RS

PATHOLOGY

MODIFIED NO. ?

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III- ASTHMA

https://pixy.org/1266846/

Color code

- Slides
- Doctor
- Additional info
- Important

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.**

- Its hallmarks are:

a) **Intermittent and reversible** (not continuous nor permanent) airway obstruction (bronchospasm),

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).

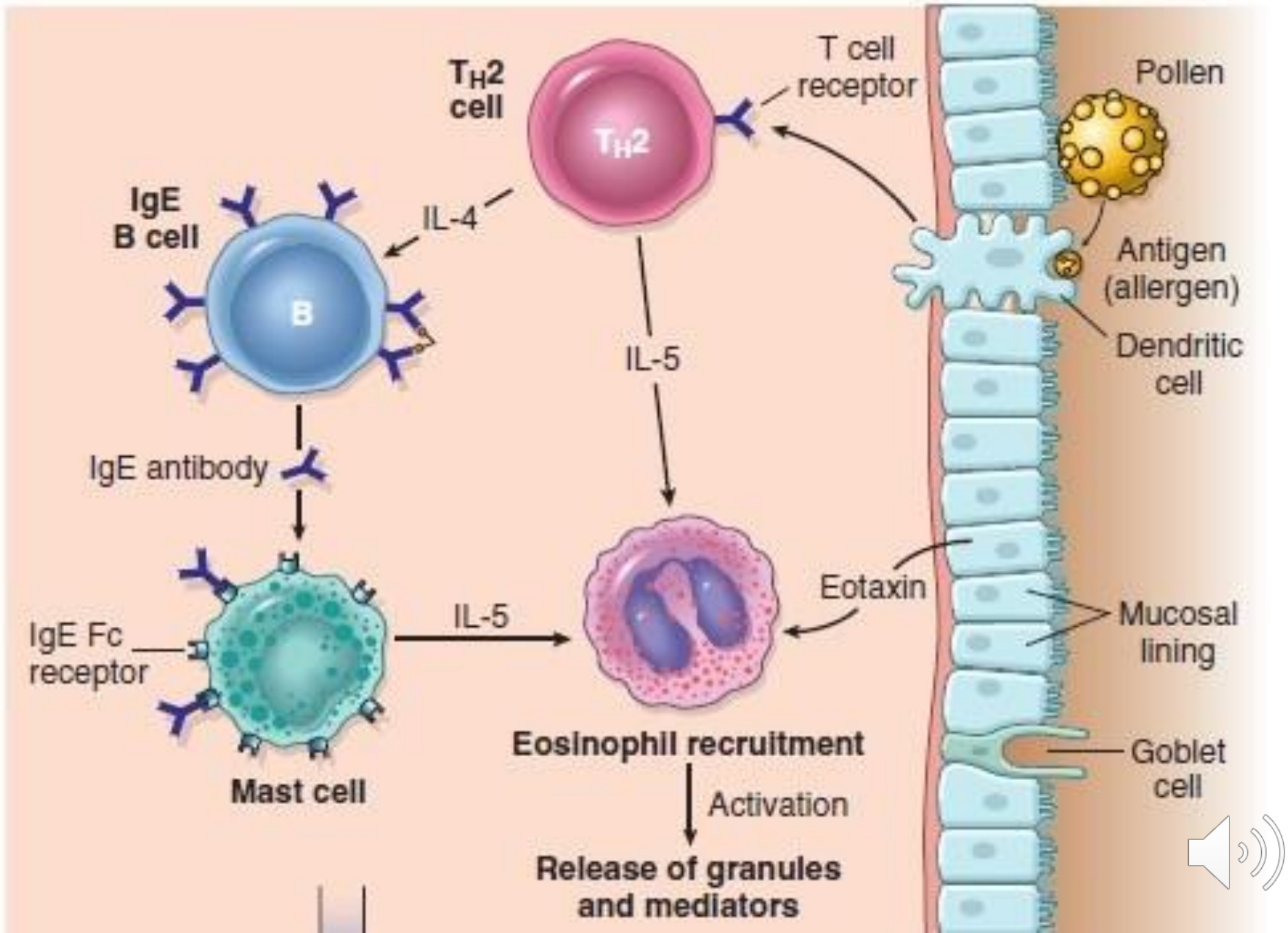
✓ Airborne irritants (smoke, fumes).

✓ Cold air.

✓ Stress.

✓ Exercise.

PATHOGENESIS


C TRIGGERING OF ASTHMA
T_H2 cell
T_H2
T cell receptor
Pollen
IgE B cell
B
IL-4
IL-5
Antigen (allergen)
Dendritic cell
IgE antibody
IgE Fc receptor
IL-5
Eotaxin
Mucosal lining
Goblet cell
Mast cell
Eosinophil recruitment
Activation
Release of granules and mediators

The previous figure shows the initial airway response after exposure to one of the inhaled allergens for the first time. The allergen or the antigen will be recognized by **antigen -presenting cells 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.

✓ IL-4 and IL-13, for example, stimulate the IgE production.
✓ IL-5 activates the eosinophils.
✓ IL-13 stimulates the mucus production.

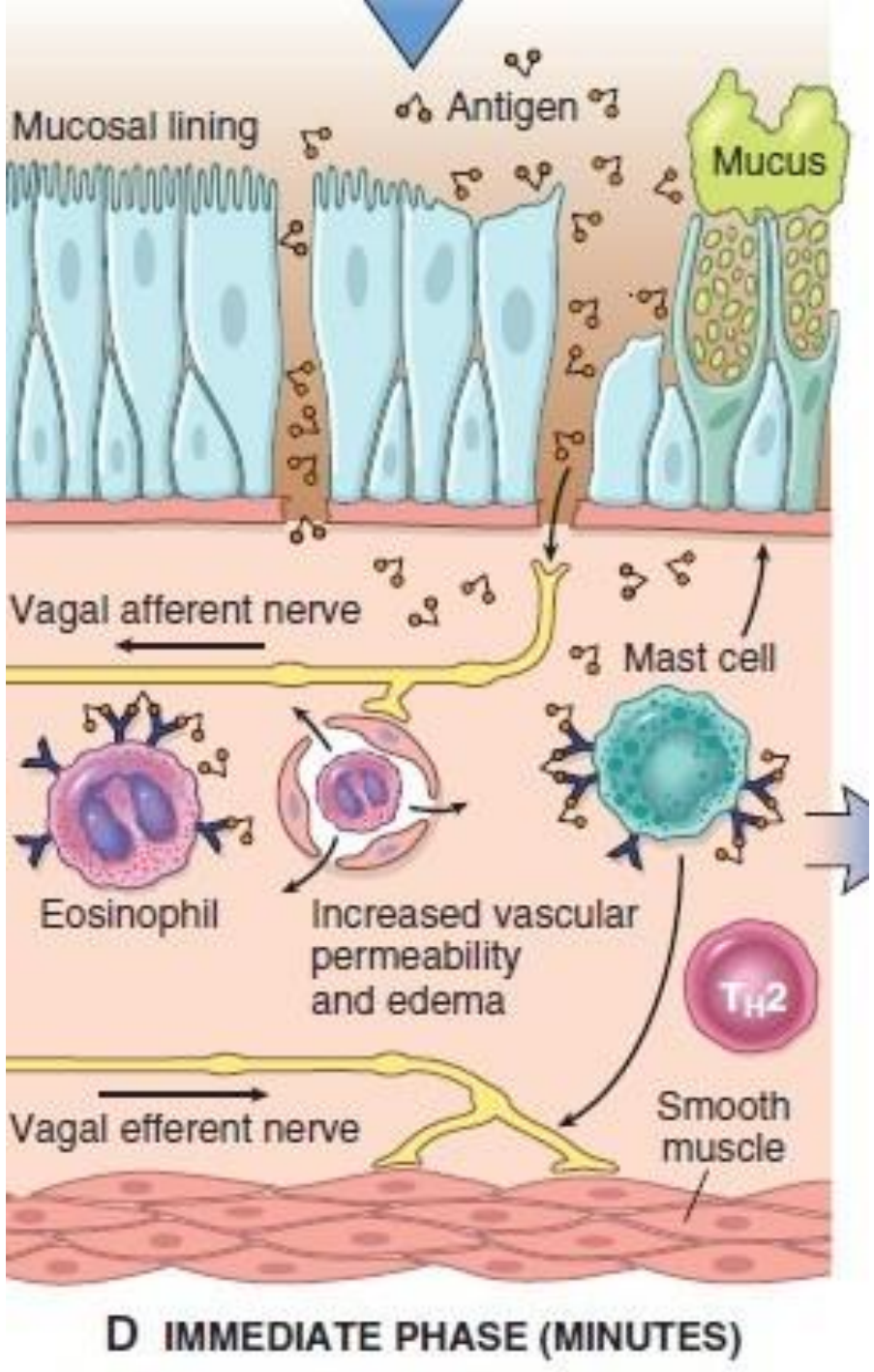
The IgE coats the submucosal mast cells. Upon the re-exposure of the mast cells to the same allergen or antigen, two waves of reaction happen: one is the early or immediate phase, and the other is the late phase.

- The early-phase reaction is dominated by:

✓ **Bronchoconstriction** → Triggered by mediators released from mast cells including histamine, prostaglandin D2, leukotrienes (e.g.leukotriene C4, D4, and E4), and by the reflux neural pathways.

✓ **increased mucus production.**

✓ **vasodilation.**



- This figure highlights the early phase reaction.

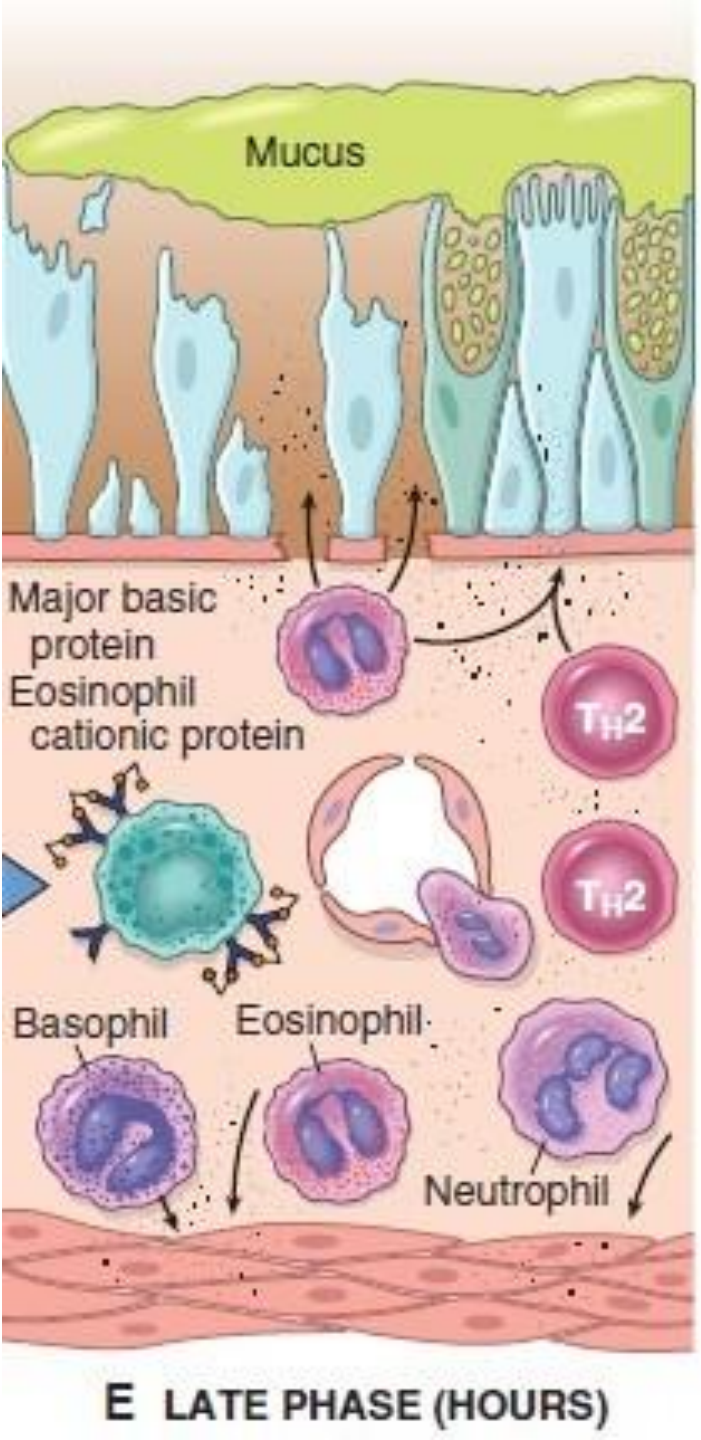
on re-exposure to an antigen (ag) → Immediate reaction

- This reaction is triggered by Ag-induced cross-linking of IgE that is already bound to FC receptors on mast cells.

- Mast cells release previously performed mediators that directly and via neuronal reflexes induce:
bronchospasm,
increased vascular permeability,
mucus production,
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 (T-helper type 2 lymphocytes),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 sub epithelial collagen.

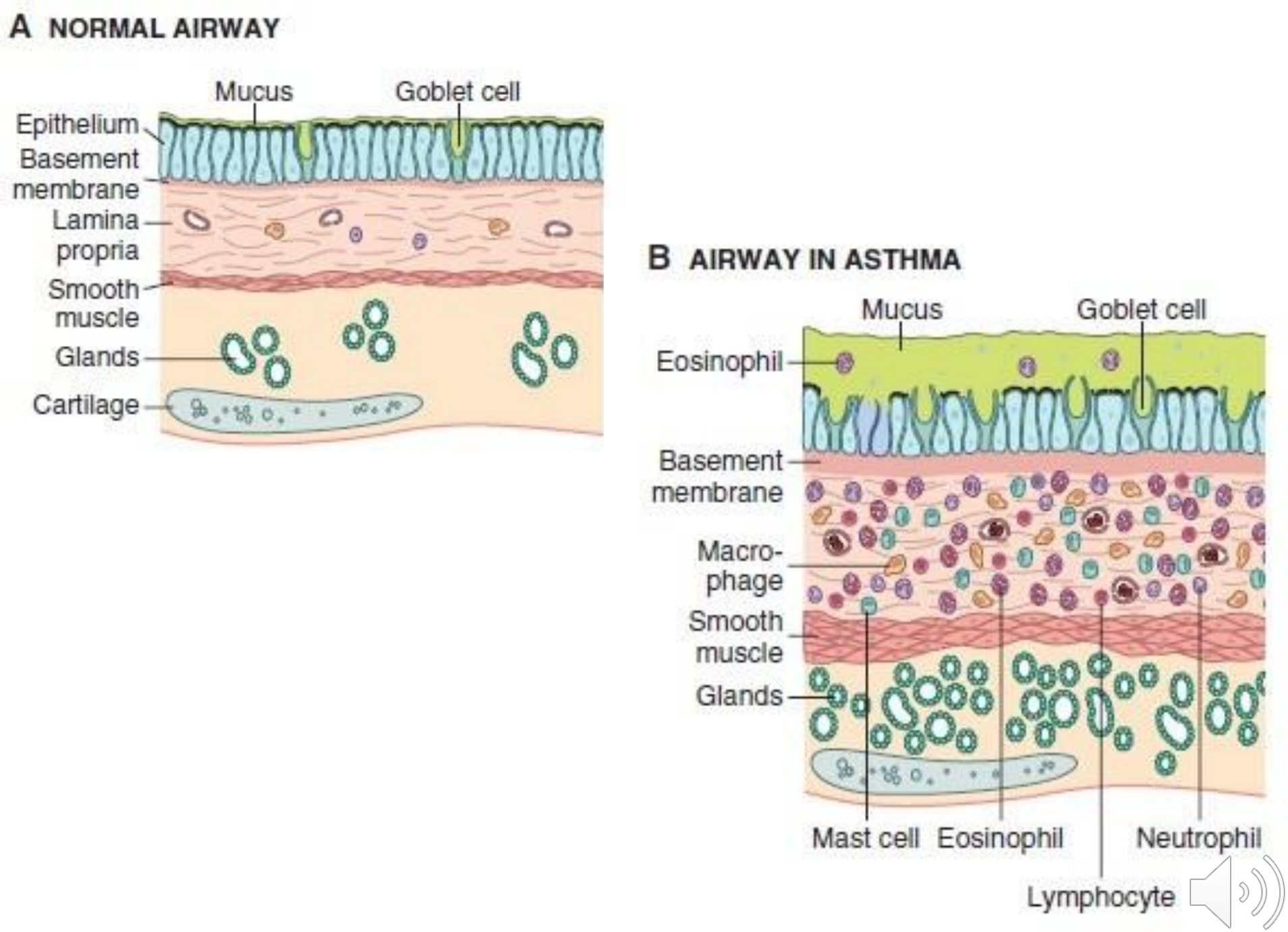
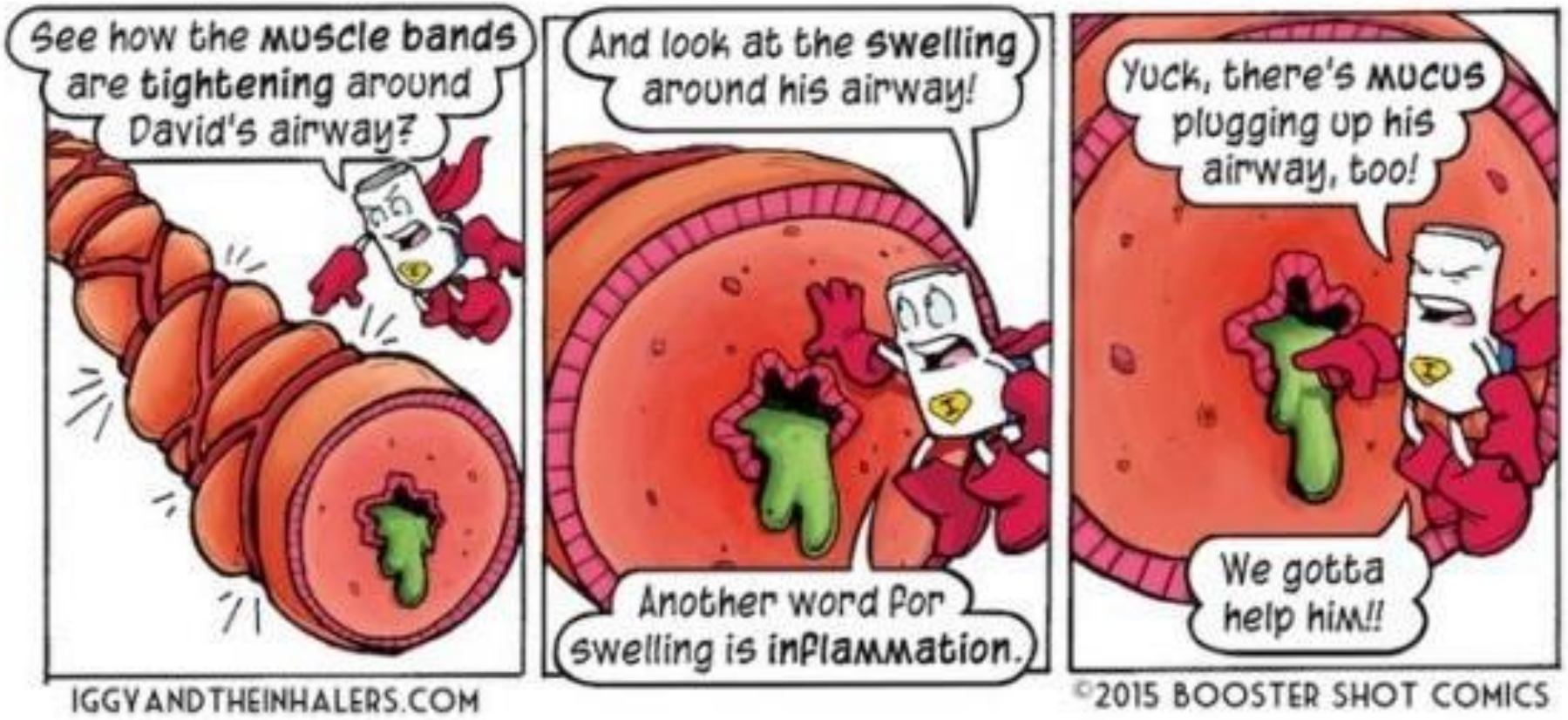


Figure 13.5 ROBBINS BASIC PATHOLOGY, 10TH EDITION

These figures show a comparison between a normal airway and an airway in asthma.

• Airway in asthma → there is a green layer of mucus overlying the surface epithelium. Asthmatic airways are marked by accumulation of mucus in the bronchial lumen, usually this happens secondary to the increased number of the mucus-secreting goblet cells in the mucosa and hypertrophy of the submucosal glands .The mucosa here is seen just below this thick layer of mucus and shows a lot of mucus-secreting goblet cells, also, the the basement membrane beneath the epithelium is thickened with intense chronic inflammation composed of eosinophils, macrophages, and other inflammatory cells, with smooth muscles hypertrophy and hyperplasia along with hypertrophy of submucosal glands.



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

- So, the **airways in patients** with asthma shows the following:

✓ Increased number of mucus-secreting goblet cells.
✓ Hypertrophy of submucosal glands.
✓ Accumulation of mucus in the bronchial lumbar .
✓ Thickened basement membrane.
✓ Intense chronic inflammation.
✓ Hypertrophy and hyperplasia of smooth muscle cells.

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 (the material that shed from animal feathers), food, or by infections.

• **Initial** exposure to the antigen → excessive activation of type 2 helper cells → Cytokines production →

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

•**Then** IgE coats submucosal mast cells → upon re-exposure → release of **Mast cell–derived mediators** → produce two waves of reaction:

1. Early (immediate) phase of reaction.
2. Late phase of reaction.

Atopic asthma can be diagnosed by two tests:

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

(eg; skin prick test and it's the most common allergy skin test). How is it done?

1. We get series of tiny drops of the allergen on the patient's back (or forearm).
2. Then quick needle pricks are made underneath each drop.
3. If the patient is allergic to that antigen, redness and itchiness will result especially at the needle prick sites.

2. Serum radioallergosorbent tests (RASTs): a blood test using radioimmunoassay to detect specific IgE antibodies, to determine the substances a subject is allergic to.

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

2- NON-ATOPIC ASTHMA :

- No evidence of allergen sensitization.

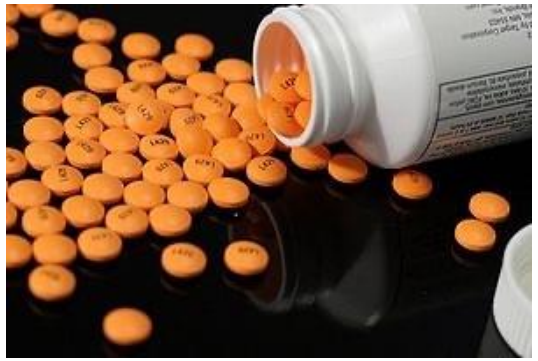
- Negative skin test.

- 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).

Although the connection between those exposures and the non-atopic asthma is not well understood, the ultimate humeral and cellular mediators of the airway obstruction are the same to both topic and non-atopic variants of asthma, so they are treated in a similar way.

3- DRUG-INDUCED ASTHMA:



• Several drugs can provoke asthmatic attacks; however, aspirin is the most important example.

• 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),animal substances and other chemicals.

- Asthma attacks usually develop after repeated exposure to the antigen.

- Examples include: farmers, animal handlers, manufacturers of foam mattresses, bakers, food processors, cotton workers and manufacturers of metals.

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

MORPHOLOGY

MORPHOLOGY

- Occlusion of bronchi and bronchioles by **thick mucous plugs** (the most striking finding).

- **Mucous plugs** contain whorls of shed epithelium **called** **Curschmann spirals.**

Curschman Spirals in sputum

Figure 13.5 ROBBINS BASIC PATHOLOGY, 10TH EDITION

The figure to the right shows a bronchial biopsy from an asthmatic patient showing the following:

- ❑ Sub basement membrane fibrosis.
- ❑ Eosinophilic inflammation.
- ❑ Smooth muscle hypertrophy and hyperplasia.

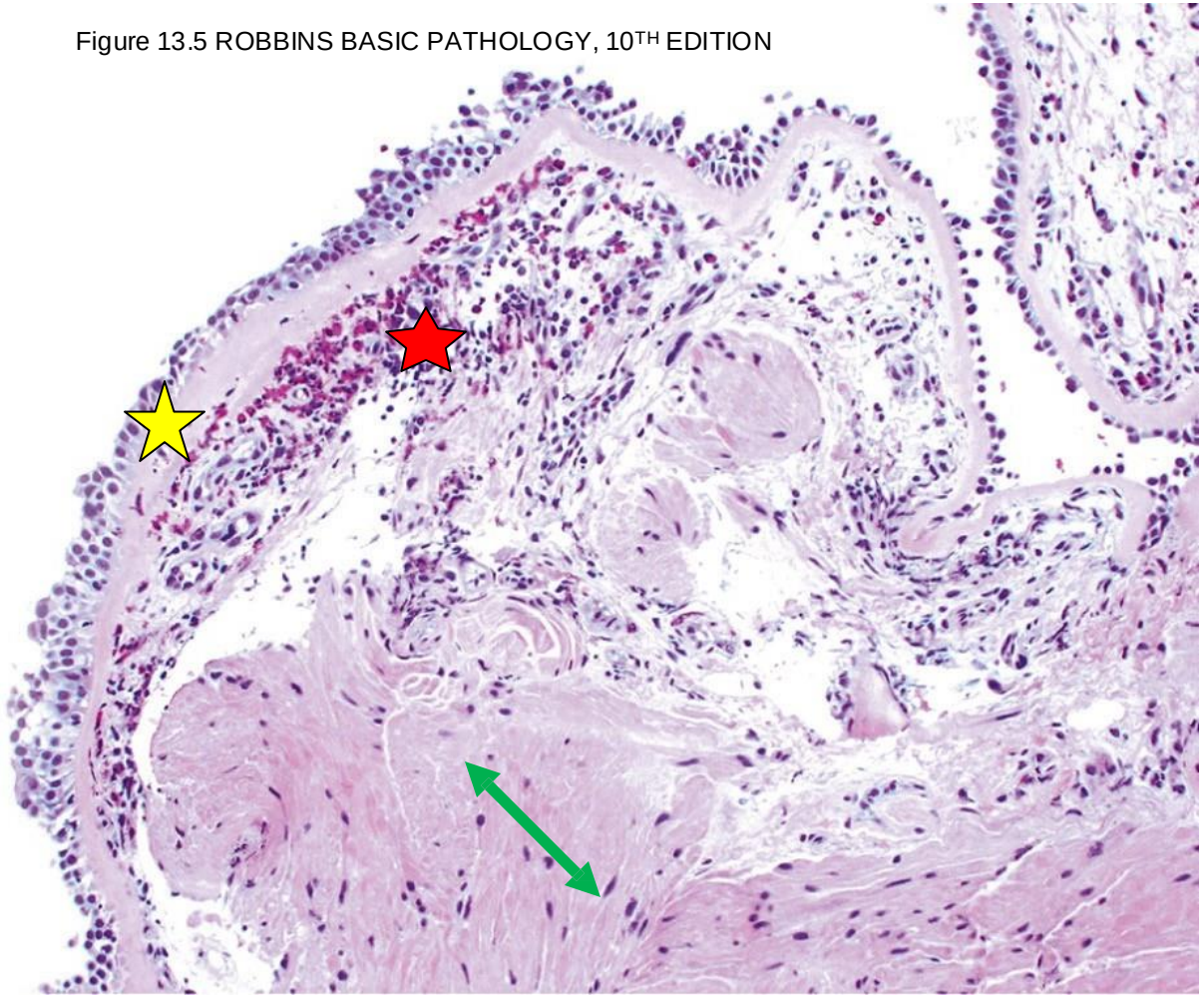
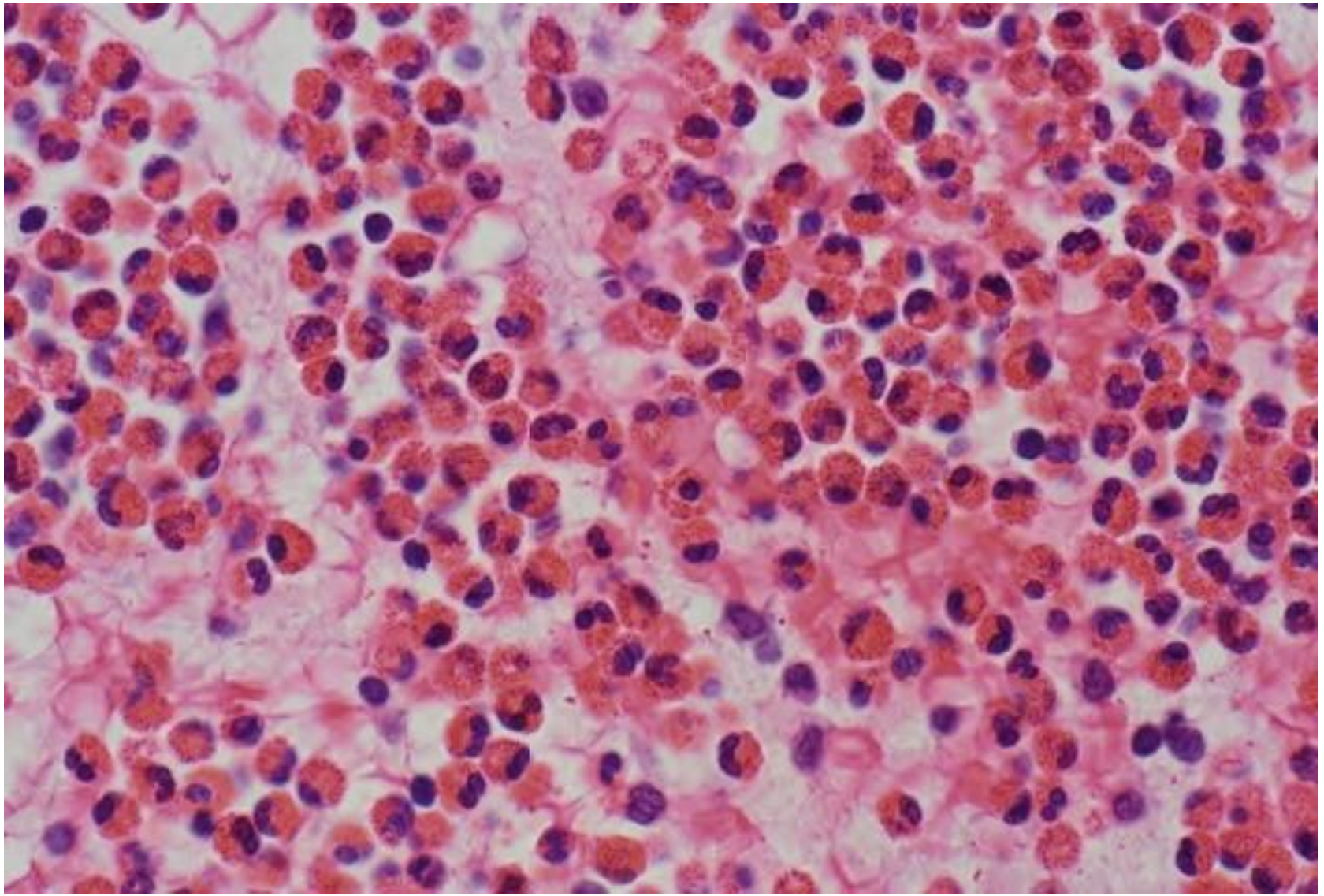


Fig. 13.11 Bronchial biopsy specimen from an asthmatic patient showin sub basement membrane fibrosis, eosinophilic inflammation, and smoot muscle hyperplasia

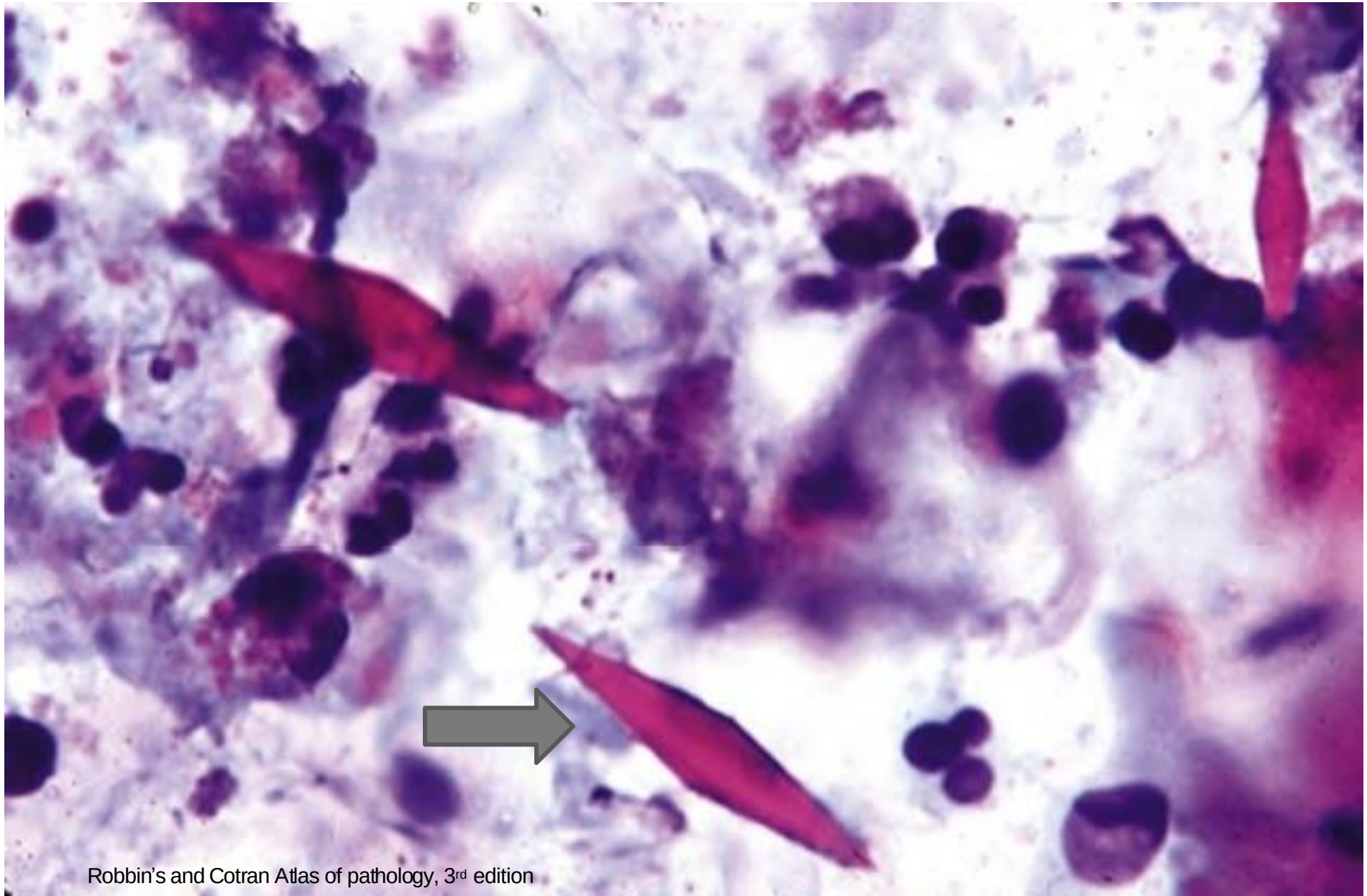
Eosinophils



•Eosinophils are the characteristic in 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.

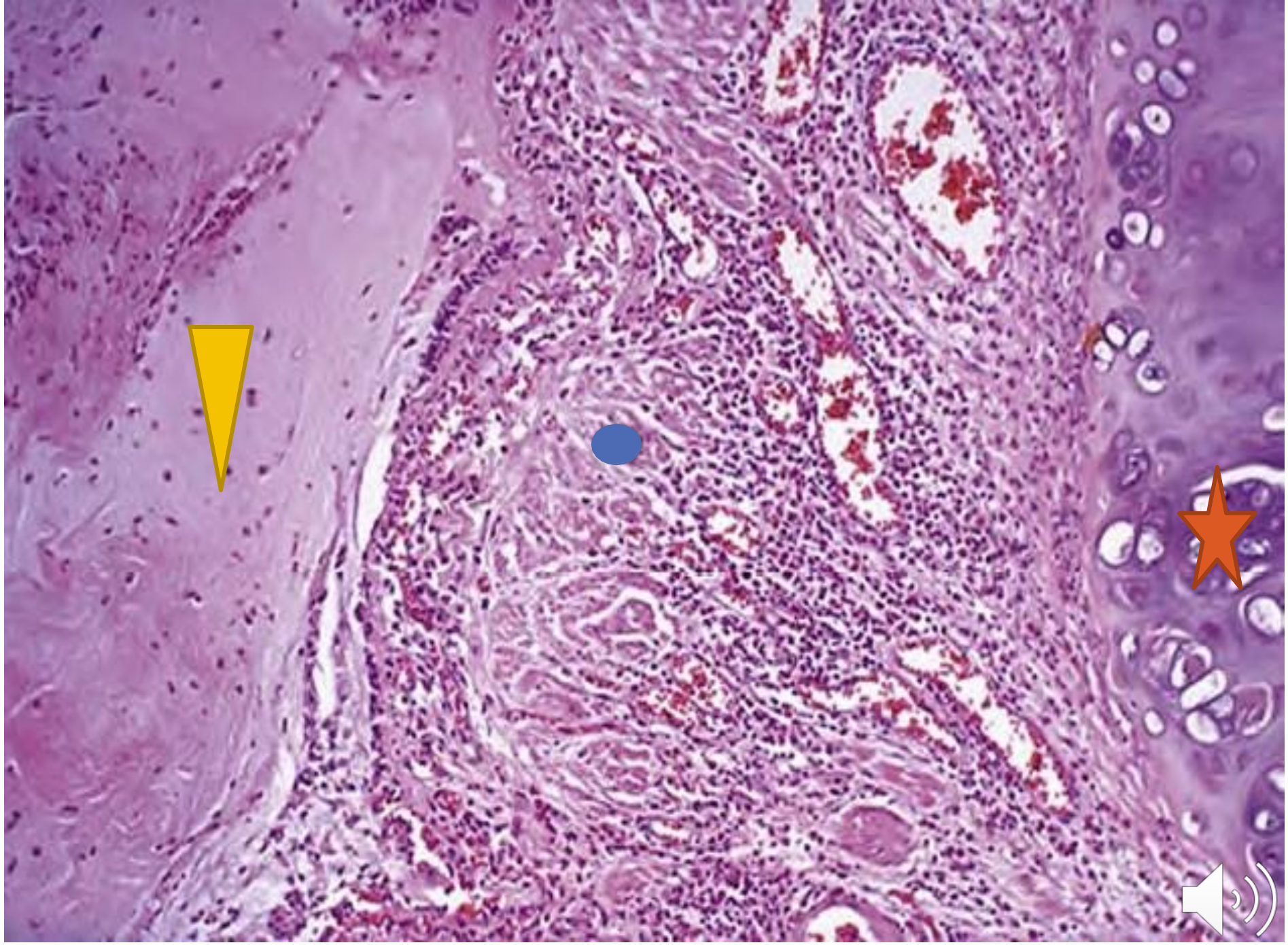


Robbin's and Cotran Atlas of pathology, 3rd edition

the characteristic morphologic changes in asthma are called 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 severe advanced cases → distension of lungs, due to the air trapping with small areas of atelectasis.



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

- The figure shows a predominantly expanded submucosa which lies between the bronchial cartilage which is marked by the red star and the bronchial lumen that is stuffed and filled with mucus and marked by the yellow arrow.
- **The submucosa is widened by smooth muscle hypertrophy, edema and inflammatory cells (mainly eosinophils).**
- Q: The mucus plugs in asthmatic patients contains whorls of shed epithelium called **curshmann spirals.**
- **Eosinophils** are the characteristic.
- Inflammatory cells in asthma patients. Charcot-leyden crystals are another finding are represent crystalloids made up of eosinophil protein galectin-10.

CLINICAL FEATURES

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

An attack of asthma is caractarised by the following:
Cough, worse at night or early morning.
Wheezing, a whistling sound especially during expiration, sometimes it can be heard easily even without a stethoscope.
Chest tightness, the patient may feel something is squeezing or stitting on their chest.
Shortness of breath or dyspnea, patients can't catch their breath or breathe deeply enough.
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, remember asthma is reversible except in advanced severe cases.
This link is for youtube video for the wheezing sound: Click for another video about the wheezing sound.

Status asthmaticus:

- **A severe paroxysm that does not respond to therapy, this type of attacks persists for days or weeks. Maybe associated with hypercapnia, acidosis, and severe hypoxia, it is fatal in some patients.**
- Hypercapnia also known as **hypercarbia** and **CO_2 retention**, is a condition of abnormally elevated carbon dioxide (CO_2) levels in the blood.

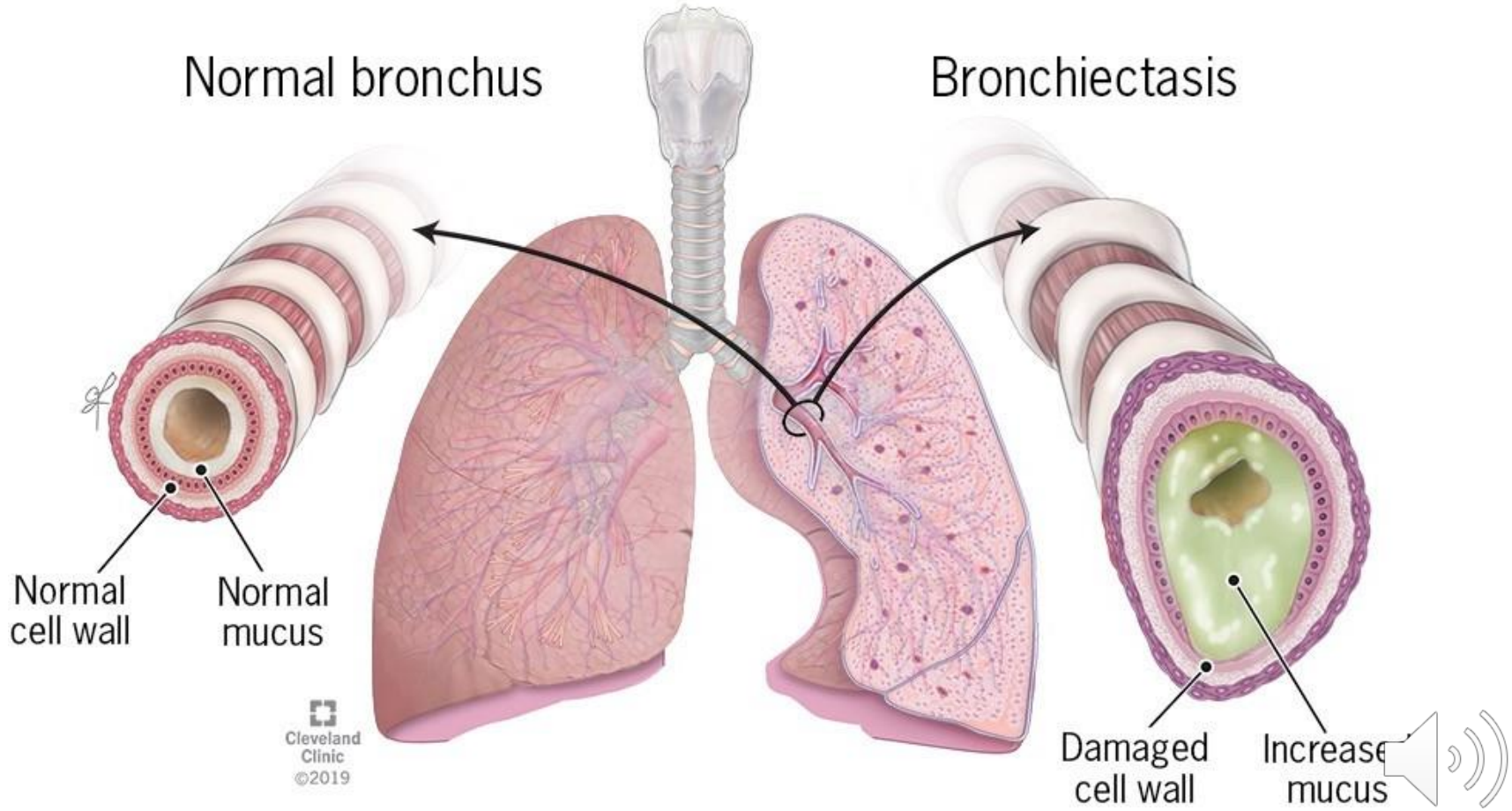
https://nurseslabs.com/status-asthmaticus-nursing-management/

MANAGEMENT:

Standard therapies include:

- Anti-inflammatory drugs (glucocorticoids).
- Bronchodilators (beta-adrenergic drugs).
- Leukotriene inhibitors, which are potent bronchoconstrictors. However those agents can block specific immune mediators such as IL-4 and IL-5, this effect can be helpful in some patients.

IV- BRONCHIECTASIS



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

- Permanent dilation of bronchi and bronchioles caused by destruction of smooth muscle and the supporting elastic tissue. It is an irreversible dilution. (You can compare it to emphysema which is defined as permanent dilation of the airways distal to the terminal bronchioles, the difference here is that the destruction of smooth muscle and elastics tissue is not primary by itself, but rather related to a primary process such as persistent infection or obstruction).

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**

- Q: Regarding bronchiectasis, one of the following statements is correct:

A. Restrictive disease
B. irreversible
C. primary process
D. Affects the acini

Ans:B

- Clinically: cough and expectoration of copious amounts of purulent sputum which usually contains white blood cells, cellular debris, dead tissue and mucus, it is typically yellow or green and can be seen in cases of bronchiectasis and lung abscess.

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

PATHOGENESIS

Two intertwined processes contribute to bronchiectasis:

✓ **Obstruction.**
✓ **Chronic infection.**

Obstruction (by a foreign body for example) → impairs clearance of secretions → superimposed infection → inflammatory damage to the bronchial wall + the accumulating exudate→ airways distention (even further) → irreversible dilation.

• Persistent necrotizing infection in the bronchi or bronchioles → poor clearance of secretions, obstruction by the accumulation of secretions, and inflammation with peribronchial fibrosis and bronchial walls damage→ irreversible dilation.

The conditions that most commonly predispose to bronchiectasis include

1. 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 lung segment.
- Atopic asthma and chronic bronchitis can also cause obstruction and bronchiectasis.

2- Congenital or hereditary conditions:-

- **Cystic fibrosis:**

- Widespread severe bronchiectasis.
- Due to obstruction caused by abnormally viscid mucus andsecondary infections.
- Remember: cystic fibrosis is a hereditary disease that affects the lungs and the digestive system.
- The body in this disease produces thick and sticky mucus that may block the lungs and obstruct the pancreas.

- Immunodeficiency states:

- Due to recurrent bacterial infections.
- Localized or diffuse.

- Primary ciliary dyskinesia (immotile cilia syndrome):

- Rare autosomal recessive disorder ⟶ abnormalities of cilia → impaires the mucociliary clearance of the airway ⟶ persistent infections.
- Bronchiectasis + sterility in males.

3- **Necrotizing, or suppurative, pneumonia:**

- Particularly with virulent organisms such as Staphylococcus aureus or Klebsiella spp.

MORPHOLOGY, MACROSCOPIC:

o Lower lobes bilaterally particularly the vertical air passages.

o Most severe involvement in distal bronchi and bronchioles.

o The airways may be dilated to as much as four times their usual diameter.

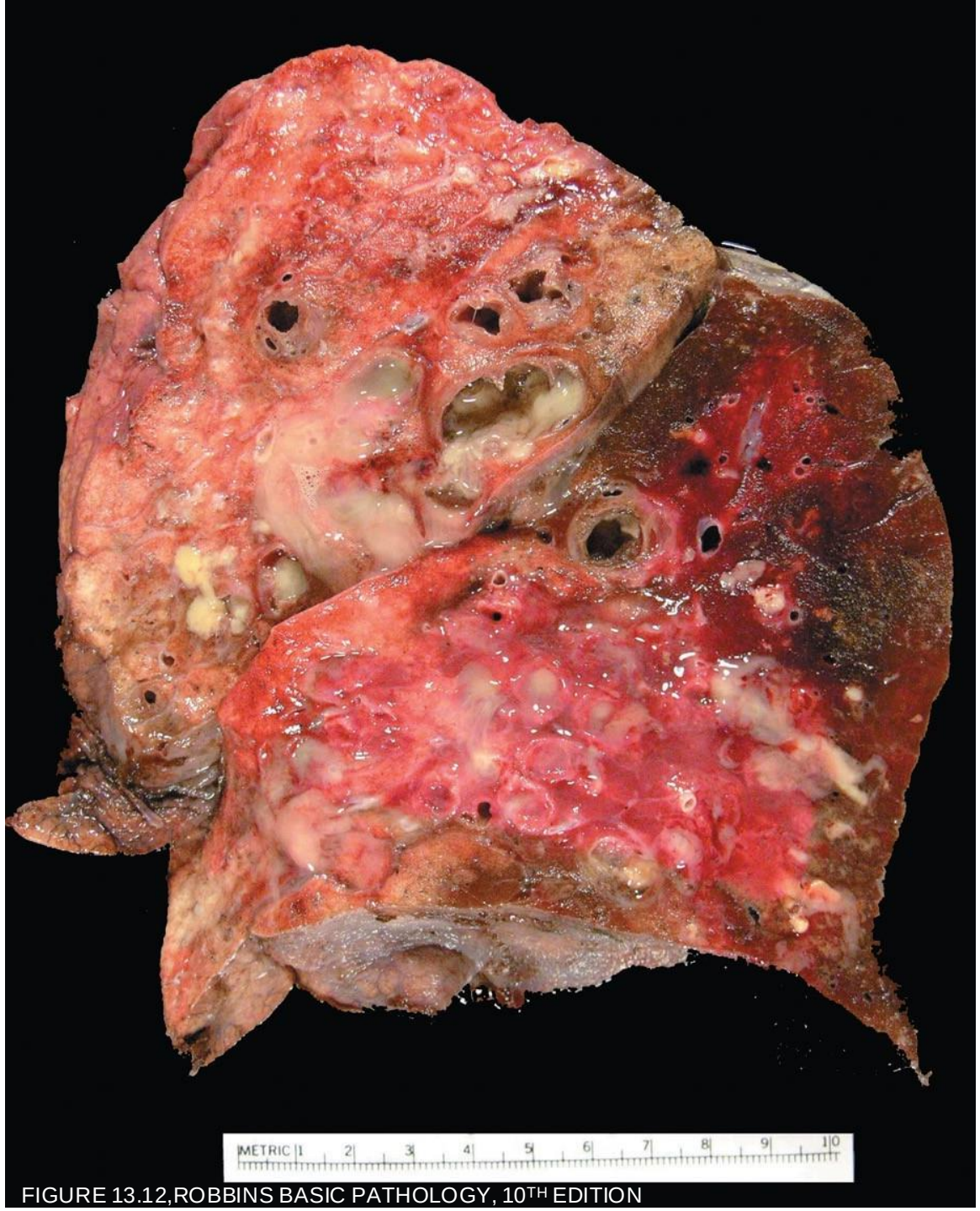


FIGURE 13.12,ROBBINS BASIC PATHOLOGY, 10TH EDITION

It is a markedly dilated bronchi filledwith purulent mucus.

- This figure shows the gross appearance of a lung that is involved by a bronchiectasis in a patient with cystic fibrosis who underwent lung reconstruction for transplantation.

MORPHOLOGY, MICROSCOPIC:

Vary with the activity and the chronicity of the disease.

In full-blown active cases:

o Intense acute and chronic inflammatory exudate within the walls of the bronchi and bronchioles → desquamation of lining epithelium and extensive ulceration due to the severe inflammation.

o Mixed flora are cultured from the sputum, the usual organisms include staphylococcus, streptococcus, pneumococcus, enteric organisms and anaerobic bacteria.

MORPHOLOGY, MICROSCOPIC:

- **When healing occurs:**

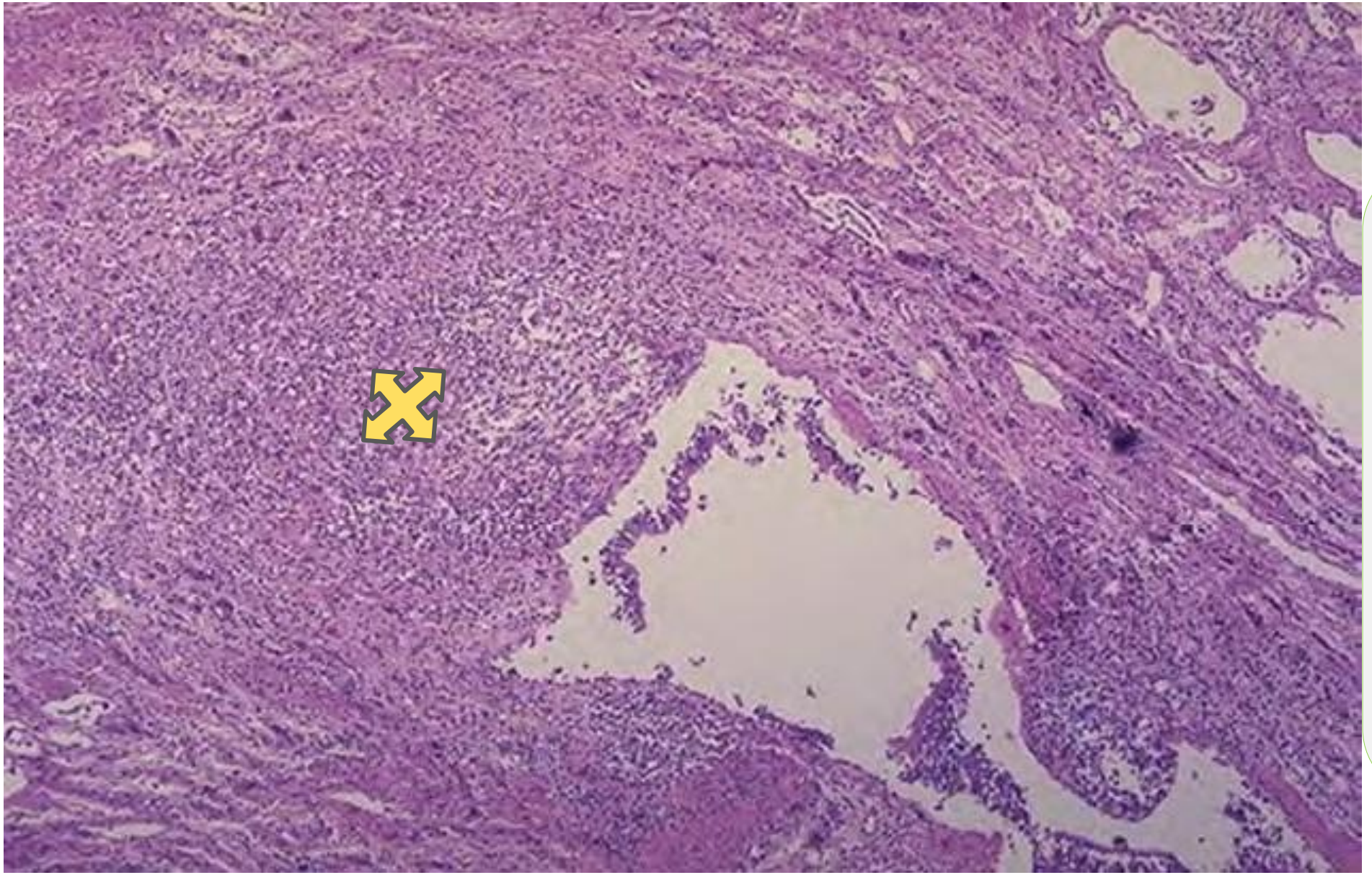
- The lining epithelium may regenerate completely; However, the injury usually cannot be repaired completely.

- Abnormal dilation and scarring (persists).

- Fibrosis of bronchial, bronchiolar walls

- peribronchiolar fibrosis.

- Abscess (cavity) formation in some cases (when the necrosis destroy the bronchial and bronchial wall).



- This figure shows the histological findings in bronchiectasis. At the centre there is an extensive necrotizing inflammation to the degree where you cannot see the mucosal lining clearly (it is mostly desqamated).

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.

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

CLINICAL FEATURES

Severe, persistent cough with mucopurulent sputum.

- Other symptoms: dyspnea (shortness of breath), rhinosinusitis, and hemoptysis.

- Symptoms are episodic.

- Precipitated or induced by URTI.

- Severe widespread bronchiectasis: may lead to significant obstructive ventilatory defects, hypoxemia, hypercapnia, pulmonary hypertension, and cor pulmonale.

However, with current treatment the outcomes have been improved and severe complications of bronchiectasis such as brain abscess 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.

THANK YOU!

Additional sources

1. Book pages
2. Youtube videos
3. Webpages…etc

آية أو حديث شريف دعاء أو نصيحة .....
اترك أثر جميل للقارئ

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2			
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!