Cough
It’s Not All It’s Hacked Up To Be

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Agenda

• Review Differential for Cough
• Discussion on the management of certain diagnoses for cough
• Practical tips
Cough

• 30 million annual outpatient visits

• Chronic > 8 weeks
  • Most common causes:
    • Upper airway cough syndrome (aka post nasal drip)
    • Asthma
    • Gastroesophageal reflux

• In children ≤ 14 years old, chronic > 4 weeks
  • Most common causes:
    • Asthma
    • Protracted bacterial bronchitis (wet cough, no other etiology, responds to antibiotics)
    • Spontaneously resolving, nonspecific cough
Cough

- Study showed that 99.4% of cough is attributable to upper airway cough syndrome, asthma, or gastroesophageal reflux, if the following criteria are met:
  1.) Non-smoker
  2.) Not taking an ACE-Inhibitor
  3.) Normal/near normal and stable chest radiograph

Pathophysiology

• Activation of chemical receptors in upper & lower respiratory tract as well as esophagus, diaphragm, stomach, and pericardium
• Afferent signal via vagus nerve to medulla
• Efferent signal via vagus, phrenic, and spinal motor nerves produce cough

Differential Diagnosis
Asthma

• Expert Panel 3 of the National Asthma Education and Prevention Program as "a common chronic disorder of the airways that is complex and characterized by variable and recurring symptoms, airflow obstruction, bronchial hyperresponsiveness, and an underlying inflammation.

• It’s a syndrome, not a “one size fits all” disorder

• Reversible airway disease...not necessarily...tissue remodeling

• Look for pattern


Types

• Allergic
  • Genetic predisposition for IgE-mediated reactions is the strongest risk factor for developing asthma
  • Avoidance of allergens (not practical)
  • Dust mite reduction

• Non-allergic
  • more likely onset during adulthood, female, greater severity, and association with eosinophilic sinusitis with nasal polyps
  • Always go back to the history (e.g. seasonal pattern correlates with relevant skin testing)

Types

• Aspirin-exacerbated Respiratory Disease (AERD)
  • Samter’s Triad = asthma + sinus disease with polyps + aspirin/NSAID sensitivity
  • Symptoms 2 to 3 hours after exposure to COX-1 inhibitor
  • 10 – 20% of asthma cases

• Non-allergic
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Pathophysiology

• Eosinophilic
  • Dependent on IL-3, IL-5, GM-CSF
  • Anti-IL-5 biologics
  • Responsive to corticosteroids

• Neutrophilic
  • Up to 50% of asthma patients
  • Less responsive to steroids

• Pauci-Granulocytic
  • Eosinophil, neutrophil, lymphocyte counts are not elevated

Pathophysiology

• Corticosteroid-resistant
  • Failure to improve FEV1 by 15% after 2 weeks of high-dose OCS

| Table 3. Factors Independently Associated With Persistent Airflow Limitation (Remodeling) in Asthma* |
|---|---|
| Risk factors | Protective factors |
| Adult onset | Childhood onset |
| Male sex | Female sex |
| African American ethnicity | Hispanic ethnicity |
| Nonallergic (intrinsic) asthma | Allergen-exacerbated asthma |
| Genetic predisposition (eg, ADAM33) | Aspirin intolerance (AERD) |
| Smoking history | |
| Abbreviation: AERD, aspirin-exacerbated respiratory disease. |

Asthma: Nocturnal Symptoms

- Nocturnal awakenings occurring ≤ 2 X / month often correlate with daytime symptoms ≤ 2 days / week and normal spirometry
- 1 to 3 nights / week correlate with daytime symptoms > 2 days / week and mild obstruction on spirometry
- 4+ nights a week correlate with symptoms throughout the day and a FEV1 < 60 % of predicted
Asthma Vs. COPD

• basement membrane thickening
• epithelial desquamation and hypertrophy
• smooth muscle cell hyperplasia and hypertrophy
• mucous gland and goblet cell hyperplasia
• increased vascularity with microvascular leakage.

Asthma Vs. COPD

- More eosinophils
- Fewer neutrophils
- Higher CD4:CD8 ratio
- Thicker reticular layer of the basement membrane
- Smooth muscle hypertrophy in the proximal airways
- Absence of characteristic changes of COPD (e.g. emphysema)

History in the Making

• Age of onset of symptoms
• Childhood atopic disease
• Triggers
• Tobacco use
Less likely asthma...

- Minimal or no reversibility after bronchodilator on spirometry
- No relief with bronchodilators
- Onset after 50 years old
- Concomitant symptoms suggestive of cardiogenic etiology
- > 20 pack year cigarette use

Spirometry

- Inspiratory reserve volume
- Tidal volume
- Expiratory reserve volume
- Total lung capacity
- Vital capacity
- Residual volume
Spirometry

• Total exhaled volume, known as the
• Forced vital capacity (FVC) = total exhaled volume
• Forced expiratory volume in one second (FEV₁) = volume exhaled in the first second
• FEV₁/FVC ration = assess airflow obstruction
Spirometry

Normal

Asthma

VCD

Flow is measured on the Y axis

"Scooped Out"

Truncated inspiratory loop

Volume is measured on the X axis
Pulmonary Function Testing

• Complete reversibility of obstruction post-bronchodilator rules out COPD

• Diffusing capacity of carbon monoxide (DLCO) – reduced in intrinsic lung disease (e.g. emphysema)
COPD

• 3\textsuperscript{rd} most common cause of death in U.S.
• Diagnosis of COPD requires demonstration of obstruction
• Associated diagnoses:
  • Emphysema (pathological diagnosis)
  • Chronic bronchitis (cough for 3 months in 2 consecutive years)
• 10 to 15 pack year smoking history is unlikely to result in COPD
• 40 pack year history is the single best predictor of obstruction on spirometry
COPD

• Alpha-1 antitrypsin deficiency
  • Check if....
  • Age of onset is < 45 years old
  • No or minimal tobacco smoke exposure
  • Emphysema is predominantly in basilar lung
  • Family history of emphysema
  • Associated liver abnormalities (e.g. LFTs)

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Vocal Cord Dysfunction

• Abduct: Inspiration (also sniffing & panting)
• Adduct: Expiration (also talking, throat clearing, coughing, swallowing, and Valsalva maneuver)
• 10-40% adduction of VC during expiration at rest
• Paradoxical adduction of vocal cords during inspiration

Traister RS, Fajt ML, Whitman-Purves E, Anderson WC, Petrov AA. A retrospective analysis comparing subjects with isolated and co-existent vocal cord dysfunction and asthma. Allergy Asthma Proc 2013;34:349-55.
Vocal Cord Dysfunction

- Cocurrent in 25% of patients with asthma
- One study, 42.4% misdiagnosed with asthma for 9 years
- Delay in diagnosis leads to increased asthma medication prescription, impaired quality of life, and increased healthcare cost.

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Vocal Cord Dysfunction
Vocal Cord Dysfunction

• Clinically:
  • Difficulty during inspiration
  • Associated throat clearing and hoarseness
  • May have throat tightness, even chest tightness
  • May be the result of uncontrolled post nasal drip and/or acid reflux
  • Older age
  • Women > men
Vocal Cord Dysfunction

• Exercise-associated
  • 14% of cases
  • Young, female athletes

• Laryngopharyngeal reflux
  • 40% of patients with acid GERD have heart burn or metallic taste
  • “Silent” acid reflux

• Psychological disorders
  • Not considered malingering
  • Stress & anxiety
Vocal Cord Dysfunction

• Diagnosis:
  • Clinical history supported by:
    • Laryngoscopy – gold standard
    • Pulmonary function test
Vocal Cord Dysfunction

• Symptoms most predictive of VCD:
  • Throat tightness
  • Odors are a trigger
  • Absence of wheezing
  • Dysphonia

Score of ≥ 4:
• Sensitivity of 83%
• Specificity of 95%
• Positive predictive value of 96%
• Negative predictive value of 77%

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Vocal Cord Dysfunction

• Management:
  • Relaxed breathing techniques
  • Episode Cessation
    • Inhale through nose
    • Exhale through mouth
  • Prevent Episode
    • Inhale through tightly rounded lips
    • Exhale through tightly rounded lips
Asthma; Differential Within
Upper Airway Cough Syndrome

• Rhinitis
  • Allergic
  • Non-allergic

• Clinically distinguished from AR by:
  • Onset at a later age
  • Absence of itching (eyes and ears) and prominent sneezing
  • Nasal congestion and postnasal drainage are prominent
  • Year round

• Triggers: strong odors/fragrances, cleaning products, newsprint, changes in temperature, and alcoholic beverages
Upper Airway Cough Syndrome

• Rule out cerebrospinal fluid (CSF) leak
  • Red flags:
    • Unilateral rhinorrhea
    • Reproducible with Valsalva
    • Associated headache
    • Recent head trauma/sinus surgery
Sinus Disease

- Acute rhinosinusitis
- Chronic rhinosinusitis
Sinus Disease
Biologics

• Omalizumab (Xolair) - average wholesale price (AWP) for a 150 mg vial is $541. For dosing every 4 weeks, the price will range from $541 to $1,000 (for 150 mg and 300 mg, respectively). For one year of treatment with these doses, the cost will range from $10,000 to $16,000.