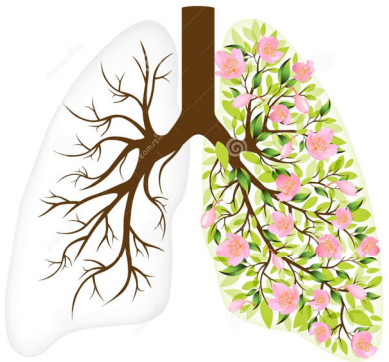

BREATHE EASIER!

Smarter Asthma Care in Primary Practice

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UK Healthcare

DISCLOSURE OF FINANCIAL INTEREST

- I DO NOT HAVE ANY RELEVANT FINANCIAL RELATIONSHIPS OR CONFLICTS OF INTEREST TO DISCLOSE

EDUCATIONAL NEED/PRACTICE GAP

1. Underdiagnosis & Undertreatment
   - Many adults with asthma are missed or not optimally managed
2. OUTDATED Management Practices
   - There were HUGE changes made to the GINA guidelines in the last few years
   - OVERUSE of SABA; underuse of inhaled corticosteroids (ICS)
3. Low Confidence with Updated Guidelines
   - GINA recommendations so new that they are not consistently being applied
4. MISSED Opportunities for Referral
   - Now can use Precision Medicine to treat asthma
   - Phenotypes and targeted treatments available

OBJECTIVES

Upon Completion of this activity, you will be able to:

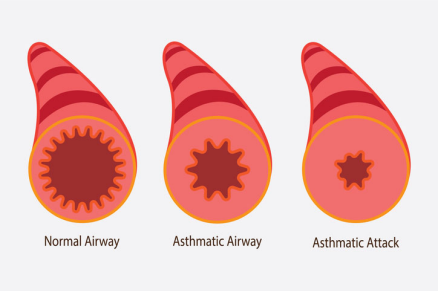
- Feel confident on how to diagnose asthma, but also recognize common challenges in diagnosing and managing adult asthma in primary care
- Recognize updated asthma/GINA guidelines and ease them into your practice
- Implement strategies to optimize patient outcomes, including education, adherence and long term asthma control
- Know when it's time to bring in pulmonary referral backup
- Empower patients to stick to their treatments and breathe easier!

EXPECTED OUTCOME

- YOU'LL FEEL READY TO SPOT ASTHMA SOONER AND TREAT IT SMARTER
- YOUR PATIENTS WILL HAVE FEWER ATTACKS AND MORE GOOD BREATHING DAYS
- YOU'LL KNOW WHEN TO MANAGE IT YOURSELF- AND WHEN TO CALL IN PULMONARY REINFORCEMENTS

OVERVIEW OF THE BASICS:

How do we define asthma?



- Asthma is a heterogenous disease with hallmarks of breathlessness, wheezing, cough, and chest tightness, particularly with triggers
  - Having more than one of the above respiratory symptoms supports asthma diagnosis
  - Triggers: allergens, respiratory infections (esp viral), exercise, cold air, pollutants, stress
- Asthma is a CHRONIC inflammatory disease
  - No, your patient did not “grow out of it” as a child, although periods of remission can occur
- Asthma is a REVERSIBLE airway disease
  - Characterized by airway hyperresponsiveness, variable airflow obstruction, & fluctuating symptoms
  - Because its variable and reversible, may have normal spirometry and/or clear lung sounds the day we see them
- Symptoms are typically worse at night or early in the AM
  - Why is this?? Circadian rhythm, supine positioning during sleep, and decreased innate plasma cortisol levels (reducing bronchodilation & increasing airway hyperresponsiveness)

POLL QUESTION

When you think of asthma, which population comes to mind first?

(There is no wrong answer!)

A. Children

B. Young adults

C. Middle aged adults

D. Older adults

E. All ages equally

When you think of asthma, which population comes to mind first?

CASE STUDY #1

Meet: ‘Albuterol Andre’

CASE STUDY #1

- 28 year old African American male, who presents to your clinic this Spring with wheezing and chest tightness directly related to running outside when exposed to tree pollen
- He has a history of childhood asthma; was on allergy IT “for a few years during elementary school”
- Other than seasonal allergic rhinitis, no other past medical history
- He has a positive family history of asthma- his Mother has asthma and his younger brother has “really bad allergies”
- He has daytime symptoms 2-3 times per week
- No night time awakenings
- VS normal today; SpO2 99% on RA; lungs CTA
- He has an old albuterol rescue inhaler and is just requesting a refill of this today

POLL QUESTION

How should we treat Albuterol Andre today?

A. Add on Singulair and cross your fingers that this will control his wheezing

B. Give the man what he wants- SABA PRN and send him on his way!

C. Give him Symbicort (ICS/LABA) and tell him to use it when needed

D. Give him an oral steroid burst to get him through the Spring

How should we treat Albuterol Andre today?

How Do I Diagnose Asthma?

- Clinical history is KEY
- Presence of variable airflow obstruction via spirometry
  - Ideally done before starting any inhaler therapy
  - Looking for a response in FEV1 by at least 12% AND at least 200 mL after bronchodilator
- If you don't have access to spirometry:
  - You can also do peak flow monitoring
  - *Empiric treatment with ICS containing inhalers
  - Methacholine challenge- a negative test really rules out asthma
- Adjunctive diagnostics:
  - FeNO (Fractional Exhaled Nitric Oxide)- measure of eosinophilic airway inflammation
  - *CBC with diff*- looking at peripheral eosinophils
    - PRO TIP: order during a flare/exacerbation!
  - Total IgE (Immunoglobulin E)- elevated levels can be indicative of allergic asthma
  - RAST testing or referral to Allergy for skin prick testing

POLL QUESTION

How many people feel comfortable ordering and knowing what to do with spirometry or PFTs?

A. Very comfortable- easy peasy!

B. Somewhat comfortable- I order them but may double check results/ask for help

C. Not very comfortable- I order them but unsure how to interpret

D. I rarely order them- I refer out for testing and interpretation

E. What's FEV1 again???

How many people feel comfortable ordering and knowing what to do with spirometry or PFTs?

THE BIG SABA SHAKE UP

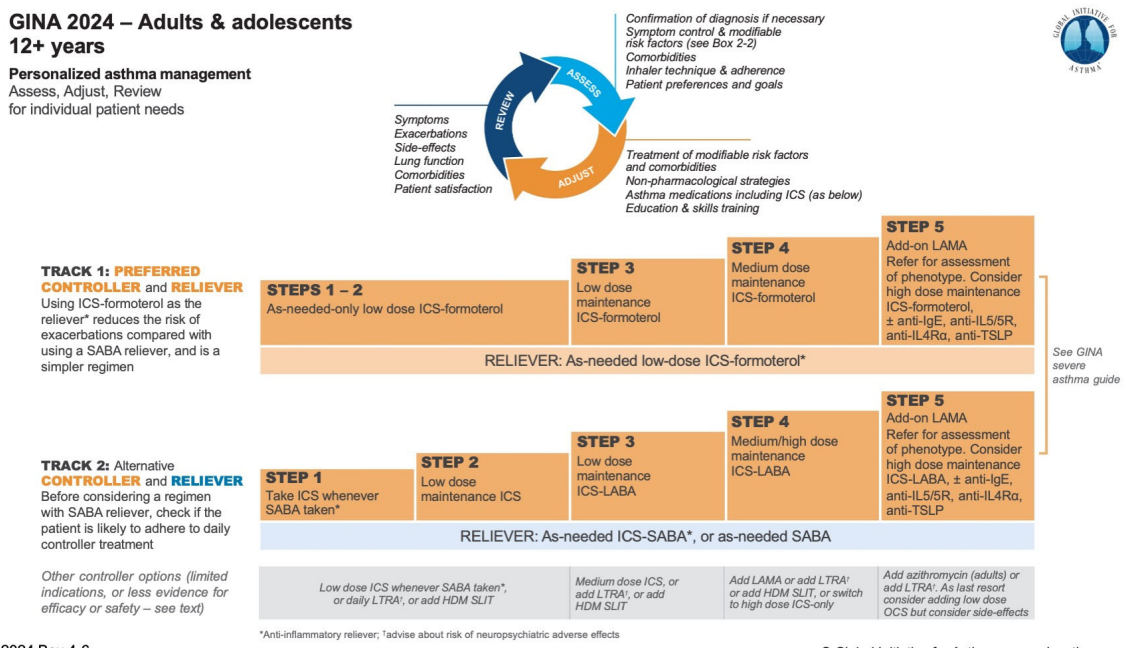
From the GINA 2019 Guidelines

- TREATMENT OF ASTHMA WITH SHORT ACTING BRONCHODILATORS (ALBUTEROL) ONLY IS NO LONGER RECOMMENDED FOR ADULTS AND ADOLESCENTS
- There is evidence that SABA overuse increases risk of exacerbations and death, and that even mild asthma involves inflammation.

THE BIG SABA SHAKE UP
From the GINA 2019 Guidelines

- This update strongly advocated for ICS to be the backbone of both maintenance AND reliever therapy
  - This recommendation is backed by strong evidence that shows this approach reduces exacerbations and improves control
- Really have to do education with your patients on this- they all want the quick fix!
- Try to avoid isolated ICS maintenance inhaler therapy only due to adherence
  - Because this doesn't have an immediate bronchodilator response, this leads to overuse and overreliance of SABA
  - "I'll just do a couple quick puffs of albuterol so I can get back to what I'm doing, I don't really need the other one"

GINA GUIDELINES 2024
Global Initiative for Asthma



GINA 2024 Box 4-6

MART THERAPY (Maintenance and Reliever Therapy)

- A single inhaler with ICS and formoterol for both maintenance AND rescue
  - LABA + ICS
  - **FORMOTEROL** has to be used because it is quick acting
  - Most common are *Symbicort/Breyna, Dulera
  - Health literacy and insurance both play a big role in this!
- Another form or idea of this is through the use of AirSupra, which is even newer
  - This is slightly different, SABA + ICS (budesonide)
  - First ever FDA approved rescue inhaler with both a bronchodilator and anti-inflammatory component
  - Approved for adults 18+ with asthma
  - Use as needed for symptoms
  - This is rescue AND prevention in one to two puffs!
  - Just started using myself in practice and have gotten great feedback from my patients

BACK TO CASE STUDY #1

Albuterol Andre

Management Plan:

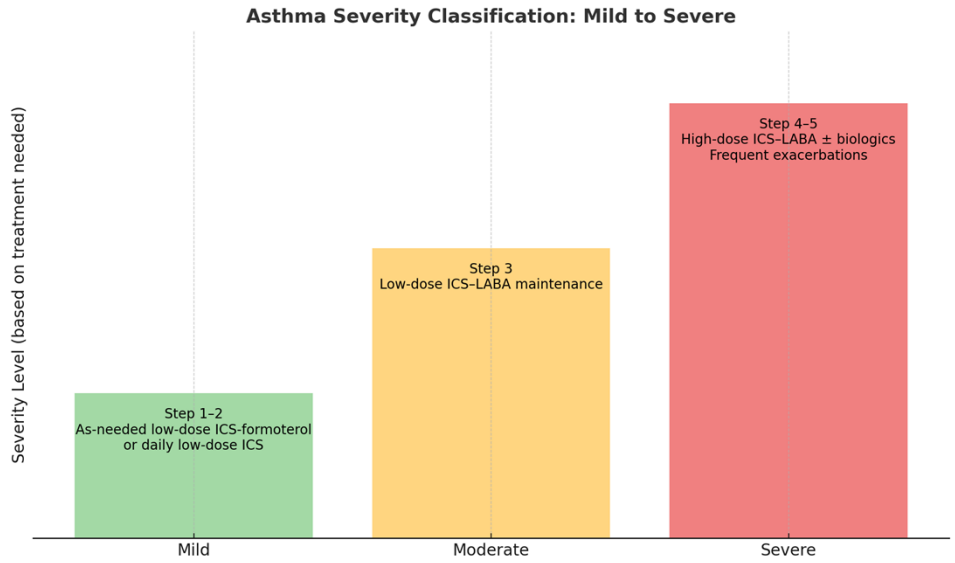
- Introduce MART therapy
  - Perfect patient for this!
- What does that look like?
  - Prescribe Symbicort 80/4.5 mcg (low dose ICS/LABA) 2 puffs PRN, up to 12 puffs per day!
  - Now addressing both symptomatic relief AND underlying inflammation
- Educate on inhaler technique
  - Spacers are amazing if available or patient willing to purchase
- Treat allergic rhinitis
  - Hard to achieve allergic asthma control when upper airway is inflamed
  - You start him on either daily antihistamine or daily intranasal corticosteroid (based on pt preference and/or chief complaint of allergy symptoms) for the remainder of the Spring allergy season

Follow up

- Return to clinic in 4-6 weeks to assess response and see if we need to STEP up therapy
- If still uncontrolled, let's say symptoms increased in frequency, then I would consider further workup with labs, spirometry, etc.
- BUT he's doing great ☺, using MART therapy 1-2 times per week; continue current plan

HOW SEVERE IS YOUR PATIENT'S ASTHMA, REALLY?

- Most recent guidelines move away from classifying their symptoms as mild, moderate severe from the start
- More related to what step of therapy achieves control
- You can only really know in hindsight what their degree of severity is



RULE OF 2's

- **IF THEY ARE HAVING…..**
  - Symptoms more than 2 days per week
  - Night time awakenings more than 2 times per month
  - Albuterol use more than 2 times per week (other than before exercise)

…….

THEN THEY ARE UNCONTROLLED!

- Step UP therapy

WHAT ELSE CAN I DO TO GET MY ASTHMA PATIENTS CONTROLLED?

- Always personalize this to the patient!
  - Add on LAMA (Spiriva 1.25 mcg 2 puffs daily is approved for asthma use)
  - Add on LTRAs (Montelukast/Singulair most common)- go over black box warning of neuropsychiatric side effects
  - Add on Allergy IT (referral to Allergy) or good allergy regimen (antihistamine, daily intranasal steroid or antihistamine, LTRA)
  - Chronic azithromycin can be helpful in some patients
  - Don't forget Non-Pharm interventions:
    - Smoking cessation, including vaping, THC
    - Avoiding allergens/exposures
    - Weight reduction
    - Physical activity/pulmonary rehab
    - Avoiding triggers- can use air purifiers, HEPA filters
    - Vaccinations: Flu, Covid-19, Prevnar-20, RSV
    - Manage comorbidities: GERD, OSA, AR, anxiety/depression, etc

IMAGING IN ASTHMA

- In reality, you don't need chest imaging all that often with asthma!
  - Imaging is helpful with mimickers of asthma, atypical presentation
  - Consider CT chest if looking for comorbidities – emphysema, bronchiectasis, ABPA
  - CT chest if hemoptysis, unintentional weight loss, other red flag symptoms
  - CT sinuses if frequent sinus infections, nasal polyps, history of sinus surgery

The GREAT Asthma Mimickers

- COPD (especially with smoking history)
- Vocal cord dysfunction (VCD)
- GERD related cough or bronchospasm
- Eosinophilic bronchitis
- Obesity related dyspnea
- CHF (especially if wheezing)
- Upper airway obstruction (tumor, thyroid goiter, foreign body)
- Chronic sinusitis/Post nasal drip
- Medication induced cough (ACE inhibitors)
- Anxiety/panic disorders

CASE STUDY #2

Meet: BREATHLESS Brenda

WHEN TO SEND TO ED

- Increased work of breathing
  - Accessory muscle use, nasal flaring, tripod positioning
  - *Unable to speak in full sentences
- SpO2 <90% on room air
  - (if this is not the norm for them)
- If they use a peak flow meter, less than 50% of personal best and not improving with treatment
- Minimal or no response to SABA/nebulizer treatments
- Altered mental status or signs of fatigue/lethargy
  - Confusion, drowsiness, falling asleep
- If history of prior ICU admission/intubation or frequent ED visits for exacerbations, send them sooner.

Okay, back to Breathless Brenda…

- This is a 45 year old Caucasian female who presents to your clinic with persistent cough, chest tightness with activity, and is frustrated because she can't do things she used to do!
  - Symptoms started around 6 months ago, worsened after having mild COVID-19
  - She describes the feeling of "just being unable to take a deep breath"
  - She has been seen in the ED twice over the past year for "lingering bronchitis" that required oral steroids; tells you she was "almost intubated" once
  - She has already been given an ICS by UTC. She is using Flovent 110 mcg 2 puffs BID and "can't really tell a big difference"
  - Someone gave her an albuterol rescue inhaler after an ED visit and it "helps a little"; she is using every day
  - She has also noticed loss of smell and feels her nose is "always stopped up"; hx of sinus surgery 10 years ago
  - She has a minimal former smoking history; smoked for 10 years, ½ PPD, prior to her first baby, and quit cold turkey after that (5 pack year history)
  - She tells you: "I can't have asthma, I didn't have asthma in childhood!"

CASE STUDY #2

Diagnostics:

- You order spirometry:
  - This shows equivocal obstruction FEV1/FVC ratio just barely above LLN
  - Her FEV1 is low at 69% predicted however she only had an equivocal response to bronchodilator with an increase in FEV1 of 180 mL/11% predicted.
    - kind of an unclear test!
- You order some routine bloodwork:
  - Normal CMP, CBC with slightly elevated WBC of 10.6 and elevated absolute eosinophil count of 600. You also order an IgE (compliments of this presentation!) and that is elevated to 400.

Treatment:

- You feel pretty confident that this patient needs at least Step 4 therapy of the GINA guidelines, so you stop Flovent 110 mcg and prescribe Dulera 100/5 mcg 2 puffs BID (this is a medium dose ICS/LABA) and add on Singulair for the sinus symptoms and IgE.

CASE STUDY #2

- She comes back in your clinic in 2-3 months for follow up, after another ED visit with exacerbation…

At this point, you refer to us!

- We order more specialized testing:
  - FeNo: 82 (yikes!) Want this less than 25
  - Type 2 high asthma inflammation is confirmed
  - Repeated full PFTs when off of inhalers for 24 hours and had mild airway obstruction with a significant response to bronchodilator (FEV1 improved by 500 mL/23%!). Now have official objective data to support asthma.
  - Didn't have to repeat labs, thanks to you!
  - Ordered chest CT without contrast to rule out comorbidities, no emphysema despite smoking history
  - Ordered CT sinuses same day as above, which showed nasal polyps. ENT Referral was initiated.
- Ultimately… this patient required
  - high dose Dulera (200/5) mcg 2 puffs BID + LAMA (Spiriva Respimat 1.25 mcg 2 puffs QD)
  - Air Supra PRN
  - Dupixent 600 mg loading dose, followed by 300 mg SQ every two weeks
    - This was chosen due to her clinical history, comorbidities, and biomarkers (IgE and eos)
    - This drastically improved both her asthma control AND her nasal polyps (along with daily Flonase)
  - Pulmonary rehab to combat physical deconditioning from where she had several months uncontrolled
  - Eventually we are able to step down treatment of her maintenance inhalers because she becomes so controlled ☺

WHEN TO REFER TO PULMONARY

- **Diagnostic uncertainty**
  - Atypical presentation, poor response to initial asthma therapy
  - Need for advanced diagnostics (full PFTs, methacholine, nitric oxide)
- **Severe or difficult to control asthma**
  - Requires GINA step 4-5 treatment
  - Persistent symptoms or frequent exacerbations despite high dose ICS/LABA + LAMA
- **Frequent exacerbations and steroid bursts**
  - ≥ 2 courses of oral corticosteroids in the past year
    - Even 4-5 LIFETIME courses of oral steroids increase cumulative risk of osteoporosis, diabetes, cataracts, heart failure, pneumonia (Price et al, J Asthma Allergy, 2018.)
  - ≥ 1 ED visits/hospital admission for asthma
- **High risk features**
  - History of ICU admission or intubation for asthma
  - Markedly reduced lung function (FEV1 < 60% predicted)
- **Advanced Phenotyping & Biologic Therapy**
  - Suspect eosinophilic or Type- 2 high asthma
  - Consider or need for biologics
- **Complex Comorbidities**
  - Uncontrolled rhinosinusitis, nasal polyps, severe obesity, COPD overlap, VCD

PRECISION MEDICINE

Phenotyping Asthma

- This is completely reshaping how we think and care for asthma patients!
- Asthma is no longer just put into one big bucket
- More focused treatments

ASTHMA PHENOTYPES:

- Allergic asthma
- Non allergic asthma
- Cough variant asthma
- Adult onset (eosinophilic) asthma
- Asthma with obesity
- Asthma with persistent airflow limitation (airway remodeling)
- Asthma/COPD overlap

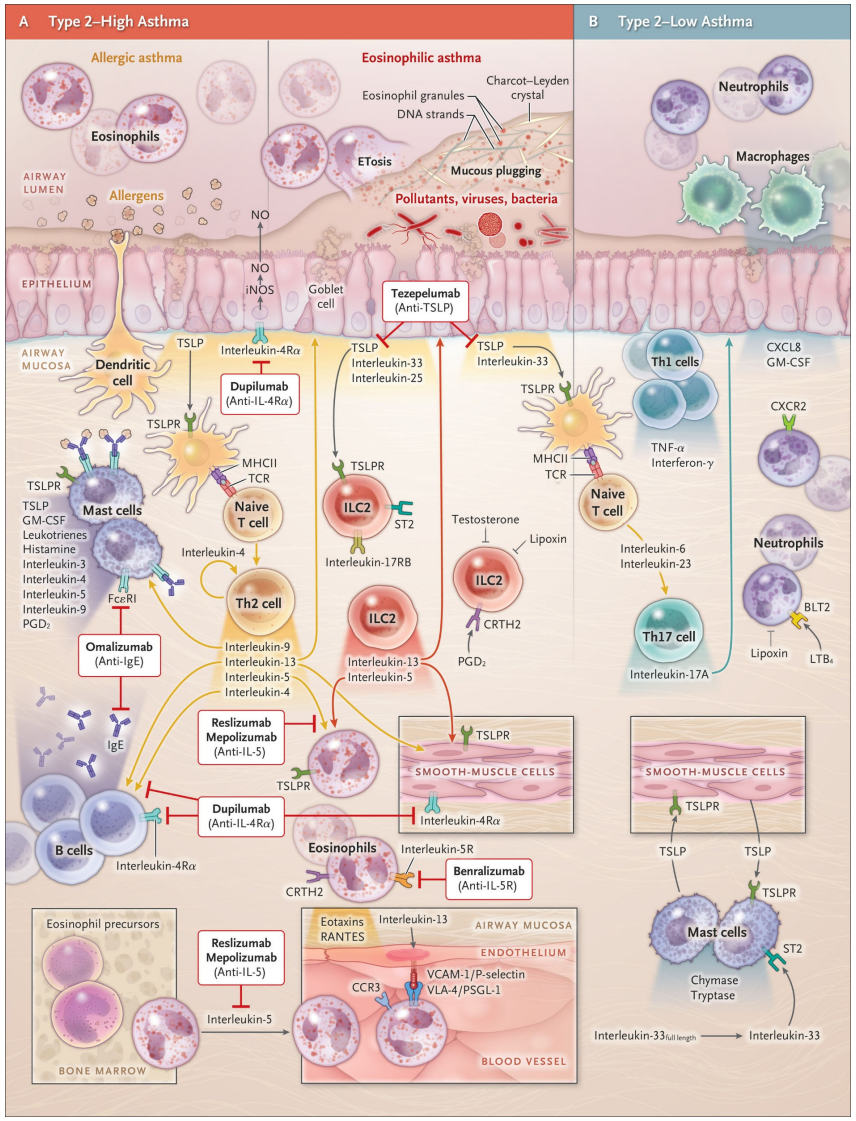
HOW WE FURTHER CHARACTERIZE ASTHMA

Type 2 High Inflammation

- Eosinophil dominant inflammatory cell
- High FeNO (> 50)
- VERY steroid responsive
- ICS cornerstone of management
- Biologics truly change these patients lives

Non Type 2 Inflammation

- Neutrophilic inflammatory cells
- Low FeNO (<25)
- Poor steroid response
- Bronchodilators (LAMA/LABA) more useful. Macrolide therapy can come into play as well.
- May be associated with obesity, smoking, and environmental pollutants
- Just came out with a biologic that targets this type!


A Type 2–High Asthma
B Type 2–Low Asthma
Allergic asthma
Eosinophilic asthma
Eosinophils
Charcot–Leyden crystal
Eosinophil granules
DNA strands
ETosis
Mucous plugging
AIRWAY LUMEN
Allergens
Pollutants, viruses, bacteria
Neutrophils
Macrophages
NO
NO
iNOS
EPITHELIUM
Goblet cell
Tezepelumab (Anti-TSLP)
AIRWAY MUCOSA
Dendritic cell
TSLP
Interleukin-4Rα
Dupilumab (Anti-IL-4Rα)
TSLPR
MHCII
TCR
Naive T cell
Mast cells
TSLP
GM-CSF
Leukotrienes
Histamine
Interleukin-3
Interleukin-4
Interleukin-5
Interleukin-9
PGD2
FcεRI
Omalizumab (Anti-IgE)
IgE
Interleukin-4
Th2 cell
Interleukin-9
Interleukin-13
Interleukin-5
Interleukin-4
Reslizumab Mepolizumab (Anti-IL-5)
Dupilumab (Anti-IL-4Rα)
B cells
Interleukin-4Rα
TSLP
Interleukin-33
Interleukin-25
ILC2
ST2
Interleukin-17RB
Testosterone
Lipoxin
ILC2
CRTH2
PGD2
ILC2
Interleukin-13
Interleukin-5
TSLPR
SMOOTH-MUSCLE CELLS
Interleukin-4Rα
Eosinophils
Interleukin-5R
CRTH2
Benralizumab (Anti-IL-5R)
Eosinophil precursors
BONE MARROW
Reslizumab Mepolizumab (Anti-IL-5)
Interleukin-5
Eotaxins
RANTES
Interleukin-13
AIRWAY MUCOSA
ENDOTHELIUM
VCAM-1/P-selectin
VLA-4/PSGL-1
CCR3
BLOOD VESSEL
TSLP
Interleukin-33
TSLPR
MHCII
TCR
Naive T cell
Th1 cells
TNF-α
Interferon-γ
CXCL8
GM-CSF
CXCR2
Neutrophils
BLT2
Lipoxin
LTB4
Interleukin-6
Interleukin-23
Th17 cell
Interleukin-17A
SMOOTH-MUSCLE CELLS
TSLPR
TSLP
TSLP
TSLPR
Mast cells
ST2
Chymase
Tryptase
Interleukin-33full length
Interleukin-33

THIS IS WHERE ASTHMA BIOLOGICS COME INTO PLAY

- These medications truly are **life changing**!!
- A great reason to refer to Pulm
- Biologics are key players in Type 2 high inflammation pathways and inflammatory mediators:
  - IgE: allergic response and mast cell activation (Xolair)
  - IL-5: production and survival of eosinophils (Fasenra and Nucala)
  - IL-4 and IL-13: airway hyperresponsiveness, mucous production, and can potentiate IgE synthesis (Dupixent)
  - TLSP- pathway that affects multiple downstream pathways
    - Tezspire if the only biologic approved for TH 2 low phenotype
- Biologics decrease steroid exposure, optimize long term lung function and prevent decline, and improve day to day symptoms
- A downside: biologics are costly, difficult to obtain without specialty pharmacy, no clearly defined off ramps
- A little bit of a science when picking the right one; sometimes there is more than one right answer!
- A lot of the time the patient will have another comorbidity that the biologic can treat simultaneously (nasal polyps, EOE, atopic dermatitis, etc)
- BONUS: Dupixent was just approved for a new indication for COPD with eosinophilia phenotype

POLL QUESTION

After today's talk, how confident do you feel in managing adult asthma?

A. Very confident!
B. Somewhat confident
C. Still have some questions…
D. Calling pulmonary immediately!

After today's talk, how confident do you feel in managing adult asthma?

TAKEAWAYS!

- ALWAYS order CBC with diff, especially if taken during an exacerbation!
- Check inhaler technique
  - Very simple but very important!
- Don't just treat their exacerbation with systemic steroids- they need treatment IN BETWEEN these flares! This can be disguised as "bronchitis"
- SABA only use in the past! Make sure you are treating with an ICS/formoterol containing maintenance inhaler as first line therapy, even for mild asthma
- If you do send a patient for spirometry and it is normal, this does NOT mean they are in the clear for an asthma diagnosis
- During follow ups, REVIEW, ASSESS, ADJUST!
  - Don't forget to consider stepping down therapy too

LET'S END WITH A LITTLE RESOURCE TOOL...

- Here are some high quality, freely available resources to teach proper inhaler technique
  - 1. American Lung Association- "How to Use Asthma Medicine Devices"
    - Link: https://www.lung.org/lung-health-diseases/lung-disease-lookup/asthma/treatment/devices
  - 2. National Jewish Health- "Inhaled Medication Instructional Videos"
    - Link: https://www.nationaljewish.org/conditions/medications/asthma-medications/devices/instructional-videos
  - 3. International Primary Care Respiratory Group (IPCRG)- "7 Steps to Using your Inhaler"
    - Link: https://www.ipcrg.org/resources/inhaler-resources

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Questions??