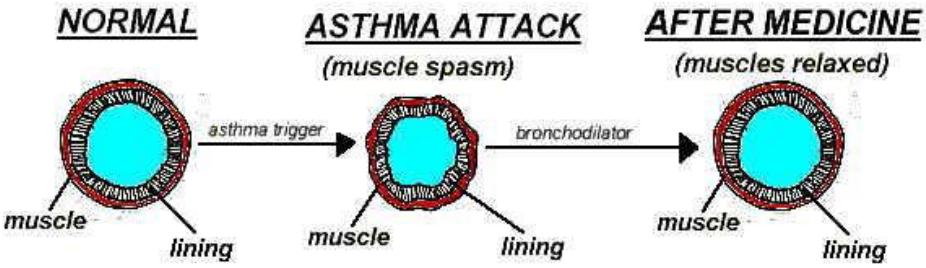
Obstructive diseases

Asthma

- A **chronic** inflammatory disorder which causes recurrent episodes of wheezing, breathlessness, cough and chest tightness.

- Characterized by **Intermittent** and **reversible** (the only reversible disorder we will talk about):
  1. Airway obstruction.
  2. The most important cell morphologically is **Eosinophil**, in pathogenesis **T2 helper cell.**
  3. Bronchial smooth muscle hypertrophy and hyper-responsiveness, more constricted will be observed.
  4. Increase in mucus secretion which is the cause of the obstruction along with smooth muscles constriction.



- Asthma affects the **terminal bronchi** and **bronchioles**.
- We said that asthma is intermittent and reversible; why it is reversible?
  Because the problem is related to smooth muscle contraction which can be reversed.

- Muscle lining normally relaxed with asthma attack muscle spasm, and after the attack finishes within 1 to several hours everything return normal, to some extent, but after several attacks there permanent changes occur.
- Clinically it will still reversible but by time it causes permanent changes in the wall.

Epidemiology

Significant increase in asthma in the last four decades in the western world.

Due to improvement in hygiene, less infections will change the immune system balance to become more responsive to normal stimuli that don't trigger any other system.

Types of asthma:

i. **Atopic:** there is evidence of **allergic** sensitization.
ii. **Non- Atopic**: **no** evidence of **allergic** sensitization.

- Both have the same mechanism, different trigger but same inflammatory cascade, same morphology, same under microscopic appearance, and similar clinical manifestations; symptoms are similar but with different history.

Etiology:

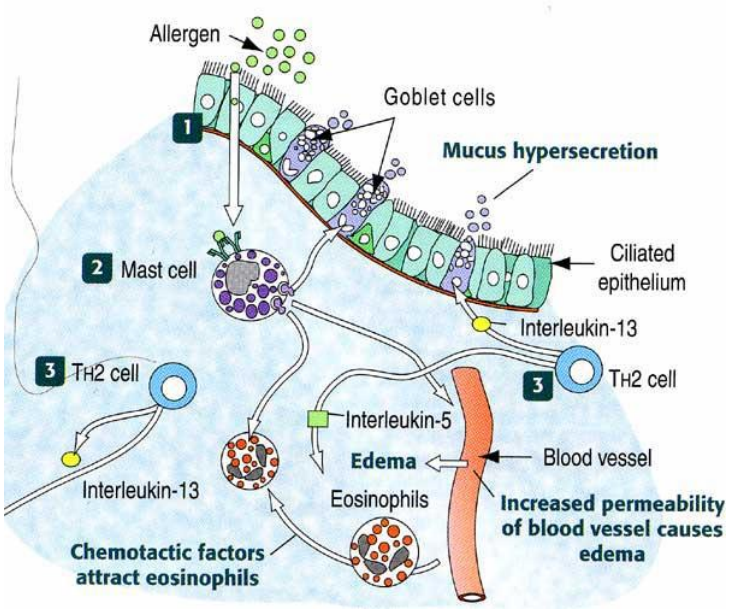
- Especially Atopic type, usually there is a genetic predisposition to **type 1 hypersensitivity**.
- Bronchial hyper-responsiveness to a variety of stimuli.
- Acute and chronic inflammation.

Inflamation:

T2 helper is critical in the pathogenesis as we said before, it releases cytokines which mediate the whole response. **IL-3,4,5**, the doctor will not ask us about their specific effects, but she read them :

•IL4…IGE PRODUCTION.
•IL5…EOSINOPHIL ACTIVATION.
•IL3…MUCUS PRODUCTION.

-When **IgE** is produced it coats mast cells which upon exposure to allergen releases the granules contents (degranulation of mast cells), releasing mediators mainly Histamine(first mediator to be released).



- **Degranulation of mast cell produces to waves of reaction**:

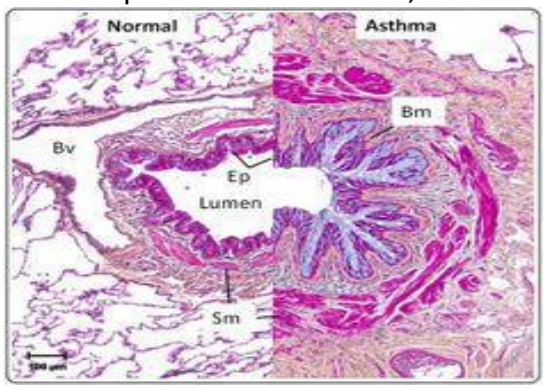
1. **Early Phase**, mediated by **already synthesized** mediators, released upon granulation .(can be called immediate phase response)
    - Causes bronchoconstriction (the cause of obstruction and wheezing), thought that it is caused by stimulation of **vagal nerve reseptors**.
    - **Increased mucus secretion**.
    - Vasodilation by **histamine**.

2. **Late Phase**, because mediators **will be synthesized** e.g: leukotrienes and porstaglandins.
   Inflammation with activation of eosinophils, neutrophils and T cells.

- We have mentioned before that the structural changes are reversible to some extent so secondary to many attacks of asthma, **Structural changes** will occur, and this is called **Airway Remodeling**.
  Airway remodeling is : Structural changes that occur secondary to many attacks of asthma.

Airway Remodeling is characterized by:

1. Hypertrophy of bronchial smooth muscles.
2. Hypertrophy of mucus glands.
3. Goblet cell metaplasia (which also happen in chronic bronchitis).
4. Increased vascularity (as the hypertrophied tissue needs more blood supply).
5. Deposition of subepithelial collagen.
   *see the pictures in slides #39,40.



Here we can see lots of goblet cells (Goblet cell metaplasia), Smooth muscles are hypertrophied , so they need more blood supply, and that's why there is **Neovascularization** (increased vascularity).

Histotlogy:

1. Mucus plugs (in acute stages and asthmatic attacks)
2. **Eosinophils**
3. **Curschman spirals** (shed epithelium accumulated is spirals), mostly seen in sputum samples. "they are remnants of dead epithelial cells"
4. **Charcot laden crystals**, which are crystalloids made up by eosinophil's protein.
   *See the pictures in slides #36, 37.

Types of asthma:

- ### Atopic
  - Allergic.
  - Most common type of asthma.
  - Begins in childhood.
  - Type 1 hyper sensitivity reaction.
  - Positive family history of allergic condition (any other allergic condition, not asthma only).
  - Triggered by allergens (environmental antigens).

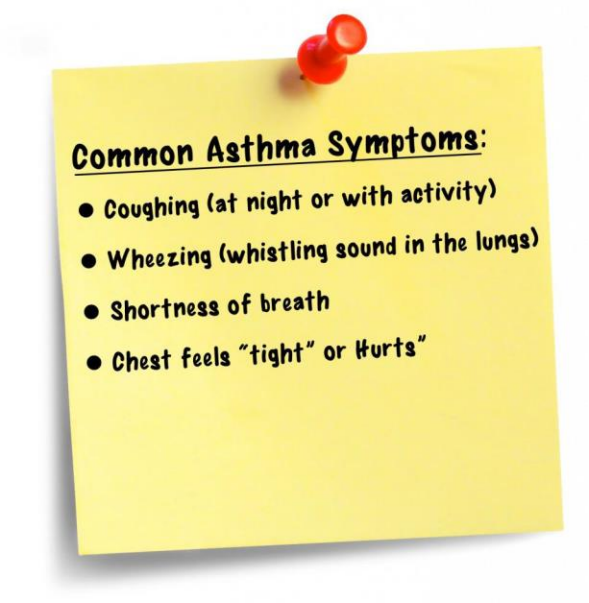
- ## Non-atopic
    - No evidence of allergic sensitization, negative skin test for allergy. “ex: skin Prick test”.
    - Less common positive family history
    - May begin later in life rather than in childhood
    - Thought that viral infection causes the sensitization.
      ((Remember that the clinical features and morphology is the same under the microscope)).

- ## Drug induced Azthma
    - Patients are sensitive to **aspirin**, here asthma is reversible, stops when they stop taking the drug.
    - The exact mechanism is unknown
    - Aspirin inhibits the cyclooxygenaxe (COX)-that produce prostaglandins- without affecting the lypooxygenase pathway (producing *leukotrienes*) so it affect their balance shifting it to **bronchospasm.**

- ## Occupatioanl Azthma
    - It is allergic asthma indeed, but caused by occupational causes hence the name, like: Plastic fumes, organic and chemical dusts; ex: wood and cotton, and some gases such as Toluene.

Clincal features:

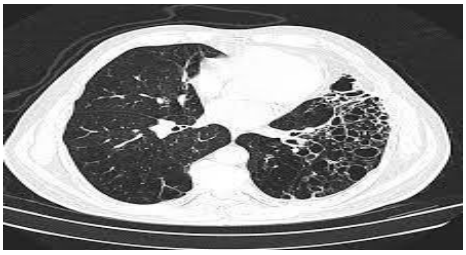
1. Severe dyspnea and wheezing.
2. Labor to inspire and cannot expire. This results in hyperinflation.
3. Attacks last from one to several hours.

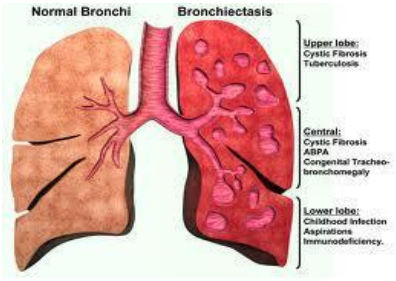


The dr. said that she found this picture on the net and that she added it to the slides because it might be useful.

Bronchiectasis

- **Permanent dilation** of bronchi and bronchioles.
- In autopsy when you open the lung, if they were normal, you cannot follow them after a certain distance, as they become very small, but if the person had bronchiectasis you can follow them till periphery because they are dilated.
- Caused by **destruction of muscles and elastic tissue** in the walls.
- Result from infection and obstruction, in a **cycle** of changes, one causes the other and ends in loss of the wall and the airway is dilated.





-This is a C.T. scan for Bronchiectasis with dilated bronchi
-this dilation is permanent.
-It's a secondary disease.

Bronchiectasis is secondary disease caused by:

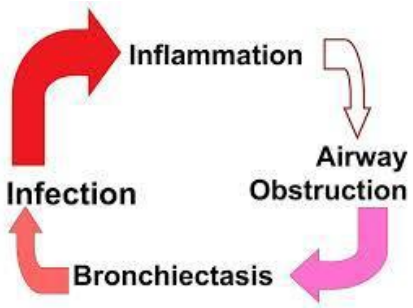
1. **Necrotizing** inflammation or suppurative pneumonia caused by (staph. aureus, TB or klebsilla).
2. Obstruction usually caused by mucus, foreign body or tumor.
   this means that any disease that cause mucus hypersecretion might lead to Bronchiectasis.
3. Congenital and Hereditary conditions "they cause obstruction and inflammation" :
   i. **Cystic fibrosis**, abnormal viscous mucus; causes mucus plugging leading to obstruction predisposes to inflammation.
   ii. **Immune deficiency** which may lead to infection, inflammation and obstruction.
   iii. **Kartagner syndrome** which is a structural abnormality of cilia which impair clearance of airways causing mucus bulging and increased susceptibility to infection.

Pathogenesis:

Obstruction and **infection;** either can come first.

- Immunodeficiency starts in infection associated with exudation which causes obstruction; obstruction predisposed to more infections.
- In cystic fibrosis obstruction leads to inflammation.
- Obstructive diseases , such as Chronic bronchitis and asthma , there is obstruction by mucus that predisposes to infection.

So, it is a cycle:



Morphology:

1. Usually affect the **lower lobe bilaterally**.
2. If the cause is obstruction by tumor the effect will be localized but by other causes diffuse bilateral involvement.
3. Dilated airways.
4. Inflammatory exudates.
5. Peribronchial Fibrosis.

Clinical features:

1. Sever persistent cough.
2. **Hemoptysis** (coughing blood), most common causes for this are: lung cancer, TB and Bronchiectasis.
   **Note that hematemesis is vomiting of blood , and it has nothing to do with Bronchiectasis.
3. Clubbing of fingers. " it's a deformity in fingers and nails, it can be seen in smokers".

Complications:

1. **Metastatic abscesses** (worst one is brain abscess); infection can metastasize through blood from the lung to any other site in the body.
2. **Reactive amyloidosis** (protein deposition) the kidney and the heart are the most common organs involved.