ECHO: When to refer to asthma specialist and biologics overview

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UAB MEDICINE PEDIATRICS

Children's of Alabama

Case

- CC: cough
- HPI: 7yo male with chronic cough, recurrent wheezing with respiratory illness
- Typically doesn't make it through respiratory illness or season change without 7-10 days of cough and wheezing.
- All illnesses typically require an MD visit and oral steroids to improve, frequent antibiotics with illness. Est. 3-4 steroids bursts in the past year
- He has a daily cough with activity and coughs throughout sleep, but doesn't often awaken

History

- PMH: full term, no complications

Respiratory symptoms developed at age 4yo

-No hospitalizations, but 2 ED visits in last year related to asthma symptoms

-No history of recurrent pneumonia or other severe infections

-Tympanostomy tubes placed at 2yo

- +eczema and allergic rhinitis
  - Allergy skin testing at allergist 2 years ago, + tree and weed pollens

- FH: Father with asthma as a child, no other chronic lung disease
- SH: lives with parents, attends school, but misses frequently
- No tobacco exposure, no environmental concerns

Additional History and Exam Findings

- Medications
  - Symbicort 80 2 puffs BID, uses spacer
    - Consistent refills
  - Albuterol nebs prn, used a few times per week
  - Albuterol MDI prn
  - Cetirizine as needed

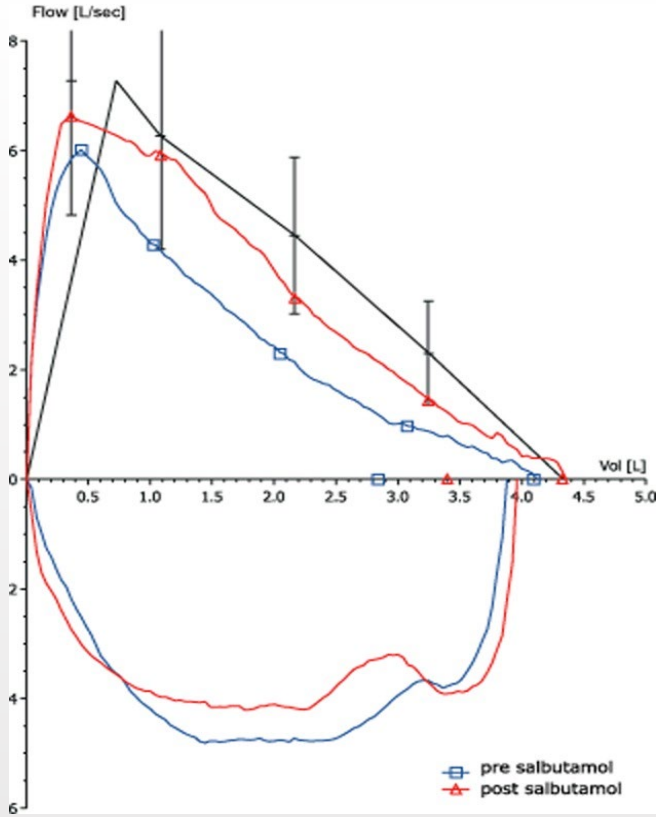
- ROS: + mild intermittent allergy symptoms, picky eater, + eczema

  No snoring, no chronic GI concerns

- Vital signs stable, well nourished
- Physical exam: + dry cough, + eczema on elbows and ankles, remainder of exam normal
- CXR: peribronchial thickening bilaterally, mild hyperexpansion

Additional Diagnostic Evaluation and Management

- Spirometry: obstructive pattern with post-bronchodilator reversibility, FEV1 improved 20%
- FeNO: 70 ppb (elevated)
- Labs: CBC Peripheral Eos 6% AEC is 640
- Upper Resp Serum RAST panel IgE 812
  - Sensitization to dust mites, tree and weed pollens, molds
- What's next?



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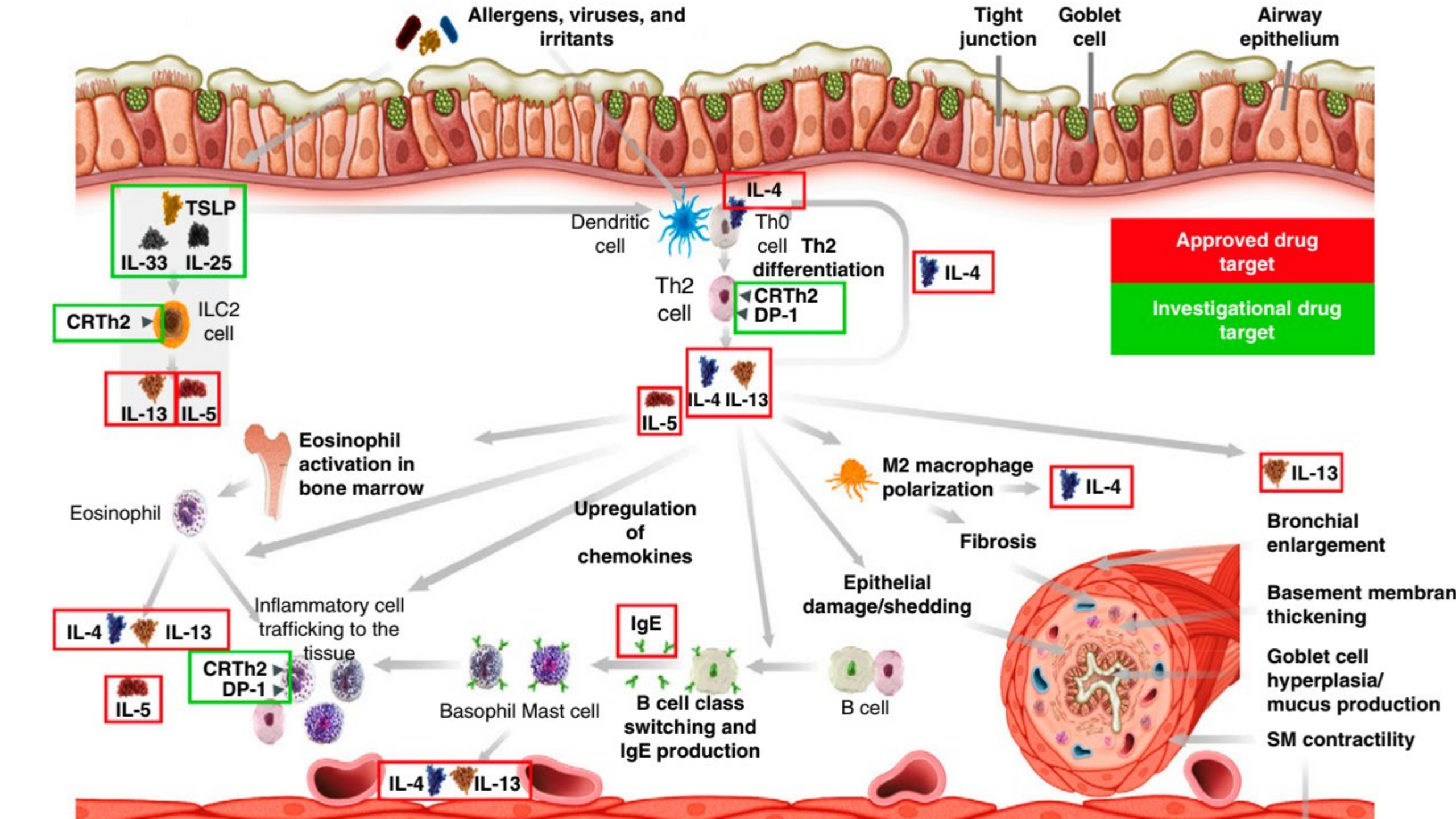
Next steps

- History doesn't point to any other contributing comorbidities
- Increase Symbicort dosing for 4-8 weeks to see if improvement
  - Consider trialing another ICS/LABA combination
- Discuss the timeline to consider biologics

Biologics for Uncontrolled Moderate to Severe Asthma

- Optimize and document asthma medication management and adherence
- Is the patient on chronic oral steroids or frequent oral steroids
- Evaluation for comorbid conditions complete
  - Food allergy, Eosinophilic Esophagitis, GERD
  - Anxiety
  - Vocal cord dysfunction
- Allergy screening: Skin testing, Environmental RAST, and CBC c diff
- Fractional exhaled Nitrous Oxide (FeNO)
- Is home administration an option?


Allergens, viruses, and irritants
Tight junction
Goblet cell
Airway epithelium
TSLP
IL-33
IL-25
IL-4
Dendritic cell
Th0 cell
Th2 differentiation
Approved drug target
Investigational drug target
CRTh2
ILC2 cell
Th2 cell
CRTh2
DP-1
IL-4
IL-13
IL-5
IL-4 IL-13
IL-5
Eosinophil activation in bone marrow
Eosinophil
M2 macrophage polarization
IL-4
IL-13
Fibrosis
Bronchial enlargement
Upregulation of chemokines
Epithelial damage/shedding
Basement membrane thickening
Goblet cell hyperplasia/ mucus production
SM contractility
IL-4 IL-13
Inflammatory cell trafficking to the tissue
IgE
CRTh2
DP-1
IL-5
Basophil Mast cell
B cell class switching and IgE production
B cell
IL-4 IL-13

New hope for severe asthma

- Biologics that target specific inflammatory modulators that have been identified to play a key role in asthma inflammation
- Omalizumab (Xolair®) IgE
- Mepolizumab (Nucala®)- IL-5
- Benralizumab (Fasenra®)-IL-5
- Dupilumab (Dupixent®)-IL-4 and IL-13
- Tezepelumab (Tezpire®)-TSLP

When to refer to asthma specialist?

- History of life-threatening asthma exacerbation
- History of 2 or more hospitalizations in the past 12 months
- Patient with poorly controlled asthma or "asthma" not behaving as asthma
  - Ideally, already on ICS with good technique
- Patient and caregivers need additional chronic disease management education.
- Symptoms are concerning for a comorbid condition that needs further evaluation.
- Evaluation for biologics

What to Refer to Pediatric Pulmonary

- Any uncontrolled OR moderate/severe persistent asthmatic
  - Pulmonary preferred:
    - Concerns for Cystic Fibrosis or Primary Ciliary Dyskinesia
    - Concerns for Aspiration
    - Comorbid congenital heart disease
    - Concerns for airway abnormalities, malacia, vascular ring
    - Concerns for OSA

- Asthma clinic
  - Severe asthma or asthma refractory to standard therapies
  - Recurrent hospitalizations and/or urgent care visits
  - Co-morbid conditions that contribute to difficult disease control
  - Unique asthma self management education needs

  https://www.childrensal.org/services/asthma-clinic/education-and-resources

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What to Refer to Allergy/Immunology

- Any uncontrolled OR moderate/severe persistent asthmatic
  - A/I preferred:
    - Food allergy history/concerns
    - Uncontrolled eczema or seasonal allergies
    - Immunodeficiency concerns
    - Eosinophilic esophagitis
- Anaphylaxis: Any & All
- Eczema: Severe/Uncontrolled – do NOT delay introduction of/eliminate foods!
- Uncontrolled rhinitis despite treatment
- Chronic urticaria that has failed quadruple normal dosing of cetirizine/levocetirizine/fexofenadine