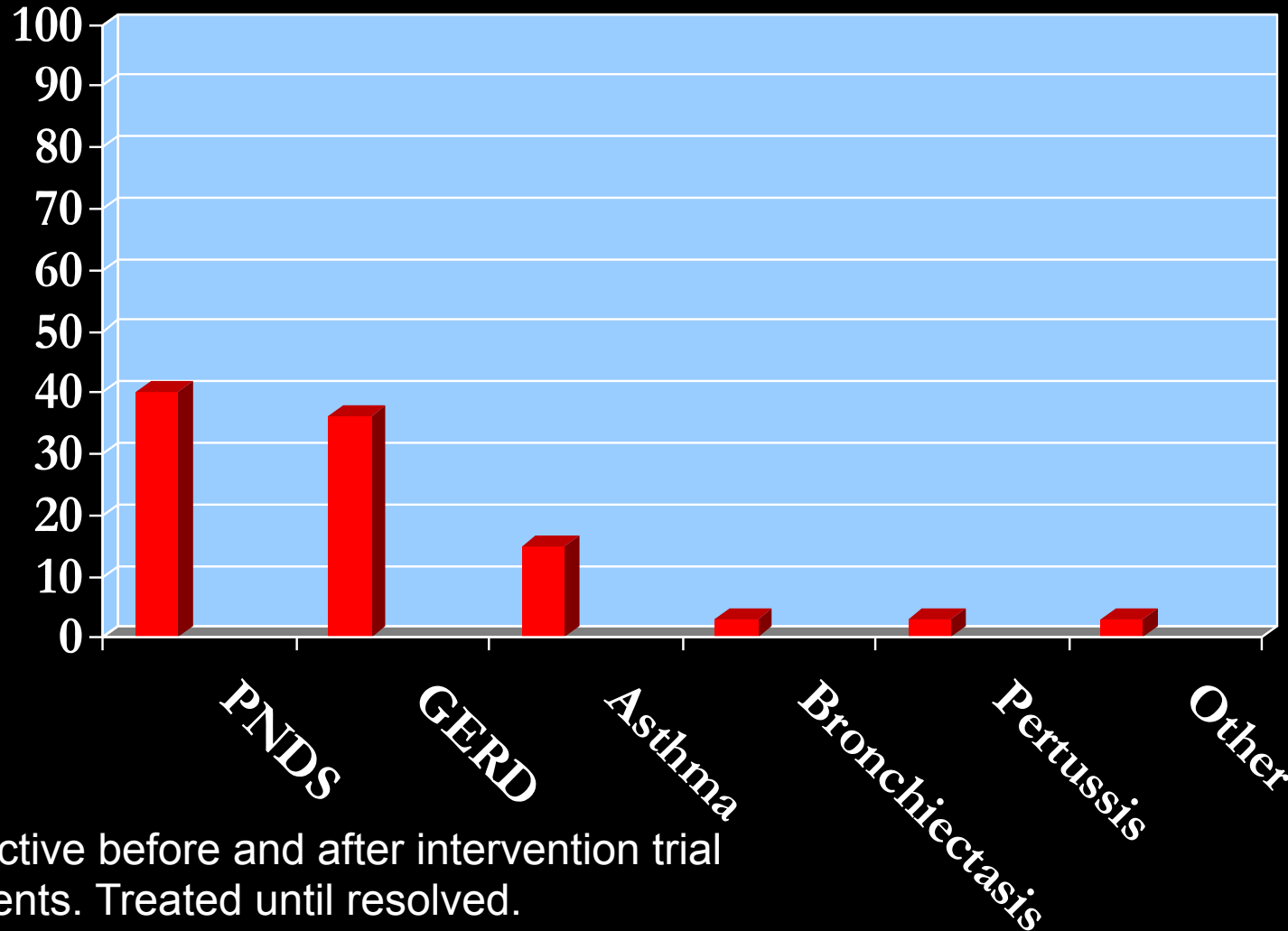


Management of Chronic Unexplained Cough

Definitions

- Chronic cough is defined as cough lasting > 8 weeks
- Unexplained chronic cough (UCC):
Chronic cough that has no determined cause after comprehensive investigation, medical assessment, and optimal trials of indicated therapy in an adherent patient (Gibson, P, et al. Chest 2016).

Causes of cough



Prospective before and after intervention trial
39 patients. Treated until resolved.

Cause based upon response

French, C, et al, Arch Intern Med, 1998

Causes of chronic cough

- “The differential diagnosis for the most common causes of chronic cough includes medications (angiotensin converting enzyme inhibitors, bisphosphonate therapy), asthma, chronic upper airway cough syndrome, and gastroesophageal reflux. Additional possibilities include non-asthmatic eosinophilic bronchitis, bronchiolitis, bronchiectasis, and malignancy.”

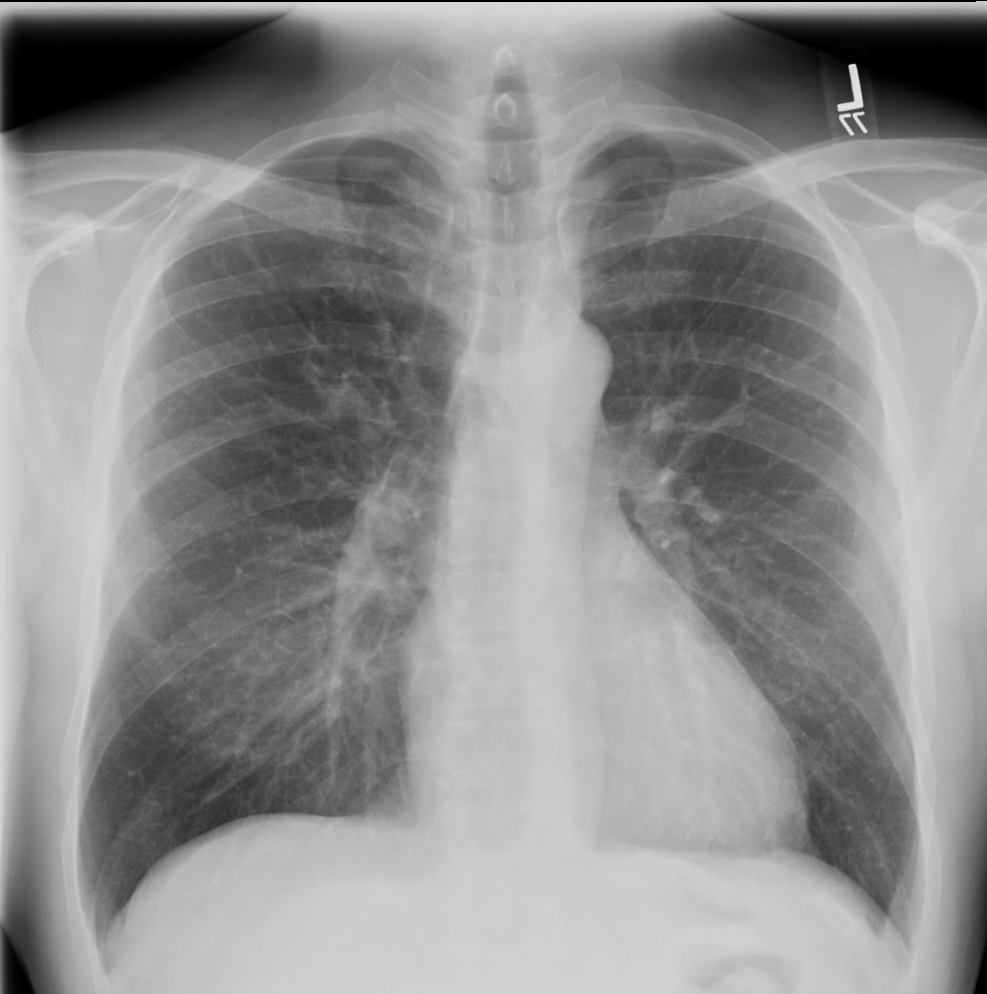
Faber, CN, EpicCare, 2009

Case Presentation:

Case 1: JE

- 57-year-old male with cough for 2 months. Cough is not productive. He does have nasal congestion. He has no GERD symptoms. Medrol has helped the cough.
- PMH: Chronic sinusitis
- Meds: Albuterol; Tessalon; Zyrtec; Flonase; Qvar 1 puff twice daily
- Exam: Clear

Case 1: CXR



Case 1

Date	FVC (%)	FEV1 (%)	FEV1/FVC	FRC	DLCO
1-21-16	4.80	3.64	76		129
	4.99	3.81	76		

Case 1

Assessment: The differential diagnosis for the most common causes of chronic cough includes medications (angiotensin converting enzyme inhibitors, bisphosphonate therapy), asthma, chronic upper airway cough syndrome, and gastroesophageal reflux. Additional possibilities include non-asthmatic eosinophilic bronchitis, bronchiolitis, bronchiectasis, and malignancy

Case 1

Plan:

- Zyrtec 10 mg daily
- Astelin 2 sprays each nostril twice daily
- Increase Qvar 4 puff twice daily. Use with spacer. Rinse and gargle after use
- If not better, then Prednisone 10 mg tablets: 4 tablets daily x 4 days; then 3 tablets daily x 4 days; then 2 tablets daily x 4 days then 1 tablet daily x 4 days

Case 1

- Ultimately needed prednisone with resolution of cough.

Case 1: Non-Asthmatic Eosinophilic Bronchitis (+/- post nasal drip)

- Definition: Non-asthmatic eosinophilic bronchitis
 - Prolonged cough
 - Normal chest film
 - FEV-1 and FVC > 80% predicted; FEV1/FVC > 0.7
 - PEFR variability < 20%
 - PC 20 > 16 mg/ml
 - Sputum eosinophilia > 3%

Case 1: Non-Asthmatic Eosinophilic Bronchitis

- 180 patients
 - 7 had steroid responsive cough but no identifiable respiratory disease
 - Non smokers
 - No wheezing, dyspnea
 - Normal FEV₁, FEV₁/FVC, negative methacholine

TABLE I—CHARACTERISTICS OF CORTICOSTEROID-RESPONSIVE NON-ASTHMATIC SUBJECTS

Subject	Age, sex	Symptom duration (months)	FEV ₁ (% predicted)	FEV ₁ /FVC (%)	PC ₂₀ (mg/ml)	Peripheral blood cell-count	
						Eosinophil (× 10 ⁹ /ml)	Basophil (× 10 ⁹ /ml)
1	40, F	9	95	76	8	113	18
2	36, F	3	101	87	12.7	152	63
3*	48, F	6	130	89	24.2	312	0
4	48, M	96	103	78	27.2	99	24
5*	36, M	3	103	89	>256	133	72
6	45, M	9	77	72	>256	30	8
7	67, F	6	110	81	>256	110	22
Mean (SE)	46 (4)	18 (13)	103 (6)	82 (3)	52.5†	136 (33)	30 (10)

*Subjects 3 and 5 had symptoms of post-nasal drip.

†Geometric mean.

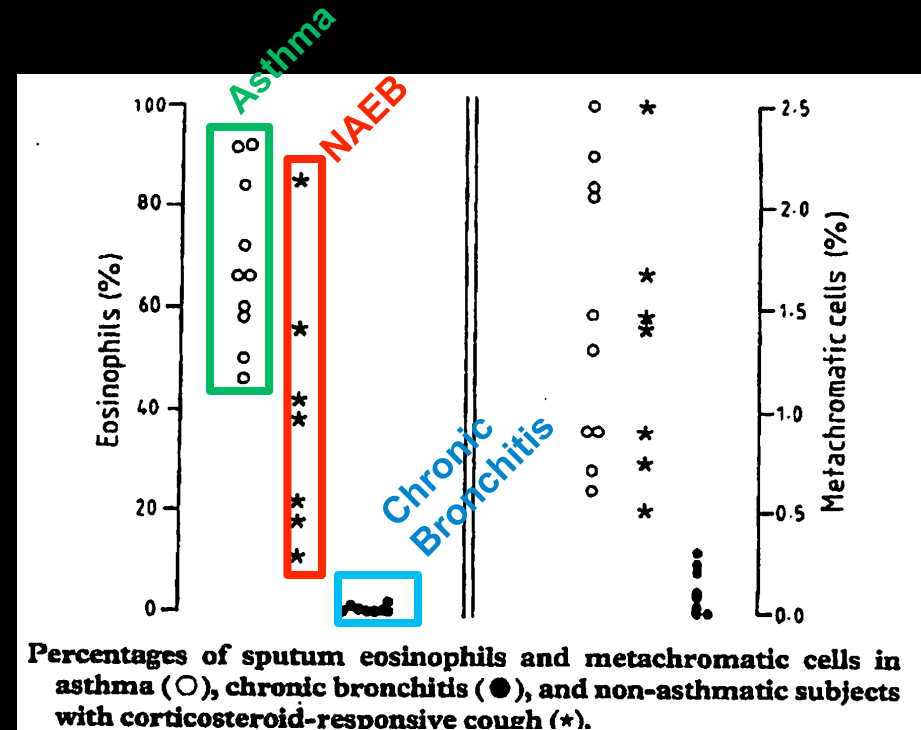
TABLE II—SPUTUM CELL-COUNTS FOR CORTICOSTEROID-RESPONSIVE NON-ASTHMATIC SUBJECTS

Subject	Total cells (× 10 ⁶ /ml)	Differential cell-count					
		Meta	Eos	Neutro	Lymph	Macro	Epi
1	18.4	0.61	17.7	6.9	3.9	60.9	9.4
2	4.8	2.50	54.8	3.2	1.6	24.4	9.4
3	11.5	0.50	85.9	6.0	0	1.7	6.0
4	13.7	1.45	42.0	0.2	1.3	51.3	3.0
5	2.8	1.60	22.9	0.4	2.5	52.6	11.4
6	19.3	0.75	37.4	8.0	5.7	44.9	4.4
7	9.1	1.41	11.5	2.2	1.9	67.5	6.0
Mean (SE)	11.4 (2.4)	1.26 (0.27)	38.9 (9.7)	5.3 (1.4)	2.4 (0.7)	43.3 (8.6)	8.6 (1.7)

Meta = metachromatic; Eos = eosinophil; Neutro = neutrophil; Lymph = lymphocyte; Macro = macrophage; Epi = epithelial.

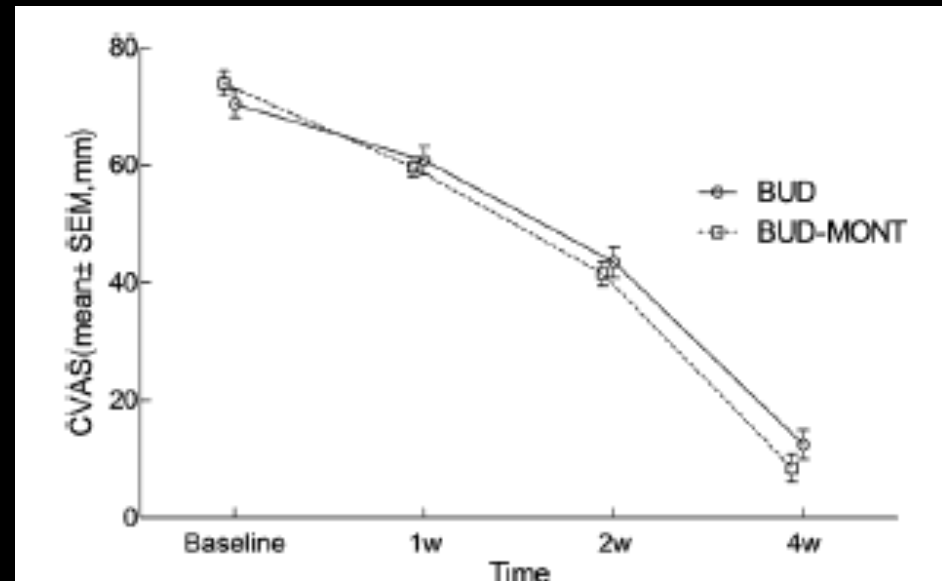
Case 1: Non-Asthmatic Eosinophilic Bronchitis

- 180 patients
 - 7 had steroid responsive cough but no identifiable respiratory disease
 - Non smokers
 - No wheezing, dyspnea
 - Normal FEV1, FEV1/FVC, negative methacholine



Treatment of NAEB

- 26 patients with NAEB and cough
 - 800 mcg/d budesonide
 - 400 mcg/d budesonide + montelukast 10 mg



Cai, C, et al. Resp Med 2012

Case Presentation:

Case 2

- 56-year-old woman presented for evaluation of chronic cough. She has seasonal exacerbations of non-productive cough and nasal congestion. Nasonex helped this a number of years ago. She receives cefuroxime intermittently which helps “slightly”. Cough has awakened in past 2 weeks, but mostly it does not awaken.

Case 2

- ROS: Nasal congestion; No GERD; snores but no daytime somnolence
- PMH: Pneumonia 1990
- PSH: Cholecystectomy
- Meds: Omega 3; B-complex; MVI; vitamin C, Calcium+D.
ClaritinD, Guaifenesin with codeine
- Social History: Non-smoker

Case 2

● Exam:

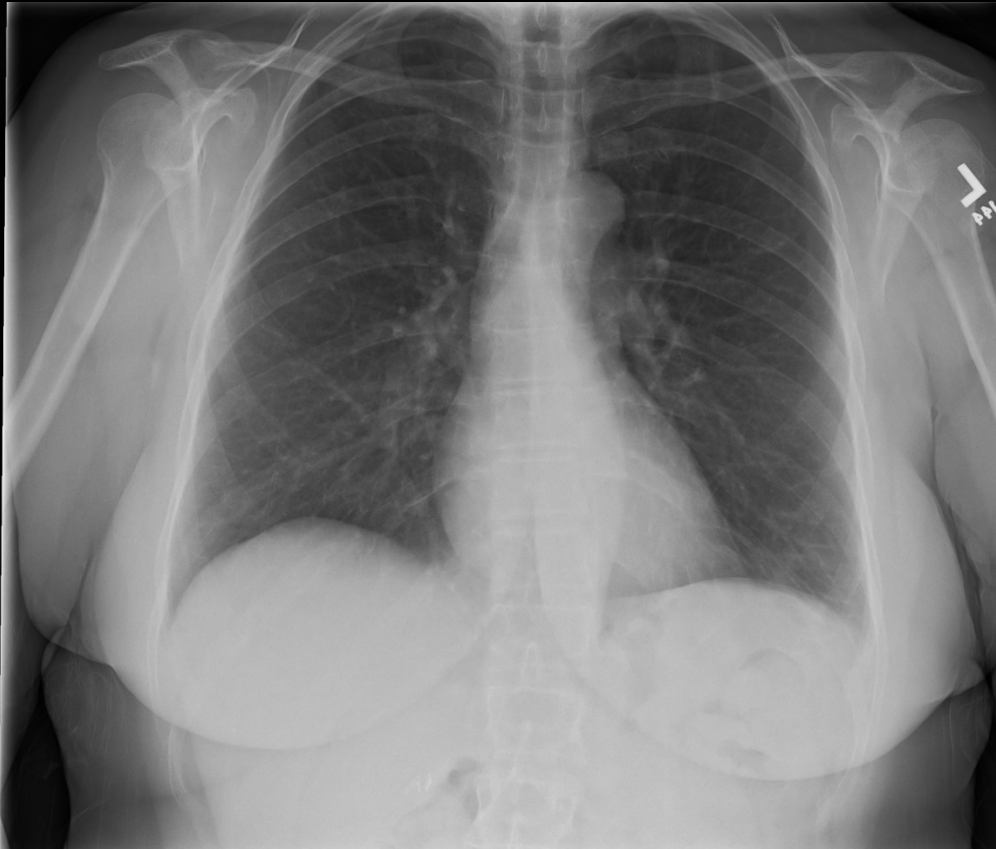
- ENT: Normal
- Cardiac: Normal
- Chest: Rales left base
- Abdomen: Normal

Case 2

● Pulmonary function

Date	FVC (%)	FEV1 (%)	FEV1/FVC	FRC	DLCO
6/21/10	2.88(94)	2.34	81		82

Case 2



FINDINGS: "Minimal left basilar atelectasis".



Case 2

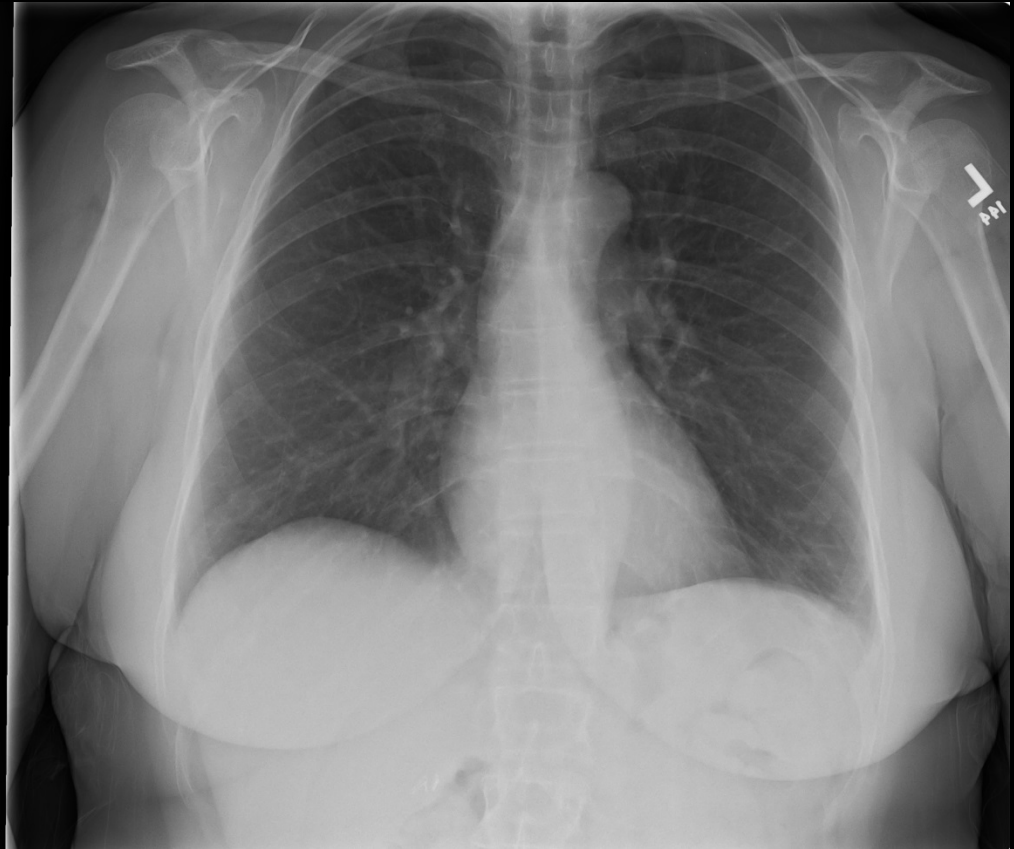
● Assessment:

- She has chronic cough that seems to have seasonal flare. She has nasal congestion that in past was helped with Nasonex.
- The differential diagnosis for the most common causes of chronic cough includes medications (angiotensin converting enzyme inhibitors, bisphosphonate therapy), asthma, chronic upper airway cough syndrome, and gastroesophageal reflux. Additional possibilities include non-asthmatic eosinophilic bronchitis, bronchiolitis, bronchiectasis, and malignancy.

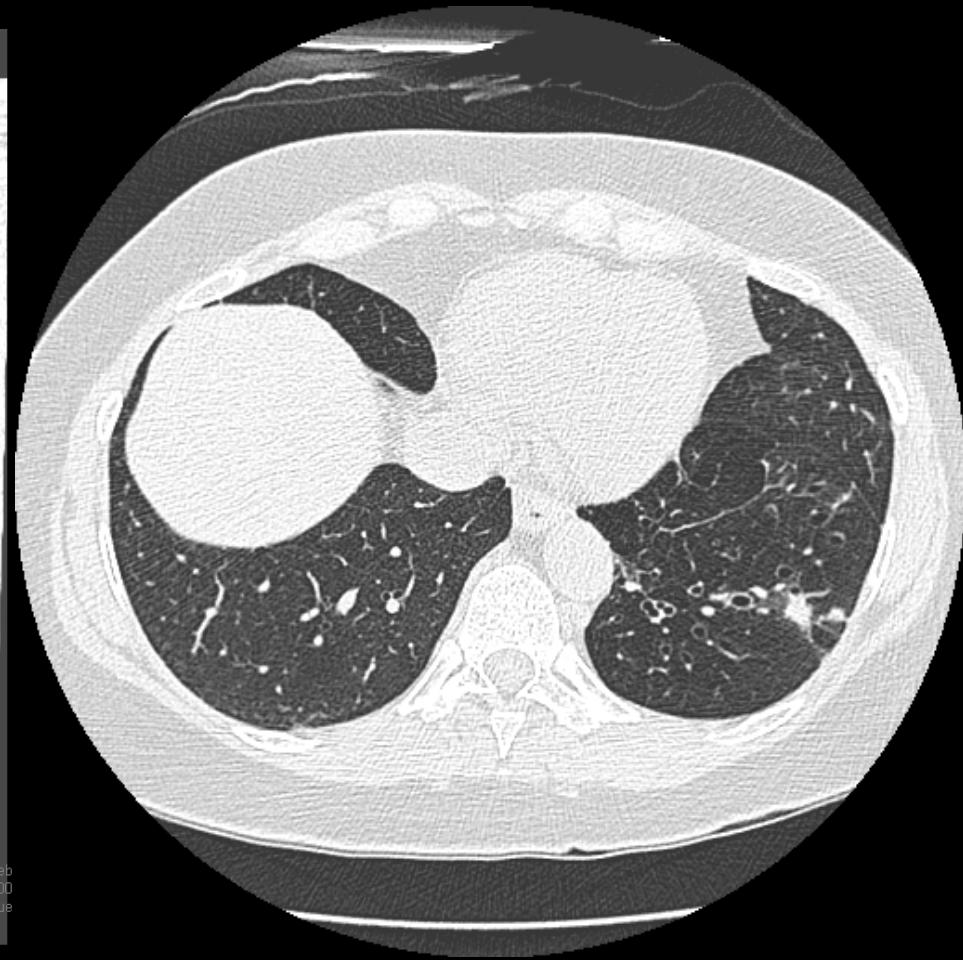
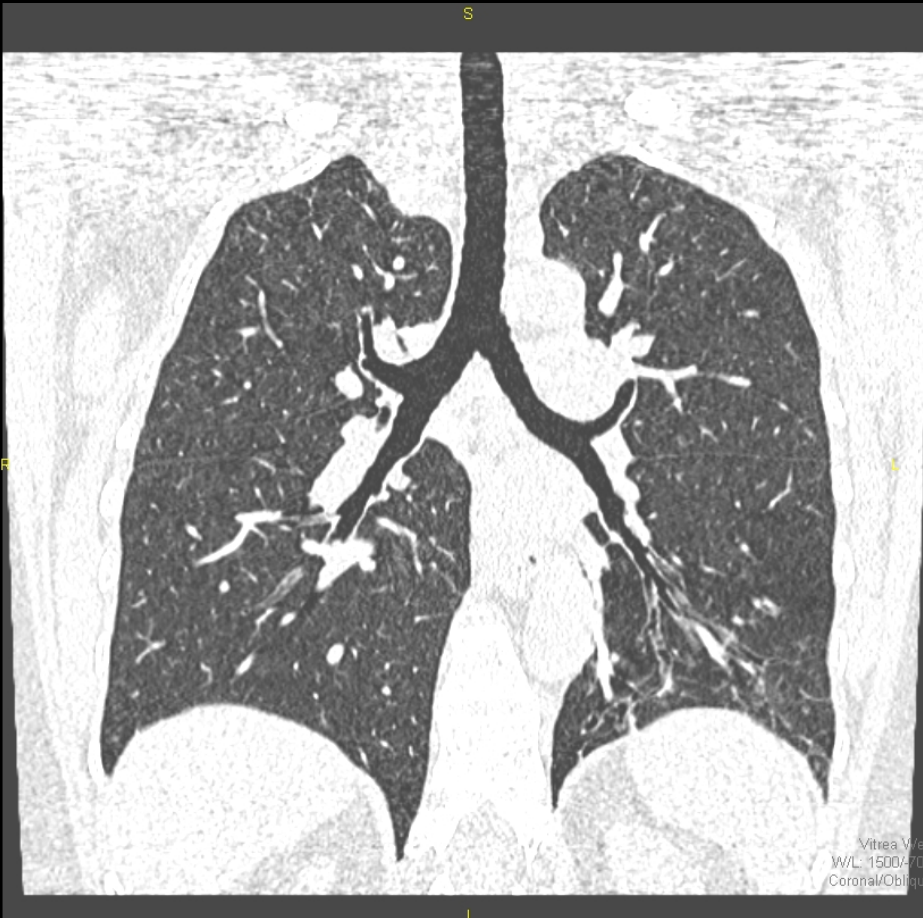
Case 2: Bronchiectasis

- Assessment: Her CXR suggested LLL bronchiectasis. The CT confirmed this. This may be the primary source of her cough. In addition to post nasal drip and reflux precaution, I will institute bronchiectasis therapy with flutter valve.

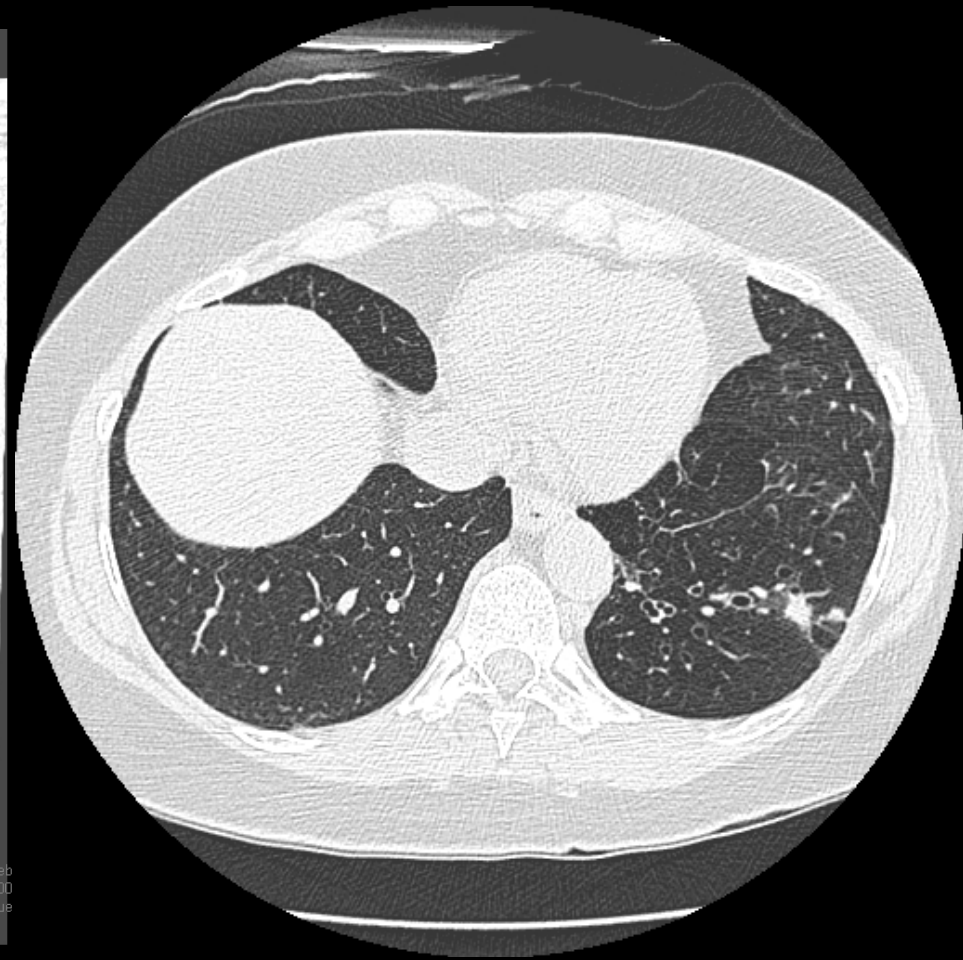
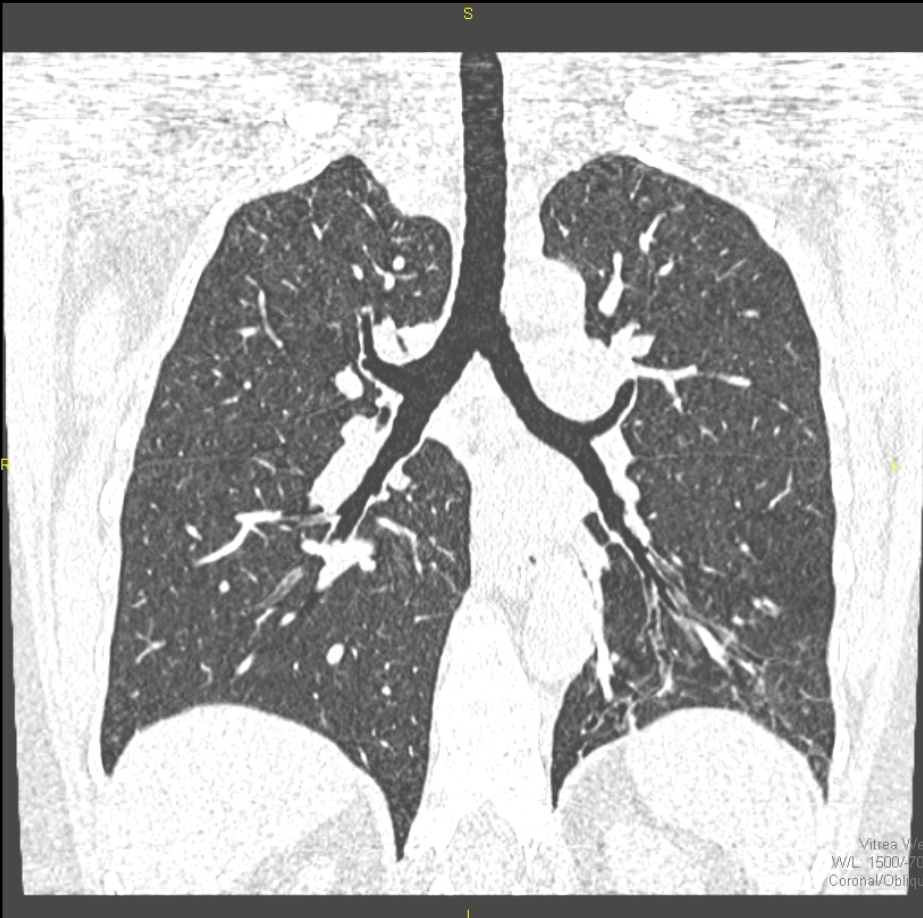
Case 2



Case 2

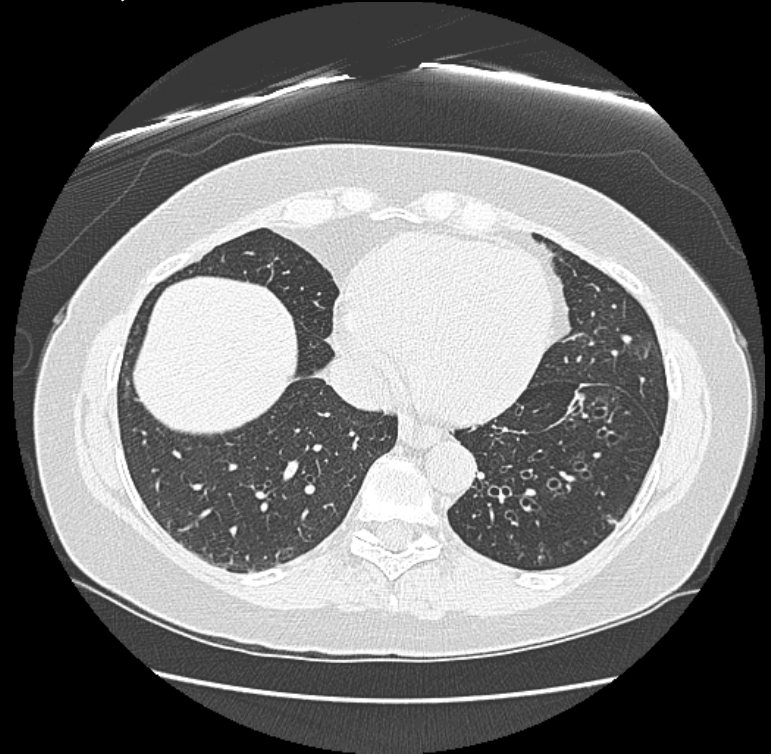
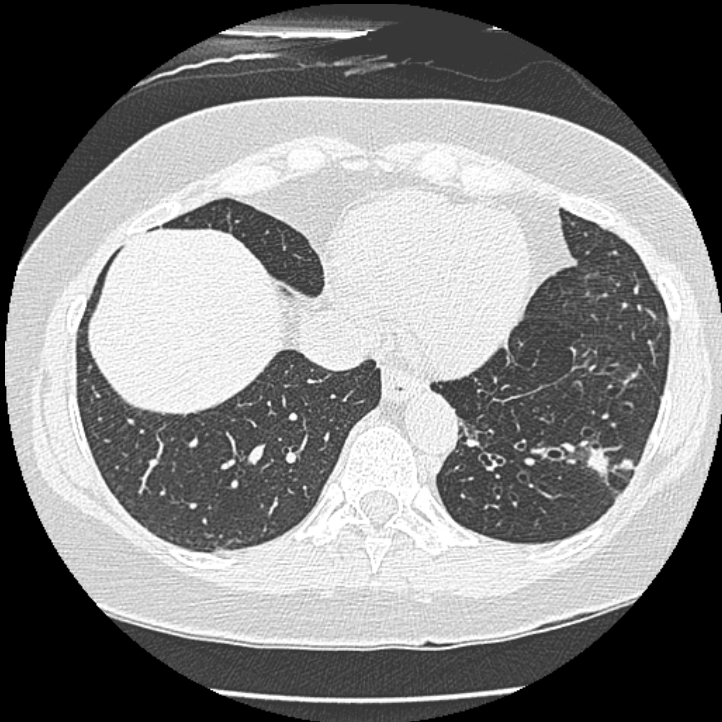


Case 2



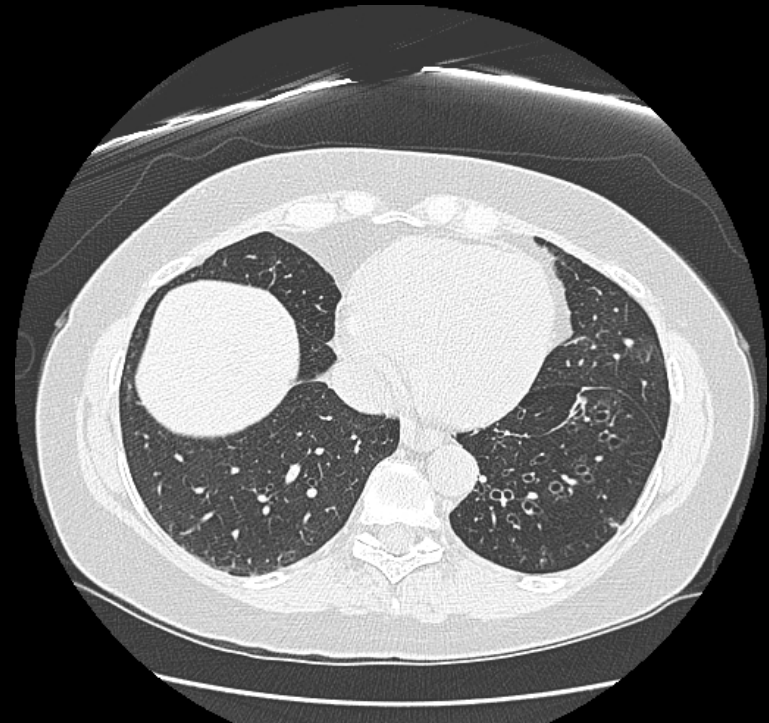
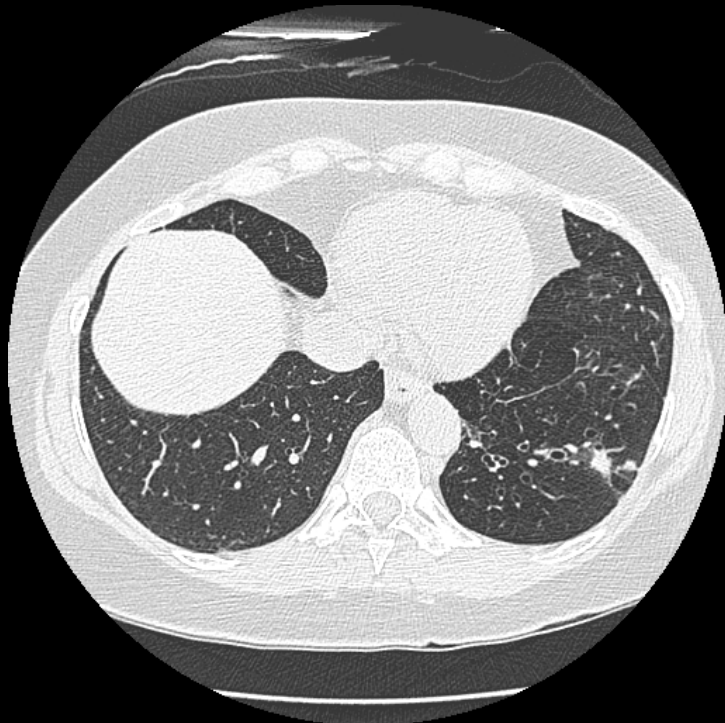
Case 2: Bronchiectasis

- T= +90 Days
- Cough resolved. She is a “different person”
- Flutter; GERD precautions; Claritin/Nasonex



Case 2: Bronchiectasis

- T= +2 years
- Cough remains resolved



Case 3

- 42-year old woman with chronic cough. This is third year in which she developed bronchitis. 7 weeks prior to visit, she developed cough to the point of gasping. Cough is productive of clear to mildly discolored mucus. She was admitted and discharged. She is currently short of breath on minimal exertion. She believes prednisone helped in May.

Case 3

- ROS:
 - Recurrent sinus congestion
 - Cough incontinence
- PMH: Hyperhydrosis; Depression; Anxiety; GERD; Endometriosis; Hypertension
- PSH: VATS/sympathetectomy; Cholecystectomy; Vertical banded gastroplasty

Case 3

● Social History

- Casual smoker (a few a week)
- 3 cats

● Medications: Augmentin; Lexapro; Flovent 110 2 BID; Astelin; Hycodan; Cozaar; Zantac

<i>Drug</i>	<i>Number of patients with cough</i>	<i>Patient-months of exposure</i>	<i>Rate per 1000 patient-months</i>	<i>95% confidence limits</i>
Enalapril	86	21 983	3.9	3.1–4.8
Lisinopril	270	18 749	14.4	12.7–16.2
Perindopril	210	12 751	16.4	14.3–18.8
Losartan	64	20 533	3.1	2.4–4.0

MacKay, F, et al. Br J Clin Pharm, 1998

Case 3

● Exam:

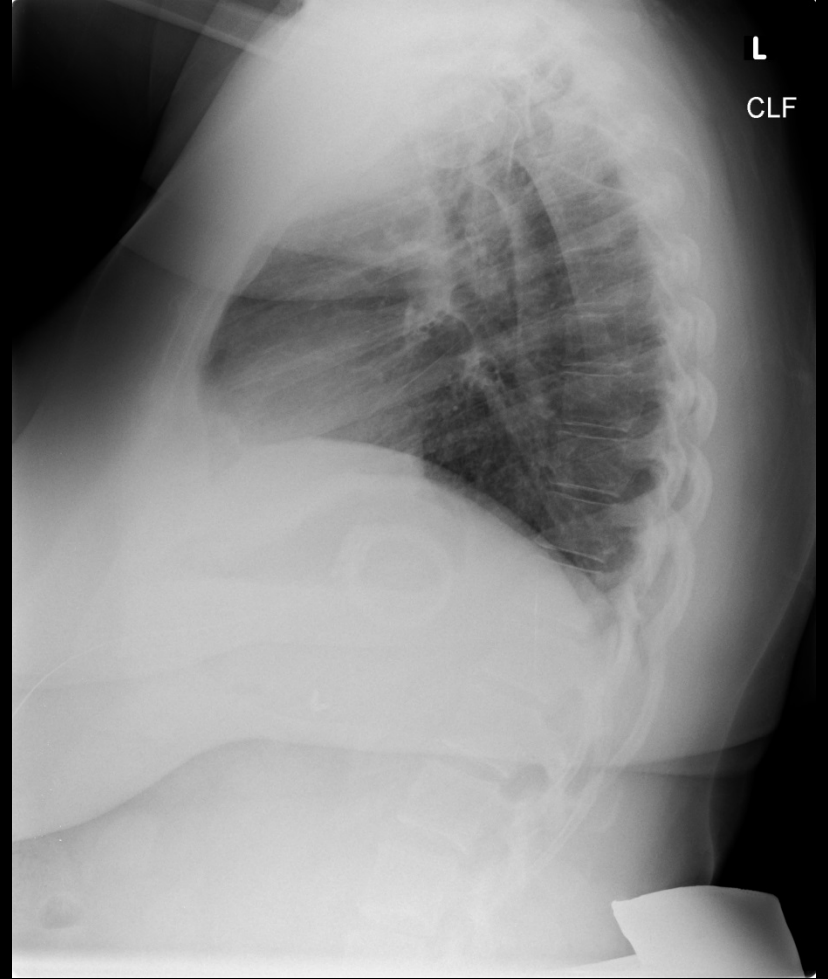
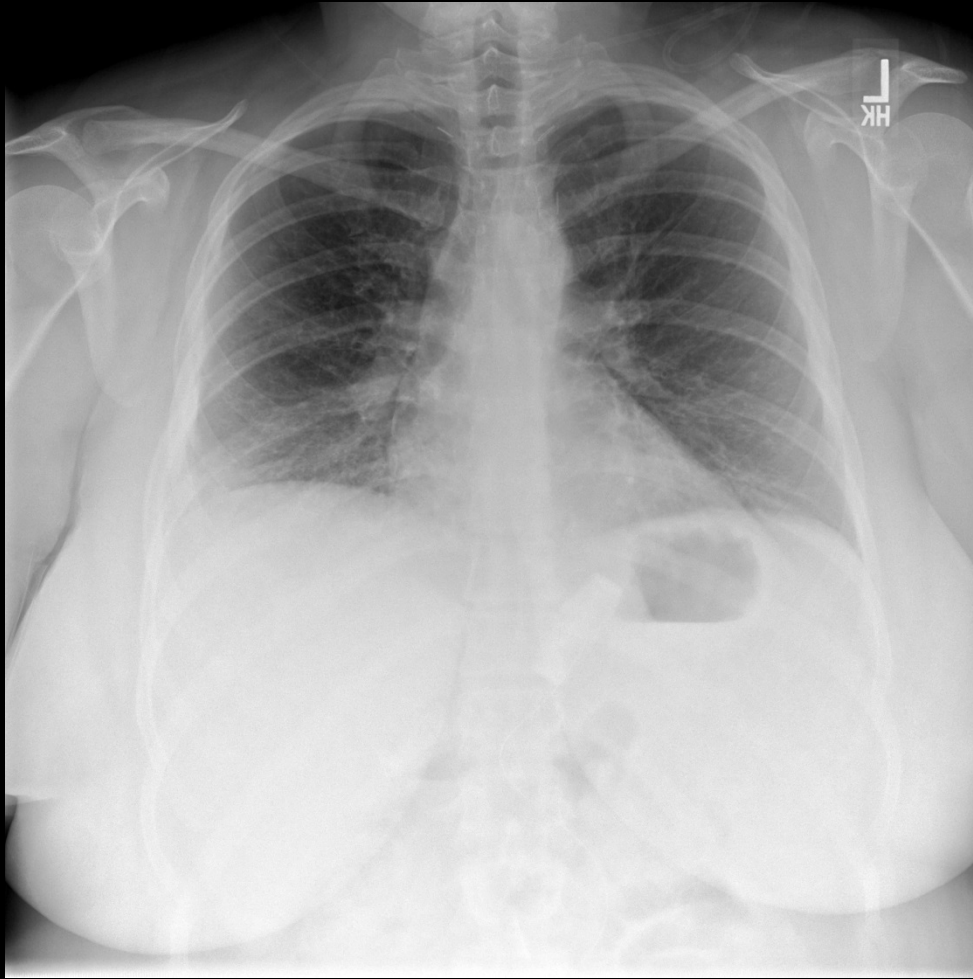
- Vitals: Normal; Saturation 95%
- ENT: bilateral nasal congestion
- Cardiac: Normal
- Chest: bilateral rales

Case 3

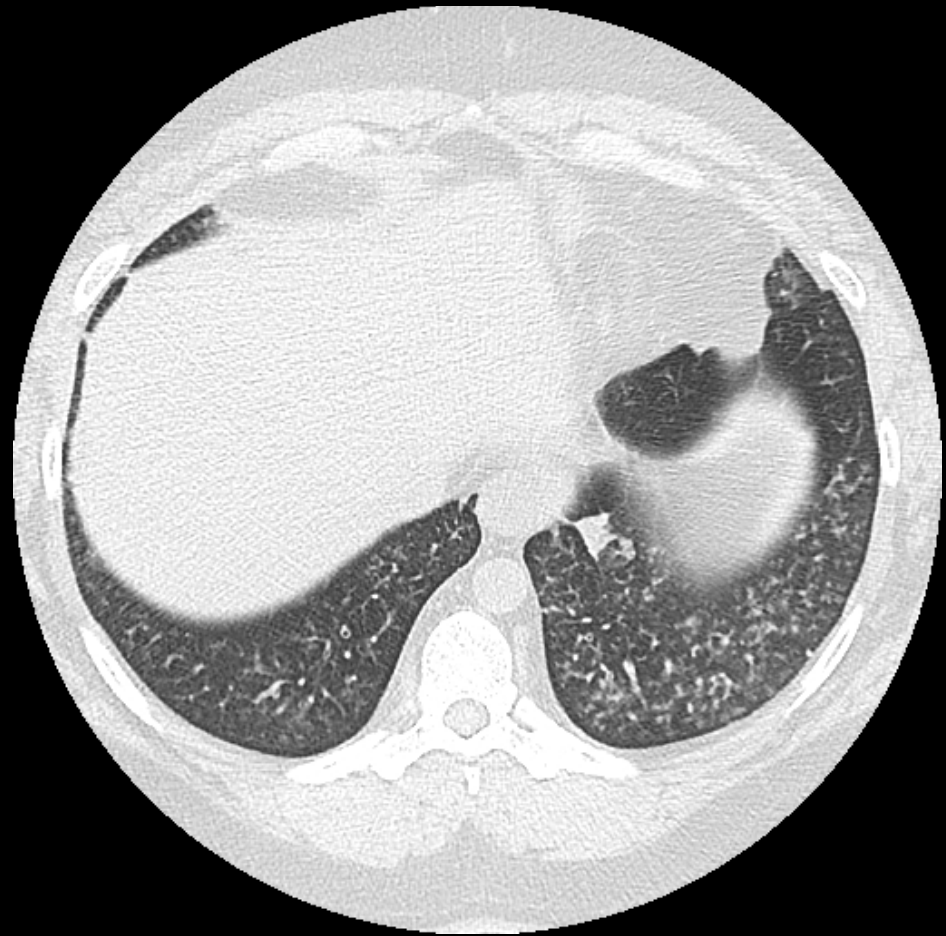
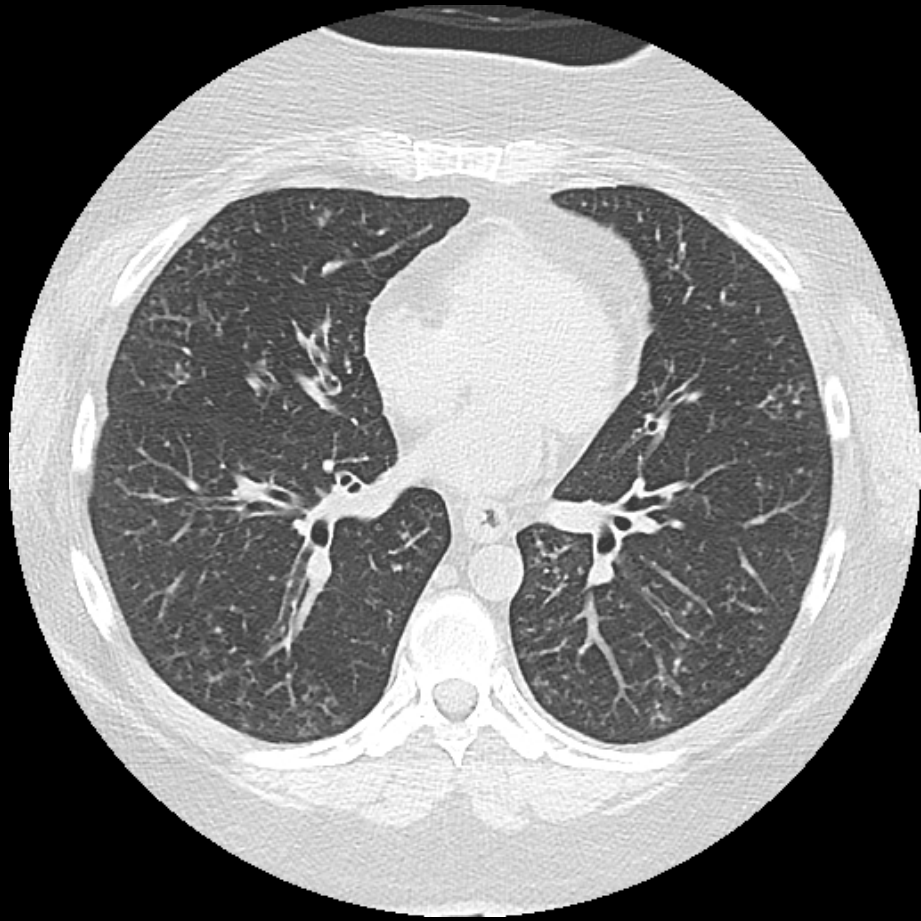
● Pulmonary function

Date	FVC (%)	FEV1 (%)	FEV1/FVC	FRC	DLCO
6/3/16	1.67(49)	1.16(44)	70		

Case 3



Case 3



Case 3

- She has recurrent episodes of cough not responsive to steroids or antibiotics.
- She has bronchiolitis (and bronchiectasis - ? Reactive). I recommend treating with macrolide and steroids and emphasize GERD precautions.

Case 2

Component	7/7/2016
B. Pertussis AB IgG	3.1 (H)
B. Pertussis AB IgM	1.1
B. Pertussis AB IgA	1.4 (H)
B. Pertussis Toxin AB	Positive

Case 3: Pertussis

- T= 42 days
- Cough persistent but much better

Date	FVC (%)	FEV1 (%)	FEV1/FVC	FRC	DLCO
6/3/16	1.67(49)	1.16(44)	70		
7/18/16	2.81	2.31	82		57
	3.25	2.65	82		
8/5/16	3.28	2.77	84		60
	3.17	2.71	85		

Case 3: Pertussis



Case 3: Pertussis

- Pertussis: Whooping Cough
 - Catarrhal phase: 1-2 weeks: malaise, rhinorrhea, fever
 - Paroxysmal phase: Severe cough, followed by inspiratory “whoop” (can last 2-3 months)
 - Convalescent phase
- Total illness 3 months: “100-day cough”

Case 3: Pertussis

● Diagnosis

- Culture/PCR if within 2 weeks
- If > 4 weeks, serology

● Treatment:

- Macrolides
- TMP/Sulfa

Case 4

- 50-year-old female presented with chronic persistent cough that did not resolve 1 year after stopping smoking. She also had wheezing and dyspnea.
- ROS: GERD
- PMH: GERD
- PSH: Meniscectomy
- Meds: Effexor; Nexium
- Family history: Stroke; heart disease
- SH: 1 PPD x 30 years; Grocer

Case 4

● Exam:

➤ Normal Vitals; Saturation 96%

➤ ENT: Negative

➤ Cardiac: Normal

➤ Chest: Bilateral wheezing

➤ Extremities: No edema

● Assessment: Chronic airflow obstruction

● Plan: Advair; Albuterol; Prednisone

Case 4

● Pulmonary Function

Date	FVC (%)	FEV1 (%)	FEV1/FVC	FRC	DLCO
2/14/07	2.73(86) 2.60(81)	1.48 (61) 1.58(65)	54 61		

Case 4

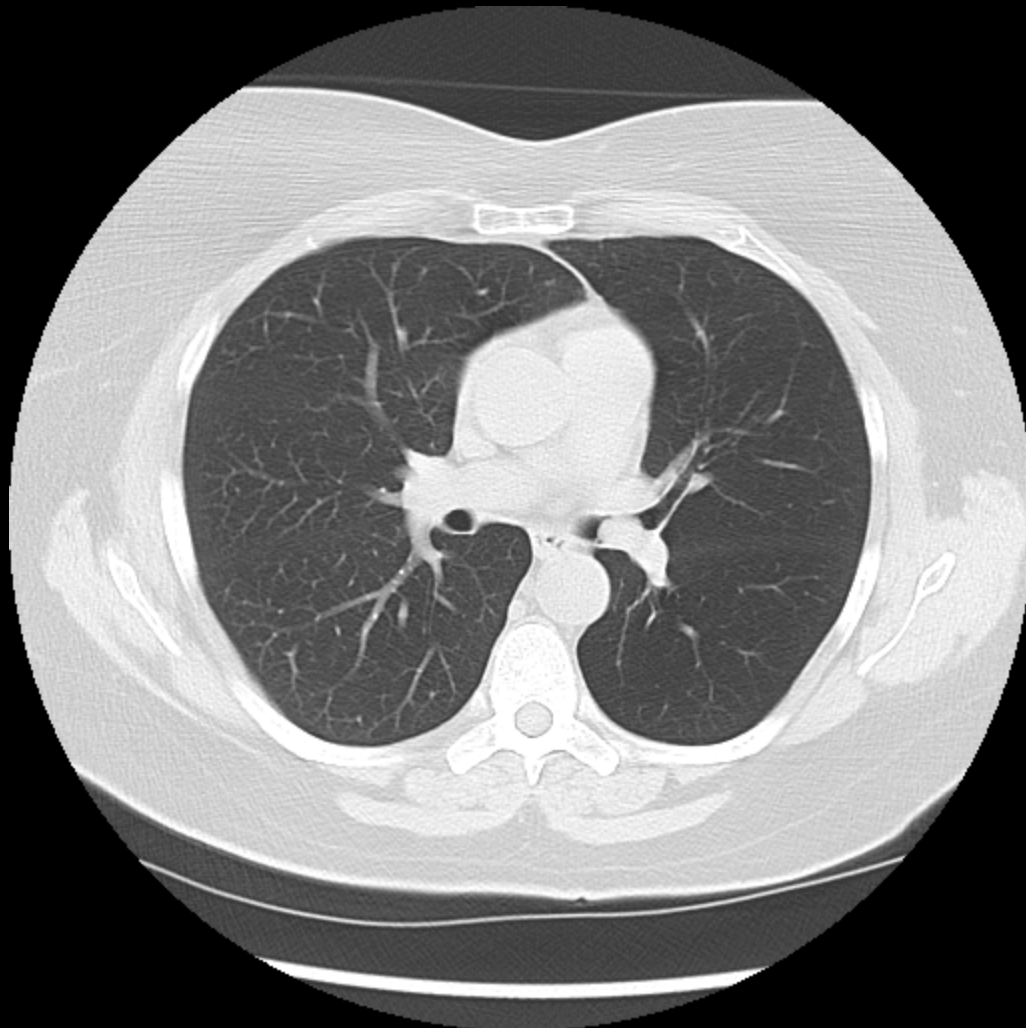
- T = 30 days
- Symptoms no better

Case 4

● Pulmonary Function (after treatment)

Date	FVC (%)	FEV1 (%)	FEV1/FVC	FRC	DLCO
2/14/07	2.73(86)	1.48 (61)	54		
	2.60(81)	1.58(65)	61		
3/14/07	2.52(79)	1.49(61)	59		
	2.59(81)	1.55(64)	60		

Case 4



Case 4: Neoplasm

- Pneumonectomy: mucoepidermoid carcinoma

Case 5

- Patient is a 61-year-old male who reported an episode of bronchitis in March and August of 2006. He had associated symptoms of cough, wheezing, chest tightness and dyspnea on exertion. He was treated with Z-pak. In August, he was treated with inhaled steroids. His cough persisted for 2 months before presenting to the office. He coughed 30 times a day and had self-limited coughing spasms immediately upon laying down.

Case 5

- Cough was associated with chest tightness and pressure so much so that he presented to UPMC Passavant ED 1 month prior to his clinic visit at which time he was admitted and underwent a cardiac evaluation. The cardiac evaluation was negative.
- PMH/PSH unremarkable
- SH: Nonsmoker; CPA
- ROS: Heartburn treated with intermittent Prevacid
- Meds: Zyrtec; Azmacort; Combivent

Case 5

- Examination: Completely normal
- CXR: normal
- PFT: Normal
- Pertussis titers strongly positive
- Assessment: Chronic cough: Possibly pertussis

Case 5

- Assessment: “The differential diagnosis for the most common causes of chronic cough includes medications (angiotensin converting enzyme inhibitors, bisphosphonate therapy), asthma, chronic upper airway cough syndrome, and gastroesophageal reflux. Additional possibilities include non-asthmatic eosinophilic bronchitis, bronchiolitis, bronchiectasis, and malignancy.”

Case 5

● Plan:

- Biaxin x 2 weeks (positive pertussis)
- Zyrtec and Astelin x 1 week; if no better then
- Asmanex x 1 week; if not better then;
- Regular treatment with proton pump inhibitor; prop head of bed up; nothing to eat for 3 hours prior to bed; avoid caffeine

Case 5: T = 4 weeks

- He improved on Biaxin and deteriorated after stopping
- Heartburn was better on regular Prevacid
- He had audible wheezing.
- Plan:
 - 6 weeks of Biaxin for pertussis
 - Continue inhaled steroids
 - Antireflux measures reinforced (he was not doing)

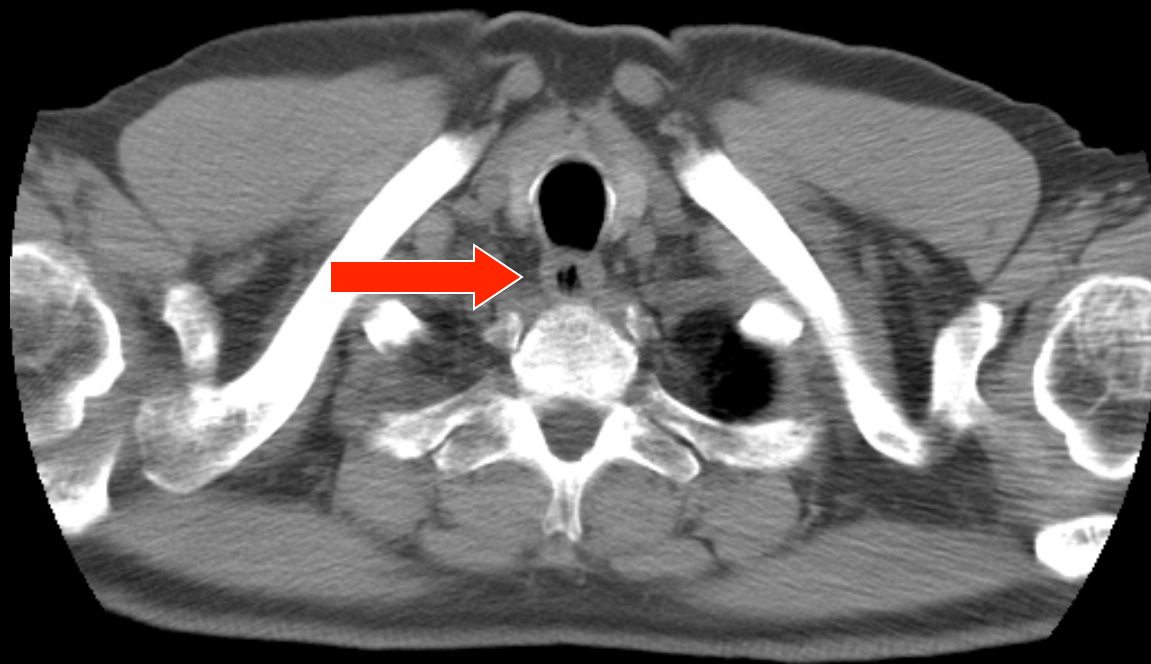
Case 5: T=6 weeks

- Patient having coughing fits now with chest pain, wheezing, and sleep disruption
- Plan: Trial of prednisone

Case 5: T=7 weeks

- Continues with severe coughing fits despite prednisone
- Exam: No wheezing
- CT: ? Thickening of proximal esophagus

Case 5: CT



Case 5: T=7 weeks

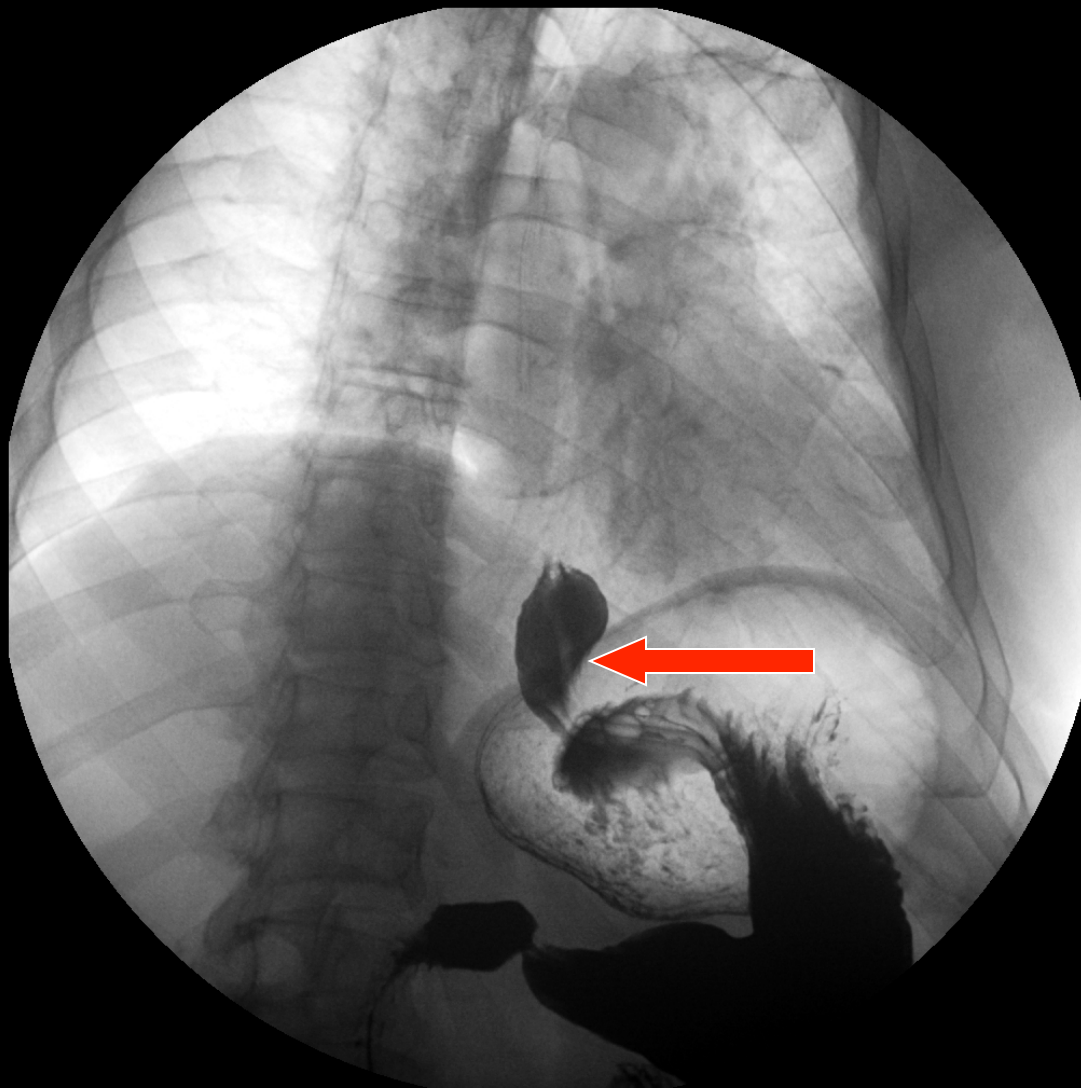
● Assess:

- Doubt asthma given absence of response to systemic steroids.
- In light of esophageal findings, could this be aspiration from diverticulum or proximal obstruction?

● Plan:

- Esophagram
- Bronchoscopy

Case 5: Barium Swallow



Case 5: T=7 weeks+1 day

- Barium swallow with hiatal hernia and reflux
- Plan:
 - Proceed with bronchoscopy
 - Reinforced anti-reflux measures

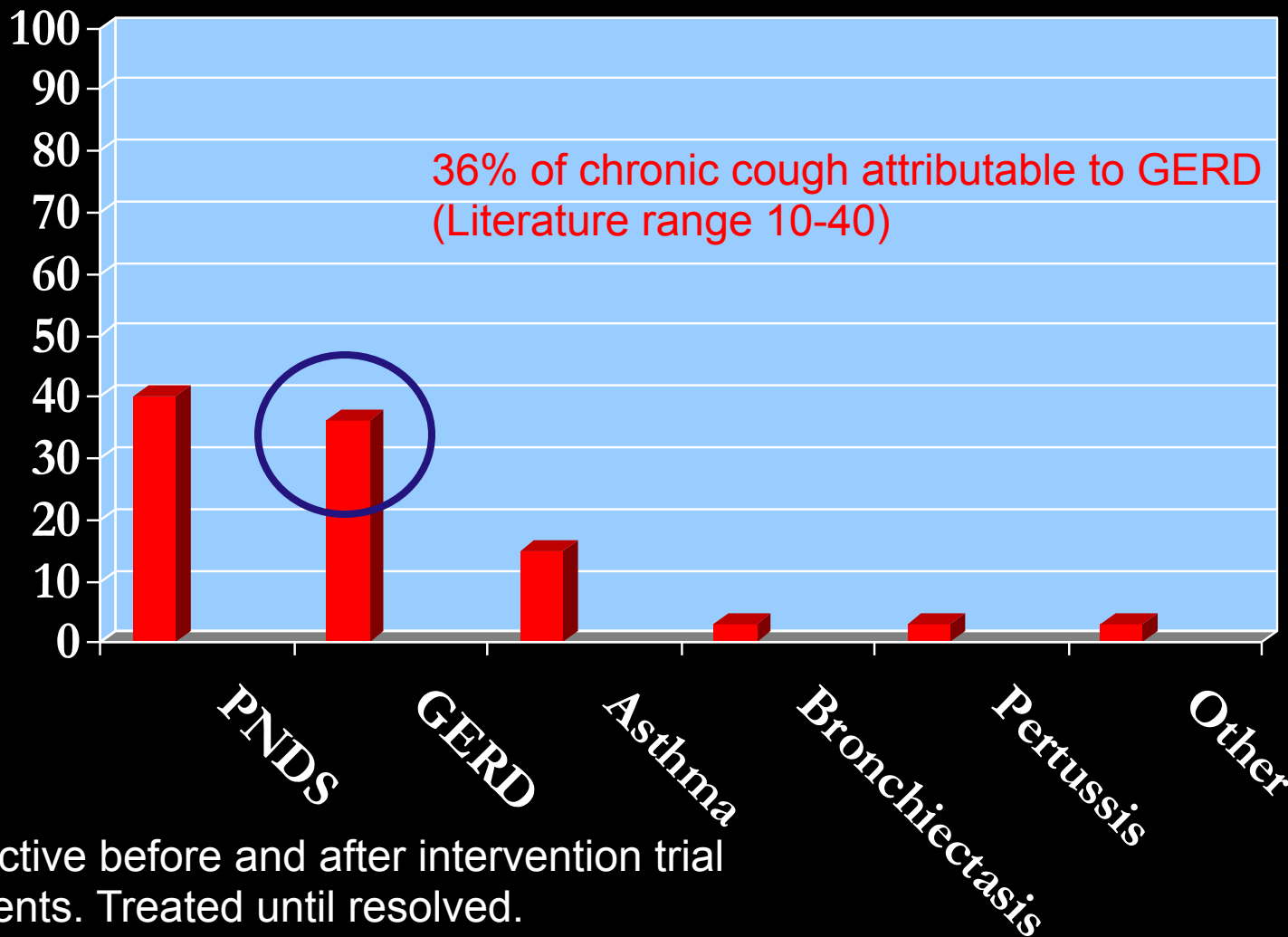
Case 5: T=7 weeks +6 days

- Patient cancelled bronchoscopy
 - Elimination of caffeine from diet resulted in complete resolution of his heartburn and cough (note he started these measures 7 weeks after I recommended them). Reported 12 caffeinated beverages/day
- EGD showed hiatal hernia but no esophagitis

Case 5: T=12 months

- Cough completely resolved
- Heartburn controlled on Pepcid, head of bed elevated, and avoidance of caffeine and alcohol.
- GERD as cause suspected but not proven.

Causes of cough



Prospective before and after intervention trial
39 patients. Treated until resolved.

Cause based upon response

French, C, et al, Arch Intern Med, 1998

GERD as a Cause of Chronic Cough: Outcomes of Treatment

	'off' PPI (<i>n</i> = 77)	'on' PPI (<i>n</i> = 23)	<i>P</i> -value
Reflux events/24 h	38 (25.5–57.5)	35 (21.5–49)	0.07
Percentage acid reflux	51.5 (33.9–73.3)	4.4 (0–18)	0.0001
Percentage weakly acidic reflux	33.3 (21–55.7)	73.6 (1–50)	0.003
Percentage weakly alkaline reflux	6.7 (0–17.4)	16.6 (0–39)	0.16

100 patients with chronic unexplained cough
Impedence pH recording

pH vs Impedance/pH monitoring

22 patient with GERD on BID PPI with persistent symptoms

Evaluated with both pH and impedance monitors

	pH +	Impedance +
+Symptoms	18%	64%

About 40% of treated patients have persistent non-acidic reflux that will not be detected with conventional pH monitoring.

Lifestyle modifications and GERD

Table 4. Treatment effects between PPI and control groups

Outcome	Control vs PPI			P value
	n	Difference	CI 95%	
<i>Primary</i>				
Total Reflux Score	37	-3.06 ± 3.90	-10.99-4.86	0.44
Sig Global Improvement	33	-3.3% ± 17.5%	-37.5%-30.9%	1.0
<i>Secondary</i>				
Reflux Severity	37	-1.67 ± 1.87	-5.46-2.12	0.38
Reflux Frequency	37	-1.39 ± 2.33	-6.12-3.33	0.55
“Typical” Symptoms	37	-0.45 ± 1.52	-3.54-2.64	0.77
“Laryngeal” Symptoms	37	-1.97 ± 1.69	-5.40-1.47	0.30
“Pharyngeal” Symptoms	37	-1.18 ± 1.57	-4.37-2.01	0.46
SF36 MCS	37	-0.92 ± 3.17	-7.36-5.51	0.77
SF36 PCS	37	3.34 ± 2.98	-2.71-9.40	0.27
Videostrobe Grade	30	-0.11 ± 0.75	-1.65-1.43	0.69

PPI did not add much to lifestyle modifications (“control”) in control of symptoms, though trends were more favorable to PPI (negative sign favors PPI over lifestyle modifications). But lifestyle modifications are very effective.

Relief of Extra-esophageal Symptoms with Fundoplication

Symptom	% Relief with Surgery
---------	-----------------------

Heartburn	93
-----------	----

Laryngeal	78
-----------	----

Chest pain	56
------------	----

Respiratory	48
-------------	----

GERD and Cough

- GERD is implicated as the cause of ~1/3 of the cases of chronic cough.
- Non-acidic reflux may contribute to cough (despite therapy) and not be detected on pH monitor
- Lifestyle modifications (including elevation of head of bed (4-6 inches), moderation in caffeine, chocolate, alcohol, fatty foods, and nothing to eat within 2-3 hours of bedtime) are important in control of reflux and extraesophageal reflux symptoms

My Approach to Chronic Cough

Algorithmic and Empiric

- Treat for identified condition if present
- If no identified cause, treat for asthma/NAEB, post-nasal drip, and GERD (with lifestyle modifications). I do this mostly concurrently and treat for at least 3 months
- If not successful
 - CT Chest
 - Consider CT sinus (though not frequently)
- If not successful
 - Speech therapy
 - Neurontin
 - Codeine

Management of Chronic Unexplained Cough

ACCP Guidelines

- In adult patients with chronic cough, we suggest that patients with chronic cough undergo a guideline/protocol based assessment process that includes objective testing for bronchial hyperresponsiveness and eosinophilic bronchitis, or a therapeutic corticosteroid trial (Ungraded Consensus-Based Statement).

Management of Chronic Unexplained Cough

ACCP Guidelines

- 3. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of multimodality speech pathology therapy (Grade 2C).

Speech Therapy and Chronic Cough

Design

87 Patients with chronic persistent cough randomly allocated to receive placebo vs speech therapy, each for 4 sessions. Twenty three symptoms rated on a 5-point scale

Table 2 Examples of strategies in the treatment programme

Component	Example
Education	No physiological benefit from cough; capacity for voluntary cough control
Strategies to reduce cough	Identify warning signs for cough and replace with modified swallow technique, pursed lip breathing exercise, or relaxed throat breath
Reduce laryngeal irritation	Increase hydration, decrease exposure to irritating stimuli
Psycho-educational counselling	Internalising locus of control; acceptance that treatment is hard work; setting realistic goals

Results

Improvement in :
Breathing
Cough
Voice
Upper airway
Limitation

Table 4 Comparison of mean (SD) pre- and post-intervention symptom scores and degree of change for participants in the treatment and placebo groups

Score	Group	Pre	Post	Difference	95% CI	p value
Total	Treatment†	35.4 (16.0)	22.7 (18.0)	12.7 (12.7)	9.0 to 16.1	<0.001*
	Placebo‡	29.9 (13.5)	28.8 (16.5)	2.9 (12.5)	-0.7 to 6.5	0.170
	Difference‡			8.5 (13.9)	4.7 to 14.9	<0.001*
Breathing	Treatment†	7.9 (4.1)	5.0 (4.2)	2.9 (3.6)	1.8 to 3.9	<0.001*
	Placebo‡	6.6 (4.7)	5.5 (3.5)	1.1 (3.4)	0.1 to 2.0	0.004*
	Difference‡			2.2 (3.7)	0.4 to 3.2	<0.001*
Cough	Treatment†	8.8 (2.8)	4.9 (3.0)	3.9 (3.2)	3.0 to 4.9	<0.001*
	Placebo‡	7.5 (3.6)	6.3 (3.5)	1.2 (3.4)	0.3 to 2.2	<0.001*
	Difference‡			2.8 (3.6)	1.3 to 4.0	0.003*
Voice	Treatment†	7.2 (6.0)	4.7 (5.2)	2.5 (4.3)	1.2 to 3.7	<0.001*
	Placebo‡	6.5 (4.6)	6.2 (5.0)	0.3 (4.1)	-0.9 to 1.5	0.959
	Difference‡			1.5 (4.5)	0.5 to 3.9	0.005*
Upper airway	Treatment†	9.2 (6.6)	6.5 (6.3)	2.7 (4.7)	1.4 to 4.1	<0.001*
	Placebo‡	7.4 (4.9)	7.4 (5.5)	0.1 (4.1)	-1.1 to 1.2	0.946
	Difference‡			1.5 (4.8)	0.9 to 4.4	0.002*
Limitation	Treatment†	2.3 (1.2)	1.6 (1.0)	0.7 (1.1)	0.4 to 1.0	<0.001*
	Placebo‡	2.2 (1.1)	2.0 (1.0)	0.3 (0.9)	0.0 to 0.6	0.038*
	Difference‡			0.5 (1.0)	0.0 to 0.8	0.011*

†Calculated using Wilcoxon signed rank test.

‡Calculated using Mann-Whitney U test.

Management of Chronic Unexplained Cough

ACCP Guidelines

- 4. In adult patients with unexplained chronic cough and negative tests for bronchial hyperresponsiveness and eosinophilia (sputum eosinophils, exhaled nitric oxide), we suggest that inhaled corticosteroids not be prescribed (Grade 2B).

Management of Chronic Unexplained Cough

ACCP Guidelines

- 5. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of gabapentin as long as the potential side effects and the risk-benefit profile are discussed with patients before use of the medication, and there is a reassessment of the risk benefit profile at 6 months before continuing the drug (Grade 2C).

Gabapentin and Chronic Cough

	Mean change from baseline to treatment period				Mean change from baseline to post-treatment period				Between-group difference in change from treatment period to post-treatment period* (95% CI)	p for interaction
	Gabapentin	Placebo	Difference* (95% CI)	p value	Gabapentin	Placebo	Difference* (95% CI)	p value		
Mean LCQ score†	+2.5	+1.1	1.80 (0.56 to 3.04)	0.004	+1.7	+1.4	0.85 (-0.75 to 2.44)	0.30	-1.22 (-2.35 to -0.09)	0.034
Cough frequency (coughs/h)	-22.5	-4.3	-27.31 (-51.75 to -2.88)	0.028	-9.7	-8.9	-3.10 (-43.31 to 37.11)	0.88	26.49 (0.49 to 52.48)	0.046
Mean cough severity (VAS score, mm)	-11.1	+0.8	-12.23 (-23.22 to -1.25)	0.029	+2.0	-4.8	5.57 (-4.93 to 16.07)	0.29	18.92 (7.71 to 30.13)	0.001
Cough reflex sensitivity at C5 (µM)	+15.1	+5.1	3.12 (-13.59 to 19.82)	0.72	+30.5	+8.6	13.15 (-14.67 to 40.97)	0.35	10.06 (-12.35 to 32.46)	0.38
Mean urge-to-cough score	-0.7	-1.4	0.59 (-0.52 to 1.70)	0.30	-0.9	-1.1	0.021 (-1.29 to 1.34)	0.98	-0.21 (-1.35 to 0.93)	0.72
Mean LDQ score	-1.6	-1.5	0.048 (-0.82 to 0.92)	0.91	-1.6	-1.8	0.44 (-0.45 to 1.33)	0.33	0.27 (-0.62 to 1.15)	0.56

Baseline refers to visit 1 (before treatment). Treatment period refers to visit 2 and visit 3 (on treatment). To calculate mean change between baseline and treatment period, an average of the score at visit 2 and visit 3 was taken away from the score at baseline. Post-treatment period refers to visit 4 and visit 5 (off treatment). To calculate mean change between baseline and post-treatment period, an average of the score of visit 4 and visit 5 was taken away from the score at baseline. LCQ=Leicester cough questionnaire. VAS=visual analogue score. C5=concentration of capsaicin needed to induce five coughs. LDQ=laryngeal dysfunction questionnaire. *Baseline differences adjusted for. †A higher score indicates a better health status.

Table 3: Efficacy analysis for gabapentin versus placebo in the treatment of refractory chronic cough

17 study patients and 6 placebo received escalating doses of gabapentin (or placebo) followed by gradual decreases in dosing and ultimately cessation

Gabapentin and Chronic Cough

	Gabapentin (n=17)	Placebo (n=6)
Blurred vision	1 (6%)	0
Depression	0	1* (17%)
Disorientation, confusion	2 (12%)	0
Dizziness	3 (18%)	1 (17%)
Dry or very dry mouth	2 (12%)	1 (17%)
Fatigue	3 (18%)	1 (17%)
Headache	1 (6%)	0
Memory loss	1 (6%)	0
Nausea, stomach pain	4 (24%)	2 (33%)

Data are number of events (%). n=total number of events associated with study drug. *Possible comorbidity (present before study).

Table 2: Adverse effects

17 study patients and 6 placebo received escalating doses of gabapentin (or placebo) followed by gradual decreases in dosing and ultimately cessation

Management of Chronic Unexplained Cough

ACCP Guidelines

- 6. In adult patients with unexplained chronic cough and a negative workup for acid gastroesophageal reflux disease, we suggest that proton pump inhibitor therapy not be prescribed (Grade 2C).

THE END



Treatment of Unexplained Cough

