Asthma Mimickers: A Case Based Approach

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March 1, 2014

Objectives

- Discuss possible causes of wheezing/cough and their treatment
- Discuss case presentations to better illustrate causes of wheezing/cough other than asthma
- Explain differences between those causes and asthma
- Identify hallmarks of clinical presentation of endobronchial foreign body

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March 2014

continuing professional education

Grand Rounds 8-9am

Cook Children's Medical Center, Hochberger Auditorium

"Asthma Mimickers with A Focus on Foreign Body Aspiration"

March 18, 2014

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Disclosure

- No financial relationships to disclose

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"If I can put everyone to sleep within the first five minutes, the rest of my presentation should go pretty well."

Case Presentation

- 5 year old male with dry intermittent cough and occasional wheezing x 7months
- Cough described as harsh, occurring day and night
- Per mother, occurs more frequently during temporal changes in weather (i.e. cold air), exercise, and “when mountain cedar levels are high”

Case Presentation

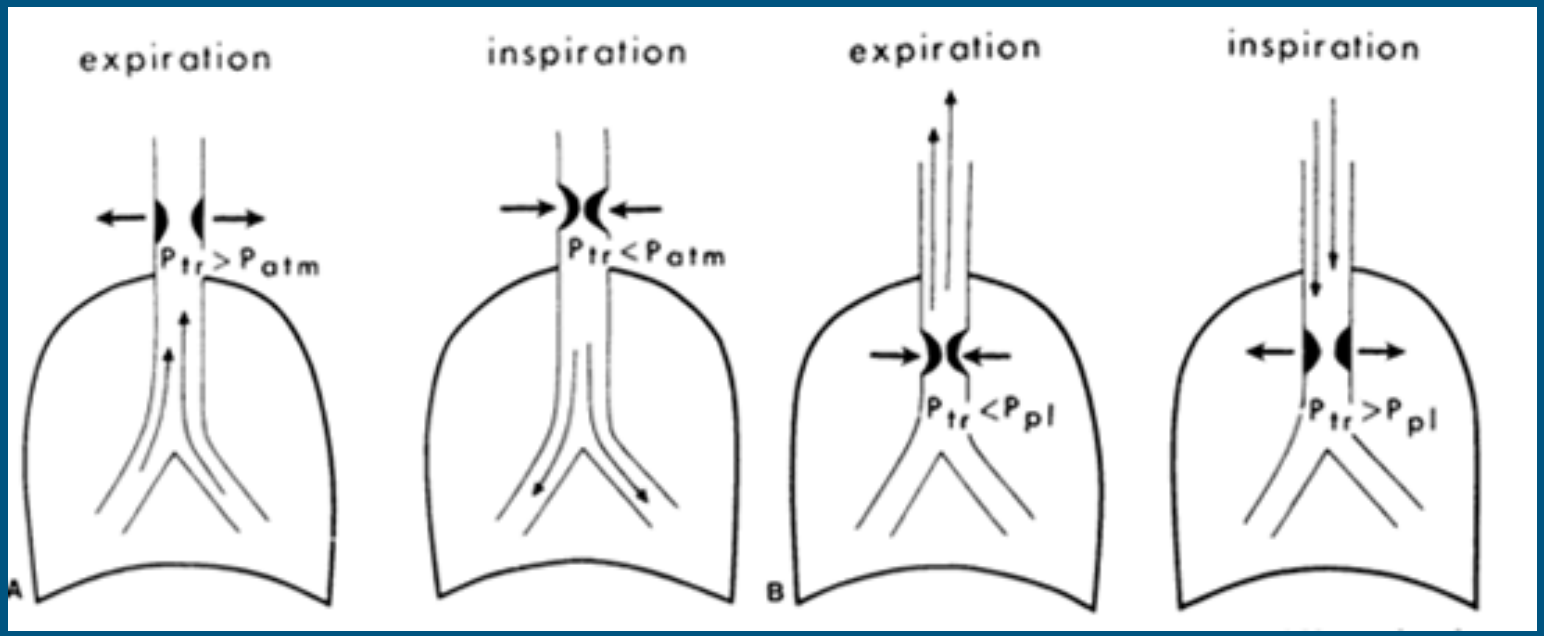
- No relation to feeds
- Denies sinus symptoms
- Symptoms NOT relieved by Albuterol
- Treatments tried:
  - Multiple short courses of oral steroids
  - Patient started on inhaled steroids
  - 10 day course of antibiotics
- Referred to pulmonary

What is “wheezing?”

- Defined as a continuous musical expiratory sound caused by intrathoracic airway obstruction
- Produced by oscillation of opposing walls of an airway that are narrowed to the point of closure

Weinberger M and Abu-Hasan M. *Pediatrics* 2007.

Wheezing



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Wheezing

- Often confused with:
  - “Rattling” (congestion)
  - A high pitched inspiratory noise (stridor)
  - A low pitched inspiratory noise (snoring)

Wheezing—exam findings

- Asthma/Lower airway obstruction: classically demonstrate high-pitched musical expiratory sounds, varying in tone and timing (“polyphonic”)
- Localized bronchial narrowing: single pitch, begins/ends at same time (“monophonic”)

What is “asthma”?

- Characterized by:
  - Hyperresponsiveness of the airways to various stimuli, leading to reversible airway obstruction
  - Airway obstruction result of bronchospasm and inflammation/mucosal edema
  - Reversibility with treatment a key component

Asthma

- Significant phenotypic variability
- Variability in clinical presentation can lead to overdiagnosis, underdiagnosis, and misdiagnosis of asthma

"All that wheezes is not asthma, and all that is asthma does not wheeze."

--A very wise person

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What else could it be?

When symptoms persist despite conventional asthma therapy, or when classic symptoms do not exist, one must consider other diagnoses

Differential diagnosis of wheezing

- Asthma
- Vocal cord dysfunction
- GER
- Chronic aspiration
- Tracheomalacia/Bronchomalacia
- Foreign body aspiration
- Cystic fibrosis
- Primary ciliary dyskinesia
- Immunodeficiency
- Cardiac disease/Vascular compression
- Bronchiolitis obliterans

Differential diagnosis of wheezing/cough

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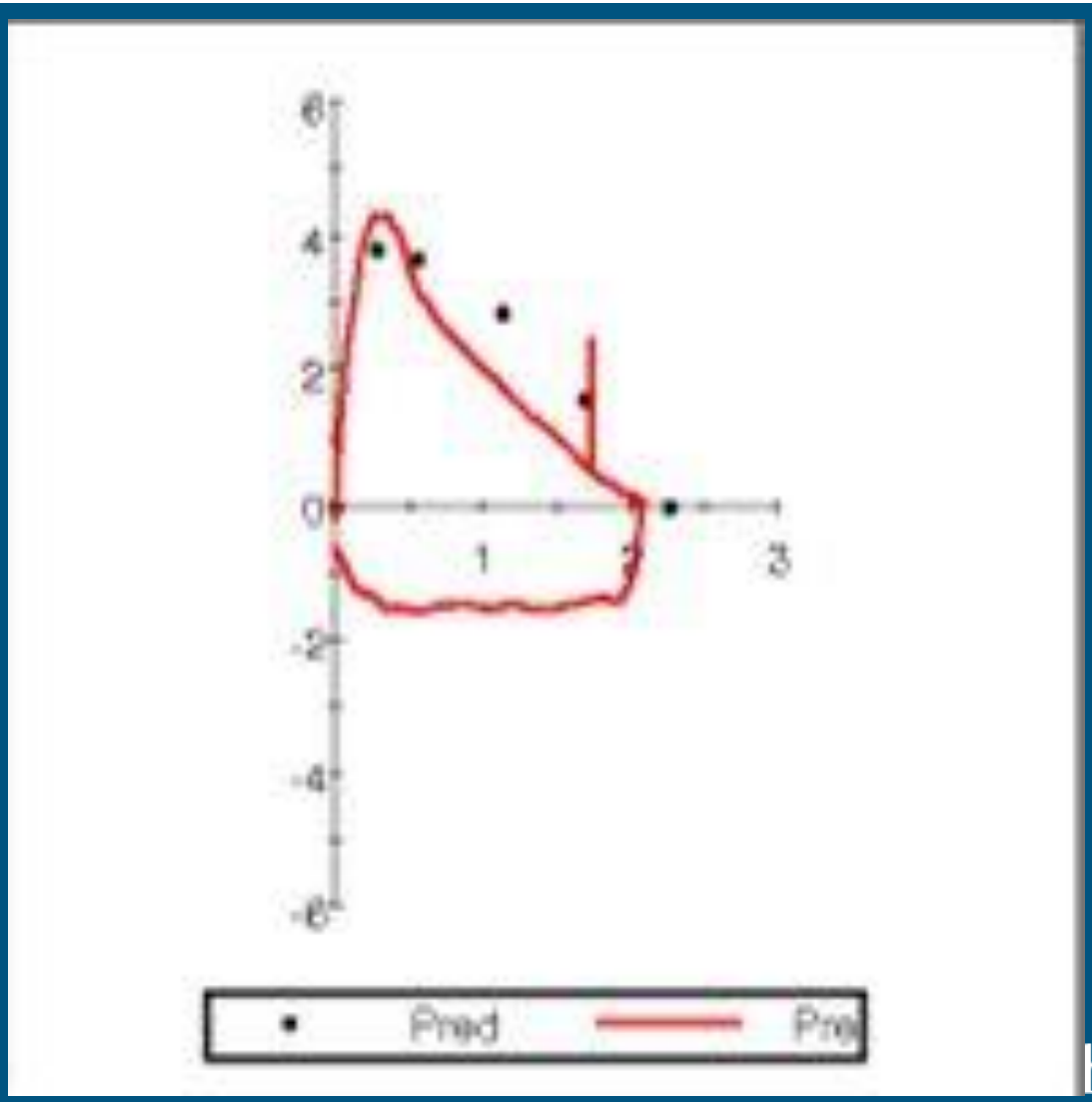
Case #1

- 10 year old female presenting for shortness of breath with activity
- Patient reports mid-sternal chest pain, wheezing
- Symptoms relieved by rest
- Diagnosed with asthma, allergic rhinitis
- Tried Albuterol, Singulair in past, but did not improve symptoms
- Fam Hx: brother with asthma

Case #1

- Due to dyspnea on exertion, seen by Cardiology, Echo done (normal); 6 min walk test normal
- Patient continued on Albuterol prn
- Seen in f/u 1 month later: symptoms not better
- Upon further questioning, patient describes dyspnea with stressful situations, also throat tightness and difficulty getting air in
- Albuterol not relieving symptoms



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Case #1

- Given constellation of symptoms and PFT findings, vocal cord dysfunction is suspected; patient referred to speech therapy after being taught abdominal breathing exercises in clinic
- After meeting with speech therapist, practicing breathing exercises, patient no longer having symptoms, and no longer using bronchodilator

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Vocal Cord Dysfunction

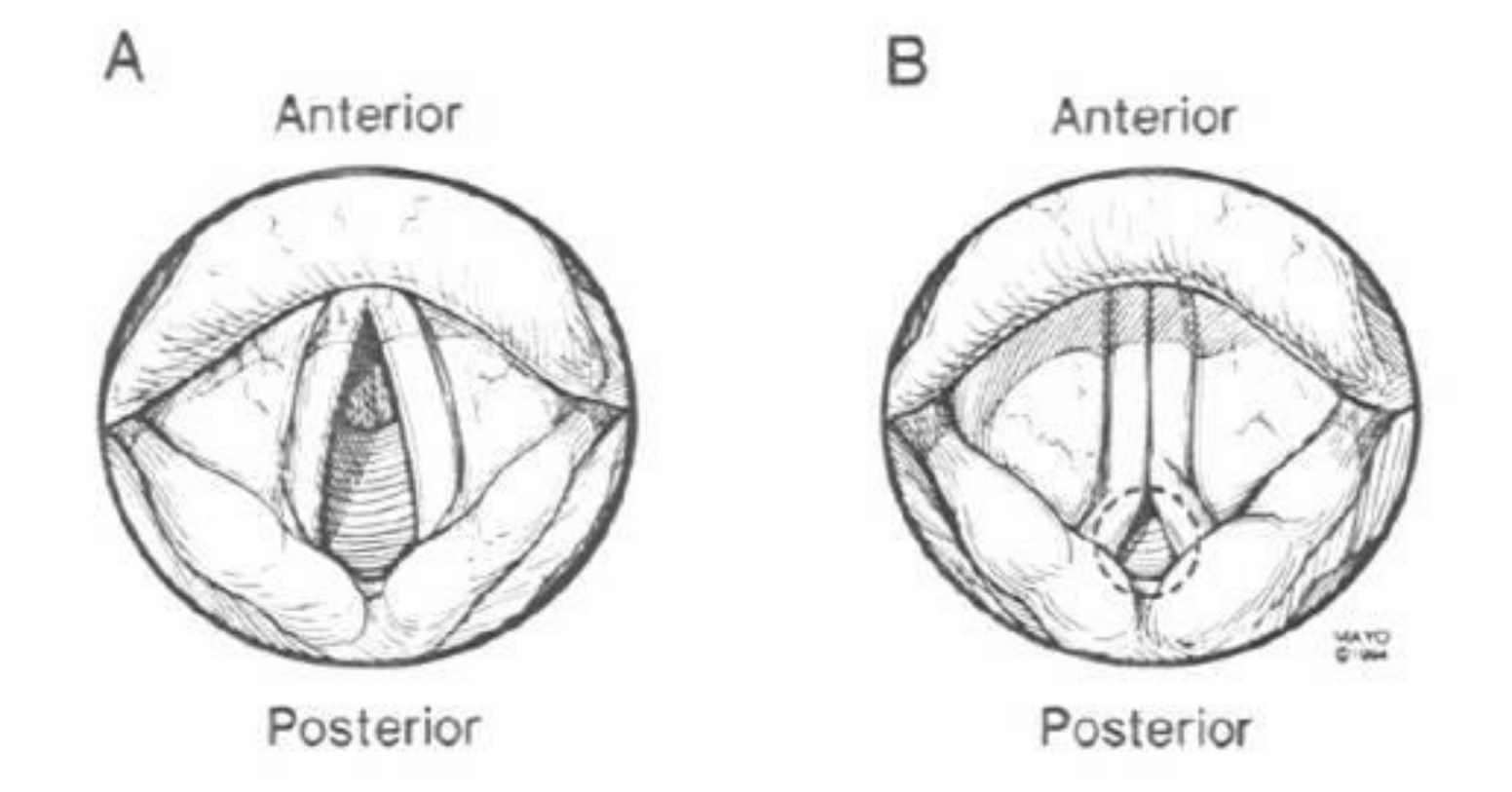
Vocal cord dysfunction

- Involves paradoxical closure of the vocal cords during inspiration and sometimes expiration, producing obstructive symptoms
- Also known as paradoxical vocal fold movement

Vocal cord dysfunction

- First described in 1842 by Dunglison
- Described disorders of the laryngeal muscles brought on by “hysteria”
- 1974—Patterson et al. “Munchausen’s stridor”
- 1983—Christopher et al described group of patients, mainly female, ages 20-40, many with history of abuse

Kenn K and Balkissoon R. *Eur Respir J* 2011.



Normal

VCD

Patterson DL et al. *Insights in Allergy* 1994.

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VCD--Presentation

-

Vocal cord dysfunction

- Classic presentation:
  - Stridor
  - Throat tightness
  - Refractory asthma
  - Female predominance (2-3 times as likely)
- Triggers:
  - Strong emotions/stress
  - Exercise
  - GER

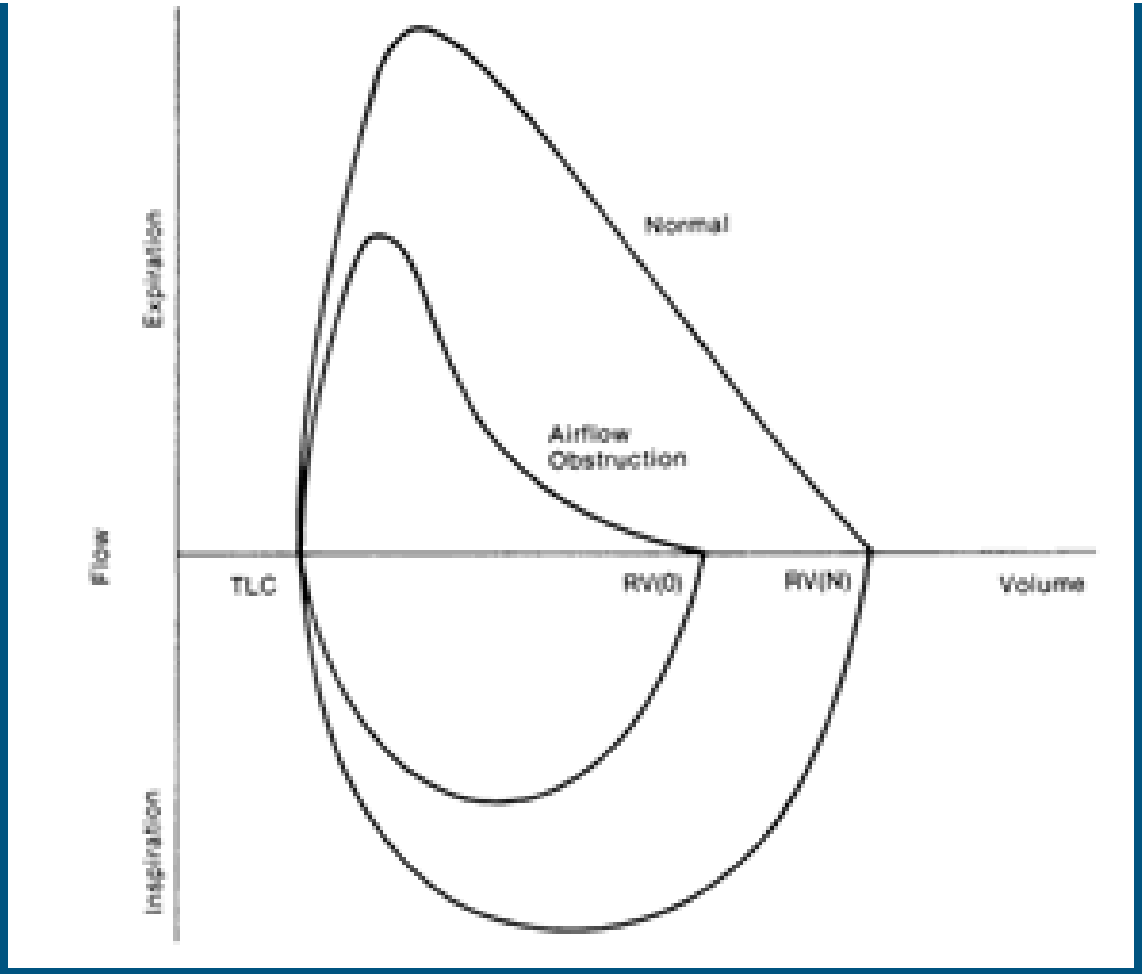
Vocal cord dysfunction

- Classic patient: adolescent female, type A personality, straight “A” student, extracurricular activities (cheerleading, gymnastics, swimming)
- Concomitance with asthma—30-60%

Comparing Asthma and VCD Exacerbations

	Asthma	Vocal cord dysfunction
Time of onset	Within minutes	Within seconds
Dyspnea during	Expiration	Inspiration
Area of obstruction	Lower airways	Throat
Effect of inhalers	Highly effective	Often ineffective
Triggers	Irritants, exercise, allergens	Irritants, exercise, stress
Hypoxemia?	More common—due to V/Q mismatch	Less common—due to hypoventilation

Pulmonary function tests



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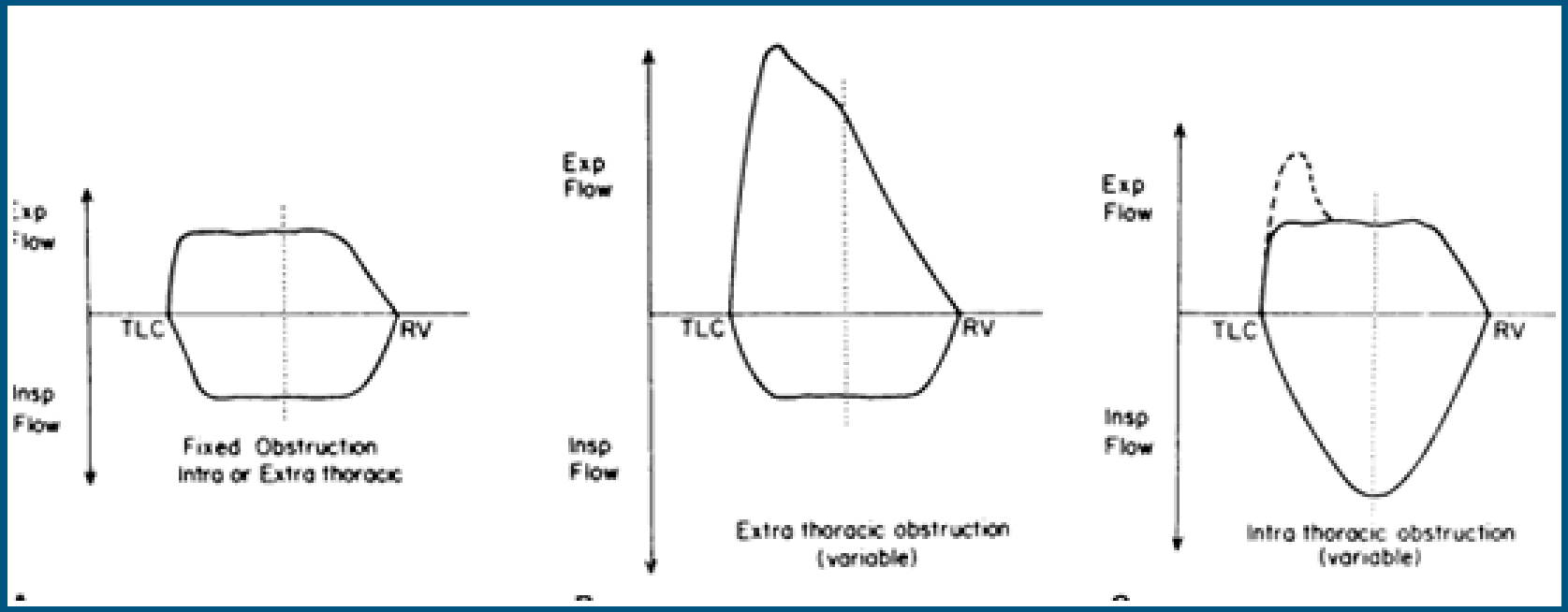
Pulmonary function tests



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VCD Treatment

- Involves breathing techniques to help manage the vocal cords, usually taught by a speech pathologist
  - Effective in 80-90% of patients if done correctly
- Anticholinergics (Ipratropium bromide inhaled) also have been shown to be of some use, esp in exercise related VCD
- Prognosis favorable

Case #2

- 7 month old male with recurrent wheezing since birth, worse after recent RSV infection
- Occurs daily, day and night
- Multiple courses of oral steroids
- Started on budesonide 0.25 mg BID inhaled
- Also started on trial of lansoprazole x 1 month

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Case #2

- Mom reports frequent spitting up, along with wheezing during/after feeds
- Patient otherwise neurologically normal
- Flexible bronchoscopy done, shows normal anatomy, occasional lipid-laden macrophages
- Swallow function study done—demonstrates aspiration, thickened feeds recommended

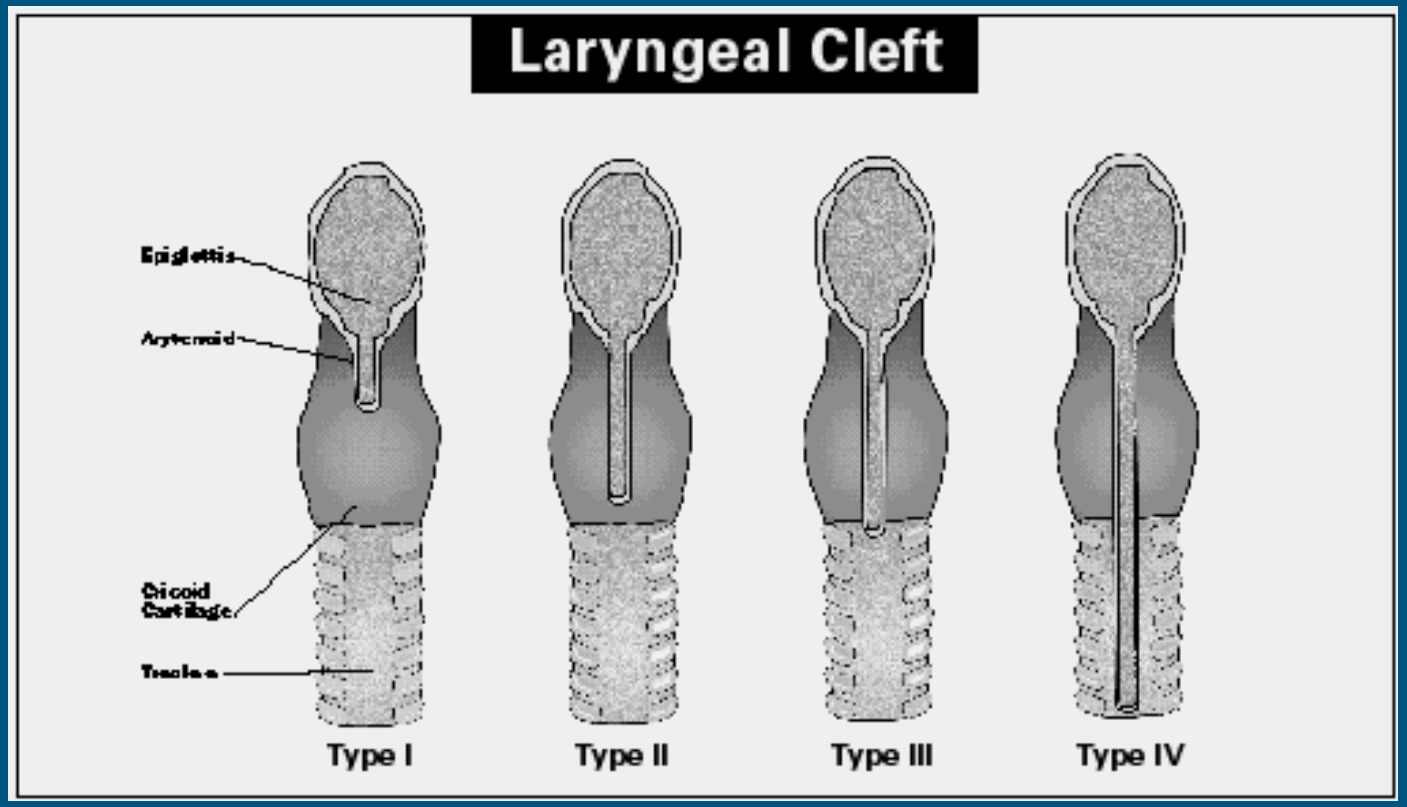
Case #2

- Only minimal relief provided, mom electively stops lansoprazole
- Repeat swallow function study done at 11 then 15 months continues to demonstrate aspiration
- Referred to ENT for further evaluation
- Rigid bronchoscopy performed, demonstrates type 1 laryngeal cleft

Swallow Dysfunction/Chronic Aspiration

Congenital causes of swallow dysfunction

- Developmental
- Anatomic
- Neurologic/Neuromuscular



Courtesy of: http://speech-language-pathology-audiology.advanceweb.com/Article/Laryngeal-Cleft-1.aspx

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Chronic Aspiration Without Gastroesophageal Reflux as a Cause of Chronic Respiratory Symptoms in Neurologically Normal Infants*

Shahid Sheikh, MD; Elizabeth Allen, MD; Richard Shell, MD; Jean Hruschak, MA; Durdana Iram, MD; Robert Castile, MD; Karen McCoy, MD

- Retrospective review of patients referred to Pediatric Pulmonary center for recurrent wheezing/stridor/cough over 3 year span

- 112 patients otherwise healthy, term infants underwent VSS and 24-h pH probe as part of workup

Sheikh S et al. *Chest* 2001.

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Aspiration and Wheezing

Both studies normal	55 infants (49%)
Abnormal pH probe	18 infants (16%)
Abnormal VSS	**13 infants (11.6%)**
Both pH probe and VSS abnormal	26 infants (23%)

Aspiration

Severity of Aspiration on VSS	Management	9-mo Follow-up		
		VSS	Feeding	Off Asthma Medications
Aspiration on thin consistencies alone (n = 7)	Thickened feeds	Improved in all	Regular	5/7
Aspiration on thin and semi-thick consistencies (n = 2)	Thickened feeds	Improved in all	Regular	1/2
Aspiration (n = 4)				
Thin/semi-thick	NJ feeds (n = 3)	Improved in all	Regular	2/2
Thick	Gastrostomy tube feeds (n = 1)	Improved	Regular	1/1

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Case #3

- 18 month old male seen for recurrent bronchitis
- Mom reports daily congestion, with purulent nasal drainage, and daily wet/dry cough
- Has had several episodes of otitis media, with chronic otorrhea, and underwent tympanostomy tube placement; he continues to have drainage

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Case #3

- Birth history significant for NICU stay for transient tachypnea of the newborn and O2 requirement; patient in NICU x 11 days

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Chest X-ray

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Case #3

- Patient underwent bronchoscopy with ciliary brush biopsy
- Diagnosis of primary ciliary dyskinesia (Kartagener syndrome) is confirmed

Primary ciliary dyskinesia

Primary ciliary dyskinesia

- Also known as immotile ciliary syndrome, Kartagener syndrome/triad
- First described in early 1900s
- 1933-Kartagener describes patients with chronic sinusitis, bronchiectasis, and situs inversus totalis
- 1976-discovery that these patients have defective ultraciliary structure

Knowles MR et al. *Am J Respir Crit Care Med* 2013.

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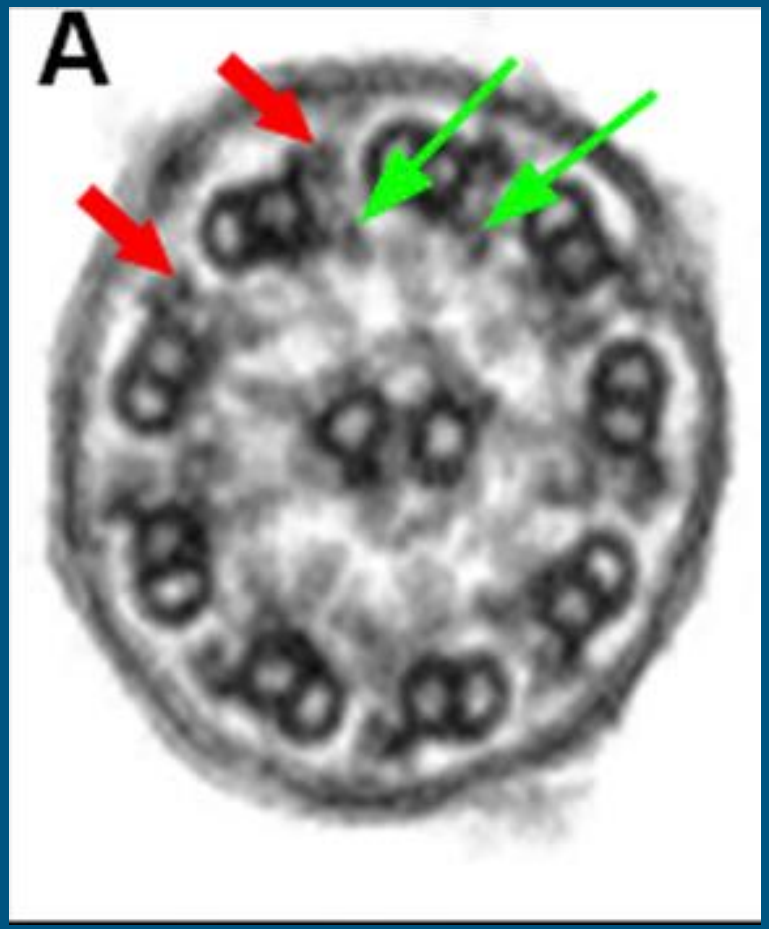
- Estimated incidence 1:10,000-20,000 live births
- Less than 1,000 confirmed cases in United States
- Underdiagnosed; Why?
  - Cardinal signs/symptoms under-recognized by clinicians
  - Diagnostic tools not readily available

Ciliary structure and function



- 9+2 configuration
- Coordinated movement responsible for clearing bacteria and toxic substances from the conducting airways, paranasal sinuses, middle ear and reproductive tract
- Also important during embryogenesis

Knowles MR et al. *AJRCCM* 2013.

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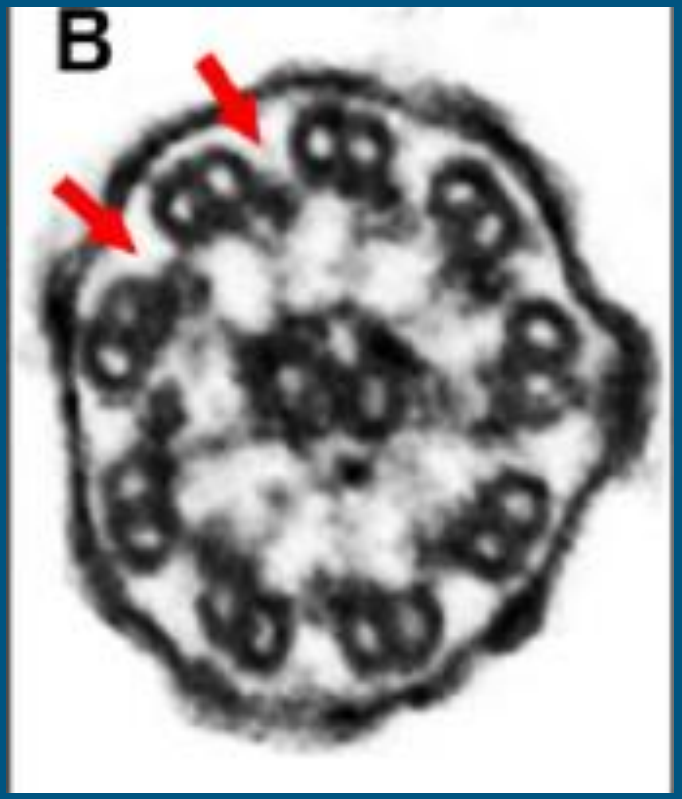

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Clinical symptoms

- Respiratory distress in neonatal period
  - 75-80% of patients with PCD have history of TTN, hypoxemia, and/or neonatal pneumonia
- Daily rhinitis and wet cough
- Chronic sinusitis and recurrent otitis media
- Progression to bronchiectasis
- Microbiome similar to that seen in cystic fibrosis
- Lung function decline not as marked as seen in CF

Non-pulmonary manifestations

- Situs inversus totalis
  - ~40-50% of patients with PCD have "Kartagener syndrome"
  - Heterotaxy, asplenia
- Infertility
- Pectus deformities

Diagnosis

- Can be difficult
- Three methods:
  - (1) Evaluation of ciliary ultrastructure via electron microscopy
    - Can be done with nasal epithelium or via bronchoscopy
    - Nasal epithelium MUST be healthy
    - Changes can be SECONDARY, and thus, false positives can be seen
    - Normal ultrastructure in about 30% of patients with PCD

Diagnosis

- Three methods:
  - (2) Nasal nitric oxide
    - Low in patients with PCD
    - Useful in patients >5 years of age
    - Only available at highly specialized centers
  - (3) Genetics
    - So far, PCD-causing mutations described in 32 genes
    - Accounts for 65-70% of patients with PCD
    - Two commercial labs available
    - Expensive

Management

- Much extrapolated from CF and non-CF bronchiectasis
- **Lung disease**: Airway clearance, antibiotic therapy, anti-inflammatory and mucolytic agents
- **Ear disease**: Placement of PE tubes controversial, as chronic otorrhea is a problem
- **Chronic sinusitis**: sinus rinses, nasal steroids, sinus surgery if needed
- Life expectancy is usually normal (compare with CF)

Findings to suggest other etiologies

History

- Onset early in infancy
- Neurologic dysfunction
- Wheezing with/after feeds
- Diarrhea
- Poor weight gain
- Stridor
- O2 requirement >1 week after onset

Exam and Other findings

- Clubbing
- Murmur
- Stridor
- Focal signs-- exam/CXR
- Crackles on exam
- Recurrent/prolonged cyanosis or hypoxemia
- Anemia
- Irreversible airflow obstruction

Fakhoury KF. *Up to date* 2012.

Approach to chronic wheeze or cough**

- First line
  - CXR
  - PFTs
- Second line
  - Trial of GER therapy
  - Sweat test
  - Infectious workup (Pertussis, TB, Mycoplasma)
- Based on H & P
  - GI studies (pH/impedance study, swallow function, Upper GI)
  - Bronchoscopy
  - Ciliary biopsy
  - Echo
  - Sinus CT
  - Chest CT
  - Immune workup

**when asthma therapies aren't working

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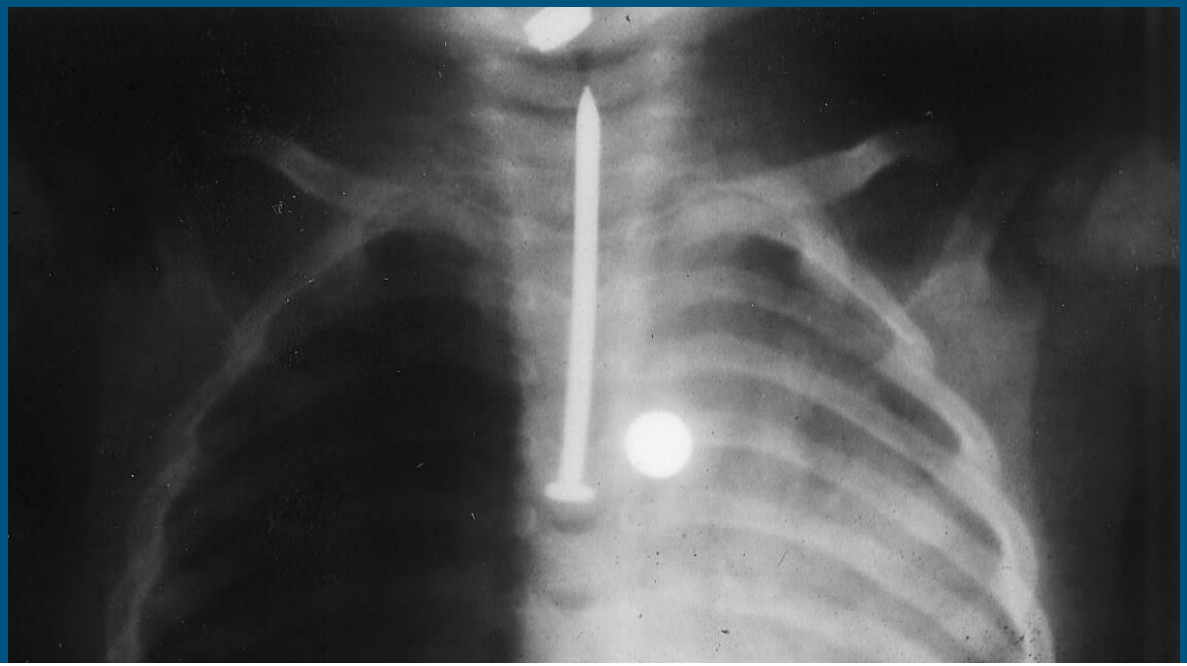

“Maybe we should wait for the radiologist for the official read…”

http://pedsinreview.aappublications.org

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Case #4

- 7 month old female with h/o GER seen at OSH for “sounding hoarse”
- Also with wheezing/barky cough along with difficulty breathing
- Given IV methylprednisolone, racemic epinephrine, albuterol, ceftriaxone, then transferred to CCMC for suspected croup
- On exam, noted to have significant stridor/wheezing, tachypnea, and sternal retractions

Case #4

- Due to significant increase in work of breathing, patient transferred to PICU
- Pediatric surgery consulted due to suspicion of foreign body
- Rigid bronchoscopy performed

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Foreign Body Aspiration

Foreign body aspiration

- Most common cause of accidental death in children < 1 year of age
- Accounts for approximately 7% of deaths in the US in children younger than 4 years of age
- 80% of aspiration events in children occur under 3 years of age
- Reasons include lack of molar teeth, exploration of objects, and poor swallowing coordination

Three phases of FB aspiration

- (1) Initial stage: choking episode followed by coughing, gagging, and airway obstruction
  - Choking event elicited in 80% of cases
- (2) Asymptomatic period
- (3) Symptoms of complications: cough, wheezing
  - Rate of serious complications, including bronchiectasis, pneumonia, is 2.5x higher when diagnosed more than 24 hours after event

Objects aspirated

Nature	Number	%
Organic FB	1751	66.7
Peanuts	1119	
Sunflower seed	144	
Almonds	60	
Ears of wheat	36	
Acorns	34	
Beans	31	
Bones	31	
Pistachio	27	
Others	269	
Inorganic FB	676	25.7
Metal	272	
Scarf pins	169	
Pins, nails, screws	50	
Others	53	
Plastic	230	
Pen caps	136	
Pearls	31	
Others	63	
Miscellaneous: stones, small light bulb, etc.	174	
Undefined	197	7.5

Boufersaoui A et al. 2013.

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Location of Aspirated foreign body

Table 4 Recent large pediatric series of inhaled foreign bodies confirmed by bronchoscopy

Author	Country	Period and type of study	Total no. of children	Age (years)	Sex (% male)	Distribution of inhaled foreign bodies
Baharloo et al. 1999 [1]	Belgium	1976–1996 Retrospective	84	Mean 2.6±1.3	60	Right bronchial tree 50% Left bronchial tree 45% Bilateral 5%
Van Looij et al. 2003 [20]	Netherlands	1990–2000 Retrospective	96	<3: 66%	68	Right bronchial 44% Left bronchial 51% Bilateral 1% Unknown 3%
				≥3: 34%		Right bronchial 81% Left bronchial 19%
Tokar et al. 2004 [19]*	Turkey	1994–2007 Retrospective	249	<3: 76%	55	Right bronchial 48% Left bronchial 32% Tracheal 14% Diffuse 6%
				>3: 24%		Right bronchial 25% Left bronchial 46% Tracheal 24% Diffuse 5%
Brkić and Umihanić 2007 [2]	Bosnia and Herzegovina	1954–2004 Retrospective	662	<3: 65%, >3: 35%	67	Right bronchial 53% Left bronchial 31% Tracheal 14% Peripheral 2%
Divisi et al. 2007 [10]	Italy	1986–2004 Retrospective	121	Mean 6 (range 4–8)	59	Right bronchial 74% Left bronchial 18% Tracheal 8%

Tahir N et al. *Eur J Pediatr* 2009.

Rigid bronchoscopy

- Therapeutic modality of choice
- Advantages:
  - Control of the airway
  - Visualization
  - Manipulation of object with wide variety of forceps
- Negative bronchoscopy rate 10-61%

Rigid Bronchoscopy--Complications

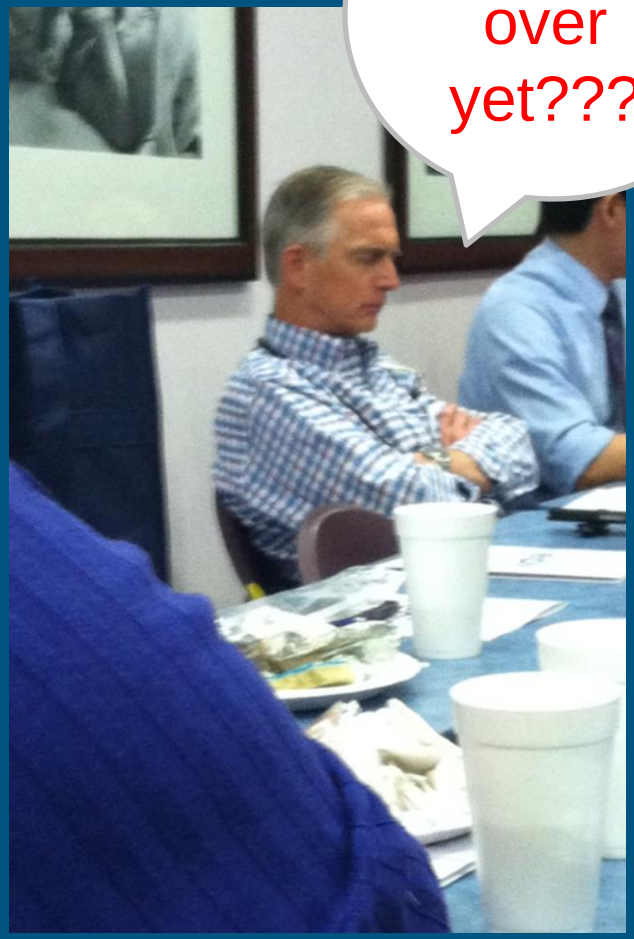
- Major iatrogenic complications <1%
- Include:
  - Laryngeal edema and/or bronchospasm
  - Pneumothorax/pneumomediastinum
  - Cardiac arrest
  - Hypoxic brain injury
  - Airway laceration

Flexible bronchoscopy

- Aids in diagnosis by visualization
- Ability to evaluate for distal FB
- Can be done with moderate sedation
- Less complication rate
- Has been more recently used for FB extraction (success rate 91-95%)

Flexible Bronch vs. Rigid Bronch

- Flexible—Less control of airway, also smaller forceps
- Rigid—higher complication rate
- American Thoracic Society recommendation: “Under most circumstances removal of foreign bodies and abnormal tissue should be carried out with the rigid bronchoscope”



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Diagnosis of FBA

Diagnostic considerations

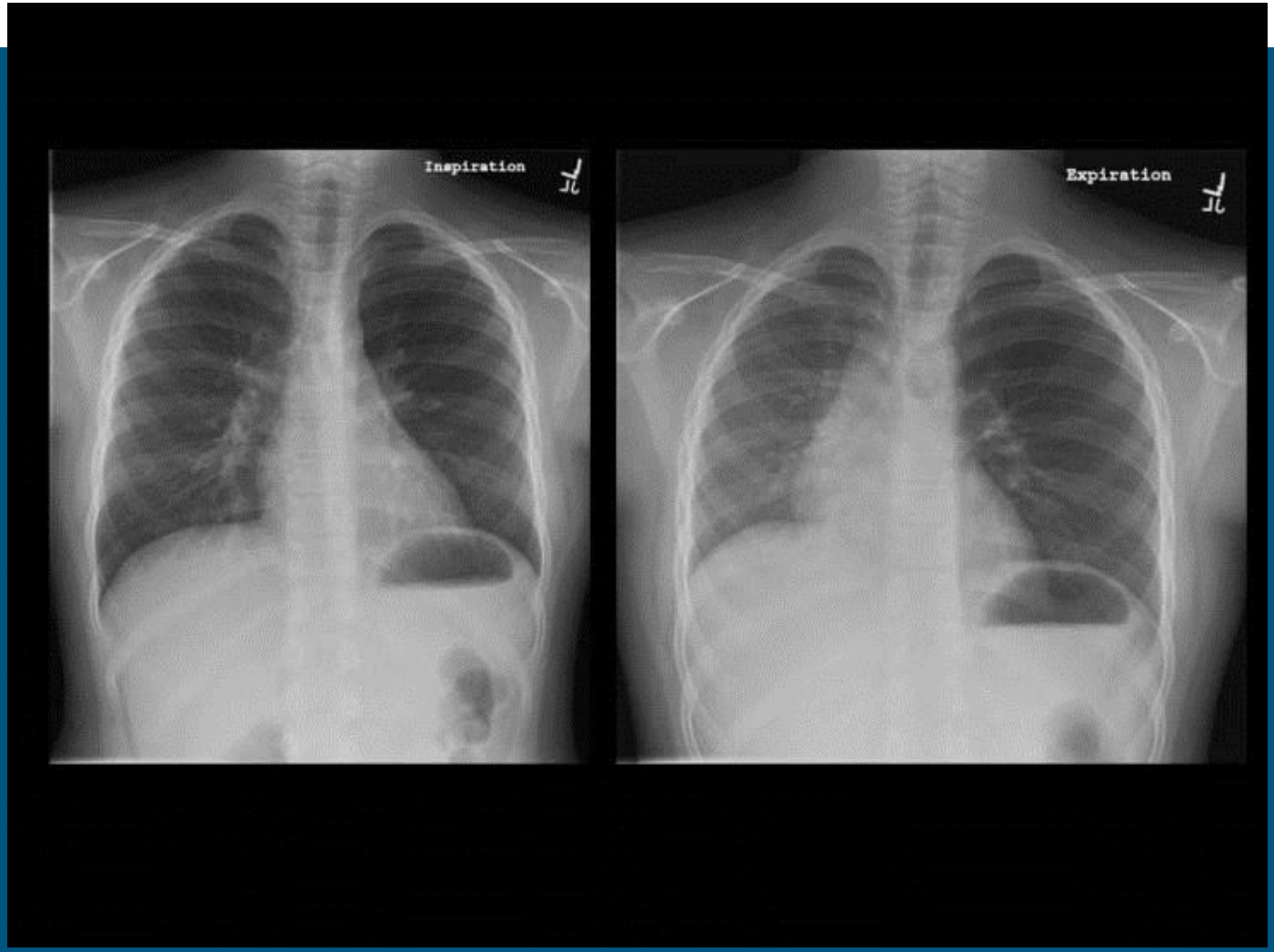
- Unfortunately, with regards to FBA, history and physical exam associated with low sensitivity/specificity
- Adjunctive diagnostic studies have been to shown to help reduce negative rigid bronchoscopy rate (from 18%→2% in one study)

Diagnostic studies

- Plain view CXR
- Special view CXRs
- Chest CT
- Flexible bronchoscopy

Chest X-ray findings

- Only approximately 10% of FB objects are radiopaque
- Indirect signs:
  - Obstructive emphysema/Unilateral hyperinflation (inspiratory/expiratory films)
  - Atelectasis
  - Mediastinal shift
- Airway fluoroscopy



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What about adjunctive chest radiographs (i.e., expiratory or decubitus films)?

- Retrospective study from Seattle Children's Hospital, 1997-2008
- 328 patients underwent standard view CXRs in addition to special view CXRs

Special view Radiographs

	Radiographs	Sensitivity	Specificity
Decubitus radiographs (n=194)	Standard 2-view	0.56	0.79
	Standard 2-view +decubitus	0.56	0.64
Expiratory radiographs (n=134)	Standard 2-view	0.33	0.70
	Standard 2-view +expiratory	0.62	0.72

Brown JC et al. *Ann Emerg Med* 2013.

Conclusions—special view radiographs

- Overall obtaining CXR added to likelihood of a foreign body if CXR suggestive (vs. history/PE alone)
- Findings demonstrated lack of clinical benefit with use of adding decubitus films
- Adding expiratory films showed an increase in true positives without adding false positives, but test accuracy was low

Diagnostic evaluations

Table 1 Sensitivity (Sens.) and specificity (Spec.) of clinical history (penetration syndrome), chest examination, chest radiograph and chest CT for the diagnosis of bronchial foreign body according to various studies.

	Penetration syndrome		Chest examination		Chest radiograph		Chest CT	
	Sens. (%)	Spec. (%)	Sens. (%)	Spec. (%)	Sens. (%)	Spec. (%)	Sens. (%)	Spec. (%)
Heyer CM, 2006	75.4	92.1	56.6	65.8	62.3	97.4		
Righini CA, 2007	88	10			88	70		
Ciftci AO, 2003	91	46	86	26	88	30		
Ayed AK, 2003	82	38	80	72	66	51		
Hong SJ, 2008							100	66.7
Cevizci N, 2008							100	86.8
Haliloglu M, 2003					85	68	100	100

Hitter A et al. *Eur Ann Otolaryngol* 2011.

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Diagnosis—Flexible Bronchoscopy

- Flexible bronchoscopy commonly used in diagnosing foreign body when diagnosis is in question
  - Close to 100% sensitive and specific

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Diagnosis—CT vs Flex Bronch

	Multidetector CT	Flexible Bronchoscopy
Advantages	Rapid No sedation needed Noninvasive High sensitivity	High sensitivity High specificity Distal aspiration (small objects)
Disadvantages	False positives due to mucus plugging Radiation	Invasive Requires sedation

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http://www.pedrad.org/associations/5364/ig/

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image gently when we care for kids! The ***image gently*** Campaign is an initiative of the Alliance for Radiation Safety in Pediatric Imaging. The campaign goal is to change practice by increasing awareness of the opportunities to promote radiation protection in the imaging of children.

Image Gently Impact

The image gently campaign launched 1/22/08. This is a snapshot of what has happened since:

21,393 medical professionals have taken the pledge

Upcoming Conferences Click here to view upcoming meetings around the world where Image Gently will be represented.

http://www.imagegently.org/

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Diagnosis FBA

Table 1 Comparison of clinical investigations, radiologic signs, and laboratory findings between children with recovery of a foreign body during bronchoscopy (FBA+, n = 122) and those without FBA (FBA−, n = 38)

	FBA+	FBA−	*P*	Odds ratio (95% CI)
Clinical investigation [n (%)]				
Auscultation	90 (74)	24 (63)	.223	1.6 (0.76-3.55)
Percussion	2 (2)	0 (0)	1.0	[a]
Decreased breath sounds	69 (57)	13 (34)	.025	2.5 (1.17-5.35)
Dyspnea	41 (34)	12 (32)	1.0	1.1 (0.5-2.4)
Choking crisis	92 (75)	3 (8)	<.001	35.8 (10.3-124.8)
Cough on admission	50 (41)	17 (45)	.710	0.86 (0.4-1.8)
Fever on admission	20 (16)	7 (18)	.806	0.87 (0.34-2.25)
Radiologic signs [n (%)]				
Infiltrate	23 (19)	6 (16)	.811	1.2 (0.46-3.31)
Atelectasis	10 (8)	1 (3)	.462	3.3 (0.4-26.7)
Bronchial wall thickening	8 (7)	2 (5)	1.0	1.3 (0.3-6.2)
Focal hyperinflation	76 (62)	1 (3)	<.001	61.1 (8.1-460.7)
Mediastinal shift	25 (21)	1 (3)	.01	9.5 (1.3-73.0)
Radiopaque foreign body	5 (4)	0 (0)	.34	[a]
Laboratory findings[b]				
CRP (mg/dL; mean ± SD)	2.5 ± 6.6	1.0 ± 1.3	.029	
CRP >0.6 mg/dL [n (%)]	17/101 (17)	4/37 (11)	.438	1.67 (0.56-4.33)
WBC count (1/μL; mean ± SD)	15,002 ± 6752	11,516 ± 5276	.005	
WBC count >10,000/μL	86/111 (78)	19/37 (51)	.004	3.3 (1.4-7.7)
pH (mean ± SD)	7.36 ± 0.071 (n = 56)	7.38 ± 0.05 (n = 18)	.335	
$PvCO_2$ (mm Hg; mean ± SD)	40.0 ± 10.7 (n = 56)	37.7 ± 4.3 (n = 18)	.409	

Heyer CM et al. *J Pediatr Surg* 2006.

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Diagnosis FBA

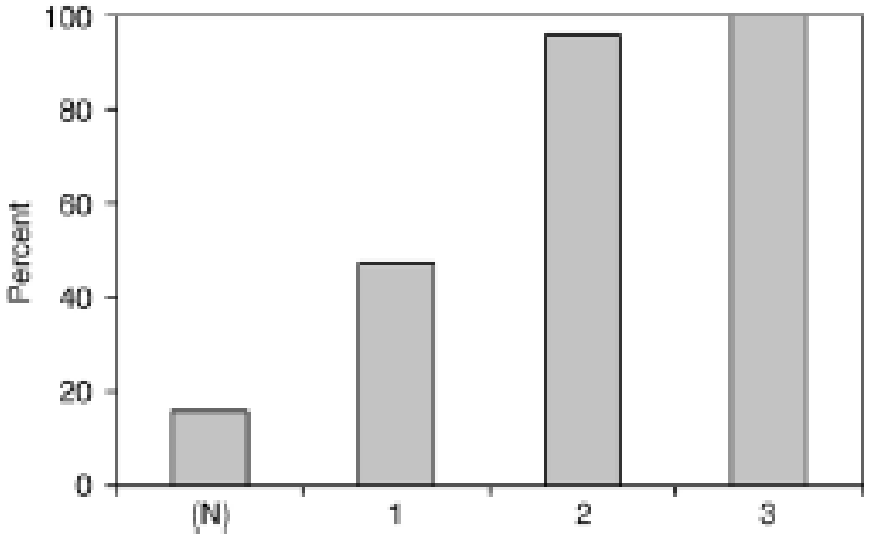

Fig. 3 Cumulative proportions of pFBA by number of risk factors (focal hyperinflation on chest radiograph, witnessed choking crisis, and/or WBC count >10,000/μL).

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Predictors of FBA

- Studies indicate poor correlation among event history, hospital presentation, and imaging to prove the absence of foreign body
- If index of suspicion exists, diagnostic bronchoscopy should be performed

Mortellaro VE et al. *J Pediatr Surg* 2013.

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http://www.healthychildren.org/English/health-issues/injuries-emergencies/Pages/Choking-Prevention.aspx

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Health Issues

Listen

Choking Prevention

Choking can be prevented. Food accounts for over 50% of choking episodes. Be alert for small objects that can cause choking, such as coins, buttons, and small toys. Check under furniture and between cushions for small items that children could find and put in their mouths. Toys are designed to be used by children within a certain age range. Age guidelines take into account the safety of a toy based on any possible choking hazard. Don't let young children play with toys designed for older children. Latex balloons are also a choking hazard. If a child bites a balloon and takes a breath, he could suck it into his airway.

Choking Hazard Items

Keep items that are choking hazards away from babies and young children. These include:

- Coins
- Buttons
- Toys with small parts
- Toys that can fit entirely in a child's mouth
- Small balls, marbles
- Balloons
- Small hair bows, barrettes, rubber bands
- Pen or marker caps
- **Small button-type batteries**
- Refrigerator **magnets**
- Pieces of dog food

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Unknown Zone (Mixed) | Protected Mode: O

Summary

- Not all that wheezes IS asthma, and with a good history/physical exam, other entities can be differentiated and managed
- Foreign body aspiration is a common life-threatening emergency; diagnosis can be difficult, esp with lack of significant exam/diagnostic findings
- If an index of suspicion exists, careful airway evaluation MUST be considered

Findings to suggest other etiologies

History

- Onset early in infancy
- Neurologic dysfunction
- Wheezing with/after feeds
- Diarrhea
- Poor weight gain
- Stridor
- O2 requirement >1 week after onset

Exam and Other findings

- Clubbing
- Murmur
- Stridor
- Focal signs-- exam/CXR
- Crackles on exam
- Recurrent/prolonged cyanosis or hypoxemia
- Anemia
- Irreversible airflow obstruction

Fakhoury KF. *Up to date* 2012.

Questions?

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