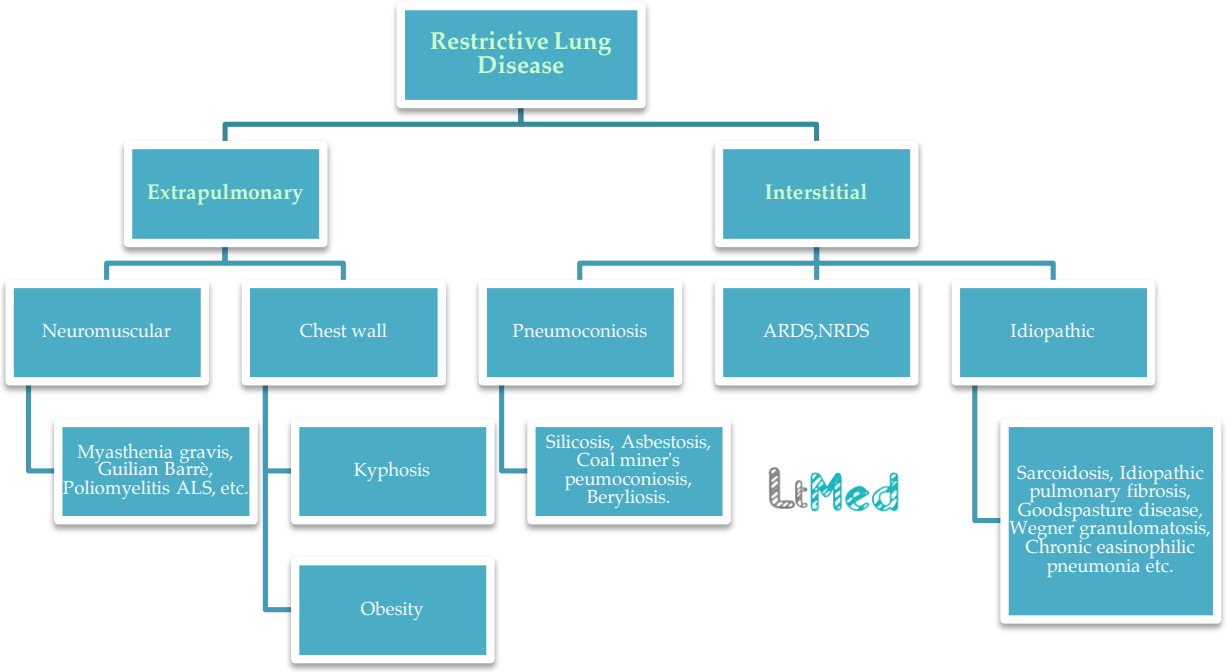
Restrictive Lung Disease (RLD)

- **Definition:** Restrictive lung disease is a chronic respiratory disorder that causes a decrease in lung volume and lung capacity due to specific causes.
  - *Lungs are **restricted** from fully expanding.*
- **Epidemiology:**
  - The prevalence of intrinsic lung diseases in the United States is 3-6 per 100,000 persons.
  - More prevalent in *elderly*.
  - Men have higher risk of developing the disease:
    - ✓ *Due to higher chances of being exposed to occupational chemicals and irritants.*
- **Types: (Based on the anatomical structure):**
  1. Intrinsic Lung Diseases (ILD): **(Parenchyma and interstitium) resulting in a pattern of either:**
     - *a.* **Interstitial lung diseases:** *Inflammation, scarring, and/or swelling of the lung's tissue.*
       - ✓ *Hallmark is reduced compliance.*
     - **b. Pneumonitis:** *Filling the alveoli with exudates and pus.*
       - ✓ *Any damage and destruction of the **alveoli** will result in: V/Q mismatch and hypoxia.*
  2. Extrinsic (extra-parenchymal) lung disease:
     - ***a.*** **Diseases that affect the components of the respiratory pump (chest wall, pleura, respiratory muscles etc.) resulting in:**
       - ✓ Lung restriction.
       - ✓ Impaired ventilator function.
       - ✓ Respiratory failure.
- **Causes:**



- **Characteristics of restrictive lung diseases:**
  1. Lung tissue Loss:
     - ✓ *Especially in interstitial lung disease ➔ irreversible fibrotic scar.*
  2. Reduction in the expandable capacity of the lung:
     - ✓ *Physical limitation restricting the lung's area of expansion (↓compliance).*
     - ✓ *Resulting in Hypoventilation, V/Q mismatch and hypoxia.*
  3. Decrease in the lung's ability to transfer gases (O_2 & CO_2) in and out of the blood.

- **Pathophysiology:**
  - **Imbalance between the inward and outward elastic recoil can cause restrictive lung disease:**
    - ✓ **Intrinsic lung disease** →lung volume is decreased due to *excessive increase in the lung's elastic recoil compared with chest wall elastic recoil.*
    - ✓ **Pleural and thoracic cage disorders** →total decrease in lung's compliance leading to reduction in total lung volume →atelectasis can occur and it can cause V/Q mismatch and hypoxemia.
    - ✓ **Neuromuscular disorders**→affect vital respiratory pump components.
    - ✓ **Obesity**→causes a physical limitation to the lung affecting its compliance.
- **Pathogenesis & morphology of idiopathic pulmonary fibrosis (IPF):**
  - *The most common ILD (prototypic type).*
    - ✓ Characterized by patchy, progressive bilateral interstitial fibrosis causing *dyspnea*.
    - ✓ Male> Female and most of the patients are>60 years.
    - ✓ *Repeated cycles of epithelial activation/injury by an unidentified agent.*
    - ✓ *Injury to type 1 pneumocytes → release TGF-β1 → induces fibroblast to differentiate into myofibroblasts → secretes collagen (fibrosis).*
    - ✓ Gross appearance of affected lungs→ *cobblestone appearance.*
    - ✓ *The end stage of interstitial lung disease (in general not only IPF) → alveolar wall collapse→Clusters of cystic spaces form lines by either hyperplastic bronchial epithelium or type 2 pneumocyte.*
    - ✓ This fibrotic cystic change is referred to as **Honeycomb changes/fibrosis** *(associated with poor prognosis).*
- **Signs & Symptoms:**
  - **Most commonly:** *dyspnoea, non-productive cough, cor pulmonale, cyanosis, clubbing and Velcro crackles*.
  - Progressive muscle weakness (in neuromuscular causes).
  - Acute or chronic respiratory failure (in neuromuscular causes as well).
  - IPF can have systemic symptoms (low-grade fever, myalgia, arthralgia, weight loss).
- **Diagnosis:**
  1. **Clinical Presentation:**
     - ✓ **Physical exam findings:**
       - **Pulmonary findings:**
         - *Velcro Crackles (fine or dry crackles) are common in most patients with interstitial disorders.*
         - Inspiratory squeaks or late inspiratory high-pitched rhonchi→ in patients with bronchiolitis.
         - Cyanosis at rest: late manifestation.
         - Digital clubbing: common in patients with IPF.
       - **Extra pulmonary findings:**
         - Erythema nodusum→sarcoidosis.
         - Hepatosplenaomegaly and lymphadenopathy→signs of systemic sarcoidosis.
         - Uveitis →sarcoidosis or ankylosing spondylitis.
         - Raynaud phenomenon.
         - Maculopapular rash →connective tissue disease, or drug-induced.

2. **Routine lab investigation→***mainly based on clinical assessment*:
    - If autoimmunity is suspected→ do autoantibody test for the suspected autoimmune disease.
    - Anaemia→ may indicate vasculitis
    - Polycythaemia→ may indicate hypoxemia in advanced cases.
    - ↑Creatine kinase→ may indicate myositis, causing restrictive lung disease.

- **Imaging: either X-ray or CT scan:**
    - ✓ **Chest X-ray:** *diagnostic*.
        - Findings for intrinsic disorders:
            - *The most common abnormal radio-graphical pattern→ reticular pattern.*
            - Honeycomb appearance in x-ray→ *advanced* fibrosis and poor prognosis.
            - Bilateral hilar lymphadenopathy→ suggest sarcoidosis.

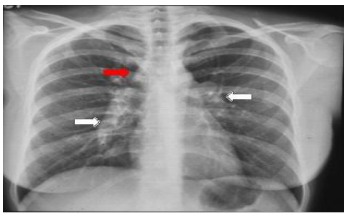


Figure 1: White arrows showing bilateral hilar lymphadenopathy.

    - ✓ **CT scan:** high radiation makes it unsuitable for every patient.

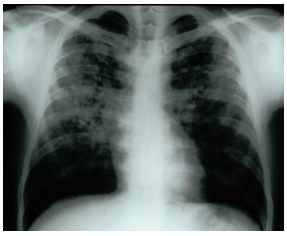


Figure 2:Reticular pattern with predominance of the upper zone.

3. **Pulmonary Function Test:**
    - ✓ Used for the diagnosis of restrictive lung disease and *determining the severity.*
4. **Spirometry and lung volume:**
    - ✓ Restrictive disorders are all associated with a *reduction in TLC, FRC and RV.*
    - ✓ Decreased FEV1 and FVC with normal or **increased FEV1:FVC ratio→** indicates a restrictive pattern.
5. **Diffusing Capacity of Carbon Monoxide (DLCO):**
    - ✓ Used *after* determining a 'restrictive pattern' in spirometry and lung volume test.
    - ✓ *It is the most sensitive parameter.*
    - ✓ The tool is used to either include or exclude intrinsic lung disease as a cause:
        - *A decrease in DLCO → intrinsic lung disease causing the restrictive pattern*
        - *A normal DLCO→ excludes intrinsic causes and includes the extrinsic causes.*
6. **Lung biopsy:**
    - ✓ It could provide information about the disease activity, exclude neoplastic or infectious processes and *predict the prognosis.*
    - ✓ *Video-assisted thoracoscopic lung biopsy is the preferred method for collecting a lung tissue sample for analysis.*
    - ✓ When suspecting sarcoidosis, good pasture syndrome or hypersensitivity pneumonitis→*Fiber optic bronchoscopy with transbronchial lung biopsy is often the initial procedure of choice.*

- **Diagnostic criteria for IPF:** *Require 4 major and ≥ 3 minors of the following:*

Clinical criteria for making a Dx of IPF in the absence of surgical lung biopsy	
Major Criteria	**Minor Criteria**
1. Exclude other causes of ILD (Drugs, connective tissue disease, and environmental exposure). 2. Evidence of restriction on spirometer, PFT, or impaired gas exchange at rest or with exercise. 3. Bibasilar reticular abnormalities. 4. Transbronchial lung biopsy or bronchoalveolar lavage showing no features to support other DDx.	1. Age>50Y/O 2. Insidious of unexplained dyspnea on exertion. 3. Illness duration ≥ 3 months. 4. Bibasilar inspiratory crackles.

- **Treatment:**
  - *Dependant on the specific diagnosis.*
  - **Lifestyle modification:** smoking cessation, weight loss.
  - **Oxygen therapy:** used when oxygen saturation is < *90%*.
  - **Preventive therapies:** the mainstay treatment of *neuromuscular* diseases.
  - **Treating extrinsic lung disease.**
  - **Pharmacological therapy:**
    - ***Corticosteroids****: first line of therapy and the most commonly used.*
    - **Cytotoxic therapy**: immunosuppressive agents, for patient who are not responding to steroids or experiencing SE.
      - Examples: methotrexate, azathioprine, or cyclophosphamide.
      - Cyclophosphamide: reserved for fulminant or refractory cases due to its potential serious toxicities.
    - **Anti-fibrotic agents (colchicine):** for fibrotic disorders, including IPF.
  - **Surgical treatment and lung transplantation.**

Failure of steroid therapy is defined as:

1. Fall in FVC or TLC by 10%.
2. Worsened radio-graphical image.
3. ↓ in gas exchange at rest or with exercise.

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