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Pediatric Pulmonology: The Lung and Short of it

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December 4th, 2024

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

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8-month-old boy with cough

History

Dry/juicy cough x 5 months

Worse when supine or agitated

Wakes from sleep 2-3x/week

Mom reports intermittent wheeze

Feeding well / gaining weight

Albuterol equivocal response

Physical exam and initial workup

Happy / comfortable	Ht and Wt 50th percentile	O2 sat 96%
Mild tachypnea / retractions	Rhonchi + wheeze bilaterally	CXR negative

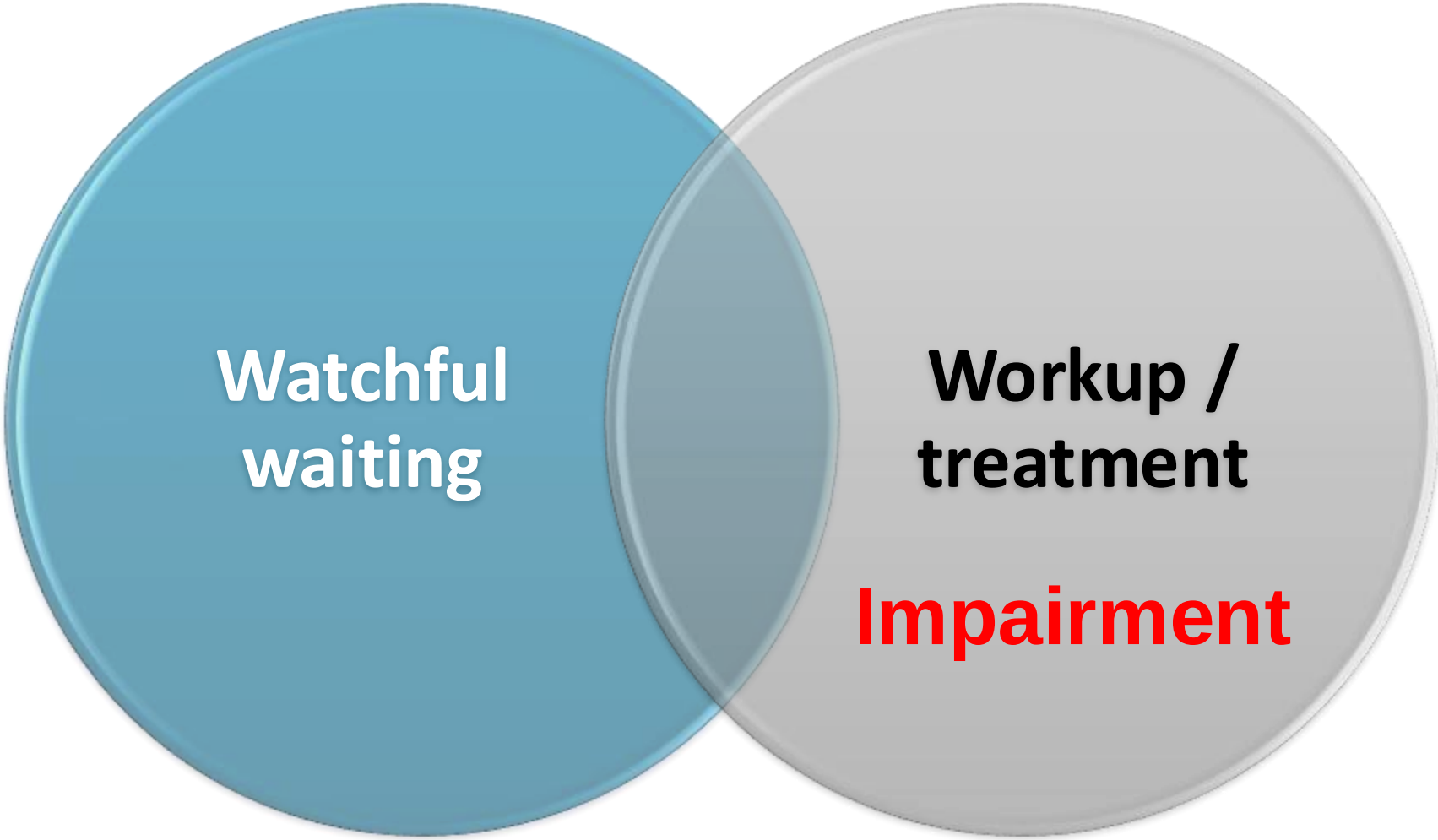
How would you treat this patient?

A. Inhaled corticosteroids
B. Prednisone
C. Albuterol
D. Ipratropium
E. Antibiotics
F. Unsure – haven't had enough coffee yet

Treatment

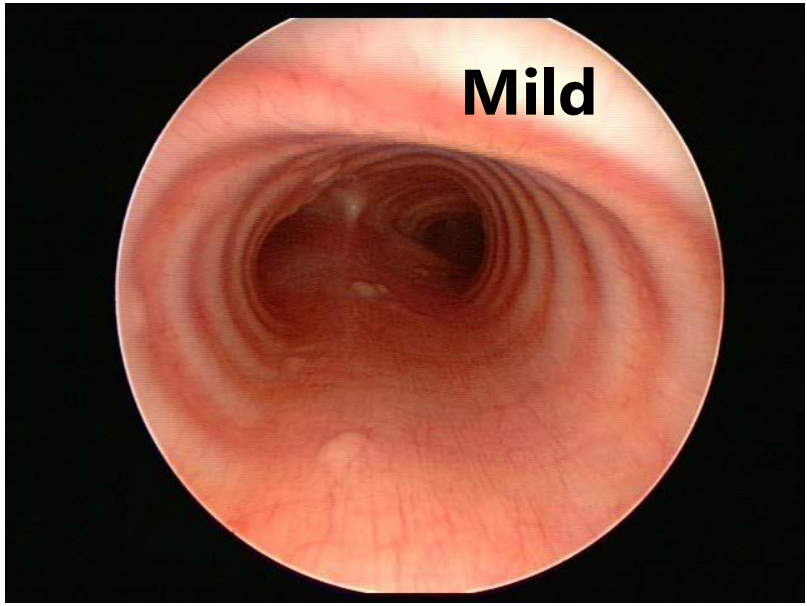

Albuterol
Inhaled corticosteroids
Prednisone
PPI
Anti-histamine

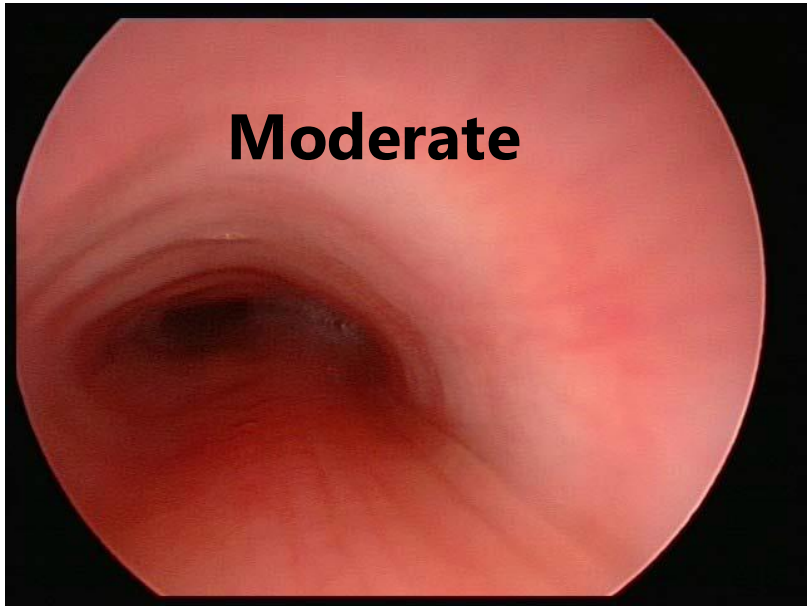
Pulmonary Clinic – chronic cough



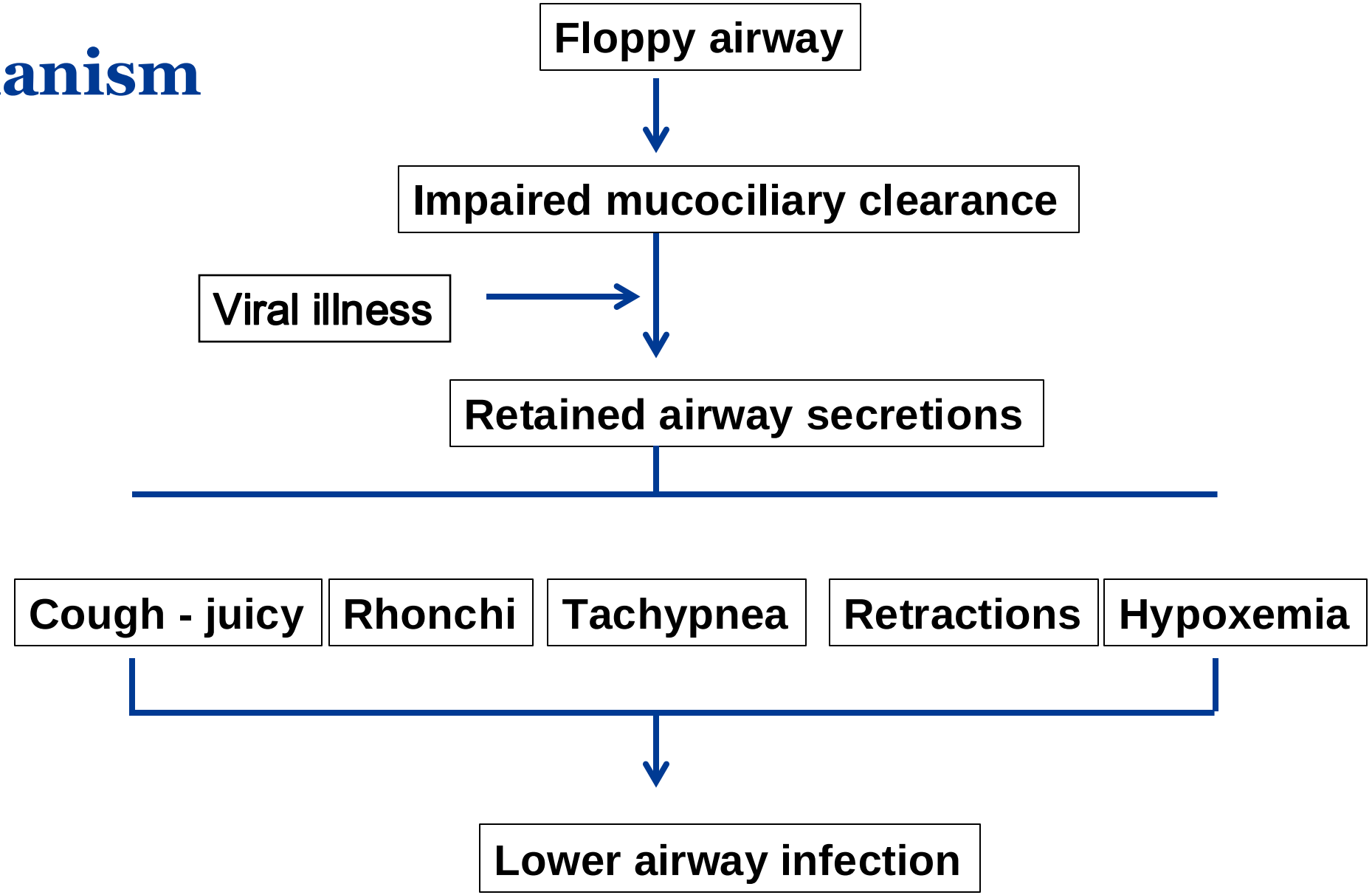
Tracheomalacia

- Weakness of the tracheal cartilage
- Incidence 1 in 1500-2000
- Cough and wheeze – not responsive to albuterol
- Can manifest first few months
- Majority outgrow by 2 years of age





Mechanism

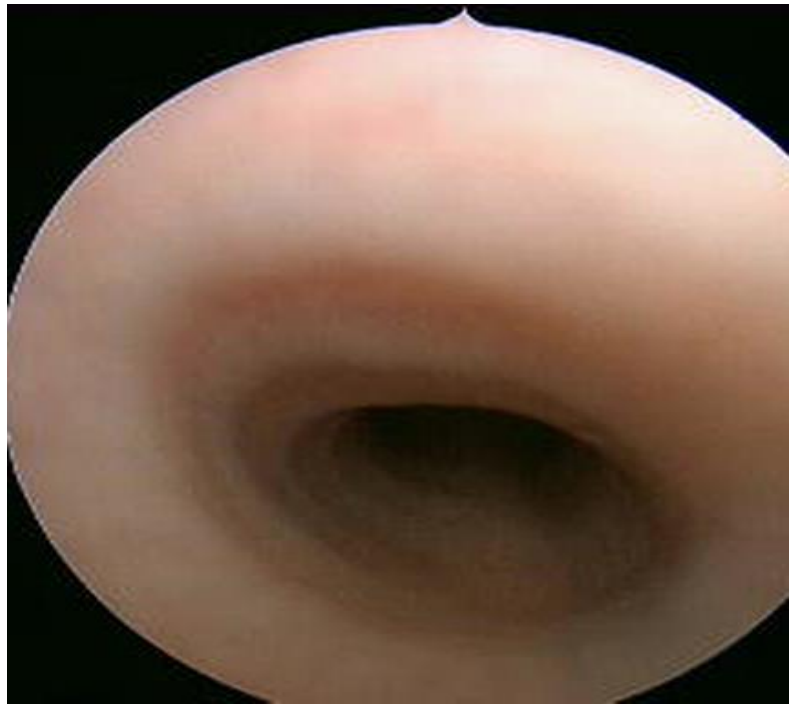

Floppy airway
Impaired mucociliary clearance
Viral illness
Retained airway secretions
Cough - juicy
Rhonchi
Tachypnea
Retractions
Hypoxemia
Lower airway infection

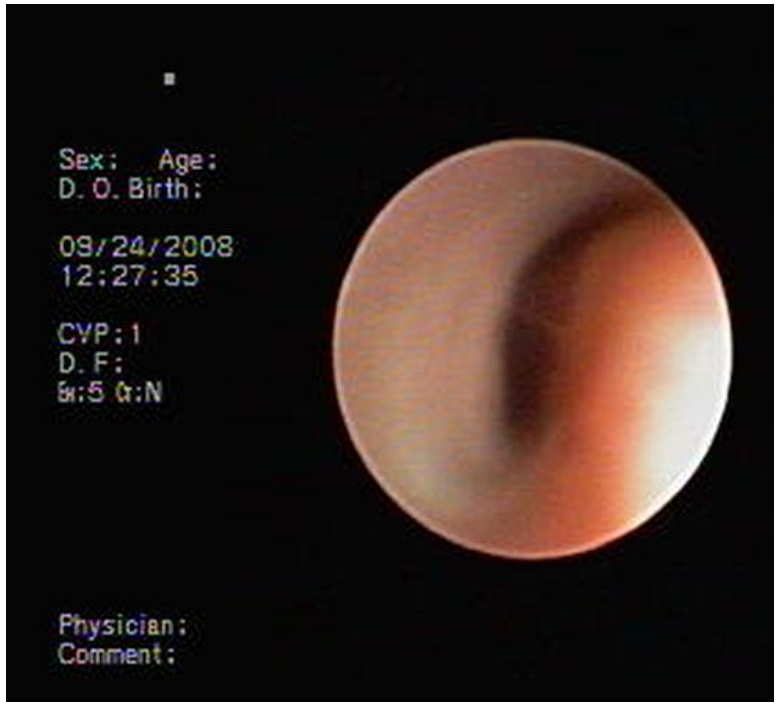
Diagnosis

Clinical	Imaging	Bronchoscopy
• Hx / PE / response to treatment	• CXR • Fluoroscopy • Dynamic CT / MRI	• Failure to thrive • Difficulty feeding • Repeated infections • Impairing daily activities

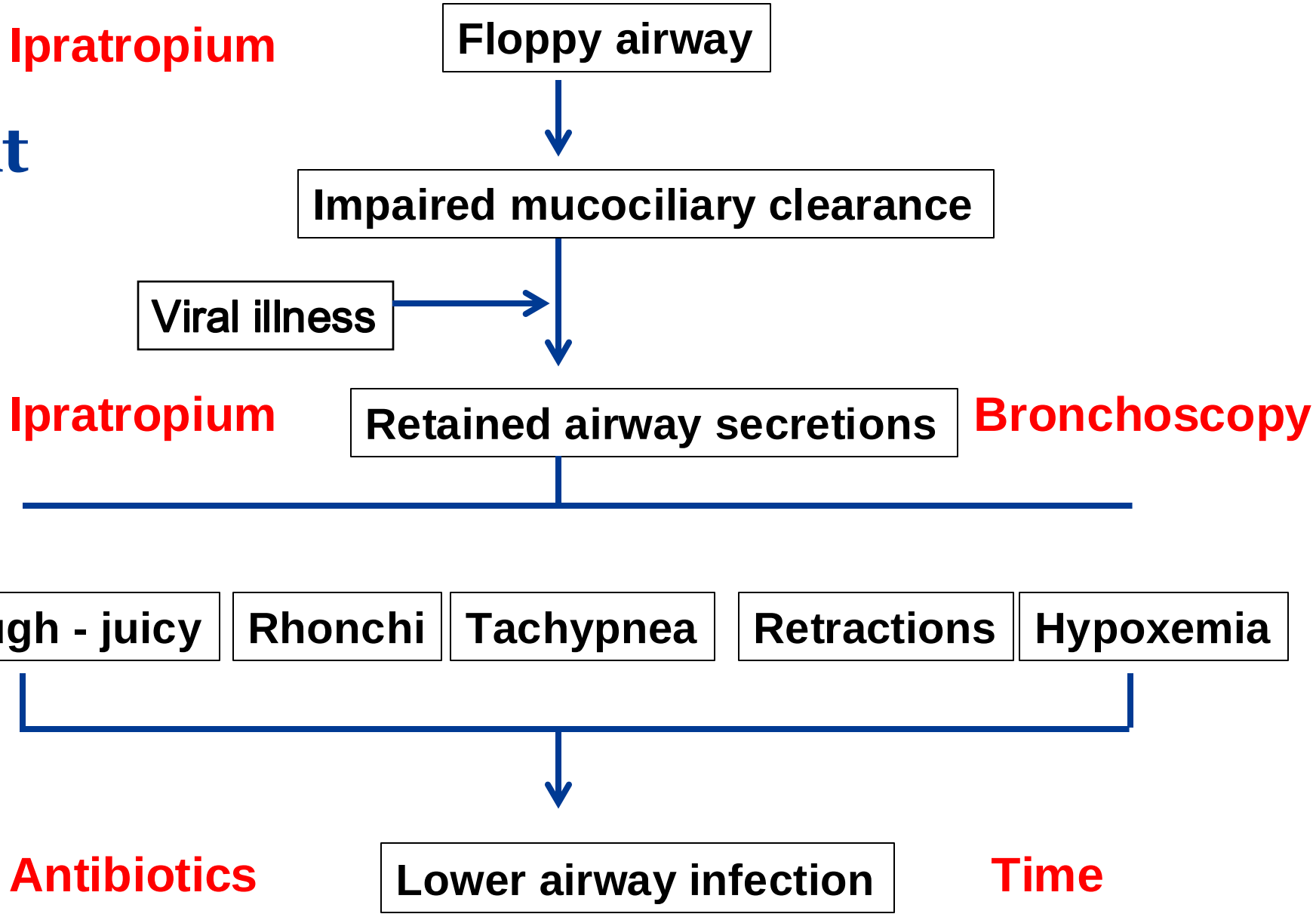
Bronchoscopy

- Diagnostic and/or therapeutic
- Rigid vs flexible





Treatment


Ipratropium
Floppy airway
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Cough - juicy
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Tachypnea
Retractions
Hypoxemia
Antibiotics
Lower airway infection
Time

Protracted Bacterial Bronchitis

Modified diagnostic criteria (PBB-clinical)
Chronic wet cough (>4 weeks)
No symptoms or signs of other causes of wet or productive cough
Resolution of the cough after a 2-week course of an appropriate oral antibiotic (amoxicillin-clavulanate)

- **Persistent infection of the conducting airways**
- **Normal CXR or minor peri-bronchial changes**
- **Not back-to-back colds**
- **Risk factor – impaired mucociliary clearance**

Annals of Thoracic Medicine - Volume 13, Issue 1, January-March 2018

Table 1: Differential diagnosis between protracted bacterial bronchitis and asthma

PBB	Asthma
Persistent wet cough	Dry cough
Cough typically worsens when changing posture	Often nocturnal cough
Children cough so much that they appear to be gasping for breath	Shortness of breath not related to cough
"Ruttle" sound (nonmusical noise generated by secretions in the larger airways that can be felt on the chest)	"Wheeze" sound
Clinical improvement after antibiotics	Clinical improvement after corticosteroids

PBB

- **Frist described 2006**
- **Misdiagnosed as asthma or inadequately treated**

Annals of Thoracic Medicine - Volume 13, Issue 1, January-March 2018

PBB - treatment

2 weeks oral abx targeting

- Streptococcus pneumoniae
- Haemophilus influenza
- Moraxella catarrhalis
  - amox/clav
  - 2nd/3rd gen cephalosporin
  - trimethoprim-sulfamethoxazole
  - macrolide

Shorter courses

- Partial resolution or relapse after a few days off antibiotics

If cough persists after 2wks antibiotics

- An additional 1-2 weeks of abx may be warranted

CHEST 2017; 151(4):884-890

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10-year-old girl with pneumonia

History

No PMH

Cough and intermittent fever x 3 weeks

Mild dyspnea with exertion

Sick contacts at home

No response to amoxicillin, amox/clavulanic acid, azithro

P/E and workup

RR 24, O2 sat 95%

Well hydrated

Bilateral wheeze and rhonchi, crackles LLL

RSV, flu, covid negative

CXR

How would you proceed?

A. Supportive care – viral

B. Order chest CT

C. Fluoroquinolone

D. Refer for bronchoscopy

E. Doxycycline

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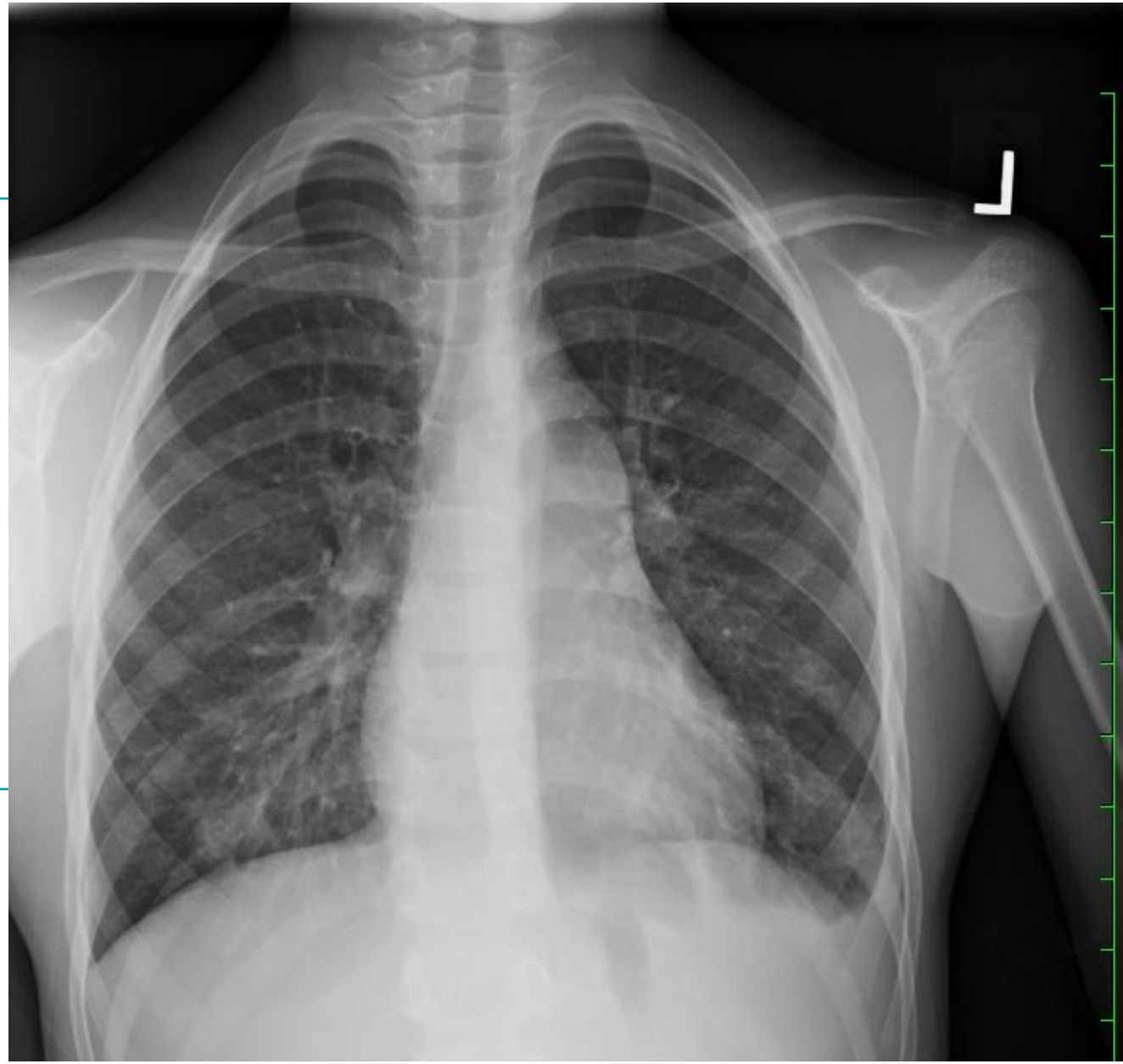


Little aside on doxycycline

3 days of fever to 104

Terrible night sweats

Lethargic

1 cause of pill esophagitis

Doxycycline <u>tablets</u>

Clinical Course

10-day course of levofloxacin and sent mycoplasma serology

- **Increasing macrolide resistance (~10%)**

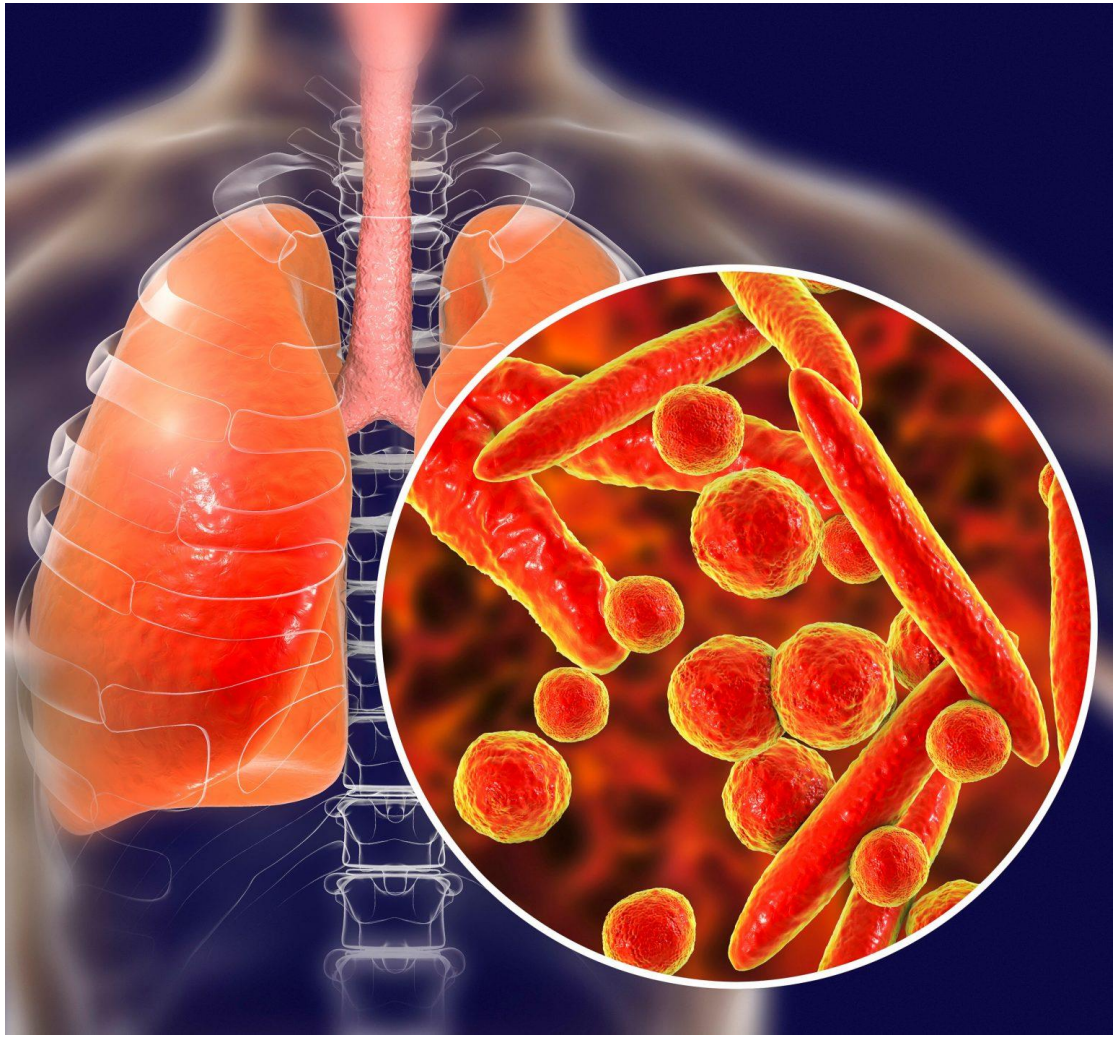
  Antimicrob Agents Chemother. 2022 Apr 19;66(4):e0243221

- **Safe**

  The Journal of Clinical Pharmacology / Vol 56 No 9 2016

Fevers and dyspnea resolved

➢**Mycoplasma serology positive**



Clinical course continued

Cough less, but now dry and worse with exercise

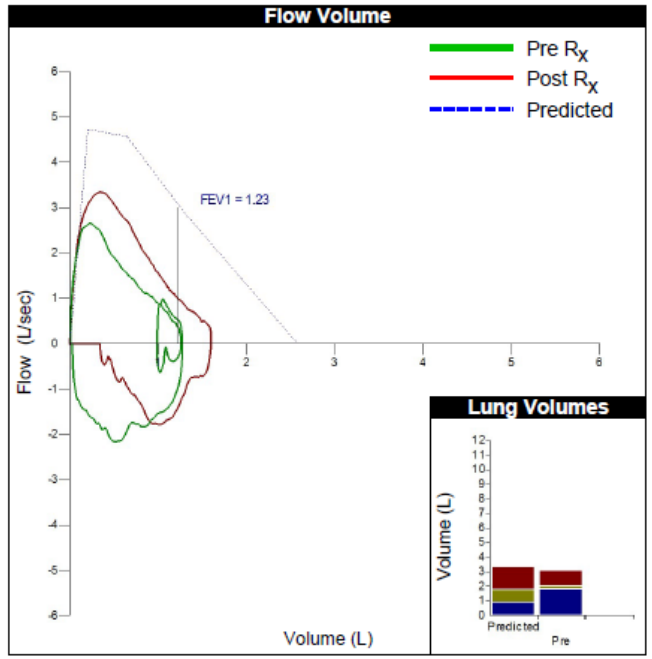
O2 sat 99%, RR 15

Expiratory wheeze bilaterally

Started inhaled corticosteroids

Albuterol as needed

Close follow up



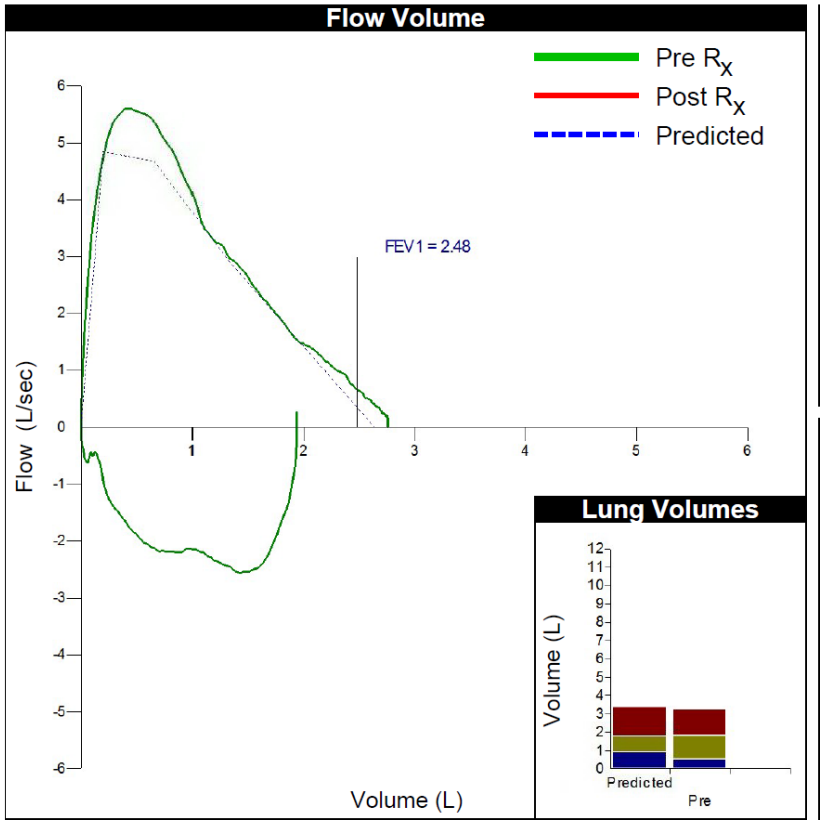
Spirometry (BTPS)

Parameter	Units	Predicted Value	Observed Pre	Observed % Pred	Observed Post	Observed % Pred	Percent Change
FVC	L	2.58	1.27	49	1.60	62	26
FEV1	L	2.24	1.23	55	1.52	68	24
FEV1/FVC	%	86	97	113	95	110	-2
FEF25	L/s	4.57	2.53	55	3.30	72	30
FEF50	L/s	2.90	1.55	53	2.09	72	35
FEF75	L/s	1.45	0.97	67	1.03	71	6
FEF25-75	L/s	2.53	1.48	58	1.89	75	28
PEFR	L/s	4.73	2.66	56	3.51	74	32
FET	sec	----	2.71	----	1.22	----	-55
PIFR	L/s	3.15	2.16	69	1.95	62	-10

3 months later – PFTs normalized

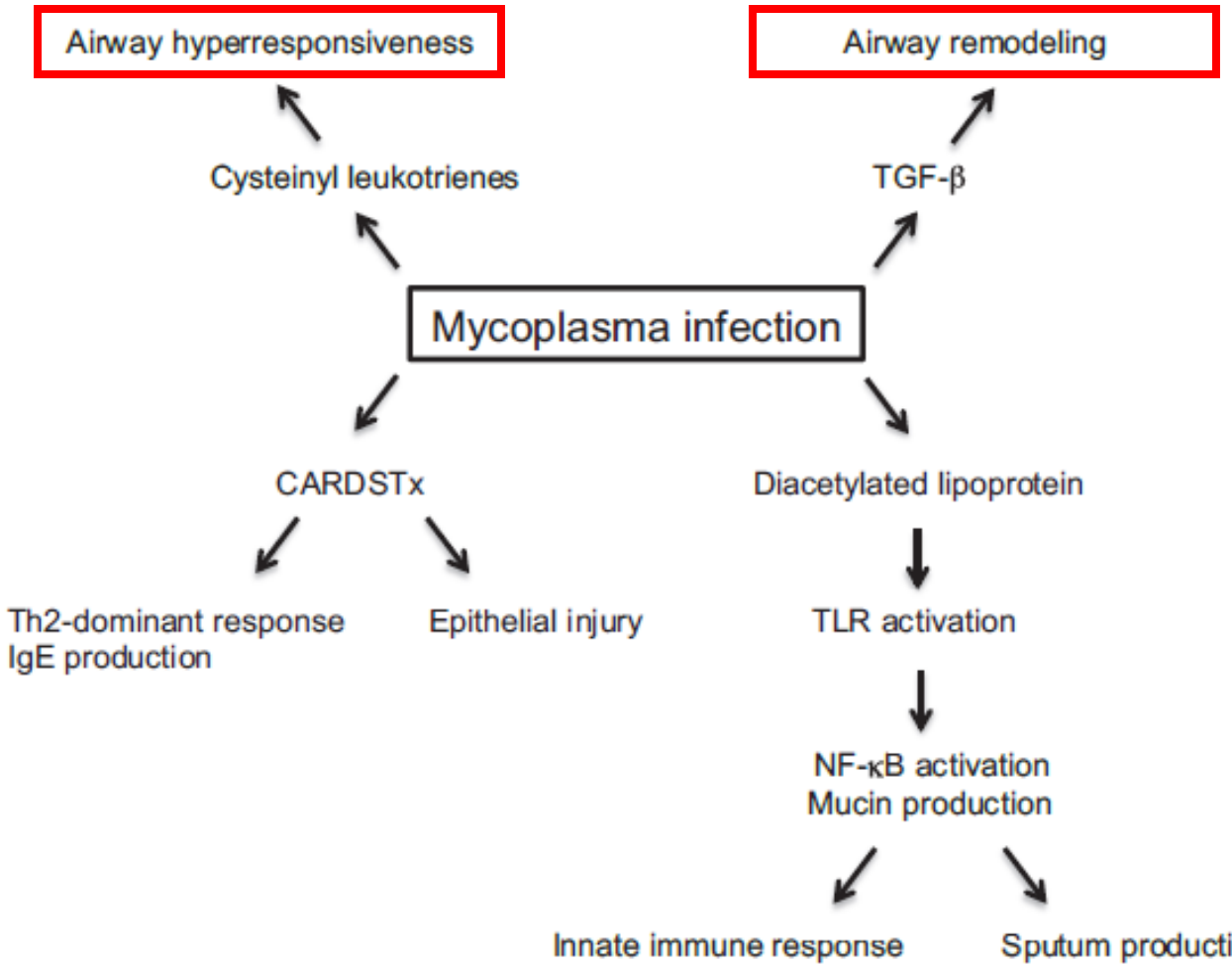
Spirometry (BTPS)

Parameter	Units	Predicted Value	Observed Pre	Observed % Pred
FVC	L	2.64	**2.76**	105
FEV1	L	2.30	**2.48**	108
FEV1/FVC	%	86	**90**	105
FEF25	L/s	4.68	**5.15**	110
FEF50	L/s	2.94	**2.89**	98
FEF75	L/s	1.46	**1.38**	95
FEF25-75	L/s	2.59	**2.54**	98
PEFR	L/s	4.84	**5.90**	122
FET	sec	----	**1.84**	----
PIFR	L/s	3.23	**4.23**	131



12 months after initial infection – weaned off inhaled steroids and has remained asymptomatic

Mycoplasma and reversible airway obstruction



Allergy asthma proc 35:204-210, 2014

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15-year-old male with cough

History

Dry cough with colds – worse at night

Triggers include viral illnesses and exercise

Asymptomatic in between illnesses

Responds well to bronchodilators and oral steroids

3 ED visits last winter

How would you treat this patient?

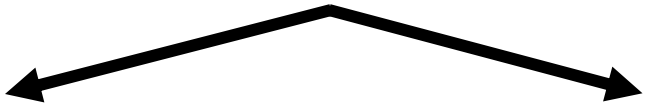
A. Albuterol prn
B. Daily inhaled steroids + albuterol prn
C. Intermittent ICS + albuterol prn
D. Daily ICS/LABA + ICS/LABA when symptomatic (SMART)
E. A different regimen
F. Transfer to your partner's schedule

Asthma Guidelines Background

Episodic exacerbations

Intermittent viral induced cough and wheeze

No controller



Intermittent inhaled steroids **Daily inhaled steroids**

Daily controller

Doubling the dose of inhaled steroids

Intermittent ICS - Is it effective?

TREXA study
5-18y - mild persistent asthma
Intermittent vs daily steroids:

- **More treatment failures**

ICS + albuterol for rescue vs albuterol alone:

- **More effective at reducing exacerbations**
- **Some is better than none?**

Conclusion:
Intermittent ICS may be an effective step-down method, but cannot be recommended over daily ICS

Lancet 2011;377:650

Intermittent ICS - Is it effective?

MIST Trial

- **278 children**
- **12-53 months of age**
- **Recurrent wheezing episodes**
- **Low degree of impairment**

Budesonide for 1 year

- **Intermittent high dose regimen - 1mg BID x 7 days at onset of illness**
- **Low dose regimen - 0.5 mg QD**

N Engl J Med. 2011 Nov 24;365(21):1990-2001

MIST Trial

Conclusion:

Daily low dose budesonide was not superior to intermittent high doses

Might be effective in a certain population

N Engl J Med. 2011 Nov 24;365(21):1990-2001

Intermittent ICS

52 week double blind trial
12 years and up
Mild asthma
3 arms:

- **SABA prn**
- **Budesonide-formoterol prn**
- **Daily inhaled steroids + SABA prn**

Conclusions:
SABA prn < as-needed budesonide–formoterol < daily ICS

N Engl J Med 2018;378:1865-76

Bottom Line

SABA < ICS + SABA prn < Daily ICS

- **Intermittent use of inhaled steroids is effective for certain populations**
- **SABA alone may be good enough for some patients**
- **Tailor therapy to individual patient**

What about doubling dose of inhaled steroids with colds?

Randomized, double-blind, parallel group trial

254 children

- **5-11 years of age**

Mild to moderate persistent asthma

- **At least 1 exacerbation requiring oral steroids within last year**

48 weeks

Low dose inhaled steroids at baseline – fluticasone 44 mcg 2p BID

Continue same dose or use a quintupled dose (220 mcg 2p BID) x 7 days at early signs of loss of asthma control

N Engl J Med 2018; 378:891-901

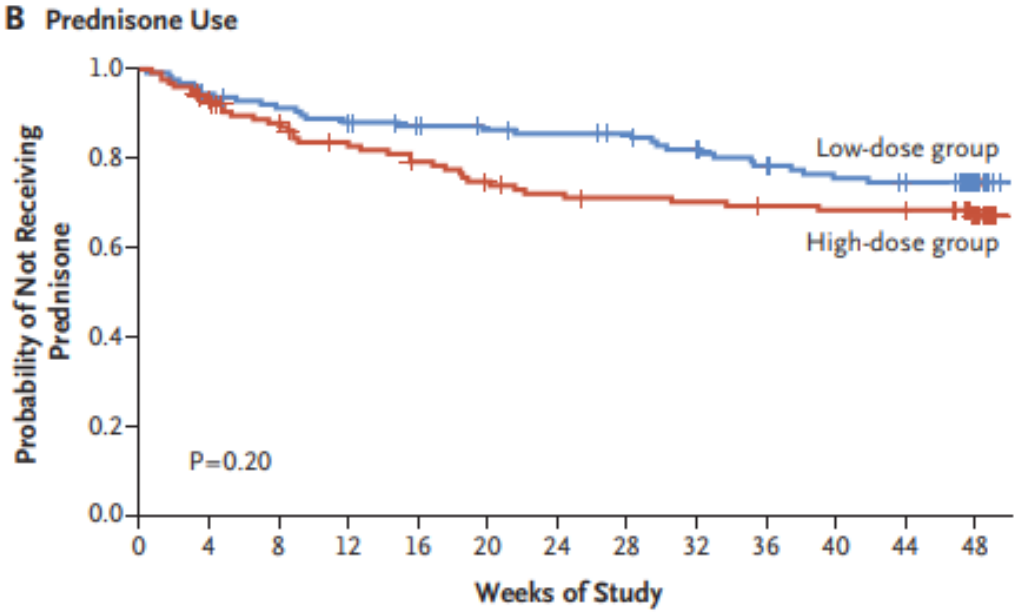
What about doubling dose of inhaled steroids with colds?

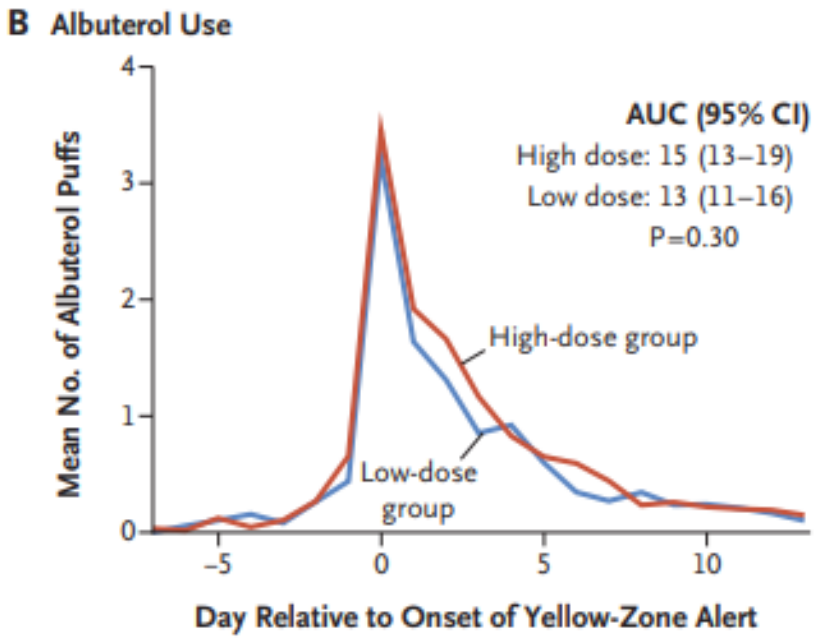
Table 2. Outcomes.*

Outcomes	Low-Dose Group (N=127)	High-Dose Group (N=127)	Treatment Effect (95% CI)†	P Value
Primary outcome				
No. of exacerbations per year (95% CI)	0.37 (0.25 to 0.55)	0.48 (0.33 to 0.70)	1.3 (0.8 to 2.1)	0.30
Secondary outcomes				
No. of emergency department or urgent care visits per year (95% CI)	0.47 (0.31 to 0.72)	0.64 (0.42 to 0.96)	1.3 (0.8 to 2.4)	0.30
No. of hospitalizations	0	4	—	0.12
Equivalent of hydrocortisone exposure — g/yr (95% CI)				
Fluticasone only	10.6 (10.4 to 10.9)	12.2 (11.9 to 12.4)	1.14 (1.10 to 1.19)	
Fluticasone and prednisone	11.1 (10.6 to 11.4)	12.8 (12.4 to 13.2)	1.16 (1.10 to 1.22)	
Growth — cm/yr (95% CI)				
Mean	5.65 (5.48 to 5.81)	5.43 (5.26 to 5.60)	−0.23 (−0.47 to 0.01)	0.06
Effect per 7-day exposure to high-dose regimen				
Overall	—	−0.07 (−0.17 to 0.03)	−0.07 (−0.17 to 0.03)	0.20
According to age group‡				
5–7 yr	—	−0.12 (−0.22 to −0.02)	−0.12 (−0.22 to −0.02)	0.02
8–11 yr	—	0.02 (−0.21 to 0.26)	0.02 (−0.21 to 0.26)	0.80

N Engl J Med 2018; 378:891-901

What about doubling dose of inhaled steroids with colds?





N Engl J Med 2018; 378:891-901

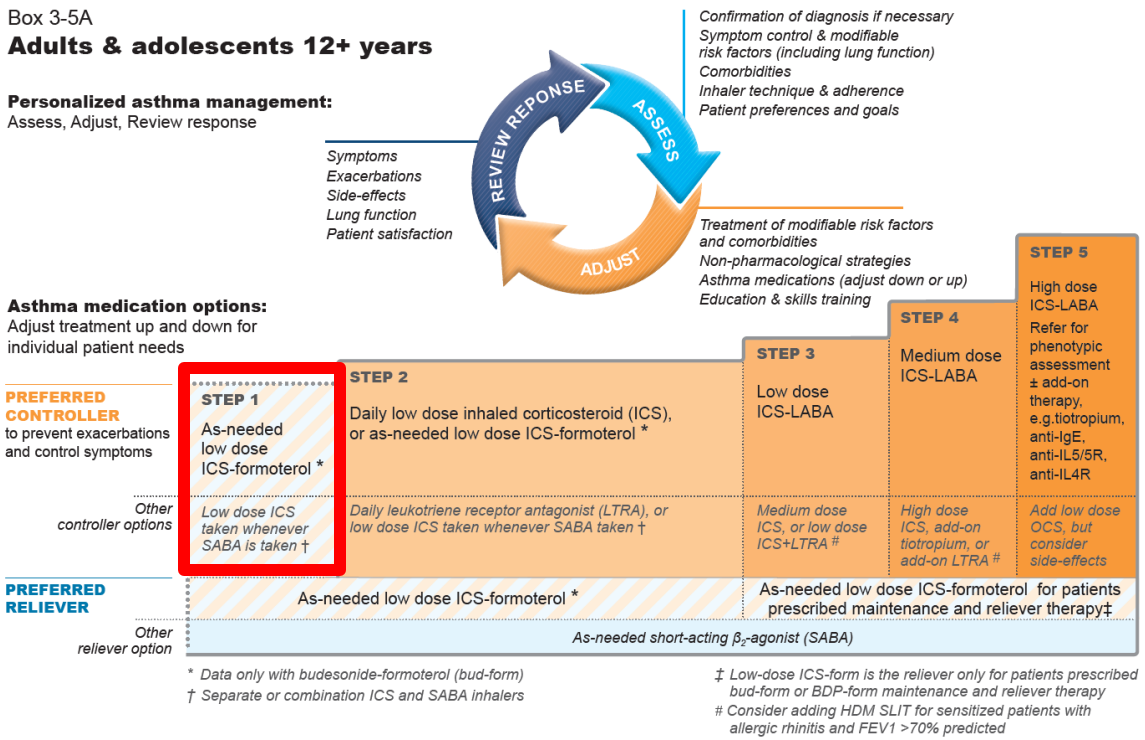
Asthma Guidelines

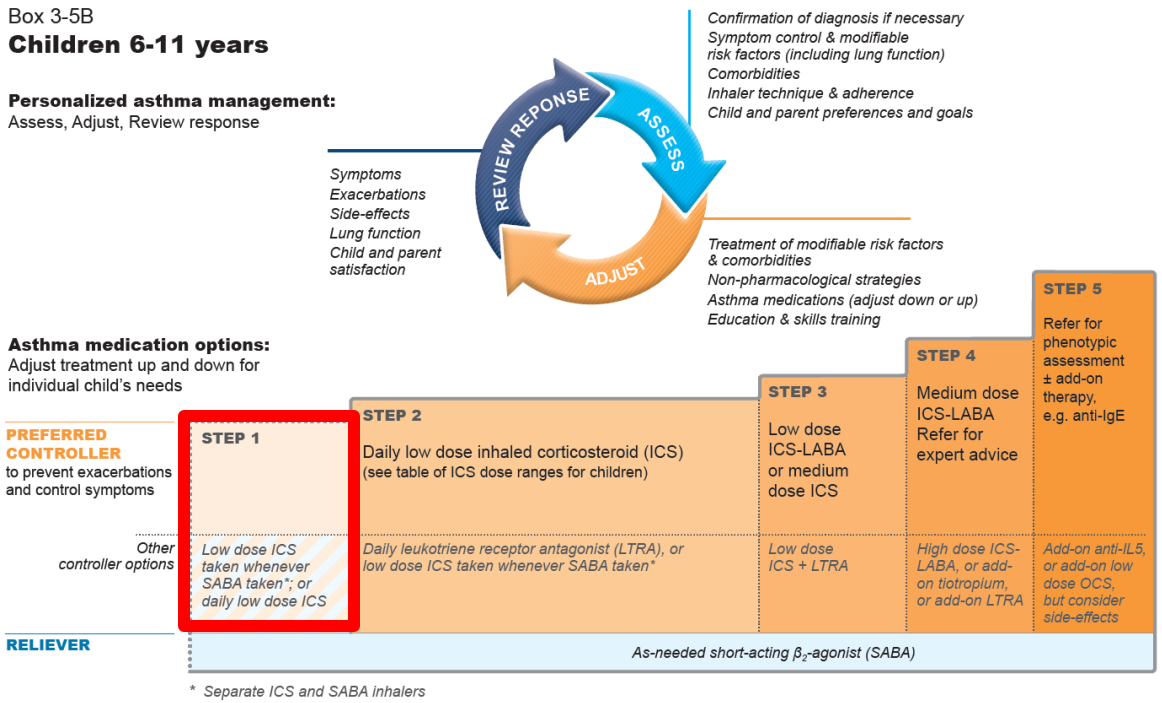
GINA: Fundamental Change – to reduce risk of exacerbations

- Adolescents and adults ≠ short acting bronchodilators alone
- Should receive symptom-driven or daily corticosteroids
- Population-level risk reduction strategy
- Early treatment and improved control – higher remission and lower recurrence
- Potentially prevent airway remodeling – improve lung function long term

Eur Respir J 2019;53:1901046

GINA: Fundamental Change – to reduce risk of exacerbations

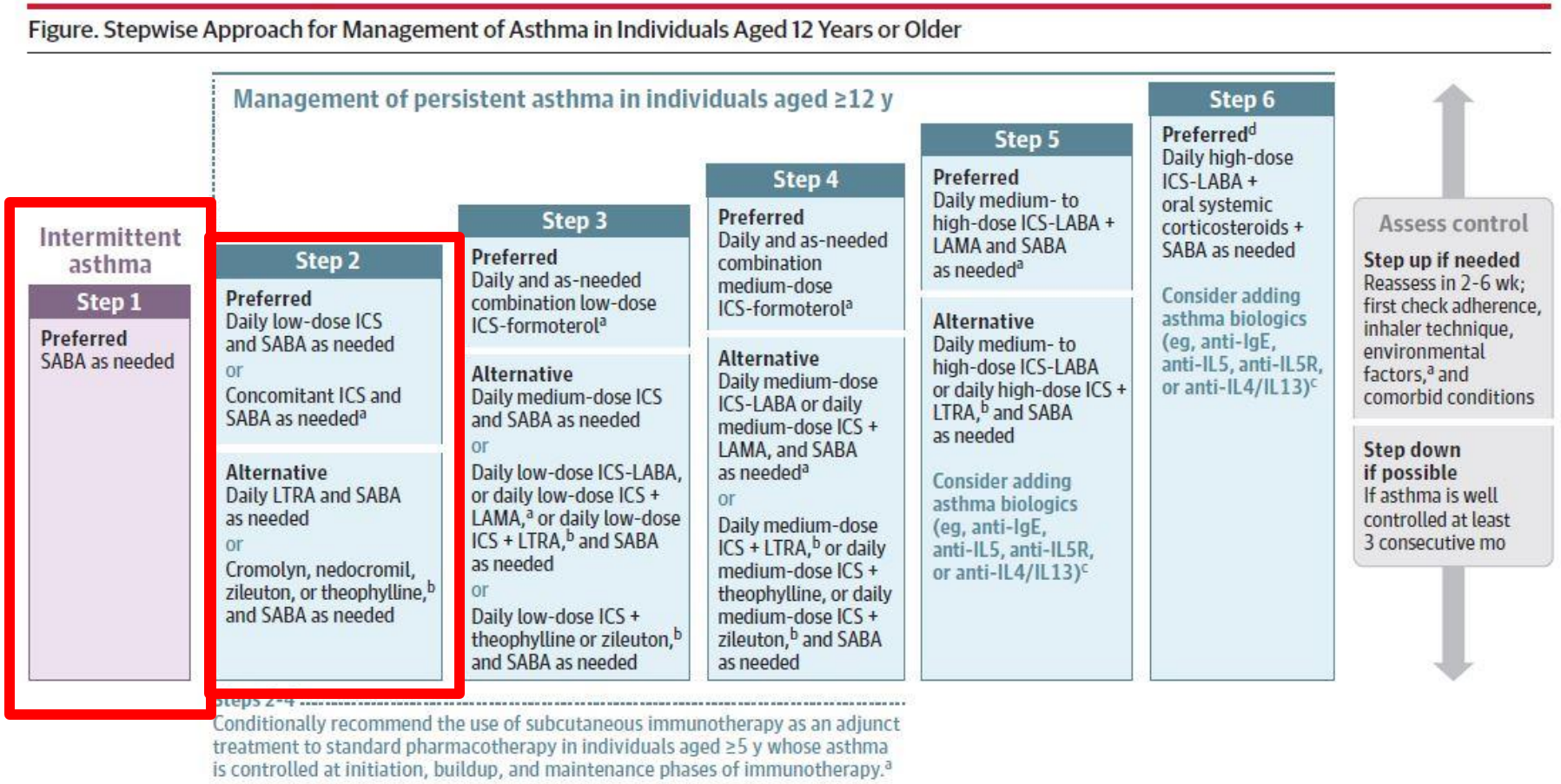




Children ≤ 5: no change

Eur Respir J 2019;53:1901046

2020 Asthma Guideline Update From the National Asthma Education and Prevention Program



JAMA. 2020;324(22):2301-2317

Takeaway

Symptoms	Risk / Impairment	Treatment
Persistent		Daily controller
Intermittent	High	Daily controller
Intermittent	Low	Intermittent ICS*

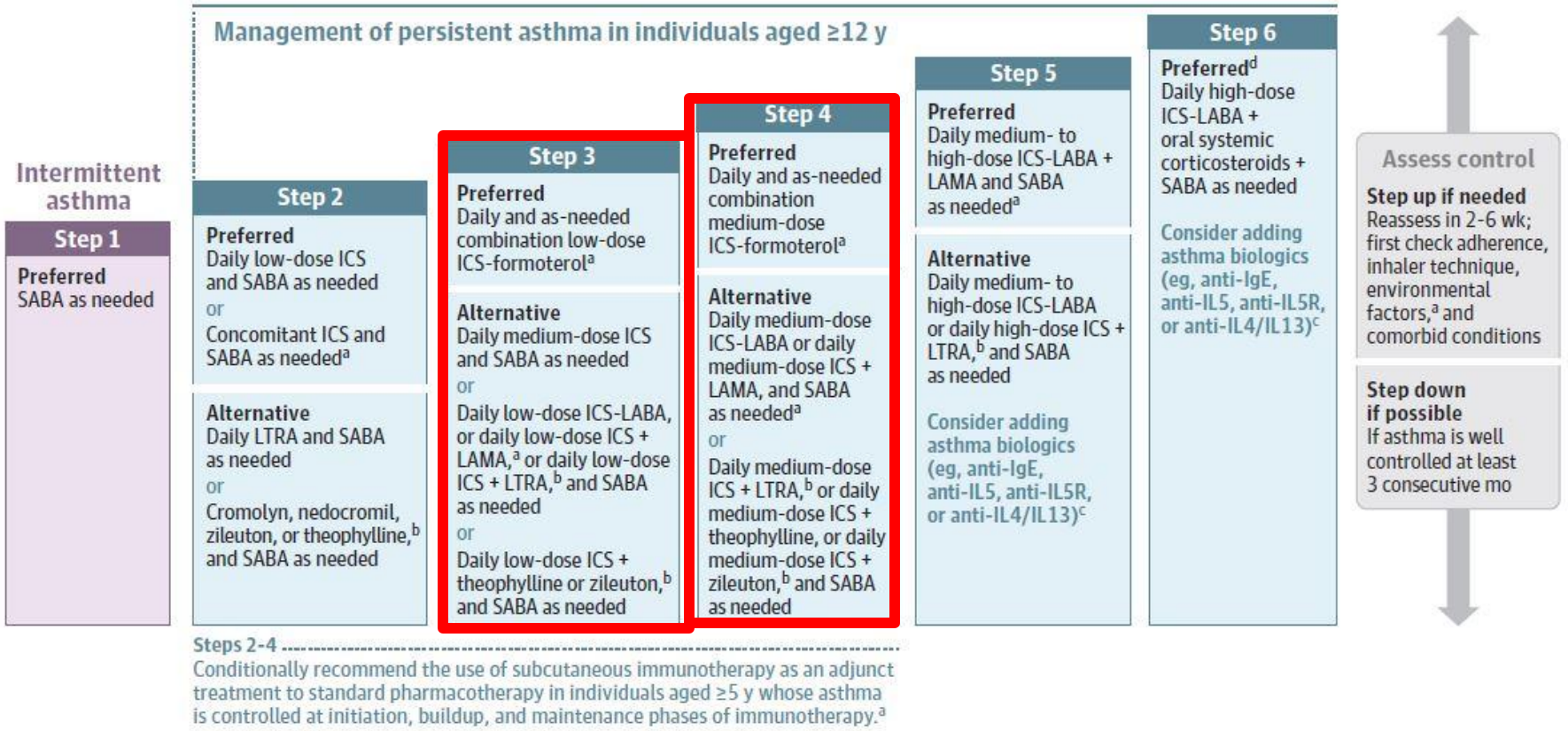
- Low threshold to start daily controller if exacerbations occur
  - This approach does not work for every patient

SMART Therapy

SMART Therapy – not initial therapy

Single maintenance and reliever therapy

Figure. Stepwise Approach for Management of Asthma in Individuals Aged 12 Years or Older



JAMA. 2020;324(22):2301-2317

Indication

Uncontrolled asthma with daily ICS-LABA + as needed SABA

- **Switch to SMART at same maintenance ICS-LABA dose before stepping up therapy**

Onset of action of formoterol = SABA

- **Cannot extrapolate to other ICS-LABA preps**

Take one inhalation whenever needed for symptom relief

Max number of puffs/day – 8 (4-11), 12 (> 12)

Good safety profile

J Allergy Clin Immunol Pract 2022;10:S31-S8

Potential Barriers

- In the US – budesonide-formoterol approved 4 years of age, but SMART not FDA approved at any age
- May need more than 1 inhaler per month
- Might not be covered by insurance
- Overall cost of inhalers

If well controlled on current regimen – don't change

J Allergy Clin Immunol Pract 2022;10:S31-S8

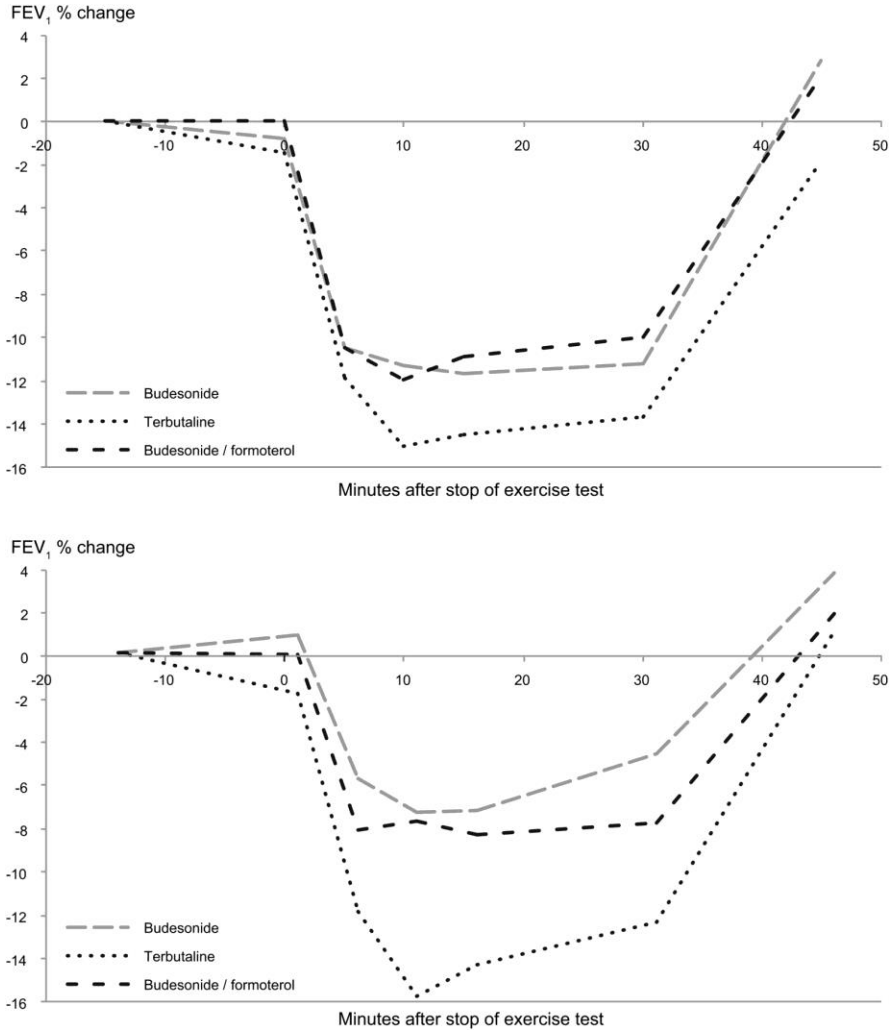
SMART Exercise

Study design

- SABA prior to exercise
- Daily budesonide + SABA prior to exercise
- Budesonide-formoterol prior to exercise?

Thorax 2014;69:130-136

Forced expiratory volume in 1 s (FEV1) before and after a 6 min standardised exercise test on a treadmill, while breathing dry air, before treatment (upper panel) and after 6 weeks of treatment (lower panel) with the three different treatments.



- **Protection against EIB:**
  - **pre-exercise bud-fom > SABA**
- **At 6 weeks:**
  - **pre-exercise bud-fom non-inferior to daily budesonide + SABA**
- **Mild EIB – may not need daily ICS**
  - **Lower dose of ICS**

Nikolaos Lazarinis et al. Thorax 2014;69:130-136

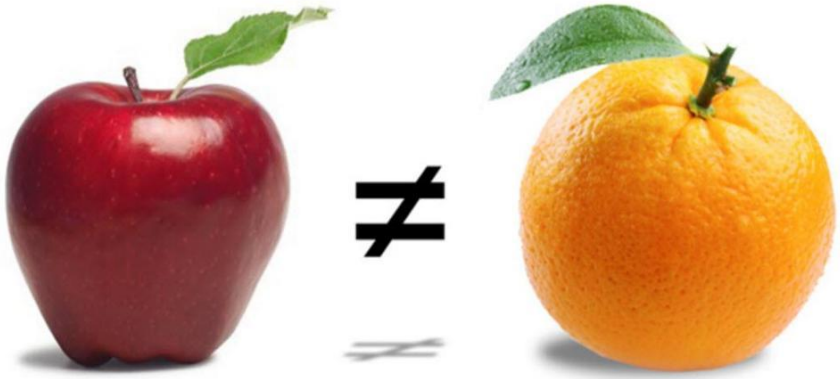
Dexamethasone in the ED

Literature

- **Single dose Dex vs 5 days pred**
  - *Pediatric Emergency Care, Altamimi, 2006*
- **Prednisone (3-5 days) vs dex (1-2 doses) in the ED: equivalent**
  - **Unplanned clinic visit, return ED visit, admission**
  - *Pediatrics. 2014 Mar;133(3):493-9*
- **Prednisone (3 days 1/kg/day) vs dex (1 dose 0.3mg/kg) – equivalent PRAM scores at day 4**
  - *Ann Emerg Med. 2016 May;67(5):593-601*
- **Prednisone (5 days 1.5mg/kg day 1, then 1mg/kg) vs dex (2 doses 0.6mg/kg): no difference asthma sx and QoL at day 7, admission rate, return to ED**
  - *J Pediatr. 2017;191:190*
- **Single dose Dex vs 2 doses**
  - *Pediatric Emergency Care, Martin 2022*

Questions

- What endpoints are most important to your patient population?
  - Primary outcome for many studies was return to ED or unscheduled PCP visit
  - Studies that looked at duration of symptoms
    - Hard to compare dosing between dex and pred
    - Concerning trend for higher return visits
- Longer half-life for Dex – does that translate to longer clinical effectiveness?
- Variability between studies
- Hard question to answer
- How do I put this into practice?



Recommendations – seeing patient in clinic after receiving 1 dose dexamethasone in ED

- No clear cut data to guide us
- Low-risk and asymptomatic: no cough or wheeze, does not need regular use of albuterol – probably no need to give further systemic steroids
- Low-risk and symptomatic: 3 days prednisone (1 mg/kg/day)
- High-risk and asymptomatic: 3 days prednisone (1 mg/kg/day)
- High-risk and symptomatic: 3 days prednisone (2mg/kg/day)

Ask me anything

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