النادي الطلابي
كلية الطب

Pathology RS

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III-
ASTHMA

https://pixy.org/1266846/

III. ASTHMA

- Chronic inflammatory disorder of the airways

- Causes recurrent episodes of **wheezing, dyspnea, chest tightness and cough** particularly at **night and/or early in the morning**
- *Dyspnea is shortness of breath.*

- **Its hallmarks are:**

a) **Intermittent and reversible** airway obstruction (bronchospasm), not continuous and not permanent

b) Chronic bronchial inflammation with **eosinophils**,

c) Bronchial **smooth muscle cell hypertrophy and hyper-reactivity**.

d) Increased **mucus secretion**.

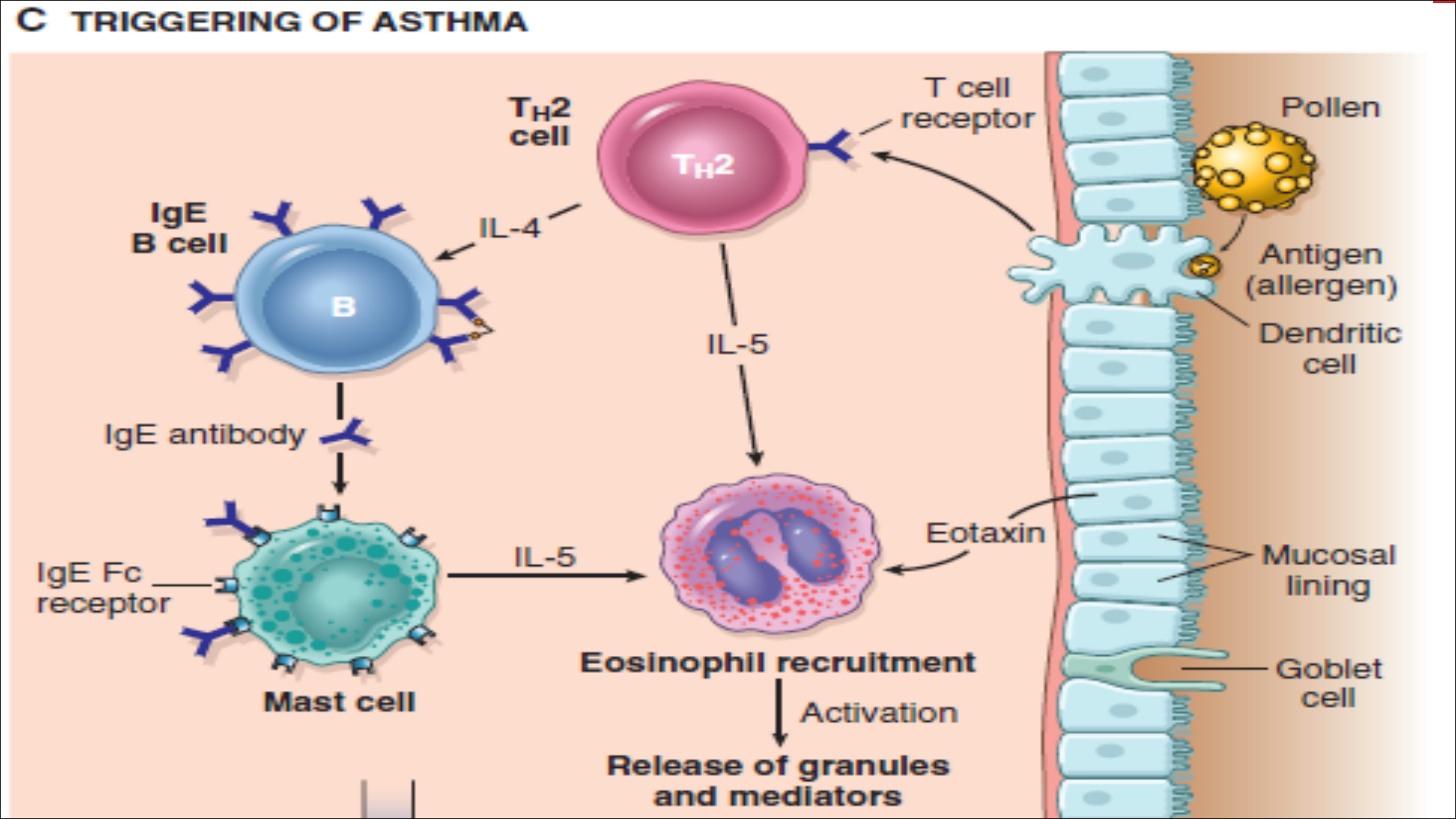
MAJOR FACTORS:

- ✓ Genetic predisposition to type I hypersensitivity (atopy)
- ✓ Acute and chronic airway inflammation
- ✓ Bronchial hyper-responsiveness to a variety of stimuli

• CAN BE TRIGGERED BY:

- ✓ Respiratory infections (especially viral)
- ✓ Airborne irritants (smoke, fumes)
- ✓ Cold air
- ✓ Stress
- ✓ Exercise

PATHOGENESIS

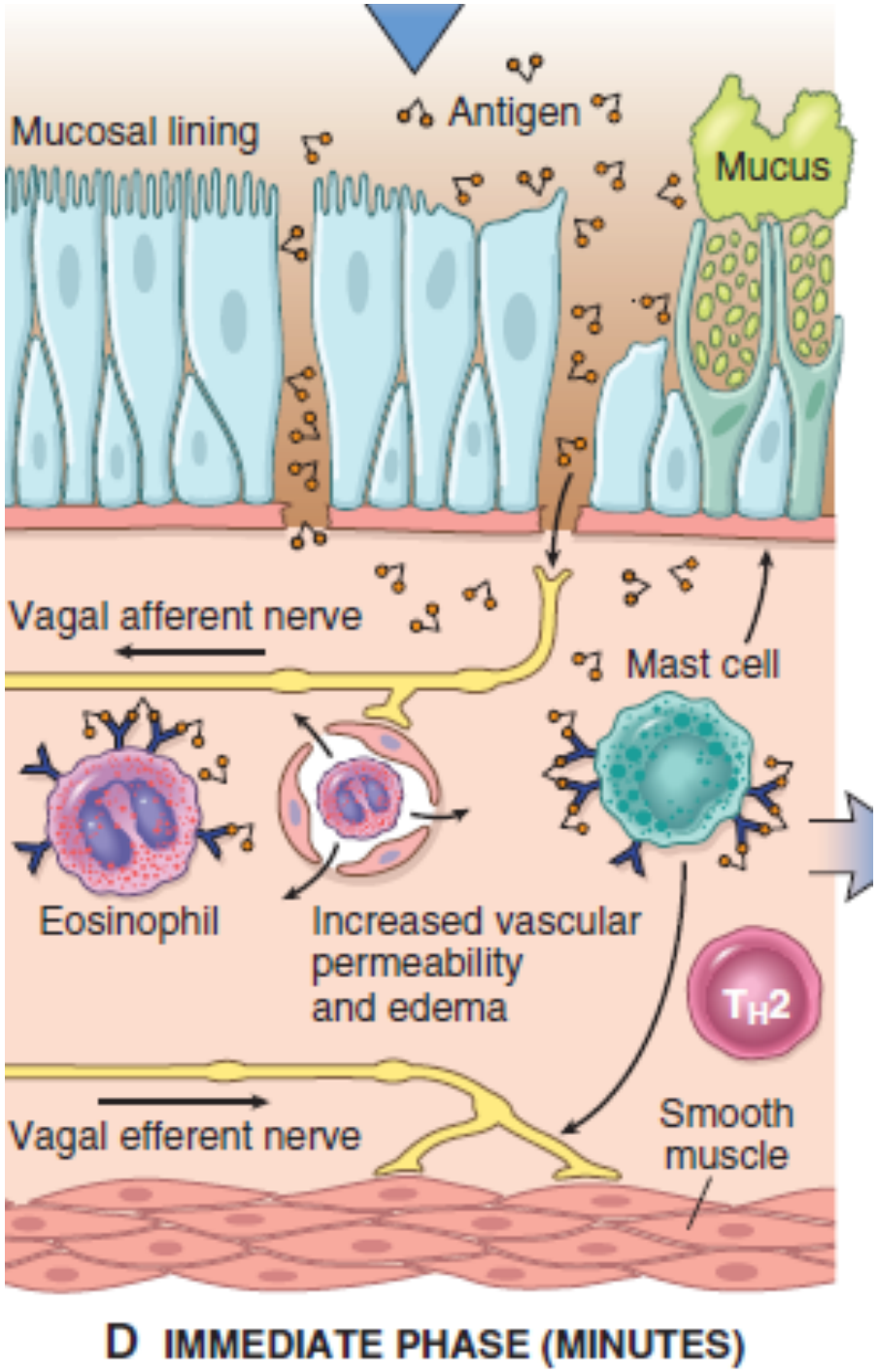

C TRIGGERING OF ASTHMA
TH2 cell
TH2
T cell receptor
Pollen
IgE B cell
B
IL-4
Antigen (allergen)
Dendritic cell
IL-5
IgE antibody
IgE Fc receptor
IL-5
Eotaxin
Mucosal lining
Goblet cell
Mast cell
Eosinophil recruitment
Activation
Release of granules and mediators

EXPLANATION OF THE PREVIOUS FIGURE

- The figure shows the initial airway response after the exposure to an inhaled allergen for the first time. The allergen (antigen) will be recognized by APCs or dendritic cells in the epithelial lining.
- As a result, T-helper lymphocytes will be activated and start releasing inflammatory mediators, resulting in IgE production and eosinophils activation and recruitment.
- IL4 and IL13 for example stimulate the IgE production, IL5 activates the eosinophils and IL13 stimulates the mucus production. IgE coats the submucosal mast cells → upon the re-exposure of the mast cells to the same allergen or antigen, two waves of reactions happen;
- 1. Early, immediate phase
- 2. Late phase

- **The early-phase reaction is dominated by:**
  - ✓ Bronchoconstriction
  - ✓ Increased mucus production
  - ✓ Vasodilation.

Bronchoconstriction is triggered by mediators released from mast cells, including histamine, PGD2, LTs for example LTC4, LTD4, LTE4 and also by the reflux neural pathways



D IMMEDIATE PHASE (MINUTES)

- This figure highlights the early phase reaction

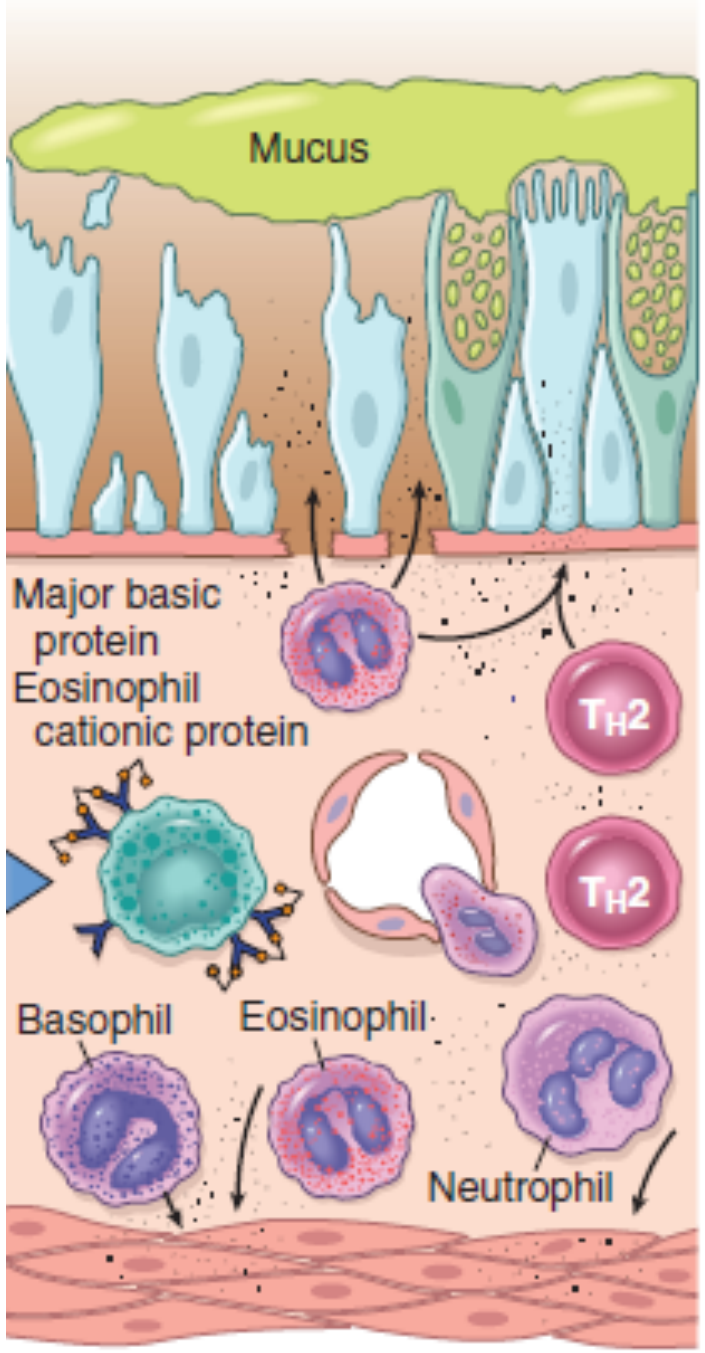
On re-exposure to antigen (ag) → immediate reaction

It is triggered by Ag-induced cross-linking of IgE bound to Fc receptors on mast cells.
Mast cells release preformed mediators that directly and via neuronal reflexes induce:

1. Bronchospasm,
2. Increased vascular permeability,
3. Mucus production
4. Recruitment of leukocytes

- **The late-phase reaction is inflammatory:**

  Inflammatory mediators → stimulate epithelial cells to produce chemokines (eotaxin) a potent chemoattractant and activator for eosinophils → recruit TH2 cells, eosinophils, and other leukocytes → amplifying the inflammatory reaction.



E LATE PHASE (HOURS)

Leukocytes recruited to the site of reaction (neutrophils, eosinophils, and basophils; lymphocytes and monocytes) → release mediators → initiate the late phase of asthma.

Eosinophils release major basic protein and eosinophil cationic protein that cause damage to the epithelium

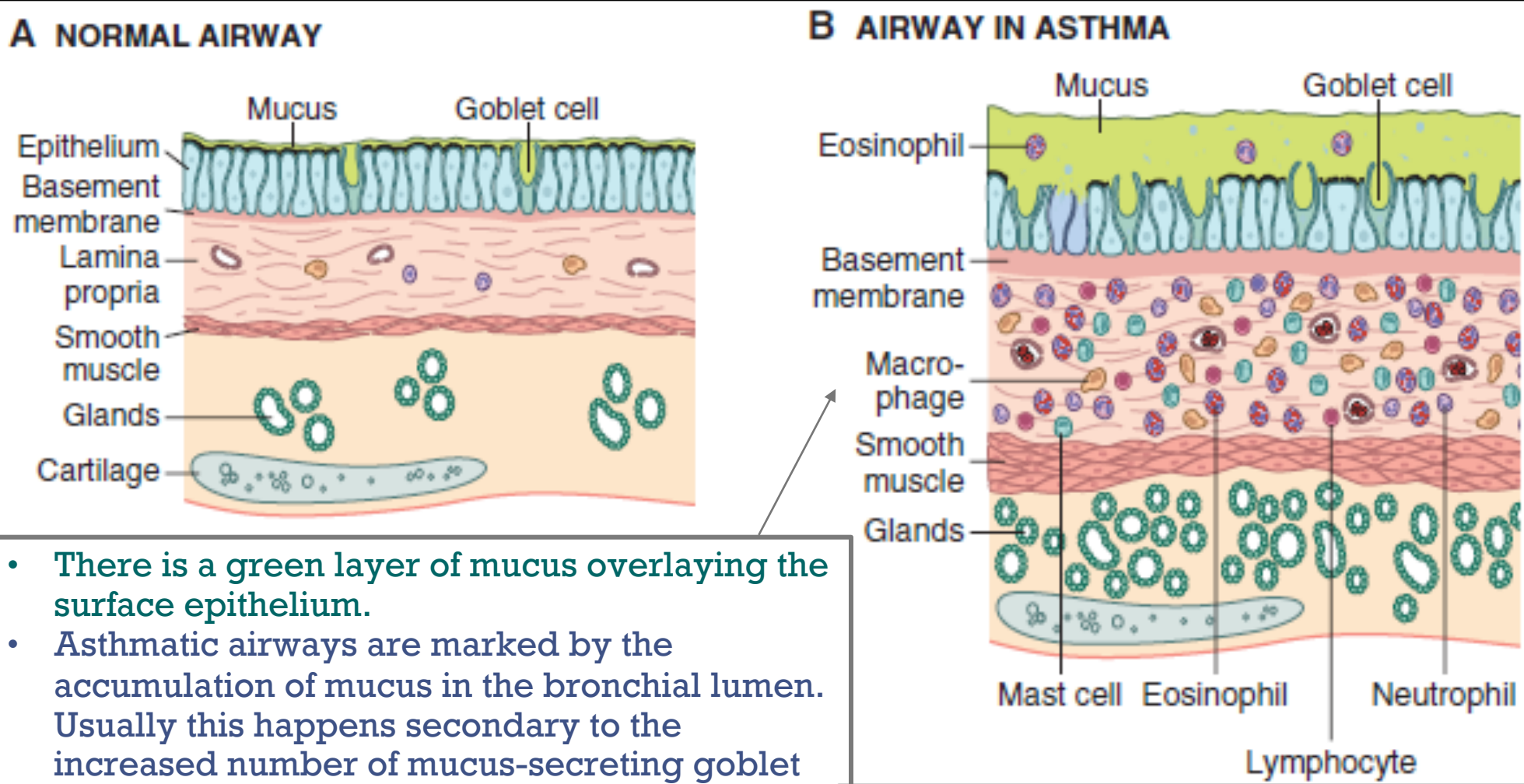
- Repeated bouts of inflammation lead to structural changes in the bronchial wall → called **airway remodeling**, including:

✓ Hypertrophy of bronchial smooth muscle

✓ Hypertrophy of mucus glands

✓ Increased vascularity

✓ Deposition of subepithelial collagen



- There is a green layer of mucus overlaying the surface epithelium.
- Asthmatic airways are marked by the accumulation of mucus in the bronchial lumen. Usually this happens secondary to the increased number of mucus-secreting goblet cells in the mucosa and hypertrophy of the submucosal glands.
- The mucosa is seen just below the thick layer of mucus and contains goblet cells.

- You can also appreciate the thickened basement membrane beneath the epithelium with intense chronic inflammation composed of eosinophils, macrophages and other inflammatory cells.
- Smooth muscle hypertrophy and hyperplasia, along with hypertrophy of the submucosal glands can be appreciated too.

Figure 13.5 ROBBINS BASIC PATHOLOGY, 10TH EDITION

Increased number of mucus-secreting goblet cells

Hypertrophy of submucosal glands

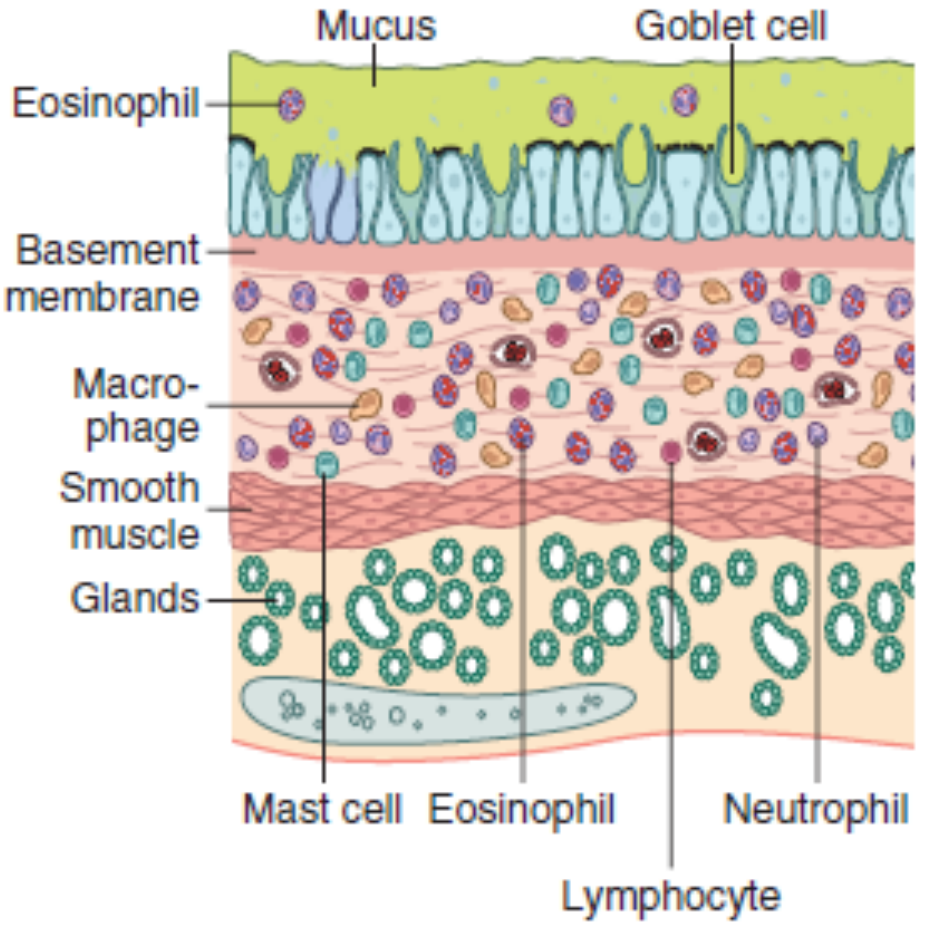
Accumulation of mucus in the bronchial lumen

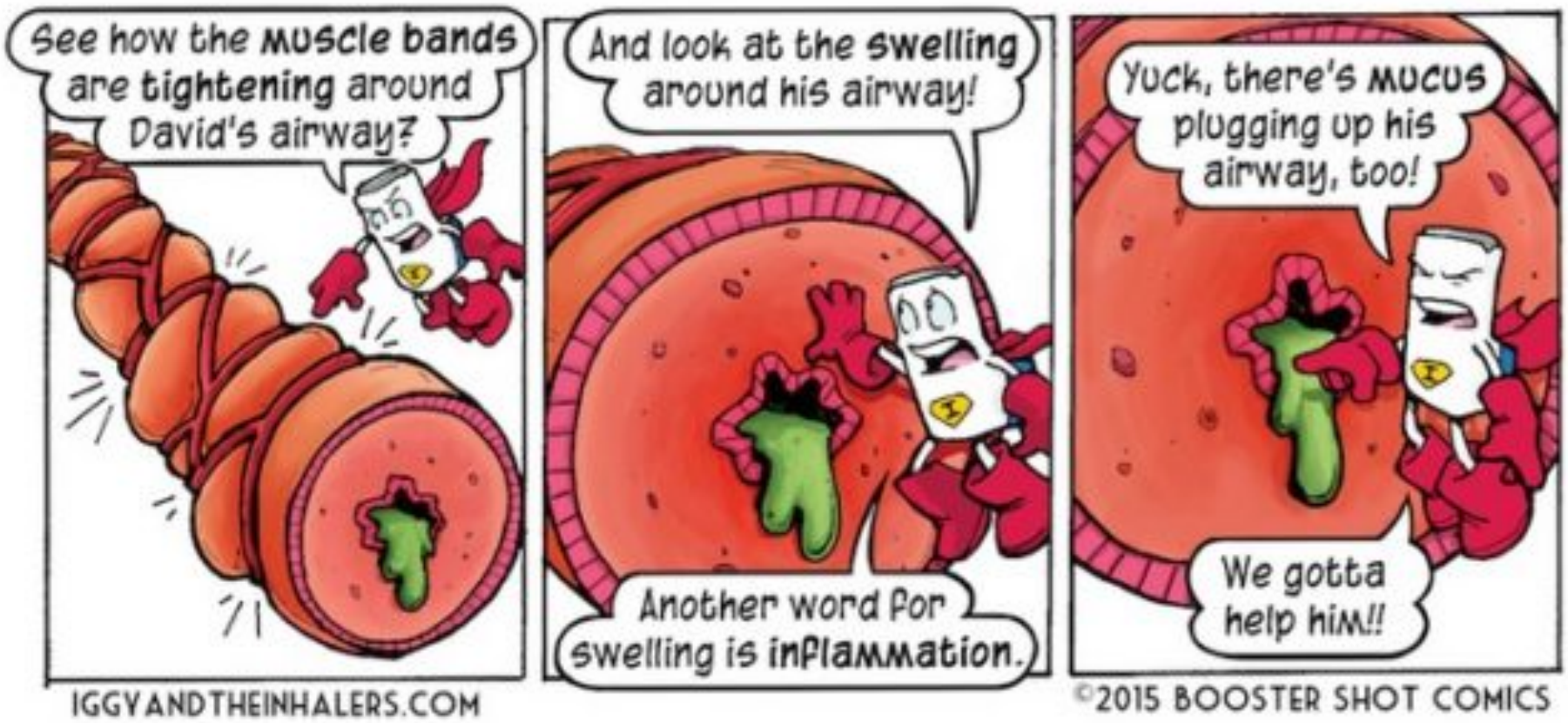
Thickened basement membrane

Intense chronic inflammation

Hypertrophy and hyperplasia of smooth muscle cells

The airways show the following ^^





https://anonhq.com/doctor-creates-animation-videos-comic-books-make-asthma-less-scary-kids/

TYPES OF ASTHMA

ATOPIC ASTHMA :

- The most common
- Classic example of type I IgE–mediated hypersensitivity reaction
- Beginning in childhood
- Positive family history of atopy and/or asthma
- Attacks are preceded by allergic rhinitis, urticaria, or eczema
- Attacks are triggered by allergens in dust, pollen, animal dander (from feathers), or food, or by infections.

- Exposure to the antigen→ excessive activation of type

2 helper cells → Cytokines production →

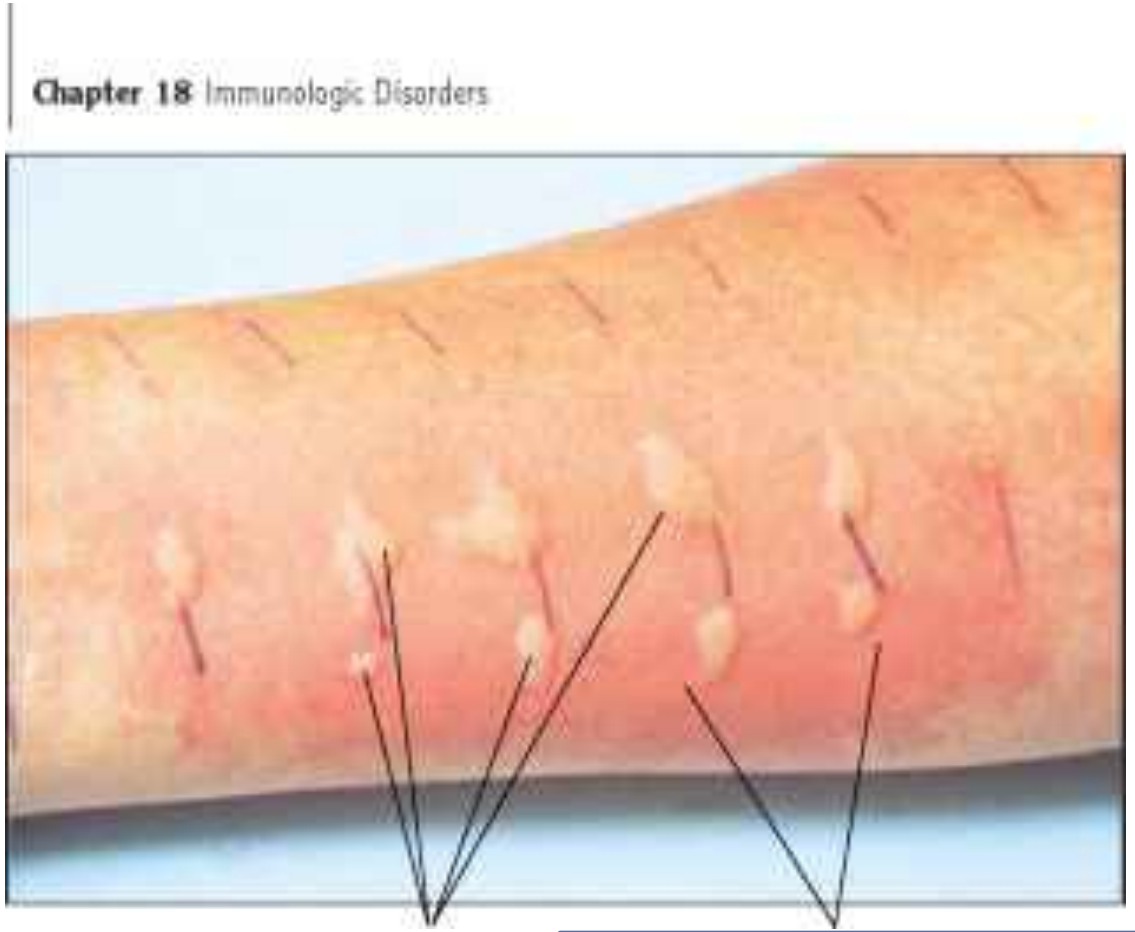
- ✓ IL-4 and IL-13 stimulates IgE production
- ✓ IL-5 activates eosinophils
- ✓ IL-13 also stimulates mucus production

- IgE coats submucosal mast cells→ release of **mast cell–derived mediators** → produce two waves of reaction:
  - Early (immediate) phase of reaction
  - Late phase of reaction

- Skin test with the antigen: immediate wheal-and-flare reaction

Skin break test: (the most common allergy skin test)

1. We get a series of tiny drops of the allergen on the back
2. Then you get a quick needle break on the skin underneath each drop
3. If the patient is allergic, he will get a red and itchy rash especially at the needle prick site



- Serum radioallergosorbent tests (RASTs) →

A blood test using radio immunoassay to detect the specific IgE antibodies and then to determine the substances the patient is allergic to

https://www.alpfmedical.info/causative-agent/type-i-hypersensitivities-immediate-igemediated.html

2- NON-ATOPIC ASTHMA :

- No evidence of allergen sensitization →
- Negative skin test
- A positive family history of asthma is less common.
- Triggered by:
  - Viral respiratory infections (rhinovirus, parainfluenza virus)
  - Inhaled air pollutants (sulfur dioxide, ozone, nitrogen dioxide).

The connections between the exposures and the non-atopic asthma are not well understood, the ultimate humoral and cell-mediators of airway obstruction are the same to both atopic and nonatopic variants of asthma, so they are treated in a similar way.

3- DRUG-INDUCED ASTHMA:

- Eg: Aspirin induced asthma →
  - Present with recurrent rhinitis ,nasal polyps , urticaria, and bronchospasm.

- The precise pathogenesis is unknown → involve some abnormality in prostaglandin metabolism from inhibition of cyclooxygenase by aspirin

https://en.wikipedia.org/wiki/Aspirin_exacerbated_respiratory_disease

4- OCCUPATIONAL ASTHMA

- Triggered by fumes (epoxy resins, plastics), organic and chemical dusts (wood, cotton, platinum), gases (toluene), and other chemicals. This happens after repeated exposure to the causing agent
- Examples include; farmers, animal handlers, manufacturers of foam mattresses, bakers, food processors, cotton workers, manufacturers of metals
- Asthma attacks usually develop after

repeated exposure to the antigen.

https://www.hopkinsmedicine.org/health/conditions-and-diseases/asthma/occupational-asthma

MORPHOLOGY

Figure 13.5 ROBBINS BASIC PATHOLOGY, 10TH EDITION

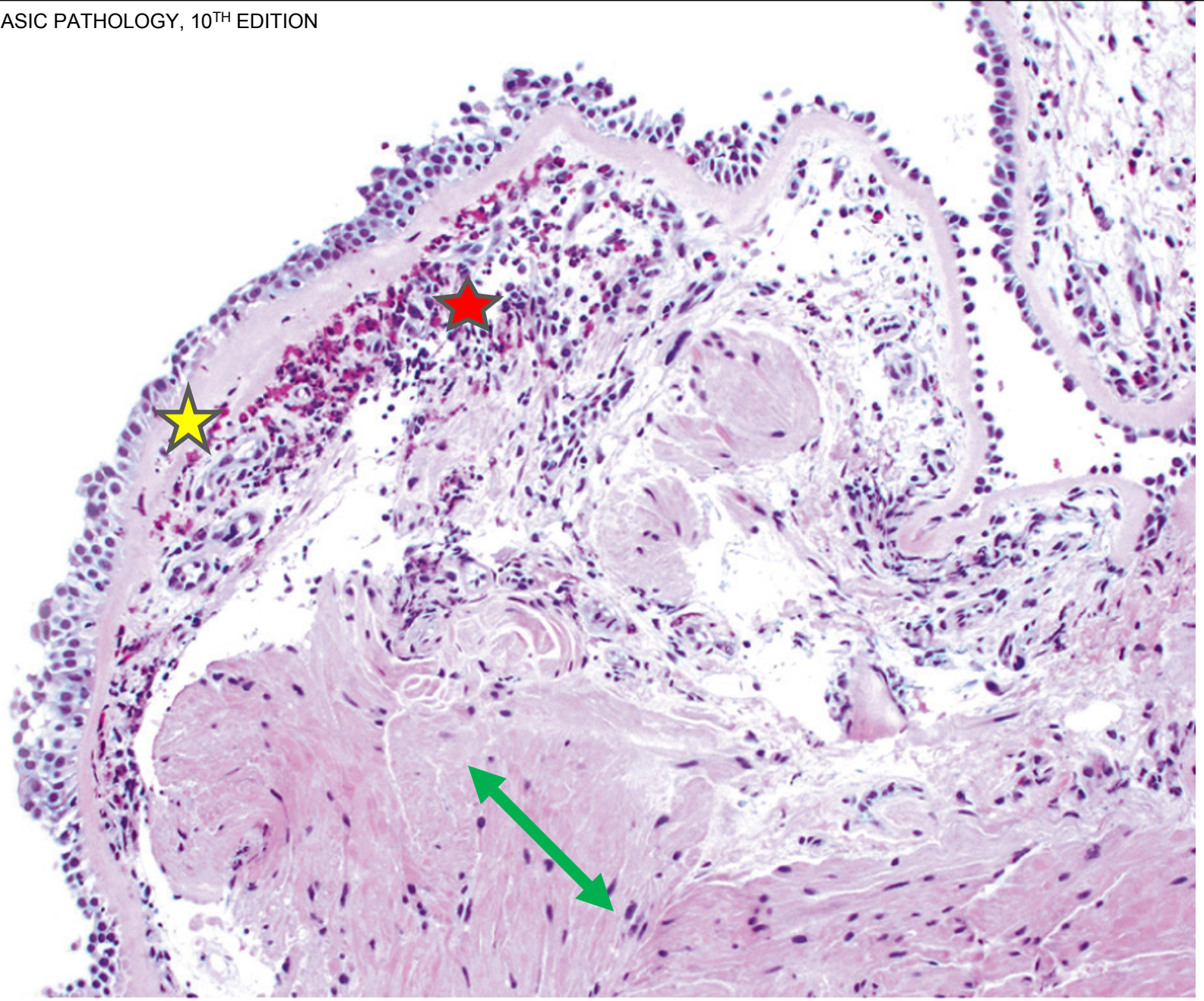
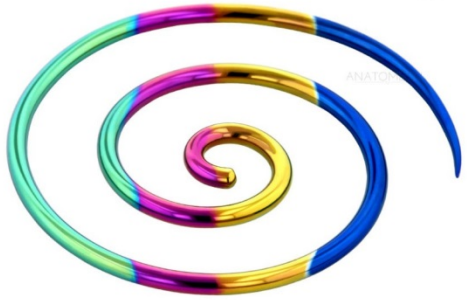


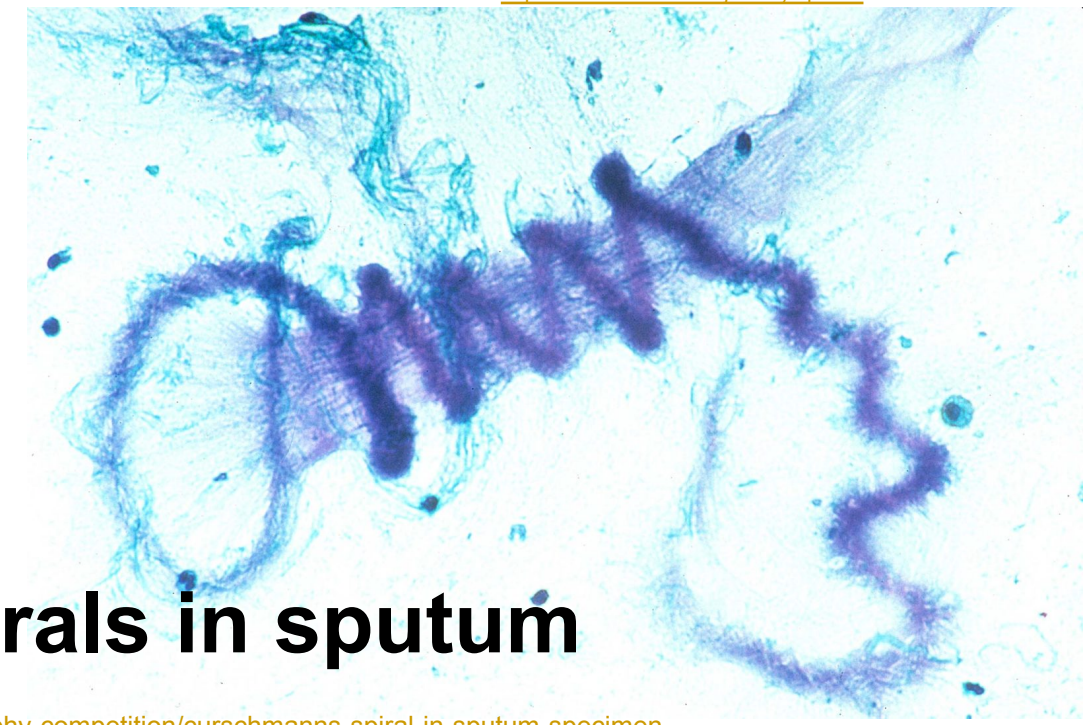
Fig. 13.11 Bronchial biopsy specimen from an asthmatic patient showing sub basement membrane fibrosis (yellow star), eosinophilic inflammation (red star), and smooth muscle hyperplasia (green arrow)

MORPHOLOGY

- Occlusion of bronchi and bronchioles by thick **mucous plugs**
- **mucous plugs** contain whorls of shed epithelium **called Curschmann spirals.**

https://anatometal.com/jewelry/spirals/

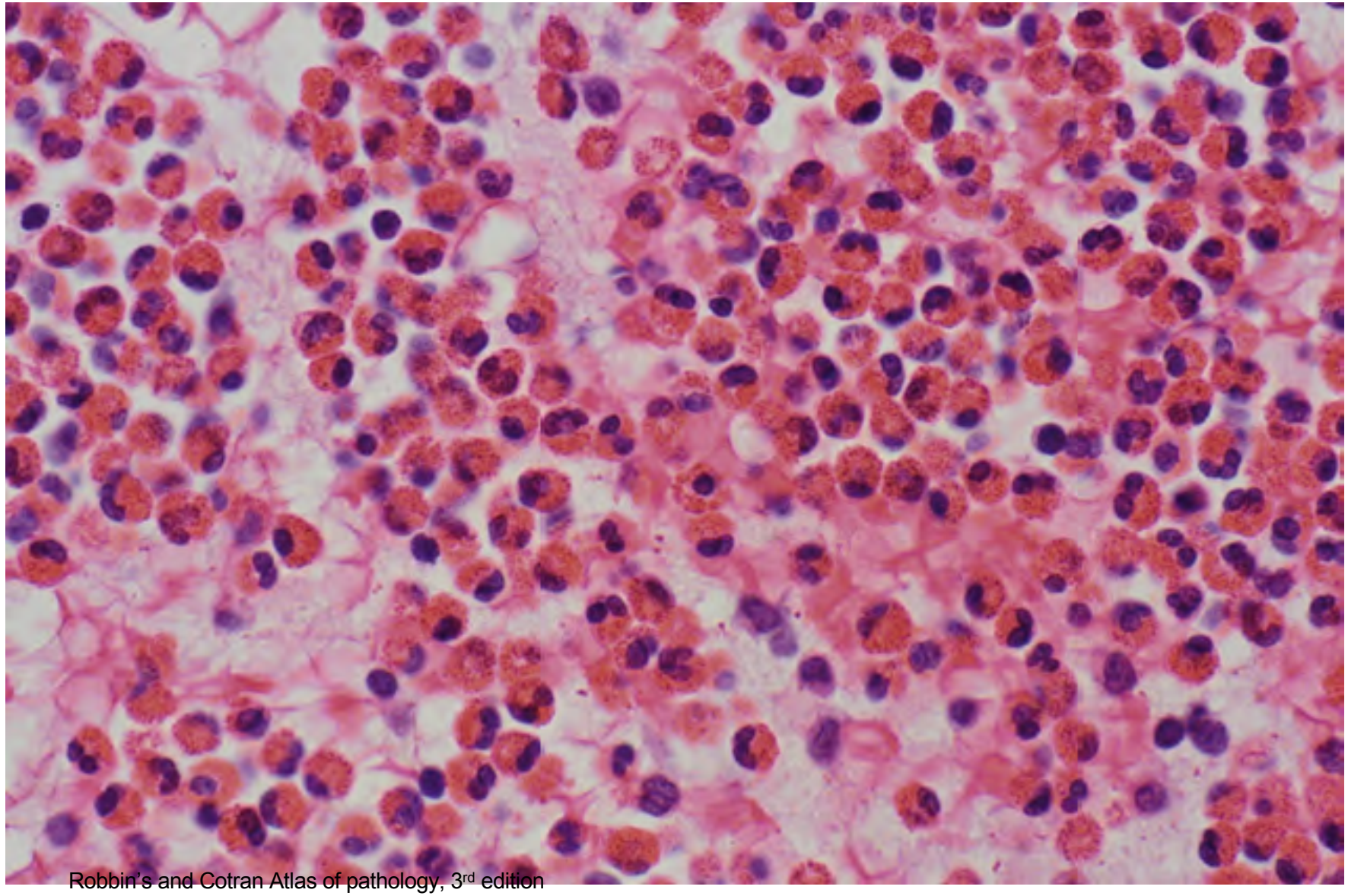




Curschman Spirals in sputum

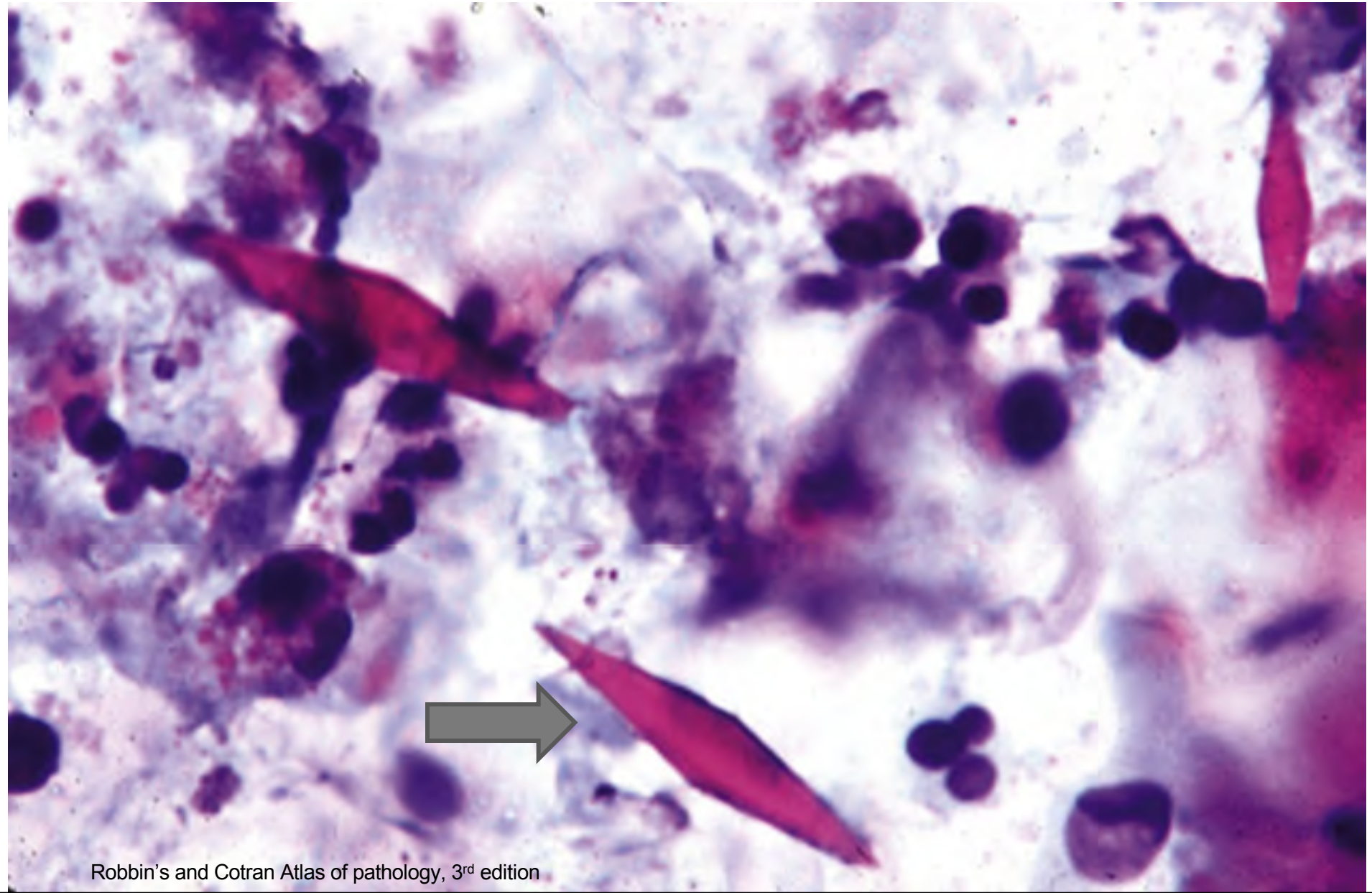
https://www.nikonsmallworld.com/galleries/1996-photomicrography-competition/curschmanns-spiral-in-sputum-specimen

- Eosinophils, they are the characteristic inflammatory cells in asthma



Robbin's and Cotran Atlas of pathology, 3rd edition

- **Charcot-Leyden crystals:** crystalloids made up of the eosinophil protein **galectin-10**



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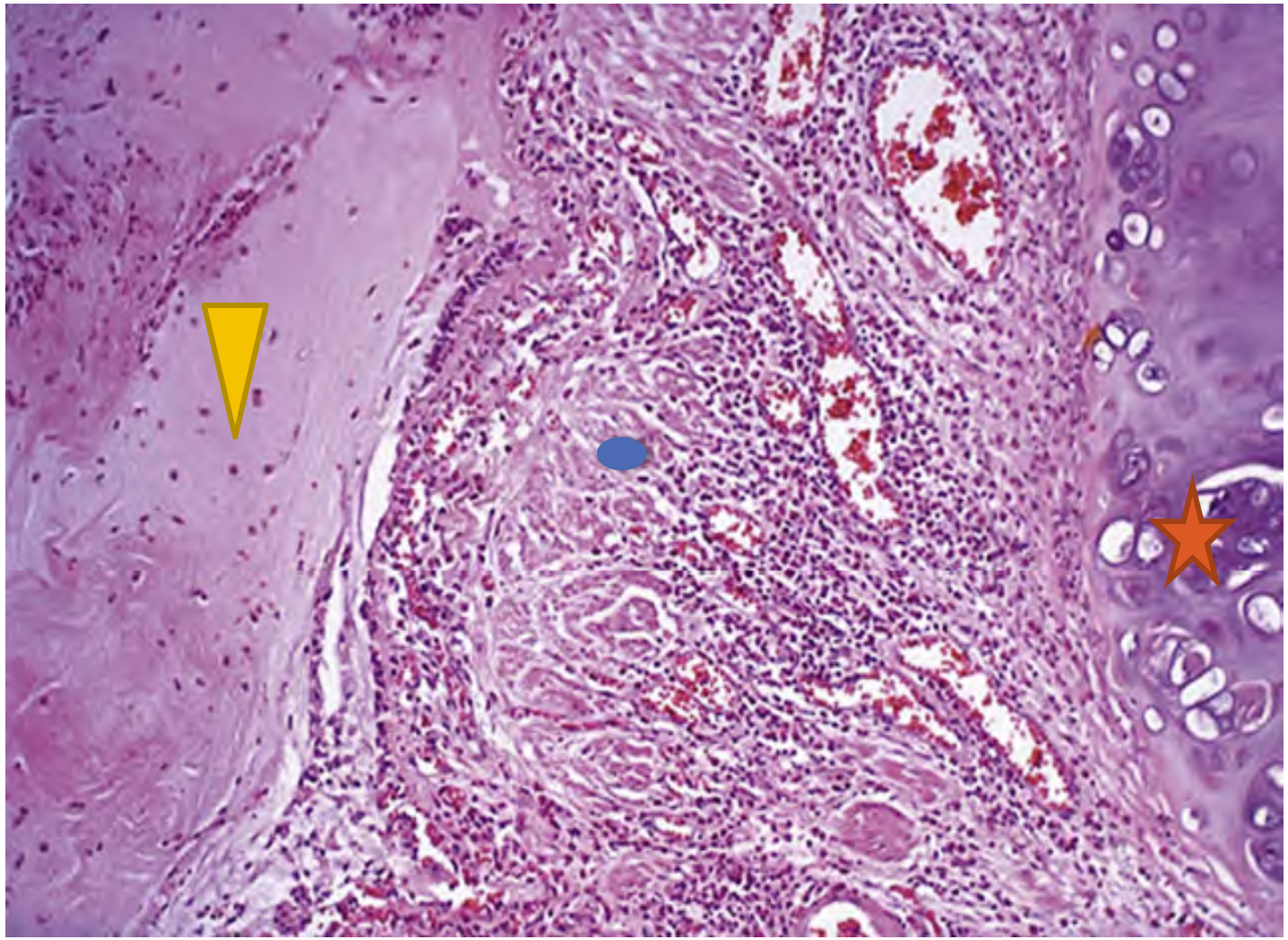
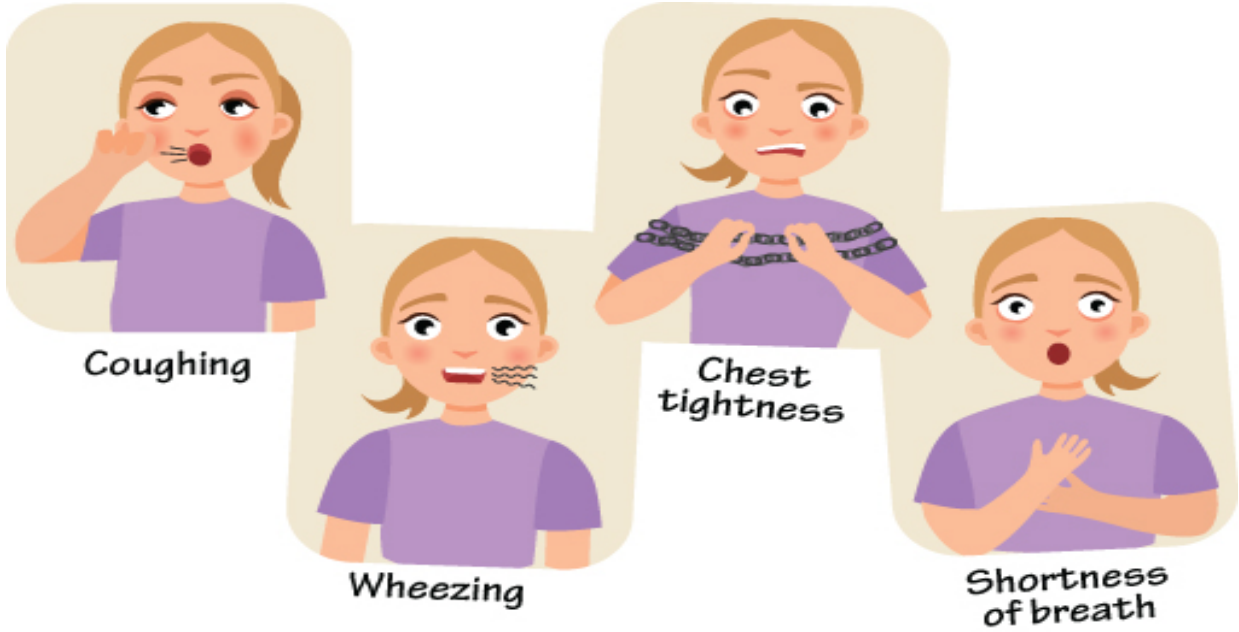
- Airway remodeling, including:
  - Thickening of airway wall
  - Sub-basement membrane fibrosis
  - Increased submucosal vascularity
  - An increase in size of the submucosal glands and goblet cell metaplasia of the airway epithelium
  - Hypertrophy and/or hyperplasia of the bronchial muscle
- In fatal cases→ distension of lungs
- They are distended due to air trapping with small areas of atelectasis



- This figure shows a predominantly expanded submucosa.
- The submucosa lies between the bronchial cartilage on the right (marked by the orange star) and the bronchial lumen that is stuffed and filled with mucus (marked by the yellow arrow head) on the left.
- The submucosa is widened by smooth muscle hypertrophy, edema, and inflammatory cells mainly eosinophils.

Robbin's and Cotran Atlas of pathology, 3rd edition

CLINICAL FEATURES OF AN ASTHMATIC ATTACK



- Cough often worsens at night or early morning
- Wheezing is a whistling sound, which occurs especially during expiration, and sometimes it can be heard easily even without a stethoscope.
- Chest tightness as the patient feels that there's something squeezing or setting on his chest
- Shorteness of breath is like you can't catch your breath
- Asthma is usually associated with difficulty in expiration.
- Each asthmatic attack may last from one to several hours and subsides either spontaneously or with therapy. The intervals between the attacks are free from the respiratory difficulties.
- Asthma is reversible except in advanced severe cases

https://allergyasthmanetwork.org/what-is-asthma/asthma-symptoms/

WHEEZING

The link below is for a youtube video for the wheezing sound

https://www.youtube.com/watch?v=7oTfvJff7go

Status asthmaticus:

https://nurseslabs.com/status-asthmaticus-nursing-management/

- **Status asthmaticus is** a severe paroxysm that does not respond to therapy and persists for days or weeks. **The associated hypercapnia, acidosis, and severe hypoxia may be fatal**
- Hypercapnia is the buildup of CO_2 in the blood.

MANAGEMENT:

- Standard therapies include:
  - Anti-inflammatory drugs (glucocorticoids)
  - Bronchodilators (beta-adrenergic drugs)
  - Leukotriene inhibitors

Leukotriene inhibitors are potent bronchoconstrictors, however these agents can block specific immune mediators such as IL4 and IL5. this effect can be helpful in some patients.

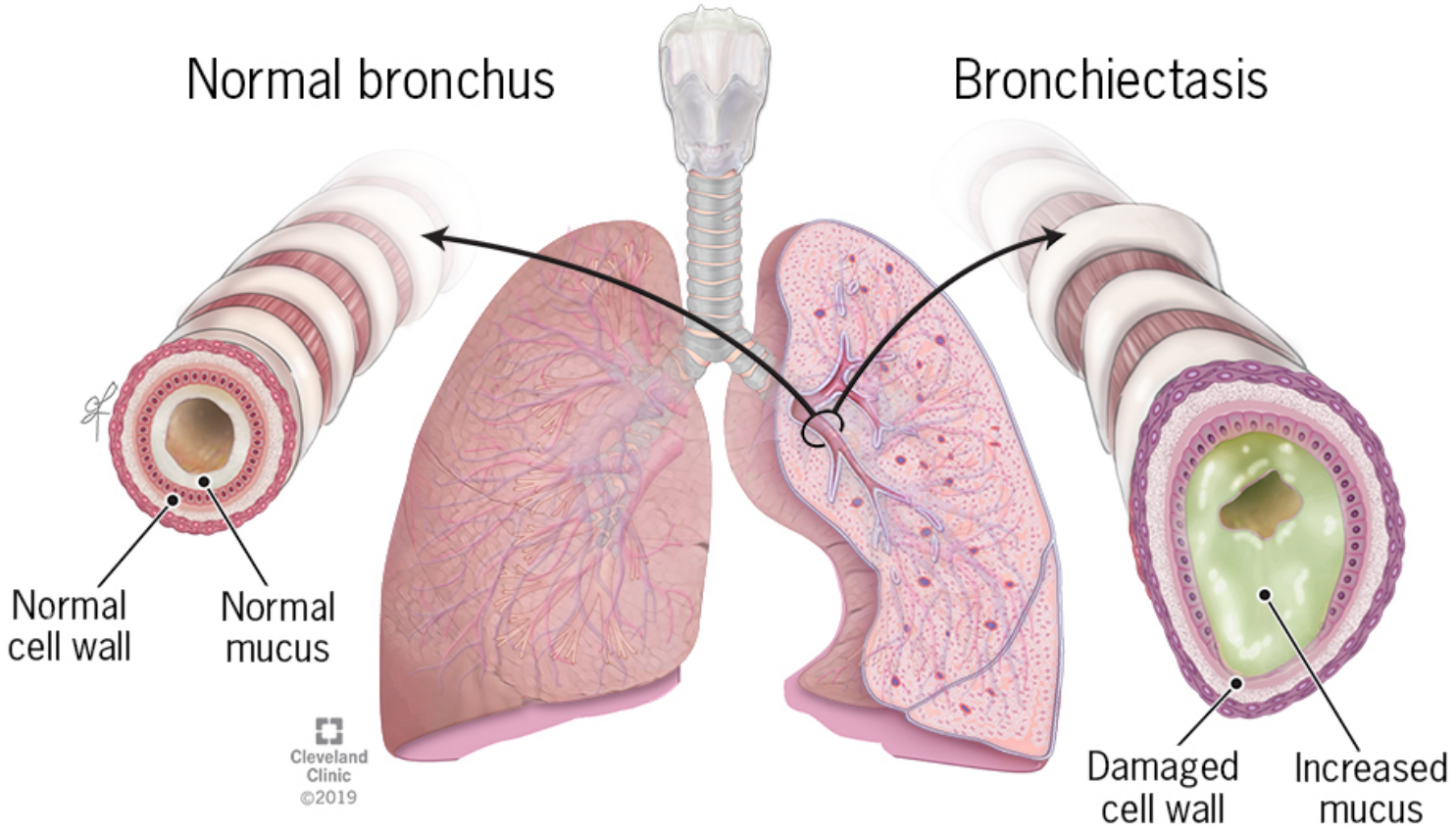
IV- BRONCHIECTASIS

- **Permanent** dilation of **bronchi and bronchioles** caused by destruction of smooth muscle and the supporting elastic tissue

- Typically **results from or is associated** with **chronic necrotizing infections**

- It is not a primary disorder, as it **always** occurs **secondary to persistent infection or obstruction**

IV- BRONCHIECTASIS



- It is an irreversible dilation.
- This time it only happens in the bronchi and bronchioles, when we compare this to emphysema, which is the permanent dilation of the airways distal to the terminal bronchioles.

https://my.clevelandclinic.org/health/diseases/21144-bronchiectasis

The characteristic symptom complex it dominated by:

- Cough and expectoration of copious amounts of **purulent** sputum
- Purulent sputum usually contains WBCs, cellular debris, dead tissue and mucus. It is typically yellow or green in color and can be seen in cases of bronchiectasis and lung abscesses.

- **Diagnosis:** appropriate **history and radiographic** demonstration of bronchial dilation.

The conditions that most commonly predispose to bronchiectasis include:

- **Bronchial obstruction:**
  - By tumors, foreign bodies, and impaction of mucus OR as a complication of atopic asthma and chronic bronchitis
  - Bronchiectasis is localized to the obstructed lund segment

- **Congenital or hereditary conditions:**

  - **Cystic fibrosis:** Widespread severe bronchiectasis
    - Due to obstruction caused by abnormally viscid mucus and secondary infections

  - **Immunodeficiency states:**
    - Due to recurrent bacterial infections
    - Localized or diffuse

  - **Primary ciliary dyskinesia (immotile cilia syndrome):**
    - rare autosomal recessive disorder→ inherited abnormalities of cilia → impairs the mucocillilary clearing of the airways →persistent infections.
    - bronchiectasis + sterility in males

Cystic fibrosis is a hereditary disease that affects the lung and the digestive system, the body produces thick and sticky mucus that may block the lungs and obstruct the pancreas.

- **Necrotizing, or suppurative, pneumonia:**
  - Particularly with virulent organisms such as Staphylococcus aureus or Klebsiella spp.

PATHOGENESIS

- Two intertwined processes contribute to bronchiectasis:
  - ✓ Obstruction
  - ✓ Chronic infection

- **OBSTRUCTION**→ impairs clearance of secretions→ the secretions start to accumulate providing a favourable media for→ superimposed infection→ inflammatory damage to the bronchial wall + the accumulating exudate→ airways distention →irreversible dilation.

- **PERSISTENT NECROTIZING INFECTION** in the bronchi or bronchioles →poor clearance of secretions, obstruction, and inflammation with peribronchial fibrosis and traction on the bronchi→ irreversible dilation

MORPHOLOGY, MACROSCOPIC:

- **Lower lobes bilaterally,** particularly the vertical air passages
- Most severe involvement in **distal bronchi and bronchioles**.
- **The airways may be dilated to as much as four times their usual diameter**

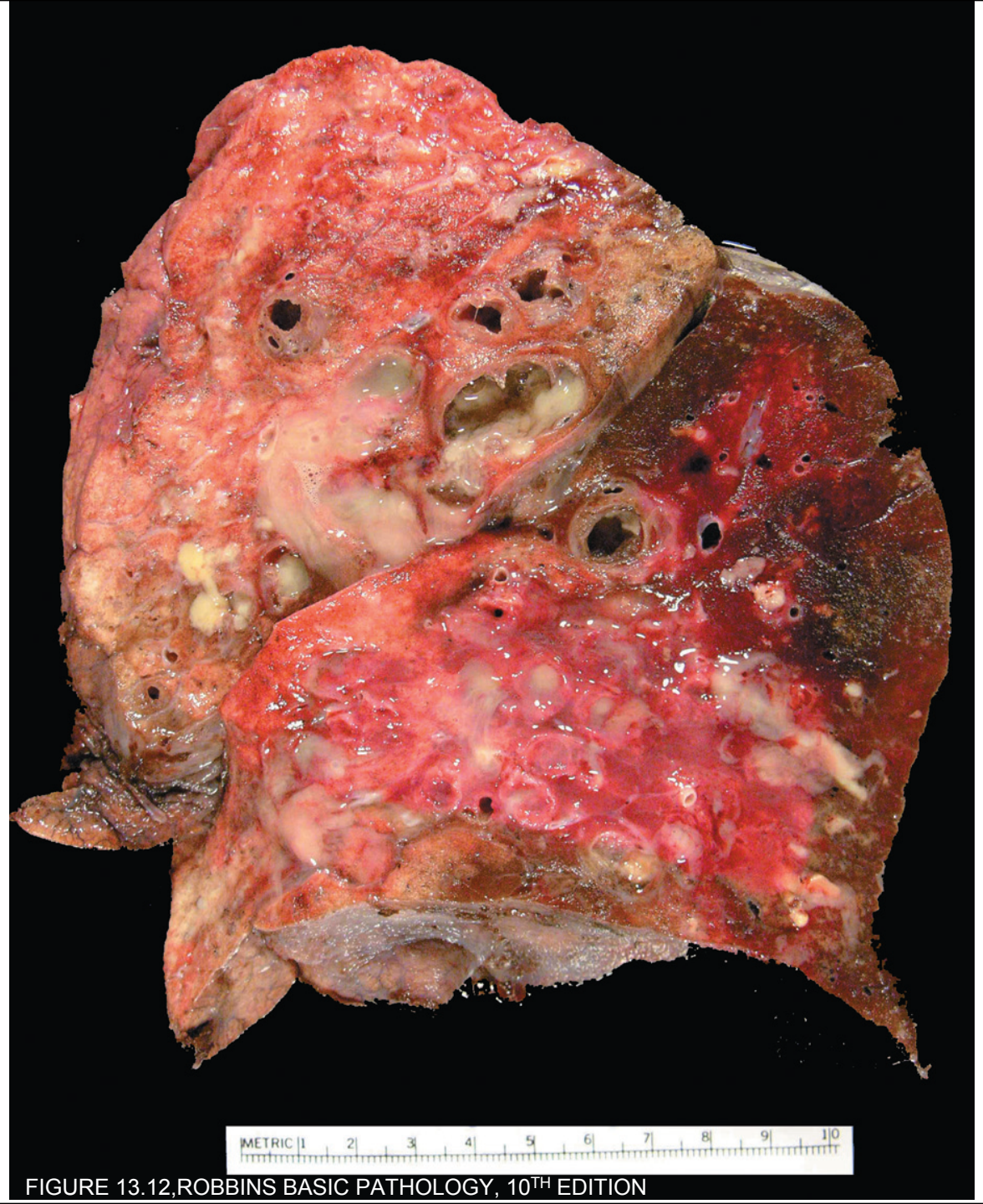


FIGURE 13.12,ROBBINS BASIC PATHOLOGY, 10TH EDITION

Markedly dilated bronchi filled with purulent mucus

The is the gross appearance of the lung that is involved by bronchiectasis in a patient with cystic fibrosis who underwent lung resection for transplantation.
The cut surface of the lung shows marked dilation of the bronchi and those bronchi are stuffed and filled with purulent mucus.

MORPHOLOGY, MICROSCOPIC:

- **In full-blown active cases:**
  - Intense acute and chronic inflammatory exudate within the walls of the bronchi and bronchioles → desquamation of lining epithelium and extensive ulceration (this happens due to the severe inflammation)
  - Mixed flora are cultured from the sputum.
  - *The usual organisms include; staphylococcus, streptococcus, pneumococcus and enteric organisms and anaerobic bacteria.*

MORPHOLOGY, MICROSCOPIC:

- **When healing occurs:**
  - The lining epithelium may regenerate completely
  - Abnormal dilation and scarring may persist, as the injury cannot be repaired completely
  - Chronic cases may have fibrosis of bronchial and bronchiolar walls
  - Peribronchiolar fibrosis (also seen in chronic cases)
  - Abscess formation in some cases (abscess cavity)

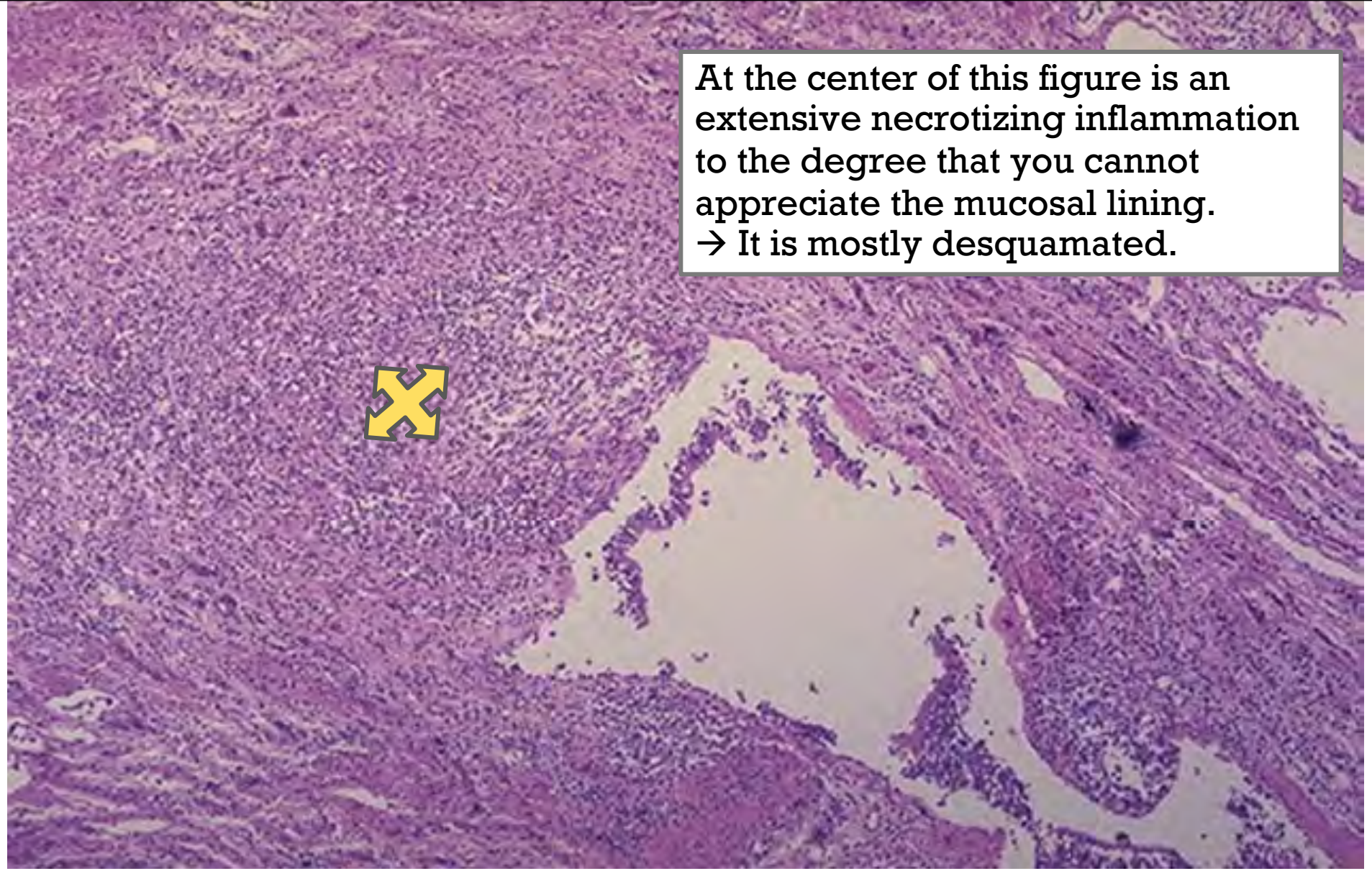


Figure 5-34 **Bronchiectasis, microscopic** dilated bronchus in which the mucosa and bronchial wall are not seen clearly because of the necrotizing inflammation with tissue destruction.

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CLINICAL FEATURES

- **Severe, persistent cough with mucopurulent sputum.**
  - Other symptoms: dyspnea, rhinosinusitis (inflammation of the nasal cavity and paranasal sinuses), and hemoptysis (spitting blood).
- Episodic
- Precipitated by URTI.
- Severe widespread bronchiectasis : significant obstructive ventilatory defects → associated with: hypoxemia, hypercapnia, pulmonary hypertension, and cor pulmonale.
- With current treatments, outcomes have been improved and severe complications such as brain abscesses and cor pulmonale are less frequent

IN SUMMARY:

Table 13.1 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.

The cough in asthma is a dry cough

The doctor read the whole table

https://baytowncrimestoppers.com/baytowns-most-wanted/unsolved-crimes/

A 45-year-old gentleman smoked two packs of cigarettes per day for 20 yrs. For the past 4 years, he has had a **chronic cough with copious mucoid expectoration**. During the past year, he has had multiple respiratory tract infections. He has also developed difficulty breathing, tightness of the chest, and **audible wheezing**. His breathing difficulty is relieved by inhalation of a β-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) α1-Antitrypsin deficiency with panlobular emphysema

B) Centrilobular emphysema with cor pulmonale

C) Chronic asthmatic bronchitis

D) Cystic fibrosis with bronchiectasis

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FOR YOUR QUESTIONS:

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Or E-learning

THANK YOU!