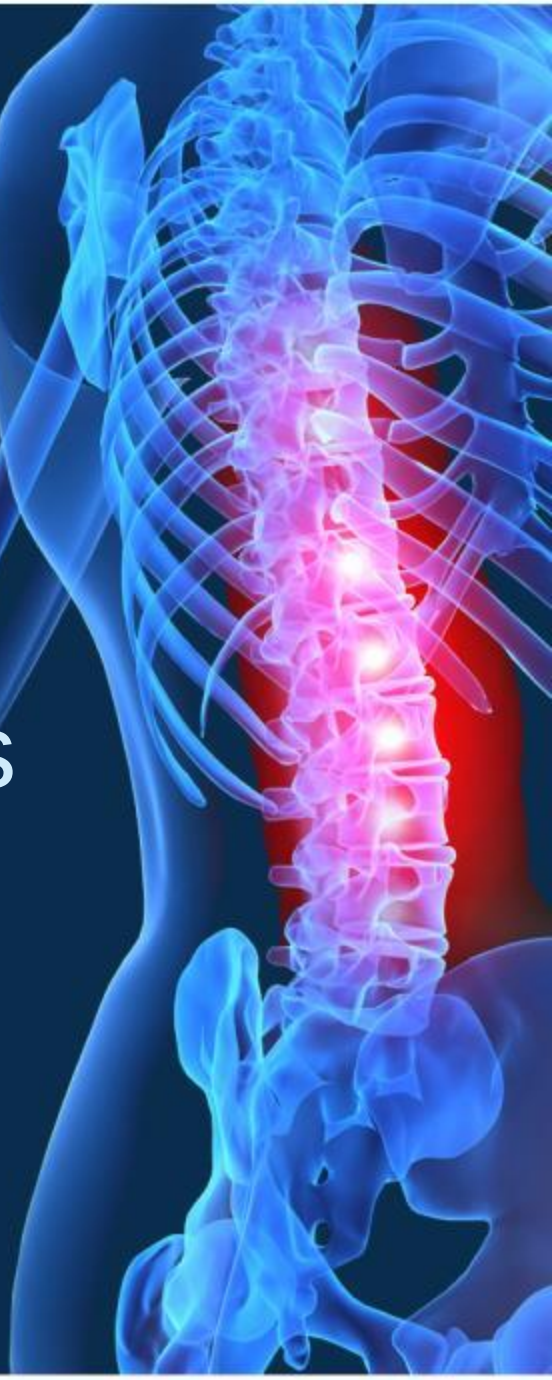
Annual Rheumatology & Therapeutics Review for Organizations & Societies



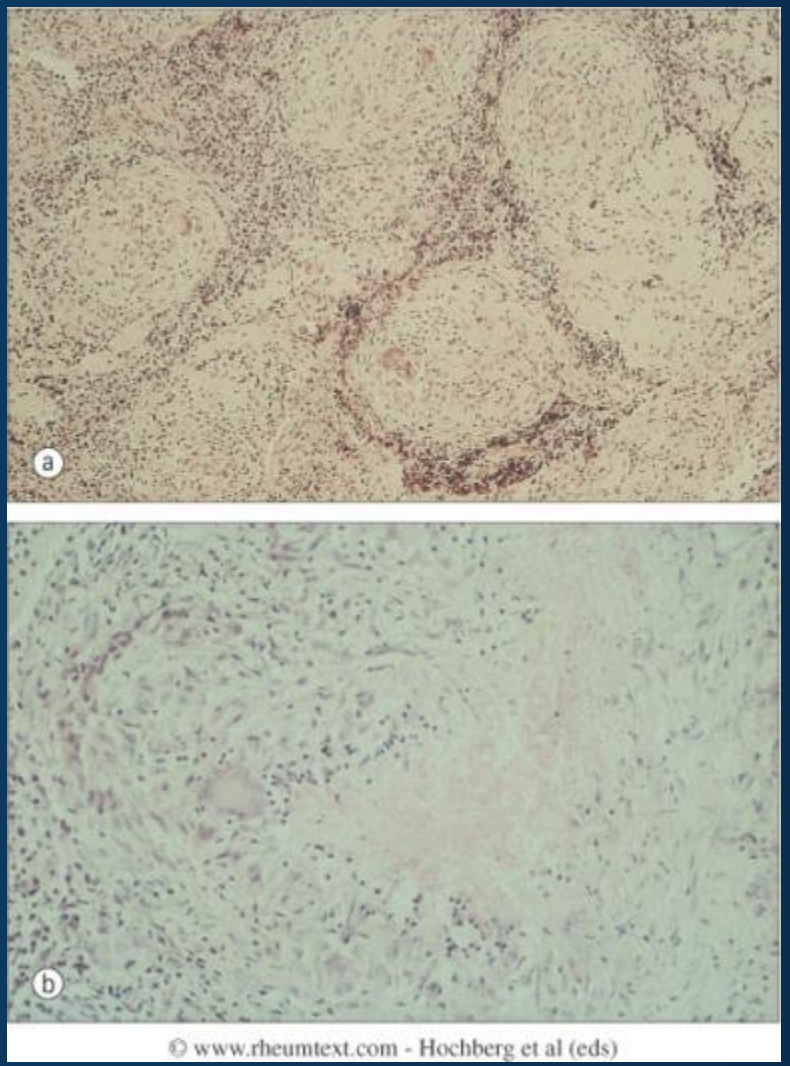
Rheumatic Manifestations of Sarcoidosis

Learning Objectives

- List the sarcoidosis manifestations which may mimic other rheumatic diseases.
- Recognize the acute arthritic presentation of sarcoidosis and discuss its prognosis.
- Identify the characteristic features of sarcoid uveitis that separates it from uveitis associated with spondyloarthropathies.
- Recognize the neurologic manifestations of sarcoidosis.
- Discuss the therapy and prognosis of extrapulmonary manifestations of sarcoidosis

Sarcoidosis

- Disease of unknown etiology.
- Characterized by noncaseating granulomas in two or more organs.
- Other causes of granulomas are excluded.



Am J Respir Crit Care Med 160: 736, 1999

Sarcoidosis: Epidemiology

- Age
  - Age 10-40 yrs: 70-90% of cases
  - All ages can be affected
- Sex
  - Females more than males (2:1)
- Race
  - U.S. incidence 3x higher for AA than whites with lifetime risk 2.4% for AA and 0.85% for whites.
- Familial clustering (genetics): 5-19%
- Seasonal clustering (April-June)-infectious causes
- Occupational clustering- environmental exposures

Hamzeh N. Med Clin N Am 95: 1223, 2011

Clinical Manifestations

- Onset of sarcoidosis
  - Acute sarcoidosis (Lofgren's): 1-20%
  - Subacute/chronic: 80%
    - Pulmonary sx onset: 70%
    - Extrapulmonary onset: 30%

Up to 50% of patients present initially with extrapulmonary sxs

Manifestation	Presenting	Cumulative
Lung	50%	95%
Constitutional	25	33-70
Adenopathy	10-20	40
Bone/Joint	1-14	4-38
Eye	5	10-20
Skin/EN	3/20-30	15-30

- Organ involvement defined early in disease. Only 23% recruit additional organ involvement during the first 2 years of followup.

Baughman RP, et al. Am J Rep Crit Care Med 164:1885, 2001

Clinical Manifestations

Manifestation	Presenting	Cumulative
Liver/spleen*	4%	5-20%
Neuro	1	5-10
Cardiac	1	5-10
Muscle*	1	1-5
ENT/Salivary	1	6
BM/Calcium	<1	10

*On biopsy 50-80% have muscle and liver involvement
Baughman RP, et al. Am J Rep Crit Care Med 164:1885, 2001

Sarcoid Manifestations Which May Present to or Be Referred to the Rheumatologist

- Musculoskeletal
  - Articular
    - Acute
    - Chronic
  - Osseous
  - Periarticular/dactylitis
  - Myopathy
- Uveitis
- Neurologic
- Other
  - FUO
  - Vasculitis
  - Upper respiratory tract: sinus, parotid
  - Lupus pernio

West SG. Sarcoidosis. In Hochberg MC et al (eds): *Rheumatology* (6th ed). Philadelphia, Elsevier, 2015.

Case #1

- A 38yo white man is referred for a one week history of acute bilateral ankle arthritis that interferes with ambulation. Patient denies fever, cough, DOE, rash, diarrhea, travel outside of Montana, or recent sexual or sick contacts.
- Physical examination including vital signs is normal except for bilateral ankle swelling, tenderness, erythema, and warmth.
- Laboratory tests done this week show normal CBC except Hct 37%, normal CMP except alkaline phos 136 U/L, and normal U/A. ESR is 48 mm/hr. RF is pending.
- Radiographs of ankles show STS.

Question

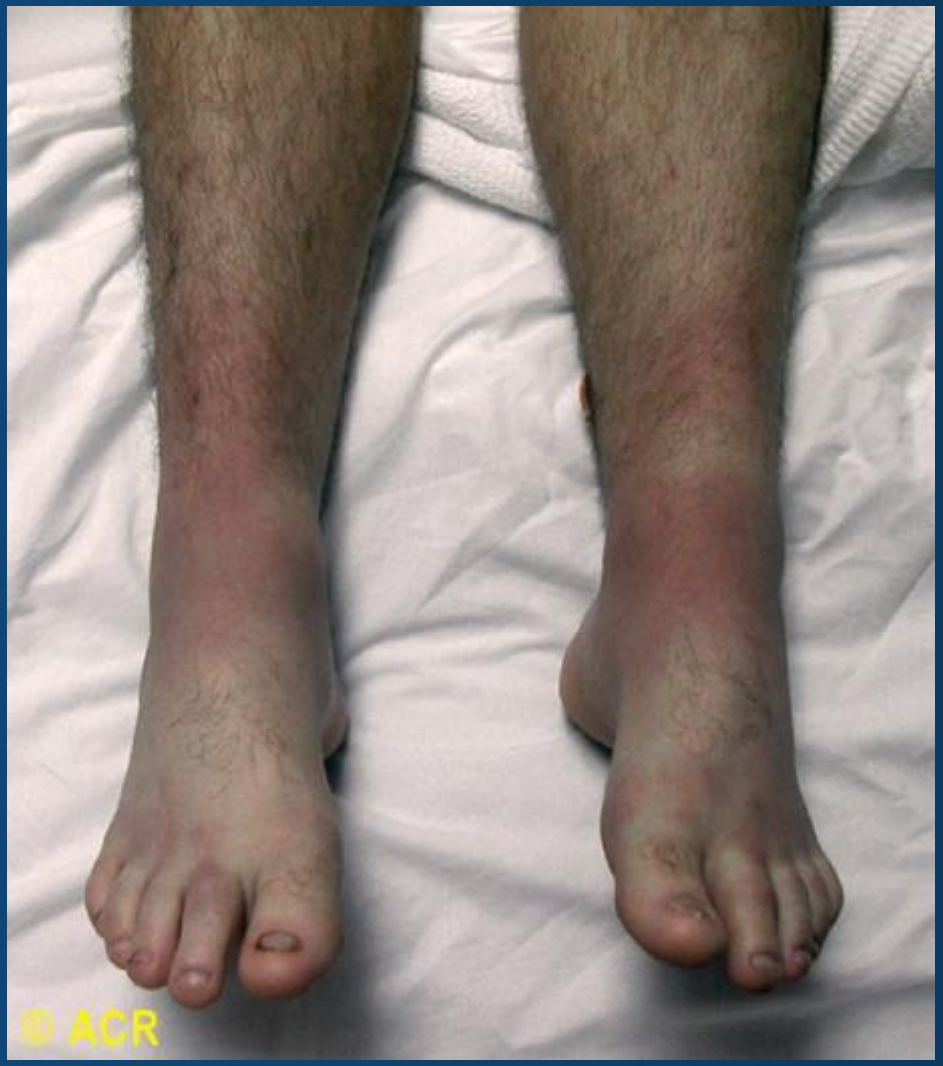
- Which one of the following tests would be most helpful in establishing a diagnosis?
  A. Chest radiograph
  B. Urethral culture for Chlamydia
  C. Aspiration of ankle joint with synovial fluid analysis
  D. Serum angiotensin converting enzyme level
  E. Coccidioides antibody titers

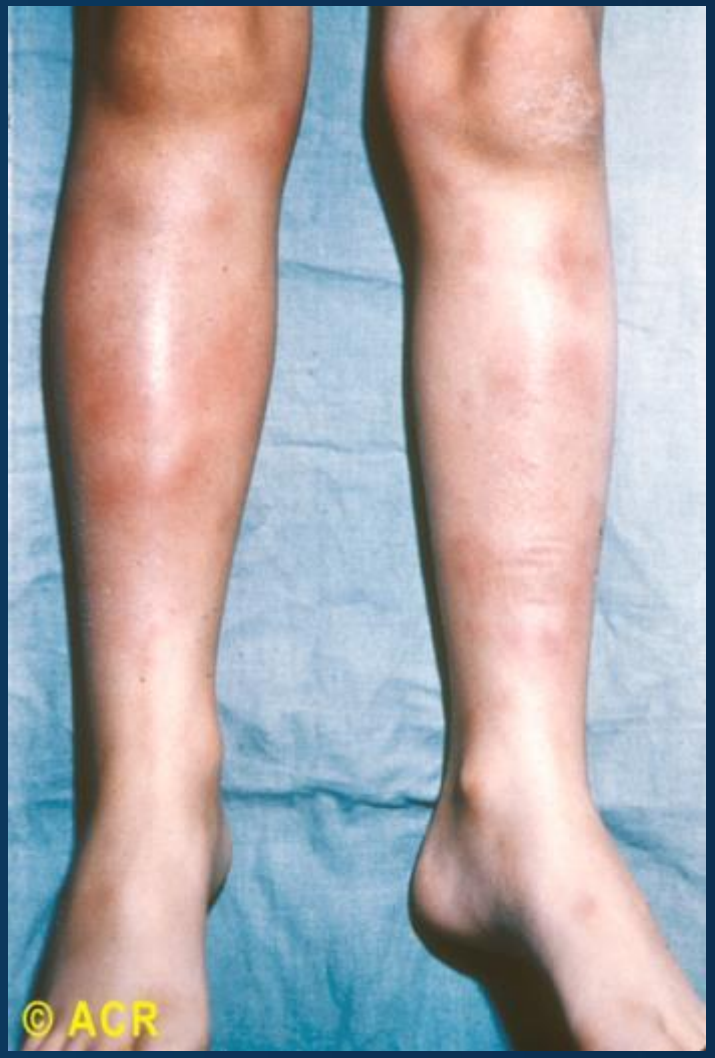
Musculoskeletal Sarcoid

- Joint involvement (4-38%)
  - Acute polyarthritis/periarthritis (20% of presentations)
    - May be migratory, intermittent, or additive
    - Can precede other manifestations by months but usually not
    - Involves ankles and knees most commonly
      - Mimics gout or infection if only 1-2 joints involved.
  - Lofgren's syndrome (70%): poly/periarthritis with bilateral hilar adenopathy(90%), E. nodosum(50-75%), fever, acute uveitis
    - Normal serum ACE level 70-85%
    - Joint pain resolves in weeks to months (avg 3 months): >70%
    - Up to 10-30% have several recurrences or persistent arthritis especially if have elevated ACE level. Synovial bx does not show granulomas. Synovial fluid hard to get.
    - Need to R/O acute histoplasmosis

Mana J,et al. Am J Med 107:240, 1999
Grunewald J et al. Am J Respir Crit Care Med 175: 40, 2007

Lofgren's Syndrome

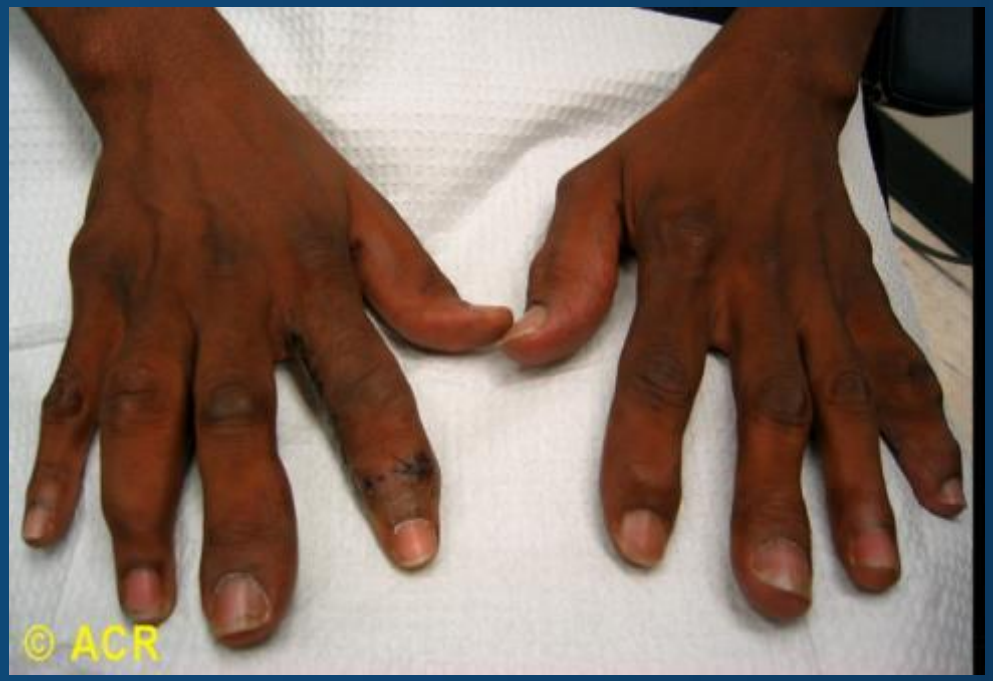




Musculoskeletal Sarcoid

- Joint involvement
  - Chronic arthritis (1-4%)
    - Most common form is a nondestructive, nondeforming oligo>monoarthritis involving knee, shoulder, wrist, ankle, and/or small joints of hands and feet. Mimics psoriatic arthritis, reactive arthritis, or chronic infection
      - Polyarthritis, costochondritis, and sacroiliitis are rare.
    - Slower onset and more common in AA pts
    - Associated with more extensive sarcoidosis, parenchymal lung involvement, and elevated ACE level.
    - SF mildly inflammatory with mononuclear predominance, xrays show STS without destruction, and synovial bx show granulomatous inflammation.
- Tenosynovitis (5-13%)
  - Finger dactylitis: may mimic psoriatic arthritis
  - Wrist, ankle, patella, or Achilles tendons

Zisman DA,et al. Semin Resp Crit Care Med 23:555, 2002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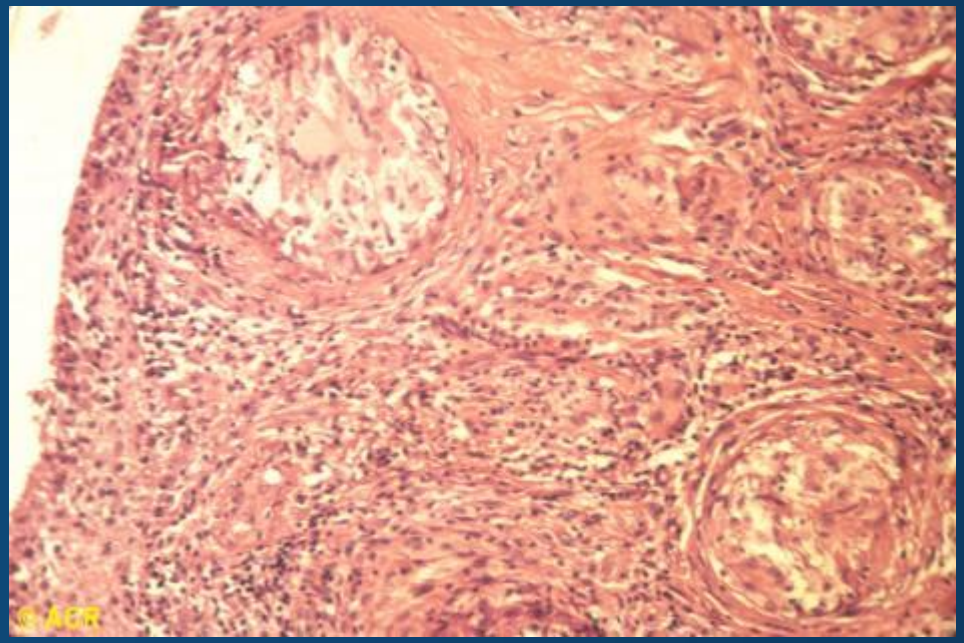
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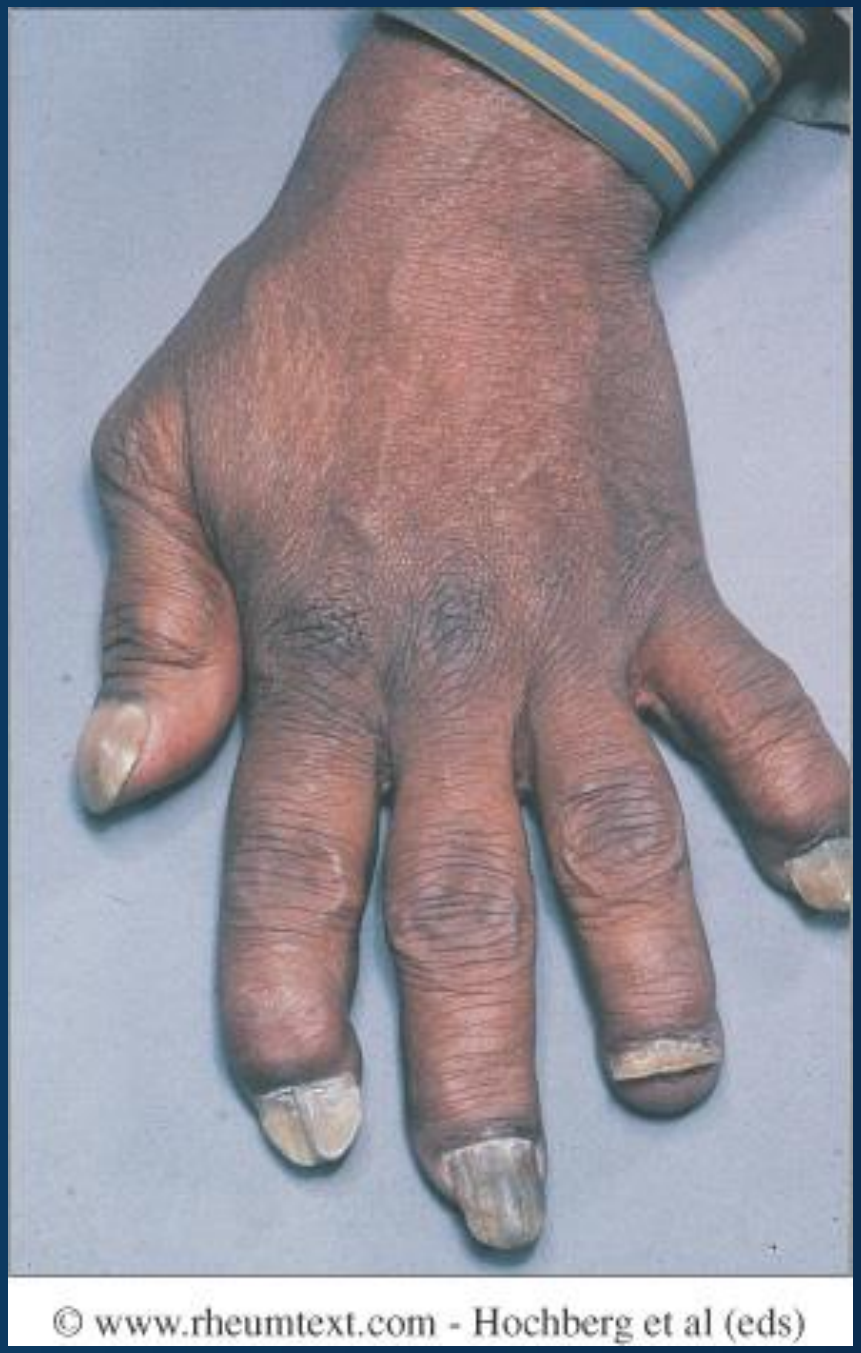
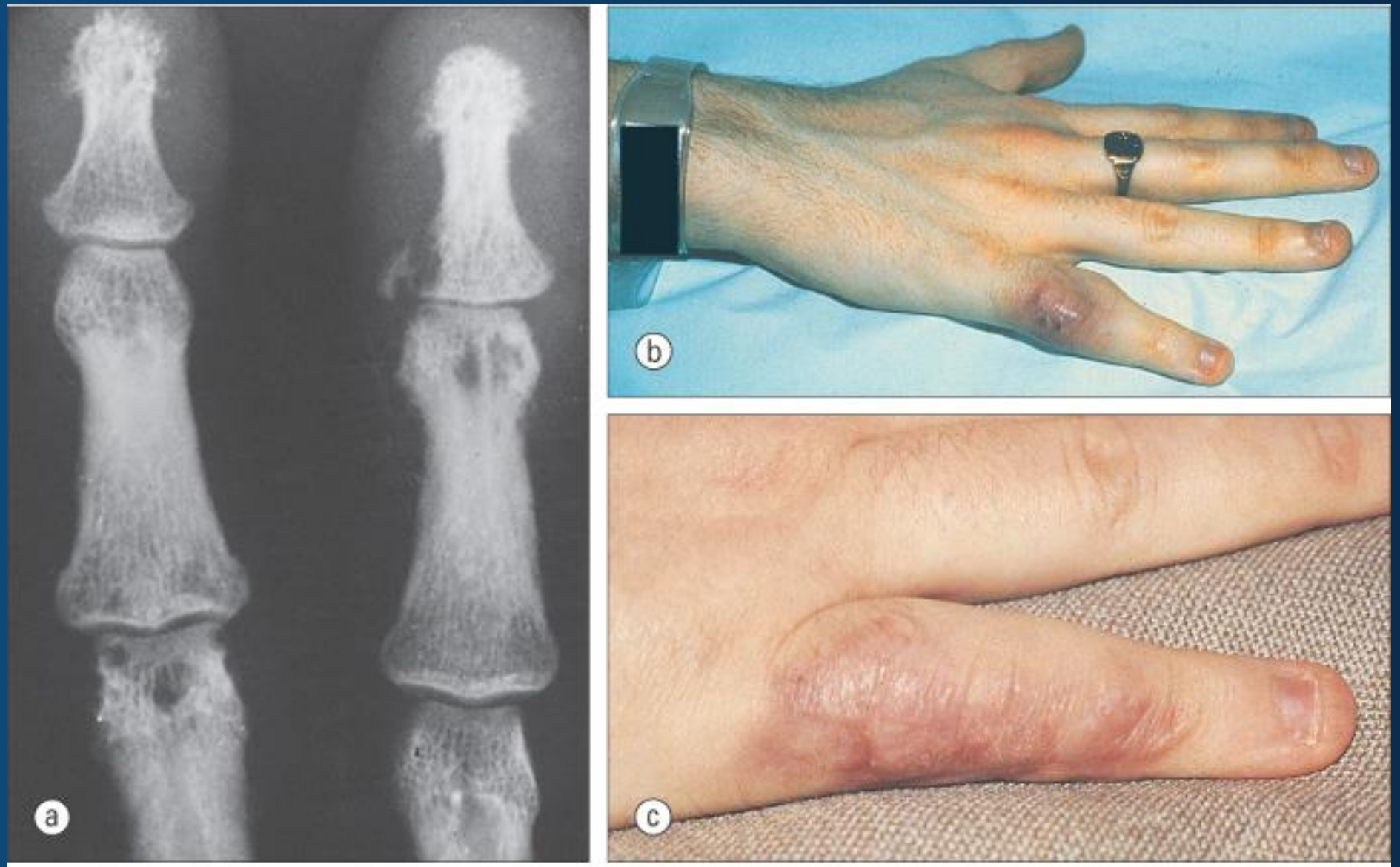
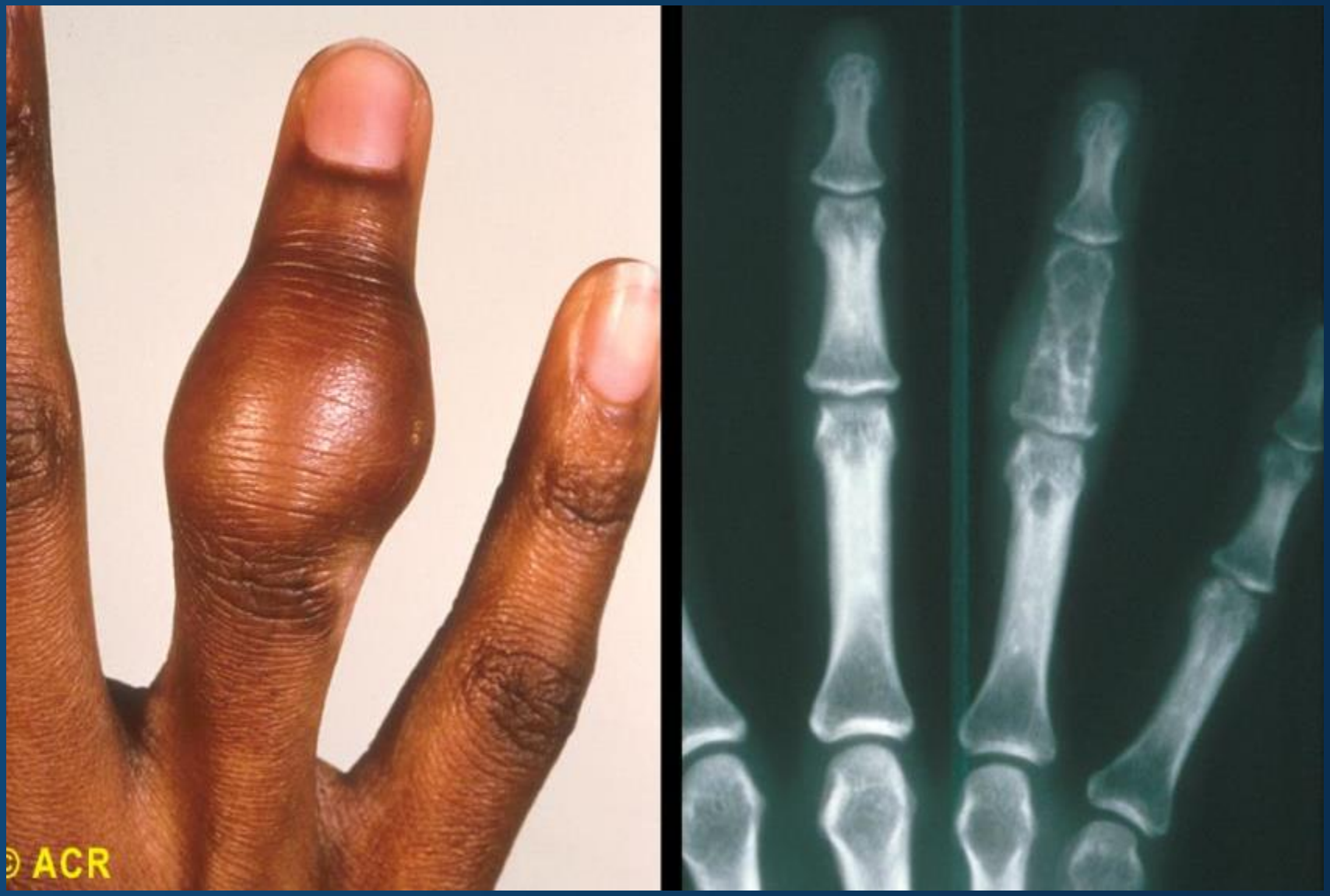

© www.rheumtext.com - Hochberg et al (eds)

Musculoskeletal Sarcoid

- Bone (osseous) involvement (1-13%)
  - More frequent in chronic and established dz. F>M (2:1). AA> other races.
  - Associated with lupus pernio and poor prognosis.
  - Cystic lesions have predilection for phalanges of hands and feet. Can have STS over lesion. Nasal bone lesions associated with lupus pernio.
  - Calcaneus, skull, vertebrae, ribs, pelvis, sternum, maxilla, and distal ends of long bones rare.
    - Sclerotic lesions of axial skeleton may mimic cancer.
  - Bone lesions on xray rarely shows periostitis or sequestra separating it from osteomyelitis.
  - MRI, PET, and bone scan more sensitive than xray since over 50% of bony lesions are asymptomatic.

Chatham W. Curr Opin Rheumatol 22:85-90, 2010
Moore SL et al. AJR 185: 154, 2005

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Muscle Sarcoid

- Muscle (1-5% symptomatic dz)
  - Up to 80% of random muscle bx in asymptomatic pts have granulomas.
  - Chronic myopathy most common form.
    Poor prognosis
    - Evolves slowly over years like muscular dystrophy. Wasting due to neurogenic atrophy from granuloma of nerves. EMG can show myopathy but muscle enzymes frequently normal. Cardiac sarcoid more common in pts with this type of myopathy.
  - Acute myositis: 20 cases. AA females
  - Muscle nodules: Muscle MRI shows “dark star”
  - Association with myasthenia gravis rarely reported

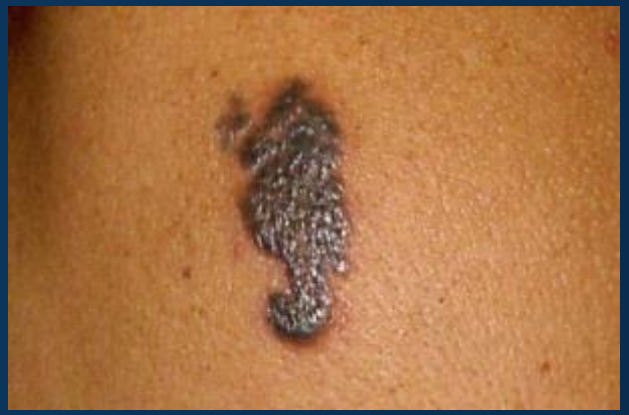
Le Roux K, et al. Muscle Nerve 35: 171, 2007
Fayad F, et al. J Rheumatol 33: 98, 2006.

Treatment of MSK Manifestations

- Acute arthritis
  - NSAIDs (Indomethacin may be best)
  - Low dose prednisone (10-20 mg/d)
  - If persists > 3-6 months, add hydroxychloroquine (HCQ)
- Chronic arthritis and tenosynovitis
  - NSAIDs, intraarticular steroids, low dose prednisone, physical therapy
  - Methotrexate +/- HCQ. Can also consider azathioprine and leflunomide
  - Biologics: anti-TNF agents (infliximab probably best)
- Osseous involvement: similar to chronic arthritis but need higher dose prednisone and early use of methotrexate and infliximab if destructive bony lesions in spine or weight-bearing bones.
- Muscle involvement
  - Acute myositis: high dose prednisone and methotrexate or azathioprine
  - Chronic myopathy: no therapy works well. Physical therapy
- Less experience with mycophenolate mofetil, IVIG, and other biologics (rituximab, abatacept)

Case #2

- A 28 yo AA woman is referred to you for evaluation of the etiology of bilateral anterior uveitis. Her evaluation shows she is HLA-B27 positive. She reports no arthritis or back pain. She denies rash but says her tattoo looks “funky”.
- Physical examination is normal including vital signs except for tattoo.
- Labs show CBC with Hct 35%,
- WBC 3800, nl plts. CMP normal.
- ESR 42 mm/hr. RF neg. ANA 1:40



Question

- Which one of the following is most likely to confirm the etiology of this patient's uveitis?
  A. Chest radiograph
  B. Serum lysozyme
  C. Radiographs of sacroiliac joints
  D. Skin biopsy of tattoo
  E. ANA profile

Ophthalmologic Manifestations

- Ophthalmologic (10-20%)
  - Presenting sx in 5%. Uveitis is most common sx, frequently bilateral, and often asymptomatic. All sarcoid patients need eye screening.
    - Anterior uveitis (75%): bilateral separates it from HLA-B27 associated dz
    - Posterior uveitis (25%): more chronic disease. Up to 20% get visual loss.
  - Other forms of eye dz: optic nerve, retinal vasculitis, orbital mass, KCS, lacrimal gland enlargement, scleral plaques, conjunctival nodules
  - Heerfordt's syndrome (uveoparotid fever): anterior uveitis, parotid gland enlargement, facial palsy, arthritis, and fever
  - Mikulicz's syndrome: enlarged lacrimal glands, enlarged parotid glands, and sicca symptoms. R/O Sjogren's, TB, lymphoma, leukemia, IgG4 Dz

Baughman RP et al. Semin Respir Crit Care Med 31: 452, 2010

Ophthalmologic Sarcoid

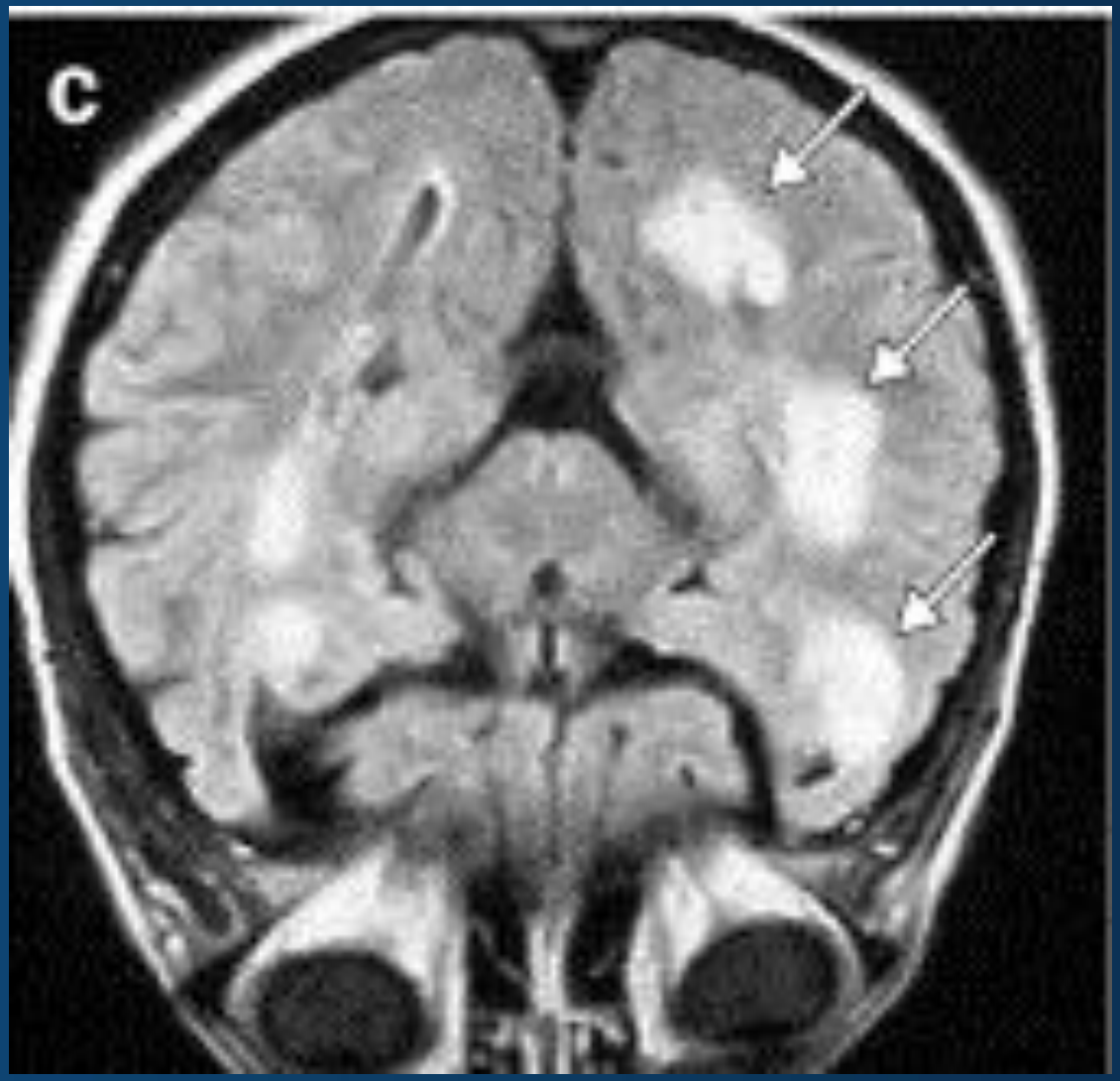
Location	Symptoms	Physical findings
Anterior chamber (iritis)	Pain, redness, blurred vision, asymptomatic	Mutton fat (KP) precipitates
Middle chamber (pars planitis)	Floaters	String of pearls, snowballs
Posterior chamber (chorioretinitis)	Decreased visual acuity	Retinitis, vasculitis, macular dz

Neurologic Sarcoid

- CNS involvement occurs in 5%. It is the initial manifestation of sarcoidosis in 50% of pts that develop neurosarcoidosis. Clinical manifestation most likely to remain chronic.
- Granulomatous basilar meningitis with infiltration and/or compression of adjacent structures causes most CNS manifestations
- Presentations (33% have more than one manifestation)
  - Cranial nerve involvement most common. Seventh nerve (Bell's palsy) most frequent (50%).
  - Perivascular granulomatous inflammation of brain or spinal cord: seizures, encephalopathy, myelopathy, radiculopathy
  - Lymphocytic meningitis- acute or chronic
  - Hydrocephalus: needs a shunt
  - Central diabetes insipidus
  - Hypothalamic hypopituitarism
  - Peripheral neuropathy: any type. Chronic sensorimotor most common pattern. Small fiber. Less frequent than CNS Dz.

Terushkin V et al. Neurologist 16: 2, 2010
Hoitsma E at al. Curr Opin Pulm Med 16: 472, 2010

Neurosarcoidosis



Neurologic Sarcoid

- Evaluation
  - Look for evidence of extraneural sarcoid if initial presentation: eye, chest CT
  - MRI with gadolinium: meningeal and/or parenchymal enhancement.
  - CSF exam (R/O infection or carcinomatous meningitis)
    - Elevated opening pressure (10%)
    - Mononuclear cell pleocytosis (50%)
    - Elevated protein (66%): up to 250mg/dl
    - Glucose can be normal or low
    - Elevated IgG index/OCBs (50%) and elevated CSF ACE level are nonspecific
  - Brain Bx: if Dx in doubt
  - EMG/NCV if peripheral neuropathy. Skin Bx for small fiber Dz

Gascon-Bayarri J et al. European J Internal Med 22, e125, 2011
Ginat DT et al. J Clin Imaging Sci 1:15, 2011

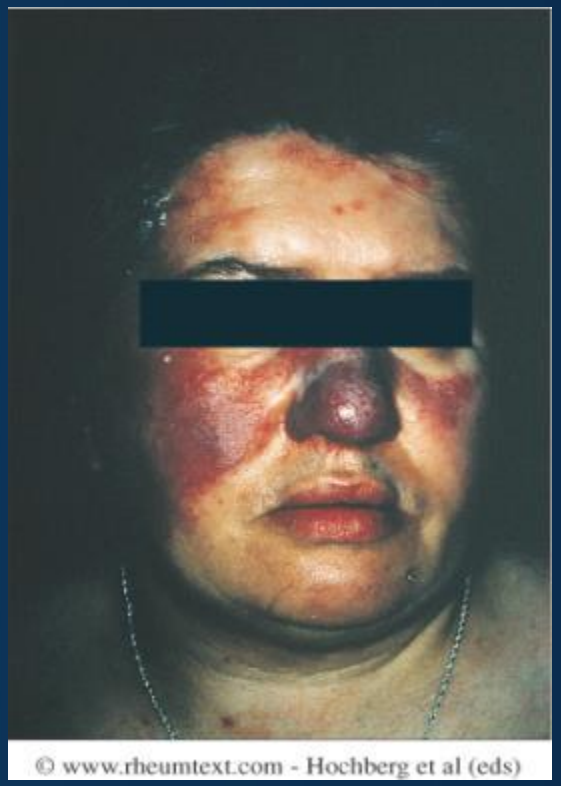
Other Extrapulmonary Presentations

- Fever
  - Usually low grade but can be up to 40°C
  - Associated with weight loss, fatigue, night sweats
  - More common in African-Americans and aged
- Vasculitis
  - Granulomatous inflammation of vessel walls of small (cutaneous, neuropathy) and medium sized vessels.
    - ANCA should be negative
    - CNS vasculitis reported
  - Large vessel involvement resembling Takayasu's in AA and Asian children (? Blau's syndrome)

Fernandes SR, et al. Semin Arthritis Rheum 30:33-46, 2000

Other Extrapulmonary Presentations

- Upper respiratory tract: larynx, pharynx, and sinuses (2-18%)
  - Parotid/salivary gland enlargement (4-6%) with sicca: may mimic Sjogren's. Anti-SS-A and anti-SS-B negative
  - Granulomatous sinusitis or laryngeal involvement: may mimic GPA
- Lupus Pernio: may mimic SLE
  - Usually AA or Puerto Rican women.
  - Most characteristic lesion.
  - Indurated, violaceous lesions on nose, cheeks, ears, lips, and fingers. Slowly progressive and disfiguring.
- Associated with upper respiratory tract dz, pulmonary fibrosis, and bony lesions in nose and phalanges.



Lodha S et al. Chest 136: 583, 2009

Case #3

- A 48 yo woman with known rheumatoid arthritis has been having problems with cough. Her arthritis is well controlled on methotrexate (7.5mg qwk) and etanercept. Chest radiograph shows bilateral hilar adenopathy. HRCT scan shows hilar adenopathy and several bronchopulmonary nodules. Transbronchial biopsy shows noncaseating granulomas. No evidence of malignancy. Cultures and stains for bacteria, fungi, and mycobacteria are negative.
- Physical examination shows normal vital signs. Heart and lung exams were normal. She has early hand deformities but no active synovitis.
- Laboratory results show CBC: Hct 35%, WBC 7800, plts nl. CMP nl except for alk phos 132 U/L. IgG level low at 550 mg/dl (nl 760-1590). ESR 38 mm/hr, ANA positive 1:160 with negative profile. RF negative. Gamma-interferon release assay negative.

Question

- Which one of the following is the most likely diagnosis?
  A. Common variable immunodeficiency
  B. Methotrexate pulmonary toxicity
  C. Etanercept-induced granulomatous lung dz
  D. Drug-induced lupus
  E. Rheumatoid lung disease

Sarcoidosis

- Childhood
  - Usually less than 5 years old presenting with painless boggy large joint polyarthritis and/or tenosynovitis, skin lesions, uveitis, and lymphadenopathy/splenomegaly without lung dz.
    - May mimic JIA except ANA negative and not oligoarticular
    - Usually have spontaneous remission.
  - Large vessel vasculitis resembling Takayasu's
  - R/O Blau's syndrome: mutation of NOD-2
- Coexistent diseases
  - Case reports of sarcoidosis occurring in patients with another autoimmune diseases (Sjogren's, SLE, RA, etc)
  - Case reports with CVID, malignancies/lymphoma, and immune reconstitution syndrome in HIV pts treated with HAART.
  - Case reports (pulmonary dz) following IL-2, interferon-α, interferon-γ, and anti-TNF-α therapy

Initial Evaluation

- History including environmental, occupational, and medication exposure
- Physical examination
- Chest xray or CT scan
- PFTs including D_LCO
- Peripheral cell blood counts
- Serum chemistries including Cr, Ca, and LAEs
  - Total immunoglobulins
- Creatine kinase
- Urinalysis
- 24 hour urine for calcium and creatinine
- Electrocardiogram with rhythm strip
- Ophthalmologic evaluation including slit-lamp exam
- Tuberculin skin test/interferon gamma release assay
- Biopsies of affected organs with special stains and cultures
- Other tests depending on organ system presentation

Am J Respir Crit Care Med 160: 736, 1999

Chest Radiograph

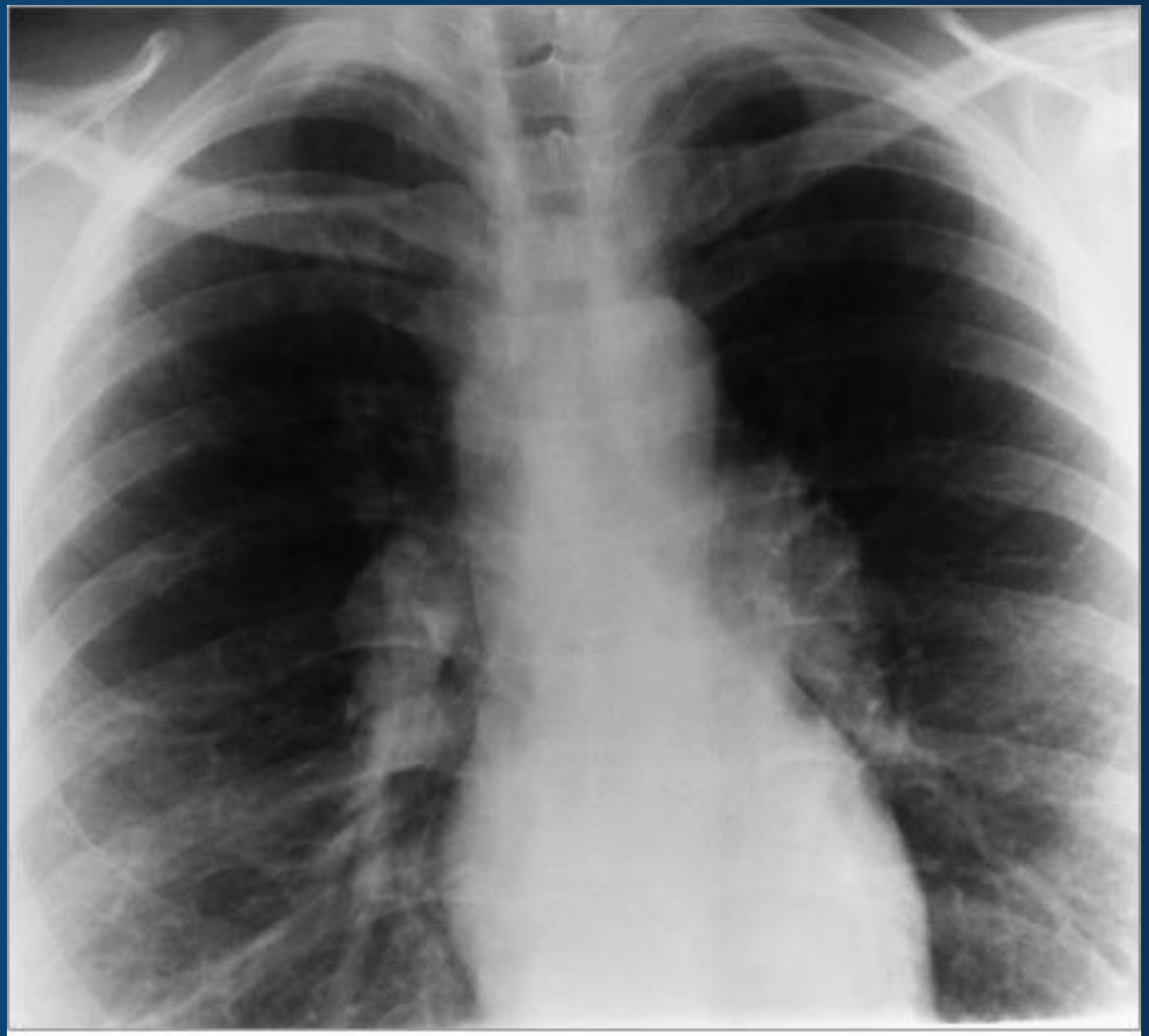
- Scadding staging system:
  - Stage 0: normal. Can have abnormal HRCT scan
  - Stage I: Bilateral hilar adenopathy with rt paratracheal adenopathy
  - Stage II: Bilateral hilar adenopathy with reticular opacities
  - Stage III: Reticular opacities
  - Stage IV: End-stage pulmonary fibrosis, volume loss, traction bronchiectasis, calcification, cavities/cysts

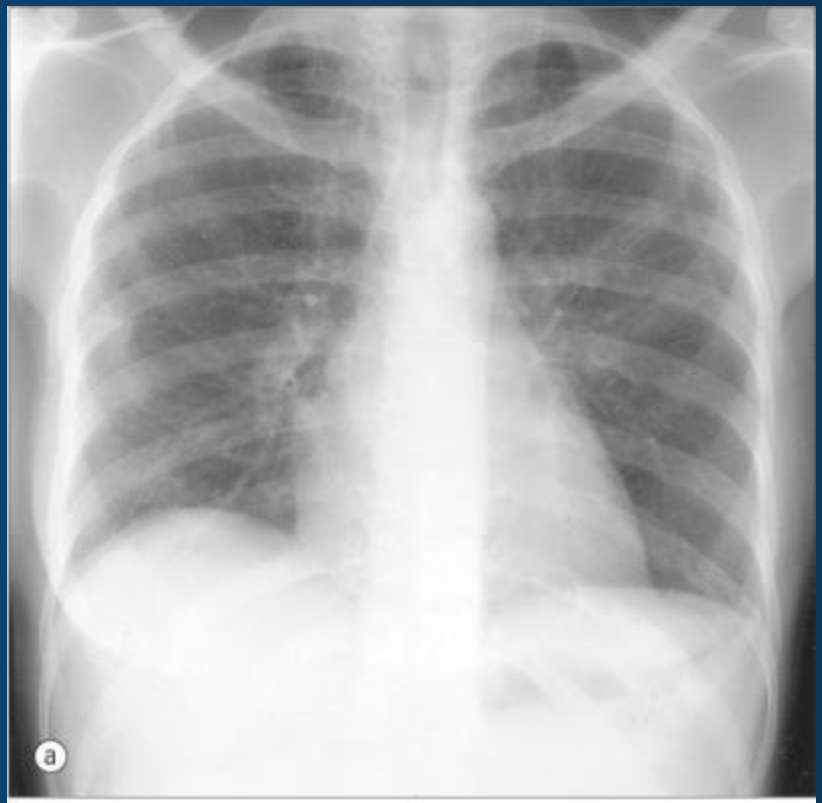
10%
50%
25%
5%
5%

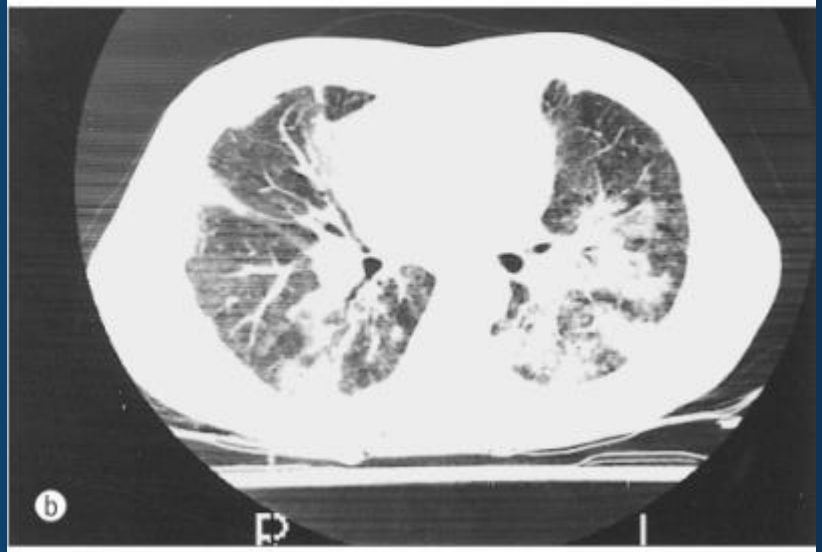
- Stages are not chronologic (don't progress from one to another over time)
- Reticular opacities in upper>lower lobes. Pleural effusions rare.
- Poor correlation between stage of lung dz and other clinical manifestations. Velcro rales < 20%. Clubbing rare.
- HRCT scan shows more abnormalities than CXR. Ground glass is granulomas and not alveolitis.
- Nodular sarcoidosis: multiple bilateral lung nodules with minimal hilar adenopathy resembling metastatic dz is rare presentation

Sarcoidosis: Stage I CXR

Prevalence at Dx 10%, Spontaneous Resolution 90%

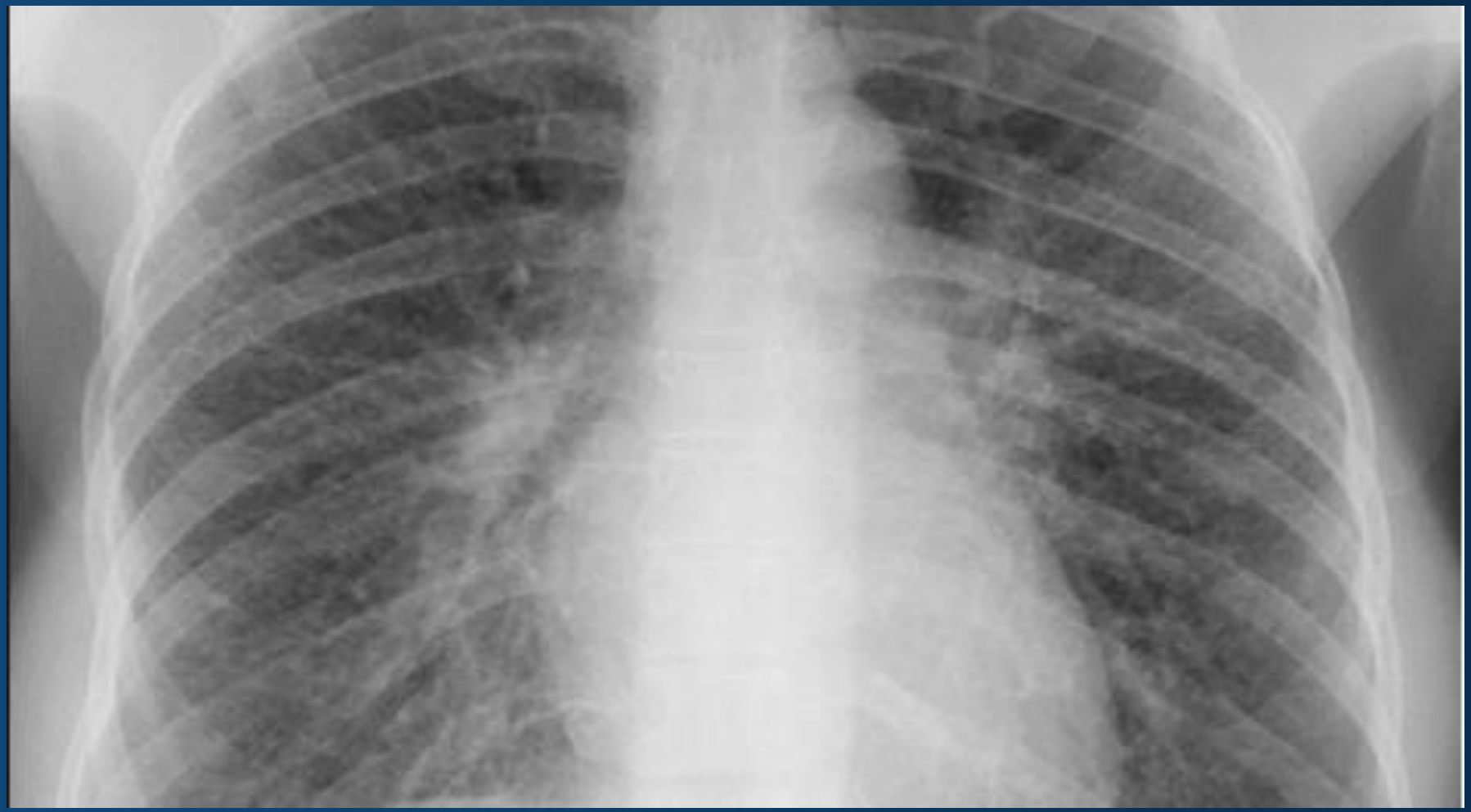






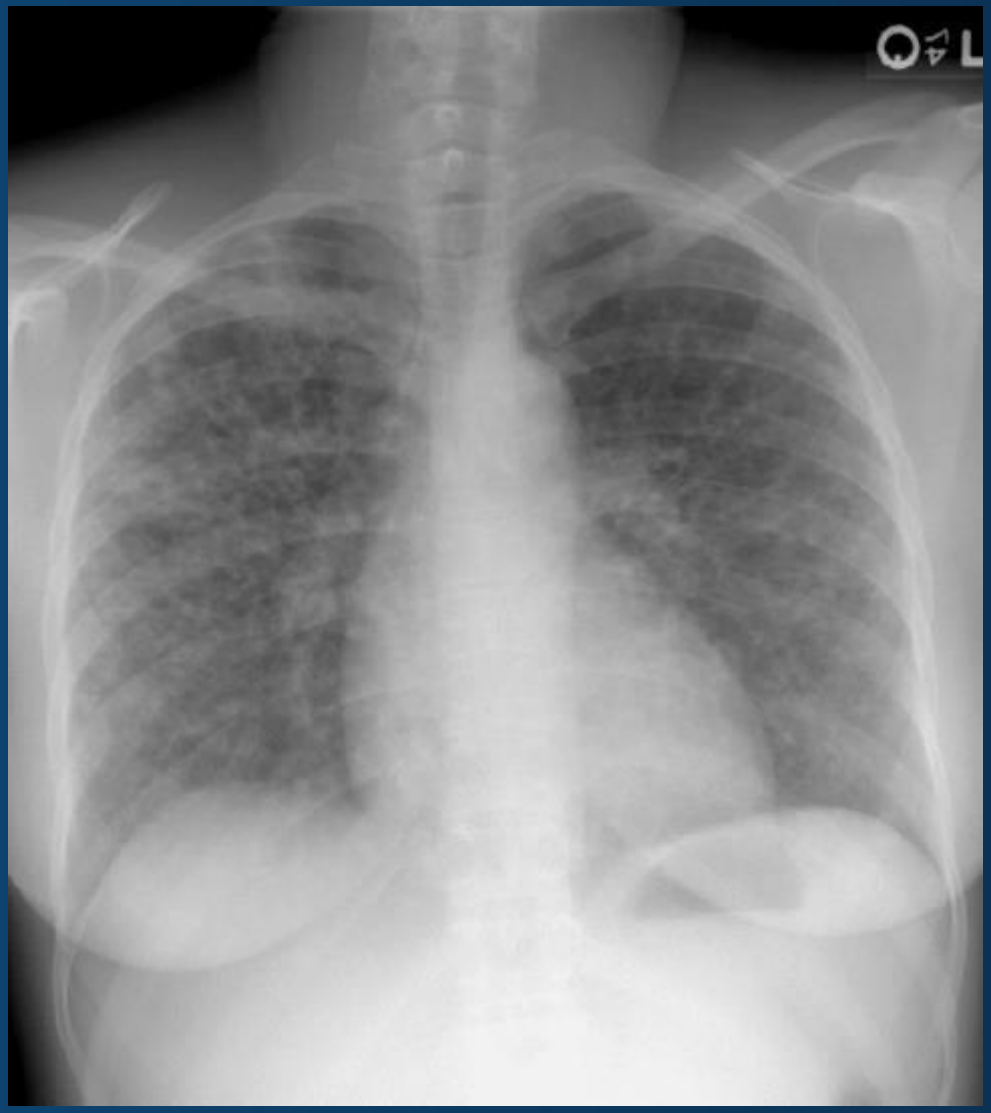
Sarcoidosis: Stage II CXR

Prevalence at Dx 25%, Spontaneous resolution 60%



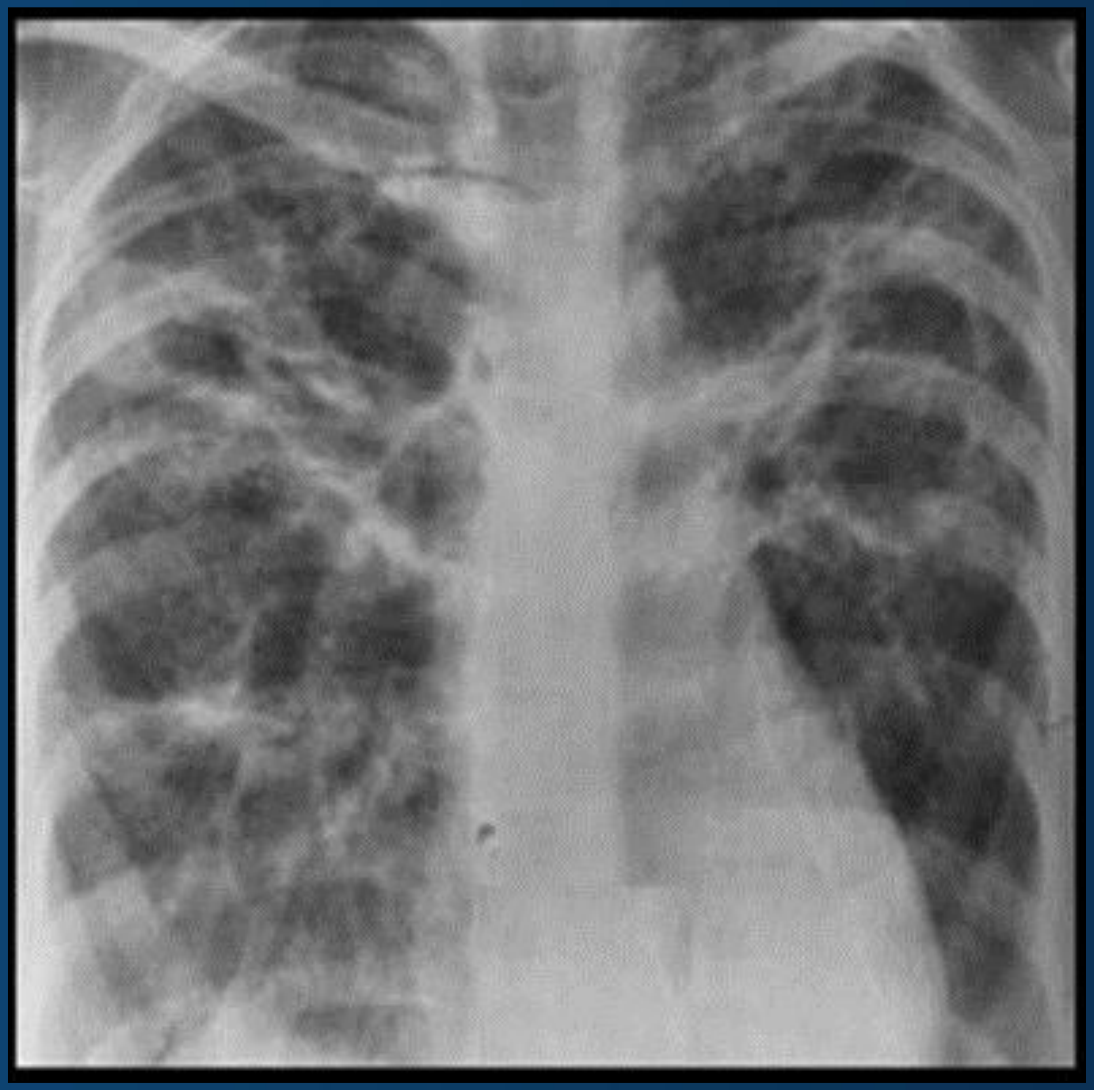
Sarcoidosis: Stage III CXR

Prevalence at Dx 5-10%, Spontaneous resolution 10%



Sarcoidosis: Stage IV

Prevalence at Dx 5%; Spontaneous resolution 0%



Laboratory Tests

- CBC
  - Anemia of chronic disease
  - Leukopenia (5%): R/O bone marrow involvement and hypersplenism
  - Eosinophilia: up to 25%
  - Thrombocytopenia: rare
- Chemistries
  - Elevated alk phos/GGT: 33%
  - Hypercalcemia (4-10%)
  - Hypercalciuria (15-20%)
- Serologies
  - Elevated ESR/CRP
  - Hypergammaglobulinemia (30-80%)
  - Low titer RF and/or ANA with speckled pattern but negative specific autoantibodies (up to 40%)
  - ANCA is negative

Supportive Diagnostic Tests

- Angiotensin converting enzyme (ACE): secreted by macrophages in granulomas. Levels affected by genetic polymorphisms and extent of organ involvement.
  - Sensitivity 73%
    - Elevated in 60-75% of patients with untreated, active sarcoidosis.
    - Elevated 15-30% of patients with Lofgren's syndrome
  - Specificity 83%
    - Multiple other causes of elevated ACE levels
    - Mild elevations (<50% above ULN) usually not concerning
    - Causes of ACE > 2x ULN: sarcoidosis, hyperthyroidism, other granulomatous diseases, genetic polymorphism
    - False positive elevations unusual (<5%)
- Lysozyme: secreted by monocytes and PMNs. Level affected by extent of organ involvement.
  - Sensitivity 69-79%: may be elevated when serum ACE is normal
  - Specificity 60-76%: multiple other causes of elevated lysozyme
- Both tests may normalize with successful therapy but value of following either to assess course of Dz unclear.

Supportive Diagnostic Tests

- PFTs and DLCO
  - Commonly restrictive pattern with decreased DLCO
  - Poor correlation with dyspnea sxs and CXR/HRCT scan
- Bronchoalveolar lavage fluid
  - CD4/CD8 ratio >4, lymphocyte percentage >16%, and TBBx showing noncaseating granulomas had 100% PPV for sarcoidosis.
  - CD4/CD8 ratio >3.5 with >30% lymphocytes has a 94% specificity and 52% sensitivity for sarcoidosis.
- HRCT scan
  - Can be abnormal with normal CXR
- MRI
  - Can be abnormal with normal radiographs
- FDG-PET scan is best test but expensive. May have role in finding sites for possible biopsy in atypical presentations.

Trelia G at al. Sarcoidosis Vasc Diffuse Lung Dis. 28: 87, 2011.

Tissue Biopsy

- Tissue biopsy is gold standard
  - Well circumscribed non-caseating granulomas of epithelioid type
  - Diagnostic yield
    - Transbronchial lung biopsy
      - Normal CXR: 30-50%
      - Abnormal CXR: >90%
    - Lymph node: >90%
      - Mediastinal/hilar node bx by endobronchial endoscopic ultrasonography (EBUS-TBNA): 79-84%
    - Skin(not EN): >90%
    - Parotid/MSG: 93%/36%
    - Synovium with chronic arthropathy: 80%
    - Asymptomatic muscle or liver; 50-80%
    - Lacrimal/conjunctival: 10-55%

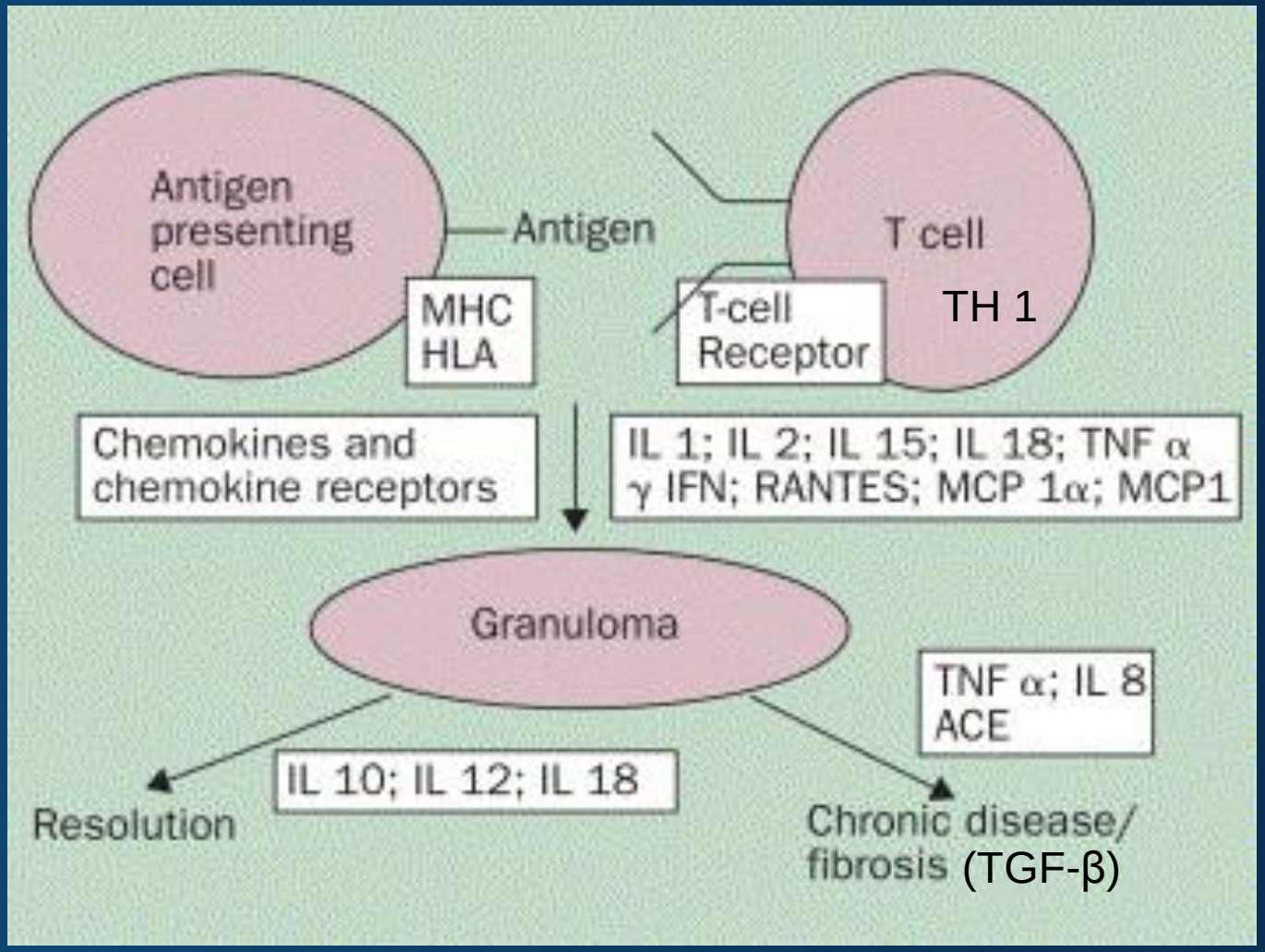
Cafulayan B et al. J Ultrasound Med 30: 1683, 2011

Etiology

- Genetics
  - Increased risk in first degree relatives: Caucasian (RR 18x), AA (RR 2.8x)
  - Monozygotic concordance 2-4X higher than dizygotic twins (RR 80x vs 7x)
  - HLA-DR/DQ(multiple), ACE polymorphisms, BTNL2, others
- Infectious
  - Mycobacterium antigens (mKatG, others)
  - Propionibacterium acnes and P. granulosum
- Environmental/occupational exposure (ACCESSS study)
  - Occupations
    - Water sources: agricultural settings, water-damaged work environments
    - Metal industry: metalworking fluids contaminated with Mycobacteria
    - Inorganic particulate matter: silicates, etc
  - Smoking is protective against developing sarcoidosis
- Autoimmunity
  - Serum amyloid A misfolding hypothesis

Newman KL, Newman LS. Curr Opin Allergy Clin Immunol 12: 145, 2012
Barnard J, et al. J Occup Environ Med 47:226, 2005
Muller-Quernheim J et al. Clin Chest Med 29: 391, 2008

Pathogenesis



Baughman RP, et al. Lancet 2003;361:1111.

Natural Hx and Prognosis

- Most patients undergo spontaneous remission(60%) within
- 2-5 yrs, additional 10-20% remit with steroids, 10-30% have a chronic course
  - At least 50% have some degree of permanent organ dysfunction
- Chronic sarcoid (10-30%)
  - 50% with chronic course have progressive lung dz.
  - 50% with chronic course have involvement of critical organs: eye (20% have visual loss), heart, and/or brain
- Poor prognostic signs: >/= 3 organ systems involved, skin involvement, AA race, disease onset after age 40, sxs lasting > 6 months, stage III-IV chest xray, pulmonary HBP
- Mortality
  - Overall mortality is 5% with half dying of pulmonary disease and half dying of cardiac/neurologic disease.
  - Pts with brain or cardiac disease: 10% mortality

Baughman RP, et al. QJM 99:307,2006
Swigris JJ et al. Am J RespirCrit Care Med 183: 1524, 2011

Management

- Patients with good prognostic signs should be observed for first 3-6 months without use of prednisone due to chance of spontaneous remission.
  - Pts with Stage I pulmonary dz and normal PFTs do not need prednisone
- Metaanalysis of prednisone use in Stage II and III pulmonary disease shows improvement in CXR and DLCO but only stabilization of FVC.
- No randomized, controlled trials to establish dose and duration of immunosuppressive therapy.
  - Usual starting dose is 20- 40mg or more of prednisone depending on manifestation
  - No guidelines for what to follow as response to therapy and when to taper therapy
    - Usually try to taper prednisone to 10mg a day by 3 months and continue that maintenance dose for 6-12 months before tapering off.

Paramothayan S et al. Cochrane Database Syst Rev 2005;2: CD001114.

Indications for Prednisone

ABSOLUTE

- Neurologic
- Cardiac
- Severe hypercalcemia
- Ocular
  - When topical therapy fails
- Organ-threatening Dz
  - Severe skin

RELATIVE

- Symptomatic Stage II/III pulmonary Dz
  - Dec FVC>15%
  - Dec TLC>10%
  - Dec D_LCO>20%
  - Inc CXR changes
- Arthritis
  - When NSAIDs fail
- Osseous (if destructive)
- Hepatic
- Systemic Sxs

Lazar CA, Culver DA. Semin Respir Crit Care Med 31: 501, 2010.

Indications for Other Immunosuppressive Rx

- Failure to taper high dose prednisone to 10mg/day by 3 months should prompt addition of a second agent.
- Severe disease
  - Cyclophosphamide (3-6 months) followed by methotrexate or azathioprine
- Moderate disease
  - Methotrexate has been studied the most
- Hydroxychloroquine should be added to other DMARDs especially for skin, arthritis, and neurologic dz.

Corticosteroids	Cytotoxic agents	Immunodulators	Other drugs
Prednisone	Methotrexate	Chloroquine/hydroxychloroquine	Minocycline
Constitutional	Azathioprine	Pentoxifylline	Clofazimine
	Cyclophosphamide	Thalidomide	
	MMF, lefunomide	Infliximab	

Paramothayan S, et al. Cochrane Database Systemic Reviews 2006; (3): CD003536.

Anti-TNF Therapy in Sarcoidosis

- Anecdotal case reports/series
  - Russell E. Semin Arthritis Rheum 43: 114, 2013 (27 pts treated with infliximab, best for extrapulmonary dz)
  - Hasni SA. Spine 35: E904, 2010 (2 pts, review)
  - Doty JD. Chest 2005; 127: 1064-1071. (10 pts)
  - Multiple case reports and series on effectiveness for skin dz.
    - Stagaki E. Chest 135: 468, 2009 (54 lupus pernio pts)
- Controlled trial
  - Rossman MD. Sarcoidosis Vasc Diffuse Lung Dis 23:201, 2006 (19 pts)
  - Baughman RP. Am J Resp Crit Care Med 2006 (138 pts)
  - Judson MA. Eur Respir J 31: 1189, 2008 (138 pts)
- Infliximab 5mg/kg IV every 4-6 weeks appears to be more effective than the other anti-TNF agents
  - Etanercept reports found etanercept not useful for pulmonary dz (Utz et al. Chest 2003;124:177-185) or for uveitis (Baughman et al. Chest 2005;128:1062-1067)
  - Retrospective study on use of adalimumab (17 pts) found it no more effective than etanercept (14 pts) and less effective than infliximab (69 pts). 40% of pts on etanercept and adalimumab actually worsened.

Summary

- Sarcoidosis is common with protean presentations and manifestations that may mimic rheumatic diseases.
- Sarcoidosis may coexist with other autoimmune diseases
- Evaluation for extrapulmonary organ involvement is a critical part of the assessment of sarcoidosis.
  - Supports the diagnosis
  - Identifies reasons for therapy
  - Provides prognostic information
- Therapy for sarcoidosis is directed for both acute and chronic disease.
  - Chronic disease may benefit from steroid-sparing agents

Thank You

Questions ???