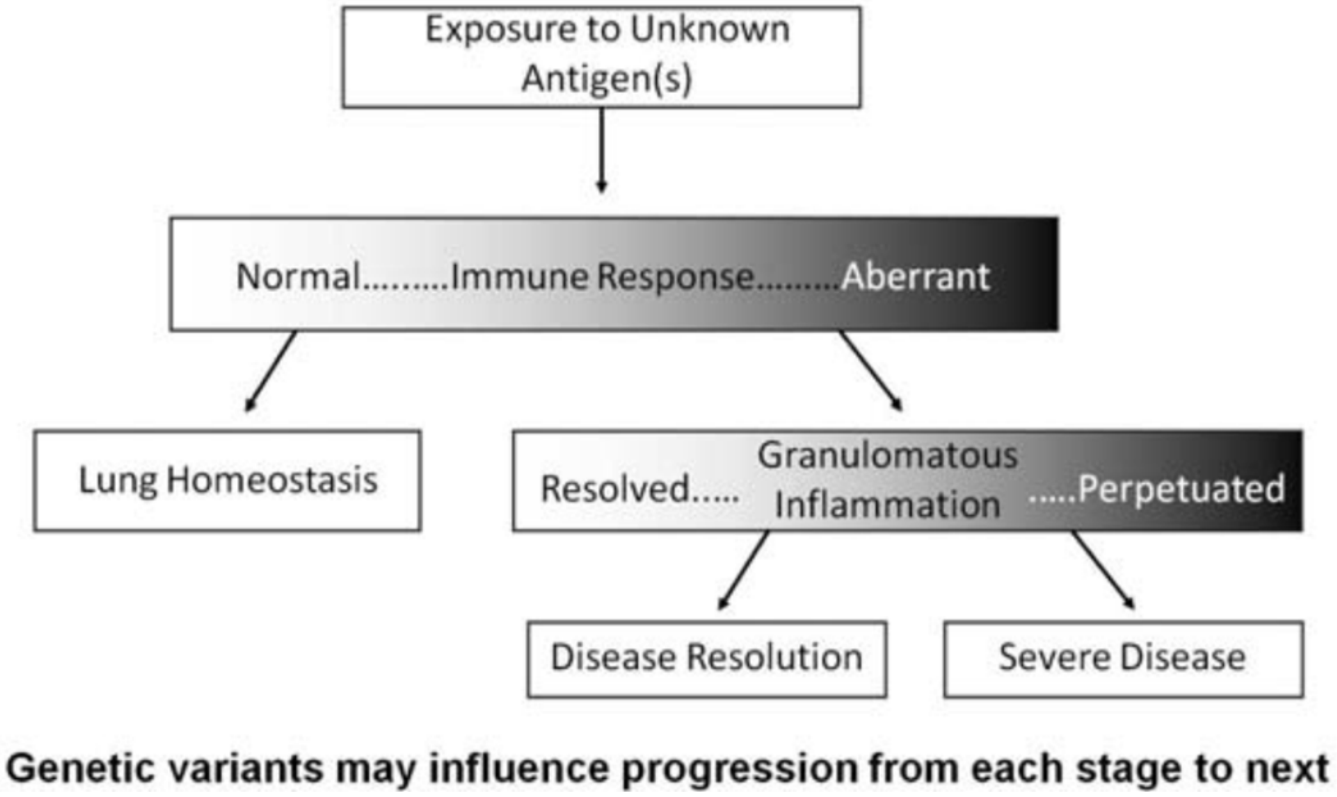
Sarcoidosis

- The cause of sarcoidosis is unclear. Genetically susceptible individuals respond to a heterogeneous set of triggers leading to an immunologic reaction characterized by the formation of noncaseating granulomas

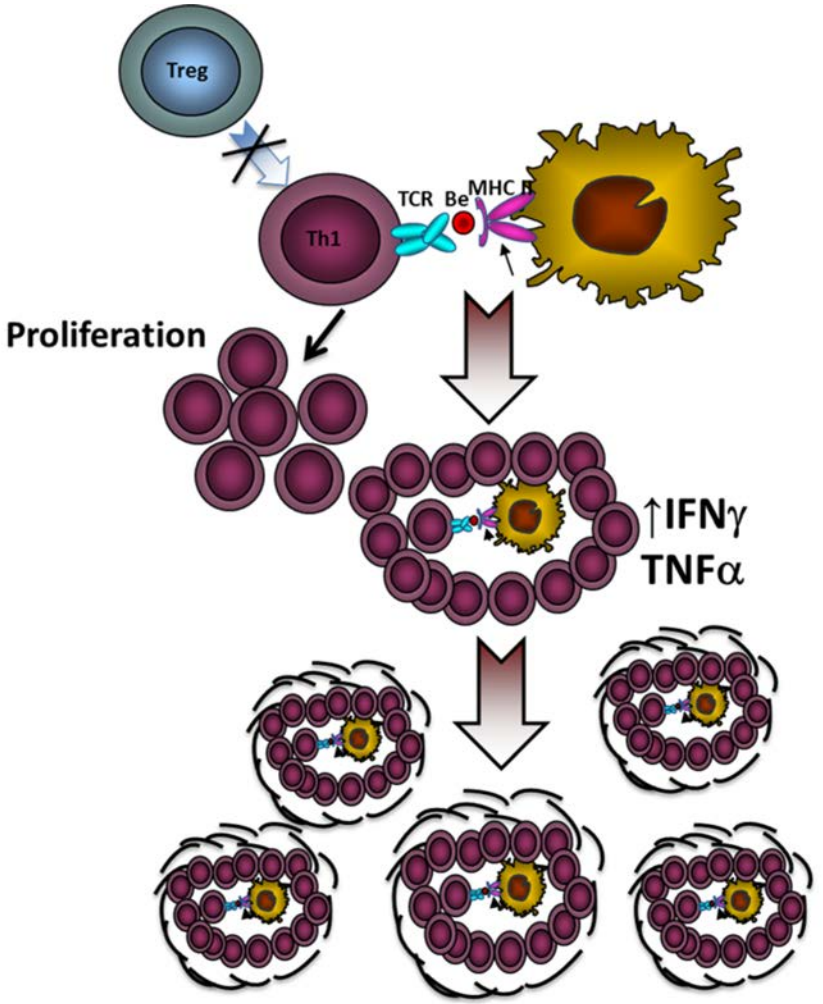
- Its presentations are heterogenous. Multiple organs of varying severity are often involved. While there is a predilection for the lungs, almost all organs can be affected

- The diagnosis is always based on a combination of the clinical context, chest imaging findings and histologic features, while eliminating other potential explanations for nocaseating granulomatous inflammation

Pathogenesis



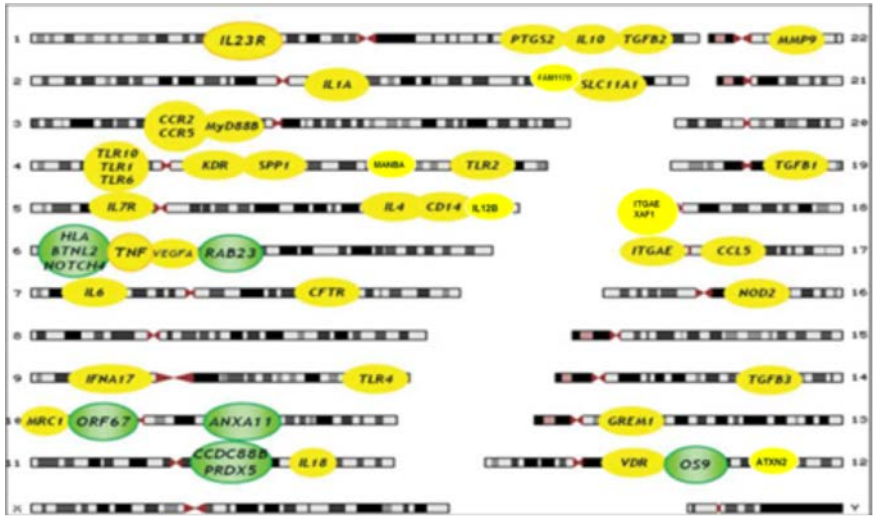
Genetic variants may influence progression from each stage to next



Exposure in Genetically Susceptible

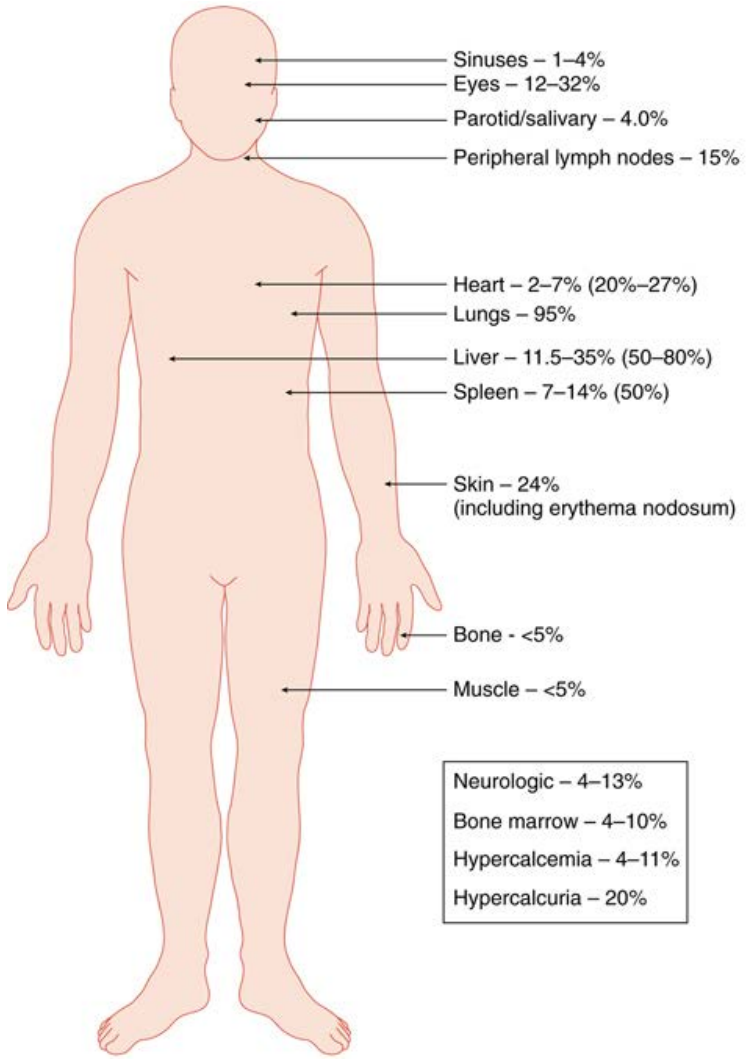
Unknown etiology

- Mycobacteria
- Proprionobacteria
- Occupational/Environmental Exposure
  - WTC
  - Agriculture
  - Pesticides
  - Military
  - Bioaerosols
  - Contact vs Dusts/Metals



Fischer et al. Semin Respir Crit Care Med 2014

It is a multisystem disease



Cleveland Clinic, Baughman AJRCCM 2001

Extrapulmonary Sarcoidosis

	Prevalence (%)	Symptoms
Skin[56]	~15	Papules, nodules, plaques, scar sarcoidosis, lupus pernio, subcutaneous sarcoidosis
Peripheral lymphadenopathy[1,57]	10–20	Mostly cervical or supraclavicular; inguinal, axillary, epitrochlear, or submandibular lymph node sites also possible; painless and mobile
Eye[58,59]	10–30	Anterior, intermediate, or posterior uveitis; retinal vascular change; conjunctival nodules; lacrimal gland enlargement
Liver[60]	20–30	Often symptom-free; abnormal liver function tests in 20–30% of patients; hepatomegaly; rarely hepatic insufficiency, chronic intrahepatic cholestasis, or portal hypertension
Spleen[57]	~10	Splenomegaly; rarely, pain or pancytopenia; very rarely, splenic rupture
Heart[48,49,61,62]	2–5	Atrioventricular or bundle branch block; ventricular tachycardia or fibrillation; congestive heart failure; pericarditis; impairment of sympathetic nerve activity; sudden death
Nervous system[63–65]	~5	Facial nerve palsy, optic neuritis, leptomeningitis, diabetes insipidus, hypopituitarism, seizures, cognitive dysfunction, deficits, hydrocephalus, psychiatric manifestations, spinal cord disease, polyneuropathy, small-fibre neuropathy

Valeyre D, Lancet 2014; 383: 1155–67

Extrapulmonary Sarcoidosis

Kidney[66]	0·5–2	Rare symptoms; increased creatininemia sometimes associated with hypercalcaemia; nephrocalcinosis; kidney stones
Parotitis[1]	4%	Symmetrical parotid swelling, Heerfordt's syndrome when associated with uveitis, fever, and facial palsy
Nose[57]	0·5–6	Nasal stuffiness, nasal bleeding, crusting, anosmia
Larynx[57]	0·5–1	Hoarseness, breathlessness, stridor, dysphagia
Bones[67]	<5	Often asymptomatic; hands and feet classically most involved, also large bones and axial skeleton
Skeletal muscles[67]	1	Proximal muscle weakness, amyotrophy, myalgia, intramuscular nodules
Genitourinary tract[1,57]	..	All organs can be involved, including breast, uterus, epididymis, and testicle
Gastrointestinal tract[1]	1	Most often symptom-free, but the oesophagus, stomach, small intestine, and colon can be involved

Valeyre D, Lancet 2014; 383: 1155–67

Sarcoidosis

- Generally a young person's disease

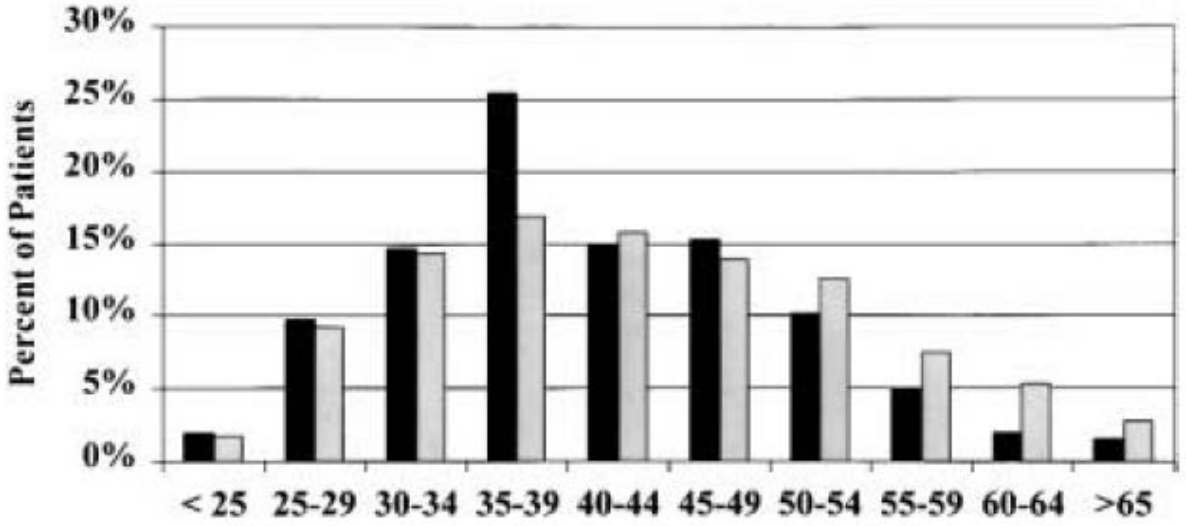


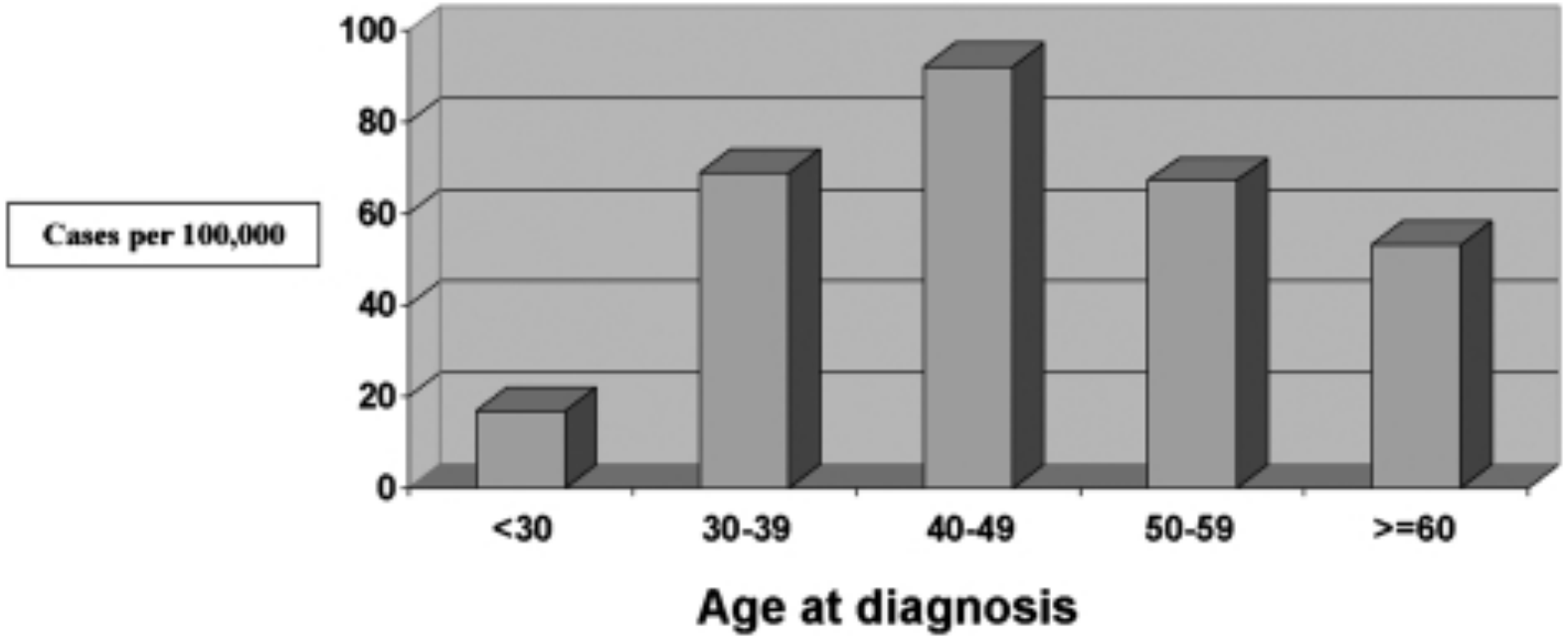
Figure 1. Distribution of patients with sarcoidosis by age at diagnosis and sex. The percentages of male and female patients are shown separately. ■ Male; □ Female.

Baughman AJRCCM 2001

Sarcoidosis

- Generally a young person's disease

Age-specific annual incidence rates of sarcoidosis in the Black Women's Health Study Cohort (1995-2007).



Cozier Chest 2011

Sarcoidosis

- Generally a young person's disease
  - Age 30-60
  - Peak incidence in patients 20-50
- US incidence rates 5.9-6.3 per 100,000 person-years
  - African Americans, Danes and Swedes appear to be at high risk
  - US annual age-adjusted incidence rates of 35.5 per 100,000 for AA
- Disease presentation and severity differs among ethnic and racial groups
  - Presence and severity of constitutional, respiratory, ocular, or skin symptoms increased in African Americans
  - Asymptomatic abnormal chest radiographic more common among Caucasians

It is a multisystem disease

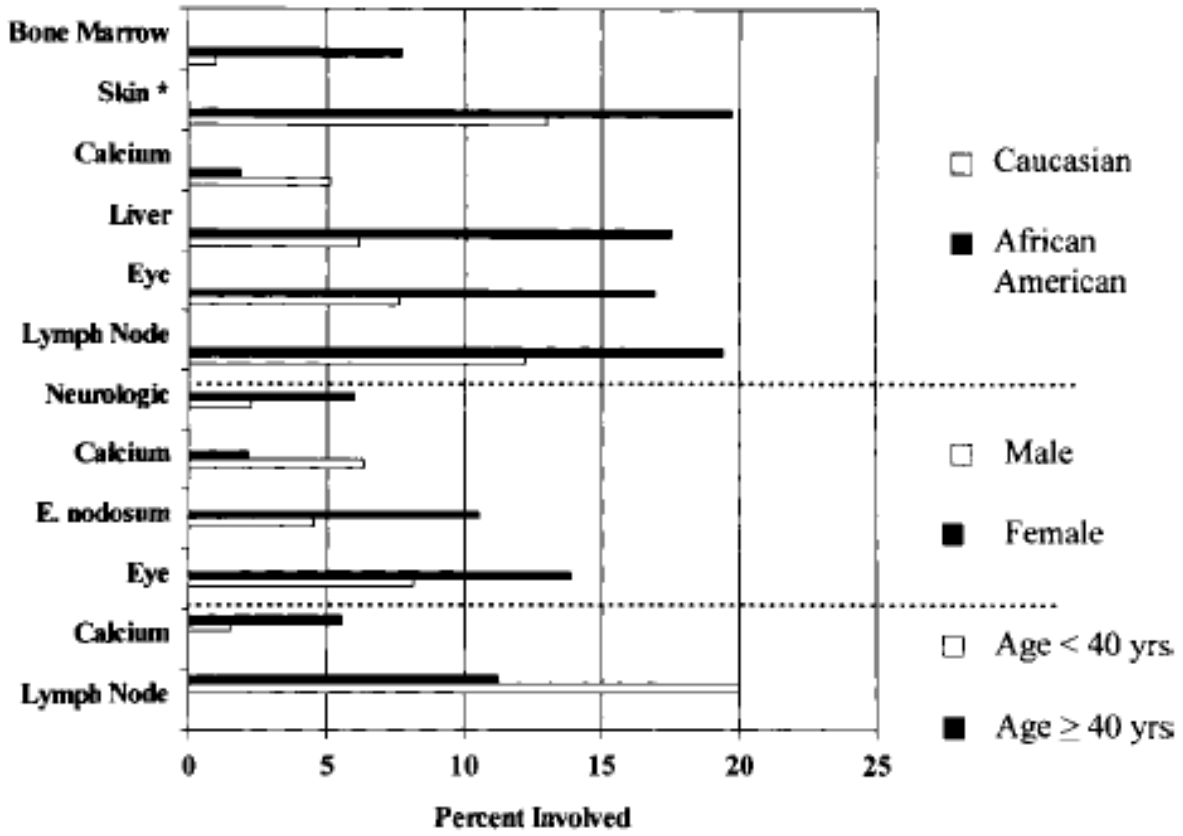


Figure 2. Comparison of proportion of organ involvement in which there was a significant difference between groups on the basis of race, sex, or age. See text for individual χ^2 values. *Skin involvement other than erythema nodosum.

Baughman AJRCCM 2001

Diagnosis

- Appropriate clinical context
  - Characteristic clinical syndrome (e.g., Lofgren's)
  - Lung involvement is common (90+%)
  - The more organs involved the more confident the diagnosis
- Find noncaseating granulomata
  - Without alternative cause (e.g.,TB, fungus, Berrylium)
- Exclusion of other diseases capable of producing a similar histologic or clinical picture
- Rare to be 100% sure of the diagnosis, reevaluation is generally necessary

Which of the following are not manifestations of sarcoidosis?

1. Cranial neuropathy
2. Mass lesion
3. Ocular symptoms that resolve spontaneously
4. Peripheral neuropathy
5. Painful patchy dysethesias that do not follow a nerve distribution

Major Pathologic Differential Diagnosis of Sarcoidosis

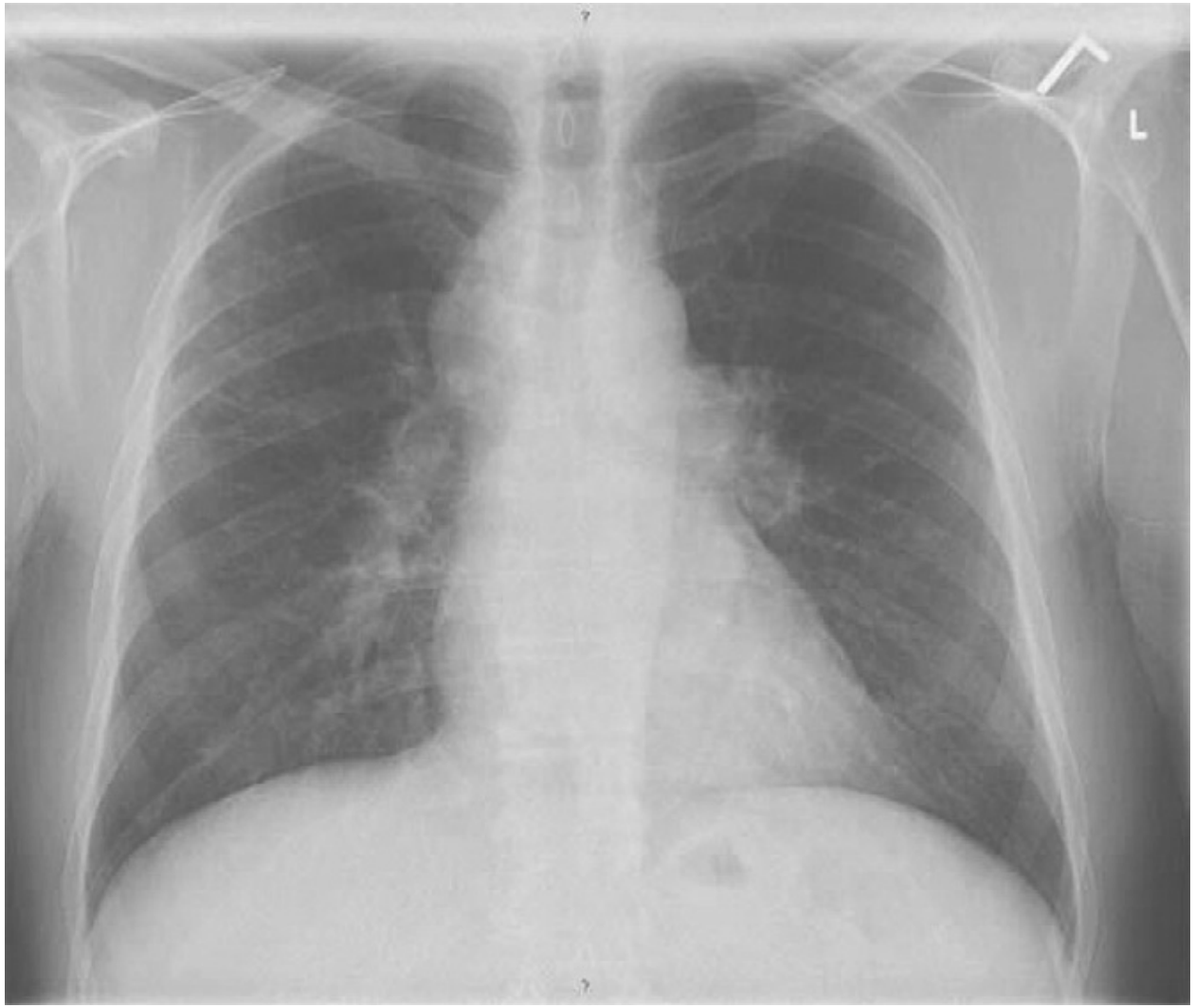
Lung	Lymph Node	Skin	Liver	Bone Marrow	Other Sites
• Tuberculosis • Atypical mycobacteriosis • Cryptococcosis • Aspergillosis • Histoplasmosis • Coccidioido-mycosis • Blastomycosis • *Pneumocystis jirovecii* • Mycoplasma, etc. • Hypersensitivity pneumonitis • Pneumoconiosis • Beryllium, titanium, aluminum • Drug reactions • Aspiration of foreign materials • Granulomatous poly-angiitis (sarcoid-type granulomas are rare) • Chronic interstitial pneumonia, such as usual and lymphocytic interstitial pneumonia • Necrotizing sarcoid granulomatosis (NSC)	• Tuberculosis • Atypical mycobacteriosis • Brucellosis • Toxoplasmosis • Granulomatous histiocytic necrotizing lymphadenitis (Kikuchi's disease) • Cat-scratch disease • Sarcoid reaction in regional lymph nodes to carcinoma • Hodgkin's disease • Non-Hodgkin's lymphomas • Granulomatous lesions of unknown significance (the GLUS syndrome)	• Tuberculosis • Atypical mycobacteriosis • Fungal infection • Reaction to foreign bodies: • Beryllium, zirconium, tattooing, paraffin, etc. • Rheumatoid nodule	• Tuberculosis • Brucellosis • Schistosomiasis • Primary biliary • cirrhosis • Crohn's disease • Hodgkin's • disease • Non-Hodgkin's • lymphomas • GLUS syndrome	• Tuberculosis • Histoplasmosis • Infectious mononucleosis • Cytomegalovirus • Hodgkin's Disease • Non-Hodgkin's • lymphomas • Drugs • GLUS syndrome	• Tuberculosis • Brucellosis • Other infections • Crohn's disease • Giant cell myocarditis • GLUS syndrome

Courtesy Prof. Kevin Flaherty

Adapted from ATS Statement on Sarcoidosis. *Am J Resp Crit Care Med.* 1999; 160: 736-755

Lofgren’s syndrome

- Fever
- Polyarthritis
- Erythema nodosum
- Bilateral hilar lymph nodes



General evaluation

Physical Examination

- Skin: Maculopapular lesions, subcu nodules, rosacea
- Head: Parotid, salivary gland enlargement
- Eyes: Conjunctival injection, lacrimal gland enlargement, slit lamp
- Nose: Missing septum
- LN: Neck, axillary, groin
- Chest: wheeze, crackles
- CV: Rhythm, S3, s/sx RVF
- Abdomen: HSM
- Joints: Synovitis, deformities
- Neuro: Central, peripheral lesions

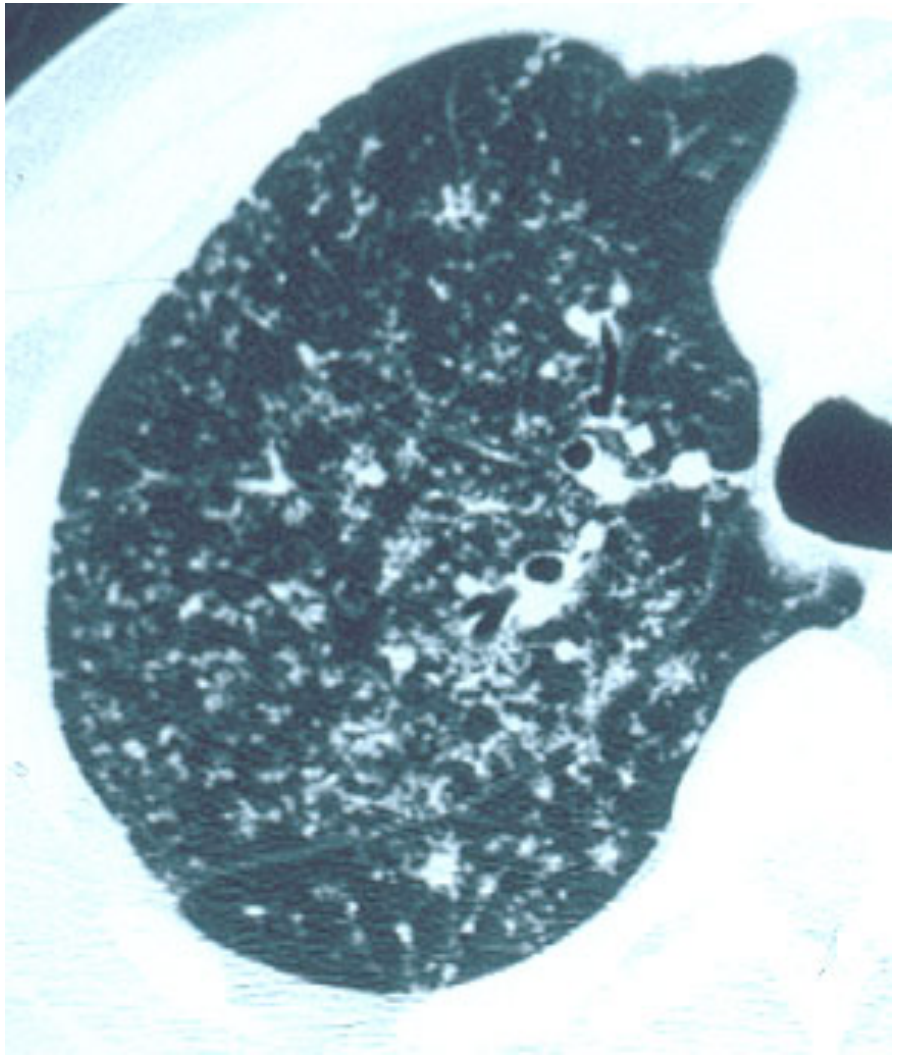
Lab testing

- CBC
- Comprehensive Chemistry
- Vit D 1,25 and 25
- PTH
- 24 hour urine Ca
- EKG
- PFT
- CXR or HRCT
- Ophthal consult
- Others depending on s/sx

Laboratory testing

- Hypercalcemia 2-10%
- Hypercalciuria 15-40%
- Anemia 4-20%
- Leukopenia up to 40%
- ACE
  - Elevated in 60% with active disease
  - Elevated in 20% with chronic disease
  - Affected by genetic polymorphisms
  - Limited prognostic value
  - Reflects granulomatous inflammation

Chest imaging



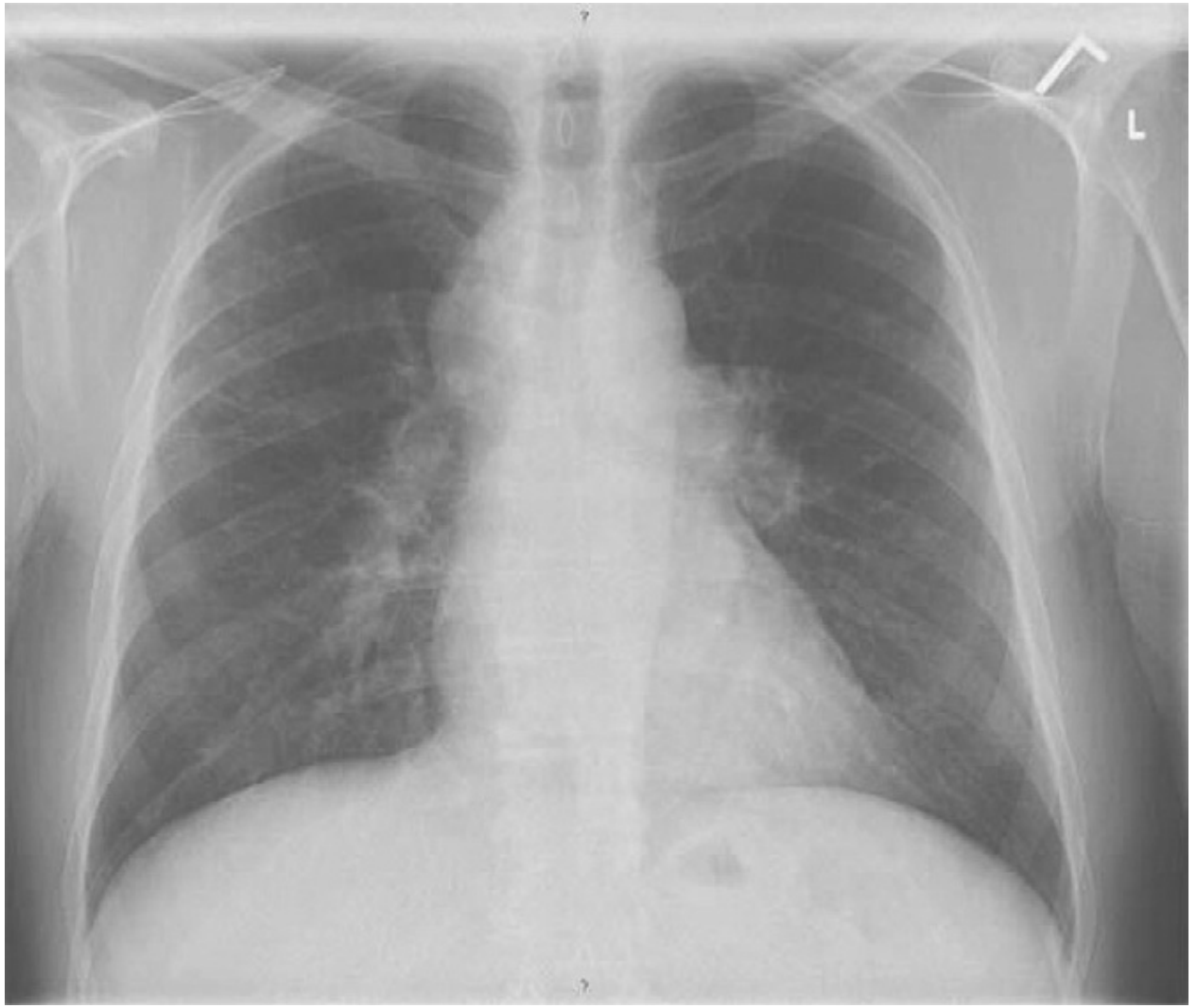
Valeyre D, Lancet 2014; 383: 1155–67

Modified Scadding Chest Radiograph Stages

Stage	Radiographic finding
0	Normal
I	Bilateral hilar lymphadenopathy
II	Bilateral hilar lymphadenopathy and pulmonary infiltrates
III	Pulmonary infiltrates without bilateral hilar lymphadenopathy
IV	Pulmonary fibrosis

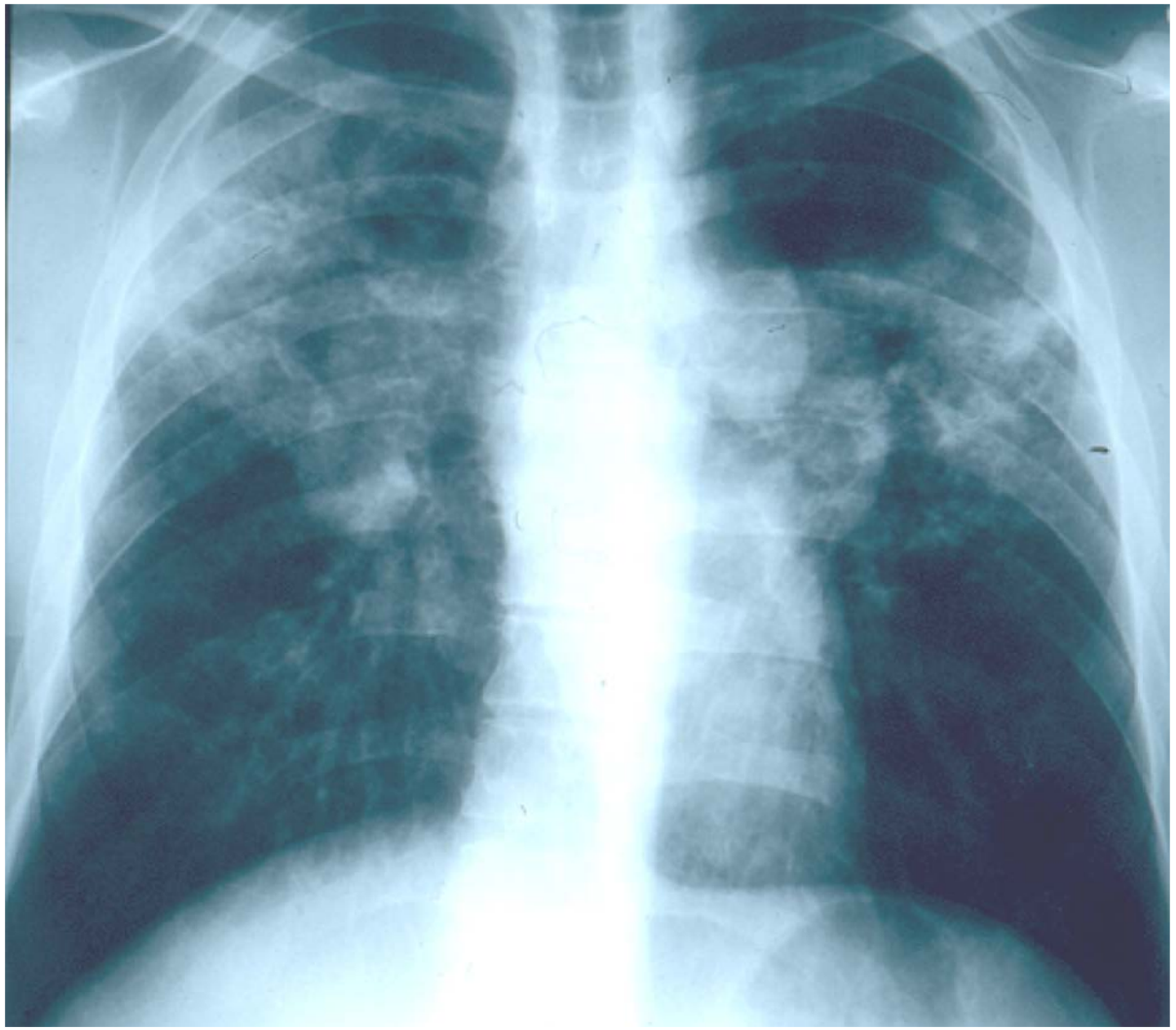
Amin et al, Ther Adv Resp Dis 2014

Stage 1

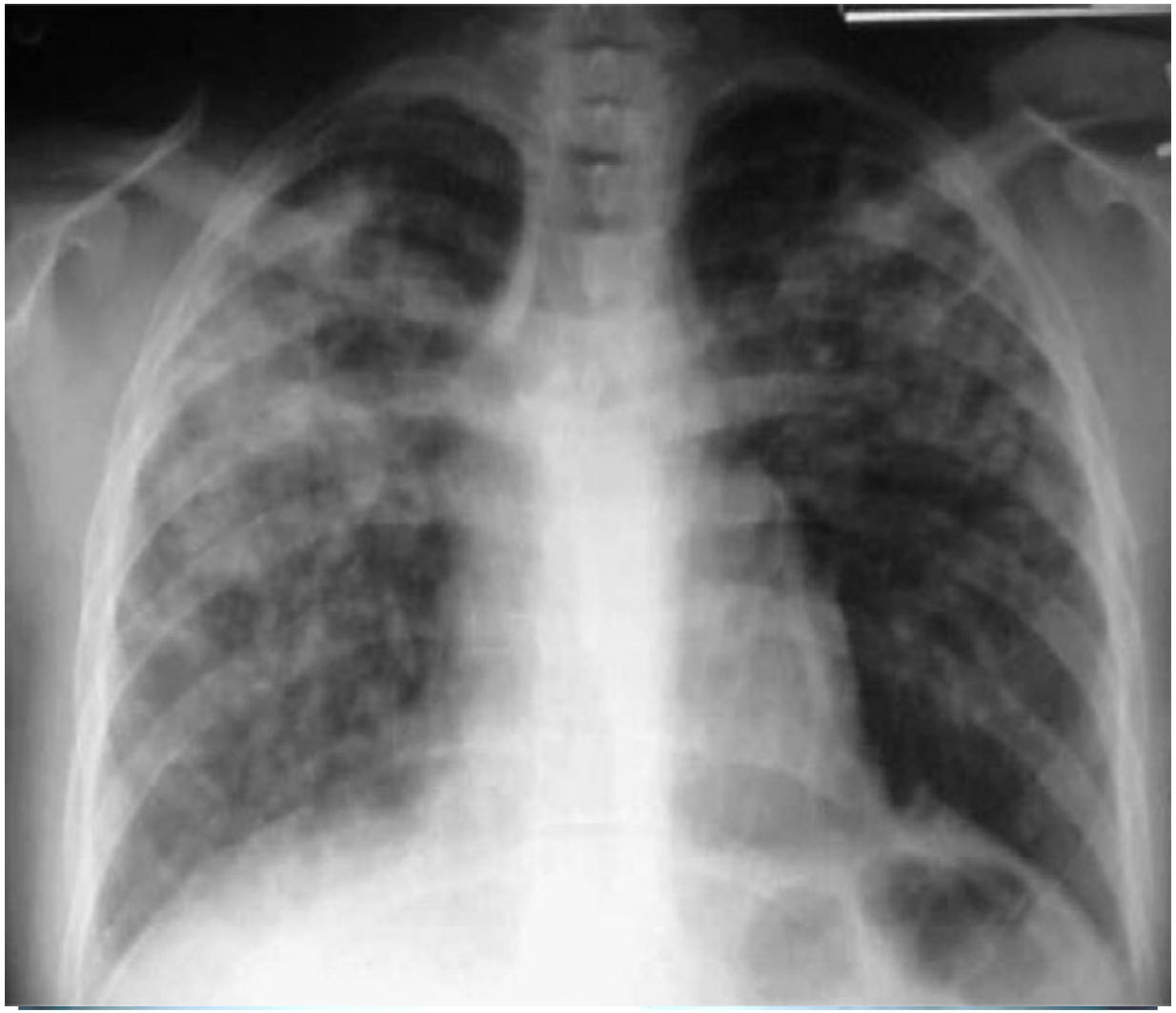


Heinle R, Autoimmunity Reviews 13 (2014) 383–387

Stage 2



Stage 3



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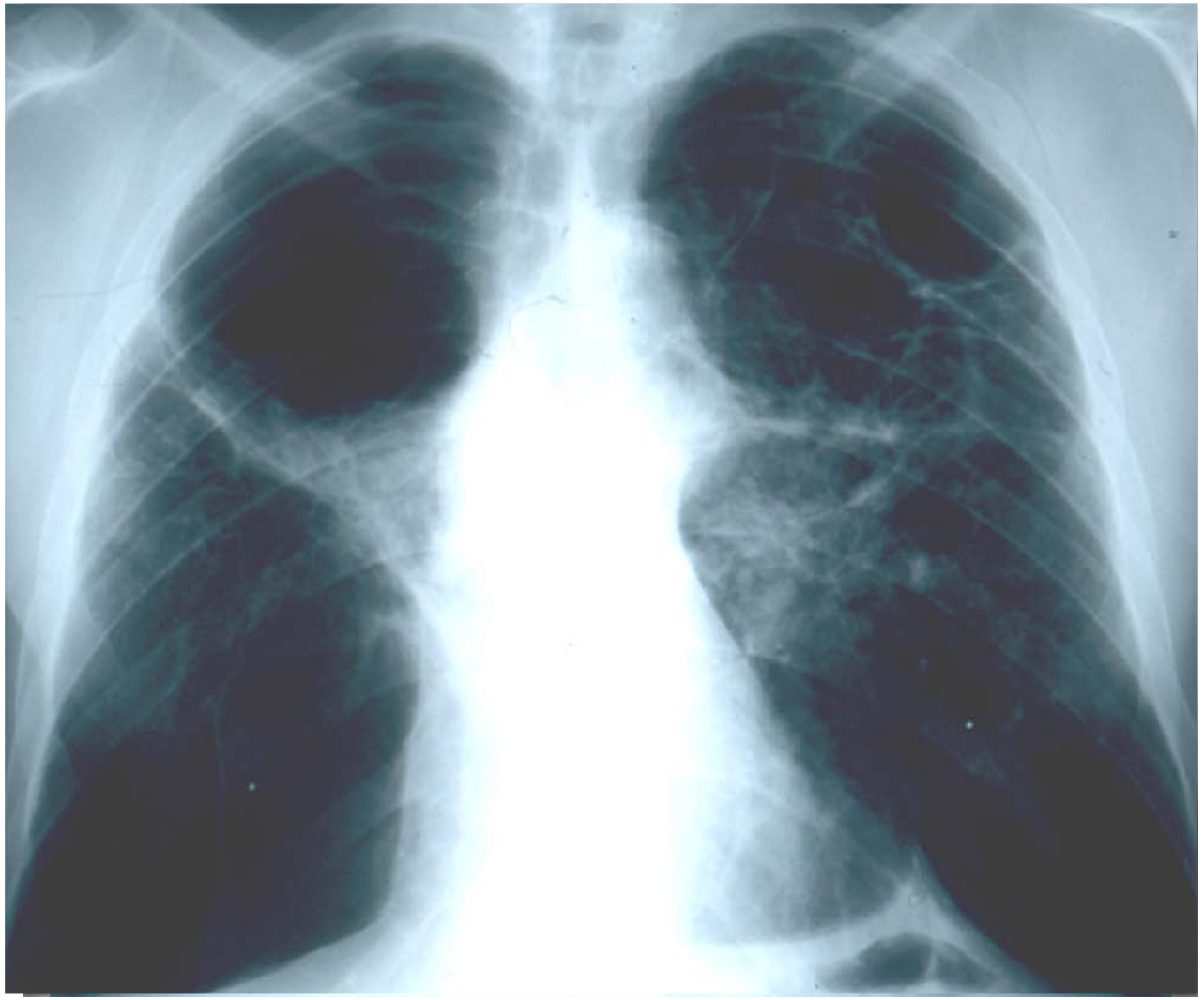
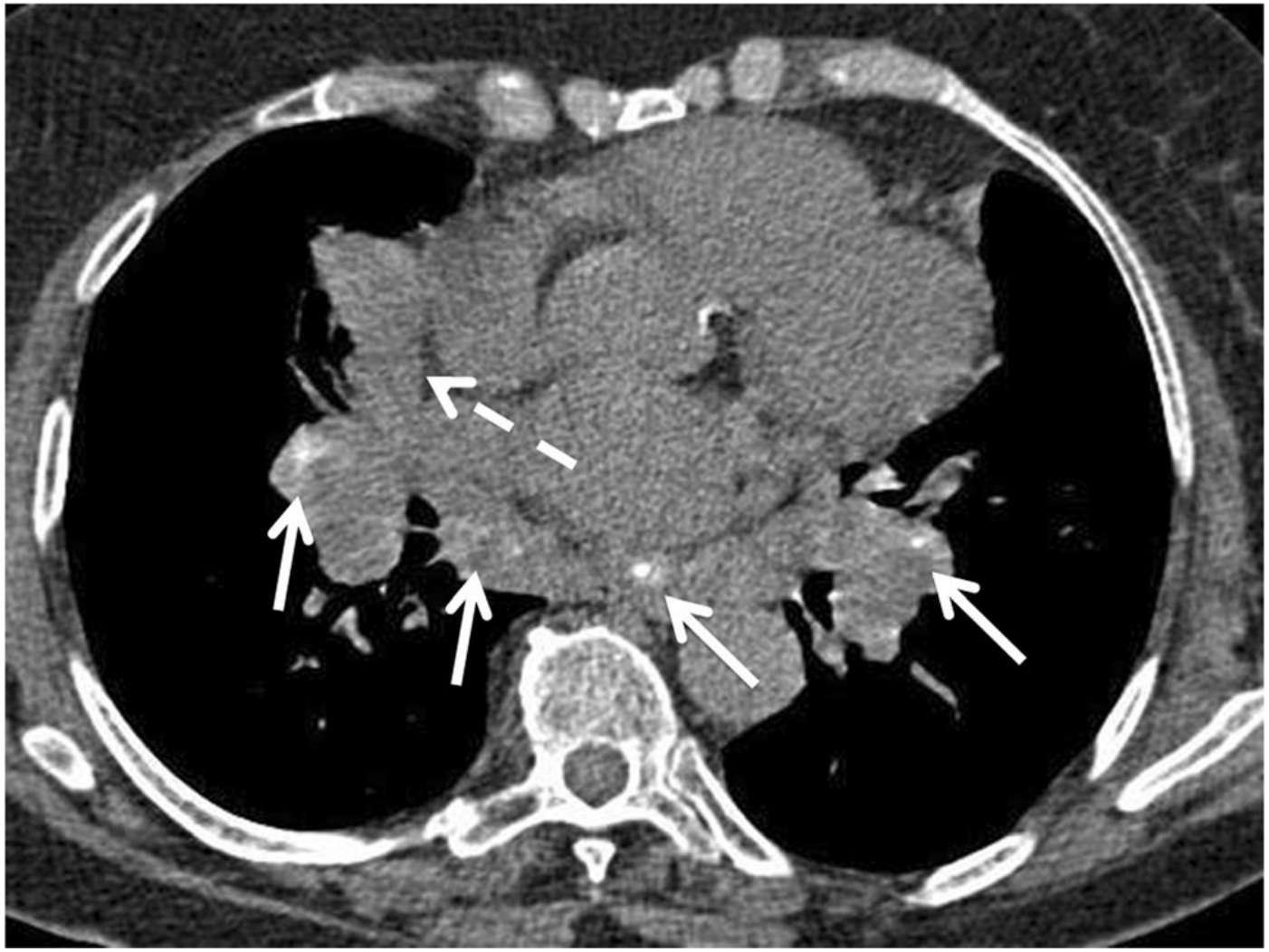
Stage 4



High Resolution CT

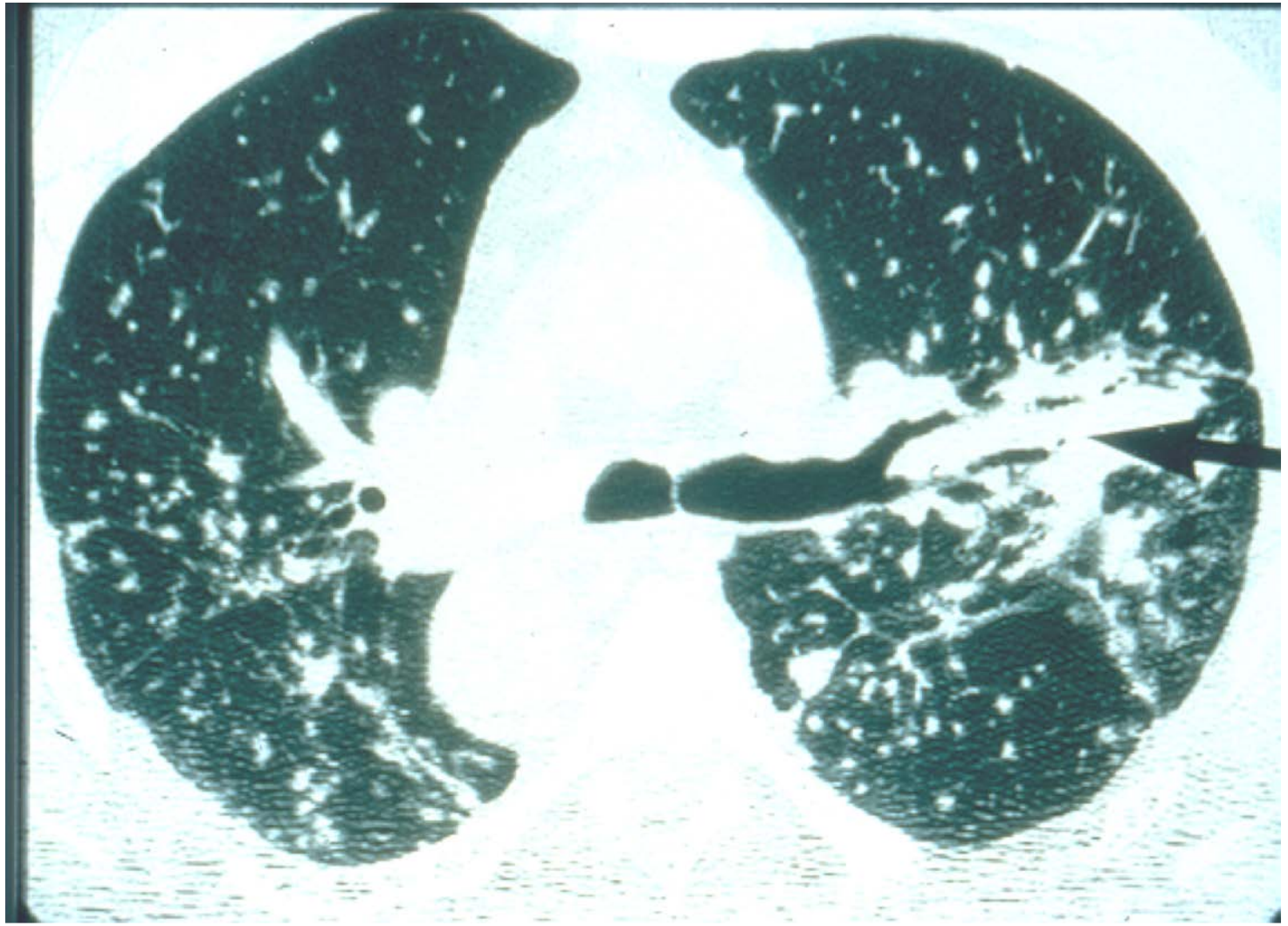
- Upper lung zone predominant
- Predilection for the central bronchovascular bundles
- Nodules
- Confluent alveolar opacities
- Late disease may show architectural distortion, fibrosis, cysts
- Complications
  - Mycetomas

High Resolution CT



Paolo S, Eur Radiol (2014) 24:807–816

High Resolution CT



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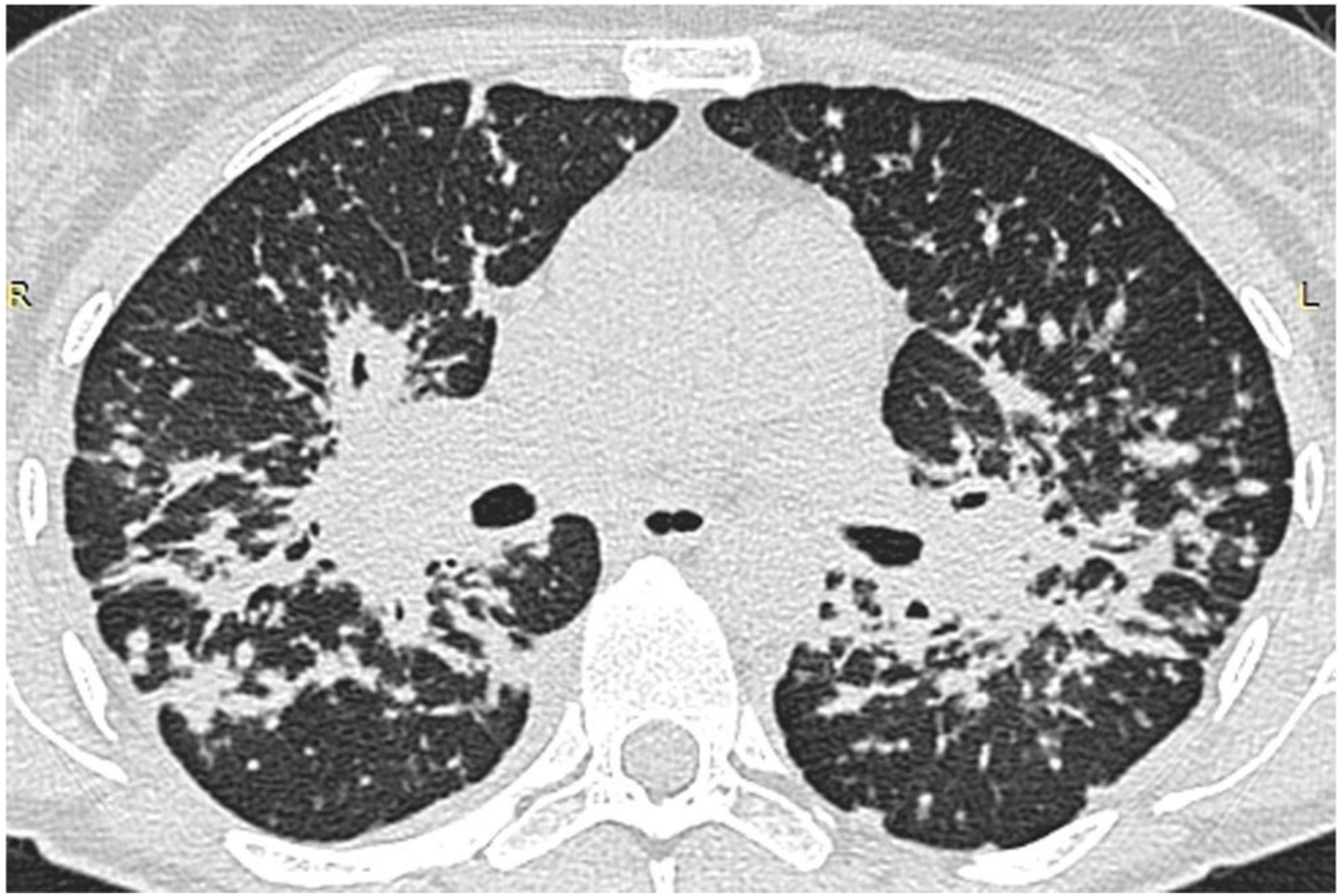

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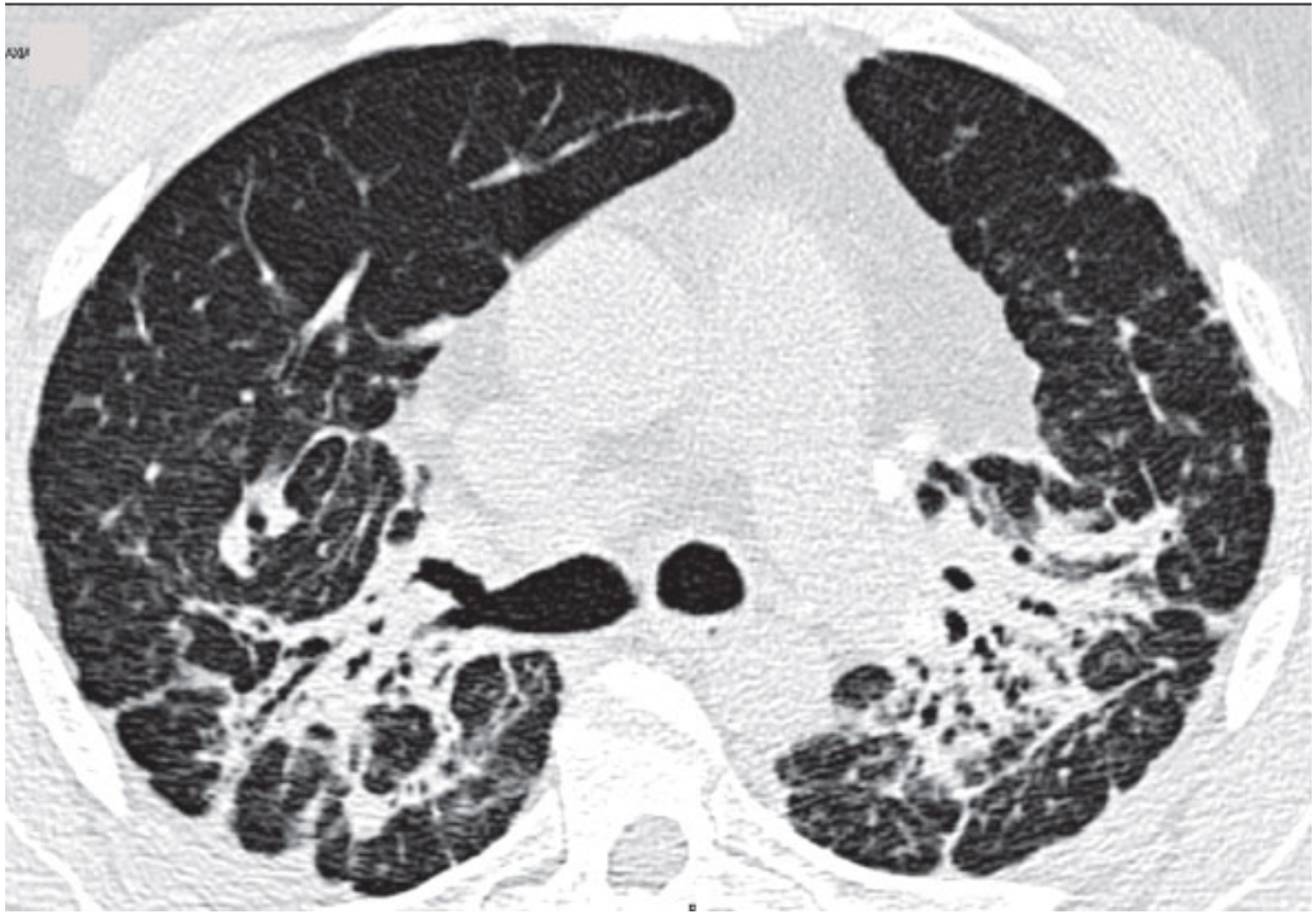

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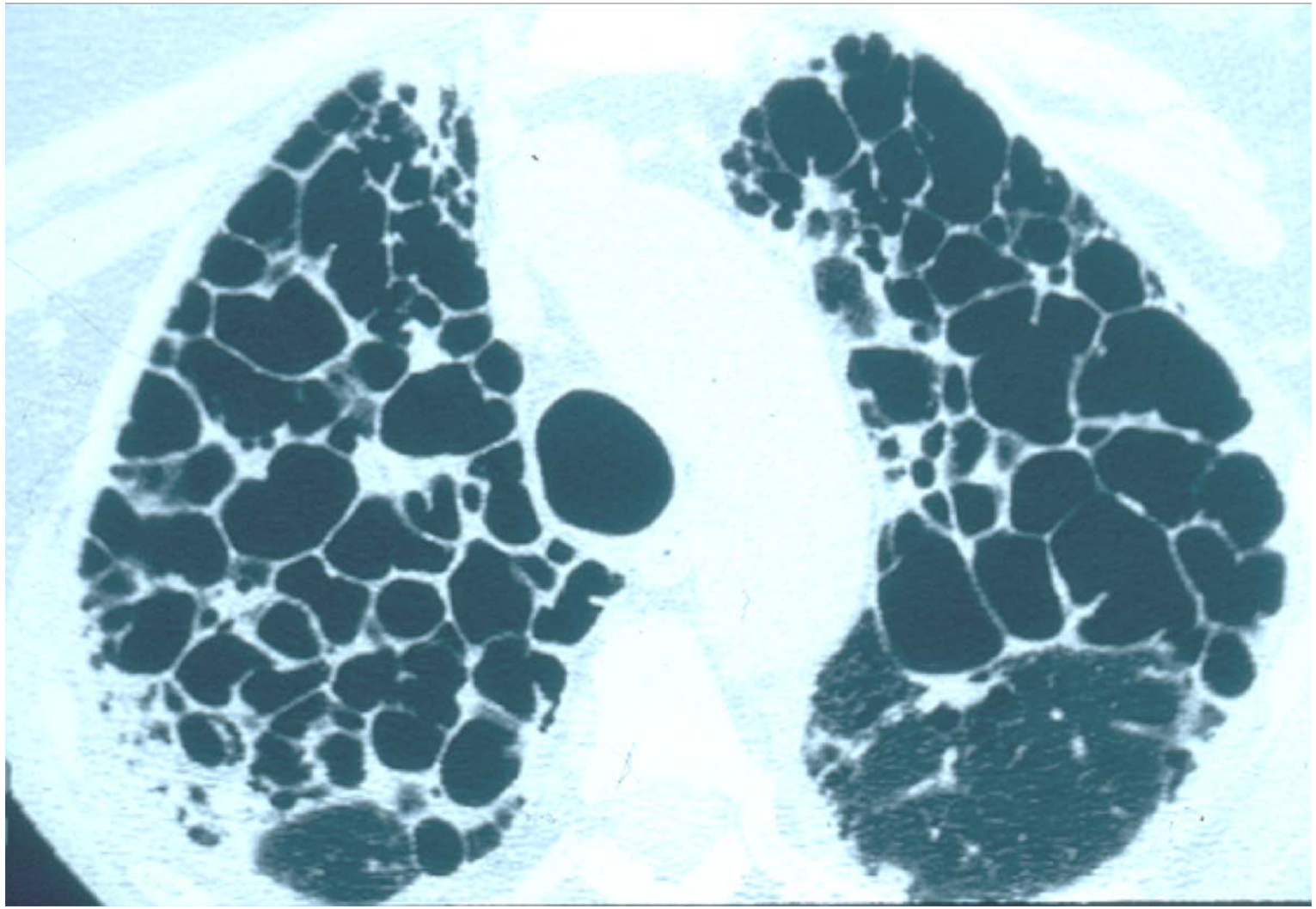

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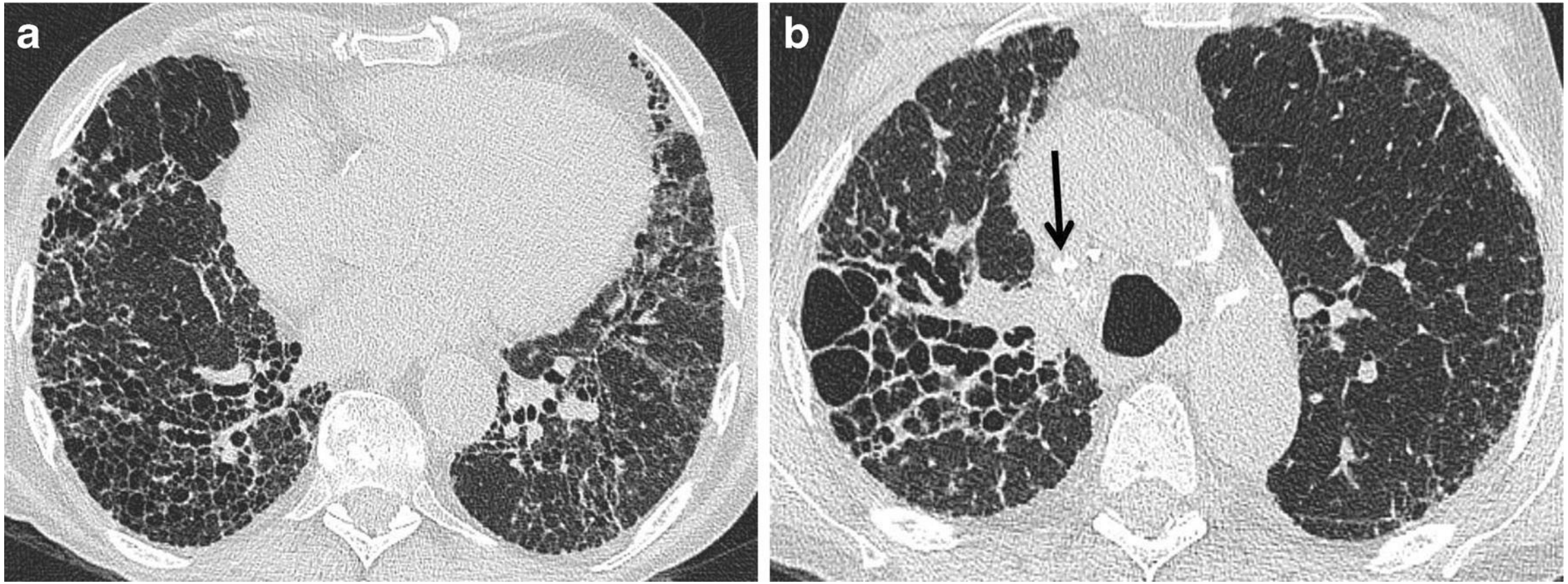

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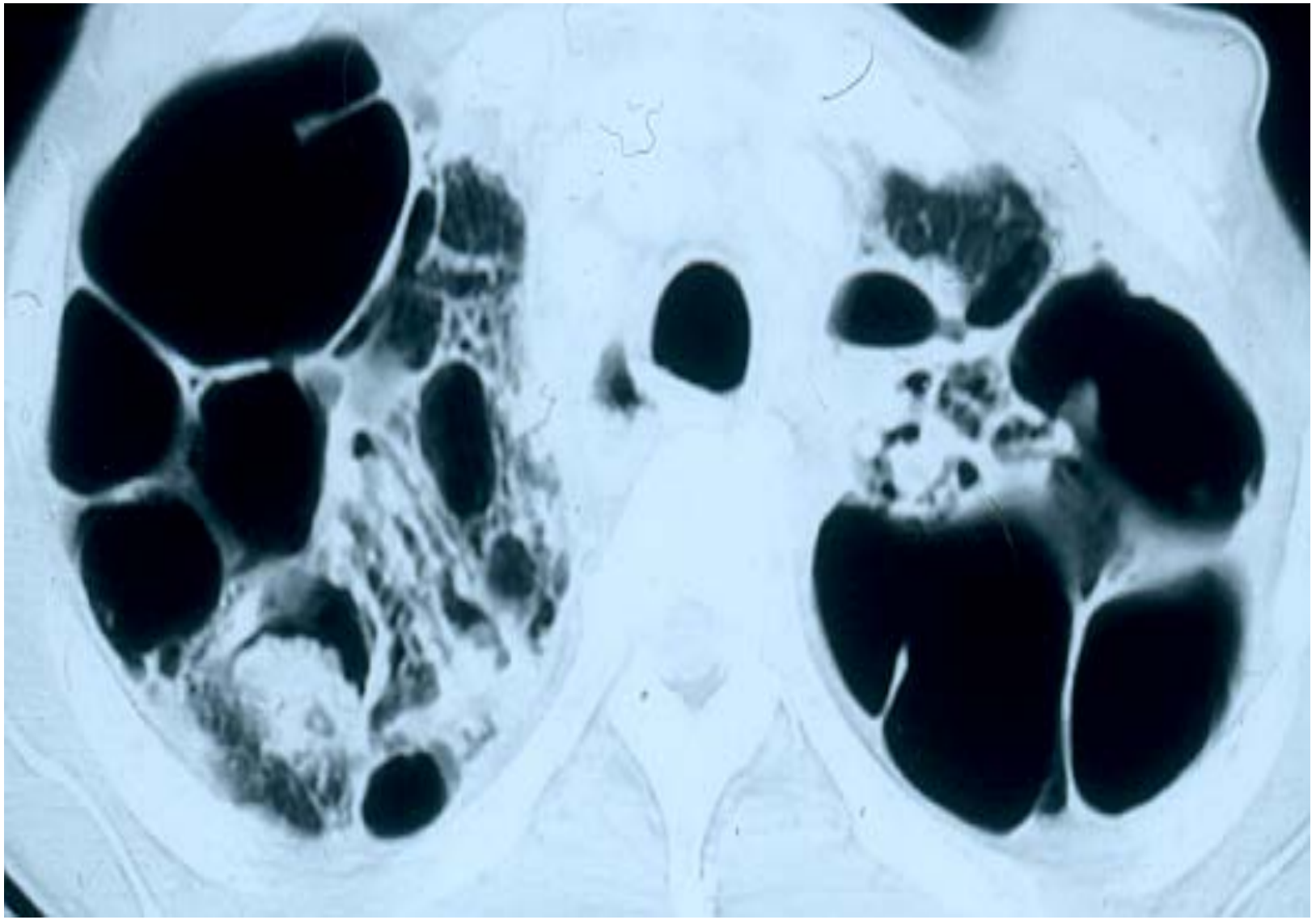

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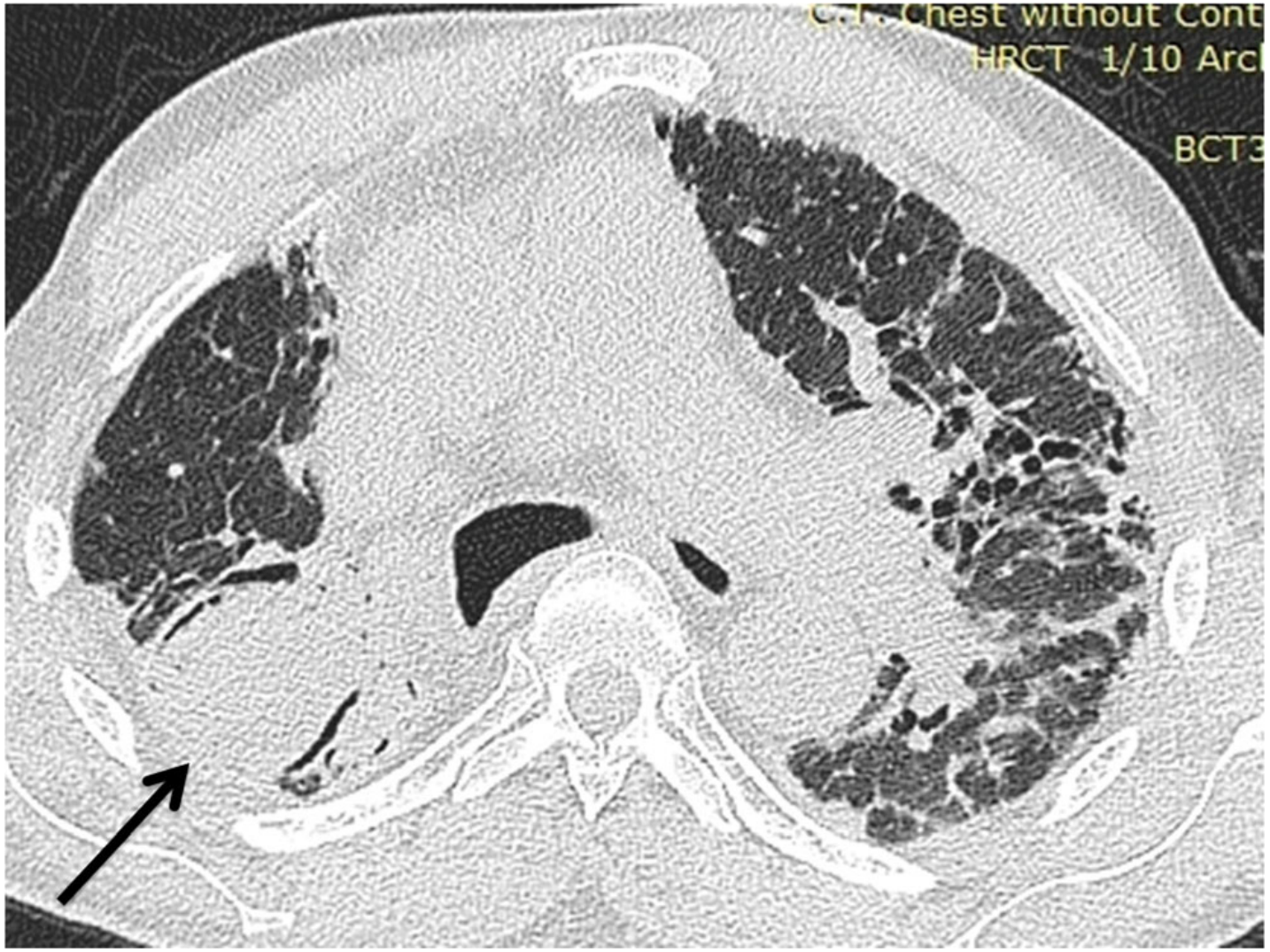

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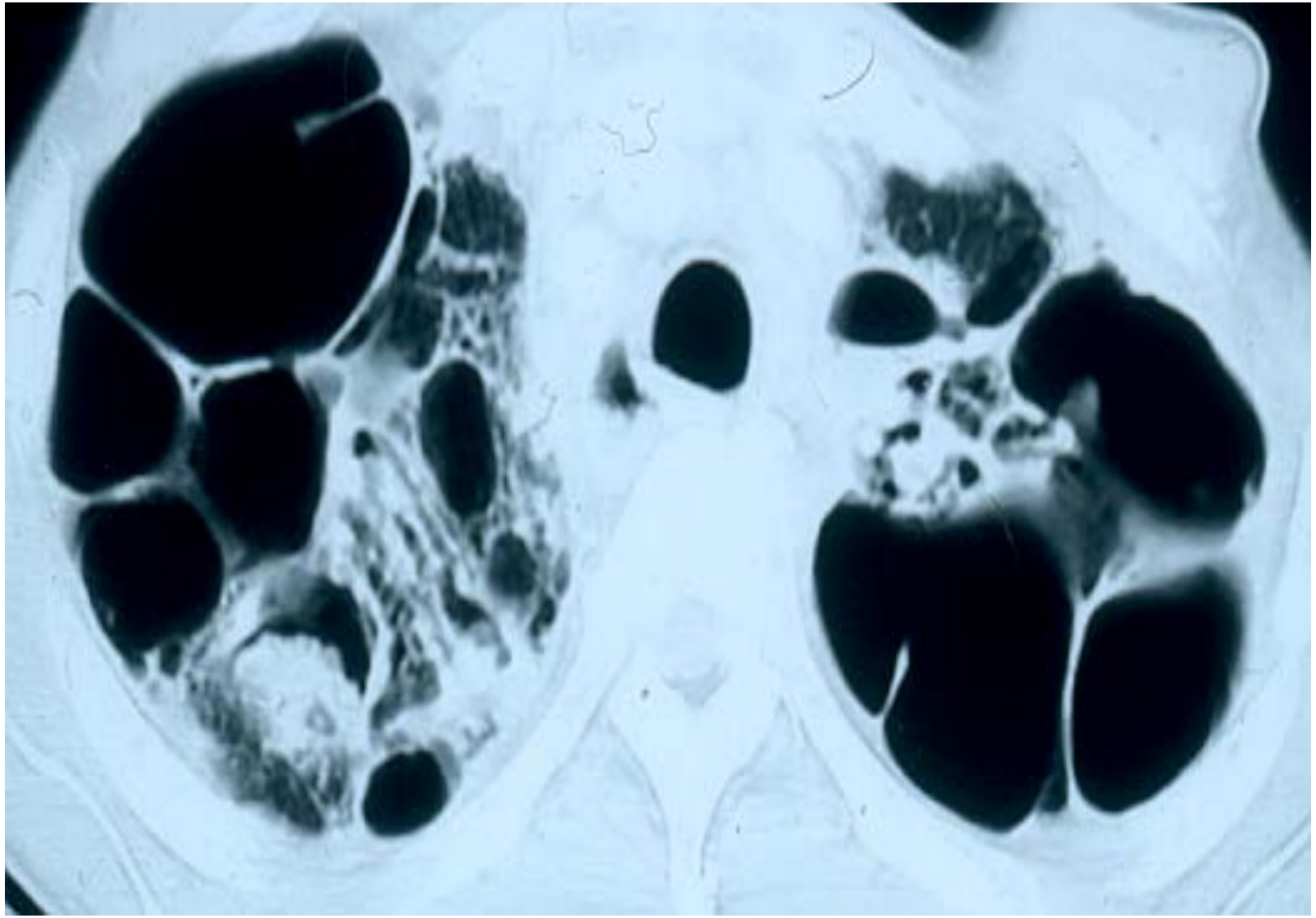


Pulmonary Physiology

- Both restrictive and obstructive defects can be seen
  - Restriction in about half (30-60%)
  - Obstruction (FEV_1) in up to 40%
- DL_{CO} can be decreased
- Hypoxemia is uncommon

Bronchoalveolar lavage (BAL)

- Relatively specific, not sensitive
- Increased CD_4, CD_4/CD_8 ratio
- Little prognostic value
- Not helpful in determining treatment

Tissue biopsy

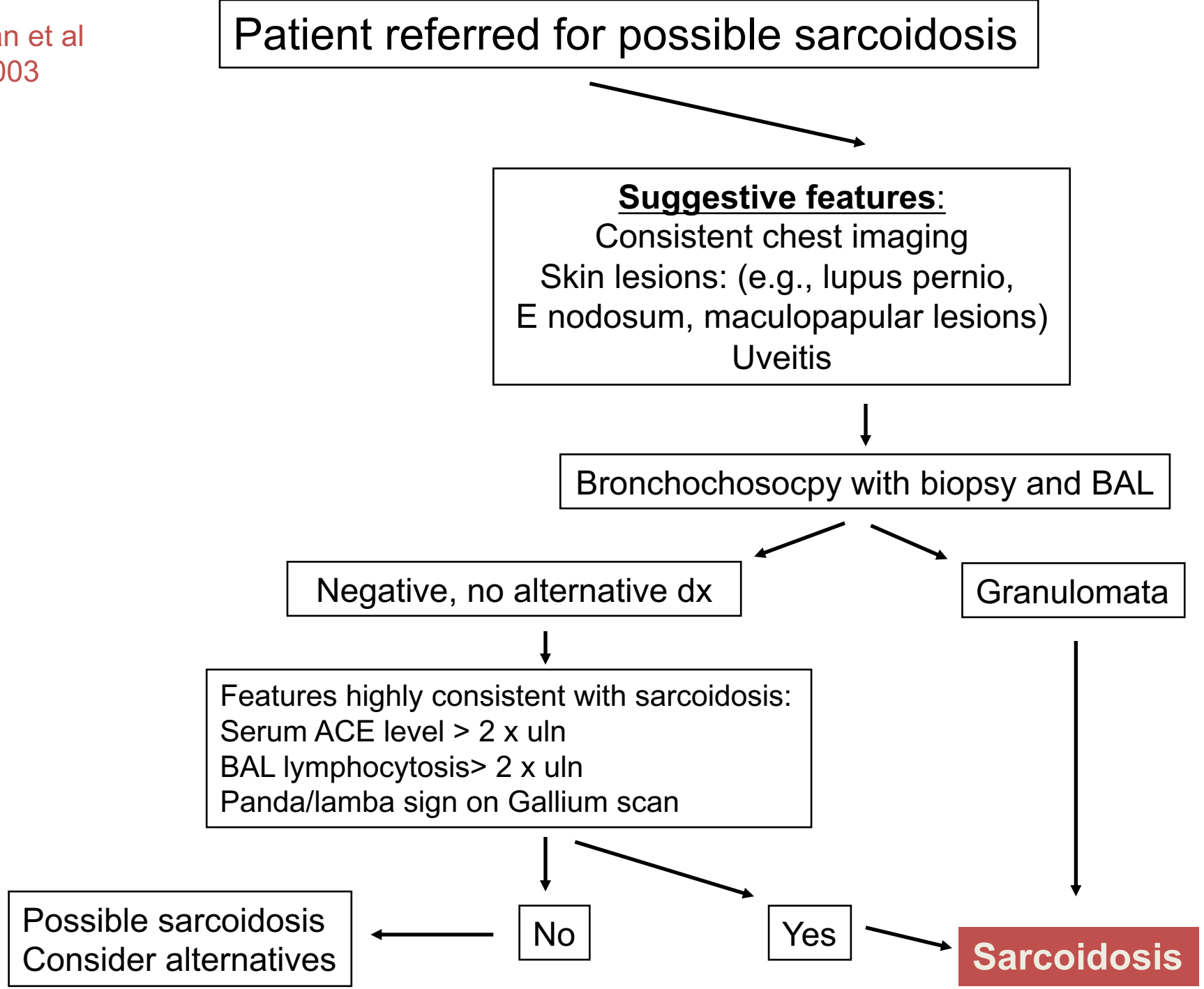
- Bronchoscopy with both endobronchial and transbronchial biopsies can provide a diagnosis in up to 90% of the cases
  - Endo bronchial biopsies
  - TBBx : at least 6-8 or more to ensure good sampling
  - BAL- 180-240 ml cell differential
  - EBUS for LN

- Diagnostic in 75% of those in whom the lung parenchyma is radiographically normal
- The bronchial mucosa will be visually abnormal in about 50% of patients
- Biopsy of erythema nodosum is not useful, as it will not show granulomas

How specific are Noncaseating Granulomas?

- Granulomas ≠ sarcoid
  - Infections (e.g., Tuberculosis)
- Cutaneous noncaseating granulomas can be seen as a result of a variety of reactions
  - Foreign body
- Hepatic granulomas are generally noncaseating, independent of cause

Baughman et al
Lancet 2003



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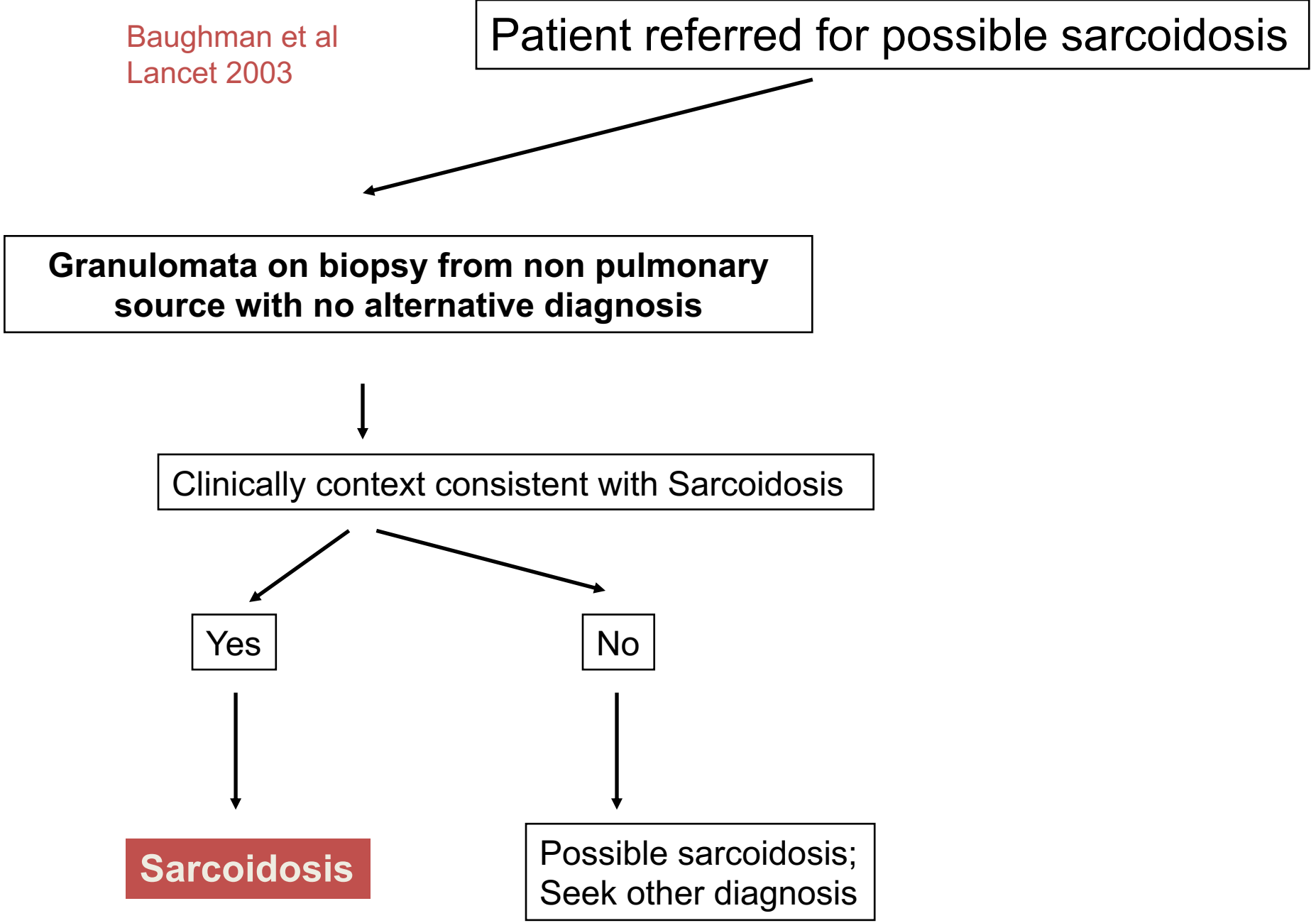


Sarcoidosis

Which statement is correct?

a) BAL demonstrates high CD8/CD4 ratio

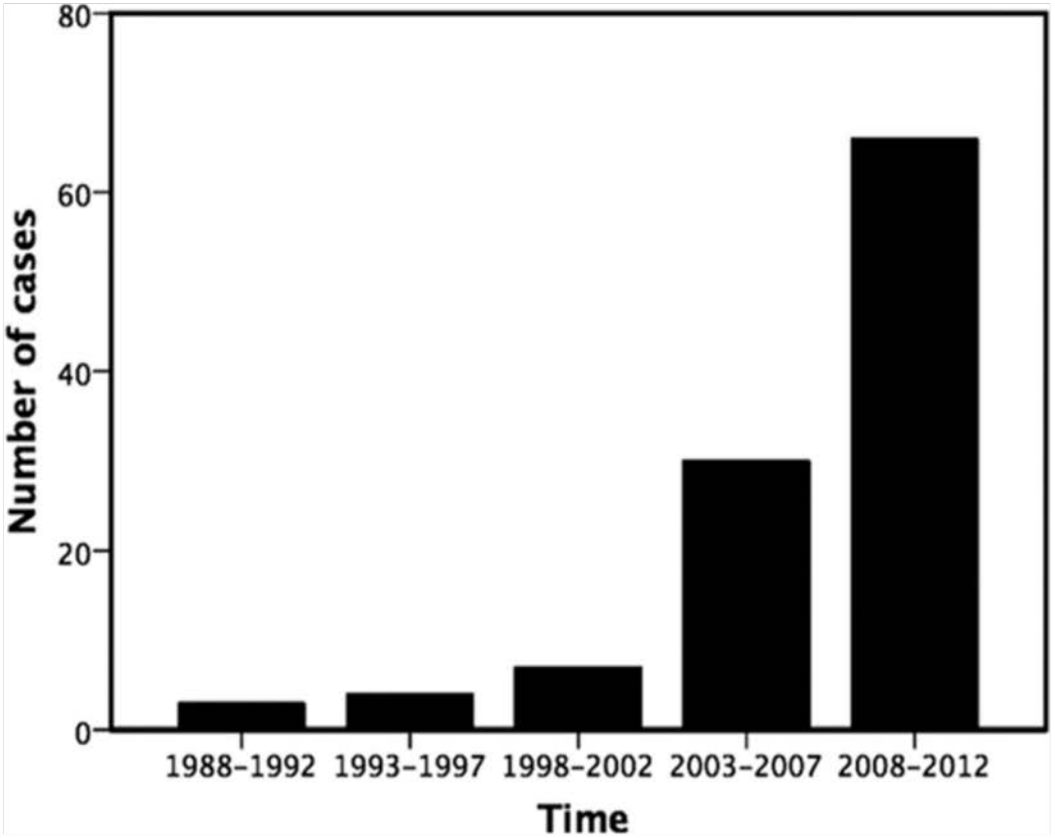
b) Pleural effusions occur in < 5 %

c) BAL cell profiles should direct therapy

d) Elevated serum ACE should prompt treatment with corticosteroids

Extrapulmonary Sarcoidosis

The number of new cases of cardiac sarcoidosis diagnosed in the 5-year periods between 1988 and 2012.



Riina Kandolin et al. Circulation. 2015;131:624-632

American Heart Association.

Consensus criteria to diagnose cardiac sarcoid

*Expert Consensus Recommendations on **Criteria for the Diagnosis of CS***

There are 2 pathways to a diagnosis of Cardiac Sarcoidosis:

1. Histological Diagnosis from Myocardial Tissue
   CS is diagnosed in the presence of non-caseating granuloma on histological examination of myocardial tissue with no alternative cause identified (including negative organismal stains if applicable).
2. Clinical Diagnosis from Invasive and Non-Invasive Studies:
   It is probable* that there is CS if:
   a) There is a histological diagnosis of extra-cardiac sarcoidosis
   and
   b) One or more of following is present
      - Steroid +/- immunosuppressant responsive cardiomyopathy or heart block
      - Unexplained reduced LVEF (<40%)
      - Unexplained sustained (spontaneous or induced) VT
      - Mobitz type II 2nd degree heart block or 3rd degree heart block
      - Patchy uptake on dedicated cardiac PET (in a pattern consistent with CS)
      - Late Gadolinium Enhancement on CMR (in a pattern consistent with CS)
      - Positive gallium uptake (in a pattern consistent with CS)

   and
   c) Other causes for the cardiac manifestation(s) have been reasonably excluded

*In general, 'probable involvement' is considered adequate to establish a clinical diagnosis of CS.[33]

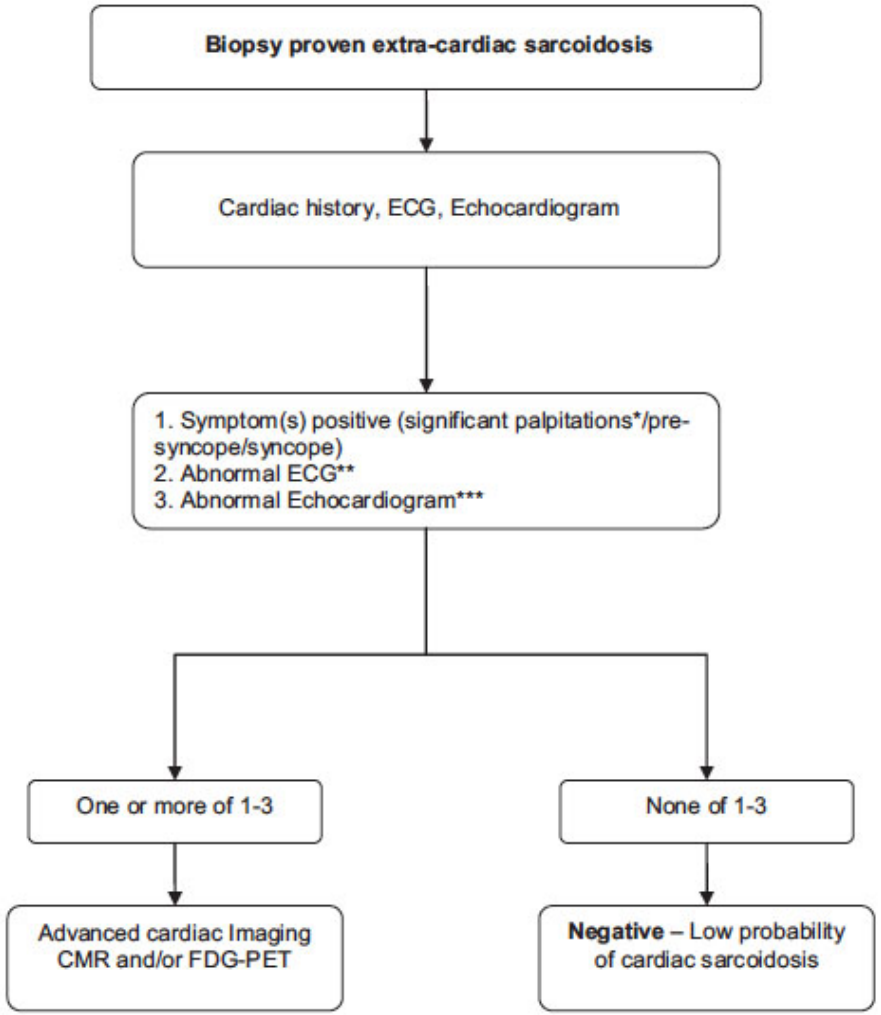
Birnie et al, Heart Rhythm 2014

Consensus criteria to diagnose cardiac sarcoid

Expert Consensus Recommendations on Screening for Cardiac Involvement in Patients With Biopsy-Proven Extracardiac Sarcoidosis	
Class I	1. It **is recommended** that patients with biopsy-proven extracardiac sarcoidosis **should be** asked about unexplained syncope/presyncope/significant palpitations*
	2. It **is recommended** that patients with biopsy-proven extracardiac sarcoidosis **should be** screened for cardiac involvement with a 12-lead electrocardiogram (ECG).
Class IIa	1. Screening for cardiac involvement with an echocardiogram **can be useful** in patients with biopsy-proven extracardiac sarcoidosis.
	2. Advanced cardiac imaging, CMR or FDG-PET, at a center with experience in CS imaging protocols **can be useful** in patients with one or more abnormalities detected on initial screening by symptoms/ECG/echocardiogram.
Class III	1. Advanced cardiac imaging, CMR or FDG-PET, **is not recommended** for patients without abnormalities on initial screening by symptoms/ECG/echocardiogram.
	*Palpitations were defined as "a prominent patient complaint lasting >2 weeks."[25]

Birnie et al, Heart Rhythm 2014

Consensus criteria to diagnose cardiac sarcoid



Birnie et al, Heart Rhythm 2014

Consensus criteria to diagnose cardiac sarcoid

- Palpitations are defined as “prominent patient complaint lasting > 2 weeks ”
- An abnormal ECG is defined as complete left or right bundle branch block and/or presence of unexplained pathological Q waves in 2 or more leads and/or sustained 2nd or 3rd degree AV block and/or sustained or non-sustained VT
- An abnormal echocardiogram defined as regional wall motion abnormalities and/or wall aneurysm and/or basal septum thinning and/or LVEF < 40%

Birnie et al, Heart Rhythm 2014

Cardiac Imaging Diagnosis of Sarcoid: No Gold Standard *Done at Specialized Center

Cardiac FDG-PET

- Prolonged fasting (low glucose)

Different from oncologic PET scans

- Thought to represent inflammation

- Patterns seen :
  - Patchy or focal uptake.
  - Patchy or focal on diffuse uptake.
  - Present in normals, ischemic CHF
  - Normal variants: No uptake, diffuse uptake, free wall uptake

- Sensitivity 79-100%, 89% meta-anal
- Specificity 38-100%, 78% meta-anal

cMRI

- Assess LV and RV function
- Scar versus inflammation
- Cannot be used with AICD

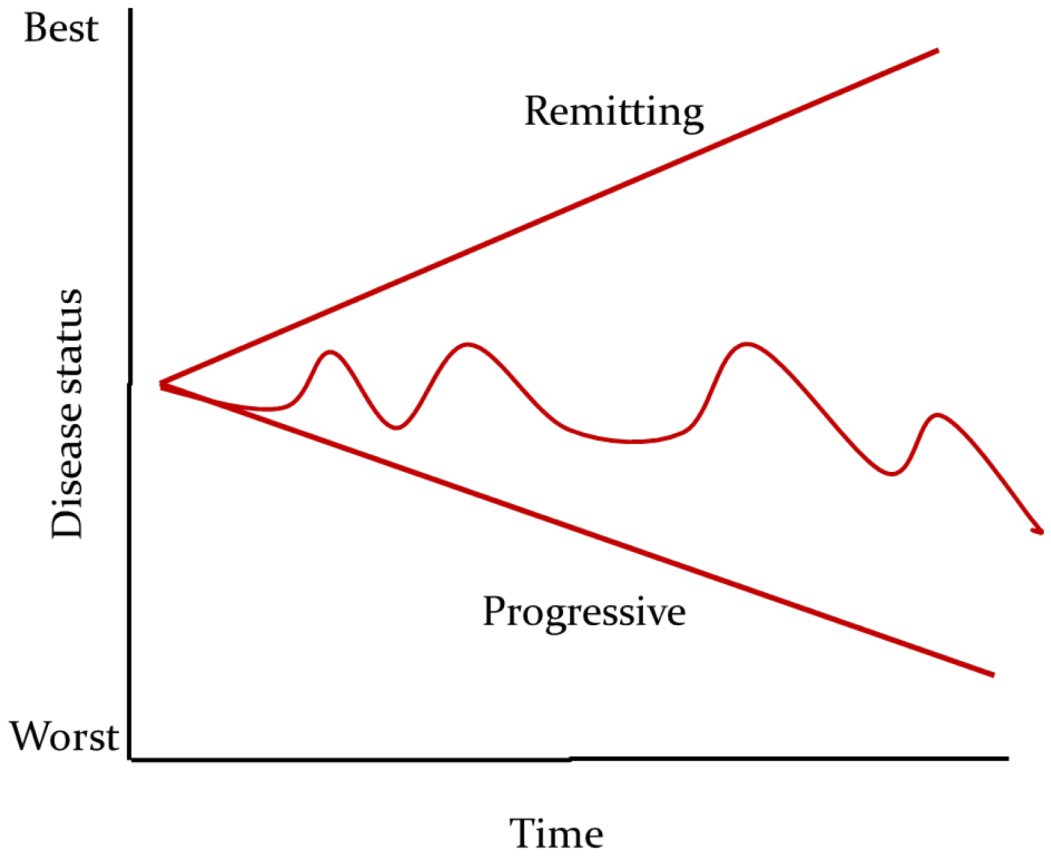
- Patterns seen :
  - Myocardial wall thickening/thinning.
  - Wall motion changes.
  - Increased T2 weighted signal (edema), may correlate with inflammation, not widely available.
  - Delayed hyperenhancement (scar / fibrosis).

- Sensitivity: 76-100%
- Specificity: 78-92%

Biopsy in Cardiac Sarcoidosis

- The disease is patchy
- Even when disease is present, endomyocardial biopsy is often negative
- Difficult to biopsy sites of involvement
- If no diagnosis of sarcoidosis from other organ: Need tissue
- Voltage map guided biopsy by EPS

Disease course



- Enormous variability
- Spontaneous remissions (up to 67%)
- Chronic or progressive (10-30%)
- Mortality (1-4%)

Disease course

Good prognostic signs:

- Löfgren's syndrome
- Radiograph Stage I
- Spontaneous remission
- HLA marker (DQB1*0201)

Poor prognostic signs:

- Lupus pernio; nasal
- Chronic uveitis
- Bone involvement
- Chronic hypercalcemia
- Pulmonary hypertension
- Certain genetic markers
  - Black race
- Late radiographic stage
  - – Honeycomb cysts, traction bronchiectasis, architectural distortion

Spontaneous remissions

- First 2 years
  - 85% of all remissions occur by 2 yrs
  - Remissions unlikely if stage II at 2 yrs (Romer, Danish Med Bull 1982)
- Löfgren's syndrome (> 85%)
- Radiographic stage I (60-85%)
- Radiographic Stage III (< 20%)
- When spontaneous remissions occur, recurrence is rare

Outcome by radiographic stage

5 years after diagnosis

Stage	#	asymptomatic (%)
I	(n=32)	97%
II	(n=40)	58%
III	(n=64)	25%

Scadding, Br Med J 1961:2;1165

Sarcoidosis

Q6. Which statement is correct?

a) Persistent infiltrates ≥ 2 years predicts spontaneous resolution in < 20%

b) Stage II or III sarcoidosis: chest X-rays have a predilection for the bases

c) Stage III sarcoidosis resolves spontaneously in 30-40% of patients.

d) Ga-67 scans are useful to stage sarcoidosis.

Treatment

- Goal is to control symptoms and critical organ involvement, and to prevent permanent organ damage
- Not all patients require therapy
  - Half never get or need treated
- Spontaneous remissions occur
- Critical organ involvement
  - CNS, Heart, Eye
- Hypercalcemia, hypercalciuria
  - Nephrolithiasis

Evidence-Based Review of Utility of Corticosteroids for Sarcoidosis

- Patients with pulmonary radiographic stage I disease, with or without erythema nodosum, and with normal lung function (VC, DLCO) **do not require** treatment with corticosteroids
  - Grade A

- Symptomatic patients with stage II-III pulmonary lesions and impaired lung function respond to treatment with oral corticosteroids
  - Grade A

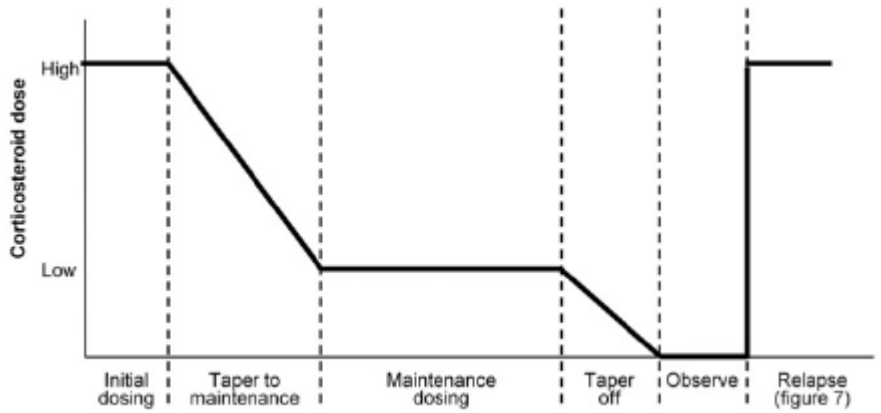
Baughman RP, Evidence-based approach to the treatment of sarcoidosis. In: Gibson PG, et al eds. Evidence-based respiratory medicine. 2005: 491-508

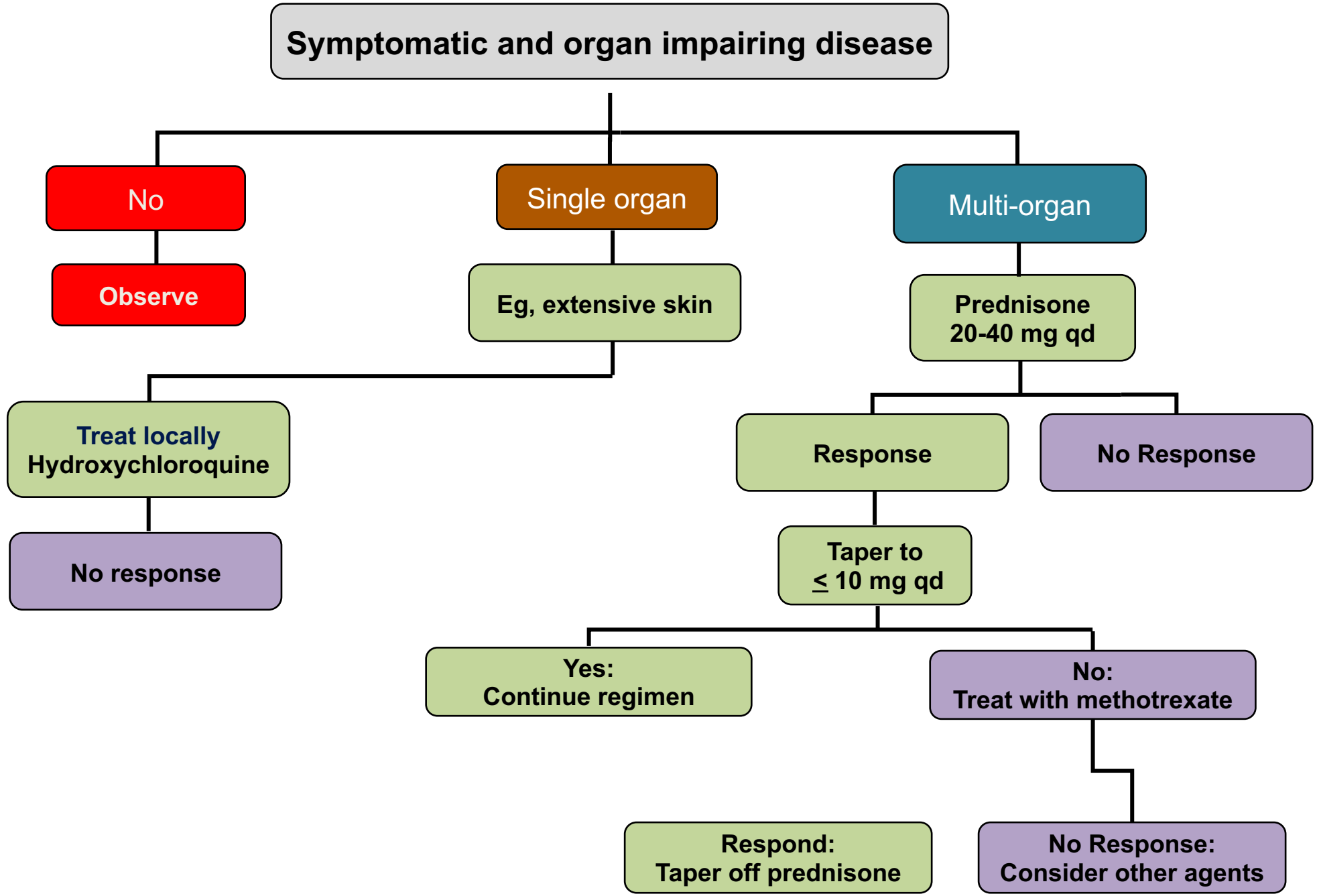
Corticosteroids should be used to treat which of the following patients with sarcoidosis?

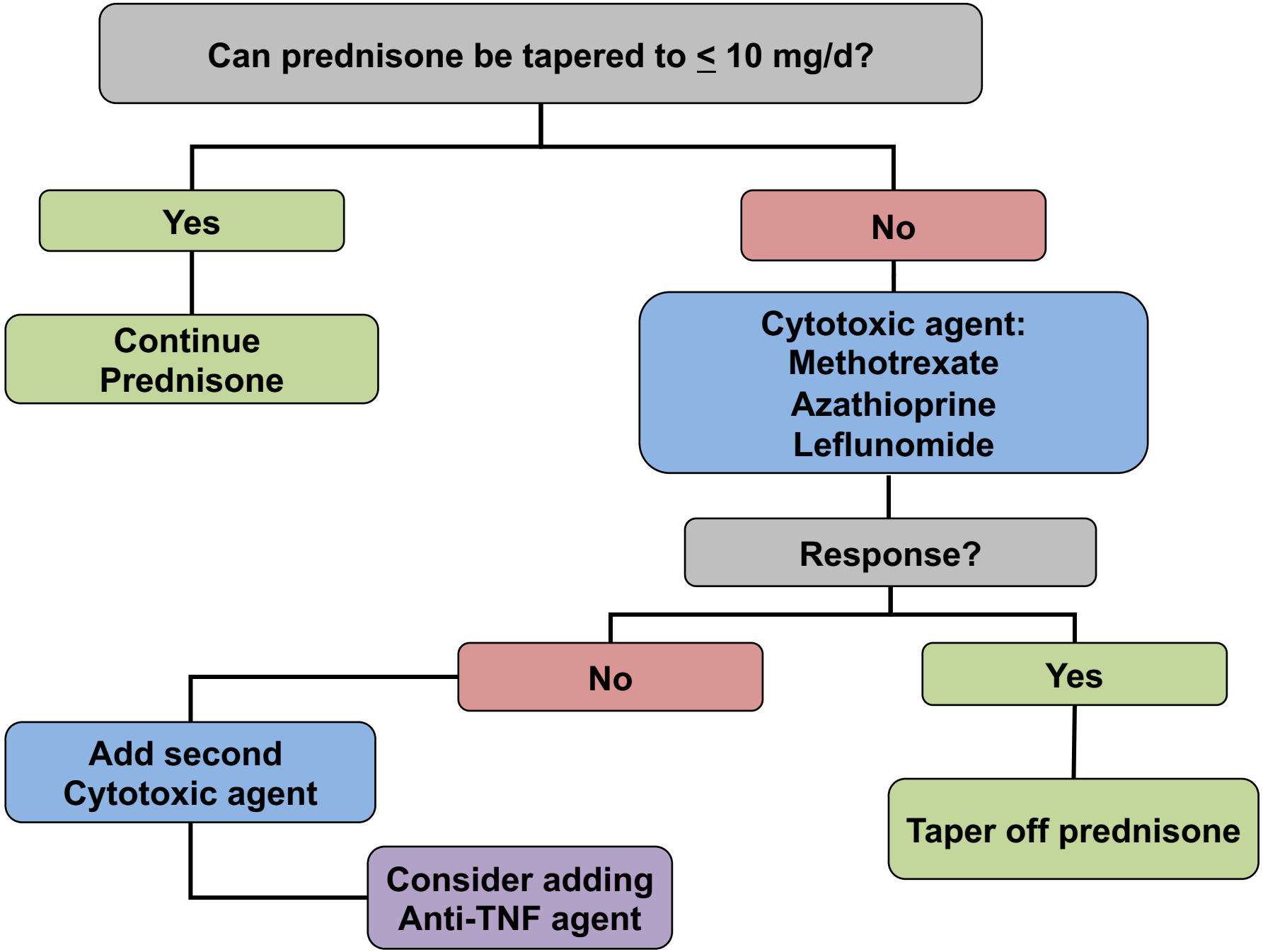
1. All newly diagnosed patients with pulmonary sarcoidosis
2. Patients with progressive organ impairment and symptoms affecting quality of life who have never been treated with corticosteroids before
3. Patients with fibrotic pulmonary sarcoidosis who have been on corticosteroids with no improvement in lung function- a higher dose is just needed

Corticosteroid therapy

- Usually starting dose 20-40mg daily
- Improved CXR, symptoms and spirometry at 3-24 months, but limited data > 2 years
- Relapses common (20-70%)
- Significant side effects




Symptomatic and organ impairing disease
No
Observe
Single organ
Eg, extensive skin
Multi-organ
Prednisone
20-40 mg qd
Treat locally
Hydroxychloroquine
No response
Response
No Response
Taper to
≤ 10 mg qd
Yes:
Continue regimen
No:
Treat with methotrexate
Respond:
Taper off prednisone
No Response:
Consider other agents


Can prednisone be tapered to ≤ 10 mg/d?
Yes
No
Continue Prednisone
Cytotoxic agent:
Methotrexate
Azathioprine
Leflunomide
Response?
No
Yes
Add second Cytotoxic agent
Taper off prednisone
Consider adding Anti-TNF agent

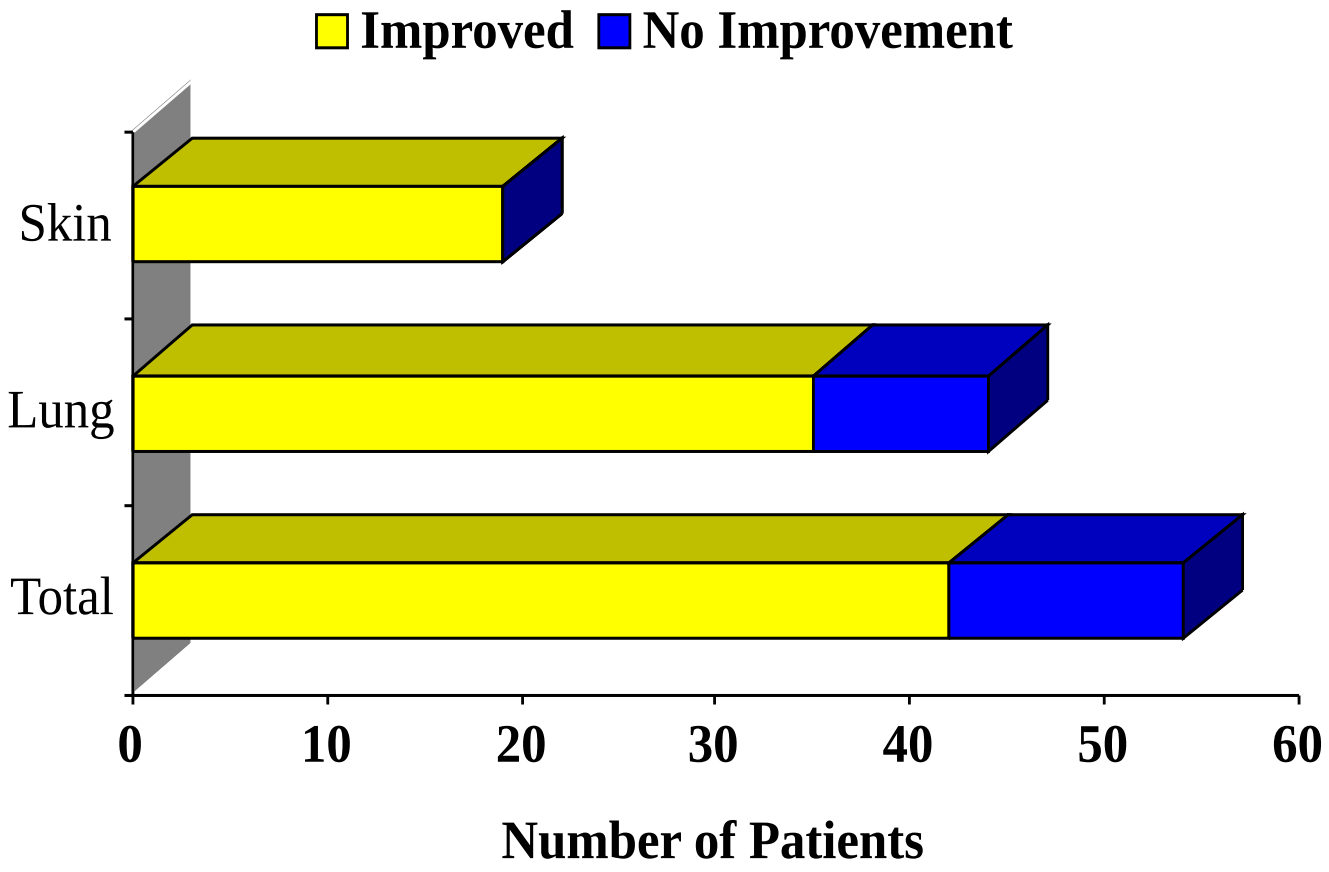
Consider additional therapy when…

- Persistent required of high-dose steroids
- Unacceptable adverse or risk for adverse steroid effects
- Disease progression despite steroids

  Consider causes of steroid failure:

  - Inadequate dose or duration
  - Steroid resistance
  - Non-adherence
  - Irreversible disease (fibrosis)
  - Complication of disease (e.g., PAH)

Treatment with Methotrexate for >2 Years: Response to Methotrexate



Lower, Baughman. Arch Intern Med 1995; 155: 846-851

Who to treat with anti-TNF therapy

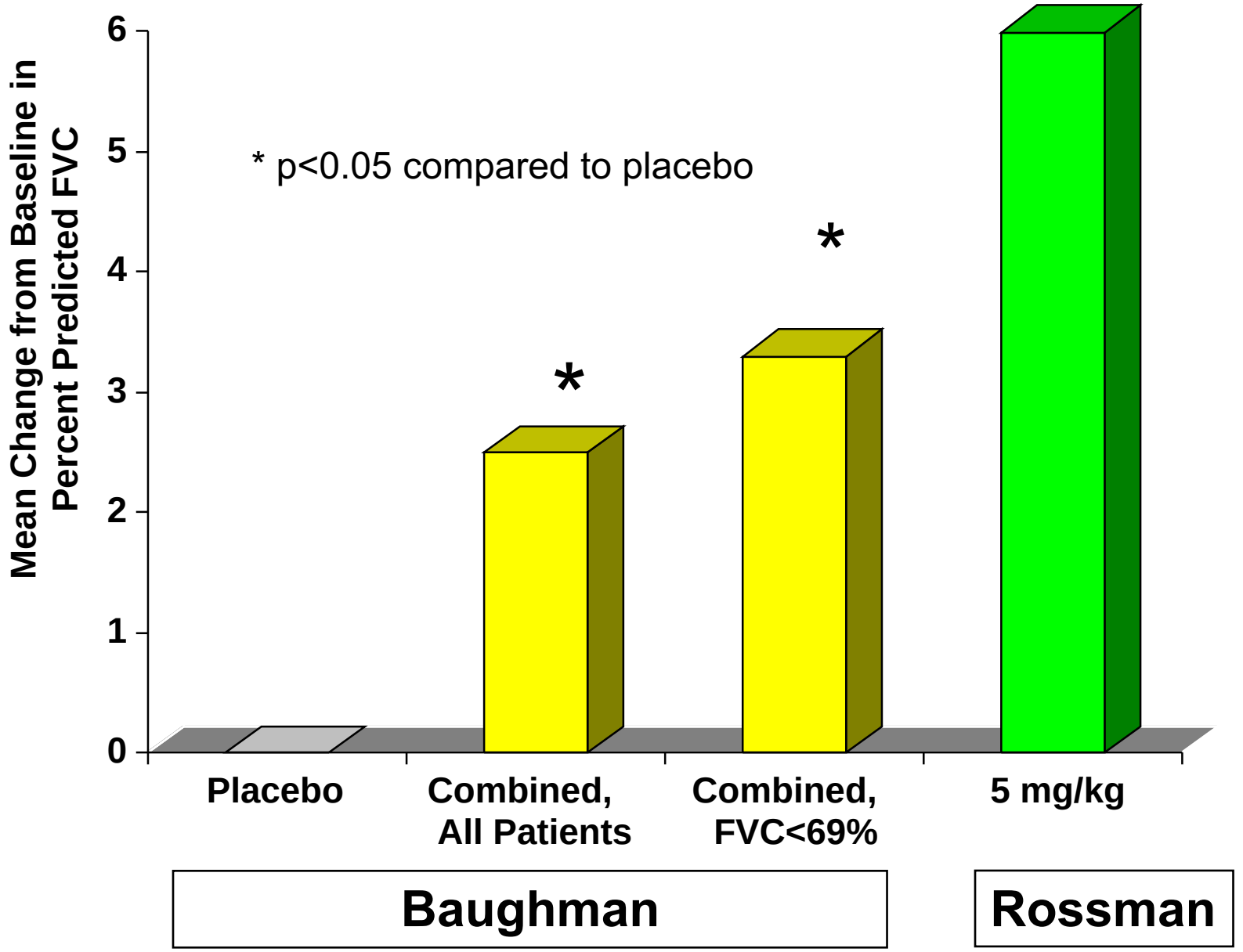
Improved response to drug

- FVC<70%
- Dyspnea ≥ 1
- Disease > 2 years
- Significant extrapulmonary disease
  - Lupus pernio
  - CNS

Possible predictors

- Elevated CRP
- TNF -308 polymorphism

Adapted from Baughman RP et Sarcoidosis 2008; 25: 76-92.



Baughman RP, et al. Am J Respir Crit Care Med 2006; 174:795-802
Rossman MD, et al Sarcoidosis Vasc Diffuse Lung Dis 2006; 23:201-208.

Additional therapy

	Usual dose	Main contraindications	Main side-effects	Monitoring needed	Comments
Cytotoxic drugs†					
Methotrexate	10–20 mg once per week orally or intramuscularly. Folate supplementation to prevent gastrointestinal toxic effects	Liver and severe renal failure; severe respiratory failure; alcohol abuse; pregnant or lactating women	Gastointestinal effects, neutropenia, liver and renal toxicity, interstitial pneumonitis, alopecia	Complete blood count liver function tests‡, and renal function every 4–12 weeks	Preferred second-line therapy for corticosteroid-resistant sarcoidosis or as a corticosteroid-sparing drug.[108] Delayed effect (up to 6 months)
Azathioprine	50–200 mg per day§	Lactating women; association with allopurinol	Gastrointestinal effects, neutropenia§, liver toxicity, photosensitivity, skin carcinoma	Complete blood count and liver function tests every 4–12 weeks; consider thiopurine S-methyltransferase genotyping§	Similar comments as methotrexate but fewer data are available.[109] can be used in men and women who want to have children, and used during pregnancy
Leflunomide	10–20 mg per day	Liver and renal failure; bone marrow dysfunction; pregnant or lactating women	Gastrointestinal effects, diarrhoea, liver toxicity, neutropenia, neuropathy, hypertension	Complete blood count and renal function tests every 4–12 weeks	Insufficient data: might be useful in patients not responding well or who are intolerant to methotrexate or as a corticosteroid-sparing drug.[110] Combination treatment with methotrexate is possible, fewer pulmonary toxic effects than with methotrexate
Cyclophosphamide	50–150 mg per day orally; or 500–1200 mg every 3–4 weeks intravenous pulse	Severe renal failure; bone marrow dysfunction; pregnant or lactating women	Neutropenia, gastrointestinal effects, haemorrhagic cystitis, possible irreversible sterility in both men and women, increased risk of malignancy, mostly bladder cancer	Complete blood count liver function tests and renal function tests every 2–4 weeks	Potentially serious side-effects that restrict its use; might be useful for refractory CNS[83] and cardiac involvement; rapid effect
Mycophenolate mofetil	500–3000 mg per day	Pregnant (insufficient data on teratogenicity) or lactating women	Neutropenia, gastrointestinal effects, diarrhoea, photosensitivity, skin carcinoma	Complete blood count and liver function tests every 4–12 weeks	Insufficient data, might be useful as a corticosteroid-sparing drug.[111] Fewer bone marrow toxic effects and infections than other immunosuppressant drugs

Valeyre D, Lancet 2014; 383: 1155–67

Additional therapy

	Usual dose	Main contraindications	Main side-effects	Monitoring needed	Comments
Cytokine modulators					
Pentoxifylline	400–2000 mg per day	Acute myocardial infarction	Nausea, diarrhoea, gastrointestinal effects	None	Insufficient and conflicting data; might be useful as a corticosteroid-sparing drug.[112] At the dose used, gastrointestinal toxic effects are very restraining[112,113]
Thalidomide	50–200 mg per day	Men refusing to wear a condom and women of childbearing age not using contraception; pregnant or lactating women; blood donation	Highly teratogenic; sleepiness, constipation, neuropathy, venous thrombosis, unexplained dyspnoea, bradycardia	Pregnancy testing every month and electromyography every 6–12 weeks	Potentially serious side-effects; useful for severe skin sarcoidosis, particularly lupus pernio; not effective for pulmonary involvement;[114] rapid effect; as early as 1 month
TNFα antagonist	Infliximab 3–5 mg per kg intravenously at week 0, 2, 6, then every 4–8 weeks¶	Pregnant (insufficient data on teratogenicity) or lactating women; New York Heart Association class 3 or 4 heart failure; tuberculosis or other infection	Allergic reaction. Increased risk of serious infections, mostly tuberculosis, and increased risk of cancer	Systematic assessment for tuberculosis before treatment	Useful for chronic and refractory sarcoidosis particularly in lupus pernio, eye, and CNS disease.[115] Efficacy for pulmonary disease,[31] but whether improvement is clinically relevant is debated. Rapid effect; as early as 2 weeks. Possible loss of response due to anti-infliximab antibody formation
Antimicrobial drugs					
Antimalarial drugs	Hydroxychloroquine 200–400 mg/day‖	Retinopathy, breastfeeding	Gastrointestinal effects, rash, retinopathy, neuromyopathy	Complete eye examination every 6–12 months	Inhibit antigen presentation by reducing degradation capacity of lysosomes; useful for moderate skin disease; hypocalcaemia, and fatigue, as well as a corticosteroid-sparing drug;[116] delayed effect up to 6 months
Tetracycline	Minocycline 200 mg/day, doxycycline 200 mg/day	Pregnancy and breastfeeding, liver failure, sun exposure	Gastrointestinal effects, anaemia, skin photosensitivity	None	Few data: might be useful for moderate skin disease

Valeyre D, Lancet 2014; 383: 1155–67

Lung transplantation…

- Who to consider
  - Severe, progressive disease (physiology)
  - Fibrotic disease (HRCT)
  - Failed aggressive medical treatment
- What to expect
  - Median survival 3.6 years
  - Recurrent disease in the allograft

Potential New Therapies for Sarcoidosis

Anti-cytokine treatments

Anti-TNF

- Adalimumab
- Golibmumab

Anti-other cytokines

- Anti-IL-12

Antibiotics

- Anti-mycobacterial therapy
- CLEAR

Rituximab

Statins

Anti-oxidants

Vasoactive inhaled peptide (VIP)

Treatment of PH

Phosphodiesterase inhibitors

Inhaled iloprost

Endothelin blockade

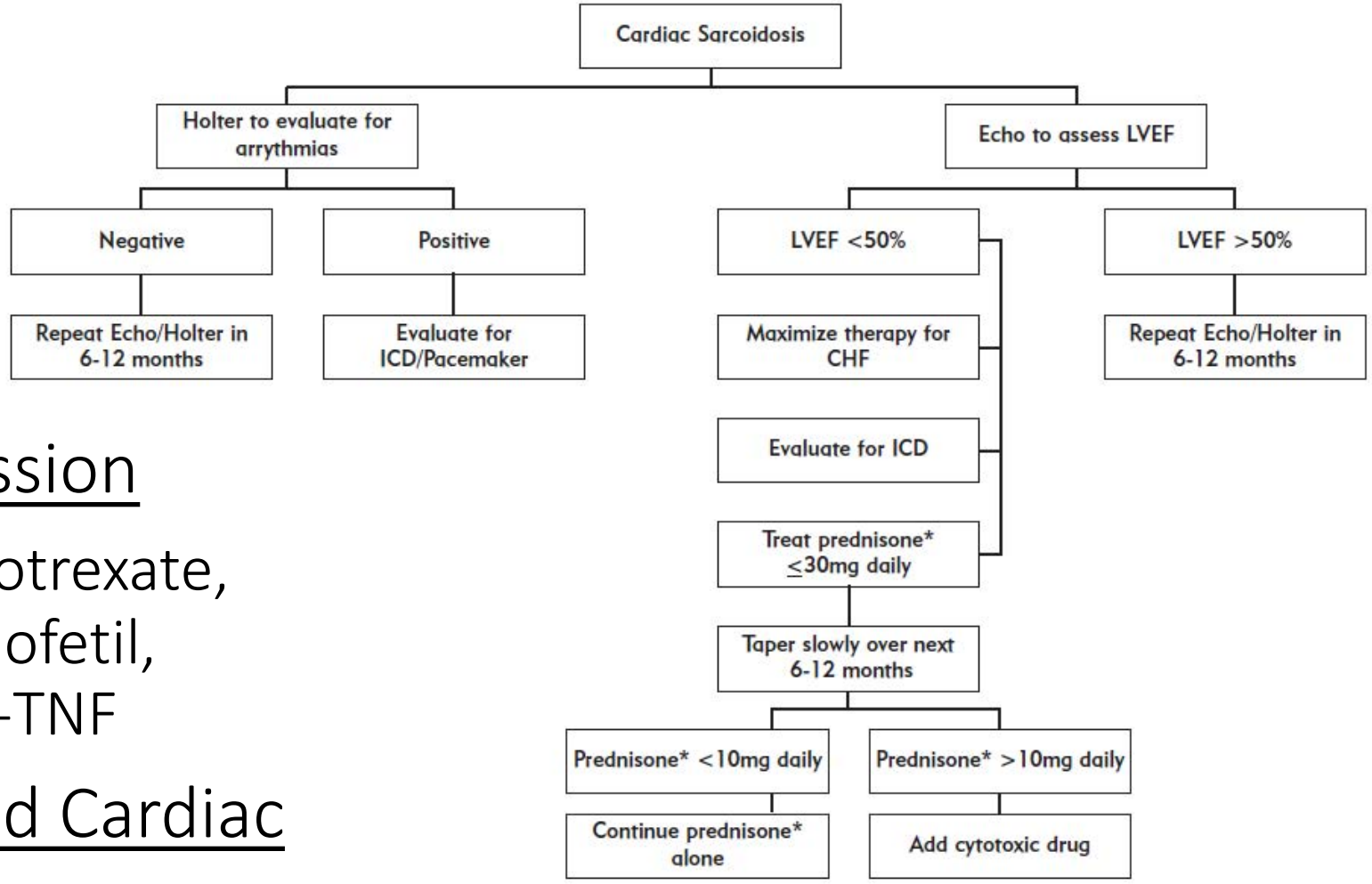
- Bosentan
- Ambisentan

Treatment of fatigue

d-MPH and armodafinil

Exercise programs

Management : cardiac sarcoid



Immunosuppression

Prednisone, Methotrexate, Mycophenolate Mofetil, Azathioprine, Anti-TNF

Heart Failure and Cardiac medications

Sarcoidosis

- The symptoms are often enigmatic; the diagnosis should be considered in all patients with multi-system symptoms of unclear etiology

- Diagnosis is one of exclusion. Serologic, radiographic, and bronchoscopic studies may be supportive but are never alone diagnostic. Except in specifics clinical scenarios, non-caseating epithelioid granulomas must be observed on a biopsy specimen

- Multiple organs are often involved; cardiac, ophthalmic, dermatologic, and neurologic evaluation should be performed

Sarcoidosis

- Treatment based on symptoms and severity of organ involvement
  - Not all patients will require therapy
- At least half of patients treated will require two years or less of therapy
- Wellness recommendations: Sleep, Diet, Exercise
- Prednisone can cause as much disability as the disease, and secondary, steroid sparing agents may reduce toxicity from therapy
- Failure to respond to therapy can be due to secondary complications
  - Pulmonary hypertension