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 1,2

Dr. Rikkabi's Note:

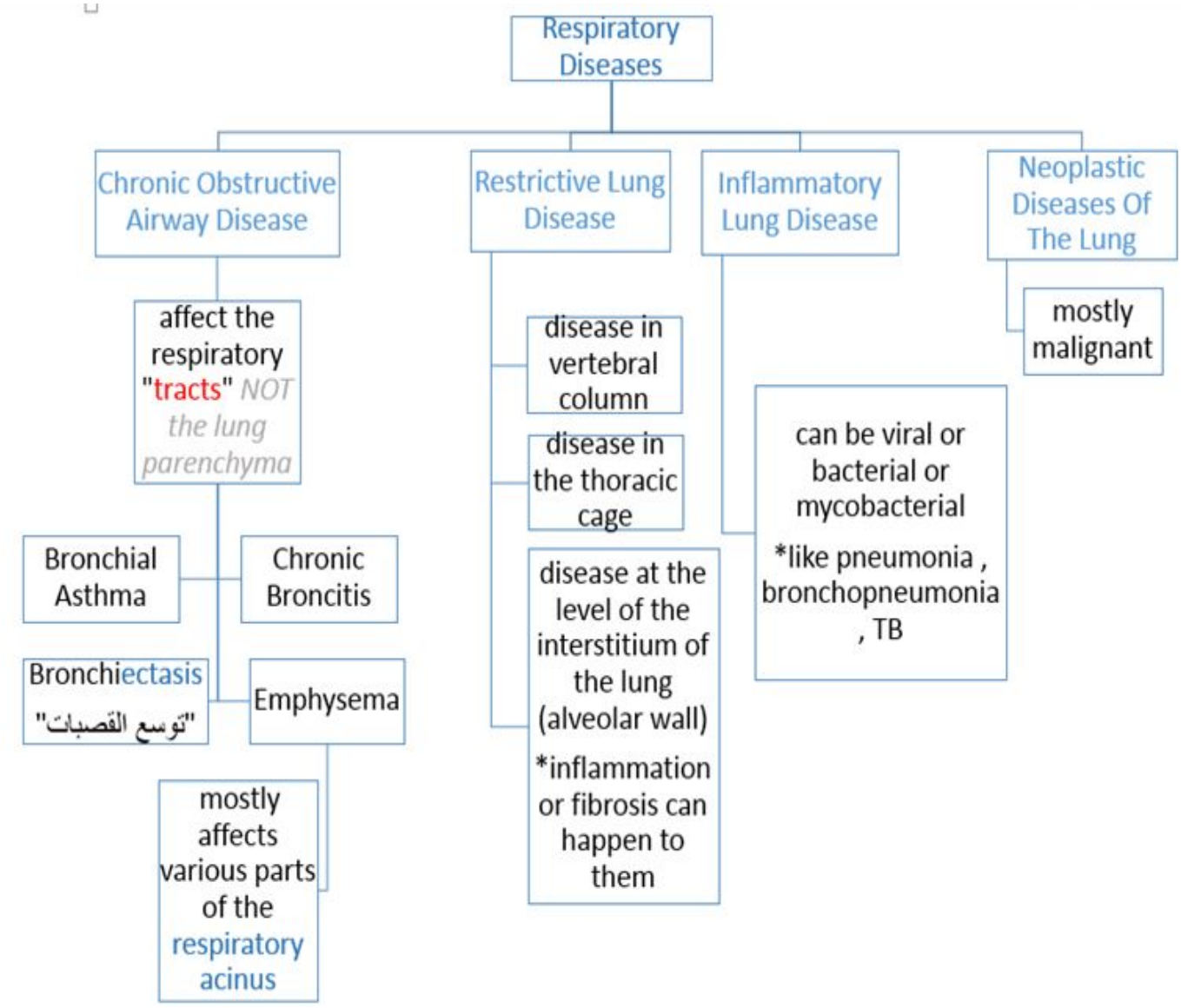
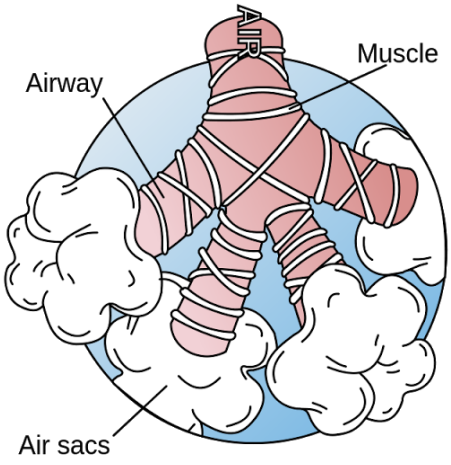


Table 12–2 Disorders Associated with Airflow Obstruction: The Spectrum of Chronic Obstructive Pulmonary Disease

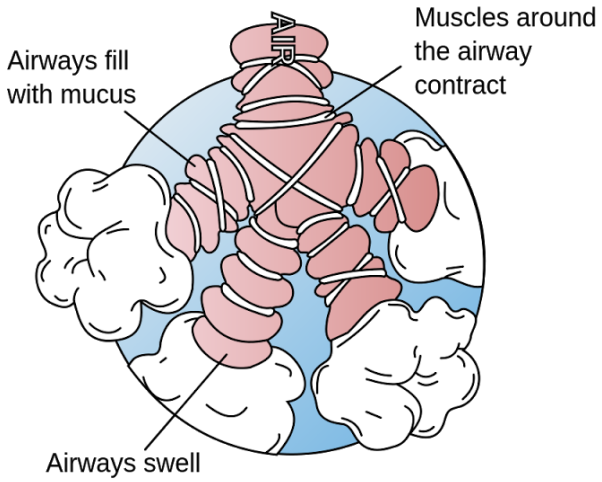
Clinical Entity	Anatomic Site	Major Pathologic Changes	Etiology	Signs/Symptoms
Chronic bronchitis	Bronchus	Mucous gland hypertrophy and hyperplasia, hypersecretion	Tobacco smoke, air pollutants	Cough, sputum production
Bronchiectasis	Bronchus	Airway dilation and scarring	Persistent or severe infections	Cough, purulent sputum, fever
Asthma	Bronchus	Smooth muscle hypertrophy and hyperplasia, excessive mucus, inflammation	Immunologic or undefined causes	Episodic wheezing, cough, dyspnea
Emphysema	Acinus	Air space enlargement, wall destruction	Tobacco smoke	Dyspnea
Small airway disease, bronchiolitis*	Bronchiole	Inflammatory scarring, partial obliteration of bronchioles	Tobacco smoke, air pollutants	Cough, dyspnea

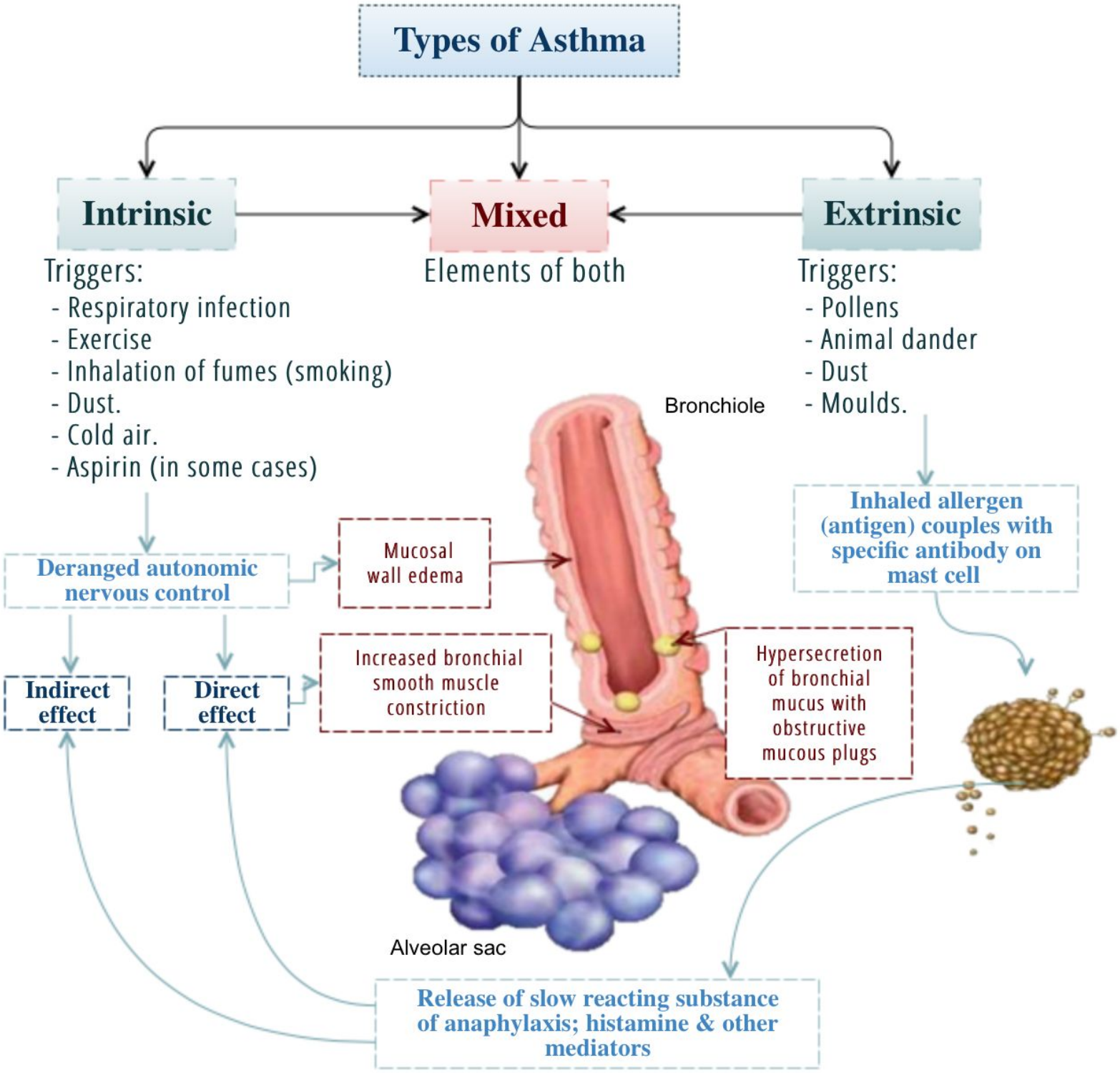
*Can be present in all forms of obstructive lung disease or by itself.

Before an asthma episode



After an asthma episode

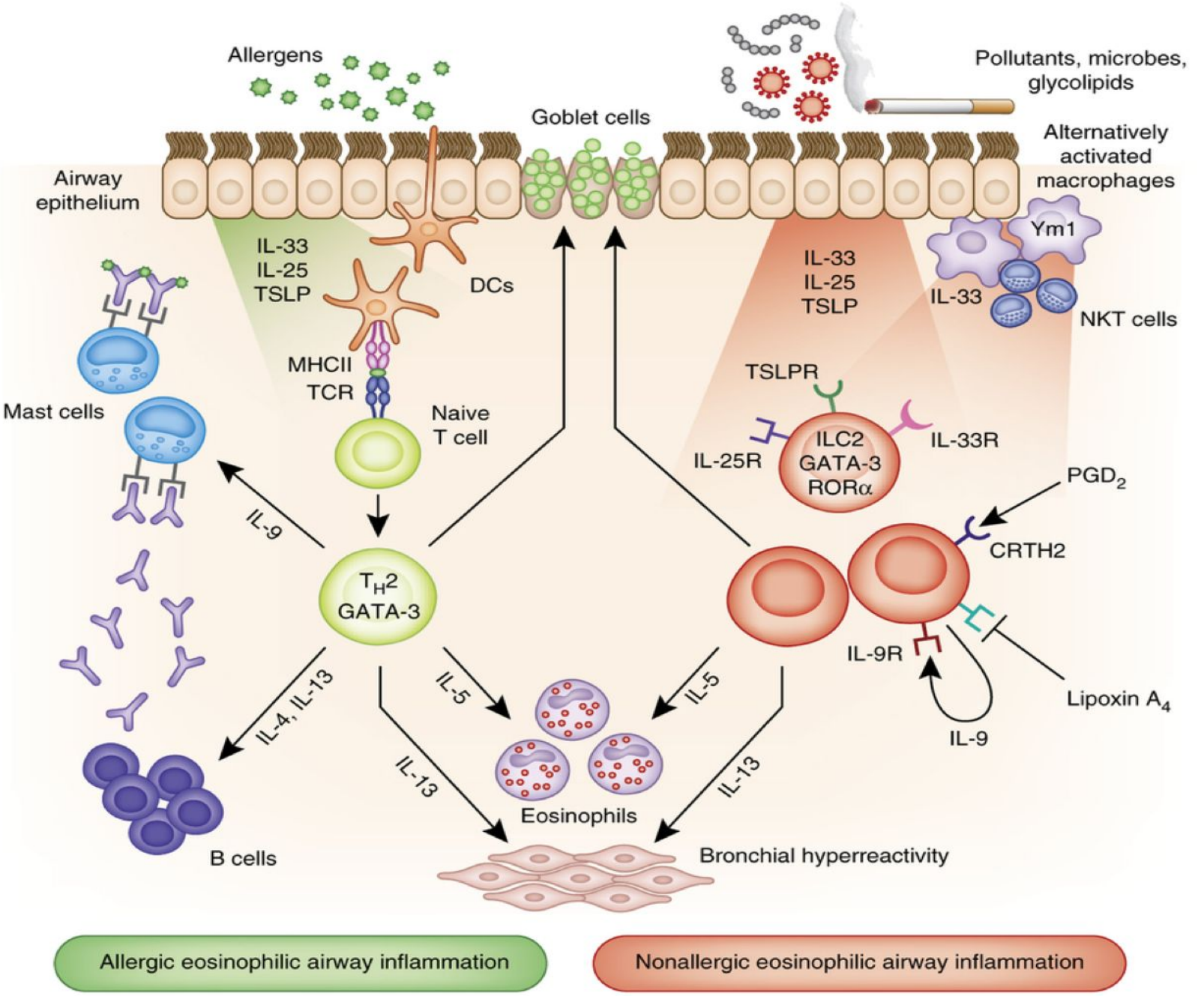



Types of Asthma
Intrinsic
Mixed
Extrinsic
Triggers:
- Respiratory infection
- Exercise
- Inhalation of fumes (smoking)
- Dust.
- Cold air.
- Aspirin (in some cases)
Elements of both
Triggers:
- Pollens
- Animal dander
- Dust
- Moulds.
Bronchiole
Deranged autonomic nervous control
Mucosal wall edema
Inhaled allergen (antigen) couples with specific antibody on mast cell
Indirect effect
Direct effect
Increased bronchial smooth muscle constriction
Hypersecretion of bronchial mucus with obstructive mucous plugs
Alveolar sac
Release of slow reacting substance of anaphylaxis; histamine & other mediators

	Extrinsic asthma	Intrinsic asthma
Definition	**Initiated by type one hypersensitivity reaction and used by exposure to an extrinsic allergen.**	**Initiated by diverse, nonimmune mechanism. Stimuli are intrinsic to body.**
Age of presentation	**Childhood**	**Adult**
Family history	**Present**	**Absent**
Preceding allergic reactions	**present in form rhinitis, urticaria, eczema**	**Absent**
Allergens	**Present**	**Absent**
Drug hypersensitivity	**Absent**	**Present, aspirin**
Serum IgE level	**Increased**	**Normal**
Skin test	**Positive**	**Negative**
Emphysema	**Unusual**	**Common**
Associated bronchitis	**Absent**	**Present**
Examples	**Atopic/ allergic asthma, occupational asthma, allergic bronchopulmonary aspergillosis.**	**Aspirin ingestion, pulmonary infection especially viral, cold, inhaled irritants, stress, exercise**

Extra

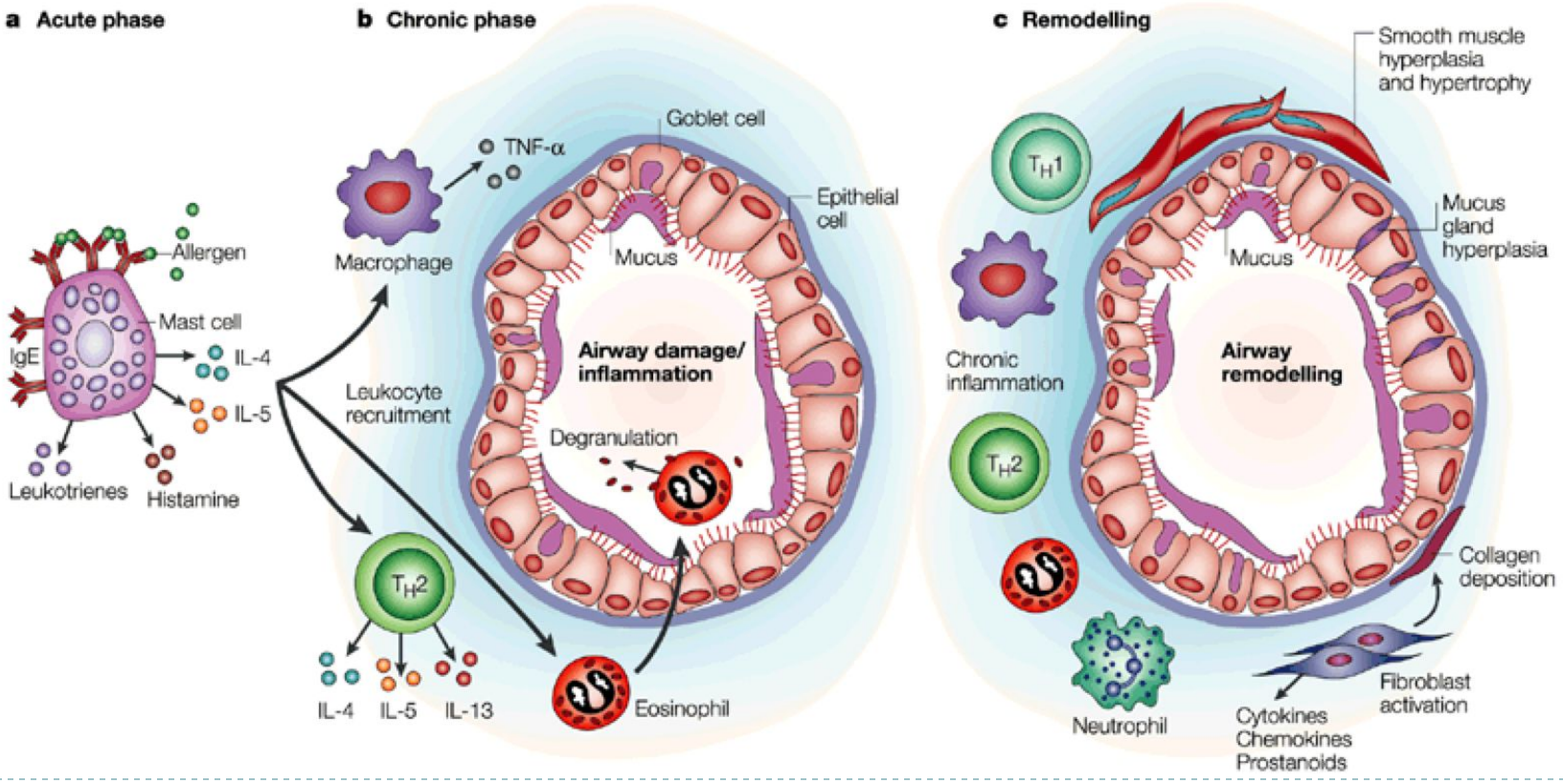
Relative roles of T_H2 cells and ILC2 cells in two forms of eosinophilic asthma.



In atopic asthma (left), eosinophilic airway inflammation and BHR are driven by adaptive T_H2 cells that are stimulated by DCs to produce IL-5, IL-13 and IL-4, the latter driving IgE synthesis. In nonatopic or intrinsic asthma (right), which is not dependent on adaptive immunity, ILC2 cells produce IL-5 and IL-13 and thus cause eosinophilia and BHR. As there is no specific allergen involved and as ILC2 cells produce little IL-4, there is no associated IgE response from B cells. Modified from ref. 185. MHCII, MHC class II; TSLPR, receptor for TSLP; NKT cells, natural killer T cells.

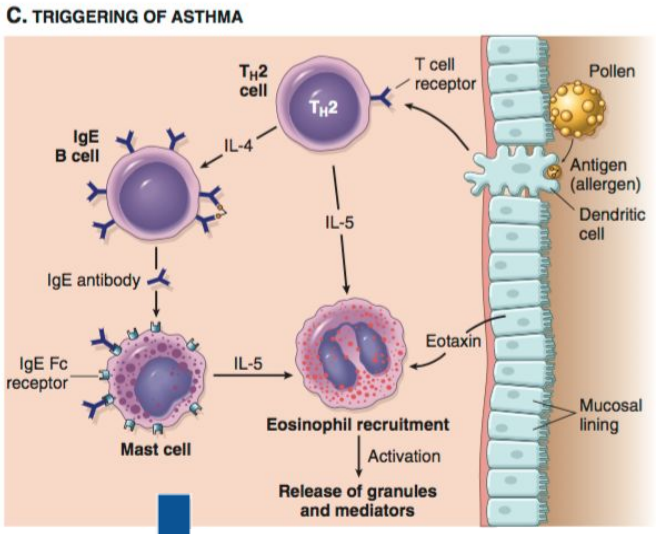
EXTRA

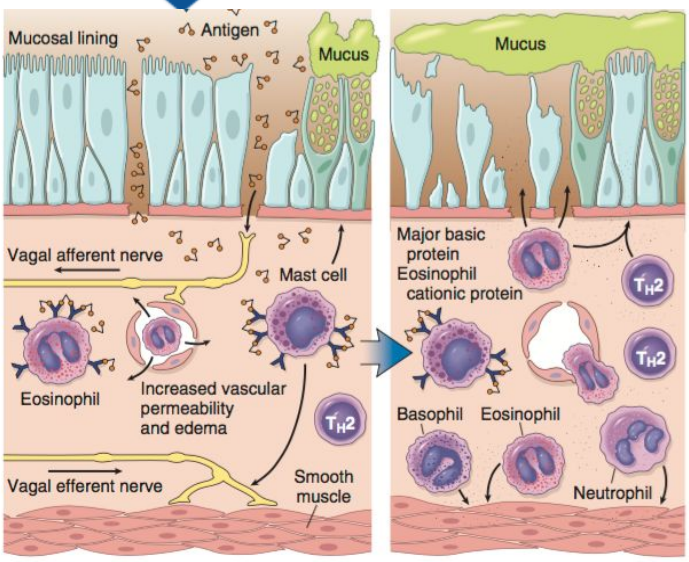
Explanation of Airway Remodeling

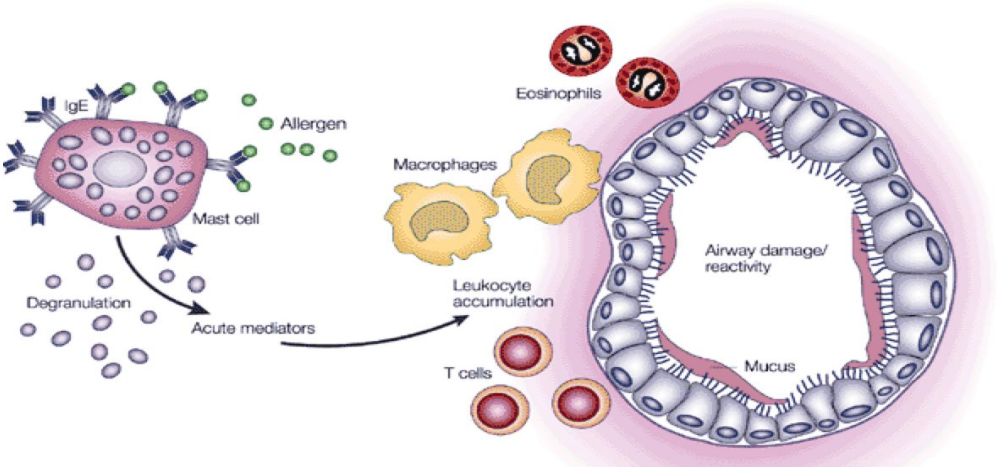


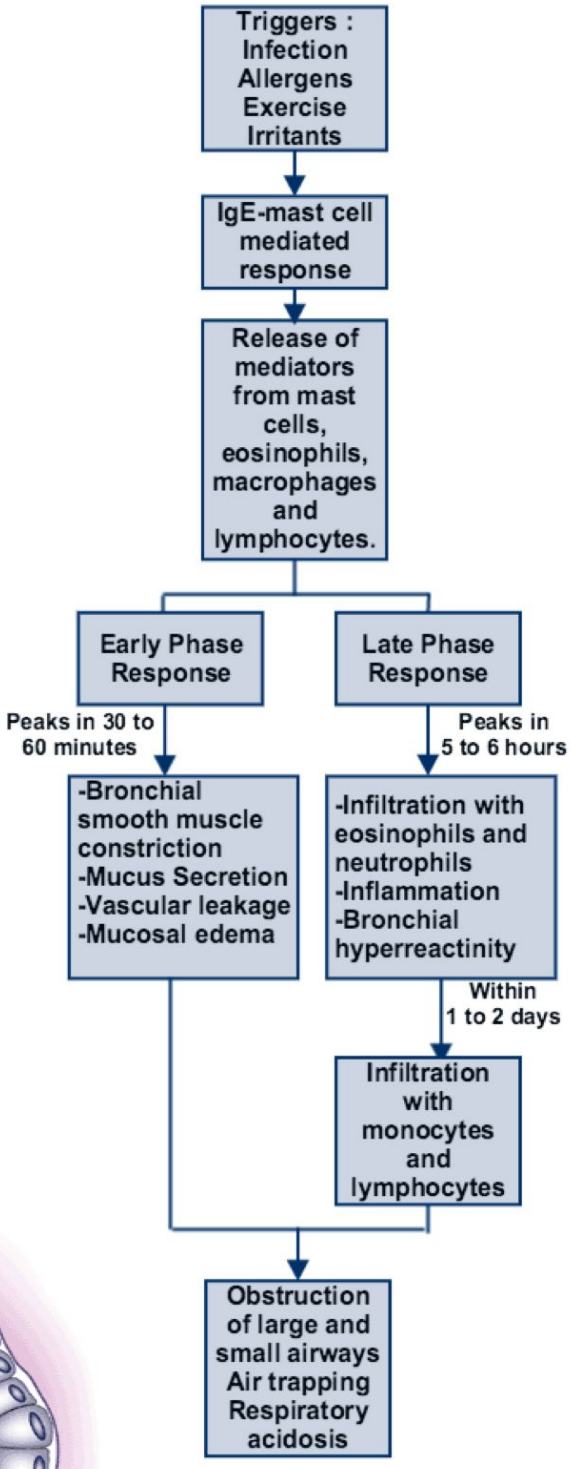
Airway remodeling refers to the structural changes that occur in both the large and the small airways of miscellaneous diseases, including asthma. In asthma, airway structural changes include subepithelial fibrosis, increased smooth muscle mass, enlargement of glands, neovascularization, and epithelial alterations. Although controversial, airway remodeling is commonly attributed to the underlying chronic inflammatory process. These remodeling changes contribute to thickening of airway walls and consequently lead to airway narrowing, bronchial hyperresponsiveness, airway edema, and mucous hypersecretion. Airway remodeling is associated with poorer clinical outcome among patients with asthma. Early diagnosis and prevention of airway remodeling has the potential to decrease disease severity, to improve control, and to prevent disease expression.

Summarized steps of the pathogenesis of Asthma





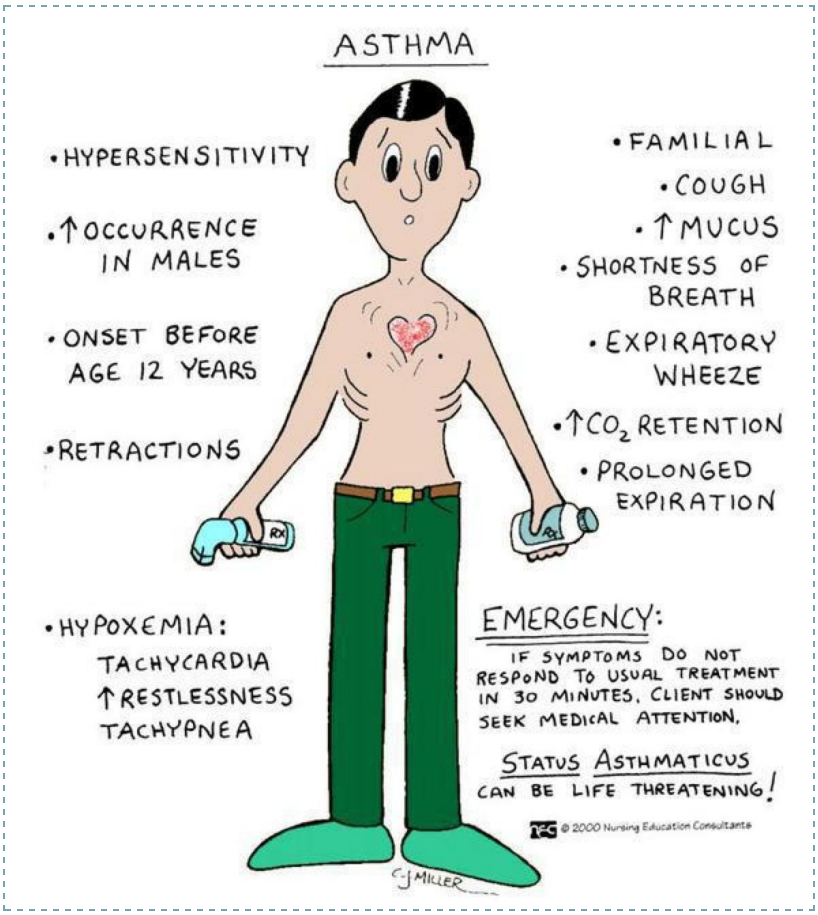




Summary of Asthma:

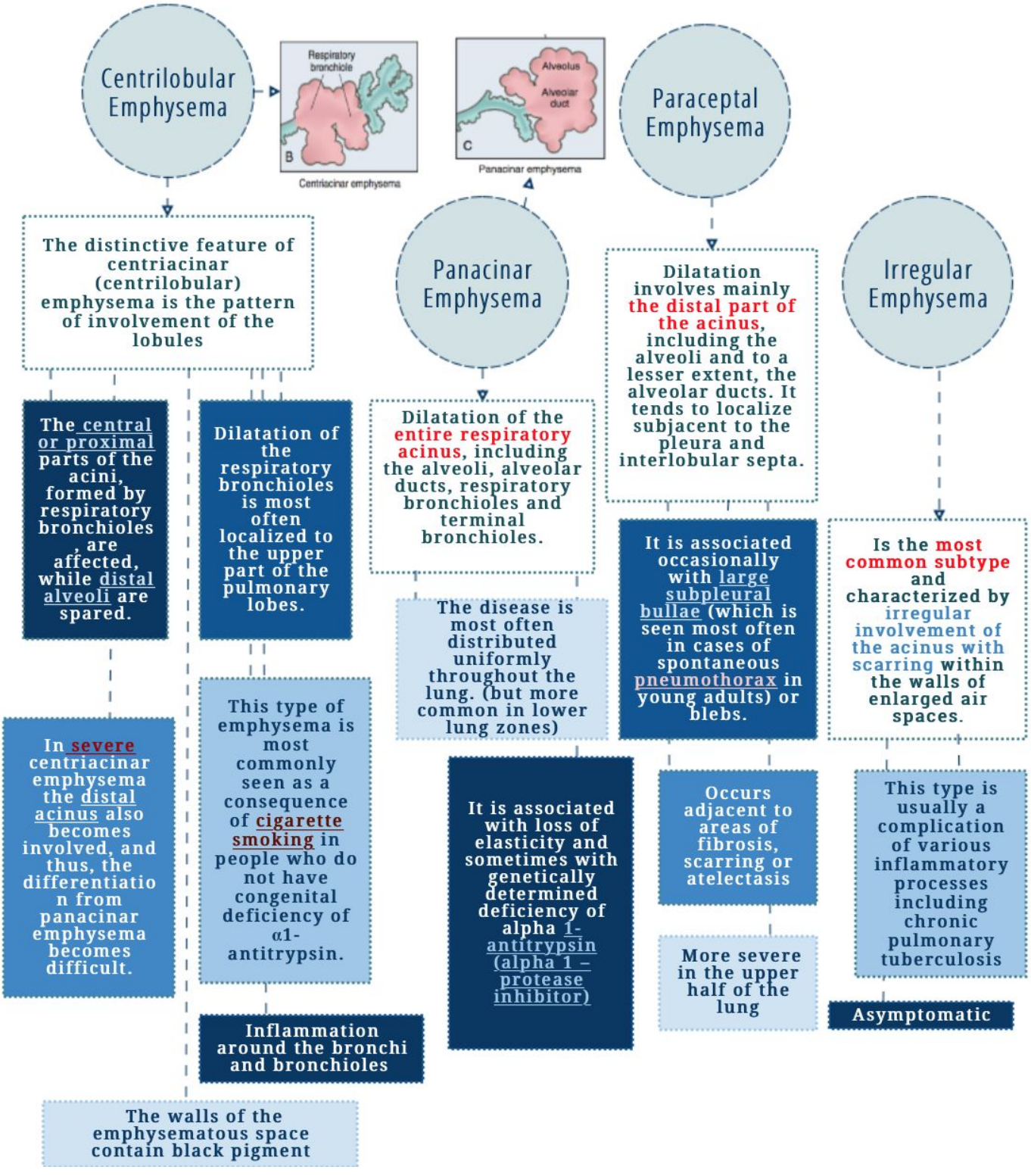
- Asthma is characterized by reversible bronchoconstriction caused by airway hyperresponsiveness to a variety of stimuli. ▫
- Atopic asthma is caused by a TH2 and IgE-mediated immunologic reaction to environmental allergens and is characterized by acute-phase (immediate) and late-phase reactions. The TH2 cytokines IL-4, IL-5, and IL-13 are important mediators. ▫
- Triggers for nonatopic asthma are less clear but include viral infections and inhaled air pollutants, which can also trigger atopic asthma. ▫
- ***Eosinophils*** are key inflammatory cells found in almost all subtypes of asthma; eosinophil products such as major basic protein are responsible for airway damage. ▫
- Airway remodeling (sub-basement membrane thickening and hypertrophy of bronchial glands and smooth muscle) adds an irreversible component to the obstructive disease.

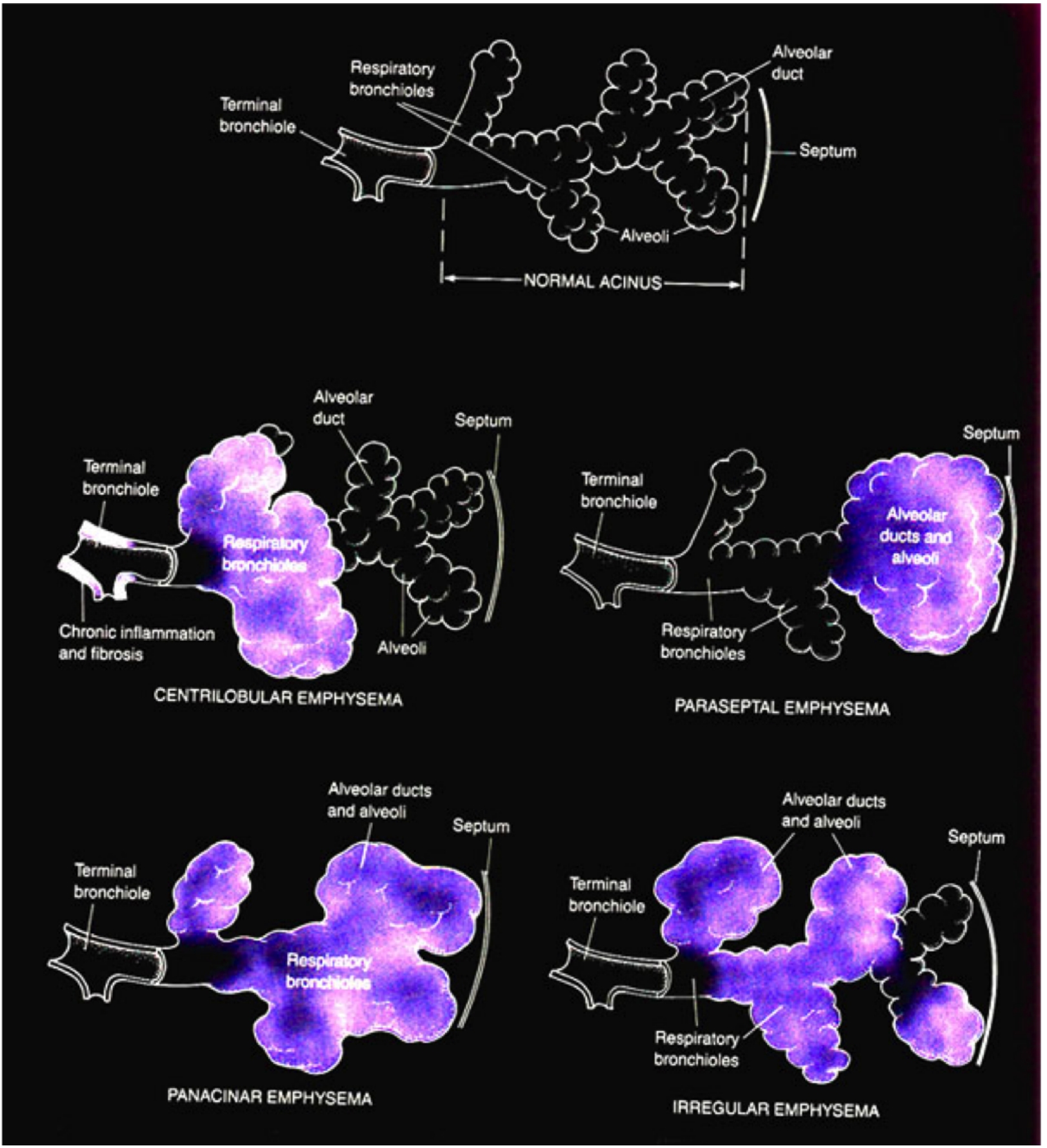
▫



Emphysema:

Types of Emphysema: Differentiated into different types depending on the parts it affects. Only the first two types cause clinically significant airway obstruction, with centriacinar emphysema being about 20 times more common than panacinar disease.




Respiratory bronchioles
Alveolar duct
Terminal bronchiole
Septum
Alveoli
NORMAL ACINUS
Alveolar duct
Septum
Terminal bronchiole
Respiratory bronchioles
Chronic inflammation and fibrosis
Alveoli
CENTRILOBULAR EMPHYSEMA
Septum
Terminal bronchiole
Alveolar ducts and alveoli
Respiratory bronchioles
PARASEPTAL EMPHYSEMA
Alveolar ducts and alveoli
Septum
Terminal bronchiole
Respiratory bronchioles
PANACINAR EMPHYSEMA
Alveolar ducts and alveoli
Septum
Terminal bronchiole
Respiratory bronchioles
IRREGULAR EMPHYSEMA

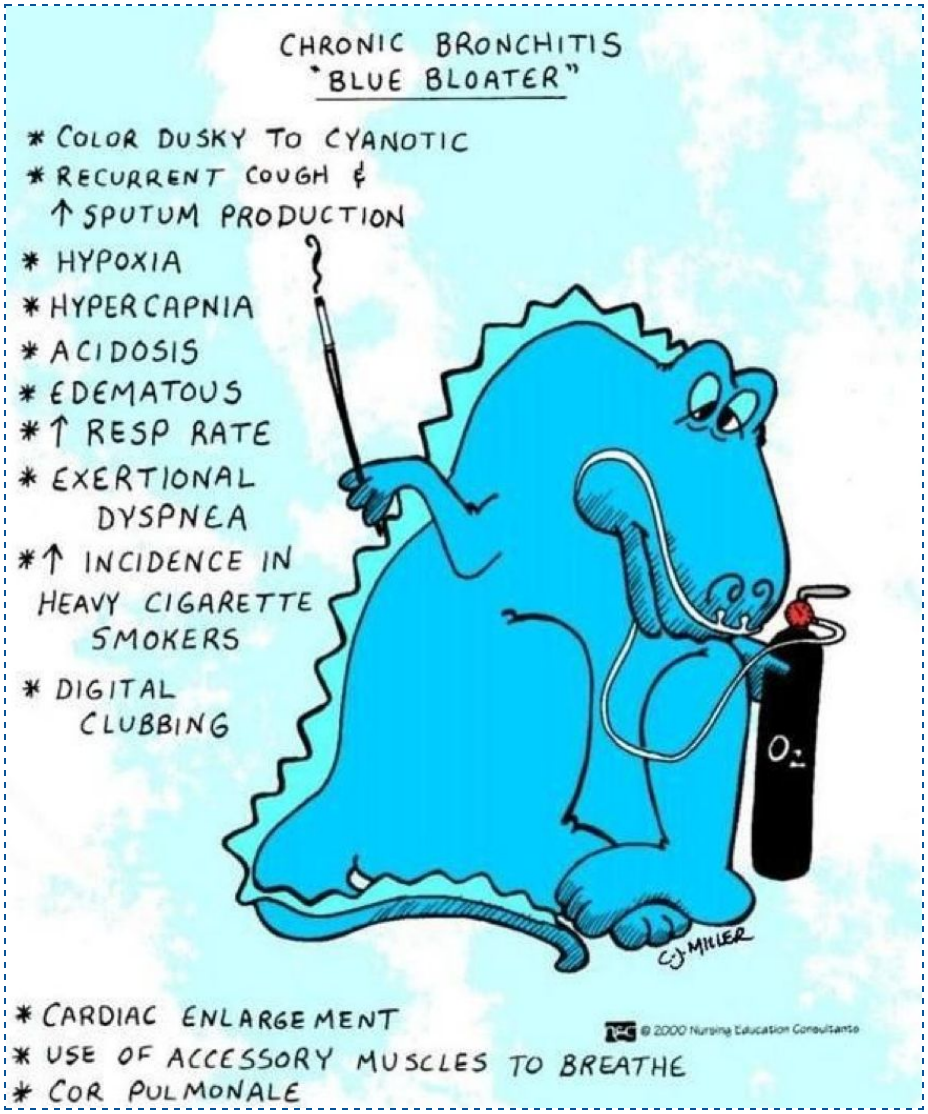
Summary of Emphysema:

- Emphysema is a chronic obstructive airway disease characterized by permanent enlargement of air spaces distal to terminal bronchioles. ▫
- Subtypes include centriacinar (most common; smoking- related), panacinar (seen in α1-antitrypsin deficiency), distal acinar, and irregular.
- Smoking and inhaled pollutants cause ongoing accumulation of inflammatory cells, releasing elastases and oxidants, which destroy the alveolar walls without adequate mesenchymal repair response. ▫
- Most patients with emphysema demonstrate elements of chronic bronchitis concurrently, since cigarette smoking is an underlying risk factor for both; patients with pure emphysema are characterized as "pink puffers." ▫

Chronic Bronchitis:

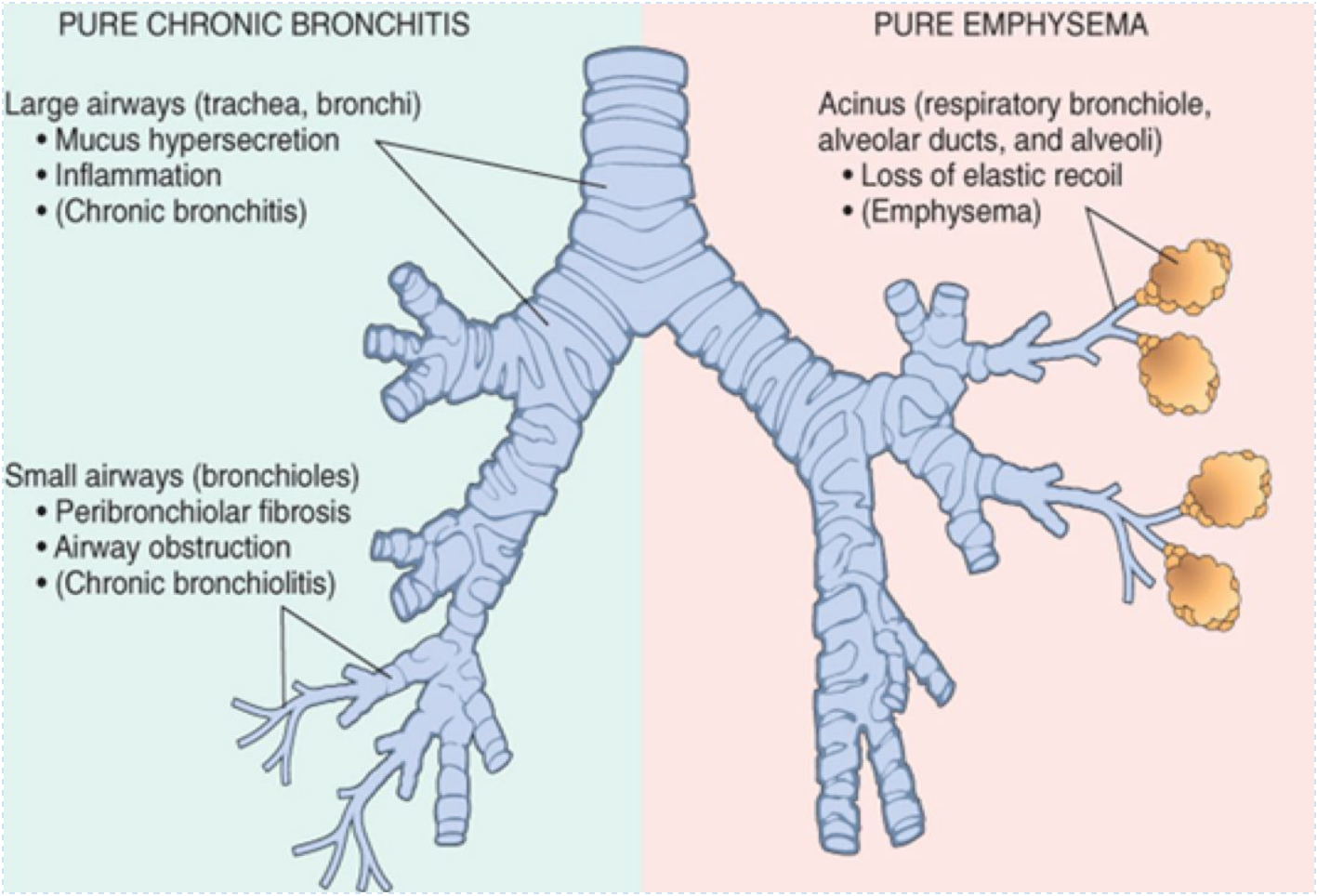
Summary of chronic bronchitis:

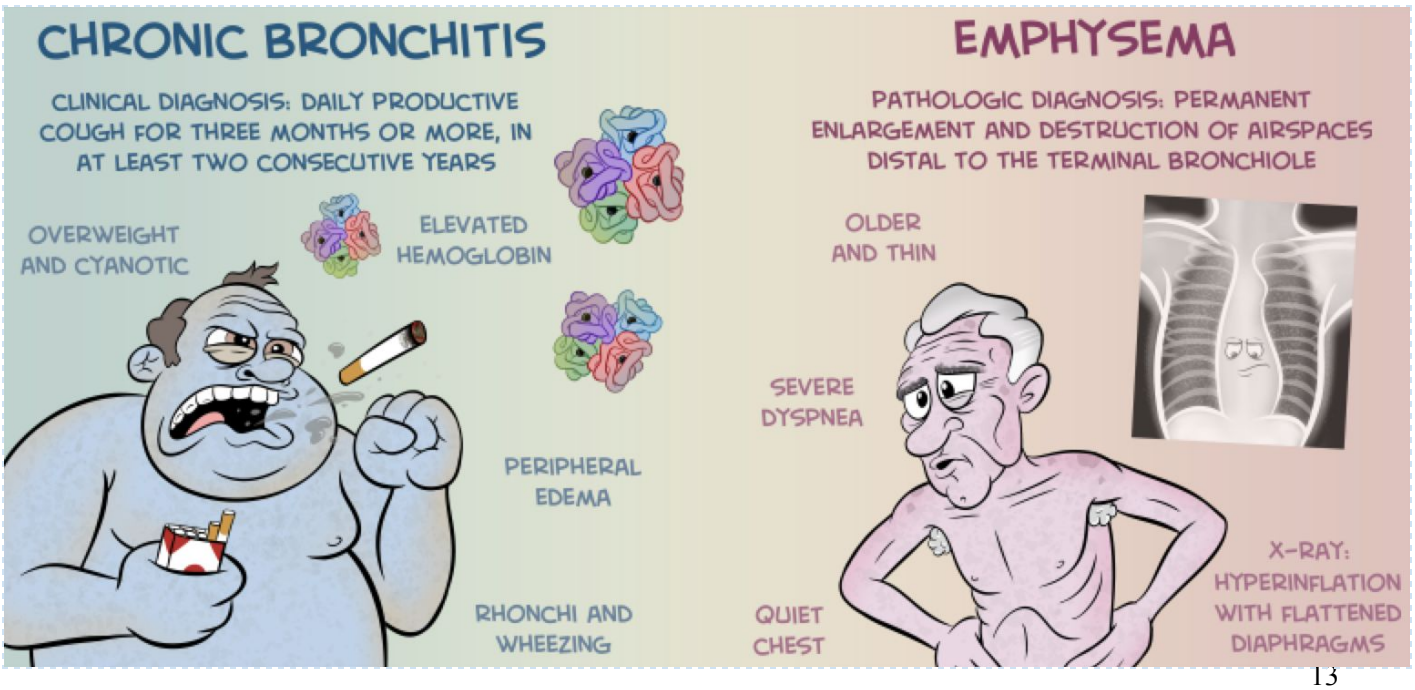
- Chronic bronchitis is defined as persistent productive cough for at least 3 consecutive months in at least 2 consecutive years. ▫
- Cigarette smoking is the most important underlying risk factor; air pollutants also contribute. ▫
- Chronic obstructive component largely results from small airway disease (chronic bronchiolitis) and coexistent emphysema. ▫
- Histologic examination demonstrates enlargement of mucus-secreting glands, goblet cell metaplasia, and bronchiolar wall fibrosis. ▫



EXTRA

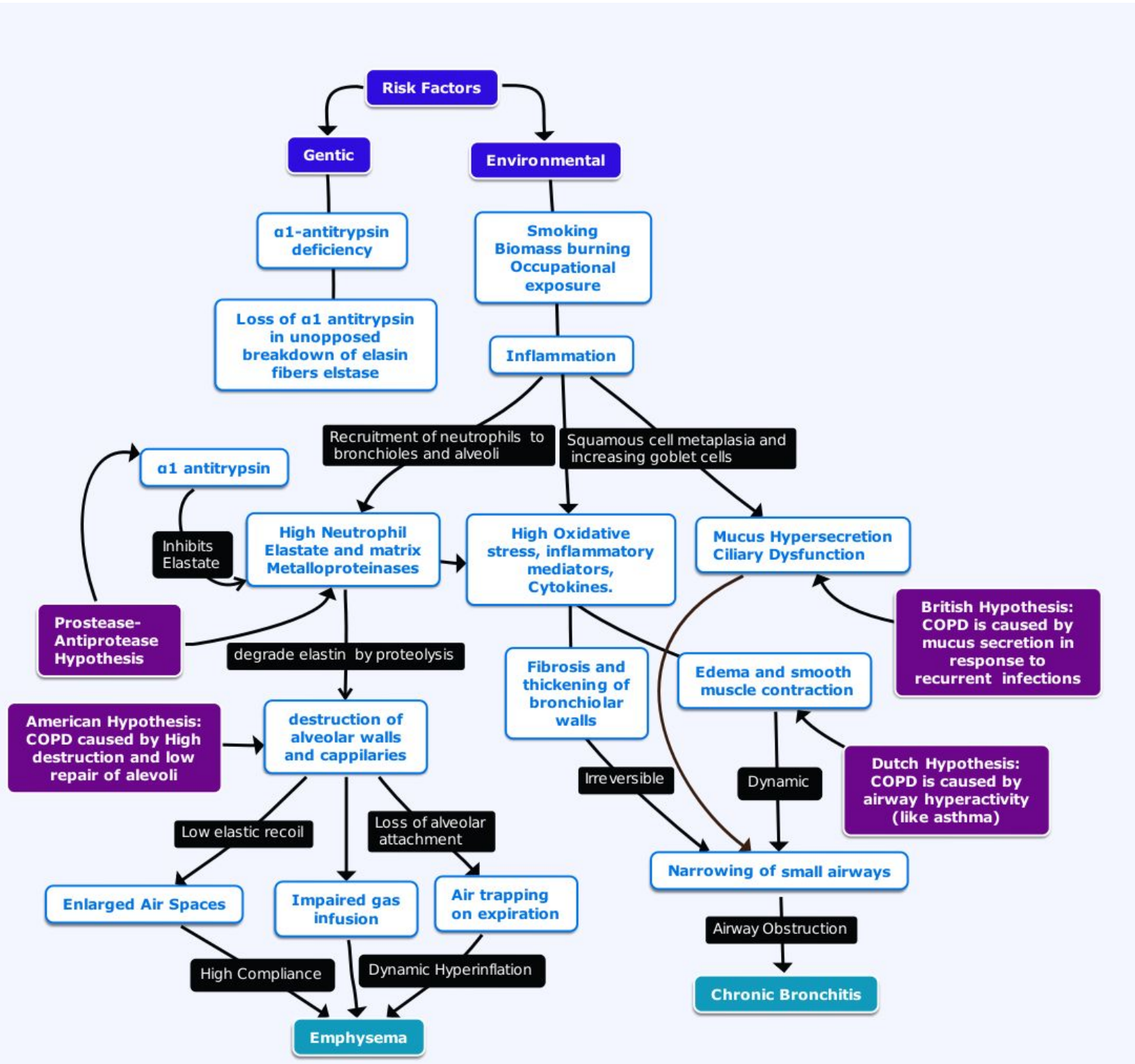
(To help you differentiate between Chronic Bronchitis and Emphysema)





EXTRA

The Difference Between the Pathogenesis of Emphysema and Chronic Bronchitis

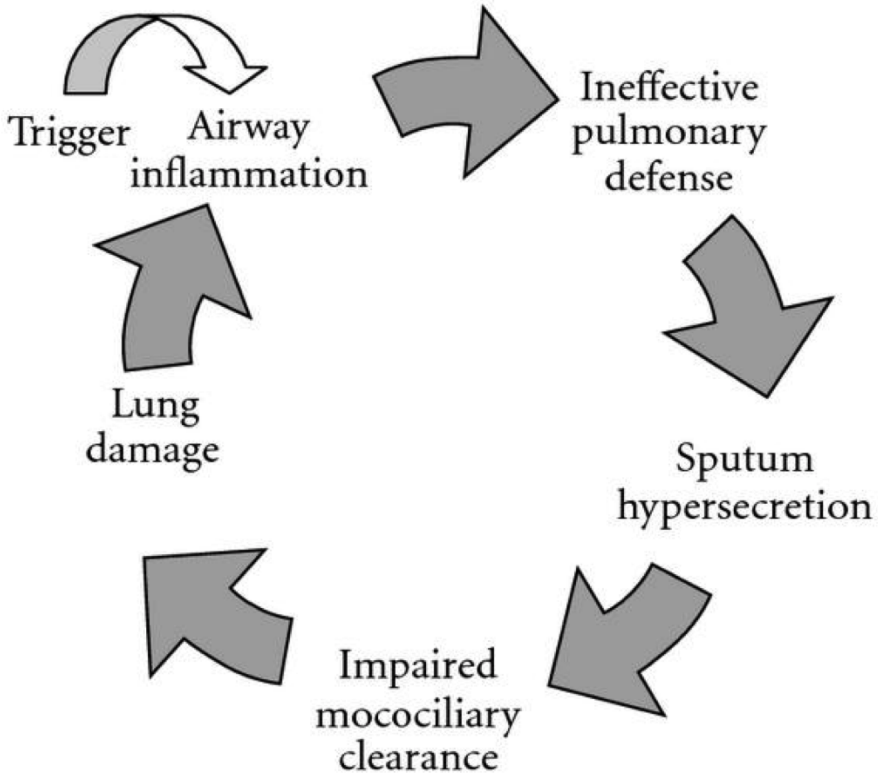


Revision of Emphysema and chronic Bronchitis

	Predominant Bronchitis	Predominant Emphysema
Appearance	Blue bloaters	Pink Puffers
Age	40-45	50-75
Dyspnea	Mild, late	Severe, early
Cough	Early, copious sputum	Late, scanty sputum
Infection	Common	Occasional
Cor pulmonale	Common	Rare, terminal
Airway resistance	Increased	Normal or slightly increased
Elastic recoil	Normal	Low
Chest radiography	Prominent vessels, large heart	Hyperinflation, small heart
$PaCO_2$	Increased	Normal to decreased
Cyanosis	Present	Absent

Bronchiectasis:

Summary of the pathogenesis:



	Asthma	Chronic Bronchitis	Emphysema	Bronchiectasis
Definition	A chronic inflammatory disorder of the airways that causes recurrent episodes of reversible bronchoconstriction caused by increased responsiveness of the tracheobronchial tree to various stimuli.	COPD which initially involves the large airways. The clinical definition of chronic bronchitis is a productive cough (with sputum) that occurs during at least 3 consecutive months over at least 2 consecutive years. "Blue Bloaters"	Abnormal permanent dilation of air spaces distal to the terminal bronchioles with destruction of alveolar walls without significant fibrosis . "Pink Puffers"	permanent and abnormal dilation of bronchi and bronchioles caused by destruction of the muscle and the supporting elastic tissue. Resulting from or associated with chronic infection with inflammation and necrosis of the bronchial wall.
Etiology	- Genetic predisposition to type I hypersensitivity - Acute and chronic airway inflammation - Bronchial hyperresponsiveness to a variety of stimuli. - Intermittent airflow obstruction that can be caused by a variety of changes.	• Cigarette smoking. • Air pollutants. • Genetic factors e.g. cystic fibrosis. • Infection.	- Cigarette smoking - Hereditary alpha 1 antitrypsin deficiency	- Bronchial obstruction. - Congenital or hereditary conditions: - Cystic fibrosis. - Immunodeficiency states - Congenital bronchiectasis. - Intralobar sequestration of the lung. - Kartagener syndrome
Damage is	Reversible	Irreversible	Irreversible	Irreversible
Complications	-Superimposed infection -COPD disease -Pneumothorax -Airway remodeling. -Cor pulmonale -Status Asthmaticus	→ Might lead to cor pulmonale. → Cyanosis in severe cases. → Coexistent emphysema	- coexistent chronic bronchitis. - Interstitial emphysema - pneumothorax. - Death due to Pulmonary failure, with respiratory acidosis, hypoxia, and coma or cor pulmonale	- Persistent Hemoptysis. - Obstruction of pulmonary function. - Rarely, pulmonary hypertension, abscess formation, amyloidosis.
Symptoms	→ Wheezing → *Dyspnea* → chest tightness. → Chronic dry cough Particularly at night and/or early in the morning.	→ In early stages of the disease, the productive cough raises mucoid sputum, but airflow is not obstructed. → hyperresponsive airways with bronchospasm and wheezing. → Increased sleepiness → Hypercapnia and hypoxemia. → chronic hypoxemia. → Dyspnea	- Dyspnea (first symptom). - Cough and wheezing. - Reduced FEV1 - "holes" in the lung tissue. - decreased Tco. - Loss of elastic recoil - Weight loss is common - (Barrell-chest) - increased total vital capacity. - Advanced: hypoxia, cyanosis, acidosis.	- Dyspnea - Chronic cough - Fever - Hemoptysis - Clubbing of the fingers - Hypoxemia - Hypercapnia.

Questions:

1. A 48-year-old man has gradually increasing dyspnea and 4-kg weight loss over the past 2 years. He has smoked two packs of cigarettes per day for 20 years, but not for the past year. Physical examination shows an increase in the anteroposterior diameter of the chest. Auscultation of the chest shows decreased breath sounds. A chest radiograph shows bilateral hyperlucent lungs; the lucency is especially marked in the upper lobes. Pulmonary function tests show that FEV1 is markedly decreased, FVC is normal, and the FEV1/FVC ratio is decreased. Which of the following is most likely to contribute to the pathogenesis of his disease?

A. Abnormal epithelial cell chloride ion transport
B. Decreased ciliary motility with irregular dynein arms
C. Impaired hepatic release of a1-antitrypsin
D. Macrophage recruitment and release of interferon-y
E. Release of elastase from neutrophils

2. A 20-year-old, previously healthy man is jogging one morning when he trips and falls to the ground. He suddenly becomes markedly short of breath. On examination in the emergency room there are no breath sound audible over the right side of the chest. A chest radiograph show shift of the mediastinum from right to left. A chest tube is inserted on the right side, and air rushes out. Which of the following underlying disease is most likely to have produced this complication?

A. Asthma
B. Bronchiectasis
C. Centriacinar emphysema
D. Chronic bronchitis
E. Distal acinar emphysema
F. Panlobular emphysema

3. A 45-year-old man has smoked two packs of cigarettes per day for 20 years. For the past 4 years, he has had chronic cough with copious mucoid expectoration. During the past year, he has had multiple respiratory tract infections diagnosed as " viral flu". He has also developed difficulty breathing, tightness of the chest, and audible wheezing. His breathing difficulty is relieved by inhalation of B- adrenergic agonist and disappears after the chest infection has resolved. Which of the following pathologic conditions is most likely responsible for his clinical condition?

A. A1-Antitrypsin deficiency with panlobular emphysema
B. Centrilobular emphysema with cor pulmonale
C. Chronic asthmatic bronchitis
D. Cystic fibrosis with bronchiectasis
E. Hypersensitivity pneumonitis with restrictive lung disease

4. A study is conducted of individuals who smoked at least one pack of cigarettes per day for 30 years. These individuals undergo pulmonary function testing, and a large subset is found to have decreased FEV1, normal to decreased FVC, and FEV1/FVC ratio less than 70%. Autopsy data from the subset of individuals in the study with a low FEV1/FVC ratio are analyzed. Which of the following respiratory tract structures in the lungs is likely to be affected most by underlying disease?

A. Alveolar duct
B. Alveolar sac
C. Bronchi
D. Respiratory bronchiole
E. Terminal bronchiole

5. A 12-year-old girl has a 7-year history of coughing and wheezing and repeated attacks of difficulty breathing. The attacks are particularly common in spring. During an episode of acute respiratory difficulty, a physical examination shows that she is afebrile. Her lungs are hyperresonant on percussion, and a chest radiograph shows increased lucency of all lung fields. Laboratory tests show an elevated serum IgE level and peripheral blood eosinophilia. A sputum sample examined microscopically also has increased numbers of eosinophils. Which of the following histologic features is most likely to characterize the lung in her condition?

A. Dilation of respiratory bronchioles with loss of elastic fibers
B. Inflammatory destruction of brionchial walls
C. Interstitial and alveolar edema with hyaline membrane formation
D. Patchy areas of consolidation with leukocytic exudate in alveoli
E. Remodeling of airways with smooth muscle hyperplasia.

6. A 33-year-old man suddenly develops severe dyspnea with wheezing. On physical examination, his vital signs are temperature, 37 C; pulse, 95/min; respirations, 35/min; and blood pressure, 130/80 mm Hg. A chest radiograph shows increased lucency in all lung fields. Arterial blood gas analysis shows Po2, 65mm Hg; Pco2, 30mm Hg; and pH, 7.48. A sputum cytologic specimen shows Curschmann spirals, Charcot-Leyden crystals, branching septate hyphae, and eosinophils in a background of abundant mucus. What is the most likely risk factor predisposing him to illness?

A. Cytokine gene polymorphisms
B. Foreign body aspiration
C. Inhalation of environmental inorganic dusts
D. Inheritance of a CFTR gene mutation
E. Reduced circulating a1-antitrypsin levels
F. Smoking cigarettes for>10

7. A pharmaceutical company is designing agents to treat the recurrent bronchospasm of bronchial asthma. Several agents that are antagonistic of bronchoconstriction are tested for efficacy in reducing the frequency and severity of acute asthmatic episodes. An inhaled drug reducing which of the following mediators is most likely to be effective in treating recurrent bronchial asthma?

A. Th1 cytokines
B. Vasoactive amines
C. Th2 cytokines
D. Leukotrienes
E. Prostaglandins

8. A 35-year-old man has a 5-year history of episodic wheezing and coughing. The episodes are more common during the winter months, and he has noticed that they often follow minor respiratory tract infections. In the period between the episodes, he can breath normally. There is no family history of asthma or other allergies. On physical examination, there are no remarkable findings. A chest radiograph shows no abnormalities. A serum IgE level and WBC count are normal. Which of the following is the most likely mechanism that contributes to the findings in his illness?

A. Accumulation of alveolar neutrophulic exudate
B. Bronchial hyperreactivity to chronic inflammation
C. Emigration of eosinophils into bronchi
D. Hyperresposiveness to Aspergillus spores
E. Secretion of interleukin (IL)-4 and IL-5 by T cells

9. A study of persons with atopic asthma reveals that they develop pathologic changes in their airways with repeated bouts. These changes include smooth muscle and mucus gland hypertrophy. It is observed that the late-phase inflammatory response to allergens potentiates epithelial cell cytokine production that promotes airway remodeling. Which of the following immune cells is most important in this excessive inflammatory response to allergens?

A. B lymphocyte
B. Cytotoxic lymphocyte
C. Natural killer cell
D. TH1 lymphocyte
E. TH2 lymphocyte
F. TH17 lymphocyte

10. A 49-year-old man has had increasing dyspnea for the past 4 years. He has an occasional cough with minimal sputum production. On physical examination, his lungs are hyperresonant with expiratory wheezes. Pulmonary function tests show increased total lung capacity (TLC) with slightly increased FVC and decreased FEV1 and FEV1/FVC ratio. Arterial blood gas measurement shows pH of 7.35; Po2, 65 mm Hg; and Pco2, 50 mm Hg. Which of the following disease processes should most often be suspected as a cause of these findings?

A. Centrilobular emphysema
B. Chronic pulmonary embolism
C. Diffuse alveolar damage
D. Nonatopic asthma

11. A 35-year-old woman has experienced multiple bouts of severe necrotizing pneumonia since childhood, with Haemophilus influenza, Staphylococcus aureus, pseudomonas aeruginosa, and Serratia marcescens cultured from her sputum. She now has a cough productive of large amounts of purulent sputum. On physical examination, there is a dullness to percussion with decreased breath sounds over the right mid to lower lung fields. A chest radiograph shows areas of right lower lobe consolidation. A bronchogram shows marked dilation of right lower lobe bronchi. Which of the following mechanisms is the most likely cause of her disease?

A. Congenital malformation of the bronchial walls
B. Damage to bronchial mucosa by major basic protein of eosinophils
C. Diffuse infiltration by bronchogenic carcinoma
D. Recurrent inflammation with bronchial wall destruction
E. Unopposed action of neutrophil-derived elastase on bronchi

12. A 33-year-old man has had increasing dyspnea for the past 8 years. He does not smoke. On examination, there are decreased breath sounds over lower lung fields. A chest radiograph shows flattened diaphragms; his CT scan is shown in the figure. Pulmonary function tests show decreased DLCO, decreased FEV1, and increased FVC. Arterial blood gas analysis shows Po2, 65 mm Hg; Pco2, 60 mm Hg; HCO3–, 32 mEq/L; and pH, 7.35. A sibling is similarly affected. What is the most likely mechanism for his pulmonary disease?

A. Atopy with IgE binding to mast cells
B. *CFTR* gene mutation
C. Increased neutrophil proteases
D. Prior infection with tuberculosis
E. Reduced antielastase activity

13. A 62-year-old man is a smoker with a 10-year history of cough productive of copious mucopurulent sputum. Over the past 6 months, he has developed progressive dyspnea. Physical examination shows bilateral pedal edema and a soft but enlarged liver. A chest radiograph shows bilateral pleural effusions and a prominent right heart border. Arterial blood gas values are Po2, 60 mm Hg; Pco2, 52 mm Hg; pH, 7.30; and HCO3−, 29 mEq/L. He is intubated and placed on a ventilator, and he requires increasing amounts of oxygen. Which of the following microscopic findings is most likely to be present in the affected lungs?

A. Bronchovascular distribution of granulomas
B. Carcinoma filling lymphatic spaces
C. Extensive interstitial fibrosis
D. Hypertrophy of bronchial submucosal glands
E. Mucosal infiltrates of eosinophils

14. A 70-year-old woman has had episodes of dyspnea with wheezing and coughing, accompanied by urticaria for the past 3 years. She has had bouts of rhinitis. She has a 10-year history of osteoarthritis. On physical examination she has nasal polyps. Use of which of the following medications is the most likely risk factor for her respiratory disease?

A. Acetaminophen
B. Aspirin
C. Gabapentin
D. Morphine
E. Prednisone

15. A study of pulmonary disease in persons who are smokers shows that tobacco used in greater amounts and for longer periods is positively correlated with the degree of lung parenchymal destruction with centrilobular emphysema. However, some persons with a history of extensive tobacco use have less lung damage than persons who smoked less. Polymorphisms involving which of the following genes are most likely to explain these differences in the repair response to lung injury in smokers?

A. AAT
B. BMPR2
C. CFTR
D. GM-CSF
E. TGF-β

16. Obstructive airway defect is characterized on pulmonary function testing by which of the following?

A. Reduced FEV1/FVC ratio
B. Decreased total lung capacity TLC
C. Reduced residual volume RV
D. Decreased residual volume /Total lung capacity RV/TLC
E. Decrease in diffusing capacity DLCO

17. Which one of the following is the first line therapy and management of acute asthma attack?

A. Steroids
B. Beta-2 agonist
C. Theophylline
D. Antibiotics
E. Magnesium sulfate

18. Which one of the following pathogens is the main cause of bronchiectasis?

A. Influenza virus
B. Rhinovirus
C. Mycoplasma pneumoniae
D. Enterovirus
E. Necrotizing fungal infections

19. In which of the following diseases would the occurrence of hemoptysis prompt a search for another disease as the cause of hemoptysis?

A. Bronchogenic carcinoma
B. Acute bronchitis
C. Emphysema
D. Bronchiectasis

20. The interstitium contains:

A. Plasma cells
B. Elastin
C. Calcium
D. Necrotic cells

21. A patient came to the clinic with asthmatic attack, his body did not respond to the drugs and it is found that he had hypoxemia. What do we call this condition?

A. Chronic bronchitis
B. Pneumonia
C. Heart attack
D. Status asthmaticus

22. Which of the following bronchial asthma characteristics is NOT true ?

A. Chronic
B. Inflammatory
C. Not reversible
D. Hyper-reactive airway

23. a 76 year old man came with dry cough and wheezing, he's been taking aspirin for 4 months as a prophylactic treatment. Which of the following is the most probable diagnosis for him?

A. Extrinsic asthma
B. Chronic bronchitis
C. Intrinsic asthma
D. Emphysema

24. Which of the following is the role of IL-4 :

A. Activation of eosinophils
B. IgE production
C. Mucus production
D. All of the above

25. A 28 year old woman with cystic fibrosis presents with increasing shortness of breath and production of abundant foul-smelling sputum. The sputum in this patient is most likely associated with which of the following pulmonary condition?

A. Atelectasis.
B. Bronchiectasis.
C. Emphysema.
D. Pneumothorax

26. Which of the following describes the Morphology of Emphysema:

A. Lungs are pale
B. Lungs are voluminous
C. Thinning and destruction of alveolar walls (histologically)
D. All of the above

27. The most important risk factor for chronic bronchitis:

A. Mycobacterium tuberculosis
B. Smoking
C. Autoimmune diseases
D. High Altitudes

28. Which of the following is the diagnosis for a patient who complain from productive cough for 3 consecutive months over 2 consecutive years?

A. Chronic bronchitis
B. Emphysema
C. Asthma
D. Bronchiectasis

29. A man has died after suffering with chronic pulmonary tuberculosis, his autopsy showed some scars in his lungs with weird-looking acinus.. The doctors included that he had a type of emphysema, which is:

A. Panacinar emphysema
B. Irregular emphysema
C. Centrilobular emphysema
D. Paraseptal emphysema

30. Metastatic brain abscess is a complication of which of the following?

A. Chronic bronchitis
B. Bronchiectasis
C. Emphysema
D. Asthma

31. 43 male patient present to the physician with dyspnea excessive sputum and blue lips and extremities chest radiography showed large heart and prominent blood vessels , which of the following is most likely the diagnosis:

A. Emphysema
B. Bronchitis
C. Bronchiectasis
D. Intrinsic asthma

32. 15 female patient present to the physician with breathlessness cough and sputum production the patient diagnosed with bronchial asthma which of the following would be found if we do sputum analysis ?

A. Curschmann spirals
B. Asbestos bodies
C. Carbon dust
D. Black coal laden macrophages

33. Asthma is mediated by what type of antigen?

A. IgA
B. IgG
C. IgE
D. IgM

34. which one of the following is not type of emphysema?

A. Centriacinar
B. Regular
C. Panacinar
D. Paraseptal

35. Which of the following diseases causes reversible bronchoconstriction?

A. Bronchiectasis
B. Chronic bronchitis
C. Emphysema
D. Asthma

36. Which of these symptoms is common is all COPDs ?

A. Dyspnea
B. Dry cough
C. Loss of elastic recoil
D. Coexistent Emphysema

37. Which of the following diseases are termed blue bloaters and pink puffers respectively?

A. Emphysema and Asthma
B. Chronic bronchitis and bronchiectasis
C. Emphysema and bronchiectasis
D. Chronic bronchitis and emphysema

38. ‘Barrel Chest’ is a characteristic of which disease?

A. Emphysema
B. Asthma
C. Chronic bronchitis
D. Bronchiectasis

39. Regarding the morphology of bronchiectasis, which of the following is <u>not</u> true?

A. Dilation of airways
B. Acute and chronic inflammation
C. Necrosis and ulceration in the wall of the bronchi and bronchioles
D. Abundant cilia

40. Abnormal dilatation of air spaces which are distal to the terminal bronchioles is a definition of which disease?

A. Asthma
B. Emphysema
C. Chronic bronchitis
D. Bronchiectasis

Answers:

1. Ans: (E) The patient’s findings are predominantly those of an obstructive lung disease—emphysema—with a centrilobular pattern of predominantly upper lobe involvement. Smoking is a major cause of this disease. The subtle but long-term inflammation that can accompany smoking leads to increased neutrophil and macrophage elaboration of elastase that is not sufficiently inhibited by the antiprotease action of α_1-antitrypsin. This results in a loss of lung tissue, not fibrogenesis, over decades. Fibrogenesis is typical of restrictive lung diseases, such as pneumoconioses, that follow inhalation of dusts. Abnormal chloride ion transport is a feature of cystic fibrosis, which leads to widespread bronchiectasis. Dynein arms are absent or abnormal in Kartagener syndrome, which leads to bronchiectasis. α_1-Antitrypsin deficiency is uncommon and leads to a panlobular pattern of emphysema. Macrophage recruitment and activation by interferon-γ released from T cells is a feature of chronic inflammatory conditions and pneumoconioses.

2. Ans: E Distal acinar (paraseptal) emphysema is localized, beneath pleura typically in an upper lung lobe, and may occur in an area of fibrosis or scar formation. Although the lesions are usually less than 2 cm in diameter, they are prone to rupture spontaneously or with minor trauma, leading to pneumothorax. They can be a cause for spontaneous pneumothorax in young adults. A “ball valve” effect can lead to air trapping in pleura, producing tension pneumothorax, as in this case. Centriacinar emphysema arises in respiratory bronchioles and is seen in smokers. Panacinar (panlobular) emphysema involves most of the lung lobule and can be seen in all lobes; α_1-antitrypsin deficiency is the most likely antecedent. Asthma results from bronchoconstriction with air trapping, but is not likely to be complicated by pneumothorax. Bronchiectasis results from inflammation with destruction of bronchi; hemoptysis is the most likely complication, not pneumothorax. Chronic bronchitis is unlikely to produce a bronchopleural fistula with pneumothorax.

3. Ans: C. This patient's disease meets the clinical definition of chronic bronchitis. He has had persistent cough with sputum production for at least 3 months in 2 consecutive years. Chronic bronchitis is a disease of smokers and individuals living in areas of poor air quality, which explains the chronic cough with mucoid sputum production. This patient's episodes of bronchoconstriction set off by viral infections suggest, however, a superimposed element of nonatopic asthma. Cor pulmonale leads to pleural effusions, not to bronchoconstriction. Centrilobular emphysema and chronic bronchitis (both complications of smoking) can overlap in clinical and pathologic findings, but significant bronchoconstriction is not a feature of emphysema. The panlobular emphysema of α_1-antitrypsin can be worsened by smoking, but there is no bronchoconstriction. Bronchiectasis results in airway dilation from destructive bronchial wall inflammation, but the onset of pulmonary disease with cystic fibrosis is typically in childhood. Hypersensitivity pneumonitis is marked by features of a restrictive lung disease, sometimes with dyspnea, but without mucus production, and is often episodic from intermittent antigen exposure.

4. Ans: D. Centrilobular emphysema results from damage to the central part of the lung acinus, with dilation that primarily affects the respiratory bronchioles. There is relative sparing of the distal alveolar ducts and alveolar sacs. Bronchi have cartilage that is not affected by emphysema. In panacinar emphysema, the lung lobule is involved from the respiratory bronchiole to the terminal alveoli. In paraseptal emphysema, the distal acinus is involved.

5. Ans: E Atopic asthma is a type I hypersensitivity reaction in which there are presensitized, IgE-coated mast cells in mucosal surfaces and submucosa of airways. Contact with an allergen results in degranulation of the mast cells, with both immediate release (minutes) of mediators such as histamine to promote bronchoconstriction, and delayed release (an hour or more) of leukotrienes and prostaglandins via the arachidonic acid pathway; these attract leukocytes, particularly eosinophils, and promote bronchoconstriction. The characteristic histologic changes in the bronchi, including remodeling of airways and smooth muscle hyperplasia, result from the episodes of inflammation. Dilation of the respiratory bronchiole is a feature of centrilobular emphysema. Bronchial dilation with inflammatory destruction is a feature of bronchiectasis. Hyaline membranes are seen with acute diffuse alveolar damage. Neutrophilic exudates with consolidation are seen in pneumonic processes, typically from bacterial infections.

6. Ans: A. Asthma, particularly extrinsic (atopic) asthma, is driven by a type I hypersensitivity response and is associated with an excessive T_H2 and T_H17 cell-mediated immune response. Genetic factors are important in the pathogenesis of atopic asthma and linkage to cytokine genes that map on 5q are strongly associated with development of asthma and other atopic allergies. The Charcot-Leyden crystals represent the breakdown products of eosinophil granules. The Curschmann spirals represent the whorls of sloughed surface epithelium within the abundant mucin. The septated hyphae are *Aspergillus* organisms colonizing the tracheobronchial tree (allergic bronchopulmonary aspergillosis). Foreign body aspiration may result in inflammation, but without eosinophils. Inorganic dust inhalation leads to restrictive, not obstructive, lung disease. *CFTR* mutations with cystic fibrosis lead to chronic widespread bronchiectasis. Inflammation with eosinophils is not a significant component of emphysema related to α_1-antitrypsin deficiency or to smoking.

7. Ans: C. The early, acute phase of bronchial asthma is triggered by release of chemical mediators, whereas the late phase is mediated by recruited inflammatory cells and the Th2 cytokines they release. Acute asthmatic episodes respond best to inhaled β-adrenergic agonists. Histamine released from mast cells acts during the early acute phase of type I hypersensitivity reactions, but antihistaminic agents are not useful for treating recurrent bouts of asthma. Th2 cytokines play an important role in recurrent asthma and antagonists of these, in particular IL-13 and IL-4, are in development. It is not clear if any one of the Th2 cytokines alone mediates recurrent bronchospasm. Among the early to late phase mediators, the leukotrienes C_4, D_4, and E_4 promote intense bronchoconstriction and mucin production. Montelukast is an agent that binds to cysteinyl leukotriene (CysLT) receptors on mast cells and eosinophils to block the lipoxygenase pathway of arachidonic acid metabolism, which generates the leukotrienes. Prostaglandin D_2 also is a bronchoconstrictor, but its role is less well defined than that of leukotrienes.

8. Ans:B .This history is typical of nonatopic, or intrinsic, asthma. There is no family history of asthma, no eosinophilia, and a normal serum IgE level. The fundamental abnormality in such cases is bronchial hyperresponsiveness (i.e., the threshold of bronchial spasm is intrinsically low). When airway inflammation occurs after viral infections, the bronchial smooth muscle spasms, and an asthmatic attack occurs. Such bronchial hyperreactivity also may be triggered by inhalation of air pollutants, such as ozone, sulfur dioxide, and nitrogen dioxides. Even exercise and cold air may act as a trigger. Accumulation of neutrophils is typical of bacterial pneumonia, which could follow viral infection, but lead to lung consolidation. Bronchopulmonary aspergillosis refers to colonization of asthmatic airways by *Aspergillus,* which is followed by development of additional IgE antibodies. Secretion of interleukin (IL)-4 and IL-5 by type 2 helper T cells also occurs in cases of allergic asthma.

9. Ans:E The T_H2 helper lymphocyte response drives cytokine production, such as IL-4, IL-5, and IL-13, that promotes eosinophil infiltration and IgE production by mast cells. This allergic response potentiates inflammation, which promotes the airway remodeling that facilitates additional airway reactivity and asthmatic episodes. The T_H1 response drives granulomatous inflammation. T_H17 lymphocytes aid in inflammatory responses to infectious agents, but may play a role in autoimmunity. B lymphocytes produce antibodies, but mainly via the action of T helper cells. Cytotoxic lymphocytes are primarily directed at intracellular infectious agents. NK cells assist in fighting infectious agents.

10. Ans: A. These findings point to an obstructive lung disease, such as emphysema, which occurs with airway narrowing and loss of elastic recoil. It has led to compensated respiratory acidosis in this man. Chronic pulmonary embolism does not affect FVC because the airways are not affected, but there is a ventilation-perfusion mismatch. Diffuse alveolar damage is an acute restrictive lung disease. Nonatopic asthma can occur at his age, but asthma is episodic and unlikely to cause permanant loss of distal airspaces. Sarcoidosis is a form of chronic restrictive lung disease. Pneumoconioses such as silicosis produce a restrictive pattern of lung disease with all lung volumes decreased, low FVC, and normal FEV_1/FVC ratio.

11. Ans:D. Bronchiectasis is a chronic obstructive airway disease from irreversible dilation of bronchi that results from inflammation and destruction of bronchial walls after prolonged infections or obstruction. Serious bouts of pneumonia can predispose to bronchiectasis. Congenital chondromalacia weakening the bronchial wall is rare. Bronchial mucosal damage by eosinophils occurs in bronchial asthma. It does not cause destruction of the bronchial wall. Bronchioloalveolar carcinoma may mimic an infiltrative pneumonia because of its lepidic pattern of spread, but it mainly produces a mass effect, and it does not start in childhood. Unopposed action of elastases damages the elastic tissue of alveoli, giving rise to emphysema.

12. (E) The extensive pulmonary involvement with increased lucency in all lung fields and increased anterior-posterior diameter is consistent with emphysema. The panlobular form, which can be worse in the lower lobes, can be due to a decrease in α1-antitrypsin, which is the major circulating antielastase. This deficiency is an inherited disease, typically with the PiZZ genotype; liver disease may also occur. Individuals with atopy are more likely to develop asthma, which has transient air trapping, not emphysema. The *CFTR* gene mutations lead to cystic fibrosis and widespread pulmonary bronchiectasis, starting in childhood. Smoking increases inflammation with neutrophils releasing proteases, mainly in upper lobes, producing the centriacinar pattern of emphysema over decades. Prior infection with tuberculosis may result in upper lobe cavitation, not emphysema.

13. (D) Chronic bronchitis can be complicated by pulmonary hypertension and cor pulmonale. There are few characteristic microscopic features of chronic bronchitis, so it is mainly defined clinically by the presence of a persistent cough with sputum production for at least 3 months in at least 2 consecutive years. Chronic bronchitis does not lead to diffuse pulmonary fibrosis. Granulomatous disease is more typical of sarcoidosis or mycobacterial infection. Lymphangitic metastases may fill lymphatic spaces and produce a reticulonodular pattern on a chest radiograph, but patients tend not to live long with such advanced cancer. Increased eosinophils are characteristic of bronchial asthma, which is an episodic disease unlikely to cause cor pulmonale.

14. (B) Drug-induced asthma is most likely to occur in older patients who develop increased sensitivity to a drug. Aspirin (acetylsalicylic acid) blocks the cyclooxygenase pathway of arachidonic acid metabolism but not the lipoxygenase pathway that potentiates bronchoconstriction. NSAIDs may have the same effect as aspirin. Angiotensin-converting enzyme (ACE) inhibitors may also induce asthmalike episodes. Acetaminophen is an analgesic that can be substituted for aspirin and is unlikely to provoke asthmatic attacks. Gabapentin and morphine act centrally as analgesics. Prednisone is an anti-inflammatory agent that is used to treat immune-mediated diseases.

15. (E) The inflammatory response to lung injury may determine the nature and extent of the pulmonary disease. The cytokine TGF-β may modulate the mesenchymal cell response to lung injury. Reduced TGF-β signaling may lead to an inadequate repair response, with loss of lung parenchyma that characterizes emphysema. The PiZZ genotype of α1-antitrypsin deficiency puts persons, especially smokers with greater tobacco use, at increased risk for panlobular emphysema. *BMPR2* is associated with development of primary pulmonary hypertension. Mutations in the *CFTR* gene are associated with development of cystic fibrosis. Mutations in *GM-CSF* are related to development of pulmonary alveolar proteinosis.

16. (A) pulmonary function tests are divided into two subgroups: obstructive and restrictive defects. The hallmark of obstructive defect is a decrease in the expiratory flow rate as manifested by a decrease In the FEV1/FVC ratio. Total lung capacity is Normal or increased. Residual volume RV is elevated owing to the air trapping during expiration, which results in an increase of the RV/TLC ratio. Vital capacity is frequently decreased in obstructive defects because of striking elevations in RV with only minor changes in TLC

17. (B) The most effective treatment for acute episodes of asthma is administration of aerosolized beta-2 agonists. And in emergency situations, they can be given every 20 minutes until the attack has subsided or the patient develops any side effects. The frequency can be reduced to every 2 to 4 hours until the attack has totally subsided. Other drugs have some role in asthma but are not the first line therapeutic agent for an acute attack.

18. (A) bronchiectasis is a consequence of inflammation and destruction of the bronchial walls. The main virus causes are influenza virus and adenovirus. Rhinovirus, mycoplasma Pneumoniae, and necrotizing fungal infections rarely cause bronchiectasis. Noninfectious causes Include immune mediated inflammation e.g., in allergic bronchopulmonary aspergillosis.

19. (D) Hemoptysis is not a feature of emphysema. In patient with emphysema who present with hemoptysis physicians must search for other causes. The most common cause of mild hemoptysis in the U.S is acute bronchitis. Hemoptysis can occur because of a tracheobronchial source, pulmonary parenchymal source, primary vascular disease, coagulopathy, or immune-mediated diseases, e.g., Goodpasture syndrome.
20. B
21. D
22. C
23. C
24. C
25. B
26. D
27. B
28. A
29. B
30. B
31. B
32. A
33. C
34. B
35. D
36. A
37. D
38. A
39. D
40. B

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قال صلى الله عليه وسلم: من سلك طريقاً يلتمس به علماً سهل الله له به طريقاً إلى الجنة.

دعواتنا لكم بالتوفيق.