Don’t bet on asthma…Not all that wheezes is Asthma

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Mercy Medical Center St. Louis, MO
Friday April 20th 2018

Lecture Objectives

- Asthma is the most common respiratory disorder seen by pediatric health care providers but NOT all that wheezes is asthma.
  - Review three interesting cases in 2017 from a local Pediatric Pulmonary Provider
  - To Explore & Expand your Differential Diagnosis (including a detailed workup) within these three pediatric wheezing or respiratory cases

Conflict of Interest Declaration

I declare that I do NOT have any affiliation with or financial relationship/interest in a commercial organization that could pose a conflict of interest with the educational content of this program.

MSRC

MISSOURI SOCIETY FOR RESPIRATORY CARE

Case #1

- 21 month White Male with a history of viral induced wheezing. First visit Jan 2017
- FH of asthma (mom as a child)
- Family lives in Rolla, MO (outreach program)
- NO admits
- Will respond to (1) SABA or Albuterol (2) OCS or Orapred (3) ABX
- H/O RSV. NO admits. Frequent sick visits by the PMD

Case #1 (continue)

- H/O ICS therapy (Pulmicort) with +/- adherence
- Family lives on a Farm
  - Two cats in the home
  - + daycare
- Wheezing free (my first visit).
- D/W mom about Flovent HFA (daily) for ease of use

Case #1 (continue)

- Next 2-3 months multiple “sick” visit for wheezing
- Improved adherence to ICS therapy (Flovent 110 HFA)
- Wheezing ONLY when sick
- Improved with therapy however needing ABX / OCS to improve his clinical course
- Seemed much worse than a typical asthma pt (however in the heart of Winter + daycare)

Case #1 (continue)

- Seen (my clinic) for several sick visits
- Seen (Rolla, MO) for a sick visit too
- Will respond (less wheezing) to a DuoNEB in the office
- We ADDed LTRA (Singulair)
- Allergy and Immune screening (negative)
- NBS (newborn screening) was negative
- CGD (given FH) was negative
- CXR (Rolla, MO) was abnormal with RLL PNA and subtle SubQ air in his neck. Likely a past airleak concern?

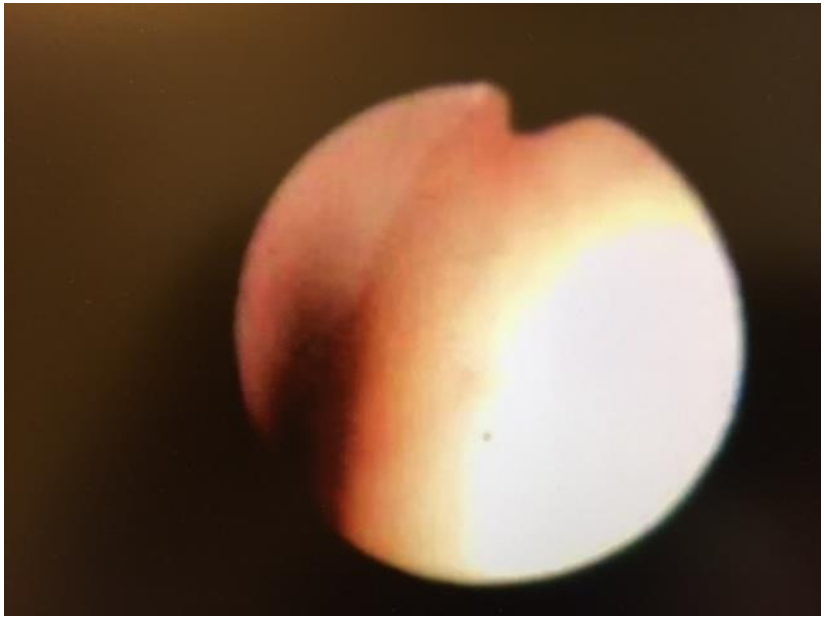
Case #1 (summary slide)

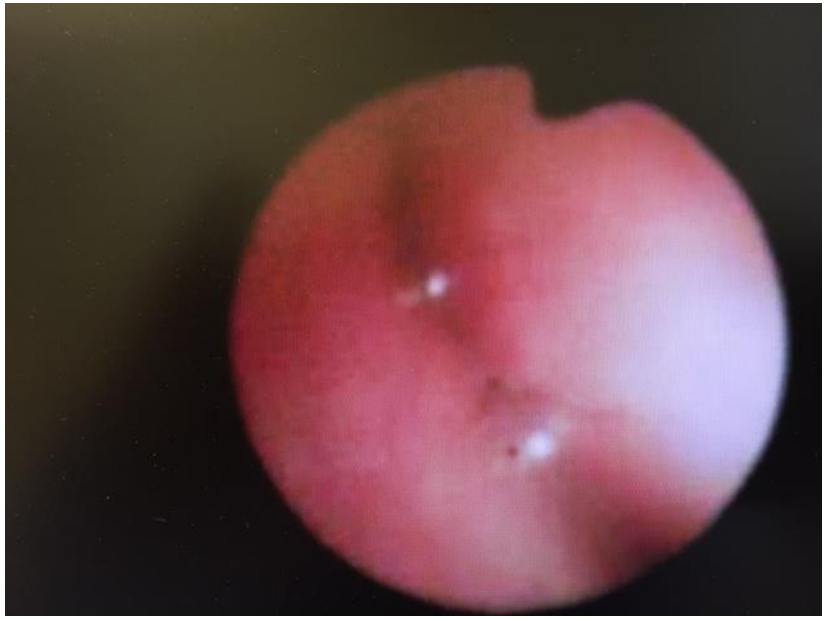
- In summary = 2 y/o child with recurrent coughing and wheezing
- Does respond to therapy
- Wheezing (can) resolve with time and treatment
- However seems MUCH sicker than your average wheezing child. Now an abnormal CXR. Screening evaluation was unremarkable to date.
- Next step = CT vs Bronchoscopy

Don’t bet on Asthma….

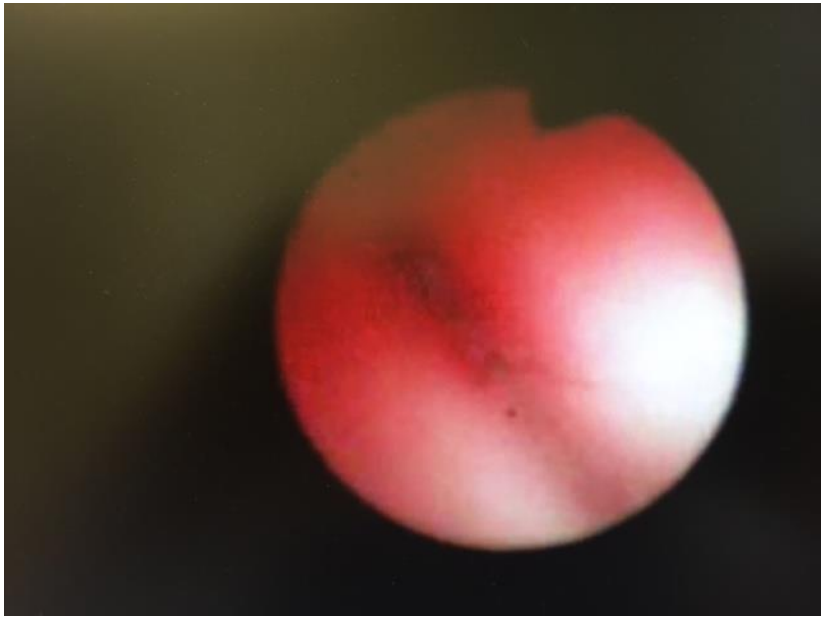
- Expand our DDx on a 2 y/o wheezer
  - CF
  - PCD
  - Fb
  - Atypical Process or Pathogen
  - Fixed mass / lesion
  - other

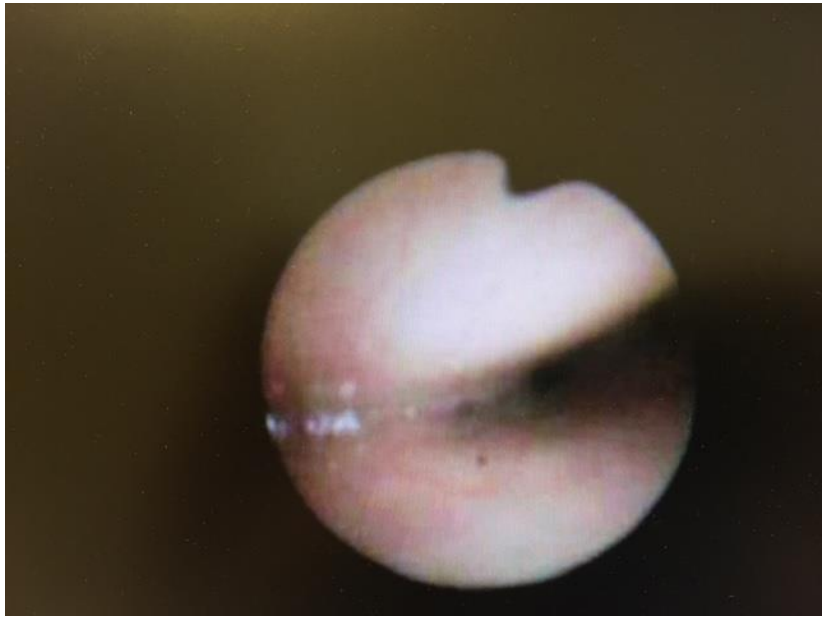
Bronchoscopy (2017)



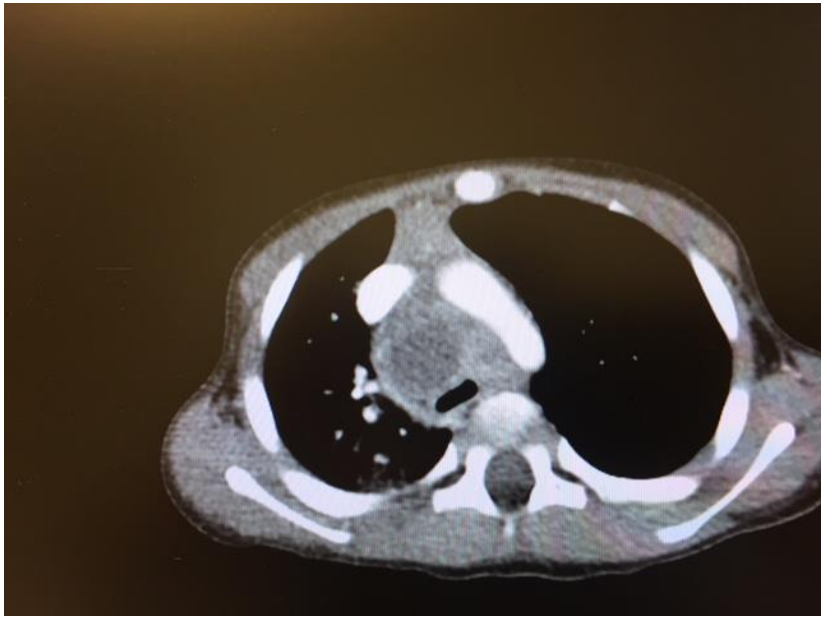


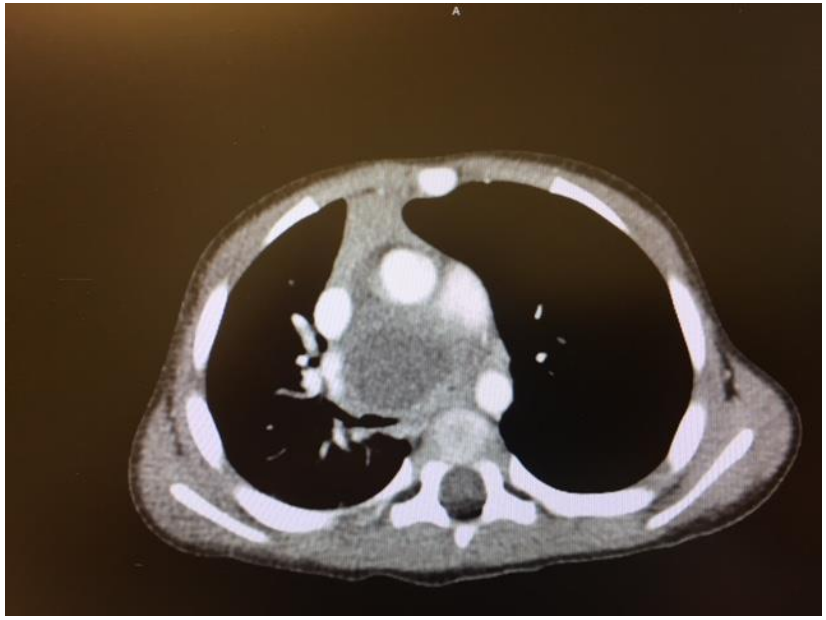
Bronchoscopy (2017)



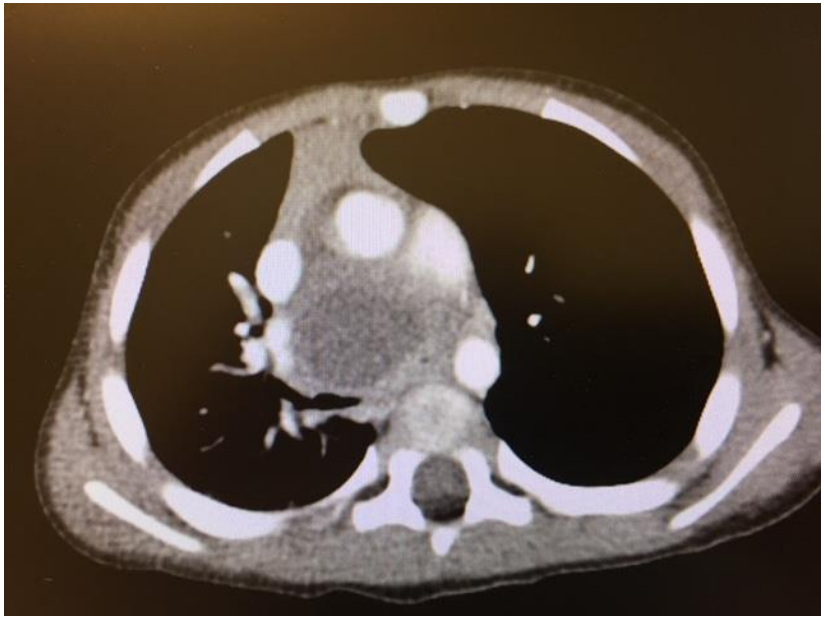


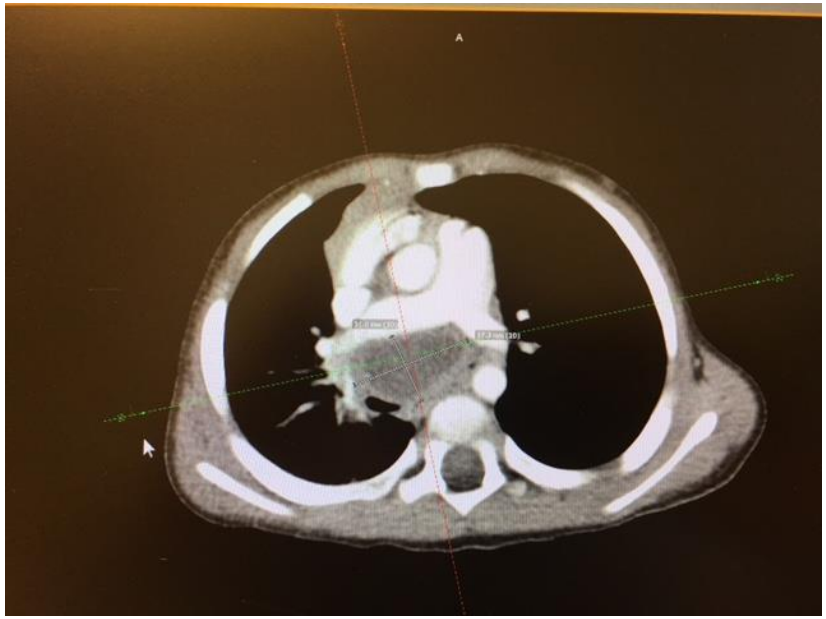
CT Chest (2017)





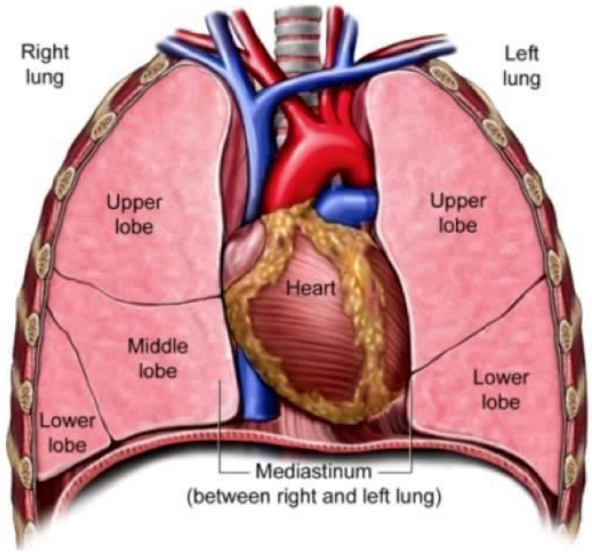
3.7 X 2.2 X 6cm mass

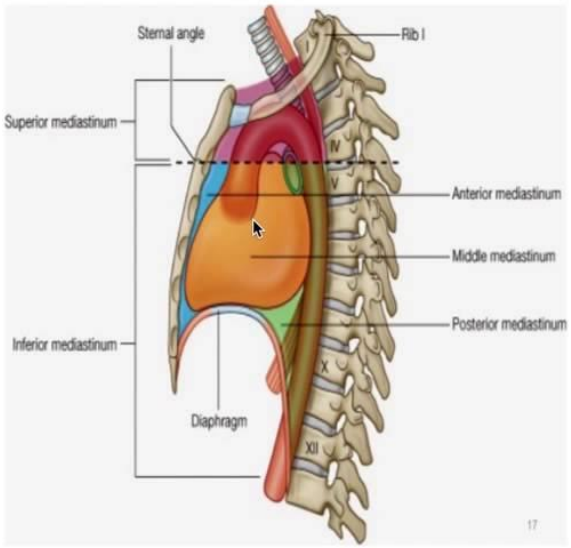




What is the Mediastinum?

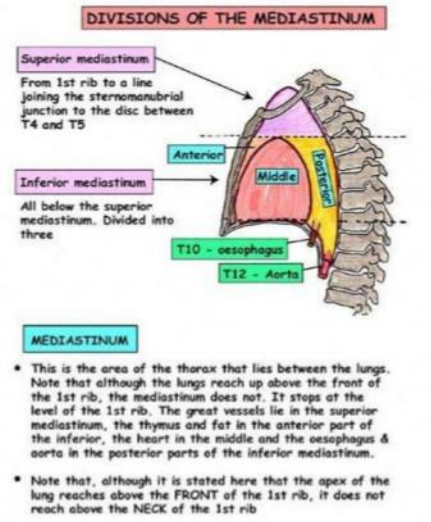
Divisions and Content





Focus on the Middle Mediastinum

Approach to mediastinal masses



Middle Mediastinum

Contents:

Heart enclosed in pericardium

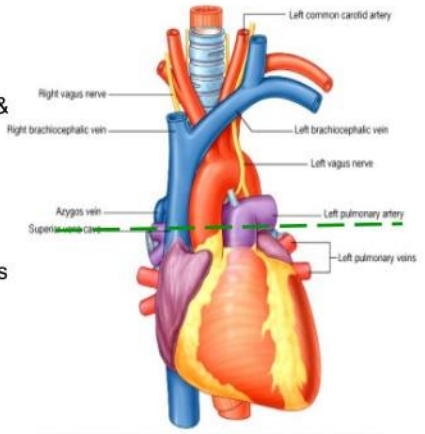
Arteries: Ascending Aorta, Pulmonary trunk with its Lt & Rt branches

Veins: SVC, Termination of Azygos, Pulmonary veins

Nerves: Phrenic, Deep cardiac plexus

Bifurcation of Trachea with two principal bronchi

Tracheobronchial lymph nodes



DDX for a Middle Mediastinum Mass

- Bronchogenic Cyst / Foregut Duplication Cyst
- Neurogenic Tumor
- Abscess or Adenopathy
- Fibrosing Mediastinitis or inflammatory process
- Infectious = Histo / Tb / Atypical Tb
- Teratoma

Labs / medical workup

- Blood work
  - Nl Uric Acid
  - Nl LDH
  - Nl CBC with diff
  - Nl CRP
  - Negative EBV, Histo, and Quantiferon Tb Gold
- Bronchoscopy labs
  - + Rhinovirus / Enterovirus
  - + S. Pneumonia (r) to Zmax
  - Negative Fungal Cx
  - Negative AFB Cx

Teratoma

- Teratoma = tumor often with normal tissue (or organs) with one or more germ layers
- Tumor has normal tissue often NOT typical for that area of the body (ex brain, liver, gut, etc)
- Can be benign
- This was removed and pathology confirmed the dx

- Tumor = benign pathologically but not anatomically with (1) compression of the LMB (2) mass effect on the airway and L lung (hyperexpanded) (3) likely some dependent collapse of the right base

Case #2

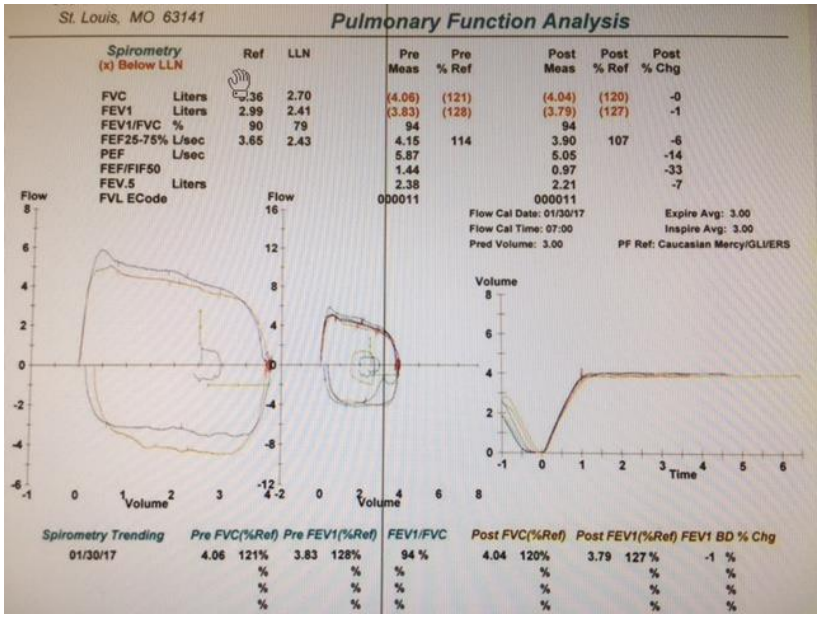
- First (only) visit in Jan 2017
- 14 y/o with a chronic cough
- NO wheezing only a persistent cough (for years)
- Cough daytime >> nighttime and will have coughing fits
- Ran case by peds pulmonary (downtown hospital) and sounded like a habit cough
- Normal exam. NO wheezing. NO distress
- Cough does resolve (while sleeping)

Don’t bet on Asthma….

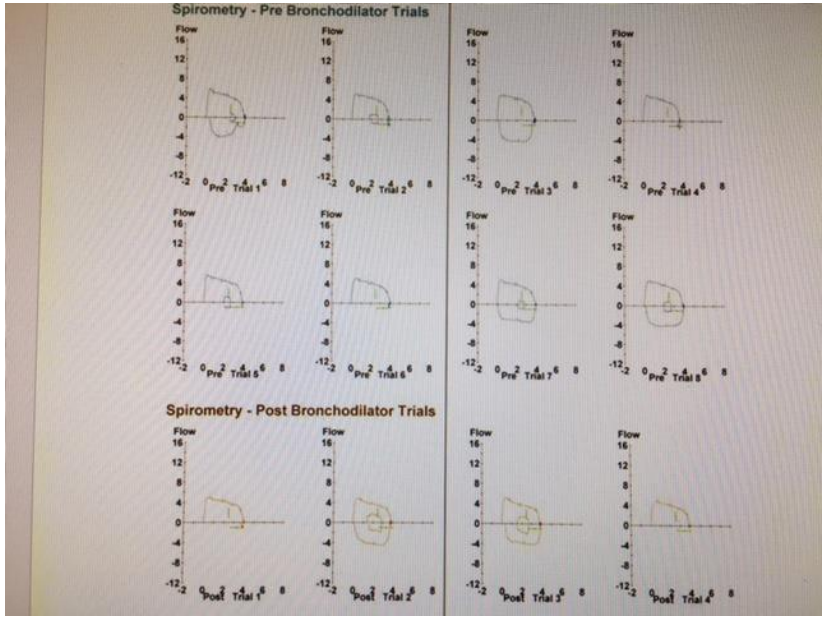
- 14 y/o with a chronic cough
- DDx to include
  - Asthma (cough variant)
  - GERD
  - Habit or irritant cough
  - Tic
  - Fb
  - Atypical Process (ex B. Pertussis)
  - other

Case #2

PFTs

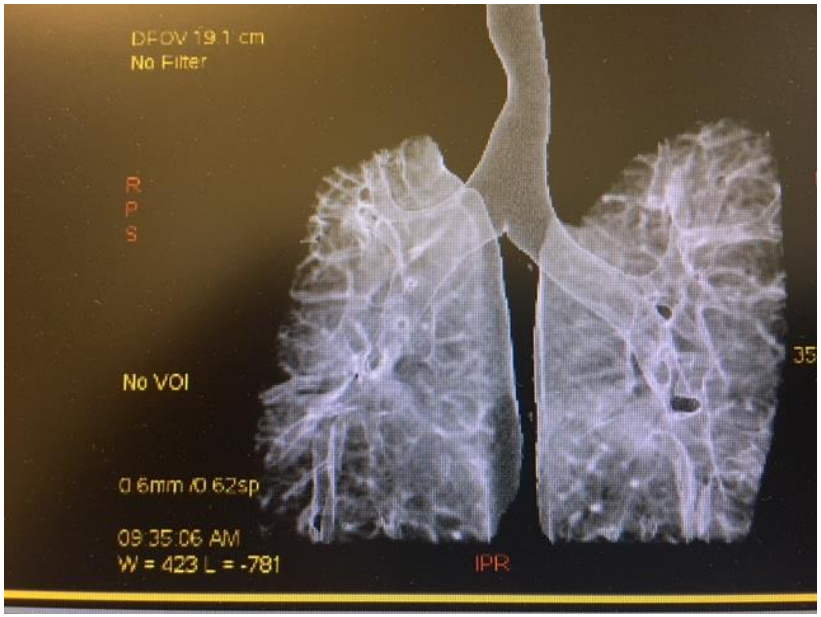


Note Shape of the PFTs

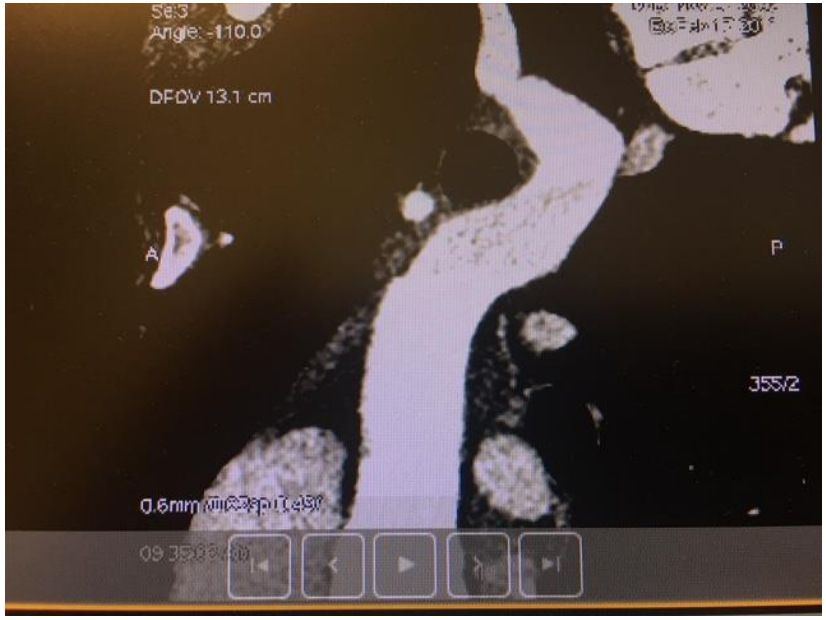


Right Sided Aortic Arch with a Vascular Ring

CT #1

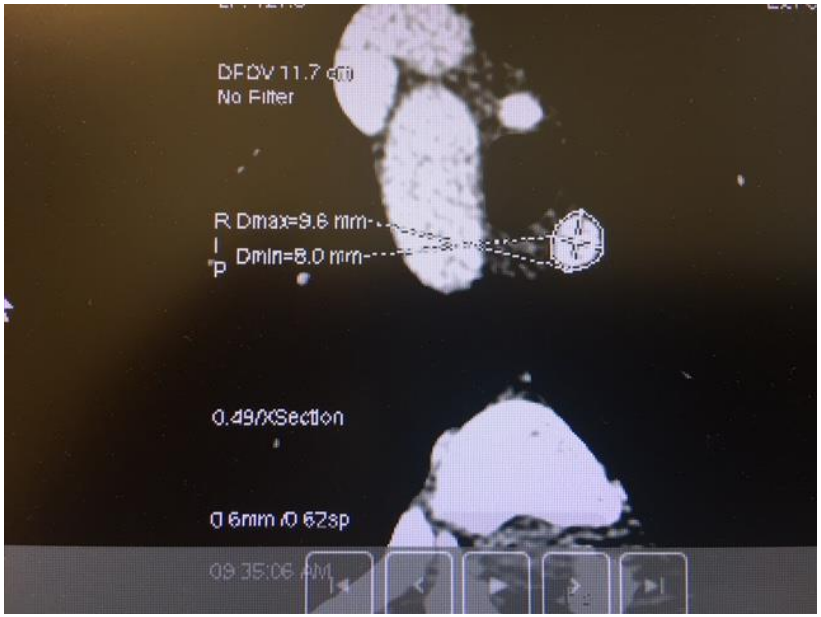


CT #2

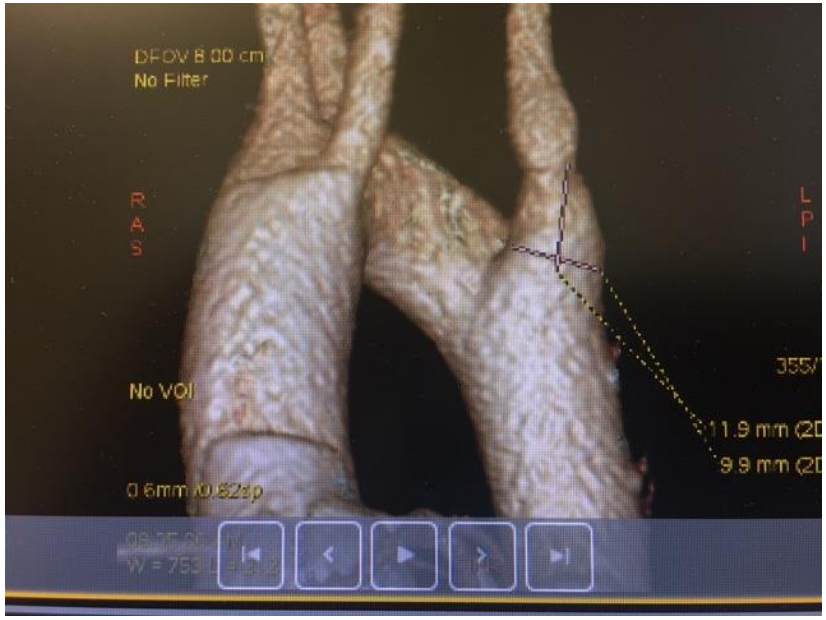


Right Sided Aortic Arch with a Vascular Ring

CT #3



CT #4



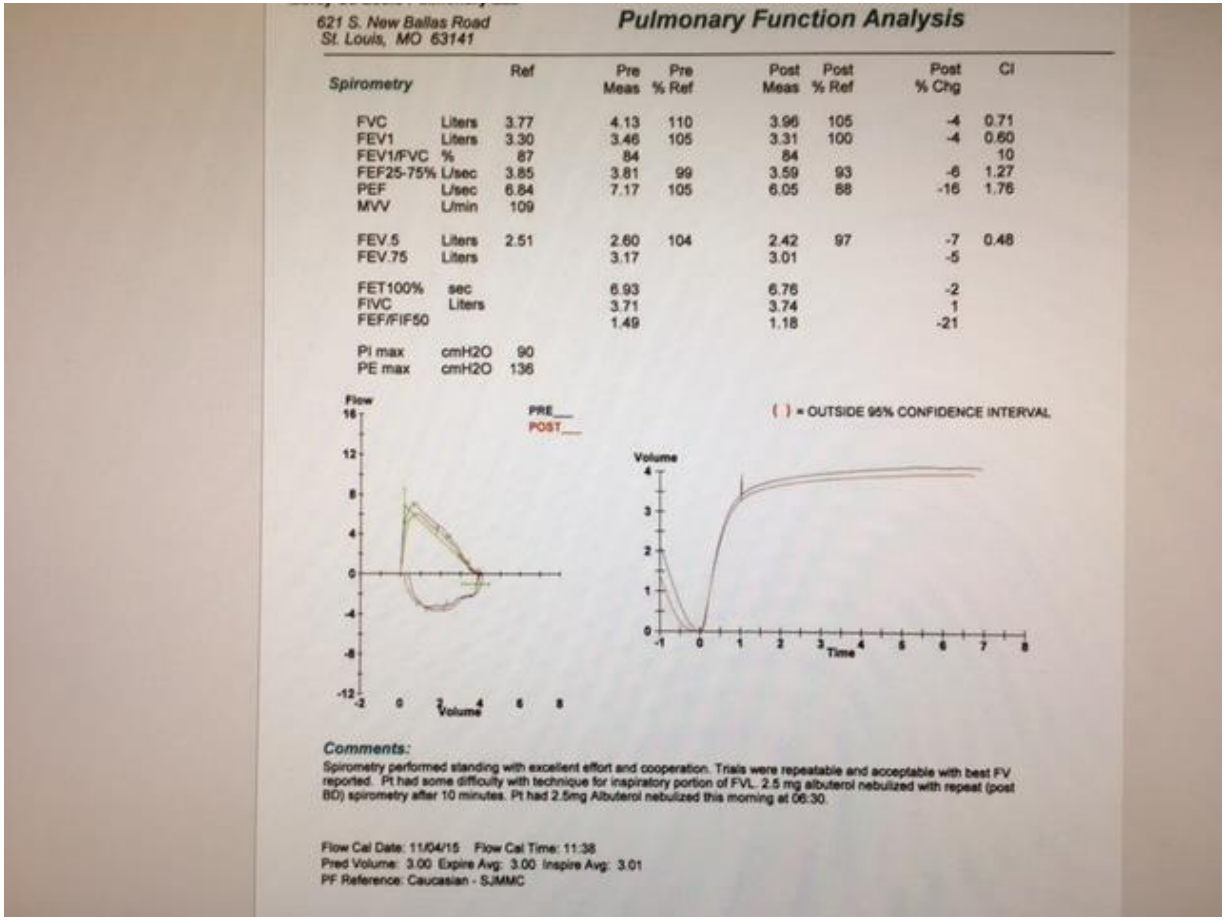
Case #3

- 16 y/o White Female with a history of asthma and atopy
- NO admits for asthma. NO ED visits
- H/O sinus surgery (with possible PA or Pseudomonas). Workup with ENT and allergy & immunology showed atopy to trees, molds, dog (no dog in the home). Immune workup was negative. NO sweat test.
- Cough + sputum >> wheezing
- Will respond to therapy

Case #3 (continue)

- Exam (first visit) did show wheezing and crackles
- HELD on PFTs (was wheezing)
- Wt 59kg
- No polyps, no clubbing
- Current Medications: Advair, Zyrtec, Singulair, and Flonase. Persistent sputum with therapy
- Placed on (1) Zmax (2) OCS (taper)
- Asked to follow up in two weeks for repeat exam and PFTs

PFT on our second visit



621 S. New Ballas Road
St. Louis, MO 63141

Pulmonary Function Analysis

Spirometry		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg	CI
FVC	Liters	3.77	4.13	110	3.96	105	-4	0.71
FEV1	Liters	3.30	3.46	105	3.31	100	-4	0.60
FEV1/FVC	%	87	84		84			10
FEF25-75%	L/sec	3.85	3.81	99	3.59	93	-6	1.27
PEF	L/sec	6.84	7.17	105	6.05	88	-16	1.76
MVV	L/min	109						
FEV.5	Liters	2.51	2.60	104	2.42	97	-7	0.48
FEV.75	Liters		3.17		3.01		-5	
FET100%	sec		6.93		6.76		-2	
FIVC	Liters		3.71		3.74		1	
FEF/FIF50			1.49		1.18		-21	
PI max	cmH2O	90						
PE max	cmH2O	136						

PRE
POST

( ) = OUTSIDE 95% CONFIDENCE INTERVAL

Flow
Volume
Volume
Time

Comments:

Spirometry performed standing with excellent effort and cooperation. Trials were repeatable and acceptable with best FV reported. Pt had some difficulty with technique for inspiratory portion of FVL. 2.5 mg albuterol nebulized with repeat (post BD) spirometry after 10 minutes. Pt had 2.5mg Albuterol nebulized this morning at 06:30.

Flow Cal Date: 11/04/15 Flow Cal Time: 11:38
Pred Volume: 3.00 Expire Avg: 3.00 Inspire Avg: 3.01
PF Reference: Caucasian - SJMMC

Case #3 (continue)

- Interesting pt
- Symptoms more coughing + sputum >> wheezing
- H/O PA?
- H/O sinus surgery
- Sputum?
- But does respond to asthma therapy

- Next evaluation = sputum (clinic)

Don’t bet on Asthma…

- 16 y/o with normal weight and normal PFTs with chronic sputum. What is your DDx
  - Asthma
  - Chronic Bronchitis
  - CF
  - PCD
  - Immune Dysfunction
  - Past lung injury or persistent bronchiectasis
  - other

Case #3 (CF diagnosis)

- Sputum grew PA (Pseudomonas) and Serratia
  - Sweat testing Sweat Cl 85/86
  - Genetic showed TWO CF related mutations or DF508 and G85E
  - Bronchoscopy (again) grew PA
  - CT chest showed bronchiectasis
  - Younger sib (too) dx with CF
  - Evaluation of PI (Pancreatic insufficiency status)
    - Fecal Elastase < 50 (PI)
    - Vit D Low

What is CF?

- CF is an autosomal recessive disease: genetic mutation in the Cystic Fibrosis Transmembrane conductance Regulator (CFTR) located on chromosome 7 resulting in abnormal Na/Cl transport resulting clinically as a multisystem disease of exocrine gland dysfunction.

Why is CF important?

- 2nd most common life-shortening childhood onset inherited disorder (#1 is SCD)
- Effects all races
- Over 30,000 affected in the US
- Costs: personal/medical/societal
- Average life span around 40+ years

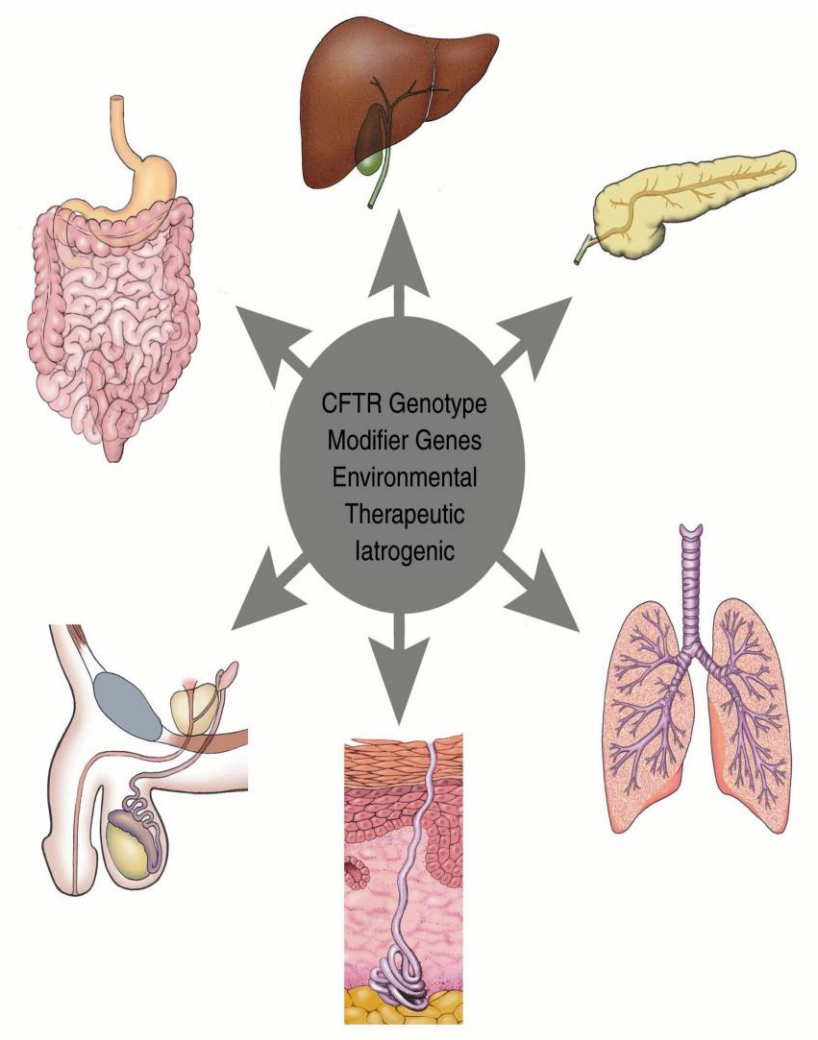
Cystic Fibrosis: Epidemiology

- Over 1800+ mutations identified
- ΔF508 66% all mutations

Race/ethnicity	Incidence
Caucasian	1:2,500
African American	1:15,000
Hispanic	1:8,000
Asian American	1:10,000
Native American	1:40,000

Cystic Fibrosis: Clinical Features

CF Involved Organs



CF Presenting Factors/symptoms

- Chronic Respiratory Symptoms 51%
- Failure to thrive/malnutrition 43%
- Steatorrhea 35%
- Meconium ileus 19%
- Family History 20%
- Electrolytes/Dehydration 5%
- Rectal prolapse 3%
- Nasal polyps/sinusitis 2%
- Hepatobiliary disease 1%

Presenting Symptoms by Age

Infancy:	Childhood:	Adol/Adulthood:
Meconium ileus	Pulmonary infections with CF organisms	Chronic bronchitis
Obstructive jaundice	Malnutrition	Pansinusitis
Failure to thrive	Heat prostration	Hemoptysis
Edema, anemia, hypoproteinemia	Atypical Asthma	Abdominal pain
Recurrent bronchiolitis	Nasal polyps	Pancreatitis
		Infertility

CF Diagnostic Criteria

One or more characteristic phenotypic features

--or a history of CF in a sibling

--or a positive newborn screening result

AND

Increased sweat chloride concentration by pilocarpine iontophoresis on two or more occasions

--or two documented CF-related genetic mutations

-- FYI: *in vivo* evaluations such as nasal epithelial potential difference are sometimes used in Atypical CF.

The Missouri State Public Health Lab (Newborn Screening) will conduct second tier te
the following CFTR mutations and 4 variants for Cystic Fibrosis (CF) when an elevate
detected in the primary screening test:

deltaF508(dF508)*	1717-1G>A*	W1282X*	2307insA
deltaI507*	R560T*	1078delT	Y1092X
G542X*	R553X*	394delTT	M1101K
G85E*	G551D*	Y122X	S1255X
R117H*	1898+1G>A*	R347H	3876delA
621+1G>T*	2184delA*	V520F	3905insT
711+1G>T*	2789+5G>A*	A559T	*5T/7T/9T*
N1303K*	3120+1G>A*	S549N	*F508C*
R334W *	R1162X*	S549R	*I507V*
R347P*	3659delC*	1898+5G>T	*I506V*
A455E*	3849+10kbC>T*	2183AA>G	

This panel includes 39 of the most common CF mutations (including the 23 mutations
recommended by the American College of Medical Genetics*).

Frequency of CFTR mutations

*US CFF Data n=28,455 (17,853 genotyped)

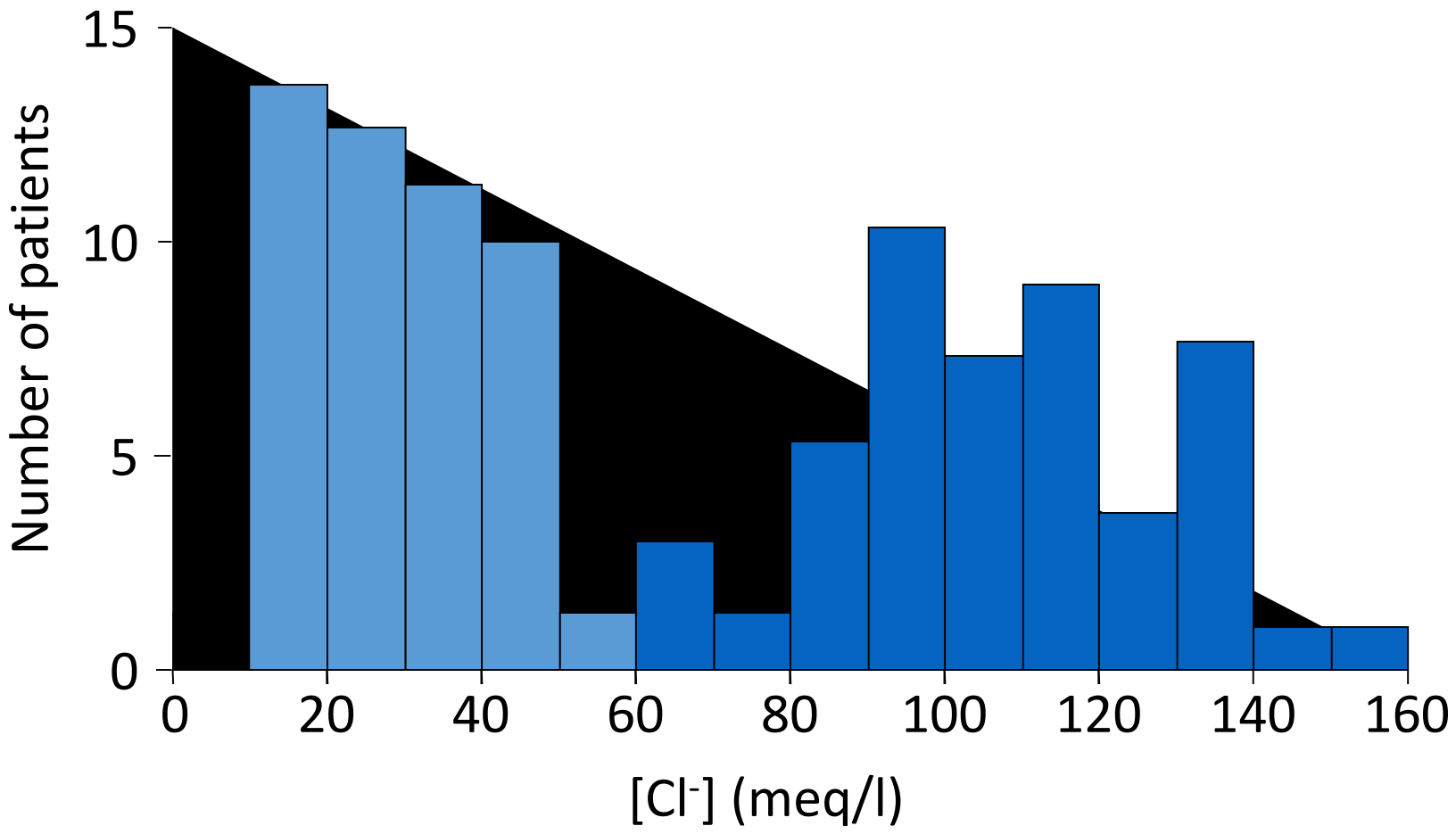
Mutations	Freq (%)
Delta F508	***69.4%***
Unknown	15.7
G542X	2.3
G551D	2.2
Delta I507	1.6
W1282X	1.4
N1303K	1.2
R553X	0.9
621+1G to T	0.8
R117H	0.7
3849 + 10kb C to T	0.7
1717 1G to A	0.5
R347P	0.3

Mutations	Freq (%)
2789 5G to A	0.3%
R1162X	0.3
G85E	**0.3**
R560T	0.2
R334W	0.2
3659DC	0.2
A455E	0.1
711 1G to T	0.1
1898 +1G to A	0.1
2148DA	0.1
S549N	0.1
1078DT	0.3

* McKone EF and et al. 2003. *Lancet*: 361:9370. 1671-76.

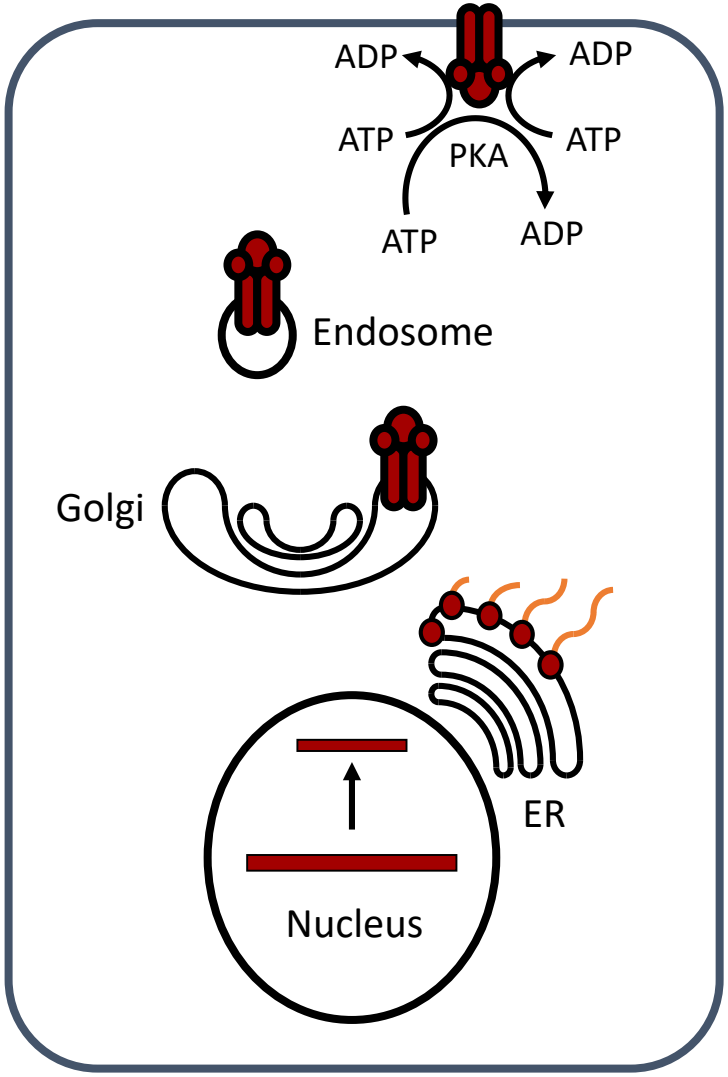
Cystic Fibrosis: Pilocarpine Iontophoresis

Di Sant'Agnese, PA., *et. al*. 1953. *Pediatrics*. **12**: 549-563.



Why such a broad clinical spectrum?
Cystic fibrosis: molecular mechanisms of CFTR dysfunction

Class 3: regulatory mutants that fail to respond normally to activation signals, e.g., G551D



Class 4: mutants that have altered channel properties, e.g., R117H

Class 2: CFTR protein degradation in the endoplasmic reticulum, e.g., ΔF508 and G85E

Class 1: premature termination of CFTR mRNA translation, e.g., W1282X

Class 5: Decreased normal CFTR protein expression, e.g., 2789 + 5 G-to-A


Project
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INTERDISCIPLINARY PANEL INCLUDES PEDIATRICS, ALLERGY, ENVIRONMENTAL ASSESSMENT, PULMONARY, NURSING AND ASTHMA EDUCATION SPECIALISTS

WHY IMPACT ASTHMA ECHO?

Asthma is a major cause of morbidity and disability among children, with 29,616 emergency room (ER) visits and 6,525 hospitalizations across Missouri in 2013 (asthma as principal diagnosis), resulting in $103.2 million in hospital charges. More than 30 percent of preschoolers and nearly 49 percent of school-age children with asthma missed one or more days of day care or school because of asthma. Connecting with the Impact Asthma ECHO team supports better quality care, lower asthma risk and reduced health care costs.

WHAT DOES IMPACT ASTHMA ECHO OFFER?

- Free CME for health care professionals*
- Collaboration, support and ongoing learning with experts and peers
- Patients get better care in home community

Missouri Telehealth Network
University of Missouri Health

HOW DOES IT WORK?

- Join an online lunch hour video conference
- Discuss and share:
  - clinical case presentations
  - a brief educational presentation by an expert in asthma

**See website for CME information*

TOPICS FOR CASE-BASED LEARNING AND DISCUSSION INCLUDE:

- Applying EPR3 guidelines
- Asthma risk panel reports
- Assessing and improving inhalation technique
- Assessing and managing environmental triggers
- Assessing "exercise-induced asthma"
- Engaging community partners
- Environmental assessments
- Managing asthma exacerbations
- Measuring and interpreting airflow
- Reimbursable preventive services
- Using validated impairment scales

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MEET OUR TEAM

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Asthma Champion (NEEF)
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Lead Trainer, Missouri School Asthma Services

John Kraemer, PhD
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Southeast Missouri State University

Paul Foreman, PhD
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Sherri Homan, FNP, PhD
Public Health Epidemiologist
Missouri Department of Health and Senior Services

Dave Zellmer, Health Literacy Expert, University of Missouri.

Claudia Preuschoff, MD, FAAP, Missouri Asthma Champion, American Academy of Pediatrics

Melissa Penkalski, DNP, PNP, AE-C
Clinical Assistant Professor, Nursing
Missouri State University

John Spivey, MD
Pediatric Pulmonologist
Mercy Hospital St. Louis

We do see Asthma and a lot more!!

Thank You!!

pulmonary disorders

Pediatric Pulmonary and Sleep Medicine

St. John's Mercy Children's Hospital
621 S. New Ballas Rd., Ste. 382-A, St. Louis, Mo. 63141
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At the Pediatric Pulmonary and Sleep Medicine clinic, Dr. Choo-Kang and Dr. Spivey offer a comprehensive approach to the diagnosis and management of a variety of acute and chronic pulmonary disorders. Dr. Choo-Kang received his medical degree from SUNY Health Science Center in Syracuse, N.Y. He completed his pediatric residency and served as chief resident at the University of Maryland Hospital for Children. Dr. Choo-Kang then completed his pediatric pulmonary medicine fellowship at the Johns Hopkins Children's Center before relocating to St. Louis in 2001. Born and raised in St. Louis, Dr. Spivey received his medical degree from Saint Louis University. He did his pediatric residency and also served as chief resident at the University of Missouri-Columbia Hospitals and Clinics. Dr. Spivey completed his postdoctoral training in pediatric pulmonary medicine at Washington University School of Medicine.

After all of their medical training, Dr. Choo-Kang and Dr. Spivey are now regarded as two of St. Louis' top pediatric doctors. They strive to achieve an optimal quality of life for all their patients. Whether they're treating a newborn baby with premature lung disease, a patient with cystic fibrosis, a school-age child with allergic asthma, an adolescent with excessive daytime sleepiness, or a college athlete experiencing decreased exercise tolerance, their philosophy is the same: "We treat the entire patient, not just the disease." Both physicians, triple-board certified in general pediatrics, pediatric pulmonary medicine, and sleep medicine, have at their disposal state-of-the-art lung-function testing facilities, an on-campus pediatric sleep laboratory, in-office allergy testing and fiber-optic airway evaluation. Close working relationships with many other pediatric disciplines, such as radiology and speech therapy, allow the physicians to offer comprehensive evaluation and treatment in an expedited fashion.

From left: Lee Robert Choo-Kang, MD and John F. Spivey, MD