Understanding What Asthma Is … and Is Not

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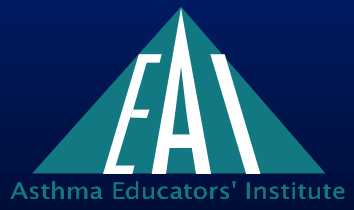

Disclosure of Conflicts of Interest

- I have no financial conflicts of interest to disclose.

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Outline

- Define asthma and its features.
- Explore the biology of asthma.
- Assess asthma severity and control.
- Identify treatments for asthma.
- Consider other diseases that may mimic asthma.

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What Is Asthma?

- The child who's always coughing, especially at night.
- *Intermittent* cough, wheeze, chest tightness, and shortness of breath.
- Symptoms brought on by characteristic stimuli or "triggers."
- Sometimes, a frightening sense of suffocation.

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Case Example

A 7-year-old boy newly develops persistent coughing and noisy, whistling breathing every time that he goes out to play in the cold air – and has similar symptoms after sitting with the pet cat.

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Asthma is Common

- It is estimated that 8-10% of all Americans have asthma.
- Asthma affects as many as 6 million children under the age of 18.
- Asthma is the most common chronic illness of childhood.

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Asthma Is a Disease of the Bronchial Tubes

- The air passageways narrow because of:
  - tightening by (involuntary) muscle that encircles the airways;
  - swelling of the airway walls; and
  - mucus partially filling the tubes.
- Air passing through narrowed tubes can elicit a whistle or “wheeze.”

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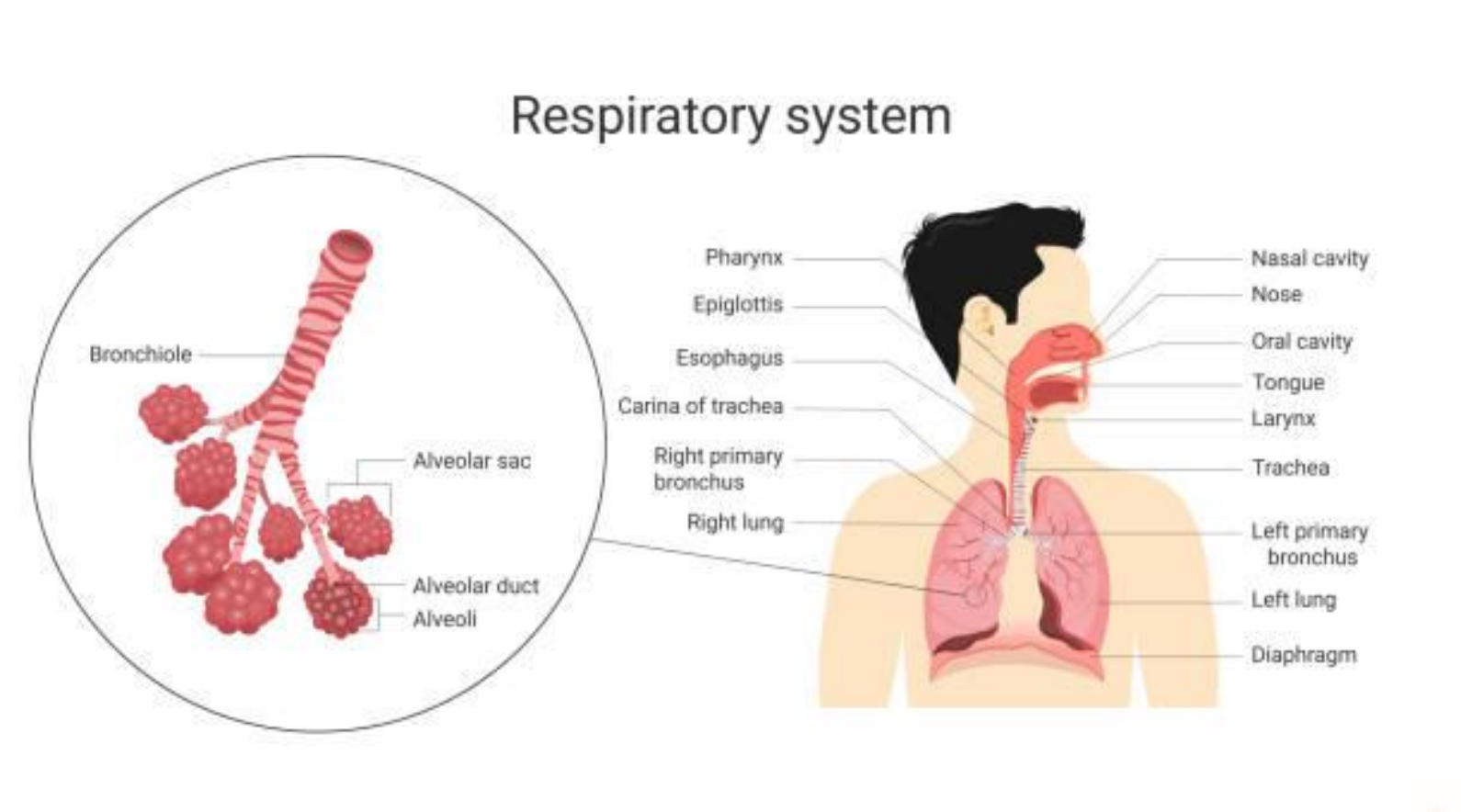
The Airways



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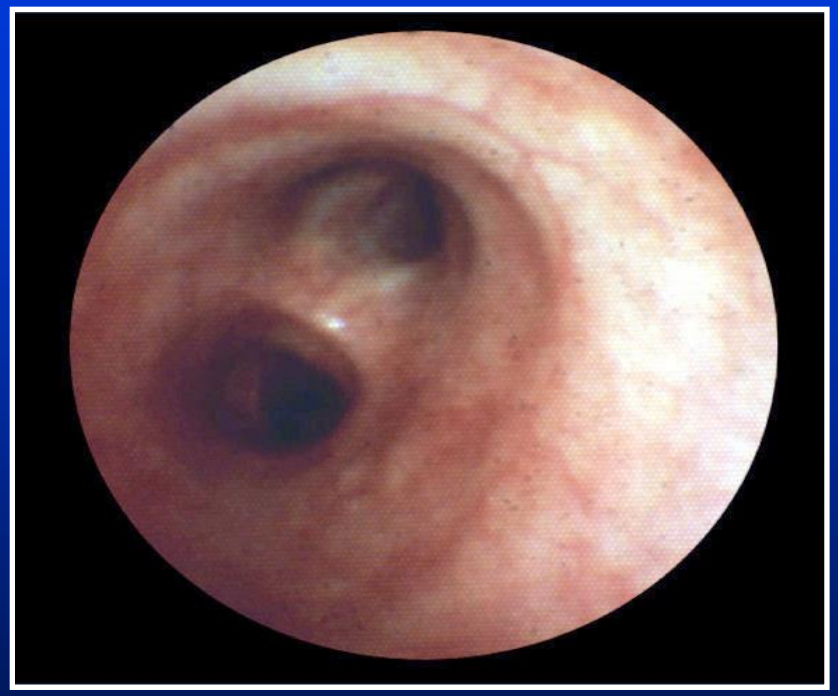
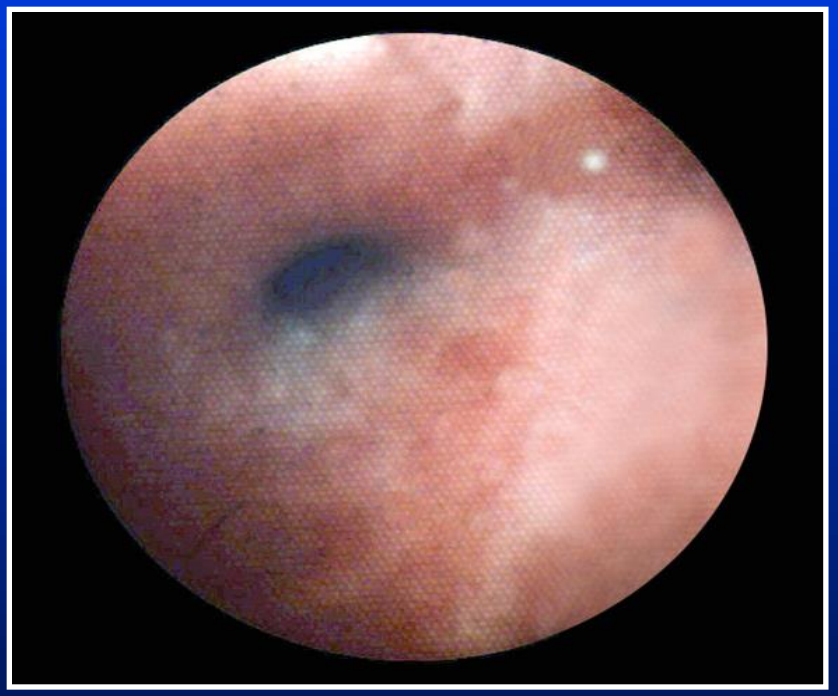
Bronchoscopic View



Before



10 minutes after allergen challenge

Components of Airway Narrowing in Asthma

- Bronchial smooth muscle contraction:

  ⟹ "bronchospasm"; "bronchoconstriction"

- Airway wall inflammation:

  ⟹ swelling with cells and edema; excess mucus production

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Measuring Airway Narrowing

- The narrower the bronchial tubes, the slower the flow of air through them.
- The rate of flow can best be measured:
  - while breathing out
  - as hard and fast as one can.
- Instruments used: spirometer (pulmonary function testing); peak flow meter

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Instruments to Measure Lung Function

Spirometer

Peak Flow Meter

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Language of Lung Function Measurements

- By spirometry:
  - Forced expiratory volume in 1 second: FEV_1
- By peak flow meter:
  - Peak expiratory flow (PEF or PEFR)
- Novel measurement of airway inflammation:
  - Concentration of exhaled nitric oxide (FeNO)

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Why Pulmonary Function Tests (PFTs) Are Important

- Many other diseases can cause cough, wheeze, shortness of breath, and/or tightness in the chest.
- The diagnosis of asthma is confirmed by PFT demonstration of variable airflow obstruction.
- The chest X-ray is typically normal in asthma; and there is no blood test to prove or disprove a diagnosis of asthma.

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What Is Asthma?

- Asthma is a disorder of the bronchial tubes in which the airways narrow too much and too easily, resulting in wheezing, chest tightness, and shortness of breath.

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Key Concept: Hyperreactive ("Twitchy") Airways

- In asthma, narrowing of the airways comes and goes.
- However, the sensitivity or "twitchiness" of the airways is always present, even when a person with asthma feels perfectly well.
- Asthma is chronic; its symptoms may come and go and vary in intensity over time.

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What Causes the "Twitchy" Airways of Asthma?

- The cause is partly in our genes and partly in our environment.
- The cause is often closely linked to allergy.
- Many persons with asthma also have allergies of their eyes, nose, and skin. This tendency towards allergies is called "atopy."
- Allergy of the bronchial tubes is asthma.

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Persistent, Mild Inflammation of the Bronchial Tubes

- Samples from the bronchial tubes of persons with asthma, even when feeling entirely well, show evidence of persistent, allergic-type inflammation.
- It is likely that persistent (chronic) inflammation contributes to the tendency of the bronchial tubes in asthma to contract too easily and too much (to be “twitchy”).

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Related Allergic Diseases

- Nose: *allergic rhinitis; nasal polyps*
- Eyes: *allergic conjunctivitis*
- Skin: *hives, eczema*
- Other: *food allergy*

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What Is Allergy?

- Allergy is a specialized reaction of the immune system.
- This part of the immune reaction likely evolved to fight worms and parasites.
- When (mis-)directed against harmless particles in the air that we breathe, it is called an allergic reaction.

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Common Allergens in Asthma*

- Animal danders (any furry animal) and bird feathers
- Dust mites
- Mold spores/mildew
- Cockroaches
- Pollens of trees, grasses, and weeds

*allergens important in asthma are:

1) proteins, and 2) inhaled.

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More About Allergy in Asthma - 1

- B-lymphocytes make proteins (antibodies) that attach to specific allergens: immunoglobulin E (IgE)
- When IgE molecules on the surface of mast cells encounter their specific allergen, they cause the mast cells to "explode," releasing many chemicals that stimulate bronchoconstriction and inflammation (like histamine and leukotrienes).

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More About Allergy in Asthma - 2

- T-lymphocytes are stimulated to make important proteins that coordinate the allergic response, including interleukins (including IL-4, IL-5, and IL-13).
- These and other chemicals (like thymic stromal lymphopoetin, TSLP) attract a type of white blood cell – eosinophils – to the walls of the bronchial tubes.

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More About Allergy in Asthma - 3

- Taken together, asthma characterized by high levels of IgE antibody in the blood, by lots of eosinophils in the blood (and sputum), and/or high concentrations of exhaled nitric oxide (FeNO) is referred to as Type-2 asthma (or Type-2-high) asthma.
- Type-1 asthma (or Type-2-low) asthma, lacking these allergic-type features, is less common.

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More About Allergy in Asthma - 4

- In recent years, new injectable therapies have become available to treat severe Type-2 asthma.
- These are manufactured antibodies that target the following proteins:
  - Immunoglobulin E (IgE) *(Xolair)*
  - Interleukin 5 *(Cinqair, Fasenra, Nucala)*
  - Interleukin 4 and 13 *(Dupixent)*
  - Thymic stromal lymphopoetin (TSLP) *(Tezspire)*

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What Is Asthma?

- Asthma is a chronic allergy-like inflammatory disorder of the bronchial tubes in which hyper-reactive airways narrow too much and too easily, resulting in wheezing, chest tightness, and shortness of breath.

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Other (Non-Allergic) Triggers

- Exercise (especially when the air is cold).
- Cigarette smoke; air pollution.
- Strong fumes/odors.
- Certain medications (beta-blockers).
- For some people with asthma, aspirin/NSAIDs.
- Emotional stresses

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Judging Asthma Severity/Control

- Frequency of symptoms, including night-time awakenings due to asthma.
- Extent of airway narrowing (lung function measurement).
- Frequency of flare-ups (“exacerbations” or “attacks” of asthma).

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Categories of Asthma Severity

- Intermittent
- Mild persistent
- Moderate persistent
- Severe persistent

Asthma control is judged as:

well-controlled or not well-controlled.

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Our Goal: Well-Controlled Asthma

- Symptoms/need for quick-relief medication no more than 2 days/week.
- Nighttime awakenings with asthma no more than 2 nights/month.
- Breathing test results within the normal range.
- At most 1 severe asthma exacerbation in the past year.

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Treating Asthma

- Avoid those things that make asthma worse, including allergens to which one is allergic (and cigarette smoke!).
- Take medications to relax the bronchial muscles (bronchodilators) and to suppress inflammation (anti-inflammatories) in the bronchial tubes.
- Allergy shots (?)

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Medical Therapy of Asthma

Bronchodilators

- Quick-onset, short-acting (4-6 hours) (inhaled)
  - e.g., albuterol *(ProAir, Proventil, Ventolin);* levalbuterol *(Xopenex)*
- Long-acting (12-24 hours) (inhaled)
  - Beta-agonist type: formoterol, salmeterol
  - Anticholinergic type: tiotropium *(Spiriva),* umeclidinium *(Incruse)*
- Theophylline (tablets and liquid): rarely used.

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Medical Therapy of Asthma (cont.)

Anti-inflammatory therapy

- Corticosteroids ("steroids") (inhaled) *(Asmanex,* fluticasone, *Pulmicort, Qvar,* and others*)*
- Steroids (tablets, liquid) *(*prednisone, *Medrol)*

Combined bronchodilator and corticosteroid:

- With short-acting bronchodilator (inhaled) *(AirSupra)*
- With long-acting bronchodilator (inhaled) *(Advair, Breo, Dulera, Symbicort, Trelegy,* and others*)*

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Other Medical Therapies

- Leukotriene blockers (tablets)
  - Montelukast *(Singulair),* zafirlukast *(Accolate)*

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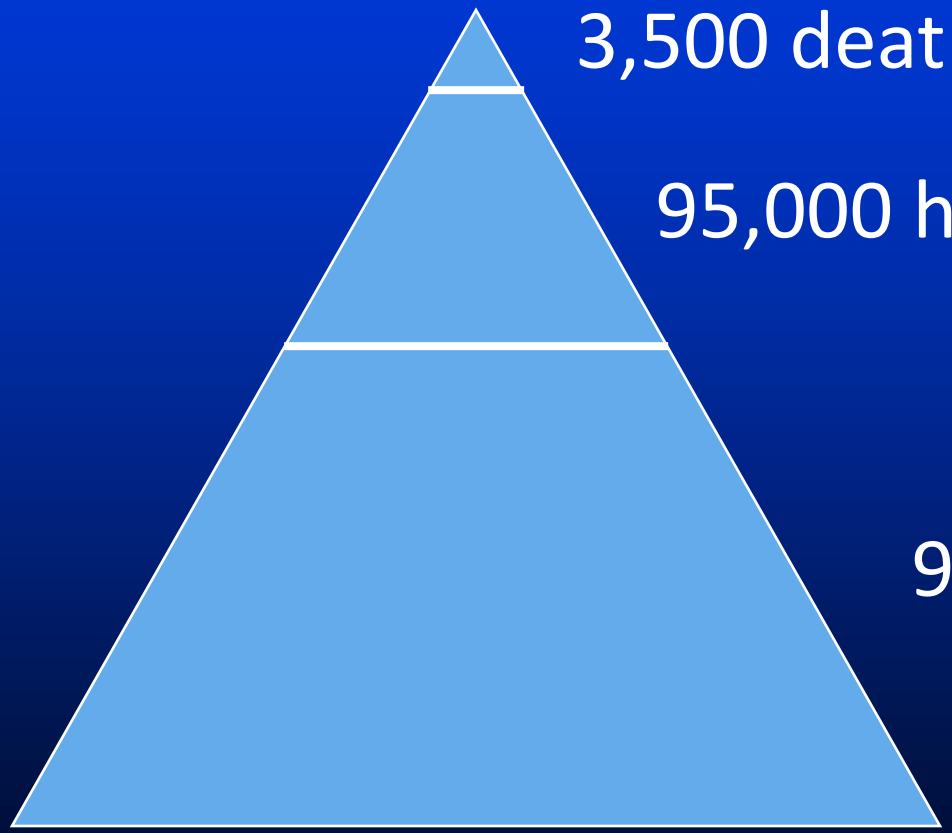
Severe Asthmatic Attacks



3,500 deaths/year

95,000 hospitalizations/year

986,000 ED visits/year

Data from www.cdc.gov/asthma

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Disparities in the Asthma Burden

- Blacks are 3-4 times more likely to be hospitalized for asthma or die from asthma than non-Hispanic whites.
- Hispanic morbidity and mortality varies with subgroup.

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Asthma and the "Social Determinants of Health"

Asthma is made worse by:

- Poor housing
- Air pollution
- Poor nutrition (obesity)
- Adverse work/school exposures
- Limited access to medical care /medications
- Stress

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What Asthma is Not

- Acute bronchitis
- Chronic bronchitis
- Emphysema

} Chronic Obstructive Pulmonary Disease (COPD)

- Chronic respiratory tract infection (e.g., bronchiectasis, cystic fibrosis, tuberculosis)

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Can One "Outgrow" One's Asthma?

- Childhood asthma often resolves spontaneously in adolescence/early adulthood (20-30%).
- Recurrence of asthma in adulthood is common (approx. 20%).
- Remission of adult asthma is rare (<10%).

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Asthma: Take-Home Points

- Usually begins in childhood.
- Is often associated with allergies.
- Is chronic, even though symptoms come and go.
- May flare up into asthma attacks.

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Asthma: Take-Home Points (cont.)

- Treatment causes bronchial muscles to relax and airway inflammation to lessen.
- Effective treatment improves asthma control and reduces the risk of asthma exacerbations.

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Our Goal: Keep Everyone in the Race!

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