NEW ASTHMA INSIGHTS AND HOW TO OVERCOME CHALLENGES

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PROFESSOR, RUTGERS SCHOOL OF HEALTH PROFESSIONS

CO-OWNER A & T LECTURES

LEARNING OIBJECTIVES

- Summarize Asthma Overview & Physiology
- Explore Updated Asthma Guidelines
- Examine Treatment Troubles & Overcoming Them
- Compare & Contrast Biologics and Bronchial Thermoplasty
- Review Conclusions
- Provide Additional Resources

Asthma

25 MILLION Americans diagnosed

1 in 10 CHILDREN

$80 BILLION annual costs

3,168 DEATHS annually

75% higher for black persons than white persons

13.8 MILLION missed school days per year

#1 reason kids miss school

14.2 MILLION missed work days per year

3 in 5 limit physical activity

71% MISUSE inhalers

1 in 5 CANNOT AFFORD medications

AllergyAsthmaNetwork.org

Allergy & Asthma NETWORK

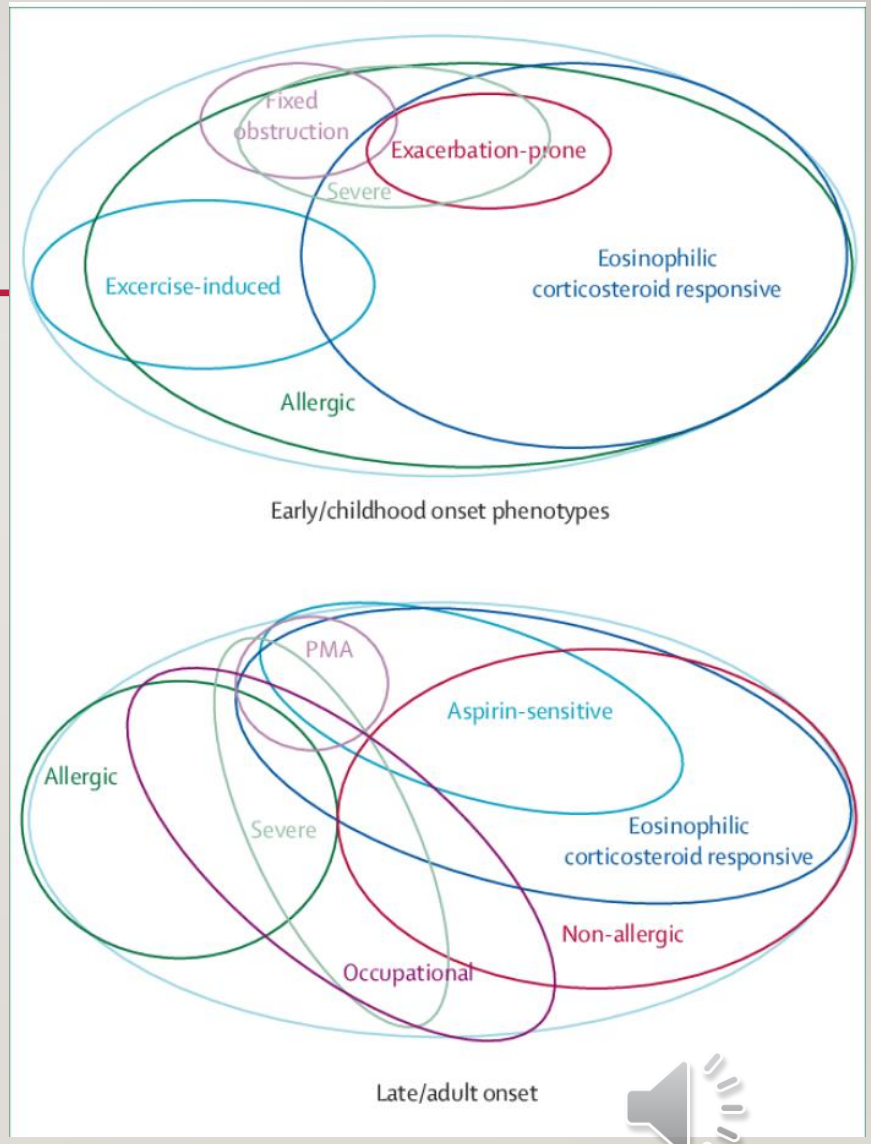
DEFINITION

- A heterogenous disease characterized by intermittent inflammation and narrowing of the airway
- Classic symptoms of SOB, wheeze, chest tightness and cough
- Varies over time and intensity
- Associated with AHR and airway inflammation

GINA. Diagnosis of Disease of Chronic Airflow Limitation: Asthma, COPD, ACOS. 2020

ASTHMA IS SYNDROME WITH HETEROGENEITY AND OVERLAP

- Allergic vs non-allergic
- Severity
- Age of Onset
- Triggers
  - Viral, occupational, allergens, irritants
- Pathophysiology
  - Eosinophilic, neutrophilic, paucigranulocytic
- Course



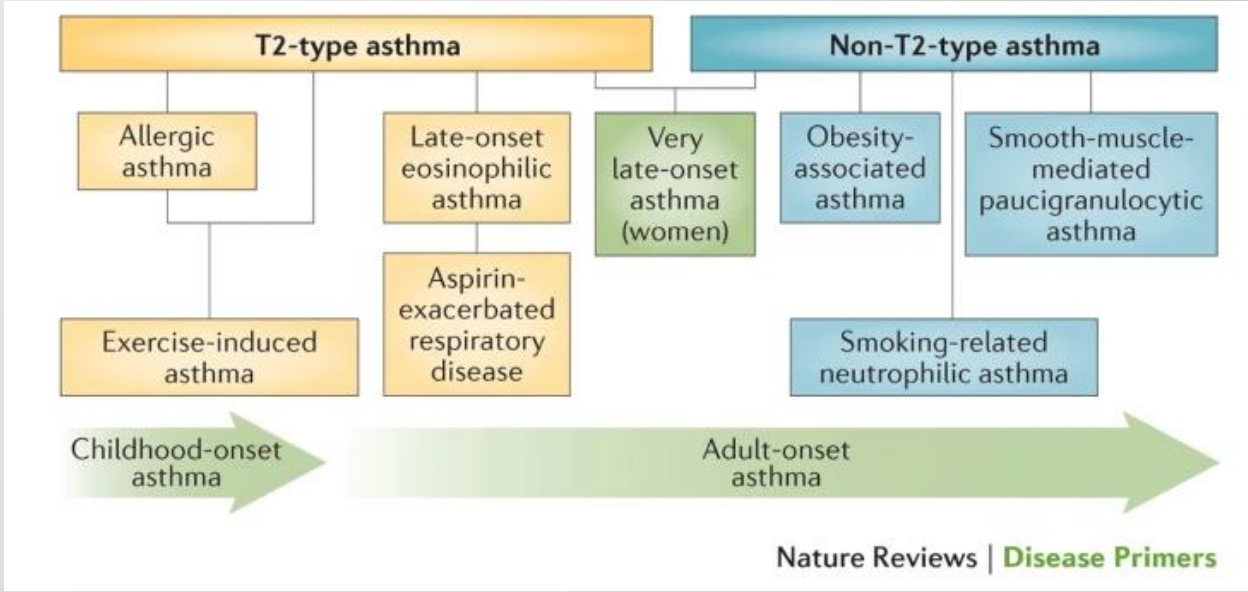
Sally Wenzel. Asthma: Defining of the persistent adult phenotypes. Lancet. 2006; 368: 804–13

RISK FACTORS FOR ASTHMA

- **Atopy – a genetic tendency for the immune system to overreact to normally harmless substances--**Strongest link
- **Allergen exposure** – Linked but not clearly causative. Dust mite and cockroach may increase risk, but farm animal and dog dander may decrease risk. Seems to be a minimum threshold but not a dose-response link
- **Viral illness** – RSV and rhinovirus in childhood are predictive but not necessarily causative
- **Gender** – Male through puberty, equal prevalence from 20 to 40 years old, and then more common in women after 40. Adult onset asthma is twice as common in women
- **Smoking** – HR for smokers is 1.43 and 1.36 (active and former), but children of smoking mothers have a HR of 2.1
- **AHR** – All asthma has AHR, but not all patients with AHR have symptoms of asthma
- **Familial history** – Not Mendelian and no specific genes known, but runs in families
- **Air pollution** - Nitrogen dioxide, ozone, volatile organic compounds, particulate matter and traffic-related air pollution
- **Obesity** – Prevalence increases with BMI. Weight loss slows the decline of FEV1 and vice versa
- **Workplace exposures** – Up to 10% of adult onset asthma

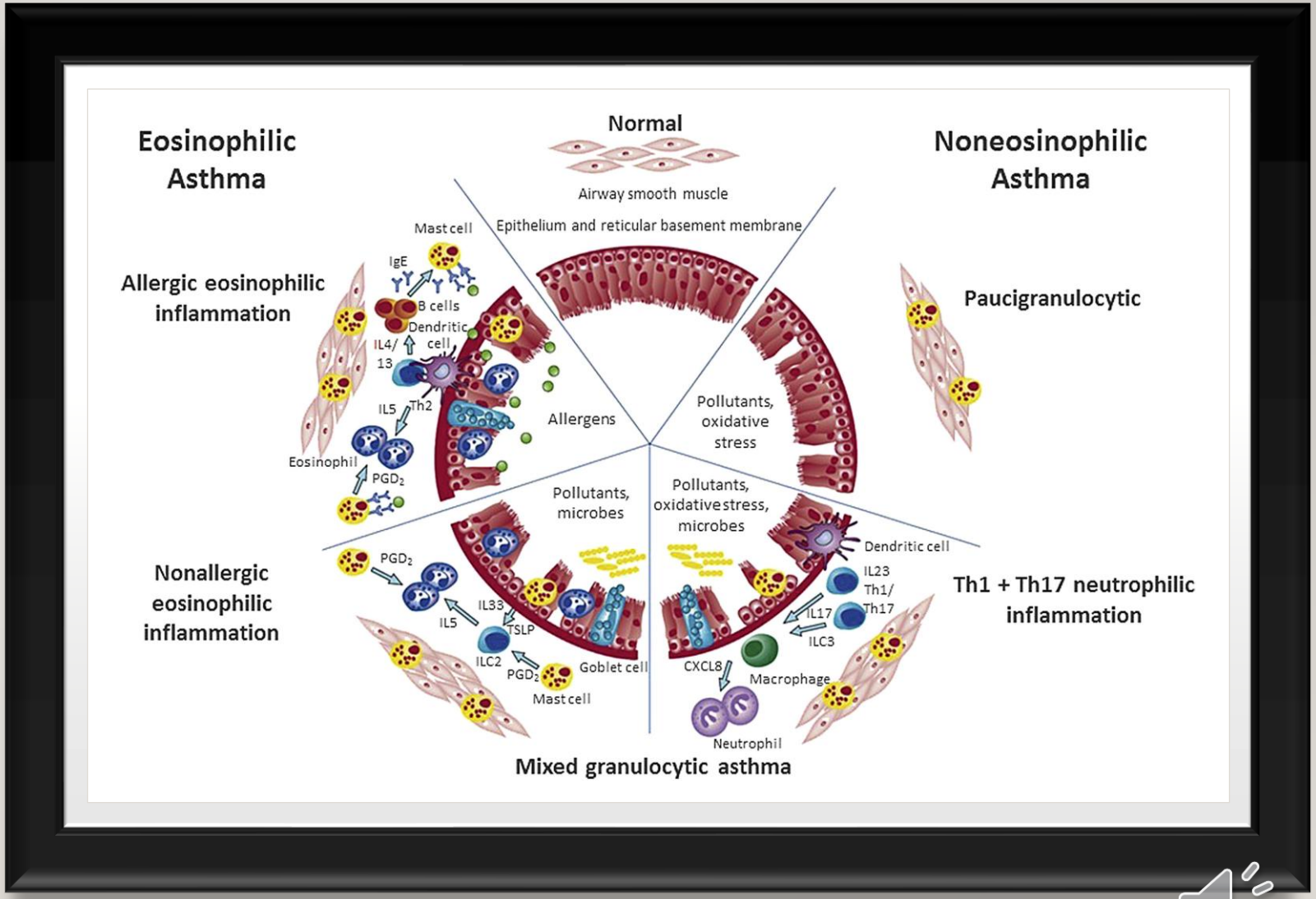
CLINICAL PHENOTYPES

- Allergic asthma – High type 2 inflammation/eosinophils
- Non-allergic asthma – Low type 2 inflammation/neutrophils
- Adult onset asthma
- Asthma with fixed obstruction
- Asthma and obesity – Little eosinophilic inflammation



Holgate, S., Wenzel, S., Postma, D. *et al.* Asthma. *Nat Rev Dis Primers* **1**, 15025 (2015). https://doi.org/10.1038/nrdp.2015.25

EOSINOPHILIC VS NON-EOSINOPHILIC PATHWAYS



William Busse. Biological treatments for severe asthma: A major advance in asthma care. Allergology International. Volume 68, Issue 2, April 2019, Pages 158-166

SEVERITY OF ASTHMA

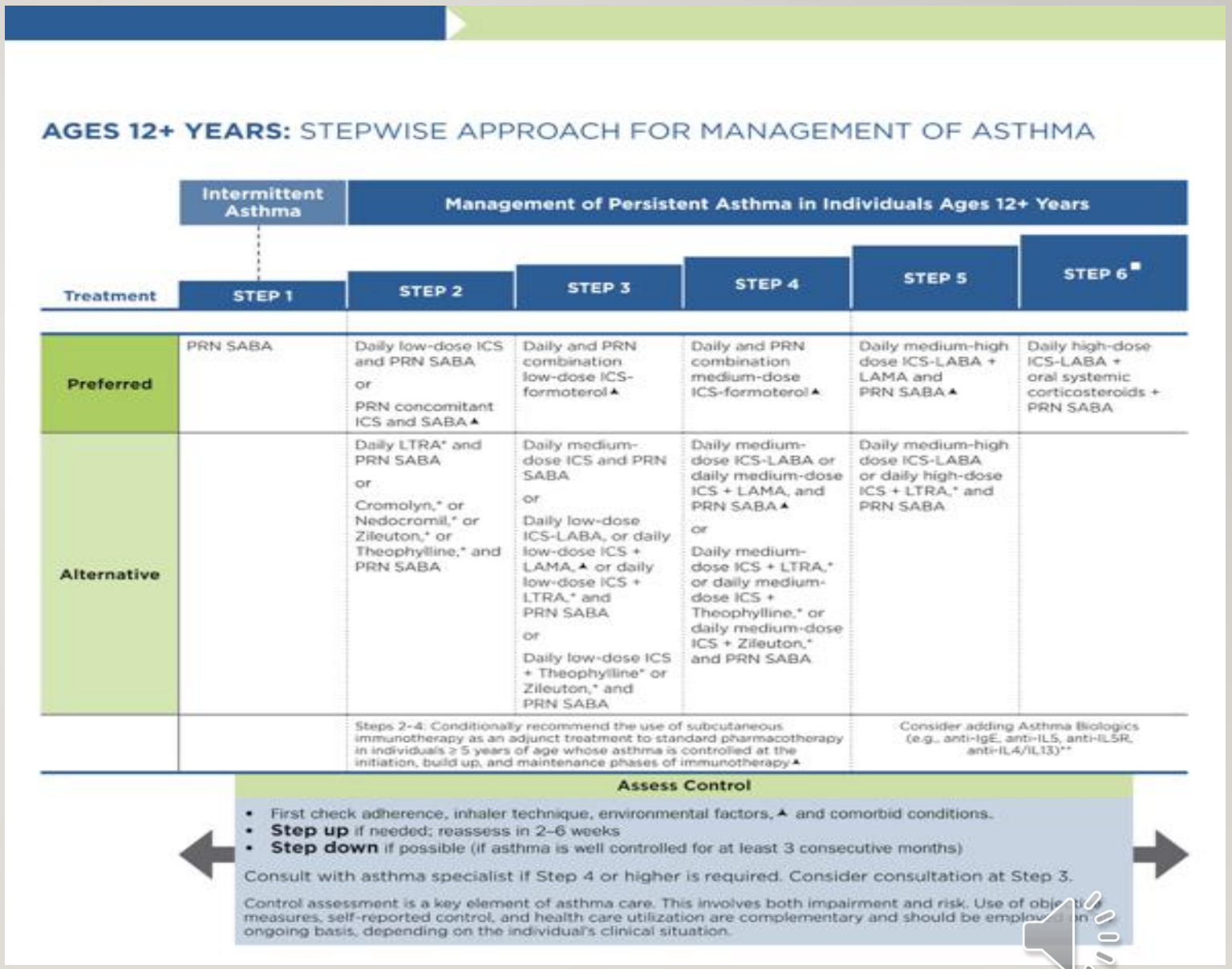
Components of Severity		Classification of Asthma Severity ≥12 years of age			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment Normal FEV_1/FVC: 8–19 yr 85% 20–39 yr 80% 40–59 yr 75% 60–80 yr 70%	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily, and not more than 1x on any day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV_1.			
Recommended Step for Initiating Treatment		Step 1	Step 2	Step 3 and consider short course of oral systemic corticosteroids	Step 4 or 5
(See figure 4–5 for treatment steps.)		In 2–6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			

Key: FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICU, intensive care u

National Asthma Education and Prevention Program, Third Expert Panel on the Diagnosis and Management of Asthma. 2020 update. Bethesda (MD): National Heart, Lung, and Blood Institute (US); 20[illegible] Aug.

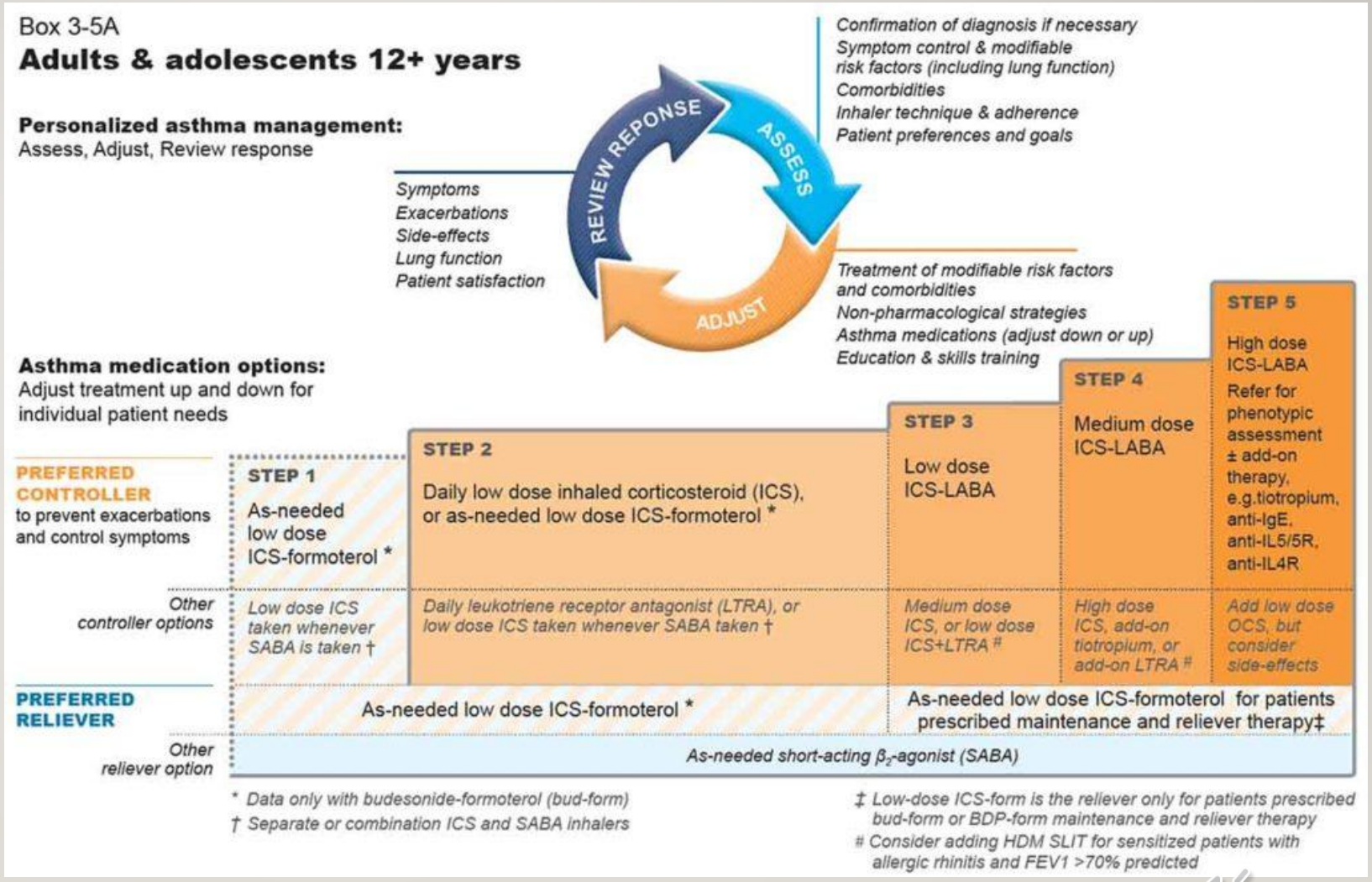
TREATMENT OF ASTHMA

Intermittent	Persistent		
	Mild	Moderate	Severe
Step 1	Step 2	Step 3 and consider short course of oral systemic corticosteroids	Step 4 or 5
In 2–6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			



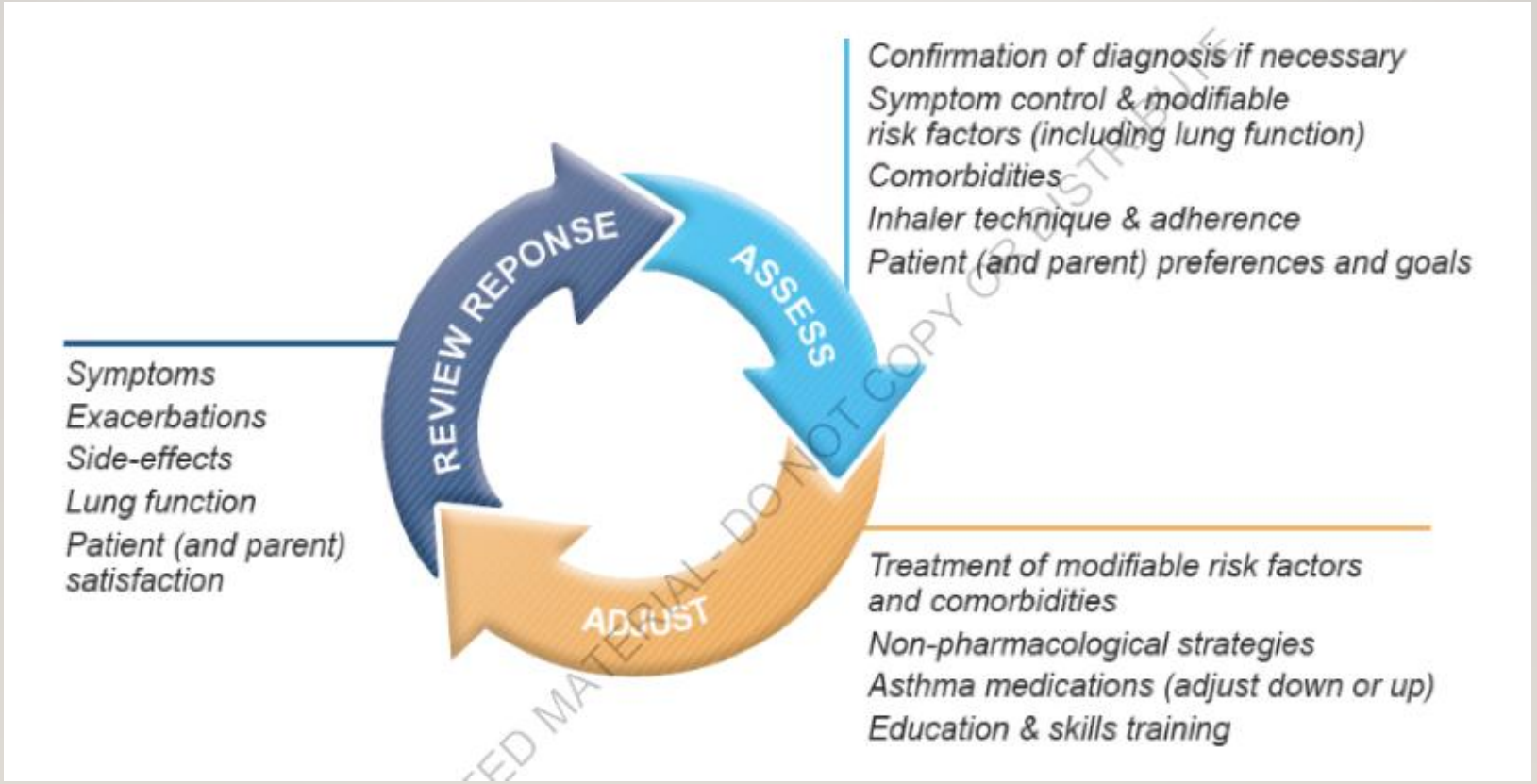
National Asthma Education and Prevention Program, Third Expert Panel on the Diagnosis and Management of Asthma. 2020 update. Bethesda (MD): National Heart, Lung, and Blood Institute (US); 2007 Aug.

TREATMENT OF ASTHMA



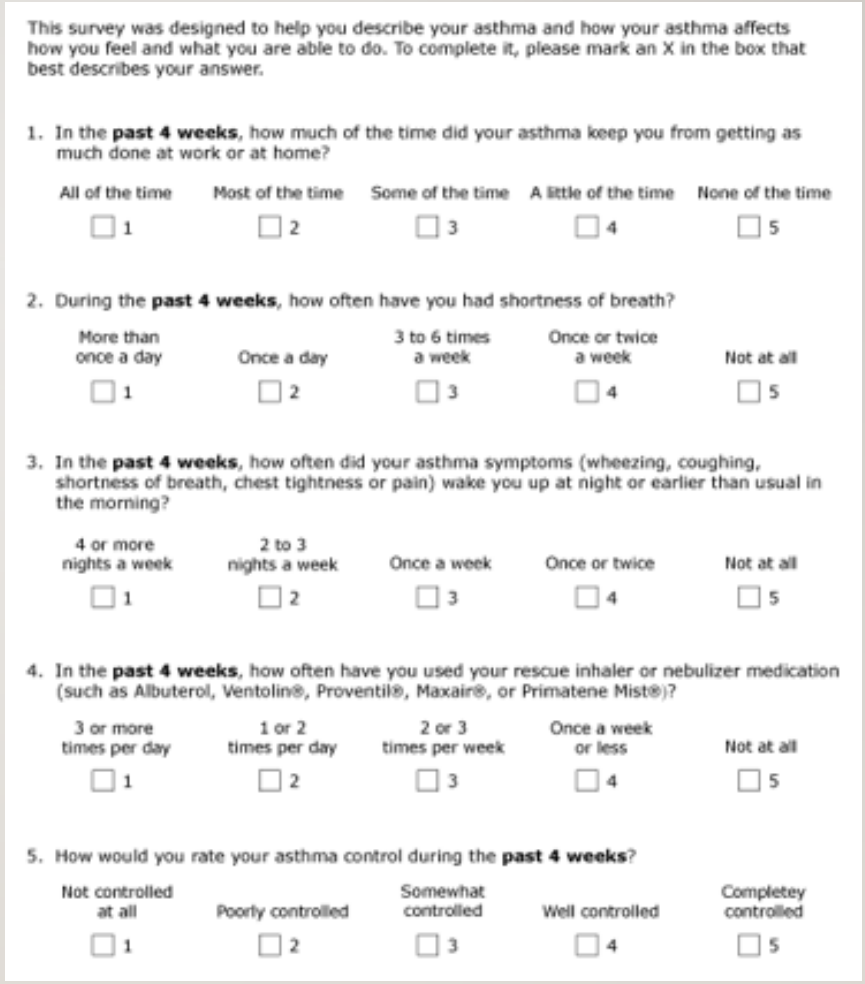
- Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. (Updated 2021. Accessed February 22, 2021)

TREATMENT OF ASTHMA



TREATMENT OF ASTHMA

- Four Components:
  - **1. Routine monitoring of symptoms and lung function**
    2. Patient education and partnership
    3. Controlling environmental factors and comorbid conditions
    4. Pharmacologic therapy
- The goal is to **reduce impairment and risk** (minimize exacerbations and ED care, prevent loss of lung function, minimize SE's of Rx)
- **Monitoring**: Frequent office follow up, peak flow meter, Asthma Control Test
- **Patient education** decreases hospitalizations, improves daily function and improves patient satisfaction
- Stepwise treatment and an asthma action plan



This survey was designed to help you describe your asthma and how your asthma affects how you feel and what you are able to do. To complete it, please mark an X in the box that best describes your answer.

1. In the **past 4 weeks**, how much of the time did your asthma keep you from getting as much done at work or at home?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. During the **past 4 weeks**, how often have you had shortness of breath?

More than once a day	Once a day	3 to 6 times a week	Once or twice a week	Not at all
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. In the **past 4 weeks**, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?

4 or more nights a week	2 to 3 nights a week	Once a week	Once or twice	Not at all
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

4. In the **past 4 weeks**, how often have you used your rescue inhaler or nebulizer medication (such as Albuterol, Ventolin®, Proventil®, Maxair®, or Primatene Mist®)?

3 or more times per day	1 or 2 times per day	2 or 3 times per week	Once a week or less	Not at all
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. How would you rate your asthma control during the **past 4 weeks**?

Not controlled at all	Poorly controlled	Somewhat controlled	Well controlled	Completey controlled
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

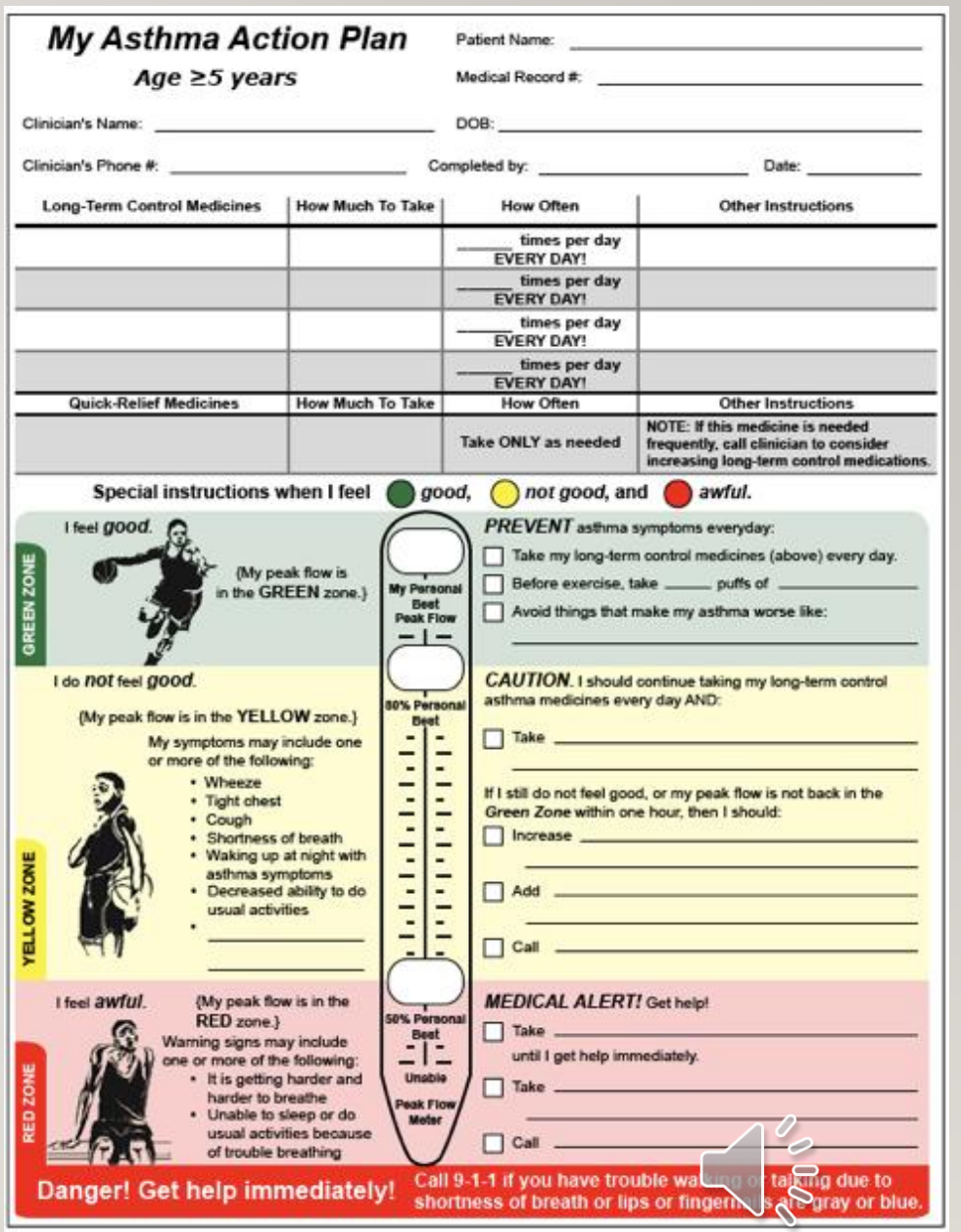
TREATMENT OF ASTHMA

Peak Flow Rate
(as % of personal best)

>80% →

50-80% →

<50% →



My Asthma Action Plan

Age ≥5 years

Patient Name: _____

Medical Record #: _____

Clinician's Name: _____ DOB: _____

Clinician's Phone #: _____ Completed by: _____ Date: _____

Long-Term Control Medicines	How Much To Take	How Often	Other Instructions
		_____ times per day EVERY DAY!	
		_____ times per day EVERY DAY!	
		_____ times per day EVERY DAY!	
		_____ times per day EVERY DAY!	
Quick-Relief Medicines	**How Much To Take**	**How Often**	**Other Instructions**
		Take ONLY as needed	NOTE: If this medicine is needed frequently, call clinician to consider increasing long-term control medications.

Special instructions when I feel good, not good, and awful.

GREEN ZONE

I feel *good*.

(My peak flow is in the GREEN zone.)

My Personal Best Peak Flow

PREVENT asthma symptoms everyday:

- ☐ Take my long-term control medicines (above) every day.
- ☐ Before exercise, take _____ puffs of _____
- ☐ Avoid things that make my asthma worse like: _____

YELLOW ZONE

I do *not* feel *good*.

(My peak flow is in the YELLOW zone.)

My symptoms may include one or more of the following:

- Wheeze
- Tight chest
- Cough
- Shortness of breath
- Waking up at night with asthma symptoms
- Decreased ability to do usual activities
- _____

80% Personal Best

CAUTION. I should continue taking my long-term control asthma medicines every day AND:

- ☐ Take _____

If I still do not feel good, or my peak flow is not back in the *Green Zone* within one hour, then I should:

- ☐ Increase _____
- ☐ Add _____
- ☐ Call _____

RED ZONE

I feel *awful*.

(My peak flow is in the RED zone.)

Warning signs may include one or more of the following:

- It is getting harder and harder to breathe
- Unable to sleep or do usual activities because of trouble breathing

50% Personal Best

Unable

Peak Flow Meter

MEDICAL ALERT! Get help!

- ☐ Take _____

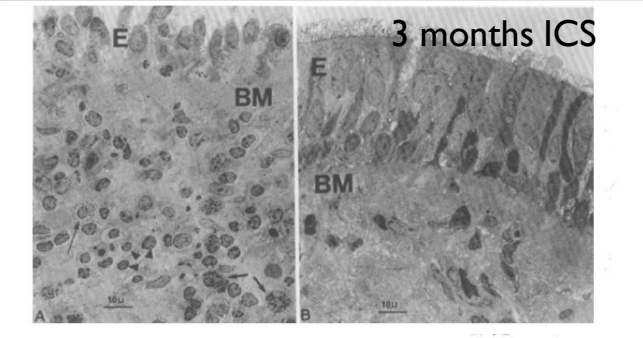
until I get help immediately.

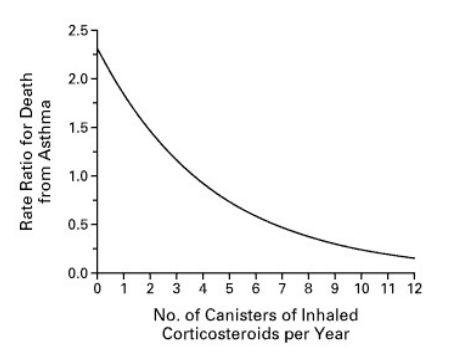
- ☐ Take _____
- ☐ Call _____

Danger! Get help immediately! Call 9-1-1 if you have trouble walking or talking due to shortness of breath or lips or fingernails are gray or blue.

AIRWAY REMODELING

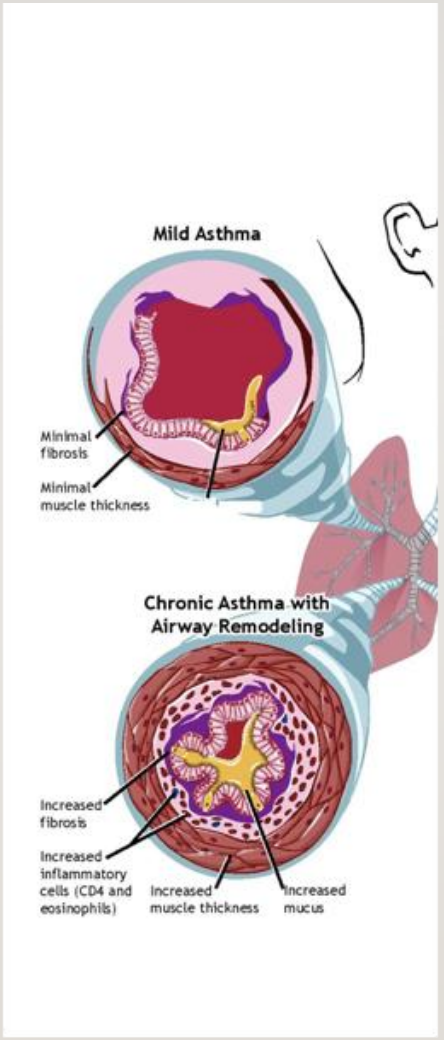
- Many patients with intermittent symptoms have normal lung function in-between
- A subset develops irreversible airflow obstruction from airway remodeling
- Use of ICS decreases inflammation, OCS use, decline in lung function by reducing exacerbations and decreases the rate ratio of death

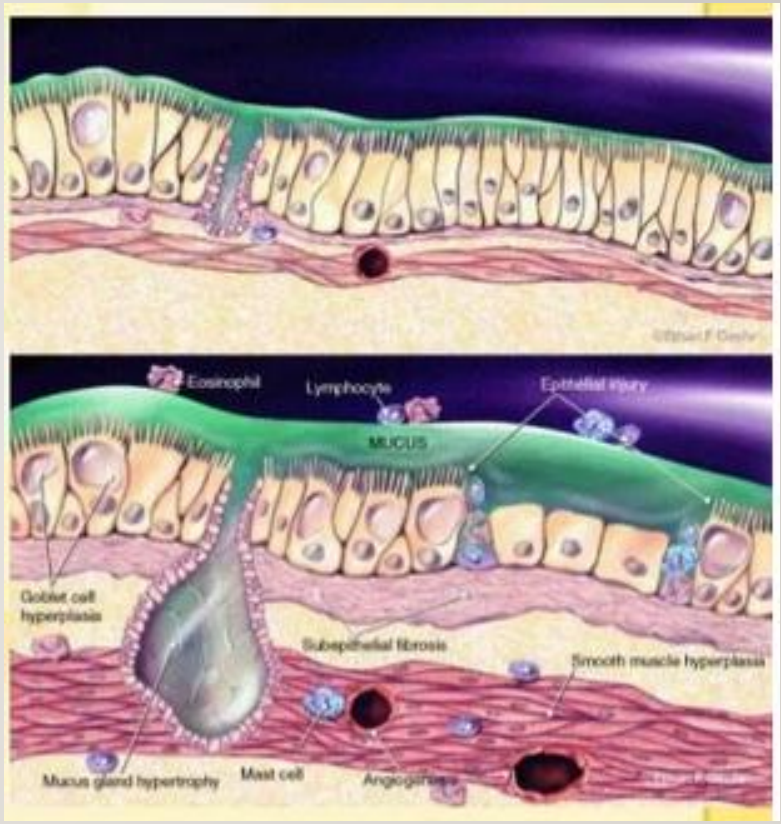




O'Byrne P, Fabbri LM, Pavord ID, Papi A, Petruzzelli S, Lange P. Asthma progression and mortality: the role of inhaled corticosteroids. Eur Respir J. 2019 Jul 18;54(1):1900491
Suissa et al. Low-Dose Inhaled Corticosteroids and the Prevention of Death from Asthma. August 3, 2000.N Engl J Med 2000; 343:332-336
Laitinen et al. A comparative study of the effects of an inhaled corticosteroid, budesonide, and a 132-agonist, terbutaline, on airway inflammation in newly diagnosed asthma: A randomized, double-blind, parallel-group controlled trial. J Allergy Clinical Immunology. July 1992

AIRWAY REMODELING





http://breathinstephen.com/double-whammy-asthma/

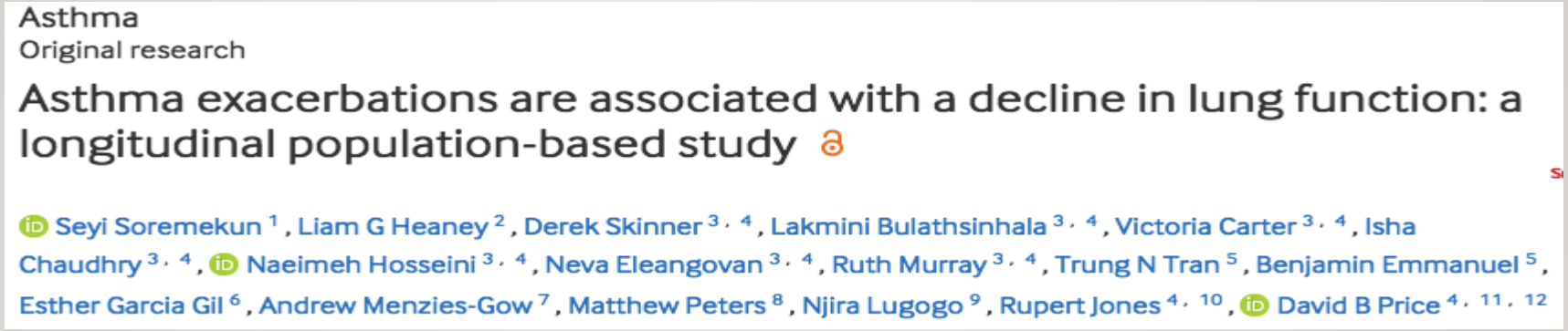
TREATMENT TROUBLES - EXACERBATIONS

- Characterized by acute worsening of symptoms and lung function
- May occur as a result of a trigger or as a new asthma presentation
  - Viral infection, allergen, noncompliance, pollution, irritants, etc
- The best treatment is **early recognition and intervention** – RT's should be in tune to subtle changes that may provide an opportunity to intervene
- One of the risk factors for asthma related deaths
  - 2 hospitalizations, 3 ED visits, 2 SABA cannisters per month, no asthma action plan, previous severe exacerbation (ICU/intubation) and non adherance

TREATMENT TROUBLES - EXACERBATIONS

- Basic principles of care – bolded are great opportunities for RT to improve patient care
  - Assess the **severity**
  - Assess the **triggers** – irritants, pollutants, allergens, medications (beta blockers or NSAIDs)
  - **Use of rapid onset medications such as SABA or ICS/Formoterol early and frequently**
  - OCS if no immediate and marked response to inhaled medications (short acting and increased ICS)
  - **Frequent objective measurements of response**
  - Transfer to an acute care facility if refractory or history of rapid progression
  - **Education for self management and recognition**

TREATMENT TROUBLES - EXACERBATIONS



Asthma

Original research

Asthma exacerbations are associated with a decline in lung function: a longitudinal population-based study

Seyi Soremekun [1], Liam G Heaney [2], Derek Skinner [3, 4], Lakmini Bulathsinhala [3, 4], Victoria Carter [3, 4], Isha Chaudhry [3, 4], Naeimeh Hosseini [3, 4], Neva Eleangovan [3, 4], Ruth Murray [3, 4], Trung N Tran [5], Benjamin Emmanuel [5], Esther Garcia Gil [6], Andrew Menzies-Gow [7], Matthew Peters [8], Njira Lugogo [9], Rupert Jones [4, 10], David B Price [4, 11, 12]

- A population based study
- It is thought that asthma exacerbations contribute to a decline in lung function
- This was for a broad and heterogeneous asthma based population
- Had to be over 18 with at least 3 PEF or FEV1 records

Soremekun S, Heaney LG, Skinner D, Bulathsinhala L, Carter V, Chaudhry I, Hosseini N, Eleangovan N, Murray R, Tran TN, Emmanuel B, Garcia Gil E, Menzies-Gow A, Peters M, Lugogo N, Jones R, Price DB. Asthma exacerbations are associated with a decline in lung function: a longitudinal population-based study. Thorax. 2022 Aug 3:thoraxjnl-2021-217032. doi: 10.1136/thorax-2021-217032.

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- 109,182 patients followed between 5 and 50 years with 75,280 having data for all variables included
- For each exacerbation there was an estimated additional loss in PEF of 1.34 L/min
- For an annual exacerbation rate >2/year between 18 and 24 at baseline, there was a loss of an additional 5.95 l/min PEF/year compared with no exacerbations
- The decline was progressively less pronounced for baseline age over 24 years
- FEV1 decline was consistent with PEF decline

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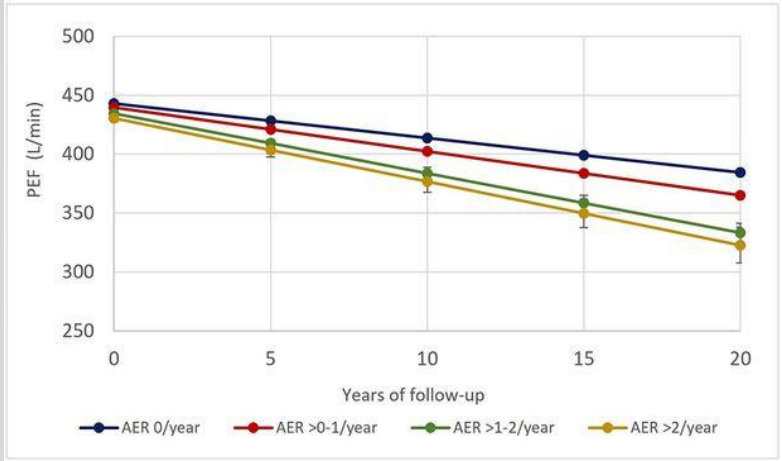
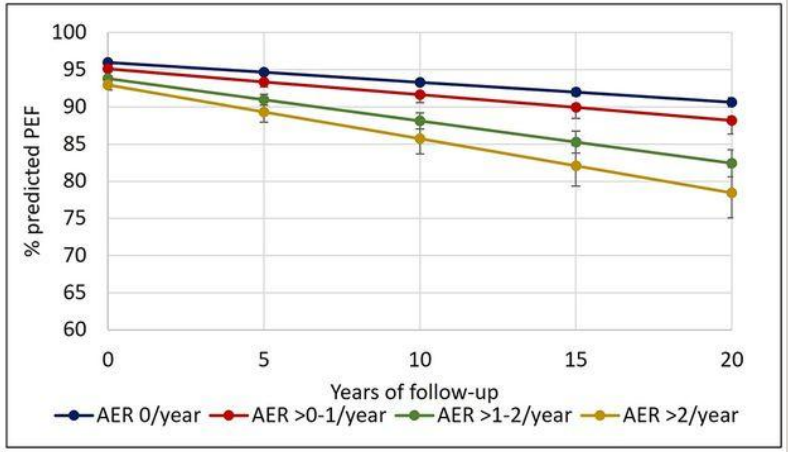


Annual exacerbation rate	Decline in PEF L/min/yr (95% CI)	Average difference in PEF L/min/yr decline between AER categories (95% CI; p)
0/yr	**-2.93 L**/min/yr (-3.04, -2.82)	
>0-1/yr	**-3.74 L**/ min/yr (-3.84, -3.64)	-0.81 L (-0.93, -0.70) p ≤0.001
>1-2/yr	**-5.05 L**/ min/yr (-5.38, -4.73)	-2.13 L (-2.46, -1.80) p ≤0.001
>2/yr	**-5.38 L**/ min/yr (-5.98, -4.78)	-2.46 L (-3.06, -1.85) p ≤0.001

B



Annual exacerbation rate	Decline in % predicted PEF (95% CI)	Average difference in % predicted PEF decline between AER categories (95% CI; p)
0/yr	**-0.27 %**/yr (-0.29, -0.24)	
>0-1/yr	**-0.35** %/yr (-0.37, -0.32)	-0.08 %/yr (-0.10, -0.05) p ≤0.001
>1-2/yr	**-0.57** %/yr (-0.64, -0.50)	-0.03 %/yr (-0.38, -0.23) p ≤0.001
>2/yr	**-0.72** %/yr (-0.86, -0.59)	-0.46 %/yr (-0.59, -0.32) p ≤0.001

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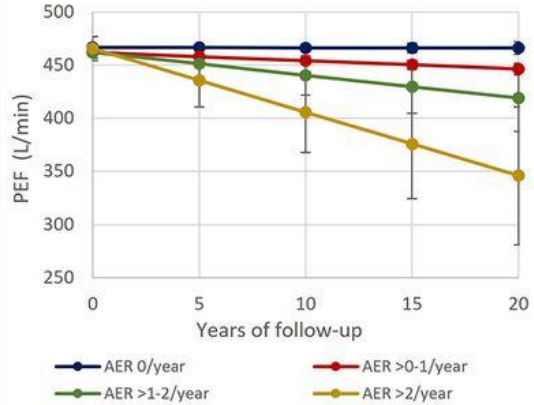
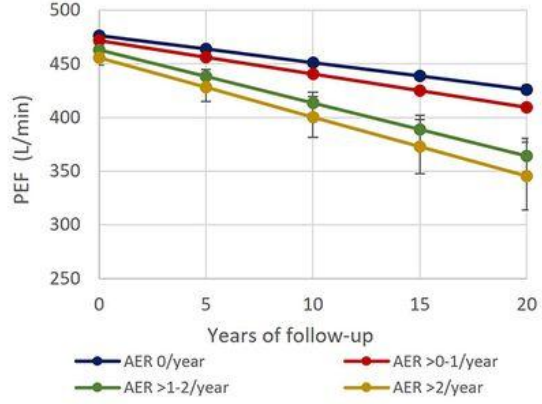
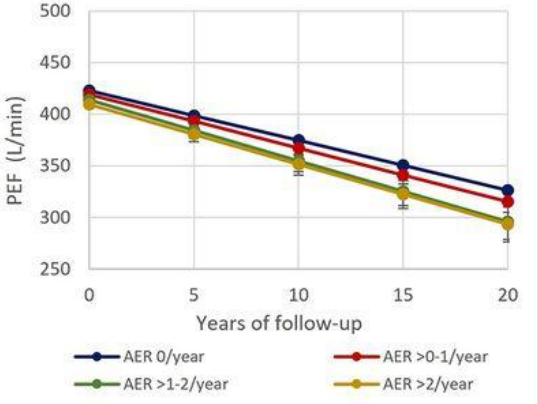
A age 18-24 at baseline



B age 25-39 at baseline



C age 40+ at baseline



AER	18 – 24 years old at baseline		25 – 39 years old at baseline		40+ years old at baseline	
	Decline in PEF L/min/yr (95% CI)	Average difference in PEF L/min/yr decline (95% CI; p)	Decline in PEF L/min/yr (95% CI)	Average difference in PEF L/min/yr decline (95% CI; p)	Decline in PEF L/min/yr (95% CI)	Average difference in PEF L/min/yr decline (95% CI; p)
0/yr	**-0.02** L/min/yr (-0.26, 0.22)	**comparator**	**-2.52** L/min/yr (-2.67, -2.36)	**comparator**	**-4.82** L/min/yr (-4.94, -4.7)	**comparator**
>0-1/yr	**-0.77** L/min/yr (-1.00, -0.54)	**-0.75** L/min/yr (-1.08, -0.41) p<0.001	**-3.11** L/min/yr (-3.24, -2.98)	**-0.59** L/min/yr (-0.79, -0.39) p<0.001	**-5.20** L/min/yr (-5.29, -5.11)	**-0.38** L/min/yr (-0.53, -0.23) p<0.001
>1-2/yr	**-2.15** L/min/yr (-3.43, -0.88)	**-2.13** L/min/yr (-3.43, -0.83) p = 0.001	**-4.93** L/min/yr (-5.57, -4.28)	**-2.41** L/min/yr (-3.07, -1.75) p<0.001	**-5.89** L/min/yr (-6.25, -5.53)	**-1.07** L/min/yr (-1.45, -0.69) p<0.001
>2/yr	**-5.98** L/min/yr (-8.64, -3.31)	**-5.95** L/min/yr (-8.63, -3.28) p<0.001	**-5.51** L/min/yr (-6.75, -4.27)	**-2.99** L/min/yr (-4.24, -1.74) p<0.001	**-5.82** L/min/yr (-6.5, -5.14)	**-1.00** L/min/yr (-1.69, -0.31) p = 0.005

TREATMENT TROUBLES - EXACERBATIONS

- Soremekun's data shows the importance of early intervention and prevention of exacerbation before reaching middle age in preventing deterioration of lung function

TREATMENT TROUBLES – PERCEPTION

Asthma management and control in the United States: results of the 2009 Asthma Insight and Management survey

Kevin R Murphy [1], Eli O Meltzer, Michael S Blaiss, Robert A Nathan, Stuart W Stoloff, Dennis E Doherty

- A telephone based survey performed in 2009 of 2500 patients
- Compared patients' perception of control vs NAEPP definition of control
- Patients over 12 years old

Murphy et al. Asthma management and control in the US: results of the 2009 asthma insight and management survey. Allergy Asthma Proc. 2012 Jan-Feb;33(1):54-64.

Asthma management and control in the United States: results of the 2009 Asthma Insight and Management survey

Kevin R Murphy [1], Eli O Meltzer, Michael S Blaiss, Robert A Nathan, Stuart W Stoloff, Dennis E Doherty

- 71% of patients believed they were completely controlled or well controlled
- Only 29% were well controlled by NAEPP definition
- Patients considered asthma well controlled if:
  - Rescue medication was used three times per week (46%)
  - Urgent care visits occurred twice per year (67%)
  - Emergency department visits occurred once per year (60%)

TREATMENT TROUBLES - PERCEPTION

- 113 patients published in 2002
- Measured a Perception of Dyspnea (POD) score by patient reported Borg scale when breathing against increasing inspiratory resistive loads to reach 30 cm H2O mouth pressure
- Patient were considered to have stable asthma and followed for 2 years

Magadle R, Berar-Yanay N, Weiner P. The risk of hospitalization and near-fatal and fatal asthma in relation to the perception of dyspnea. Chest. 2002 Feb;121(2):329-33. doi: 10.1378/chest.121.2.329.

The Risk of Hospitalization and Near-Fatal and Fatal Asthma in Relation to the Perception of Dyspnea

Rasmi Magadle, MD • Noa Berar-Yanay, MD • Paltiel Weiner, MD

Variable	Low POD (n 29 – 26%)	Normal POD (n 67 – 59%)	High POD (n 17 15%)
Hospitalization	22 (76%)	4 (6%)	3 (17.6%)
Near Fatal Asthma	13 (45%)	2 (3%)	1 (5.9%)
Death	6 (20.6%)	1 (1.5%)	0

- There were more severe asthmatics in the low POD group compared with the normal, but there was no difference in numbers of severe asthmatics between the low and high POD groups
- Rescue inhaler use was significantly lower in the low POD group than the high POD group
- Low POD had a higher female/male ratio and skewed older

TREATMENT TROUBLES - ADHERENCE

- Underuse of controller medications leads to increased hospitalizations, exacerbations and ED visits
- It is estimated that poor adherence leads to up to 60% of hospitalizations
- It is suggested that asthma control requires at least 75% adherence

Williams LK, Peterson EL, Wells K, Ahmedani BK, Kumar R, Burchard EG, Chowdhry VK, Favro D, Lanfear DE, Pladevall M. Quantifying the proportion of severe asthma exacerbations attributable to inhaled corticosteroid nonadherence. *J Allergy Clin Immunol*. 2011;128:1185–1191.e2.
Williams LK, Joseph CL, Peterson EL, Wells K, Wang M, Chowdhry VK, Walsh M, Campbell J, Rand CS, Apter AJ, et al. Patients with asthma who do not fill their inhaled corticosteroids: a study of primary nonadherence. *J Allergy Clin Immunol*. 2007;120:1153–1159.
Lasmar L, Camargos P, Champs NS, Fonseca MT, Fontes MJ, Ibiapina C, Alvim C, Moura JA. Adherence rate to inhaled corticosteroids and their impact on asthma control. *Allergy*. 2009;64:784–789.

TREATMENT TROUBLES – ADHERENCE

Primary Adherence to Controller Medications for Asthma Is Poor

Ann Chen Wu,[1,2,3] Melissa G. Butler,[4] Lingling Li,[1] Vicki Fung,[5] Elyse O. Kharbanda,[6] Emma K. Larkin,[7] William M. Vollmer,[8] Irina Miroshnik,[1] Robert L. Davis,[9] Tracy A. Lieu,[1,2,3,10] and Stephen B. Soumerai[1]

- Retrospective cohort from 5 large health plans (far from perfect approach)
- 69,652 subjects with probable persistent asthma based on ICD-9 code
- Prescribed ICS, LTRA or ICS/LABA
- Mean age was 37 years and 58% were female.
- The study measured if the first prescription was filled, if there was a refill between 31 and 180 days and the proportion of days covered (number of days with prescription/number of days since prescription written)

Ann Chen Wu et al. Primary adherence to controller medications for asthma is poor. Ann AmThorac Soc. 2015 Feb; 12(2): 161–166.

Primary Adherence to Controller Medications for Asthma Is Poor

Ann Chen Wu,[1,2,3] Melissa G. Butler,[4] Lingling Li,[1] Vicki Fung,[5] Elyse O. Kharbanda,[6] Emma K. Larkin,[7] William M. Vollmer,[8] Irina Miroshnik,[1] Robert L. Davis,[9] Tracy A. Lieu,[1,2,3,10] and Stephen B. Soumerai[1]

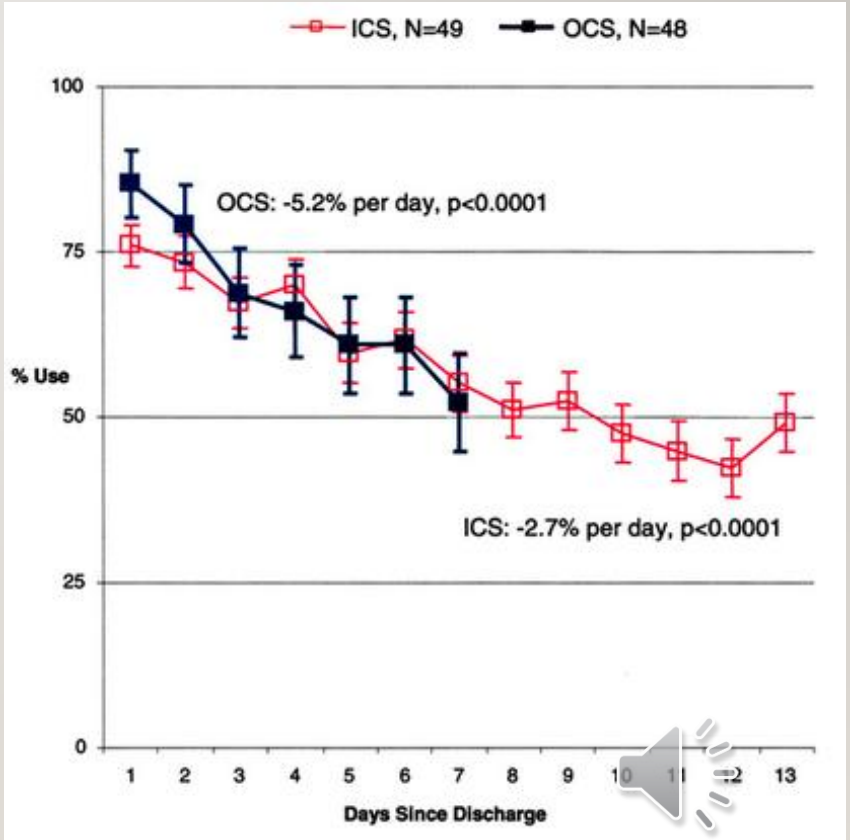
Outcomes by new episodes for subjects with probable persistent asthma who were prescribed no other controller medications in the prior 365 days

	n = 69,652			ICS/LABA vs. ICS	LTRA vs. ICS
	ICS (*n* = *63,998*)	ICS/LABA (*n* = *3,457*)	LTRA (*n* = *2,197*)		
Primary adherence	86% (54,731)	82% (2,836)	80% (1,755)	$P < 0.0001$	$P < 0.0001$
Early-stage persistence	64% (40,842)	60% (2,091)	76% (1,661)	$P < 0.0001$	$P < 0.0001$
Adjusted PDC > 75%	3% (1,748)	7% (239)	13% (282)	$P < 0.0001$	$P < 0.0001$
Mean adjusted PDC	21% (19%)	25% (27%)	30% (32%)	$P < 0.0001$	$P < 0.0001$

- 14–20% of subjects did not fill their first prescriptions.
- 24-40% did not refill their prescription
- Mean PDC was 21% for ICS, 30% for LTRA, and 25% for ICS/LABA
- Subjects prescribed LTRA were less likely to be primary adherent than subjects prescribed ICS (OR 0.82) or ICS/LABA (OR 0.88)

TREATMENT TROUBLES - ADHERENCE

- 2 week prospective study in 2001-2002 (old!)
- Patients admitted with an asthma exacerbation to an inner-city academic medical center
  - 60 patients
  - Most were female (65%), unmarried (88%), unemployed (70%) and African American (98%),
  - Average age 42
- Discharged with 40 mg Pred x 7 days, Fluticasone via spacer and albuterol PRN
- Adherence measures by patient report, electronic monitoring, inhaler weight and pill counts



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TREATMENT TROUBLES - TECHNIQUE

TREATMENT TROUBLES - TECHNIQUE

Improper inhaler technique is associated with poor asthma control and frequent emergency department visits

Hamdan AL-Jahdali, Anwar Ahmed, Abdullah AL-Harbi, Mohd Khan, Salim Baharoon, Salih Bin Salih, Rabih Halwani & Saleh Al-Muhsen

- 450 patients who visited the ED in two Saudi Arabia academic hospitals
- 176 (39.1%) were males
- Mean age of 42.3 ±16.7 years
- Mean duration of asthma was 155.9 ± 127.1 weeks.

Hamdan Al-Jahdali, et al. Improper inhaler technique is associated with poor asthma control and frequent emergency department visits. Allergy, Asthma & Clinical Immunology volume 9, Article number: 8 (2013)

Improper inhaler technique is associated with poor asthma control and frequent emergency department visits

Hamdan AL-Jahdali, Anwar Ahmed, Abdullah AL-Harbi, Mohd Khan, Salim Baharoon, Salih Bin Salih, Rabih Halwani & Saleh Al-Muhsen

- Improper use of asthma inhaler devices was observed in 203(45%)
- Improper use was associated with:
  - Irregular clinic follow-ups (p = 0.0001)
  - Lack of asthma education (p = 0.0009)
  - Uncontrolled asthma ACT (score ≤ 15) (p = 0.001)
  - Three or more ED visits (p = 0.0497)
  - Duration of asthma of less than 52 weeks (p = 0.005).
- **Lack of education (OR =1.65) and lack of regular follow-up (OR =1.73) were the most likely factor to lead to bad technique**

TREATMENT TROUBLES - COMORBITIES

- Often overlooked or leads to an improper diagnosis
- Can exacerbate or mimic asthma
  - GERD
  - Rhinitis/Sinusitis
  - COPD
  - Other pulmonary diseases
  - VCD
  - Cardiac disease

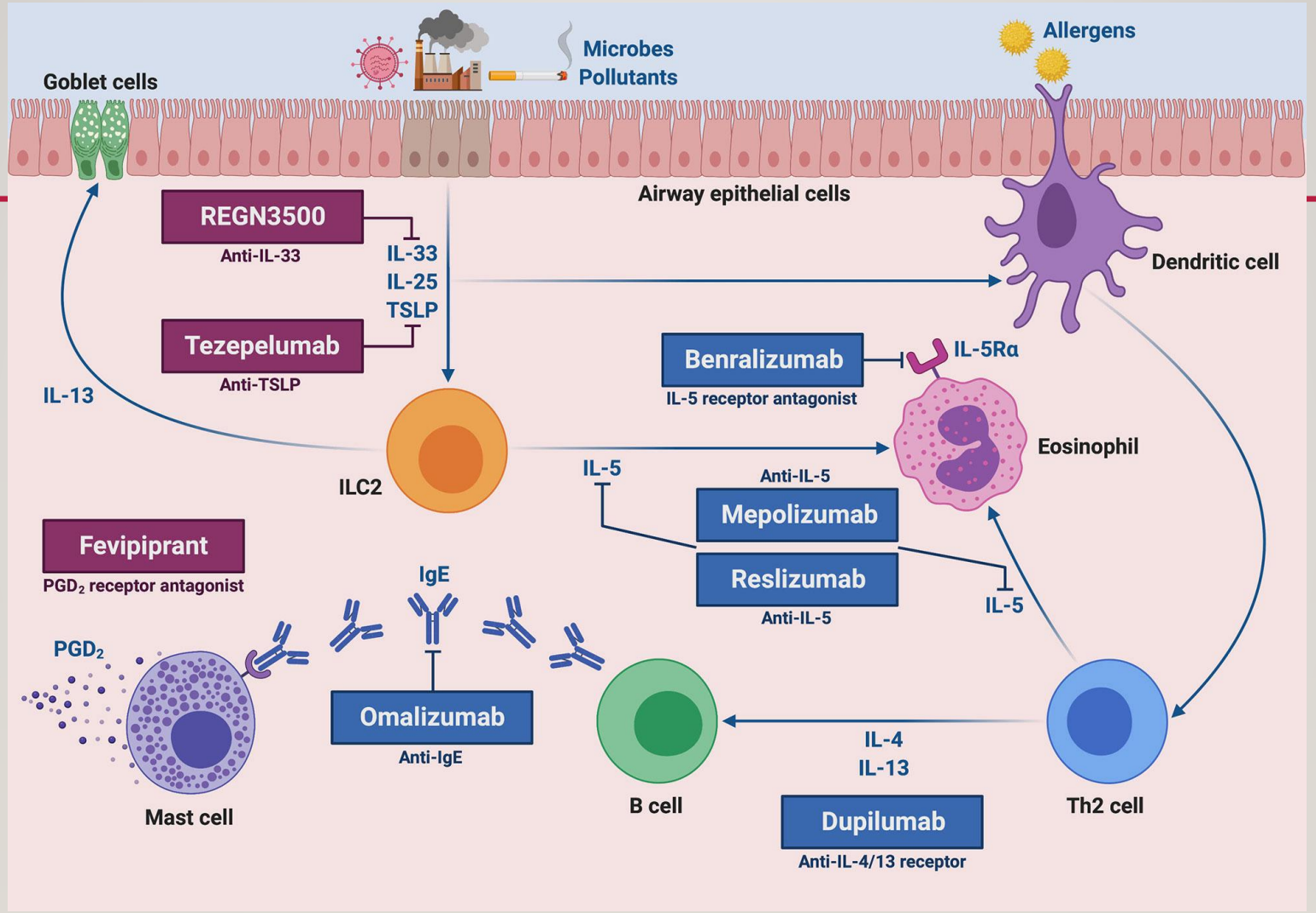
TREATMENT

You have verified the diagnosis, treated the confounders, optimized and maximized inhaler and oral therapy, performed extensive teaching and have had frequent follow-up but the patient is still complaining of a poor quality of life, frequent exacerbations and recurrent steroid use. **Now what!!!**

BIOLOGIC THERAPY

- Life changing for many of our patients
- Currently, there are agents that target anti-IgE, anti-IL 5, anti-IL5R, anti-IL-4R/13 and anti-TSLP (thymic stromal lymphopoietin)
- There are no head to head trials
- Choice is based heavily on suspected phenotype, concurrent disease, IgE level, eosinophils, patient preference (home vs. observed) and personal experience

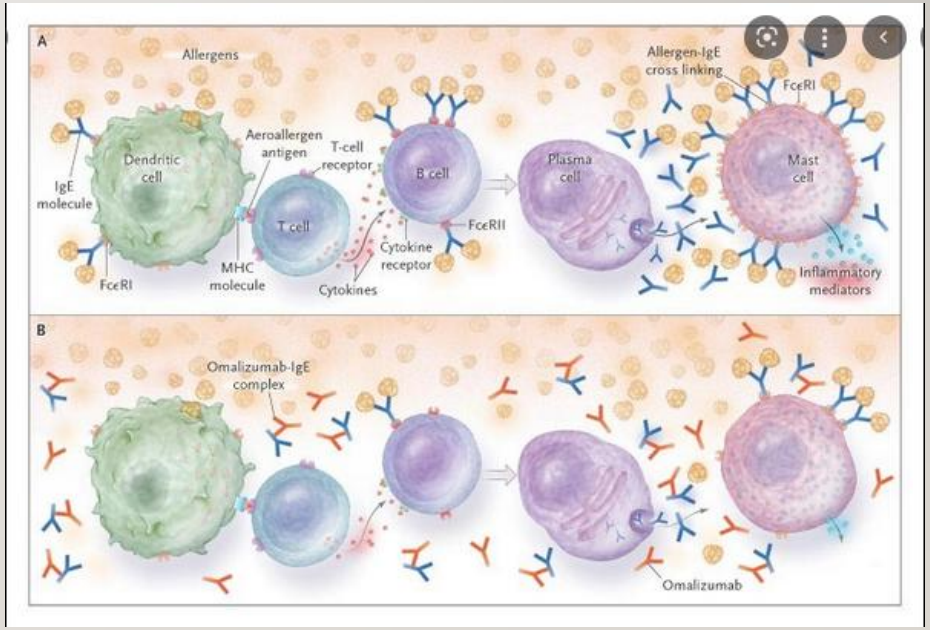
MOLECULAR TARGETS OF BIOLOGIC THERAPY



Pelaia et al. Molecular Targets for Biological Therapies of Severe Asthma. Front. Immunol., 30 November 2020

BIOLOGIC THERAPY – OMELIZUMAB (XOLAIR)

- **The OG** anti-IgE therapy
- Forms complexes to prevent binding to mast cells
- Approval for over **6 yo with IgE 30-700** IU/mL, positive allergen testing and incomplete control of mod-severe asthma
- SubQ every 2-4 weeks - **Self administered** or observed
- Decrease the rate of asthma exacerbations by 25%
- May cause sustained improvement in FEV1 at 5, 7 and 9 years
- Improvement in symptom control, QoL, OCS use, and a lower loss of working and school days has also been shown



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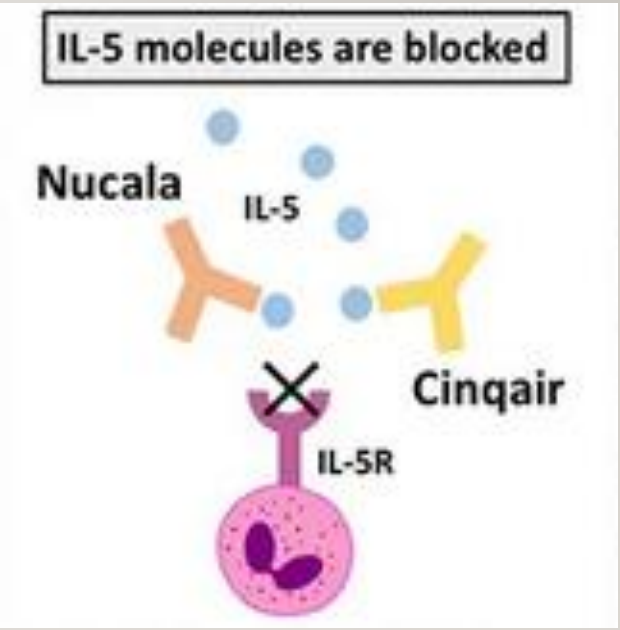
Strunk et al. Omalizumab for asthma. June 22, 2006. N Engl J Med 2006; 354:2689-2695

MEPOLIZUMAB (NUCALA)

- Anti-IL 5
- Over **6 yo** with severe asthma with eosinophilia > 150/microL (preferably >300)
- Also approved for chronic **rhinosinusitis and nasal polyposis**
- SubQ 100 mg every 4 weeks and can be **self-administered** or observed
- Significant reduction in exacerbations (50-60% reduction)
- Improved QoL
- Steroid reduction of 50% compared with placebo



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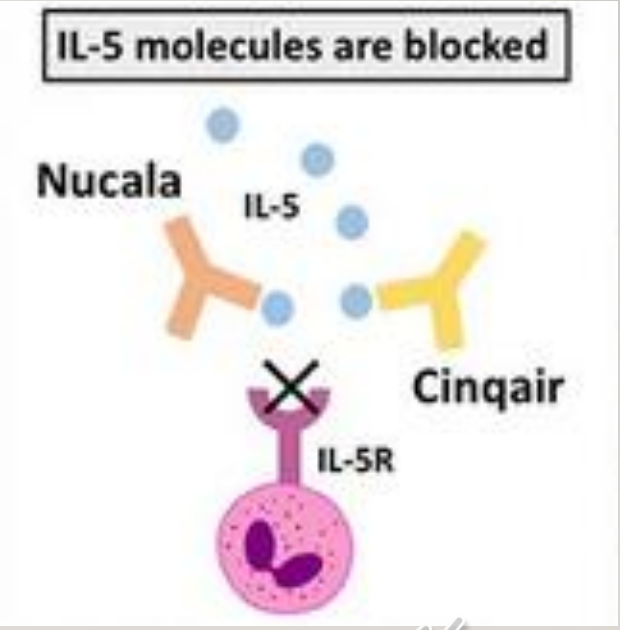
RESLIZUMAB (CINQAIR)

- Anti IL-5
- Over **18 yo** with severe asthma with eos > 400
- **IV administration** over 20-50 minutes every 4 weeks
- Decrease in exacerbation by 50%, improved symptoms and QoL and improved FEV1 (115-220 mL)
- Limited data shows a reduction in steroid use (250 vs 610 mg over 52 weeks



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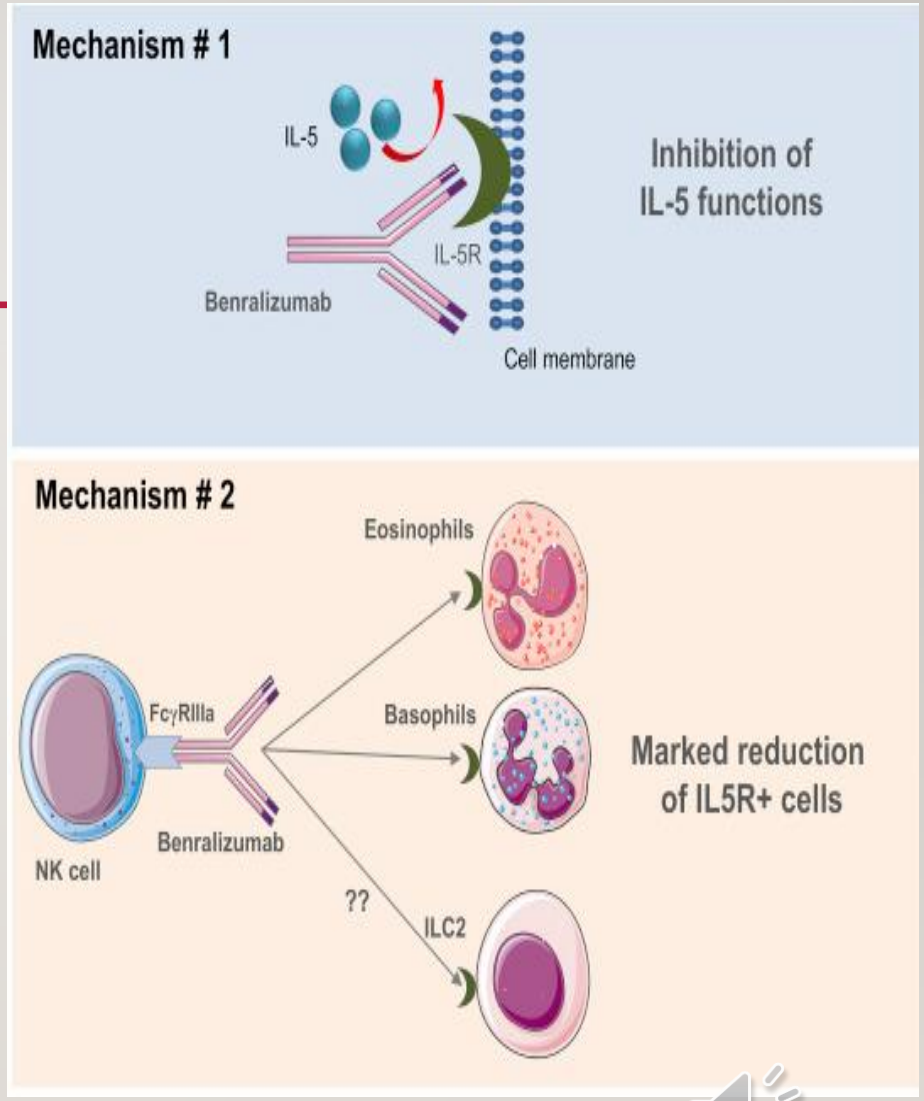
BENRALIZUMAB - FASENRA

- Anti IL-5 receptor alpha works to **both** block IL-5 from binding and to induce apoptosis of eosinophils
- Over 12 yo with severe asthma and eos > 150 cell/microL
- SubQ q4 weeks for 3 doses and **then every 8 weeks** and can be self-administered
- **Reduces exacerbations** with RR 0.49, 0.51 or 0.55 depending on the study. This was most pronounced if eos > 300
  - Meaning those on Fasenra lowers exacerbations by 49, 51 or 55%.
- Steroid reduction by 75% and elimination in 62% of patient



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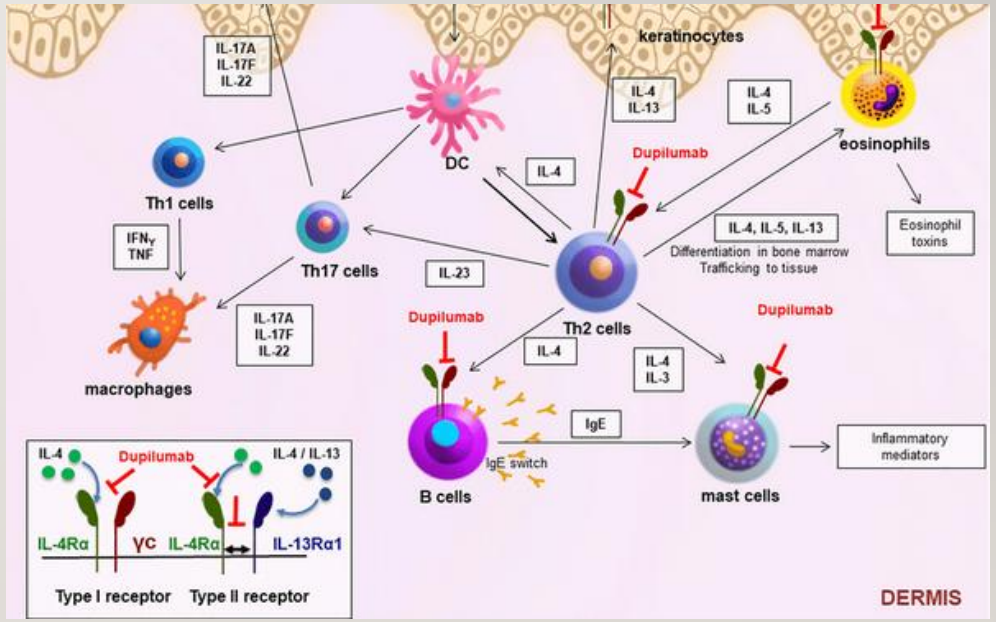
DUPILUMAB (DUPIXENT)

- Anti IL-4 receptor alpha subunit
- Inhibits both IL-4 and IL-13
- Approved for **moderate-severe** with eos > 150 in patient > 6 yo
- Also used for **eczema, chronic rhinosinusitis, nasal polypsis,** eosinophilic esophagitis and prurigo nodularis
- Decreases exacerbations by 67% (eos > 300), 40% (150-300) and –4% (< 150)
- Decreases steroid dose by 70% vs 42% in placebo
- Increases FEV1 by 150 mL



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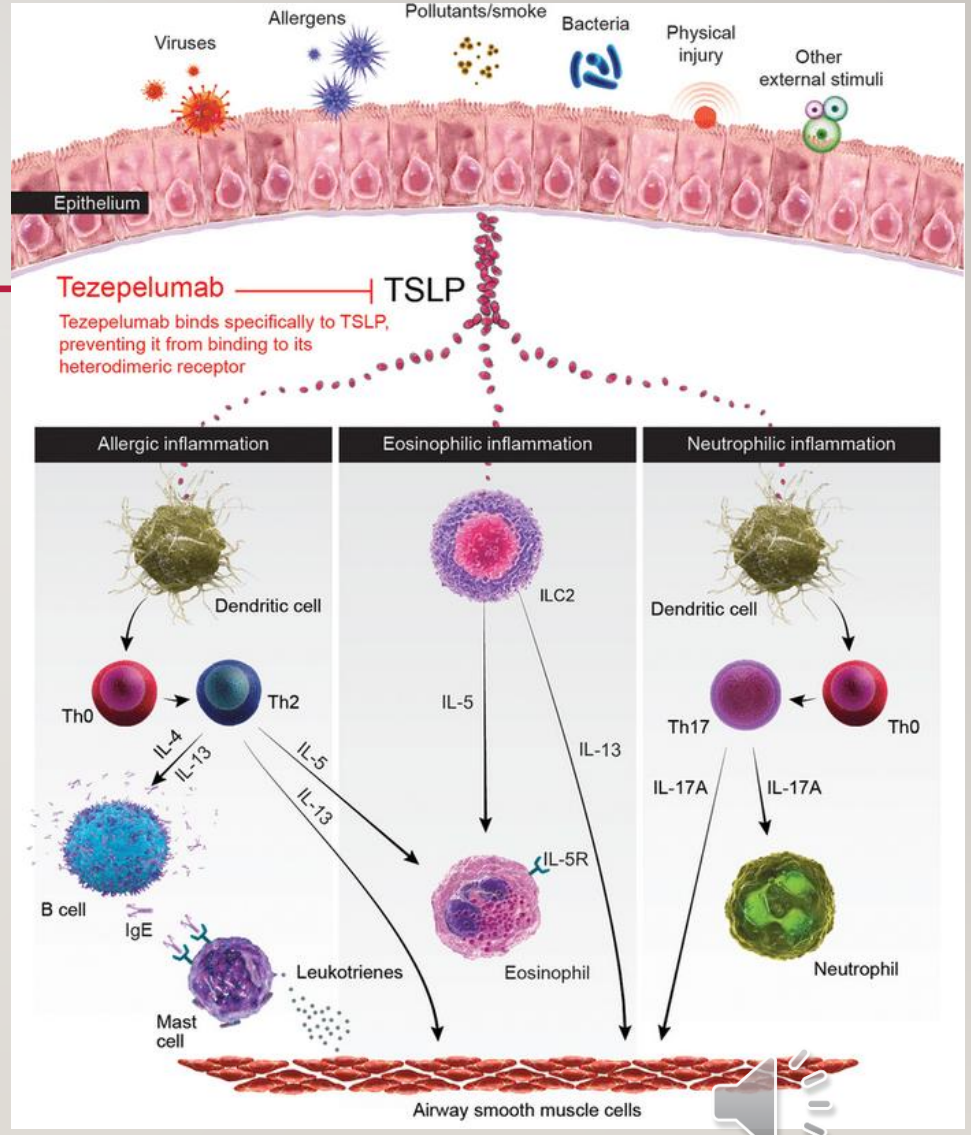
TEZEPELUMAB (TEZSPIRE)

- Newly approved anti thymic stromal lymphopoietin (TSLP) - a cytokine produced from the epithelial cells
- Severe asthma over the age of 12 with no requirement for FeNO or eos
- SubQ every 4 weeks
- 56-71% reduction in exacerbations
- Reduced ED visits (1.2% vs 3.6%)
- Reduction in steroid use was only apparent for eos>150



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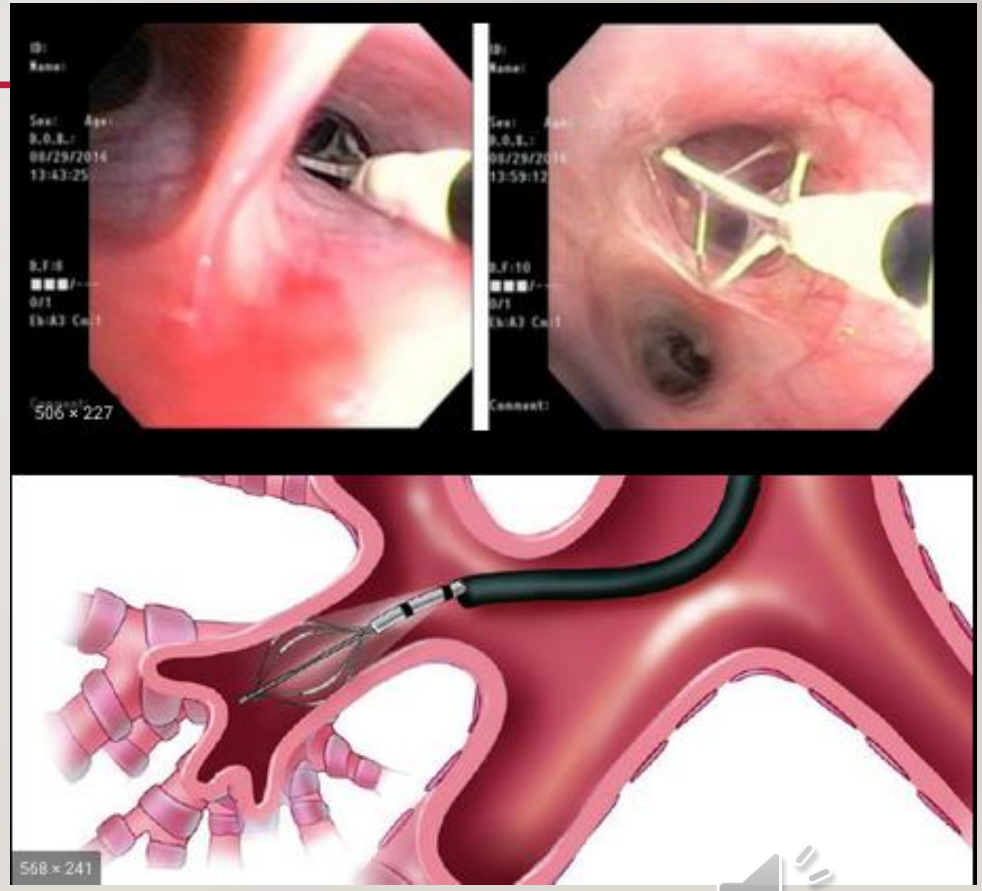
Licensed biological therapies	Targets	Molecular mechanisms of action	Effects in the control of severe asthma
Omalizumab	IgE	Generation of IgE/anti-IgE immune complexes that inhibit IgE-mediated allergic cascade	↓ Exacerbations ↑ Quality of life and symptom control ↑ FEV1
Mepolizumab	IL-5	Prevention of IL-5 binding to IL-5Rα	↓ Blood and sputum eosinophils ↓ Exacerbations ↑ Quality of life and symptom control ↓ OCS intake ↑ FEV1
Reslizumab	IL-5	Prevention of IL-5 binding to IL-5Rα	↓ Blood and sputum eosinophils ↓ Exacerbations ↑ Quality of life and symptom control ↑ FEV1
Benralizumab	IL-5Rα	Blockade of IL-5Rα ADCC-induced eosinophil apoptosis	↓ Blood eosinophils ↓ Exacerbations ↑ Quality of life and symptom control ↓ OCS intake ↑ FEV1
Dupilumab	IL-4Rα	Dual receptor antagonism of IL-4/IL-13	↓ Exacerbations ↓ OCS intake ↑ FEV1

Pelaia et al. Molecular Targets for Biological Therapies of Severe Asthma. Front. Immunol., 30 November 2020

BRONCHIAL THERMOPLASTY

- Applying heat to all airways (3-10 mm) except the RML – **3 separate procedures separated by 3 weeks**
- Reduces SM mass
- Indications
  - Poorly controlled on ICS and LABA
  - Non-smoker > 1 year
  - FEV1>60% of predicted
  - No life-threatening exacerbations
  - <3 hospitalizations in the last 12 months
- Effect
  - **May** reduce exacerbations
  - No change in control , QoL or hospitalizations
- Side effects
  - 7% developed bronchiectasis at 10 years
  - Severe exacerbations (56%)
  - ED visits (16%)



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https://www.chestmed.theclinics.com/article/S0272-5231(17)30121-1/fulltext

CASE 1- BEST CASE: BIOLOGIC RESPONSIVE

- A patient who is reasonably well controlled with inhaled steroids, monitoring and early intervention when exacerbations occur.
- However, exacerbations continue to occur occasionally inhibiting activities of daily living (ADLs).
- As a result, testing was conducted which implicated IL-5 as a contributing mediator to the patient asthma.
- As a result, the patient was stated on Mepolizumab (Nucala) via SubQ 100 mg every 4 weeks.
- Patient continues to monitor symptoms, but has been largely symptom free for two years.

CASE 2- WORST CASE- ASTHMA DISASTER

- An adult asthmatic patient believes his asthma is well controlled. However, he uses his rescue medication at least 3 times per week, has had two urgent care and one ER visit in the past year.
- Needless to say, his asthma is not well controlled.
- He also does not have a pulmonologist, despite repeated referrals to see one from his primary care doctor, who prescribes his albuterol rescue inhaler and from whom he has basic education.
- During an abrupt and severe exacerbation at home, he receives no relief from his Albuterol MDI.
- His symptoms worsen and he calls 911, who find him unconscious when they arrive.
- He intubated in the field and codes in the ambulance.
- Despite multiple round of CPR, the patient is pronounced dead in the ER.

PULMONOLOGIST LED ASTHMA CENTERS

- Newer initiative introduced by many pulmonology practices.
- The goal is to assess and treat patients with difficult to control symptoms, high health care utilization, steroid use and recurrent exacerbations.
- They incorporate patient education into each visit and insure proper follow up.
- Many patients have already been identified as misdiagnosed or who's symptoms were predominantly caused or exacerbated by other disease processes.
- Objective data (symptom-free days, miss work, ER visits) and subjective feedback (QOL) improve dramatically in most patients with Asthma Center involvement.

CONCLUSIONS

- Asthma is a heterogeneous disease and treatment needs to be tailored to each patient
- Education and follow up are imperative
- Treatment confounders include patient perception of symptoms, adherence to therapy, inhaler technique, exacerbations and comorbid conditions
- Biologic therapies have been a game changer
- Bronchial thermoplasty has a very limited role currently
- **Respiratory therapists can be a HUGE part in improving patient education, treatment and outcome**

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