"Hold off on increasing that dose": Addressing asthma co-morbidities

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AAE Association of Asthma Educators

No disclosures

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Objectives:

- After attending this presentation the learner should be able to:

1. Identify three areas before considering step-up therapy for asthma
2. Recognize the different co-morbidities associated with poor control of asthma
3. Demonstrate multifaceted treatment approaches including medical management, environmental control and behavior modification

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What are the three areas to identify before considering step-up therapy for asthma?

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Step Up Therapy

Step 1
Preferred:
SABA prn

Step 2
Preferred:
Low-dose ICS

Alternative:
Cromolyn , LTRA, Nedocromil or Theophylline

Step 3
Preferred:
Low-dose ICS + LABA
OR
Med.-dose ICS

Alternative:
Low-dose ICS + either LTRA, Theophylline or Zileuton

2nd

Step 4
Preferred:
Medium-dose ICS + LABA

Alternative:
Med.-dose ICS + either LTRA, Theophylline or Zileuton

Step 5
Preferred:
High dose ICS + LABA

AND

Consider Omalizumab for Patients who have allergies

Step 6
High dose ICS + LABA+ oral Corticosteroid

AND

Consider Omalizumab for Patients who have allergies

1st
Step up if needed
(first, check adherence, inhaler technique, environmental control)

Assess Control

Step down if possible
(and asthma is well controlled at leaset 3 months)

Patient Education, Environmental Control and Management of Comorbidites at Each Step
Consider subcutaneous allergen immunotherapy for patients who have allergic asthma at steps 2 though 4

Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma . NIH Publication No. 08-4051

Think outside the box

Co-morbidities

- rhinitis
- sinusitis
- gastroesophageal reflux disease
- obstructive sleep apnea
- obesity
- hormonal disorders
- Psychopathologies (depression/stress)

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Population study

- Health administration data of 12 million children and adults (1.5 million of had asthma)

(1) Allergic rhinitis

(2)Atherosclerotic cardiac disease and circulatory disorders

(3) Bronchitis and bronchopneumonia

(4) Connective tissue diseases

(5) Dermatologic conditions (eczema)

Plos One 2012; 7:e34967.

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Population study (2)

(6) Gastroesophageal reflux (GERD) and other gastrointestinal disease

(7) Immunologic and hematologic diseases

(8) Metabolic disorders

(9) Neurologic disorders

(10) Obesity

(11) Obstructive lung disease (COPD)

Plos One 2012; 7:e34967.

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Population study (3)

(12) Paradoxical vocal fold movement [vocal cord dysfunction (VCD)

(13) Pregnancy

(14) Psychologic disease (anxiety, depression, behavioral disorders)

(15) Respiratory infection

(16) Rhinitis and rhinosinusitis

Plos One 2012; 7:e34967.

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How they may affect asthma

- share a common pathophysiological mechanism with asthma
- influence asthma control and response to treatment
- more prevalent in asthmatic patients but without obvious influence on this disease

Expert Rev Respir Med 2011 Jun;5(3):377-93.

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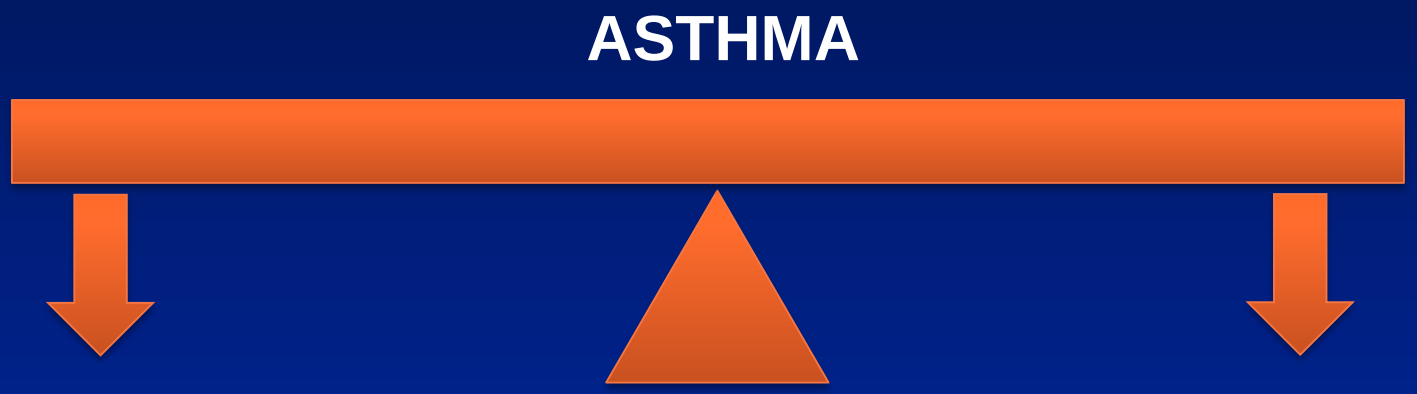
Balance



Poor control
Too little

Medication side effects
Too much

In between

Co-morbidities

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History taking

- Multiple courses of oral steroids
- High dose steroids
- Poor control of asthma
- Frequent ED and urgent care visits
- PICU admissions

- Above are the same criteria for severe asthma

But may also be your prompt for looking for co-morbidities

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Physical examination

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Physical examination (2)

Definition of co-morbidity

- refer to either
  - coexisting conditions
  - interacting conditions (having a more significant influence on the management of asthma)

do not respond or respond inconsistently to treatment often have a comorbidity

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Bad outcomes

- Comorbidities may result
  - misdiagnosis
  - misinterpretation of symptoms
  - aggravation of one or both diseases
  - decreased adherence

Eur Respir J 2009; 33:897–906.
Expert Rev Clin Immunol 2008; 4:731–742.

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Goal

- Recognition of these comorbidities
  - facilitates more appropriate therapy
  - reduction of potentially risky therapies, such as systemic corticosteroids

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Frequent asthma exacerbations

- Comorbidities increase the likelihood of poorly controlled asthma
- Survey of 136 individuals
  - Increased odds ratio (O.R.) of asthma exacerbation
    - 10.8-fold by depression
    - 4.9-fold by GERD
    - 3.7-fold by severe sinus disease
    - 3.4-fold by obstructive sleep apnea

Eur Respir J 2007; 26:812–818.

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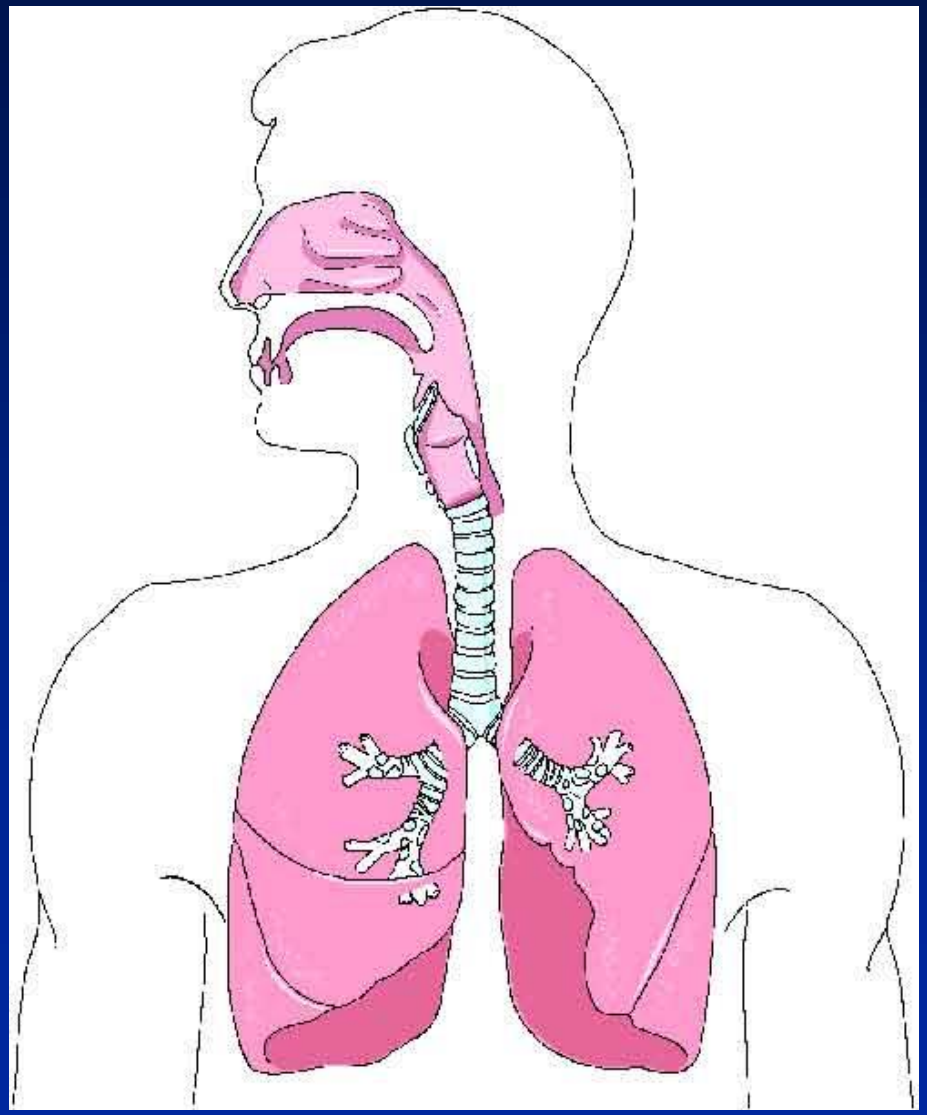
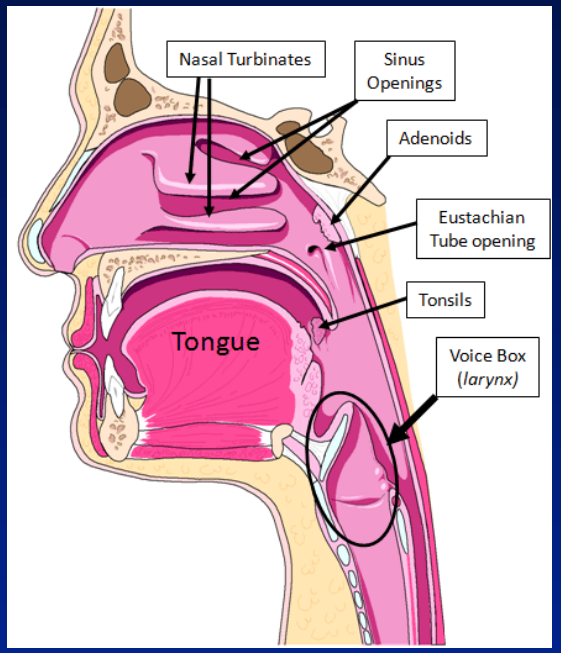
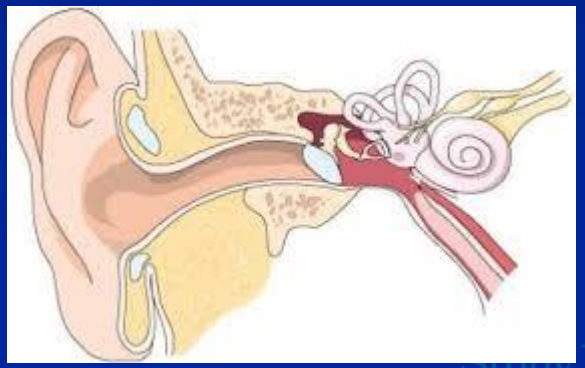
Upper airway disease







Postnasal drip

- Allergic rhinitis is the most common form of rhinitis, affecting approximately 20% of adults and over 30% of children
- Sinusitis is more likely in individuals with rhinitis
  - chronic sinusitis is coincident with nasal inflammation (rhinosinusitis)

J Allergy Clin Immunol 2001; 107:73–80.

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Multifactorial

- linking asthma exacerbation of asthma with upper airway disease
  - release of systemic immune mediators from the upper airway
  - drainage of inflammatory mediators
  - neurogenic responses resulting in more generalized airway inflammation
  - common inhalant mechanisms with allergens

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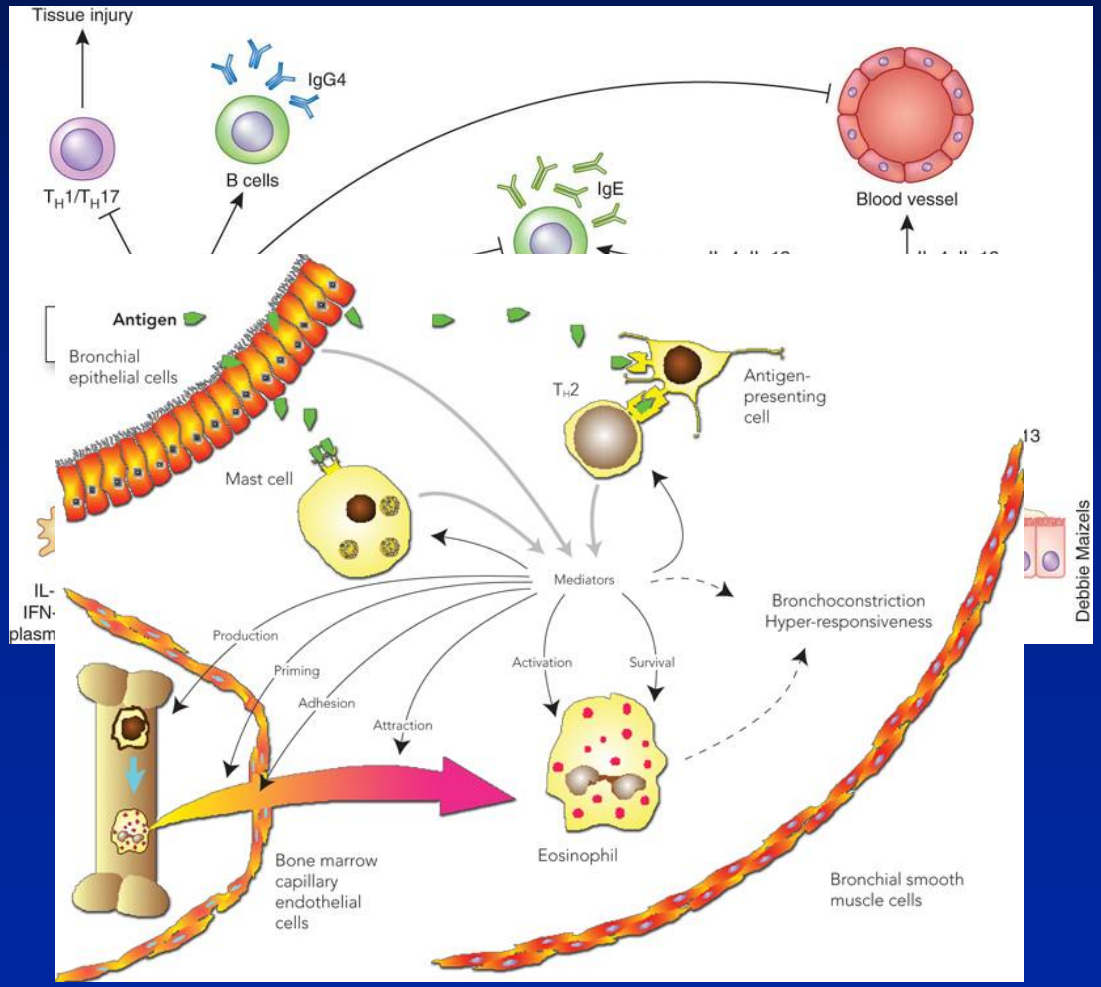
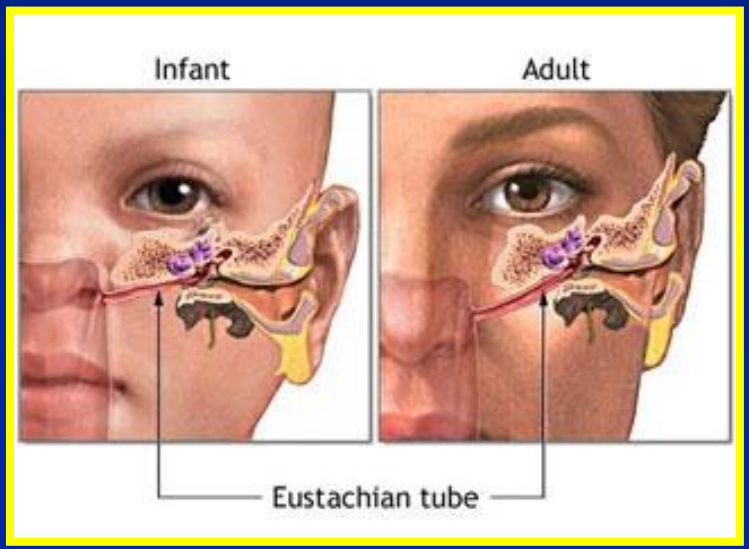
Two significant factors

- Inflammation
- Anatomy





Relationship to asthma

- Asthma is almost always associated with nasal disease in up to 95% of cases in some studies
- Chronic rhinosinusitis and nasal polyposis are frequently linked to persistent, severe asthma
- It is a given: ideal management of asthma is generally not achieved without control of upper airway disease

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Allergic march

- Rhinitis may also precede the diagnosis of asthma with the relative risk of subsequent asthma development
  - increased by 2.7–3.5 in a study of 6461 adults, aged 20–44 years
- What is the unique sensitivity that increased risk of developing asthma?
  - Allergic rhinitis with dust mite allergy

Lancet 2008; 372:1049–1057.

Diagnostic and therapeutic considerations

- the primary symptom of rhinitis or rhinosinusitis?
  - Cough
- Therefore, persistent asthma can suggest that greater consideration be given to optimal management of the upper airway disease
  - oral leukotriene modifiers, allergen immunotherapy or omalizumab, and allergen avoidance
- sleep disturbance, a common comorbidity with asthma

Gastroesophageal disease

- retrograde movement of gastric contents into the esophagus is termed **GERD**
- if the refluxate reaches the larynx, **laryngopharyngeal reflux**

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How common is GERD

- General adult population
  - 10–20% in western countries (5% in Asia)
- Pediatric studies
  - 2–8%
- Atypical symptoms of GERD
  - throat tightness, throat clearing, cough, chest tightness, and hoarseness
  - Sensation

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Laryngopharyngeal reflux cough

- Usually described as originating in the larynx or pharynx rather than the chest
  - But subject to patient perception

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Relationship of asthma and GERD

- Epidemiologic studies: variable prevalence of GERD in asthma (12 to 85%)
- asthma more commonly in GERD patients
- increased upper airway complaints in GERD patients
- Asthma therapies (theophylline and albuterol)
  - decrease lower esophageal sphincter tone, (asthma therapy may increase GERD)

Am J Respir Crit Care Med 2001; 164:72–76.

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Therapy of GERD improves asthma?

- conflicting evidence
- Double-blind, prospective, controlled trials
  - demonstrate that treatment of asymptomatic GERD does not improve asthma in adults or children

N Engl J Med 2009; 360:1487–1499. (Adult)
JAMA 2012;307:373–381. (Pediatrics)

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Asthma and symptomatic GERD?

- double-blind studies of individuals with asthma and symptomatic GERD shows a benefit
  - asthma quality of life and number of exacerbations
  - inconsistent effects on asthma symptoms, albuterol use, and pulmonary function

Chest 2005; 128:1128–1135.
Am J Med 1996;100:395–405.

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Watch out for effects of your asthma medications

- Bronchodilators
  - may reduce esophageal sphincter tone
- systemic corticosteroids
  - may increase gastric acid production
- inhaled corticosteroids
  - May cause hoarseness similar to the hoarseness caused by GERD

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Review of all GERD/asthma studies

- Cochrane review of all controlled trials of GERD therapy (adults and children) with asthma
  - lack of benefit in achieving asthma control
  - But a suggestion of reduced albuterol use and clinical benefit in an undefined subset of patients

Cochrane Database Syst Revs 2003:CD-0-1496.

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Vocal cord dysfunction

- WHAT?
  - maladaptive process; seems to occur in response to irritation of the larynx or hypopharynx or secondary to emotional or physical stress
- SYMPTOMS
  - wheezing (may be more prominent with inspiration)
  - hoarseness, dysphonia
  - cough
  - globus pharyngeus

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Characterize VCD

- ‘chest tightness’

(superior to the sternal notch)

- often episodic

with rapid resolution, with or without therapy

- ‘wheeze’

(high pitched and musical or stridorous)

- TRIGGERS (“provokes”):
  - respiratory or laryngeal irritants
  - exercise
  - stress

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How common is VCD

- Prevalence
  - difficult to determine (dynamic, episodic condition), which may not be evident or easily provoked at the time of the examination
- 'hyperreactivity' of the larynx'
  - Through histamine inhalation challenge (J Allergy Clin Immunol 2011; 127:412–419.)
- extreme or elite athletes?
  - Exercise is a common trigger
  - misdiagnosed as exercise-induced bronchospasm

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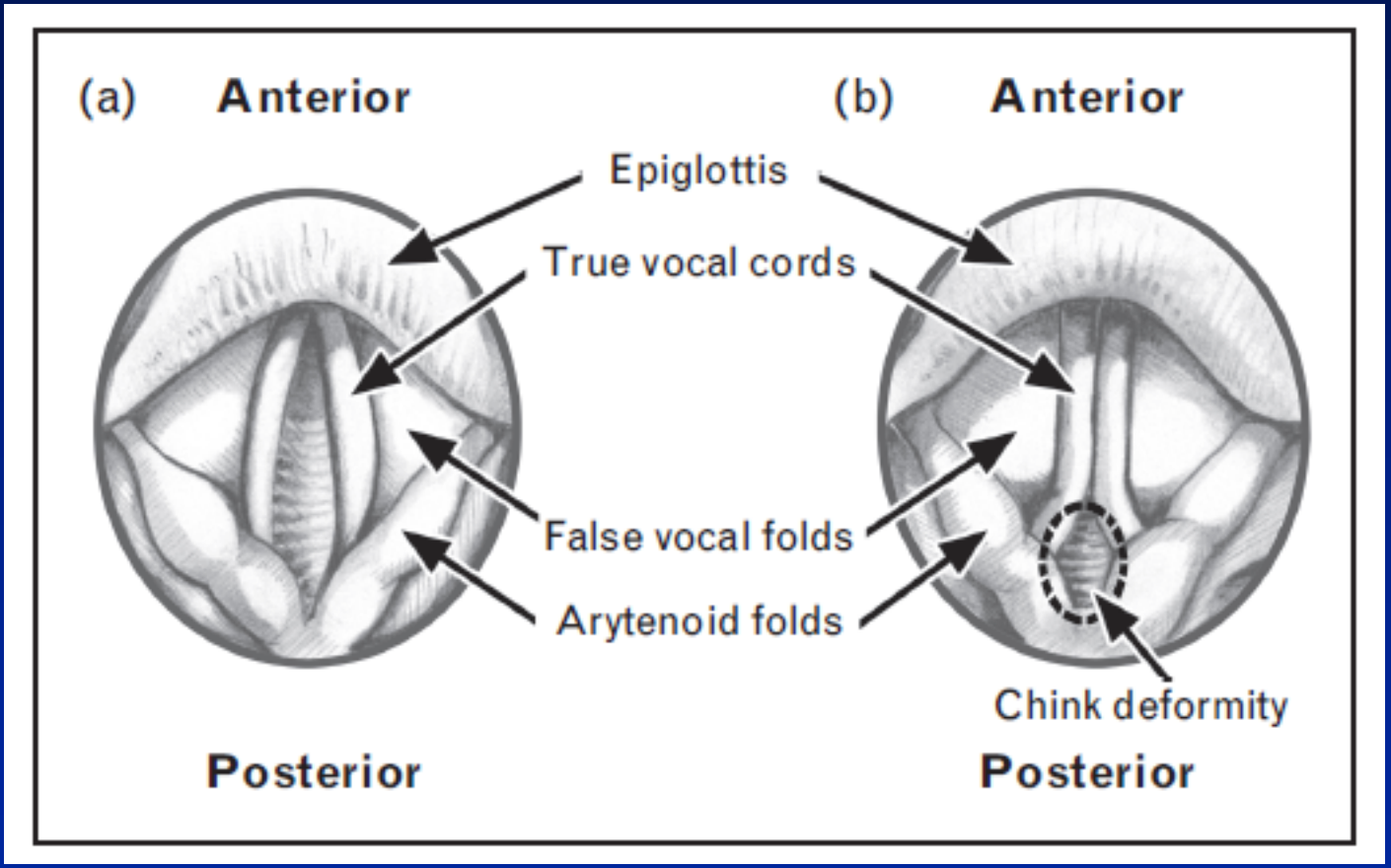
Diamond-shaped opening between the vocal folds



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Other clues of VCD

- inflammation of the larynx
- variable motion or quivering of the vocal folds
- inflammation of the larynx
  - Related with GERD or laryngopharyngeal reflux
  - Treatment of GERD may improve VCD

  (not been confirmed in prospective trials)

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Misdiagnosis of asthma

- VCD - wheezing/asthma-like symptoms
- VCD and asthma simultaneously
  - distinguishing the two conditions – challenging
  - may require direct visualization of the vocal folds during a symptomatic episode to be certain of the diagnosis

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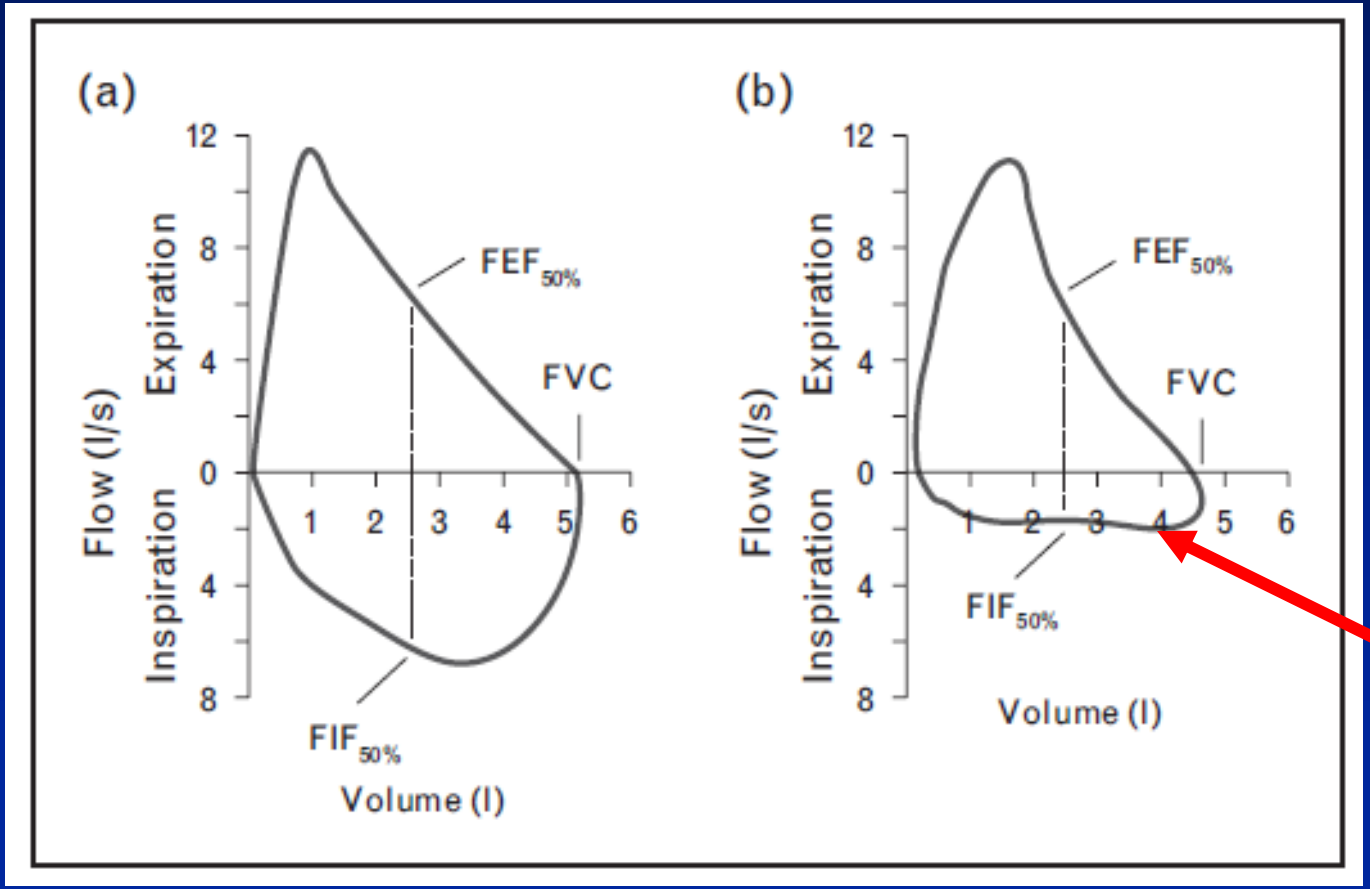
Diagnostics

- difficult-to-control asthma –assess for VCD
- flow volume loop



Truncated (wavy, flattened curve)

Diagnostics (continued)

- Confirmation: visualize the vocal folds, usually with a flexible nasolaryngoscope, during symptoms.
- VIDEOS

Pediatrics. 2007 Oct;120(4):855-64.

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Management

- Biofeedback therapy
  - relaxation techniques to minimize muscle tension in the larynx (relief of symptoms and resolution of wheeze)/hypnotherapy
  - speech therapist or speech pathologist (knowledgeable about VCD) can be very helpful in treating this disorder
- psychological dysfunction
  - significant contributor or predisposing factor in VCD (association of asthma symptoms with anxiety and depression)

Factors associated with VCD

(1) Anxiety disorders

(2) Family members of healthcare profession

(3) History of psychiatric disease, particularly depression

(4) Perfectionists or obsessive/compulsive personalities

(5) Victims of remote sexual abuse or trauma

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COPD

- Chronic obstructive lung disease
  - airflow obstruction that is not fully reversible
  - However, 60% of participants in COPD trials
    - 15% improvement in FEV1 with aggressive bronchodilator therapy but not improvement to normal
- associated with cigarette smoking
  - but up to 15–20% of affected – no significant history of cigarette smoking
  - host factors, in addition to irritants to the cigarette smoke, are essential for disease development

COPD and asthma

- 24 million people in the United States were estimated to have COPD in 2008
- symptoms of COPD and asthma are very similar
  - cough, mucous production, and shortness of breath, wheezing
- Another diagnostic challenge: there is a subset of asthmatic patients who develop irreversible airflow obstruction, resembling COPD

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Diagnostic considerations

- support a diagnosis of asthma.
  - Onset of symptoms prior to the age of 30 years
  - a personal or family history of atopic disease, upper airway disease
  - mucosal and/or peripheral blood eosinophilia
- Cigarette smoking increases the likelihood of COPD

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Treatment considerations

- Treatment of both is similar
  - the focus for COPD is regular bronchodilator therapy with inhaled corticosteroids added for more severe disease
  - Inhaled anticholinergic therapy is approved in COPD but not asthma, although anticholinergic therapy is effective in asthma

- COPD and asthma share clinical features confounding the diagnosis of the two conditions

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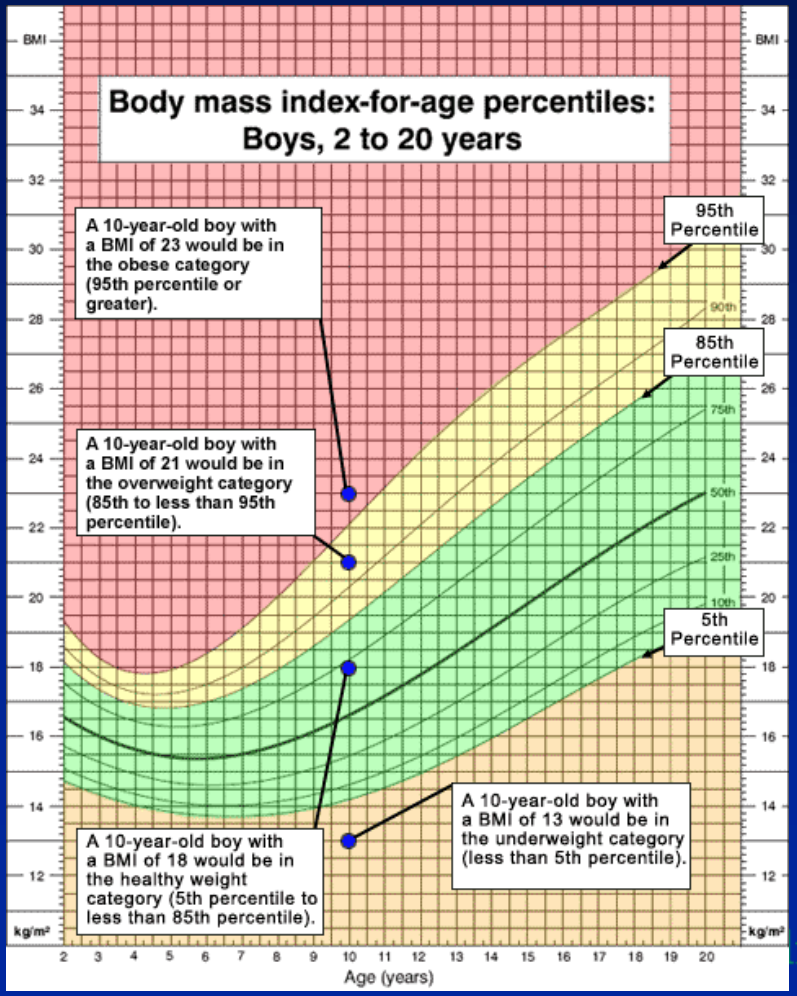
Obesity

Adults:

BMI (weight in kg divided by height in m2)

- normal weight = less than 25 kg/m2
- Overweight=25–30 kg/m2
- Obesity = greater than 30 kg/m2

Children:



Obesity and asthma

- Development of asthma?
  - In most of these papers, obesity precedes asthma
- increased severity of asthma?
  - 3095 participants (National Asthma Survey, 2008)
    - persistence of symptoms
    - increased work absence
    - greater use of inhaled beta agonists and corticosteroids
    - decrease in asthma control

BMC Public Health 2009; 9:88. 32.
Chest 2008; 134:317–323.
Thorax 2008; 63:14–20.

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Misdiagnosis of asthma in obesity

- Symptoms
  - shortness of breath
  - exercise-induced dyspnea
  - chest tightness
- ideal outcomes are dependent on losing weight
- most effective therapy for asthma, inhaled corticosteroids, may be less effective in the obese individual

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Conclusions

- Asthma is a common condition that is very responsive to appropriate therapy
- Confirmation of the diagnosis by history, physical examination, and spirometry with a flow volume loop is essential

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Think outside the box if it does not make sense or something does not fit

- Recognize the comorbidities
  - reach the goal of asthma control
  - avoid the complications of adverse
  - limit the side-effects of inappropriate doses of therapeutics