Coughing and Kids: When It's Not Just Asthma

Satellite Conference and Live Webcast
Thursday, May 16, 2013
12:00 – 2:00 p.m. Central Time

Produced by the Alabama Department of Public Health
Video Communications and Distance Learning Division

Faculty

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Parent of a Child with a Chronic Respiratory Condition

Faculty

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Presentation Overview

- Case Presentation and Parent Interview
  - 20 minutes
- Functional and Pathophysiologic Cough
- Airway Clearance – Innate Defense

Presentation Overview

- Diagnostic Evaluation of Cough
  - 40 minutes
  - Break (15 minutes)
- Case Reviews
  - 25 minutes
- Questions
  - 5 minutes

Disclosures

- Dr. Hoover
  - No personal disclosures
  - Cystic Fibrosis Research Funding
    - Cystic Fibrosis Foundation
    - Gilead Pharmaceuticals
  - Will indicate non-FDA approved treatment strategies (**)

Disclosures

- Ms. Bradford has no disclosures

Objectives

- Explore the parental experience of dealing with chronic cough and undiagnosed illness
- Identify the functional nature of coughing
- Associate the relationship of coughing to pathologic states in the respiratory tract

Objectives

- Identify differential diagnoses associated with chronic coughing that may indicate diagnoses other than asthma

Chronic Cough: A Parent's Perspective

Jacob's Medical Journey

- Concern
- Frustration
- Disappointment
- Hope
- Resolution
- Maintenance

Jacob's Cough

- Began at age two
- Rarely productive but occasionally produces green sputum

Jacob's Cough

- **Multiple visits with few answers and little improvement**
  - **Recurrent use of antibiotics, cough and cold medicines, allergy medicines, inhalers**
    - **Nothing seemed to work**

Frustration

"I knew something was wrong with him but did not know where to turn."

Disappointment

"I figured that a doctor, if there was something really wrong, would find it and fix it."

Chronic Fever and Cough

- **Jacob, age 12, experienced fevers over 9 months up to 103F associated with cough**
- **Ultimately he was evaluated by a new physician and referred to infectious disease specialist following a CT scan demonstrating bronchectasis**

Chronic Fever and Cough

- **Subsequent referral to pulmonary for evaluation of chronic cough March 2012**

Hope

"This was the first time I thought that a doctor actually cared about my child."

Jacob's Cough and Bronchiectasis

- Jacob's differential diagnosis
  - Asthma
  - Cystic Fibrosis
  - Immune Deficiency
  - Primary Ciliary Dyskinesia
  - Hypersensitivity Pneumonitis
  - Aspiration of foreign body

Evaluation

- History and PE
  - Chronic wet productive cough
- PFTs confirm asthma
- CT sinuses: Pan Sinusitis
- Immune w/u negative
- Sweat CL: negative

Evaluation

- IgE elevated 531 and Rast c/w Environmental Allergies (ABPA neg)
- Admitted with pneumonia May 2012
  - Bronchoscopy: Purulent Bronchitis

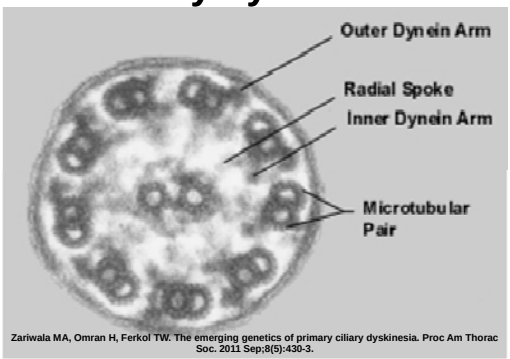
Bronchoscopy

- Aleveolar Lavage
  - G+ Cocci
  - 12,815 WBC/uL
  - 440 RBC/uL
  - 93% PMNs
  - 500,000 CFU
    - Strep Pneumonia

Ciliary Dyskinesia

- Electron Microscopy Revealed Normal Ultrastructure
- PCD Gene Sequence Identified Heterozygous Mutation in DNAH11
  - Zariwala MA, Omran H, Ferkol TW. The emerging genetics of primary ciliary dyskinesia. Proc Am Thorac Soc. 2011 Sep;8(5):430-3.

Ciliary Dyskinesia



Zariwala MA, Omran H, Ferkol TW. The emerging genetics of primary ciliary dyskinesia. Proc Am Thorac Soc. 2011 Sep;8(5):430-3.

Diagnosis of PCD

- Difficult diagnosis with emerging tools
  - Gold standard: nasal brushing and EM
    - Demonstrating ultrastructural abnormality has a high specificity for disease
    - Normal structure does NOT rule our PCD

Diagnosis of PCD

- Emerging tools
  - Genetics
    - Ready for prime time?
    - Much debate
  - Nasal NO
    - Good NPV / limited availability

Diagnosis of PCD

- Ciliary motility study
  - Difficult / affected by virus
- See references for further reading

Treatment for PCD and Asthma

- Daily chest physiotherapy
- Mometosone / Fomoterol 100/5mcg 2 puffs BID with spacer
- Montelukast 5mg QHS
- Albuterol HFA 2-4 puffs prn with spacer

Treatment for PCD and Asthma

- Azithromycin 250mg Mon., Wed., and Fri.**
- Gentamicin 80mg nebulized BID QOM**

"Relieved"

"Now I finally know what is wrong with Jacob."

Staying Healthy is Hard Work!

"I don't feel Jacob's care is a burden. He is able to actively play sports and lead an almost normal life."

Mechanical Defenses of the Lung

- Nasal and upper airway filtration of larger particles (>10um)
- Muscosal surface and mucous secretion
- Mucociliary clearance

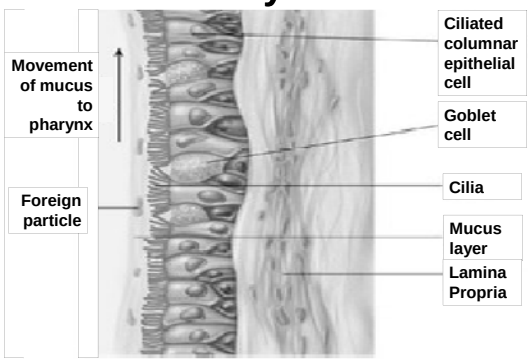
Mechanical Defenses of the Lung

- Neurally mediated responses
  - Cough
  - Sneezing
  - Bronchoconstriction

Mucociliary Clearance

- Ciliated cells present at 13 WGA
- Present on mucosal surfaces with up to 200 cilia present per cell
- Beat in frequency at 12-22 hz to sweep mucous along mucosal surfaces
- Ciliary function can be disrupted due to structural or dyskinetic beat

Mucociliary Clearance



Neurally Mediated Clearance

- Sneezing
  - Response to particulate matter or irritants in the nose or nasopharnyx
- Cough
  - Response generated to stimulation of laryngeal or airway receptors

Neurally Mediated Clearance

- Bronchoconstriction
  - Increased lower airway tone in response to receptor stimulation to limit dispersion of inspired particles

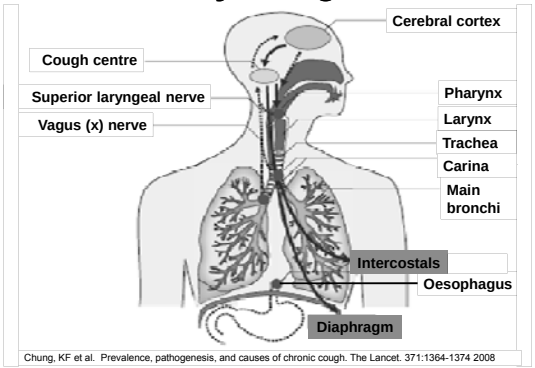
Why Cough?

- Larnyx
  - Irritant
  - Thermal
- Trachea
  - RARs - Irritant
  - SARs - Facilitate

Why Cough?

- Lower Airways
  - C-Fibers
- Esophagus

Why Cough?



Chung, KF et al. Prevalence, pathogenesis, and causes of chronic cough. The Lancet. 371:1364-1374 2008

What Is a Cough

- Coughing is a physiologic reflex that augments airflow thus enhancing mucociliary clearance and expelling large accumulations of mucous
- Coughing is in effect a normal response to a pathophysiologic state
- Cough can be both reflexive and controlled

How Do We Cough

- Initial inspiration above tidal breathing to a point in IRV but below TLC
- Glotic closure with contraction of abdominal and thoracic muscles raises transpulmonary pressure
- Opening / closing glotis in repetition allows high velocity air flow transients to propel mucous

High Velocity Air Flow Moves Liquids!

Is a Cough Always Bad

- Coughing is a normal and protective physiologic defense
- Chronic coughing represents ongoing response to a pathophysiologic state
- Generally a cough lasting more than four weeks requires further investigation

Is a Cough Always Bad

- A cough that is acutely worsening likewise requires more attention

Cough: Efficient Accurate Diagnosis

- Chronic cough in association with chronic lower airway inflammation results in permanent lung injury
  - Bronchiectasis is permanent and progressive

Cough: Efficient Accurate Diagnosis

- Morbidity and physiologic limitations associated with chronic coughing significantly disrupts daily activity
  - School, sleep, activity, parental concern

So Many Coughs: Where to Start?

- History is the key!

Characterize It: Types of Cough

- Clinical descriptors of cough help tremendously
- Character
  - Wet or productive?
  - Dry and hacky?
  - Barking or seal-like?

Characterize It: Types of Cough

- Setting and stimulus
  - During wakefulness or asleep?
  - During exercise or at rest?
  - Following meals or drinking?
  - Continuous or disruptive in nature?

Wet and Productive

- Generally associated with excessive mucous production, ineffective clearance, and inflammation
  - Asthma: “wet” asthma vs. “dry” asthma
  - Bronchitis: chronic or acute
  - Pneumonia: infectious or non-infectious

Wet and Productive

  - Impaired airway clearance: innate or acquired
  - Consider CF, PCD, foreign bodies and focal airway obstructions
    - Intrinsic / extrinsic mass

Dry and Hacky

- Generally associated with upper airway stimulation
  - Asthma
  - Allergic rhinitis
  - Sinusitis
  - Gastroesophageal reflux
  - Post infectious hypersensitivity
    - Psychogenic

Barking or Seal-like

- Generally not a chronic finding but more a qualitative descriptor – think acute
  - Croup / laryngotrachobronchitis
  - Characteristic of tracheomalacia
    - History of T-E fistula

Barking or Seal-like

- External / internal airway compression
- Psychogenic – honking quality

Setting or Stimulus

- Awake or asleep?
  - Pathologic coughing usually continues and disrupts sleep
  - A cough that resolves during sleep and resumes on awakening raises concern of psychogenic etiology **diagnosis of exclusion

Setting or Stimulus

- During exercise or rest
  - Coughing only with exercise represents a physiologic change
    - Asthma, EIB, GERD, environmental factors
  - A cough that occurs at rest is most common in the pathologic state and usually is exacerbated by activity

Setting or Stimulus

- Continuous or disruptive in nature
  - Coughing that is seemingly uncontrollable or disruptive is often psychogenic in nature
  - While this is a diagnosis of exclusion and requires careful assessment, a chronic cough is generally responsive to active suppression

Setting or Stimulus

- Following meals or drinking
  - Generally would be triggered by irritant receptors independently or in association with lower airway disease
    - Think aspiration: vocal cord paralysis, laryngeal clefts, primary aspiration, thermal sensitivity

Setting or Stimulus

- GERD
- Gustatory responses

Evaluation of Chronic Coughing

- History, history, history
- Physical examination
- Routine diagnostic testing
  - What is done by the primary care provider
- Subspecialty evaluation
  - Advanced diagnostics available at tertiary care centers

Physical Exam

- HEENT
  - Chronic OM, sinusitis?
  - Auscultation of the neck?
- Cardiac
  - Ccardiac and vascular abnormalities?

Physical Exam

- Pulmonary
  - Wheezing, crackles, rhonchi, tight / prolonged expiration, auscultation pre / during / post cough
- Neurologic
  - Weakness
- Extremity
  - Clubbing

Routine Diagnostic Testing: Primary Care Setting

- Pulse Oximetry
- CXR
- Office Based Spirometry
- Upper GI
- Baseline Immunologic Evaluation
- Rast Allergy Evaluation

Advanced Diagnostic Evaluation: Subspecialty Setting

- Advanced pulmonary function testing
- HRCT
  - Capability of advanced imaging techniques
- Bronchoscopy and BAL
  - A +/- ENT or GI - Aerodigestive Evaluation

Advanced Diagnostic Evaluation: Subspecialty Setting

- Nasal brushing biopsy - EM
- Genetic testing
- Advanced immunologic evaluation
  - Often done in collaboration with immunology

Summary

- Cough duration > four weeks requires further intervention
- Evaluation and treatment begins in the primary care setting
- Characterization of the cough is highly important in guiding diagnosis

Summary

- Advanced diagnostics and subspecialty evaluation may be necessary
- Primary goal is accurate diagnosis and treatment to prevent morbidity and permanent lung damage

References

- Taussig LM, Landau LI, et al. Pediatric Respiratory Medicine. St. Louis: Mosby, 1999
- Chung, KF et al. Prevalence, pathogenesis, and causes of chronic cough. The Lancet. 371:1364-1374 2008
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- Knowles MR, Leigh MW, Carson JL, Davis SD, et al.; Genetic Disorders of Mucociliary Clearance Consortium. Mutations of DNAH11 in patients with primary ciliary dyskinesia with normal ciliary ultrastructure. Thorax. 2012 May;67(5):433-41.

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- Grüber C, Lehmann C, Weiss C, Niggemann B. Somatoform respiratory disorders in children and adolescents-proposals for a practical approach to definition and classification. Pediatr Pulmonol. 2012 Feb;47(2):199-205. doi: 10.1002/ppul.21533. Epub 2011 Sep 8.

Case 1

- 7-year-old female presents with cough and chest pain worsened with exercise
- Diagnosed as asthma
- ROS
  - Constipation and abdominal pain
- PMHx
  - Seen by GI and allergist

Case 1

- FAMHx
  - Negative for childhood disease
- Social
  - Outside smoking by parents

Previous Treatment

- Allergist diagnosed allergic rhinitis and asthma
- Treated with multiple ICS, nasal steroids without improvement
- Recently increased to ADVAIR 250/50 BID, flonase BID, zyrtec 10mg qd, tessalon pearls 2-4 daily PRN
- Neg CXR by hx but no spirometry

Cough

- Dry and barky
- Often associated with clearing of throat
- Occurs at rest and activity
- At times seems worse after eating
- Does not occur at night during sleep

Cough

- Chest pain is vague and difficult to characterize
  - Mostly when coughing and it is getting worse

Exam

- VSS O2 Sat 99% Ht and Wt at 45%
- General: Well Appearing
- CV: RRR w/o murmur 2+ Pulses
- Chest: Clear BS Bilaterally
- Abdomen: Benign
- Extremities: ? 1+ clubbing and CR <2 sec

Endoscopy / Bronchoscopy

- Bronchoscopy and BAL were completely normal
- Upper endoscopy revealed severe esophagitis with white plaques
  - Esophagus: mixed eosinophillic and neutrophillic microascesses with budding yeast and pseudohyphae
  - Dx: invassive candidal esophagitis

Evaluation and Treatment

- Immunologic evaluation was negative
- ICS felt to contribute in the setting of GERD
- All asthma and allergy meds stopped with addition of BID PPI and Diflucan
- At follow up pt was symptom free with no chest pain or cough

Summary

- While asthma is the most common association with cough in children, this cough was NOT completely characteristic of asthma
- Spirometry should be used in the diagnosis of refractory asthma
  - Children as young as 4-5 y/o
- Ultimately escalation of treatment contributed to nosocomial disease

Case 2

- 14 y/o male with coughing, fatigue, shortness of breath and a "racing heart" while walking or climbing stairs
- Increasing exertional dyspnea of the last three weeks
- Cough that worsens with activity and when supine

Case 2

- Nasal congestion and sinusitis
  - Tx with Augmentin
- Started on ADVAIR 250/50 2 weeks ago without improvement

ROS

- Neuro / psych
  - Baseline Asperger Syndrome
- CV
  - Racing heart, dyspnea with walking
- Pulm
  - Cough which is worsened supine

Cough

- Improves with rest and sitting up
- Cannot lie supine
  - Immediately starts coughing
- Cough is harsh and honking
- Activity also causes the cough to worsen but not like lying down

PMHx

- Asthma: since childhood
- Recurrent hemolytic anemia and thrombocytopenia
- Multiple cutaneous and hepatic hemangiomata
  - Involuted at 13 months
- Resolved VSD

PMHx

- Asperger syndrome
  - Learning disability
    - Verbal and reading IQ 70
    - Overall IQ 85

PSHx

- Bilaterl inguinal hernia – 1991
- Left leg cellulitis w/debridement - 1996

BHx

- Term delivery: 5lb, 14oz
- Hemolytic anemia and thrombocytopenia
- VSD

FHx

- Asthma in 9 y/o sibling
- HTN in adults
- No anemia
- No other cardiopulmonary disease

SHx

- Lives with mother, father, and sibling
- Lives in the city
- Italian descent

Feeding Hx

- Breast fed for eight months
- Tolerated addition of fruits and vegetables
- Developed vomiting and diarrhea with addition of cow milk and table food which resolved after several months and after trying soy milk

Feeding Hx

- Doesn't eat much meat or dairy products
- Prefers corn, potatoes, cookies, and chips

Exam

- VS
  - Hr 125, r 18, bp 110/48 o2 96% ra
- Gen
  - Alert without distress
  - Thin habitus
- HEENT
  - Scleral icterus

Exam

- CV
  - S1 with loud single s2 and a 3/6 blowing diastolic murmur 2+ peripheral pulses
- Lungs
  - Clear BS but coughing with deep inspiration and supine position

Exam

- AB
  - Soft and NT /ND
  - No hepatomegaly with spleen tip down 3 cm
- Ext
  - Cr 2 seconds and no clubbing

Evaluation

- ECHO: Pulmonary HTN
  - Predicted pulmonary artery pressure of 125 systolic and 55 diastolic
  - RVH and LVH with diastolic pulmonary valve insufficiency otherwise normal intracardiac anatomy

Evaluation

- Spirometry
  - Moderate obstructive and restrictive disease
  - Patient had difficulty performing the test

Problem List

- Severe pulmonary hypertension
- Chronic hemolytic anemia and thrombocytopenia
- Low-normal IQ and learning disability
- History of multiple hemangiomata
- Questionable dietary aversion to protein

DD

- Idiopathic pulmonary hypertension
- Metabolic disease
  - Lysinuric protein intolerance, gaucher, etc.
- Hereditary hemorrhagic telangiectasia
- Hemoglobinopathies

DD

- PVOD
- Thrombosis (chronic)
- Collagen vascular disease
- Arterial-venous shunting

Hematologic Evaluation

- WBC 9, HgB 10 and PLT 50s
- Smear mircoangiopathic hemolysis
- INR 1.7
  - All coagulation factors slightly low except fibrinogen and factor VII activity
- LDH 1500s

Hematologic Evaluation

- Historical evaluation of immune and non-immune hemolysis negative

Metabolic Evaluation

- Fasting ammonia: 39
- Post-prandial ammonia: 90-120
- Urine amino and organic acids: normal
- Serum amino acids: normal
- Metabolic storage diseases: normal
- Acylcarnitine profile: normal

Hepatic Evaluation

- AST, ALT, GGT and AlkP: normal
- Albumin: 2.0
- Prealbumin: 5
- TB: 3-4 (unconjugated)
- Normal electrolytes

Congenital Extrahepatic Portocaval Shunts

- The Abernathy Malformation – 1793
  - Type 1
    - End to side anastomosis and congenital absence of the portal vein
  - Associated with dextrocardia, transposition, and polysplenia

Congenital Extrahepatic Portocaval Shunts

  - Type 2
    - Side to side
    - Not associated with other anomalies but associated with encephalopathy

– Howard E and Davenport M, J Ped Surg, 32; 494-97, 1997

Summary

- Coughing, even as the presenting CC can be a distracter and delay diagnosis
- Coughing is not specific to lung disease

Summary

- Focusing on basic history and adhering to the concept that pediatric disease is most frequently of common primary etiology
- Always listen and hear parental instincts