Team 435

PATHOLOGY

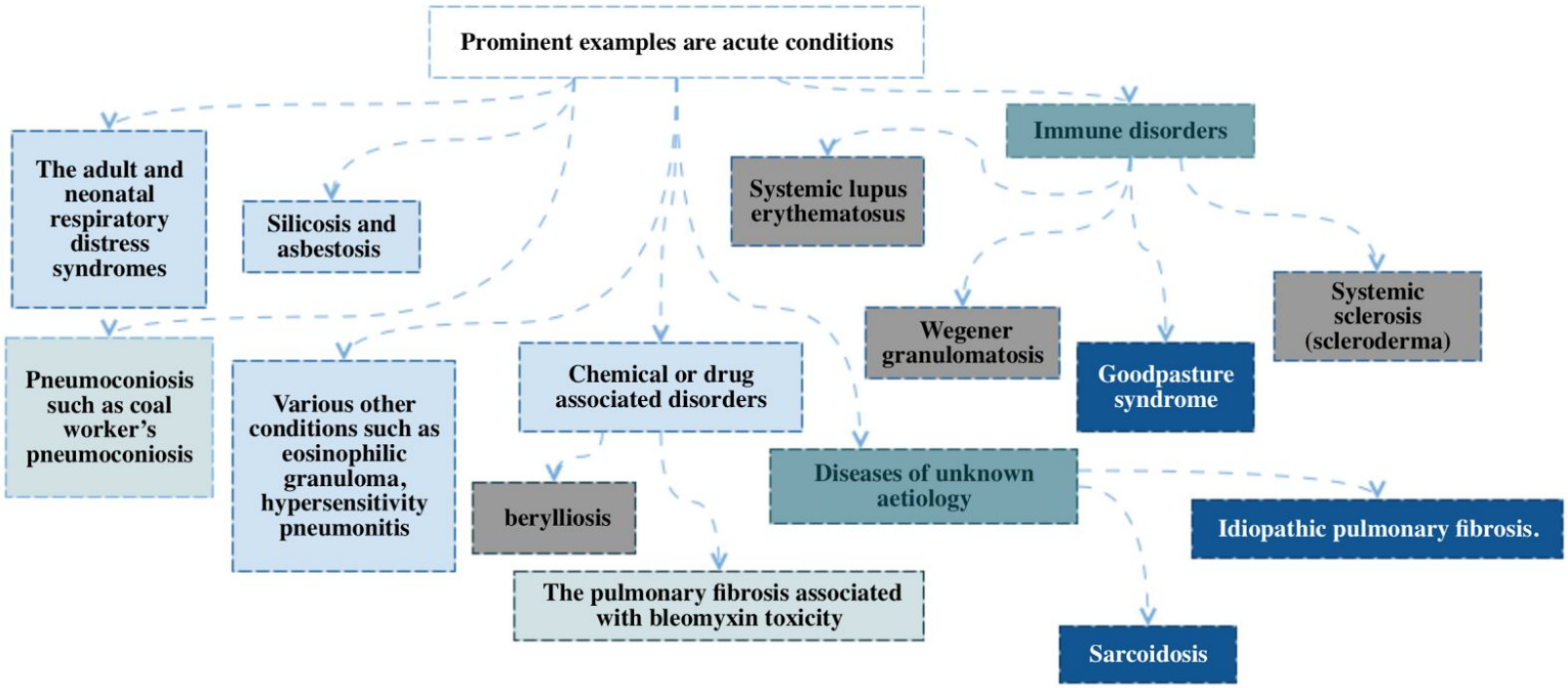
As a doctor you should know what can threaten your patient's life
should know what makes your patient suffers from pain

That's why you study pathology

Lecture 3

Restrictive Pulmonary Diseases:

A group of disorders characterized by reduced expansion of the lung, reduction in total lung capacity, increased work of breathing and inadequate ventilation and/or oxygenation (decreased lung compliance).



The hallmark feature of these disorders is reduced compliance (i.e., more pressure is required to expand the lungs because they are stiff), which in turn causes difficulty in breathing (dyspnea).

Divided into:

1. **Intrinsic lung diseases/ diseases of the lung parenchyma/primary interstitial lung disease**
2. **Extrinsic disorders or extraparenchymal diseases:**

   The chest wall, pleura, and respiratory muscles are the components of the respiratory pump, and they need to function normally for effective ventilation.

Pulmonary interstitium:

It is the area of the lung between the alveolar epithelial and capillary endothelial basement membranes (fused in the thinnest portions)

It is composed of:

- Elastic tissue.
- A few mast cells.
- Fibroblasts.
- Occasional mononuclear cells.

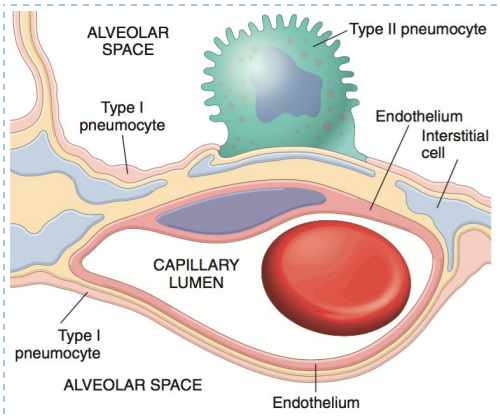


Figure 12–1 Microscopic structure of the alveolar wall. Note that the basement membrane *(yellow)* is thin on one side and widened where it is continuous with the interstitial space. Portions of interstitial cells are shown.

What are the changes that occur?

- ❏ Hypoxia.
- ❏ Diffuse infiltration by small nodules, irregular lines, or "ground-glass shadows." With progression, patients can develop respiratory failure, often in association with pulmonary hypertension and cor pulmonale.
- ❏ "Honeycomb" lung.

Major Categories of Chronic Interstitial Lung Disease:

1. **Occupational:**
   Pneumoconiosis:
   - Anthracosis and coal worker's pneumoconiosis.
   - Silicosis.
   - Asbestosis.
2. **Fibrosing:** (occupational diseases are also fibrosing diseases)
   Usual interstitial pneumonia (idiopathic pulmonary fibrosis).
3. **Immune diseases:**
   - **Sarcoidosis.**
   - **Goodpasture syndrome.**
   - **Hypersensitibity pneumonitis(extrinsic allergic alveolitis).**
   - Systemic lupus erythematosus.
   - Systemic sclerosis (scleroderma).
   - Wegener granulomatosis.
4. **Drugs:** **Chemotherapy, methotrexate, bleomyxin toxicity.**
5. **Radiation Reactions.**
6. **Smoking related:**
   - **Eosinophilic granuloma.**
   - **Desquamative interstitial pneumonia.**
   - **Respiratory bronchiolitis-associated interstitial lung disease.**

Table 12–3 Major Categories of Chronic Interstitial Lung Disease

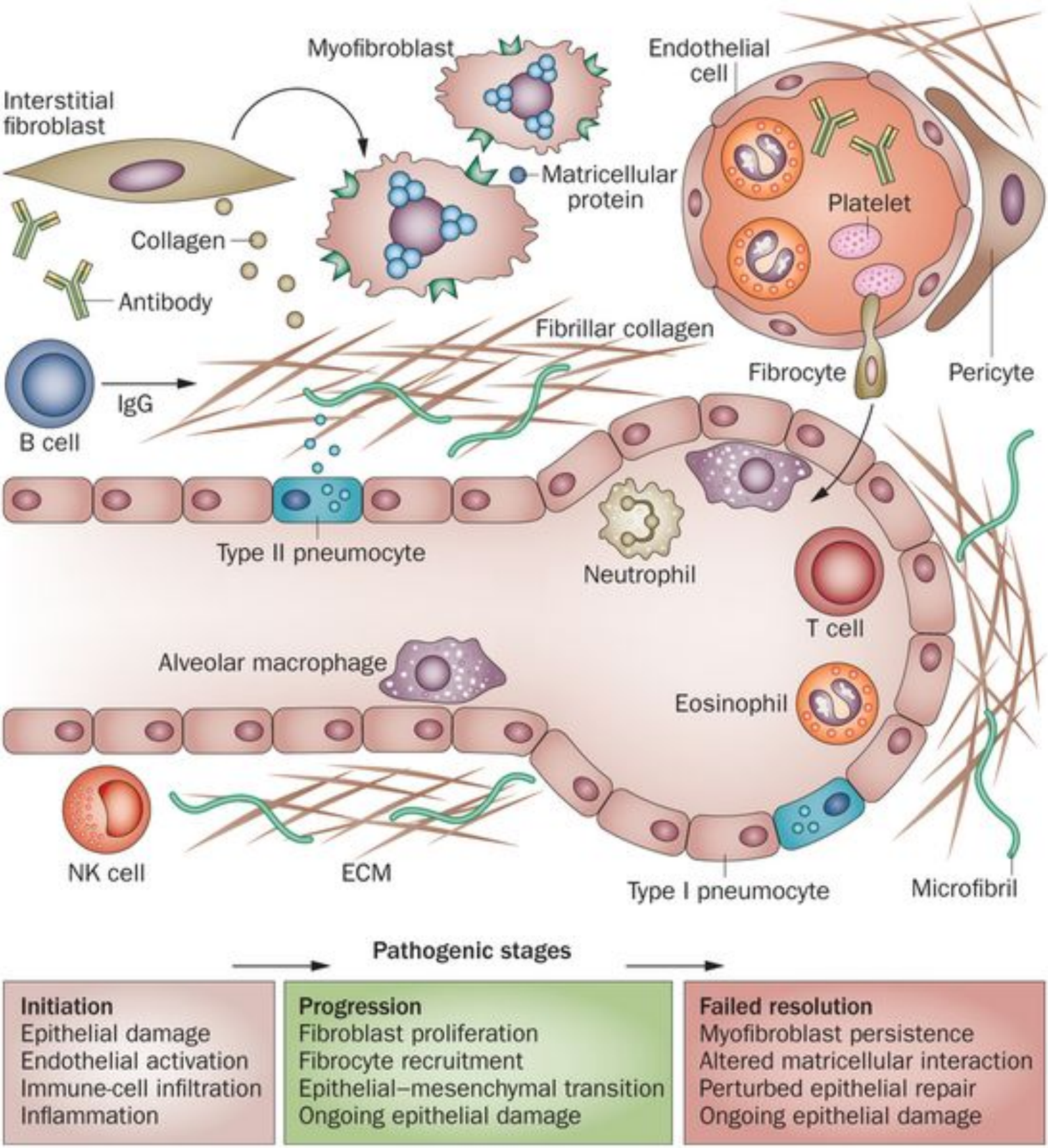
Fibrosing
Usual interstitial pneumonia (idiopathic pulmonary fibrosis)
Nonspecific interstitial pneumonia
Cryptogenic organizing pneumonia
Associated with collagen vascular disease
Pneumoconiosis
Associated with therapies (drugs, radiation)
Granulomatous
Sarcoidosis
Hypersensitivity pneumonia
Eosinophilic
Loeffler syndrome
Drug allergy–related
Idiopathic chronic eosinophilic pneumonia
Smoking-Related
Desquamative interstitial pneumonia
Respiratory bronchiolitis

Pathogenesis:

- Influx of inflammatory cells into the alveoli and alveolar walls.
- Distortion of the normal structure of alveoli.
- Release of chemical mediators.
- Promotion of fibrosis.

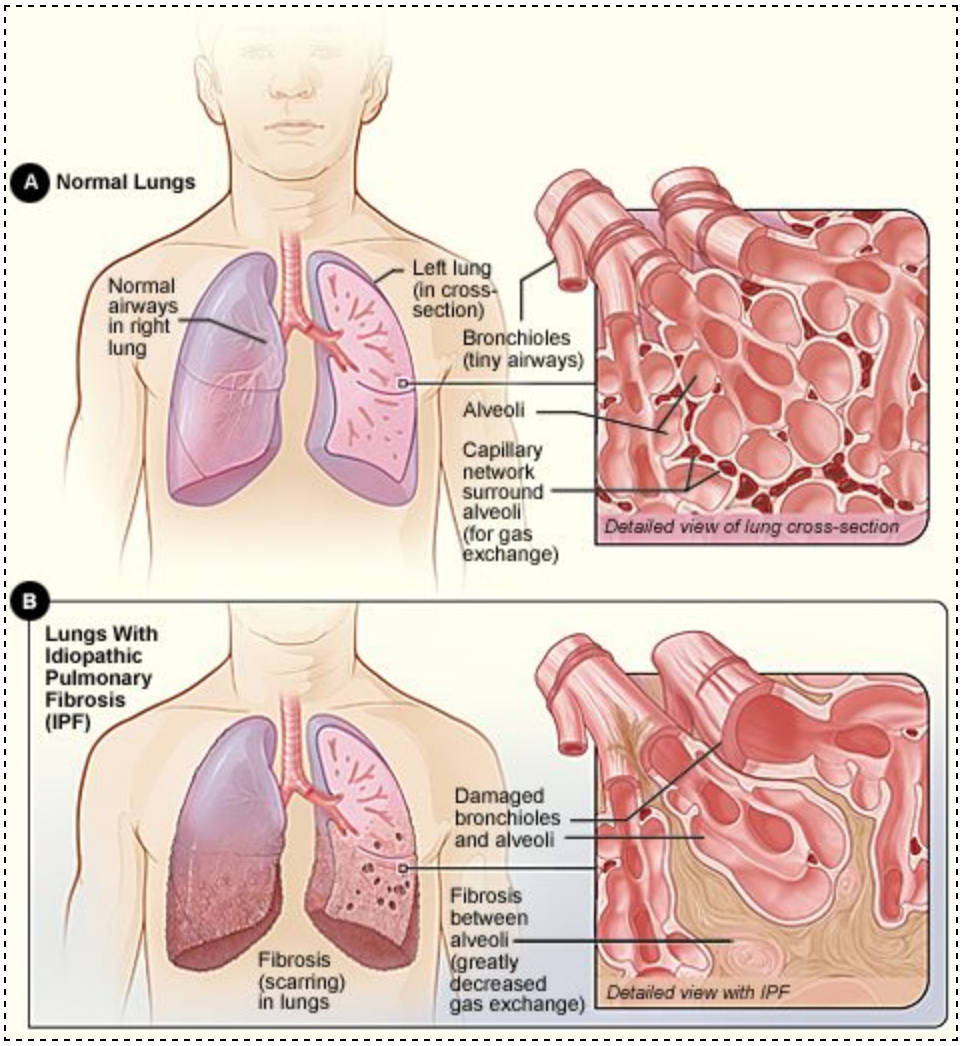
EXTRA

The summarized pathogenesis of Restrictive Lung Diseases



SUMMARY

- Diffuse interstitial fibrosis of the lung gives rise to restrictive lung diseases characterized by reduced lung compliance and reduced forced vital capacity (FVC). The ratio of FEV to FVC is normal.
- The diseases that cause diffuse interstitial fibrosis are heterogeneous. The unifying pathogenetic factor is injury to the alveoli with activation of macrophages and release of fibrogenic cytokines such as TGF-β. □
- Idiopathic pulmonary fibrosis is prototypic of restrictive lung diseases. It is characterized by patchy interstitial fibrosis, fibroblastic foci, and formation of cystic spaces (honeycomb lung). This histologic pattern is known as *usual interstitial pneumonia* (UIP). □

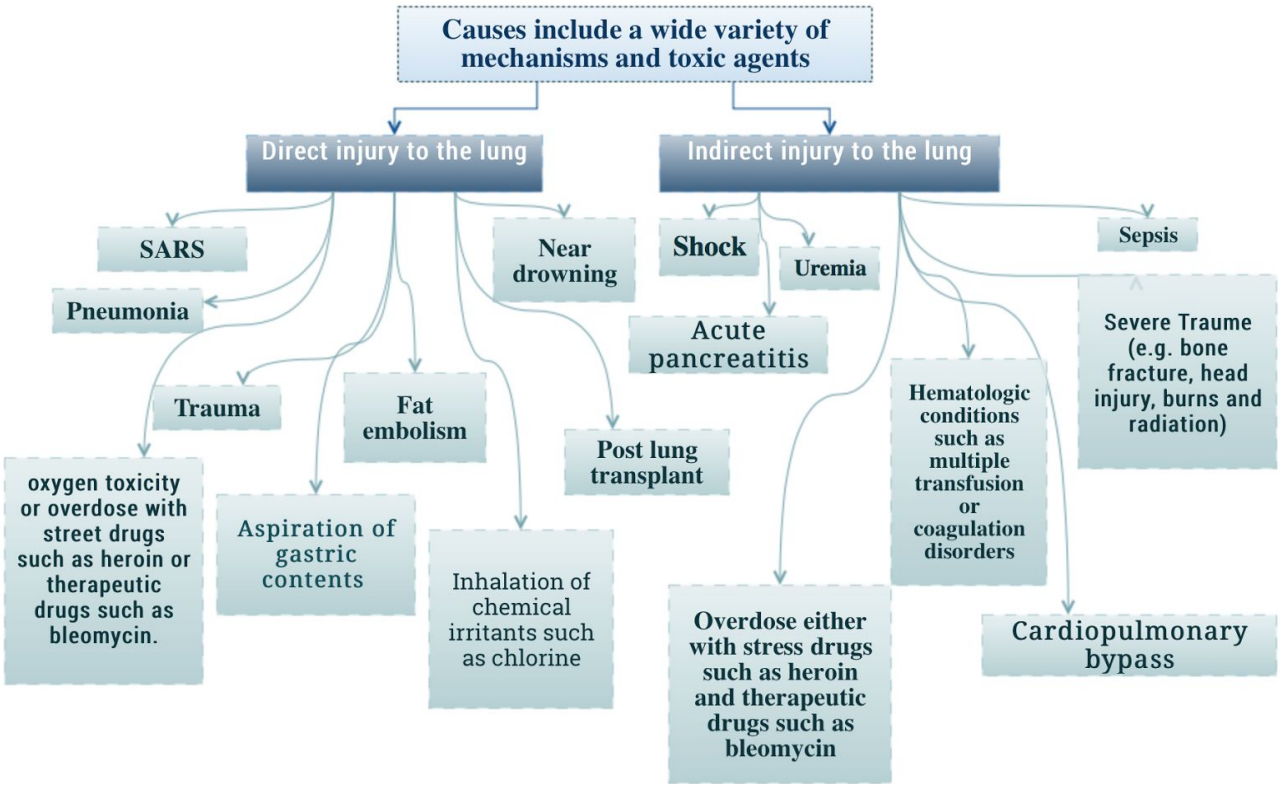


Acute Respiratory Distress Syndrome (ARDS): (Affects both adults and neonatal)

Adult respiratory distress syndrome:

ARDS is a severe form of acute lung injury with diffuse alveolar injury. Produced by diffuse alveolar damage with resultant increase in alveolar capillary permeability, causing leakage of protein-rich fluid into alveoli.

It is also known as shock lung/ diffuse alveolar damage/ adult respiratory failure/acute alveolar injury/ traumatic wet lung.
Characteristics include the formation of an **intra-alveolar hyaline membrane** composed of fibrin and cellular debris.



➔ ARDS can be a manifestation of the severe acute respiratory syndrome (SARS).

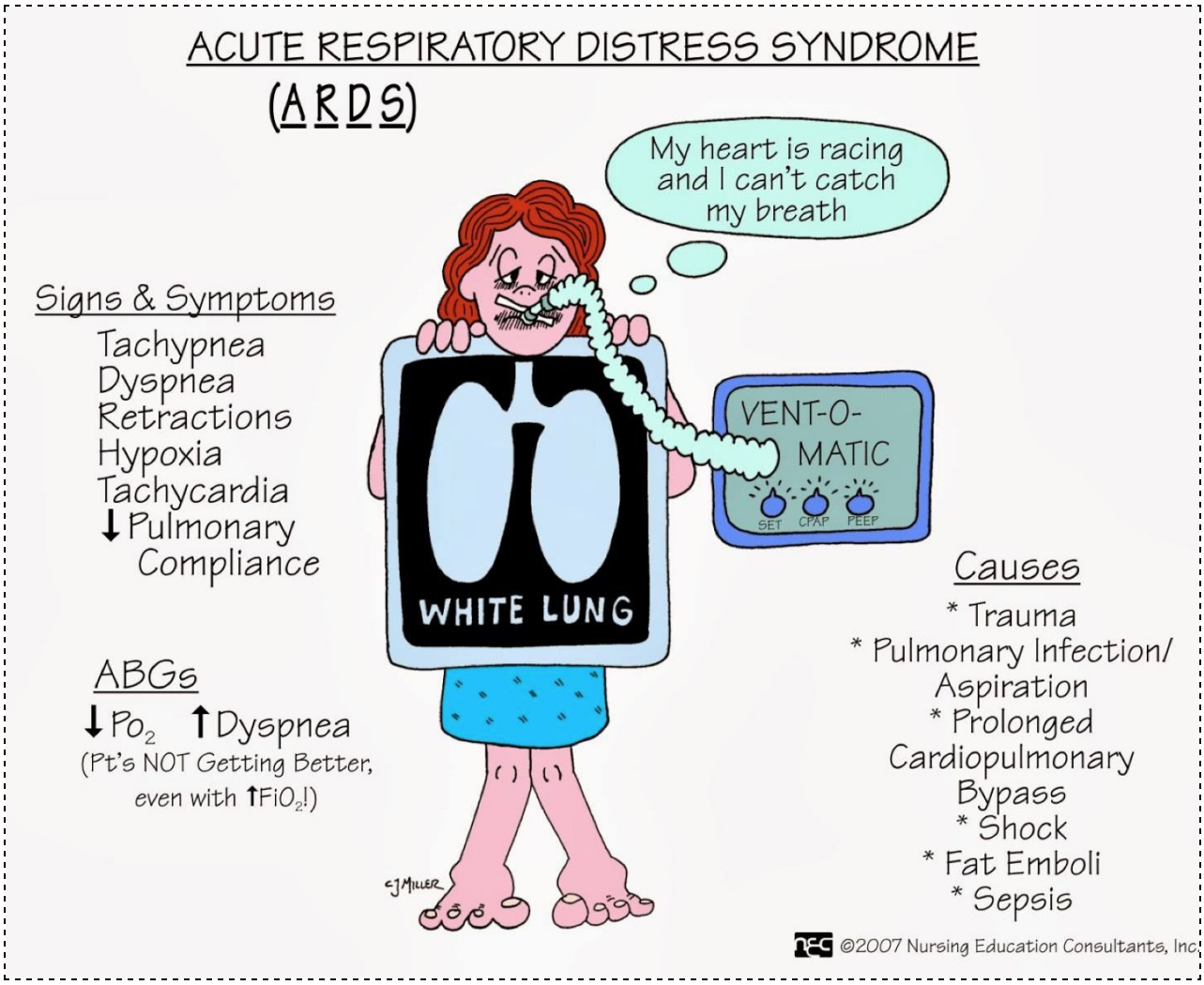
➔ ARDS is initiated by damage to alveolar capillary endothelium and alveolar epithelium.

It is:

- Rapid acute onset progressive severe life threatening respiratory insufficiency, cyanosis, severe arterial hypoxia.
- Decreased arterial oxygen pressure.
- Refractory to oxygen therapy and that may progress to multiorgan failure.
- Bilateral pulmonary infiltrates (edema).
- Absence of evidence of left sided heart failure.
- It is the most common cause of non- cardiogenic pulmonary edema

Clinical features characterized by:

- Cyanosis.
- May progress to multisystem organ failure.



Dr. Rikabbi's Note:

Usually caused by:

- Major trauma
- Aspiration of gastric juice
- Septicaemia
- Severe infections
- Shocks.

There are two types of ARDS:

- Direct:

  If the injury is in the interstitial area.. like the damage of the lining cells.

- Indirect:

  When there is a septicaemia which can cause some problems to the alveolar capillaries and then the alveoli.

Pathogenesis:

Diffuse alveolar damage which leads to → increase in alveolar capillary permeability which leads to →leakage protein rich fluid which leads to (in order of appearance):

1. **Exudative stage:**

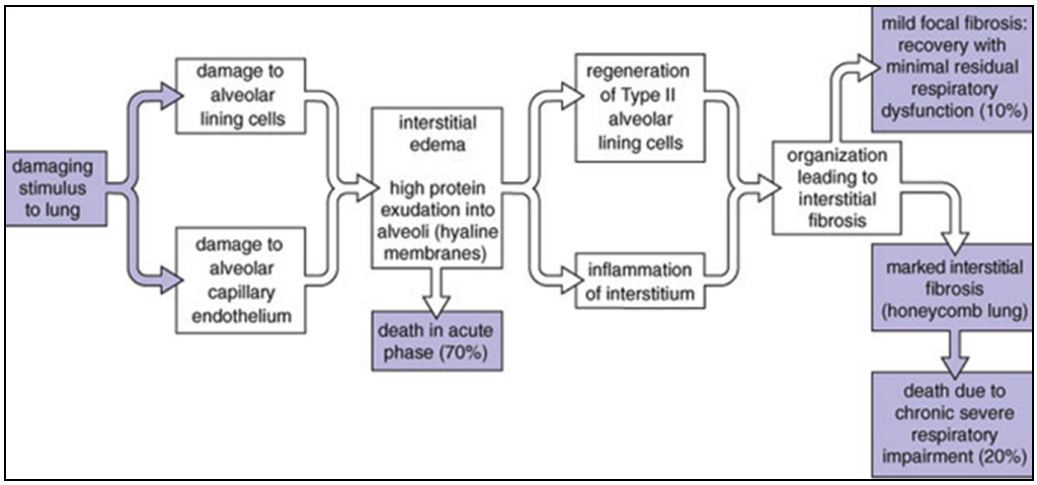
   The protein and necrotic cells layer out on the alveolar septae, forming hyaline membranes (composed of fibrin and cellular debris).

   The lungs become remarkably heavy and stiff due to inflammation and edema.

2. **Proliferative stage:**

   Occurs in response to the damage. Type II pneumocytes undergo hyperplasia (type I can't regenerate).

3. **Fibrosis.**



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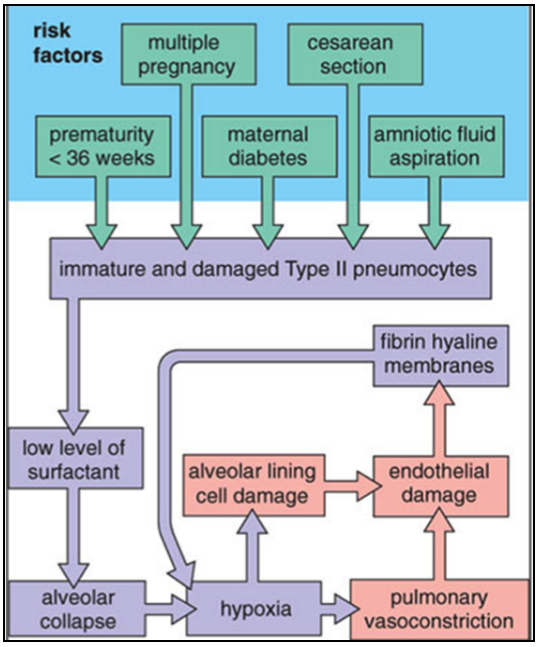
Neonatal Respiratory Distress Syndrome (Hyaline Membrane Disease)

General Considerations:



- Most common cause of respiratory failure in the newborn and is the most common cause of death in premature infants.
- It is the same as ARDS except that it is caused by a deficiency of pulmonary surfactants in new borns, most often as a result of immaturity.
- Marked by dyspnea, cyanosis and tachypnea shortly after birth.

Fibrosing Diseases:

1. Pneumoconiosis:

A group of pulmonary diseases caused by chronic exposure to inorganic mineral dust inhalation and this leads to lung damage. More than 40 inhaled minerals can cause lung problems. They include **carbon dust, silica, asbestos**, beryllium...

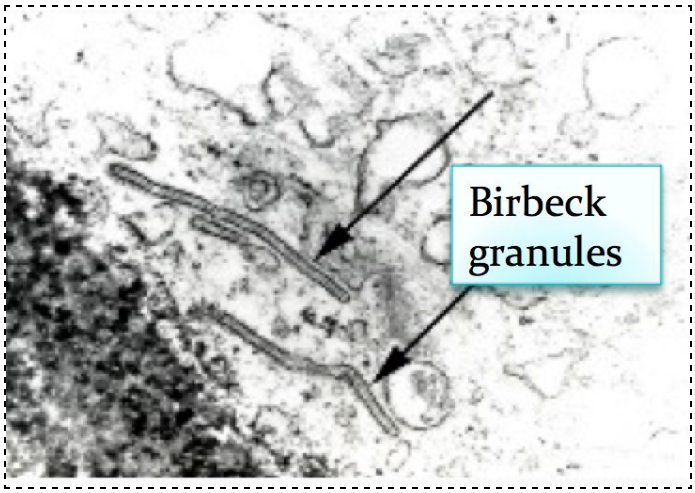
Pathophysiology:

- Alveolar macrophages ingest the particles, become activated, and release cytokines and chemotactic factors that recruit other inflammatory cells.
- The ensuing inflammation damages lung cells and also damages the interstitium of the lung by degrading the extracellular matrix glycoproteins.
- The inhaled particles also stimulate the fibroblasts to proliferate and produce collagen; fibrosis results.
- As the disease progresses the blood vessels become compromised, and ischemic necrosis ensues.

Eosinophilic Granuloma:

Proliferation of histiocytic cells related to Langerhan's cells of the skin.

- An uncommon interstitial lung disease in which there is accumulation of Langerhans cells in the lungs.
- It is considered as a form of smoking-related interstitial lung disease.
- Some patients recover completely after they stop smoking, but others develop long-term complications such as pulmonary fibrosis and pulmonary hypertension.
- It chiefly affects young adults in the third or fourth decades of life.
- It commonly involves the lungs. Other organ systems like bone, skin and lymph nodes may also be affected.
- They may be identified by immunohistochemical staining with CD1a or by the presence of rod like Birbeck granules via electron microscopy.



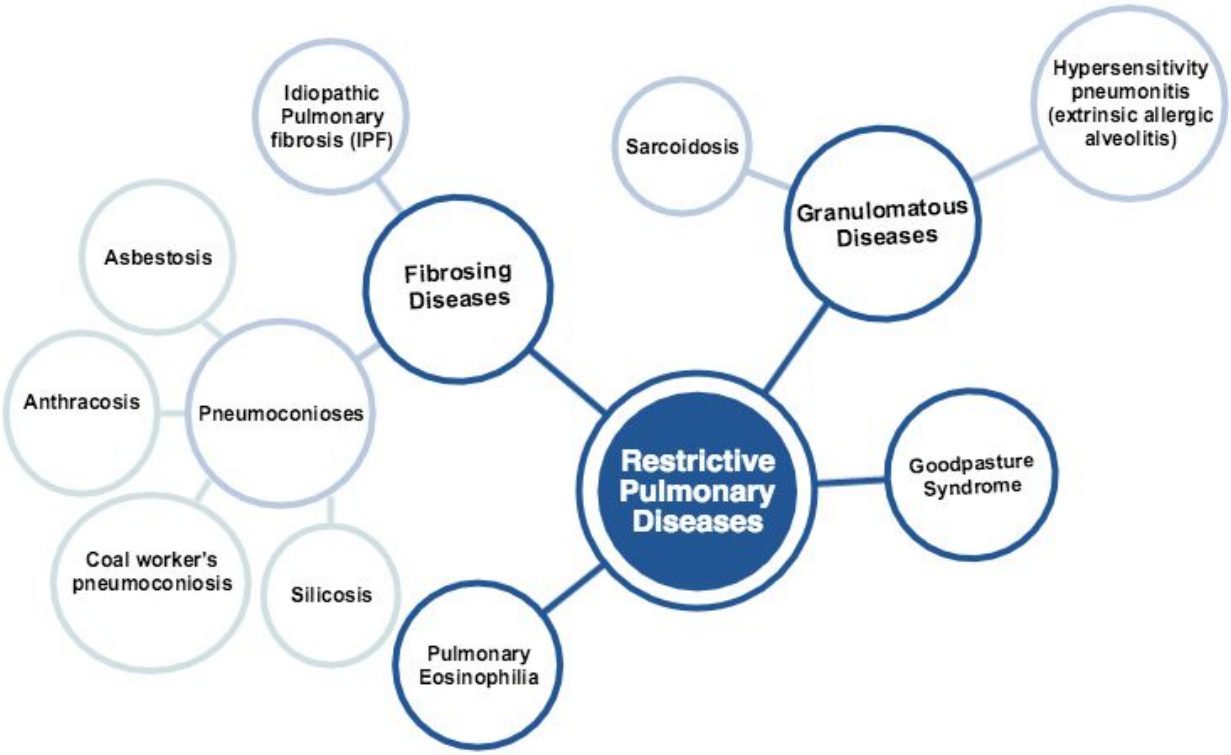
Hypersensitivity pneumonitis vs Asthma:

Primarily affects the **alveoli** ,called ***allergic alveolitis***	Affects the **larger airways**
Type 3&4, NO IgE antibodies or eosinophilia	**Type 1** hypersensitivity(IgE antibodies)

Summary

Name	Description	Characterized by	Classification	Extra Notes
Anthracosis	**Caused by inhalation of carbon dust.**	**Carbon-carrying macrophages, it results in irregular black patches visible on gross inspection**	**Fibrosing Disease, pneumoconiosis**	**Endemic in urban areas and causes no harm.**
Simple Coal worker's pneumoconiosis	**Caused by inhalation of coal dust, which contains both carbon and silica.**	**Coal macules around the bronchioles, formed by ingestion of coal dust particles by macrophages.**	**Fibrosing Disease, pneumoconiosis**	**Inconsequential and produces no disability.**
Progressive massive fibrosis, Coal worker's pneumoconiosis	**Caused by inhalation of coal dust, which contains both carbon and silica.**	**Fibrotic nodules filled with necrotic black fluid.**	**Fibrosing Disease, pneumoconiosis**	**It can result in bronchiectasis, pulmonary hypertension, or death from respiratory failure or cor pulmonale**
Silicosis	**Chronic occupational lung disease caused by exposure to free silica dust**	**A fine nodularity in the upper zones of the lung (called Silicotic nodules that enlarge and eventually obstruct the airways and blood vessels but pulmonary function is either normal or only moderately affected.**	**Fibrosing Disease, pneumoconiosis**	**Ingestion of silica dust by alveolar macrophages initiates an inflammatory response mediated by lysosomal enzymes increased susceptibility to tuberculosis**
Asbestosis	**Caused by inhalation of asbestos fibers.**	**The presence of ferruginous bodies and Dense hyalinized fibrocalcific plaques of the parietal pleura Marked predisposition to bronchogenic carcinoma and to malignant mesothelioma of the pleura or peritoneum. progressively worsening dyspnea cough & sputum.**	**Fibrosing Disease, pneumoconiosis**	**A fibroblastic response occurs, probably from release of fibroblast-stimulation growth factors by macrophages and leads to diffuse interstitial fibrosis mainly in the lower lobes.**
Idiopathic Pulmonary fibrosis (IPF)	**Immune complex disease with progressive fibrosis of the alveolar wall. Refers to a pulmonary disorder of unknown etiology.**	**- Fibroblast foci. - Temporal heterogeneity - Honeycomb fibrosis. - "dry" or "Velcro"-like crackles during physical examination inspiration.**	**Fibrosing Disease**	**- nonproductive cough - progressive dyspnea - Cyanosis - The mean survival is 3 years or less. - Lung transplantation is the treatment**

Name	Description	Characterized by	Classification	Extra Notes
Hypersensitivity pneumonitis	Interstitial pneumonia caused by inhalation of various antigenic substances exemplified by inhalation of spores of thermophilic actionomycetes from moldy hay causing "farmer's lung"	1. Acute Hypersensitivity Pneumonitis: Characterized by fever, cough, dyspnea, and constitutional signs and symptoms arising 4 to 8 hours after exposure, resolves with removal of the exposure. 2. Chronic Hypersensitivity Pneumonitis: Characterized by insidious onset cough, dyspnea, malaise, and weight loss.	Granulomatous Diseases	Failure to remove the inciting agent from the environment eventually results in an irreversible chronic interstitial pulmonary disease. Called extrinsic allergic alveolitis
Sarcoidosis	Multisystem disease of unknown etiology characterized by noncaseating granulomas in many tissues and organs	- Asymptomatic patients: Present with hilar lymphadenopathy - Symptomatic cases: Gradual appearance of respiratory symptoms (shortness of breath, dry cough, or vague substernal discomfort) or constitutional signs and symptoms (fever, fatigue, weight loss, anorexia, night sweats).	Granulomatous Diseases	- Increased incidence in nonsmokers. - The remissions may be spontaneous or initiated by steroid therapy and often are permanent. - Some develop permanent lung dysfunction or visual impairment and others develop progressive pulmonary fibrosis and cor pulmonale.
Goodpasture Syndrome	Hemorrhagic pneumonitis and glomerulonephritis caused by antibodies directed against glomerular basement membranes.	1. Hemoptysis 2. Later, glomerulonephritis and renal failure, 3. Progressing to uremia(blood in urine) and death.	Diffuse Alveolar hemorrhage syndrome	-



Questions:

1. A 63-year-old man has had progressively worsening dyspnea over the past 10 years. He has noticed a 5-kg weight loss in the past 2 years. He has a chronic cough with minimal sputum production and no chest pain. On physical examination, he is afebrile and normotensive. A chest radiograph shows extensive interstitial disease. Pulmonary function tests show diminished DLCO, low FVC, and normal FEV1/FVC ratio. Increased exposure to which of the following pollutants is most likely to produce these findings?

A. Carbon monoxide
B. Ozone
C. Silica
D. Tobacco smoke
E. Wood dust

2. A study of persons with a history of mining occupational exposure to inhaled dusts is performed. Though found in urban air in small amounts, this dust consists of 1- to 5-micron particles that are inert and insoluble. Fibrosis occurs only with large amounts of dust accumulation, mainly in upper lobes, with nodular opacities larger than 1 cm seen on chest radiographs. What is most likely in this dust?

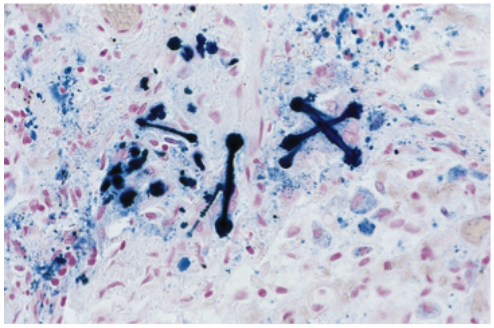
A. Asbestos
B. Beryllium
C. Carbon
D. Iron
E. Sulfur dioxide

3. A 76-year-old man has experienced increasing dyspnea for the past 4 years. On physical examination, he is afebrile, with a pulse of 70/min, respirations 30/min, and blood pressure 120/75 mm Hg. A chest radiograph shows increased interstitial markings, but no effusions. The right heart border and the pulmonary arteries are prominent. A transbronchial biopsy is performed; the figure shows the microscopic appearance with Prussian blue stain. Which of the following is the most likely diagnosis?

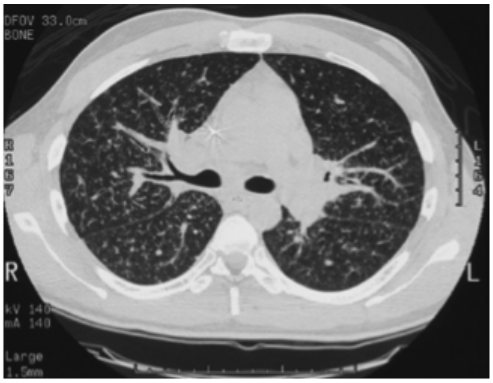
A. Anthracosis
B. Asbestosis
C. Berylliosis
D. Calcinosis
E. Silicosis

4. A radiographic study of inhalational lung diseases is conducted. One pattern of involvement is seen in persons whose total lung capacity, diffusing capacity, and compliance is decreased. This pattern consists of numerous bilateral nodular opacifications on chest radiographs. Polarizable needlelike crystals are seen on microscopic examination of these nodules. What inhaled substance is most likely to produce these findings?

A. Cigarette smoke
B. Mold spores
C. Silica dust
D. Sulfur dioxide
E. Wood particles



5. A 36-year-old woman has had a low-grade fever and worsening nonproductive cough and dyspnea for the past 2 years. On examination, she has breath sounds in all lung fields. A chest CT scan shows the findings in the figure. An arterial blood gas shows pH, 7.45; Po2, 83 mm Hg; Pco2, 30 mm Hg; and HCO3–, 19 mEq/L. Pulmonary function tests show total lung capacity 3 L (60% of predicted), FEV1 2.5 (66% of predicted), and DLCO 10 mL/min/mm Hg (50% of predicted). Her pulmonary compliance is reduced. What is the most likely diagnosis?



A. α1-Antitrypsin deficiency
B. Chronic bronchitis
C. Diffuse alveolar damage
D. Goodpasture syndrome
E. Nonatopic asthma
F. Sarcoidosis

6. A 65-year-old man worked in a shipyard for 10 years, and then he worked for 5 years for a company that installed fire retardant insulation. He experienced increasing dyspnea for 11 years with progressive respiratory failure and hypoxemia. A CT scan of his chest now shows a large mass encasing the left lung. Which of the following findings is most likely to be seen on a chest radiograph in this patient?

A. Bilateral fluffy perihilar infiltrates
B. Bilateral upper lobe cavitation
C. Diaphragmatic pleural calcified plaques
D. Endobronchial mass with atelectasis
E. Pleural effusions

7. A 61-year-old woman has noted increasing dyspnea and a nonproductive cough for 5 months. On physical examination, her temperature is 37.7° C. A chest radiograph shows prominent hilar lymphadenopathy with reticulonodular infiltrates bilaterally. A transbronchial biopsy is performed, and the microscopic findings include interstitial fibrosis and small, noncaseating granulomas. One granuloma contains an asteroid body in a Langhans giant cell. The medical history indicates that she smoked cigarettes for 10 years, but stopped 5 years ago. Which of the following is the most likely cause of her illness?

A. T cell-mediated response to unknown antigen
B. Antibody-mediated diffuse alveolar damage
C. Deposition of immune complexes
D. Infection with atypical mycobacteria
E. Smoke inhalation with loss of bronchioles

8. A 64-year-old alfalfa farmer has a 15-year history of increasing dyspnea. On physical examination, his temperature is 37.6° C. A chest radiograph shows a bilateral increase in linear markings. Pulmonary function tests show reduced FVC with a normal FEV1. A transbronchial lung biopsy specimen shows interstitial infiltrates of lymphocytes and plasma cells, minimal interstitial fibrosis, and small granulomas. What is the most likely cause of this clinical and pathologic picture?

A. Autoantibodies against alveolar basement membranes
B. Chronic inhalation of silica particles
C. Hypersensitivity to spores of actinomycetes
D. Infection with *Mycobacterium tuberculosis*
E. Prolonged exposure to inorganic dusts

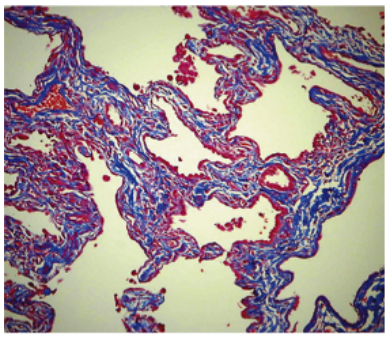
9. A 25-year-old man experiences acute onset of fever, cough, dyspnea, headache, and malaise a day after moving into a new apartment. His symptoms subside over 3 days when he visits a friend in another city. On the day of his return, the symptoms recur. There are no remarkable findings on physical examination. A chest radiograph also is unremarkable. Which of the following pathogenic mechanisms is most likely to produce these findings?

A. Antigen-antibody complex-mediated injury
B. Antibody-mediated injury to basement membrane
C. Formation of mycolic acid as a result of tubercular infection
D. Generation of prostaglandins by basophil recruitment
E. Release of histamine from mast cells
F. Toxic injury to type I pneumocytes caused by inhaled dust

10. A 29-year-old man who has had no major illnesses experiences acute onset of hemoptysis. On physical examination, he has a temperature of 37° C, pulse of 83/min, respirations of 28/min, and blood pressure of 150/95 mm Hg. A chest radiograph shows bilateral fluffy infiltrates. A transbronchial lung biopsy on microscopic examination shows focal necrosis of alveolar walls associated with prominent intra-alveolar hemorrhage. Two days later, he has oliguria. The serum creatinine level is 2.9 mg/dL, and urea nitrogen is 31 mg/dL. Which of the following antibodies is most likely involved in the pathogenesis of his condition?

A. Anti–DNA topoisomerase I antibody
B. Anti–glomerular basement membrane antibody
C. Antimitochondrial antibody
D. Antinuclear antibody

11. A 41-year-old man has a 6-year history of increasing shortness of breath and weakness. On physical examination, he is afebrile and normotensive. A radiograph of his chest shows diffuse interstitial markings. Pulmonary function tests indicate diminished FVC, decreased DLCO (diffusing capacity), and a normal FEV1/FVC ratio. Which of the following sets of pathologic changes is most likely to be found in his lungs?



A. Acute inflammation of bronchial walls with prominence of eosinophils
B. Chronic inflammation with bronchial mucus gland hypertrophy
C. Dilation of airspaces distal to respiratory bronchioles
D. Honeycomb lung with extensive alveolar septal fibrosis
E. Widespread alveolar epithelial necrosis and prominent hyaline membranes

12. A 68-year-old man has had worsening dyspnea with a nonproductive cough for the past 9 months. On physical examination, he is afebrile and normotensive. On auscultation of the chest, diffuse dry crackles are heard in all lung fields. A chest radiograph shows irregular opacifications throughout both lungs. A transbronchial biopsy is obtained and the microscopic findings with trichrome stain are shown in the figure. Laboratory studies include negative serologic tests for ANA, anti–DNA topoisomerase I, ANCA, and anticentromere antibody. Despite glucocorticoid therapy, his condition does not improve, and he dies 2 years later. What is the most likely diagnosis?

A. Goodpasture syndrome
B. Hypersensitivity pneumonitis
C. Idiopathic pulmonary fibrosis
D. Sarcoidosis
E. Systemic sclerosis

13. A 19-year-old man has a history of recurrent mucoid rhinorrhea with chronic sinusitis and otitis media since childhood. He has experienced multiple bouts of pneumonia. His temperature is 37.7° C. On examination of his chest, there is tactile fremitus, rhonchi, and rales in lower lung fields. Nasal polyps are noted. A chest radiograph shows bronchial dilation with bronchial wall thickening, focal atelectasis, and areas of hyperinflation; his heart shadow appears mainly on the right. Which of the following abnormalities is he most likely to have?

A. α1-Antitrypsin deficiency
B. Atopy
C. Chloride ion channel dysfunction
D. Ciliary dyskinesia
E. HIV infection

14. A 26-year-old woman with postpartum sepsis is afebrile on antibiotic therapy, but she has had worsening oxygenation over the past 3 days. Her chest radiograph shows scattered bilateral pulmonary opacifications. A ventilation-perfusion scan shows areas of mismatch. Which of the following microscopic findings is most likely to be present in her lungs?

A. Alveolar hyaline membranes
B. Arterial plexiform lesions
C. Interstitial fibrosis
D. Lymphocytic infiltrates

15. After a hemicolectomy to remove a colon carcinoma, a 56-year-old man develops respiratory distress. He is intubated and receives mechanical ventilation with 100% oxygen. Three days later, his arterial oxygen saturation decreases to 60%. A chest radiograph shows increasing opacification in all lung fields. A transbronchial lung biopsy specimen on microscopic examination shows hyaline membranes lining distended alveolar ducts and sacs. Which of the following is the most likely mechanism underlying these morphologic changes?

A. Aspiration of oropharyngeal contents
B. Intravascular thrombi with coagulopathy
C. Leukocyte-mediated injury to alveolar capillaries
D. Reduced production of surfactant
E. Release of fibrogenic cytokines by macrophages

16. A 78-year-old man has had increasing dyspnea without cough or increased sputum production for the past 4 months. On physical examination, he is afebrile. Breath sounds are reduced in all lung fields. A chest CT scan shows a dense, brightly attenuated pleural mass encasing most of the left lung. Microscopic examination of a pleural biopsy specimen shows spindle and cuboidal cells that invade adipose tissue. Inhalation of which of the following pollutants is the most likely factor in the pathogenesis of this mass?

A. Asbestos
B. Bird dust
C. Coal dust
D. Cotton fibers
E. Silica

17. Hypersensitivity pneumonitis is of type ..... Hypersensitivity:

A. III & VI
B. II & IV
C. III & IV
D. II & VI

18. Non-caseating interstitial granulomas is a characteristic of:

A. Hypersensitivity pneumonitis
B. Asbestosis
C. Anthracosis
D. Silicosis

19. Which oF of the following diseases is found in the insulation workers?

A. Asbestosis
B. Silicosis
C. Sarcoidosis

20. All are true about Sarcoidosis EXCEPT :

A. Characterized by caseating / necrotizing granulomas in affected organ tissue.
B. Unknown cause
C. Affecting all races
D. Affecting both sexes equally

21. Development of pneumoconiosis is dependent on:
    A. Infections
    B. Smoking
    C. Amount of fluid retained in the lungs
    D. Fibrosis of the parenchyma

22. A 35 year old woman who a long history of dyspnea, chronic cough, sputum production, and wheezing dies of respiratory failure following a bout of labor pneumonia.
She was a non-smoker and did not drink alcoholic beverage. This patient most likely has?
    A. Alpha 1 antitrypsin deficiency.
    B. Cystic fibrosis.
    C. Goodpasture syndrome.
    D. Hypersensitivity pneumonia.

23. Which of the following is considered to be a diffuse alveolar hemorrhage syndrome?
    A. Asthma
    B. Goodpasture Syndrome
    C. Hypersensitivity Pneumonitis
    D. Emphysema

24. Which of the following is an asymptomatic accumulation of coal pigment/carbon particles without consequent cellular reaction?
    A. Coal worker's pneumoconiosis
    B. Silicosis
    C. Anthracosis
    D. Asbestosis

25. Which of the following is not a fibrosing disease?
    A. Anthracosis
    B. Asbestosis
    C. Coal worker's pneumoconiosis
    D. Hypersensitivity pneumonitis

26. Which of the following is true about silicosis?
    A. Mesothelioma is a complication of psittacosis
    B. It is caused by exposure to asbestos fibers
    C. An increased risk exists of developing tuberculosis in patients with silicosis
    D. Patients with silicosis should not receive any antituberculous therapy

27. A 57-year-old man complains of long-standing respiratory distress that he worked for most of his adult life in locomotive repair shop.On examination he does not have fever, palpable lymph nodes or abnormal lung findings duct which one of the following is likely to be found on test roentgenogram?

A. Pulmonary vascular prominence
B. Pleural blebs
C. Enlarged right ventricle
D. Acute bronchopneumonia
E. Diffuse interstitial pulmonary fibrosis with irregular Or linear opacities

28.Workers exposed to asbestos have a risk to develop which type of cancer?

A. Mesothelioma
B. Bladder cancer
C. Bone cancer

29. 28-year-old man works in mining presents to the physician with dyspnea and blackish sputum. Further investigation showed that he suffers from rheumatoid arthritis, which of the following is most probably diagnosis :

A. Adult respiratory distress syndrome
B. Hyaline membrane disease
C. Goodpasture syndrome
D. Caplan syndrome

30. which one of the following is indirect injury to lung:

A. Far embolism
B. Sepsis
C. Pneumonia
D. Trauma

Answers:

1. **(C)** Silica crystals incite a fibrogenic response after inhalation and ingestion by pulmonary macrophages. The greater the exposure to silica dust and the longer the time of exposure, the greater is the lung injury. Silica is a major component of the earth's crust, including sand, which contains the mineral quartz. Mining, manufacturing, farming, and construction/renovation activities generate small silica crystals that can be inhaled, and their buoyancy allows them to be carried to alveoli. There, they are ingested by macrophages, which secrete cytokines that recruit other inflammatory cells and promote fibrogenesis. Carbon monoxide readily crosses the alveolar walls and binds avidly to hemoglobin, but does not injure the lung directly. Ozone, a component of smog, has no obvious pathologic effects. Tobacco smoke leads mainly to loss of lung tissue and emphysema, not to fibrosis. Particulate matter such as wood dust is mainly screened out by the mucociliary apparatus of the upper airways, but may invoke bronchoconstriction.

2. **(C)** Coal worker's pneumoconiosis (CWP) is now less common because of workplace safeguards in mining. Coal dust is relatively inert, so that large amounts must be inhaled before a fibrogenic response occurs, but the response continues over many years. The other listed substances are more reactive. Asbestos produces ferruginous bodies. Chronic berylliosis tends to be associated with sarcoid like granulomas. Iron produces siderosis with fibrosis. Sulfur dioxide is a gas that contributes to obstructive lung diseases, particularly chronic bronchitis and asthma.

3. **(B)** The ferruginous bodies shown in the figure are long, thin crystals of asbestos that have become encrusted with iron and calcium. The inflammatory reaction incited by these crystals promotes fibrogenesis and resultant pneumoconiosis. Anthracosis is a benign process seen in city dwellers as a consequence of inhaled carbonaceous dust. Chronic berylliosis is marked by noncaseating granulomas. Calcium deposition may rarely occur along alveolar walls when the serum calcium level is very high (metastatic calcification). Silica crystals are not covered by iron and tend to result in formation of fibrous nodules (silicotic nodules).

4. **(C)** Silicotic nodules form when the silica crystals ingested by macrophages elicit a fibrogenic response as cytokines, such as tumor necrosis factor, are released. The nodules may become confluent with progressive massive fibrosis. Pneumoconioses such as silicosis lead to restrictive lung disease. Cigarette smoke contributes to loss of lung parenchyma with emphysema. Mold spores tend to elicit a hypersensitivity pneumonitis that rarely goes on to extensive restrictive lung disease. Sulfur dioxide in polluted air tends to drive chronic obstructive lung disease. Wood dust tends to elicit an asthmatic response.

5. **(F)** She has a restrictive lung disease; the figure shows hilar adenopathy and a reticulonodular pattern of infiltrates characteristic of sarcoid. The blood gas values show mild hypoxemia with a compensated respiratory alkalosis. Because there is no obstructive disease, the CO2 can be normal or low from increased respirations to compensate for the diffusion block (with low DLCO). α1-Antitrypsin deficiency and chronic bronchitis lead to obstructive lung disease with increased total lung capacity and diminished FEV1 and respiratory acidosis. Chronic bronchitis is defined by prolonged sputum production. Diffuse alveolar damage is an acute restrictive lung disease from a severe underlying injury, such as sepsis. Goodpasture syndrome results in pulmonary hemorrhage with hemoptysis. Asthma is an acute obstructive lung disease with dyspnea and wheezing.

6. **(C)** This patient has an occupational risk of asbestos exposure. The inhaled asbestos fibers become encrusted with iron and appear as the characteristic ferruginous bodies with iron stain. The firm, tan mass encasing the pleura is most likely a malignant mesothelioma. Asbestosis more commonly gives rise to pleural fibrosis and interstitial lung disease, similar to other pneumoconioses. This is seen grossly as a dense pleural plaque, which often is calcified. Asbestosis can give rise to bronchogenic carcinoma, especially in smokers. Fluffy infiltrates suggest an infectious process. Upper lobe cavitation suggests secondary tuberculosis. An endobronchial mass could be a carcinoid tumor, which is not related to asbestosis. The pleural mass likely leads to obliteration of the pleural space, with no effusion.

7. **(A)** The clinical and morphologic features strongly suggest sarcoidosis. This granulomatous disease has an unknown cause, but the presence of granulomas and activated T cells in the lungs indicates a delayed hypersensitivity response to some inhaled antigen. Lung involvement, occurring in about one third of cases, may be asymptomatic or may lead to restrictive lung disease. Sarcoidosis can involve multiple organs, particularly those of the mononuclear phagocyte system, especially lymph nodes. Diffuse alveolar damage is an acute lung injury seen in acute respiratory distress syndrome. Hypersensitivity pneumonitis is an immune complex disease that is triggered by inhaled allergens. This form of lung disease is characterized by acute dyspneic episodes. The disease starts with type III hypersensitivity, but there can sometimes be granulomas in the lung, and lymph node enlargement is not seen. Atypical mycobacteria cause caseating granulomas, as does *Mycobacterium tuberculosis.* Smoking causes chronic bronchitis and emphysema.

8. **(C)** Farmer's lung is a form of hypersensitivity pneumonitis caused by inhalation of actinomycete spores in moldy hay. These spores contain the antigen that incites the hypersensitivity reaction. Because type III (early) and type IV immune hypersensitivity reactions are involved, granuloma formation can occur. The disease abates when the patient is no longer exposed to the antigen. Chronic exposure can lead to more extensive interstitial lung disease. Antibodies directed against pulmonary basement membrane are a feature of Goodpasture syndrome, which mainly produces pulmonary hemorrhage. Silicosis can produce a restrictive lung disease with fibrosis, but there are nodules of fibrosis that develop over years with minimal inflammation. Pulmonary tuberculosis can produce granulomas, but the pattern would be miliary, and it is unlikely that it would continue for 15 years. Pneumoconioses with exposure to dusts such as silica can produce interstitial fibrosis over many years, and the risk of neoplasia is increased slightly for silicosis and greatly for asbestosis.

9. **(A)** Hypersensitivity pneumonitis has acute symptoms that occur soon after exposure to an antigen, often actinomycetes or fungi (molds) growing in contaminated HVAC systems (air conditioner or ventilation ducts). The symptoms improve when the patient leaves the environment where the antigen is located. The pulmonary pathologic changes are usually minimal, with interstitial mononuclear infiltrates. It is mainly a type III hypersensitivity reaction, but with more chronic exposure to the antigen, there may be a component of type IV hypersensitivity with granulomatous inflammation and fibrosis. Attachment of antibody to basement membrane occurs in Goodpasture syndrome. Mycolic acid is a component of the cell wall of mycobacteria, and infections with these organisms are chronic, not episodic. Prostaglandins are produced by the cyclooxygenase pathway of arachidonic acid metabolism during acute inflammation, and they mediate pain and vasodilation. Histamine release is characteristic of a type I hypersensitivity reaction that more typically occurs in allergic disease. A toxic injury is more typical of inhalation of a toxic gas, such as sulfur dioxide (so-called silo filler's disease).

10. **(B)** Goodpasture syndrome leads to renal and pulmonary lesions produced by an antibody directed against an antigen common to the basement membrane in glomerulus and alveolus. This leads to a type II hypersensitivity reaction. The anti–DNA topoisomerase I antibody is a marker for scleroderma. Antimitochondrial antibody is associated with primary biliary cirrhosis. C-ANCA and P-ANCA are best known as markers for various forms of systemic vasculitis. ANA is used as a general screening test for various autoimmune conditions, typically collagen vascular diseases such as systemic lupus erythematosus.

11. (D) The pulmonary function data suggest a restrictive lung disease process. The progressive pulmonary interstitial fibrosis of a restrictive lung disease such as a pneumoconiosis can eventually lead to dilation of remaining residual proximal airspaces, giving a honeycomb appearance. The loss of lung tissue with emphysema also leads to airspace dilation, but without alveolar wall fibrogenesis. Eosinophilic infiltrates suggest atopic asthma, an episodic disease without fibrogenesis. The increase in mucous glands with chronic bronchitis leads to copious sputum production, but not fibrogenesis. Hyaline membranes, edema, inflammation, and focal necrosis are features of diffuse alveolar damage (acute respiratory distress syndrome) in the acute phase; if patients survive for weeks, diffuse alveolar damage may resolve to honeycomb change.

12. (C) The cause of many slowly progressive cases of restrictive lung disease is unknown, and the frustrated but empathetic health care provider can only say, "I am sorry, but there is nothing more that we can do." These cases must be distinguished from cases with identifiable causes, such as infection, collagen vascular disease, drug use, and pneumoconioses. Idiopathic pulmonary fibrosis leads to progressive restrictive lung disease. An unknown antigen incites the TH2 inflammatory process with activated macrophage release of cytokines such as fibroblast growth factor and TGF-β1. TGF-β1 down-regulates telomerase activity and leads to epithelial cell apoptosis. TGF-β1 diminishes caveolin-1, a protein that inhibits fibrosis. Goodpasture syndrome is a form of type II hypersensitivity characterized by diffuse pulmonary hemorrhage superimposed upon normal lung. Hypersensitivity pneumonitis may have an element of type IV hypersensitivity with some fibrosis, but usually not as severe or rapid as in this case. Sarcoidosis is marked by granulomatous inflammation. In this case, scleroderma is less likely because of the negative serologic test result.

13. (D) He has Kartagener syndrome (sinusitis, bronchiectasis, and situs inversus associated with ciliary dyskinesia). There is an abnormality of ciliary dynein arms that diminishes the mucociliary function of the respiratory epithelium, predisposing to recurrent and chronic infections of both upper and lower respiratory tract. Bronchiectasis is ongoing destruction and dilation of bronchi with infection and airway obstruction. α1-Antitrypsin deficiency leads to panlobular emphysema, mainly of lower lobes, and the upper respiratory tract is not involved. Atopy may be associated with nasal polyps, but leads to asthma, not bronchiectasis. Cystic fibrosis with *CFTR* gene mutations involving chloride ion channels can lead to widespread bronchiectasis, but generally not upper airway problems, and not situs inversus. HIV infection is marked by opportunistic infections with progression to AIDS, but usually without bronchiectasis, and no situs inversus.

14. (A) She has acute lung injury with noncardiogenic pulmonary edema and development of diffuse alveolar damage (DAD), clinically known as *acute respiratory distress syndrome* (ARDS). Inciting sepsis, trauma, or other forms of lung injury leads to a vicious cycle of inflammation with ongoing damage, mainly through the action of neutrophils. Plexiform lesions are characteristic for pulmonary hypertension. Though ARDS may eventually proceed to fibrosis, most patients do not survive that long. Lymphocytic infiltrates may be seen with infections such as viral pneumonias or immune-mediated lung diseases. Destruction of respiratory bronchioles is a feature of centrilobular emphysema.

15. (C) This clinical and morphologic picture is that of acute lung injury (ALI), which, when severe, leads to acute respiratory distress syndrome (ARDS). ARDS is characterized by the pathologic finding of diffuse alveolar damage (DAD), which is initiated in most cases by injury to capillary endothelium, with neutrophils and macrophages that aggregate in alveolar capillaries and release toxic oxygen metabolites, cytokines, and eicosanoids. Oxygen toxicity from high levels of inspired oxygen exacerbate DAD. The damage to the capillary endothelium allows leakage of protein-rich fluids. Eventually, the overlying alveolar epithelium also is damaged. Aspiration of bacteria causes bronchopneumonia. ARDS and disseminated intravascular coagulation (DIC) together can complicate septic shock, but DIC is not the cause of ARDS. Release of fibrogenic cytokines is an important cause of chronic diffuse pulmonary fibrosis. Reduced surfactant production causes respiratory distress syndrome with hyaline membrane disease in newborns.

16. (A). Malignant mesothelioma is a rare tumor even in individuals with a history of asbestos exposure. The tumor may appear decades after exposure, and is not related to amount or length of exposure. Bronchogenic carcinoma is more common in individuals with asbestos exposure, particularly when there is a history of smoking. Bird dust inhalation can lead to hypersensitivity pneumonitis. Coal dust inhalation can lead to marked anthracosis, but without a significant risk of lung cancer. Inhalation of cotton fibers (byssinosis) leads to symptoms resembling asthma related to bronchoconstriction. Ozone and nitrogen oxides in smog can cause acute respiratory discomfort, but are not known to be promoters of neoplasia. Silicosis is typified by interstitial fibrosis and causes a slight increase in the risk of bronchogenic carcinoma.

17. C

18. A

19. A

20. A

21. B

22. A

23. B

24. C

25. D

26. (C) Workers exposed through sandblasting, tunneling through rock with high quartz content or manufacture of abrasive soaps Silicosis. Chest x-ray findings include reticular pattern of irregular densities mostly in the upper lung zones. The nodular fibrosis may be progressive with formation of a irregular masses of greater than 1 cm each. These masses can become quite large and coalesce to progressive massive fibrosis. Calcification of hilar lymph nodes may occur in as little as 20% of cases and can produce the characteristic 'egg shell' calcification. Patients with silicosis are at higher risk of acquiring mycobacterium tuberculosis and atypical mycobacterial infections. Treatment or prophylaxis for tuberculosis is indicated in patients with silicosis and a positive tuberculin test.

27. (E) In locomotive repair shops, the workers are exposed to asbestos from the brake linings. on x-ray examination asbestos exposure causes diffuse interstitial pulmonary fibrosis that is slowly evolving and characterized by linear or irregular opacities of the lung. Usually, about 10 years elapse since first exposure to asbestos and the development of asbestosis. benign pleural effusions occur and these may resolve without treatment however enlargement of the right ventricle and decreased prominence of the pulmonary vascular are not features of asbestos on x-ray.

28. A

29. D

30. B

Contact us: pathology435@gmail.com

Team members

Nouf Altwaijri

Aljohara Almazroua

Ghaida Aljamili

Kowthar Almousa

Nojood Alhaidri

Nouf Alabdulkarim

Raghad Alnafisah

Rawan Aldhuwayhi

Reem AlAgeel

Samar AlOtaibi

Wael Al Oud

Abdulaziz AlHammad

Abdullah AlGhizzi

Abdulrahman Thekry

Ahmad Alkhiary

Ammar Almansour

Anas Ali

Faris Alwarhi

Khalid Ali Alghsoon

Mana AlMuhaideb

Naif Alhadi

Saleh Alkhalifa

Rayan Almuneef

Salem Al Ammari

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