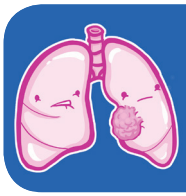

NOTES
RESTRICTIVE LUNG DISEASE

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Inflammatory disorders of lung parenchyma
- Restricts lung expansion → decreases lung volume, ventilation, gas exchange → difficulty breathing

RISK FACTORS

- Exposure to occupational, biological dusts

SIGNS & SYMPTOMS

- Dyspnea, cough

DIAGNOSIS

DIAGNOSTIC IMAGING

High resolution chest CT scan

LAB RESULTS

- Lung biopsy

OTHER INTERVENTIONS

- Spirometry
  - ↓ Vital capacity
  - ↓ Total lung volume
  - ↓ Forced expiratory volume in one second (FEV1)
  - ↓ Diffusion capacity of carbon monoxide
- Bronchopulmonary lavage

TREATMENT

SURGERY

- Lung transplant (definitive)

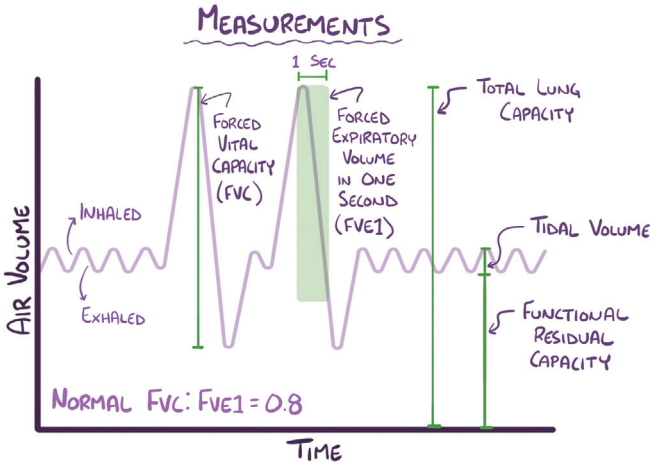

Figure 131.1 Illustration depicting the various criteria examined during a spirometric test.

IDIOPATHIC PULMONARY FIBROSIS

osms.it/idiopathic-pulmonary-fibrosis

PATHOLOGY & CAUSES

- Abnormal pulmonary healing process: pulmonary insult heals → excess deposits of collagen, fibrotic tissue → progressive scarring of lung tissue → loss of lung compliance → dyspnea worsens, lung function declines → hypoxemia
- Affects pulmonary interstitium: tissue between alveoli, airspaces, peripheral airways, vessels
- Chronic, irreversible, ultimately fatal disease

CAUSES

- Overproliferation of type 2 pneumocytes → excessive myofibroblast population → excessive collagen production → collagen accumulates → interstitial layer thickens between alveoli, capillary → poor ventilation/gas exchange, lung parenchyma stiffens → restricted lung expansion (restrictive lung disease)

RISK FACTORS

- Ages 50–70, history of smoking, more common in individuals who are biologically male, exposure to occupational dusts (e.g. metal, wood, coal, silica, stone), biologic dusts (e.g. hay, molds, spores, agricultural products, livestock), gastroesophageal reflux disease, genetic

SIGNS & SYMPTOMS

- Worsens over time, coughing (dry non-productive cough, worse on exertion), dyspnea (progressive exertional), cyanosis, digital clubbing, dry inspiratory bibasilar crackles on auscultation, significant respiratory failure with increasing tissue loss

DIAGNOSIS

- Exclude known causes of interstitial lung disease (e.g. hypersensitivity pneumonitis, pulmonary Langerhans cell histiocytosis, asbestosis, collagen vascular disease)

DIAGNOSTIC IMAGING

High-resolution chest CT scan

- Usual interstitial pneumonia (UIP) pattern
  - Honeycombing with well-defined walls
  - Reticular opacities with/without traction bronchiectasis (ground glass opacities, honeycombing, cystic spaces)
  - Subpleural, basal lung fields
  - Absence of features inconsistent with UIP (mid to upper predominance; peribronchovascular predominance; extensive ground glass appearance; profuse micronodules; discrete cysts away from areas of honeycombing; diffuse air-trapping)
  - Bronchopulmonary consolidation
- Thickening of interstitial walls
  - Fibrotic changes
  - Bases, periphery

LAB RESULTS

Biopsy

- Taken from three different areas, large enough to show underlying lung architecture (bronchoscopic biopsies insufficient; thoracotomy/thoracoscopy prefered)
- Histology
  - Interstitial fibrosis in patchwork pattern; interstitial scarring; honeycomb changes; fibroblastic foci (dense collections of myofibroblasts, scar tissue)

OTHER INTERVENTIONS

Broncheolar lavage

- Cytology
  - Exclude alternative diagnoses (e.g. malignancy, infection, eosinophilic pneumonia, histiocytosis X, alveolar proteinosis)
- Lymphocytes > 30%
  - Exclude idiopathic pulmonary fibrosis

Spirometry

- Restrictive pattern decreased
  - Total lung capacity
  - Forced vital capacity (FVC)
  - FEV1
- Decreased diffusing capacity of lungs for carbon monoxide

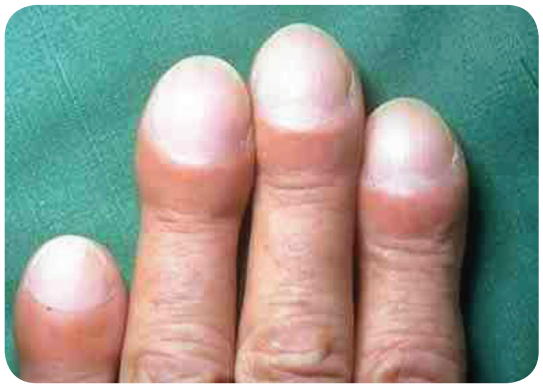

Figure 131.2 The clinical appearance of digital clubbing as seen in a case of idiopathic pulmonary fibrosis.

TREATMENT

MEDICATIONS

- Antifibrotic medication
  - Slows progression
- Seasonal influenza vaccine

SURGERY

- Lung transplant (definitive)

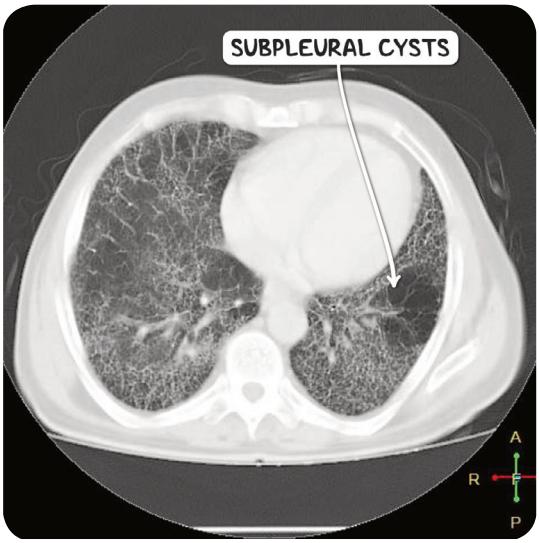

Figure 131.3 A CT scan of the chest in the axial plane demonstrating marked honeycombing of the lung and a collection of subpleural cysts in an individual with idiopathic pulmonary fibrosis.

SARCOIDOSIS

osms.it/sarcoidosis

PATHOLOGY & CAUSES

- Disease involving formation of noncaseating granulomata (clumps of inflammatory cells)
- Can affect any organ system
  - Accumulation of monocytes, epithelioid macrophages, activated T-lymphocytes
  - Macrophages may aggregate to form multinucleated giant cells (AKA Langhans giant cells)
  - Increased production of inflammatory mediators (Th-1 mediated)
  - Cytokines released from activated immune cells → systemic effects

CAUSES

- Unknown; may be triggered by immune reaction in genetically predisposed individuals

RISK FACTORS

- Genetic, previous episode of sarcoidosis, biological females, 20–50 age group

COMPLICATIONS

Paradoxical effect on immune reactivity

- Increased macrophage and CD4 helper T-cell activation → accelerated inflammation
- But antigen challenges, e.g. tuberculin skin test are suppressed
- This paradoxical hyper-/hypo-activity is immunological anergy → increased risk of infections, cancer

Pulmonary pathology

- > 90% of affected individuals
- Bilateral hilar lymphadenopathy (up to 90% of affected individuals)
- Predominantly upper lobe parenchymal infiltration
- Airway involvement → airway hyperresponsiveness (increased sensitivity to inhaled triggers)
- Pulmonary hypertension → cor pulmonale

Ocular pathology

- Up to 25%
- Significantly more common in Asian people of Japanese descent (>70%)
- Anterior uveitis
- Uveoparotitis (inflammation of uvea, parotid gland)
- Retinitis

Cardiac pathology

- 5% symptomatic, autopsy reports 25–70% subclinical involvement
- Significantly more common in Asian people of Japanese descent
- Conduction defects
  - Asymptomatic conduction abnormalities
  - Fatal ventricular arrhythmias
  - Complete heart block
  - Sudden cardiac death
- Cardiac fibrosis, interstitial fluid accumulation, heart failure, valvular dysfunction, pericardial disease

Nervous system pathology

- ~5%
- AKA neurosarcoidosis
- Variable presentation
  - Cranial nerves most commonly affected
  - Neuroendocrine changes
  - Chronic meningitis

Endocrine/exocrine pathology

- Sarcoidosis of anterior pituitary
  - Deficiency of adrenocorticotropic hormone, thyroid-stimulating hormone, follicle-stimulating hormone, luteinizing hormone, insulin-like growth factor 1
- Hypothalamic dysfunction
  - Hypersecretion of prolactin

- Increase in 1,25-dihydroxyvitamin D (active form of vitamin D)
  - Hydroxylation usually occurs in kidney; in sarcoidosis it may occur in sarcoid granulomata due to activated macrophages → hypercalcemia → hypercalciuria

Hepatic pathology

- Liver granulomata very common (70%)
- Only 20–30% have detectable aberrant liver function
- Liver granlomata → cholestatic pattern → raised alkaline phosphatase, mildly elevated bilirubin, aminotransferases

Nephrological pathology

- < 5%
- Can cause nephritis, but renal injury from hypercalcemia more common
- Nephrocalcinosis, nephrolithiasis

Gynecological/Urological

- Uncommonly epididymis, tesicles, prostate, ovaries, fallopian tubes, uterus or vulva may be affected
- Biological males → infertility

Hematological

- Sequestration of lymphocytes into areas of inflammation → lymphopenia
- Anemia
- Leukopenia
  - May reflect bone marrow involvement or redistribution of T-cells to disease sites
- Monocytosis
- Polyclonal hypergammaglobulinemia

Rheumatological

- 10%
- Acute polyarthritis
- Enthesitis
  - Inflammation at sites where tendons or ligaments insert into bone
- Chronic sarcoid arthritis
  - Diffuse organ involvement
  - Periosteal bone resorption

SIGNS & SYMPTOMS

- Varies by organ. May be asymptomatic.

General

- Peripheral lymphadenopathy, fatigue (not relieved by sleep), weight loss, arthralgia, dry eyes

Lower respiratory manifestations

- Wheezing, cough, dyspnea, chest pain, hemoptysis, crackles

Upper respiratory sarcoidosis (uncommon)

- *Laryngeal sarcoid:* involves supraglottis, occasionally subglottis
  - *Subglottis:* dysphagia, dyspnea, cough, hoarseness
- *Nasal and sinus sarcoidosis:* nasal obstruction, nasal crusting, anosmia, epistaxis, nasal polyposis

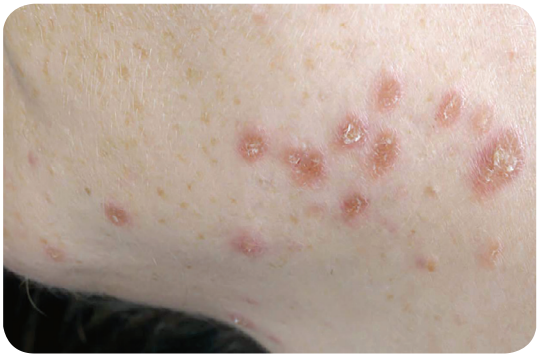

Figure 131.4 The clinical appearance of cutaneous sarcoidosis.

Skin

- Erythema nodosum
  - Inflammation of subcutaneous adipose tissue → painful nodules
  - Affects anterior surface of lower extremities
- Plaques
  - Often seen in chronic forms
  - Affects shoulders arms, back and buttocks
- Maculopapular eruptions
  - Common manifestation

- Affects alae, nares, lips, eyelids, forehead, nape of neck, sites of previous trauma
- Subcutaneous nodules
  - Affects face, trunk, extensor surfaces
- Lupus pernio
  - Violaceous or erythematous indurated papules, plaques/nodules
  - Primarily affects nose, cheeks, chin, ears

Ocular involvement

- Photophobia, blurred vision
- Increased tearing or dry eyes
- Loss of visual acuity → blindness
- Heerfordt syndrome: anterior uveitis, parotitis, cranial nerve VII palsy, fever

Cardiac involvement

- Palpitations, dizziness, chest pain

Nervous system

- Hearing abnormalities, headache, altered consciousness level, changes in peripheral sensation

Endocrine & exocrine changes

- *General:* changes in body temperature, mood alterations, swelling of salivary/parotid glands
- *Biological females:* amenorrhea, galactorrhea, nonpuerperal mastitis, changes in menstrual cycle
- *Biological males:* hypogonadism
- Other clinical manifestations of hypopituitarism, e.g. diabetes insipidus, hypothyroidism, adrenal insufficiency

Hepatic

- Hepatomegaly

Nephrological

- Reduced creatinine clearance
- Proteinuria
- Signs and symptoms of renal calculi

Hematological

- Signs and symptoms of anemia, immunodeficiency
- Splenomegaly
- Immunological abnormalities
  - Allergies to test antigens, e.g. candida or purified protein derivative

Rheumatological

- Acute polyarthritis
- Symmetric involvement of ankle joints
- Usually periarthritis not true arthritis
- May be present in isolation or as part of Löfgren syndrome
- Löfgren syndrome
  - Acute form of sarcoidosis
  - 95% specificity for sarcoidosis
  - Predominantly occurs in biological females of Scandinavian, Irish, and Puerto Rican descent
  - Bilaterally enlarged hilar lymph nodes
  - Erythema nodosum (tender red nodules, typically pretibial surface)
  - Arthritis most commonly occurring in ankles > knees > wrists > elbows > metacarpophalangeal joints; usually not true arthritis, but periarthritis affecting soft tissue around joints
  - Enthesitis (inflammation sites where tendons/ligaments insert into the bone)
- Chronic sarcoid arthritis
  - Diffuse organ involvement
  - Ankles, knees, wrists, elbows, hands may be affected (polyarticular pattern)
  - Dactylitis (inflammation of entire digit)
  - Pain, stiffness

MNEMONIC: SARCOIDOSIS

Features of Sarcoidosis

Schaumann calcifications

Asteroid bodies/**A**CE increase/**A**nergy

Respiratory complications/**R**enal calculi/**R**estrictive lung disease/**R**estrictive cardiomyopathy

Calcium increase in serum and urine/**C**D4 helper cells

Ocular lesions

Immune mediated noncaseating granulomas/**I**g increase

Diabetes insipidus/**D** vit. increase/**D**yspnea

Osteopathy

Skin: subcutaneous nodules, erythema nodosum

Interstitial lung fibrosis/**I**L-1

Seventh CN palsy

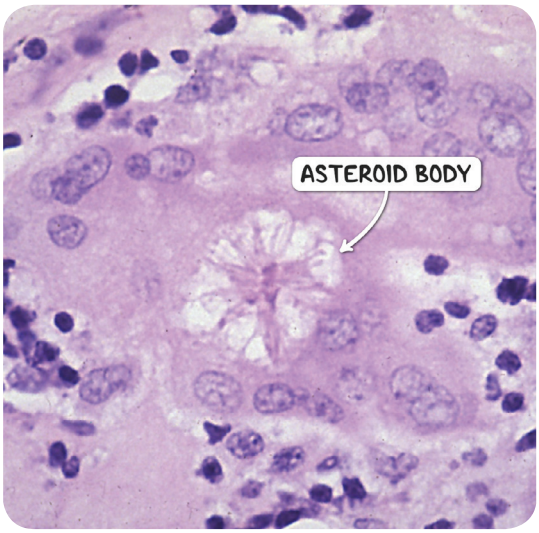

Figure 131.5 A giant cell containing an asteroid body in a case of pulmonary sarcoidosis.

DIAGNOSIS

- Diagnosis of exclusion
- Usually dependent on biopsy of organ involved
    - Noncaseating granulomata
    - Tuberculin skin test (tuberculosis, sarcoidosis share many clinical features)
    - Exclusion of other granulomatous causes

DIAGNOSTIC IMAGING

X-ray, CT scan

- Staged according to extent of lung involvement (Siltzbach classification system)
    - *Stage 0:* normal lung at presentation
    - *Stage I:* bilateral hilar lymphadenopathy only (60% resolution within 1–2 years)
    - *Stage II:* bilateral hilar lymphadenopathy with pulmonary infiltrates (46%)
    - *Stage III:* pulmonary infiltrates without bilateral hilar lymphadenopathy (12%)
    - *Stage IV:* pulmonary fibrosis
- CT scan-/ultrasound-guided biopsy/fine-needle aspiration of mediastinal lymph nodes
    - Flow cytometry
    - Microscopy and staining
    - Culture

PET scan

- Lamba sign → gallium uptake in paratracheal, hilar lymph nodes
- Panda sign → lacrimal, parotid, submandibular glands with normal nasopharyngeal uptake
- Combination of two specific for sarcoidosis

LAB RESULTS

- High blood calcium (normal parathyroid level)
- Elevated angiotensin converting enzyme (level correlates with total granuloma load)
    - Can be used for monitoring treatment and disease progression

OTHER DIAGNOSTICS

Lung function testing

- Determine level of function
- Monitor course of disease
- Typically reveals restrictive pattern (reduced vital/total lung capacity)

- Endobronchial sarcoid may lead to impairment of airflow, obstructive pattern

Diffusion of carbon monoxide (DLCO)

- Most sensitive test for interstitial lung disease

Bronchoscopy

- Biopsy
- Bronchoalveolar lavage
  - CD4/CD8 T cell ratio in bronchoalveolar lavage is raised > 3.5 (can be normal/low)

Ophthalmological exam

ECG

TREATMENT

- May resolve spontaneously over years
- Dermatological involvement typically resolves without treatment
- Acute disease
  - No therapy is a viable option for mild symptoms
  - Topical/local therapy preferred for organ-confined disease

MEDICATIONS

Anti-inflammatory drugs

- NSAIDS
  - Up to 75% of individuals may achieve sufficient symptomatic control on these alone
- Corticosteroids
  - If long course required, consider steroid-sparing agents

Antimetabolites

- Methorexatem, chloroquine, azathioprine

Immunosuppressants

- Cyclophosphamide, cladribine, chlorambucil, cyclosporine
- Anti-tumor necrosis factor treatment
  - These agents have also been reported to cause sarcoidosis-like illness

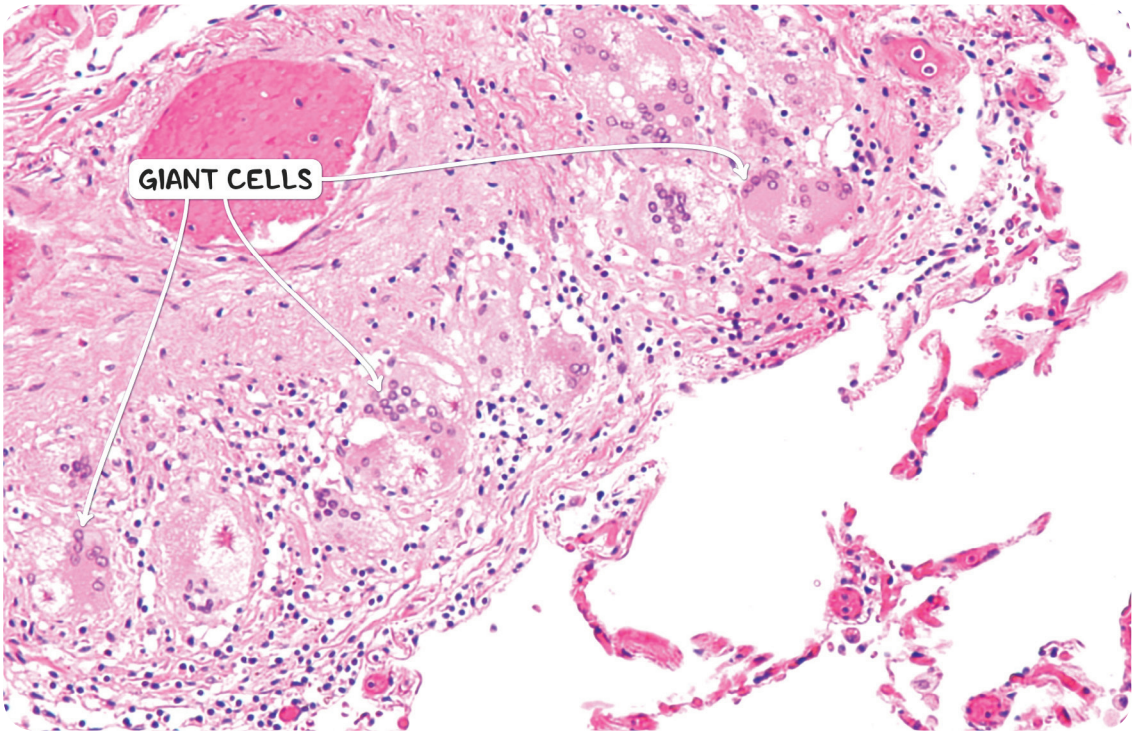

Figure 131.6 The histological appearance of pulmonary sarcoidosis. There are large numbers of giant cells visible.