



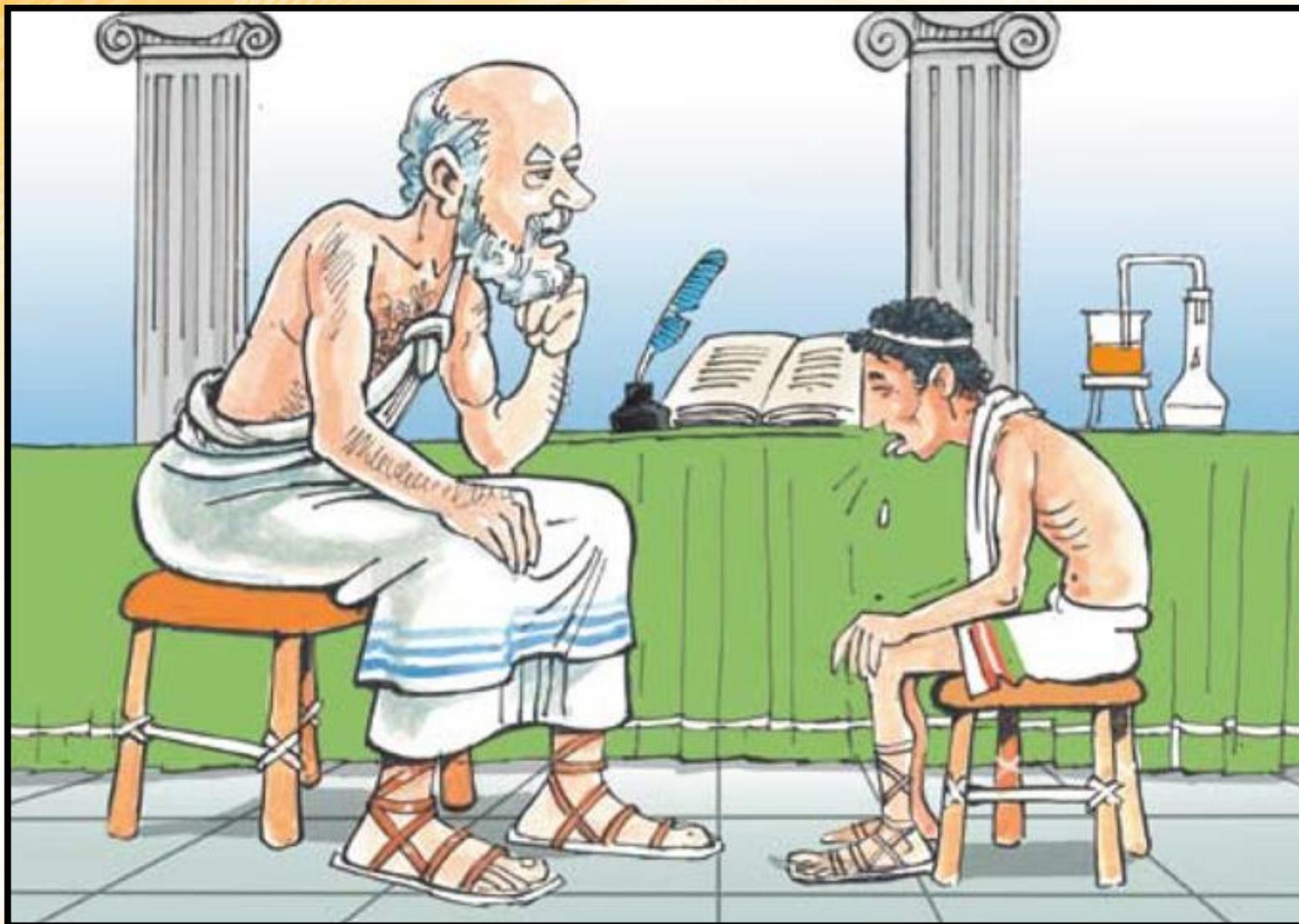
Current Trends In Asthma Part I

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Clinical Educator
Wellness Champion
Lehigh Valley Health Network
Allentown, Penna.*

Presentation Objectives

- Describe the pathophysiology associated with the asthmatic patient.
- Define what is asthma and describe the epidemiological prevalence.
- Define clinical end-points when treating the asthmatic patient.

What is Asthma??



The term Asthma comes from the **Greek verb aazein**, meaning to pant, to exhale with the open mouth, sharp breath. In The *Iliad*, a Greek epic poem (attributed to Homer) describing the siege of Troy, the expression asthma appeared for the first time.

The Corpus Hippocraticum, (collection of ancient Greek Medical works) is the earliest text where the word asthma is found as a medical term. We are not sure whether it meant asthma as a clinical entity or as merely a symptom. Hippocrates said spasm linked to asthma were more likely to occur among carpenters, tailors and metalworkers.

Galen (130-200 AD), the greatest physician of ancient Rome described asthma as bronchial obstructions and treated it with owl's blood mixed in wine in his post- operative patients.

Historical Perspectives Of Asthma



Bernardino Ramazzini (1633-1714 AD), known to some as the father of sports medicine, detected a link between asthma and organic dust. He also recognized exercise-induced asthma.

At the beginning of the 20th century asthma was seen as a psychosomatic disease. During the 1930s to 1950s, **asthma was known as one of the holy seven psychosomatic illnesses.**

Asthma was described as psychological, with treatment often involving, as its primary component, psychoanalysis and other **'talking cures'**. A child's wheeze was seen as a suppressed cry his or her mother. Psychoanalysts thought that patients with asthma should be treated for depression. This psychiatric theory was eventually refuted, and asthma became known as a physical condition.



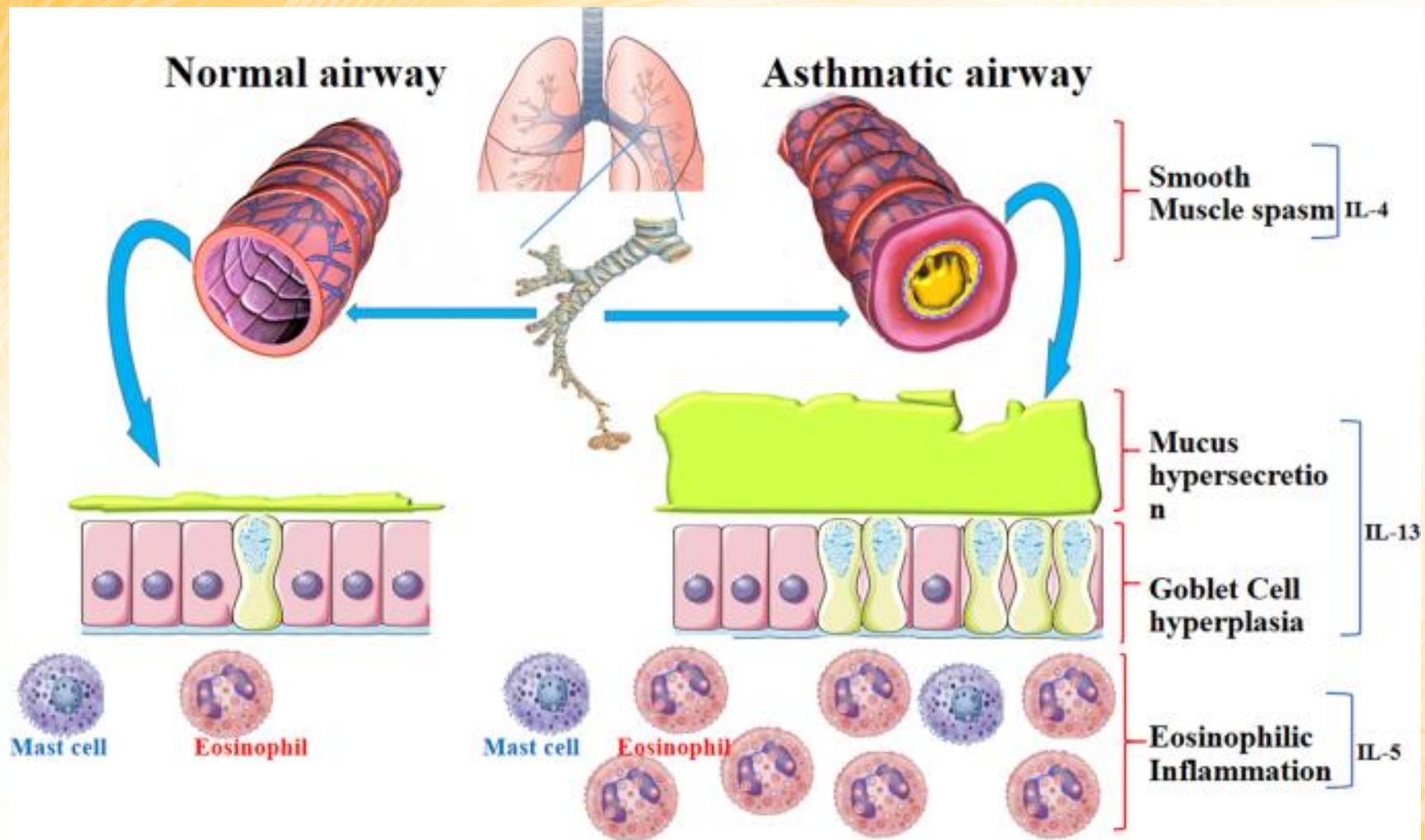
Asthma, as an inflammatory disease, was not really recognized until the 1960s when anti-inflammatory medications started being used.

What is Asthma 2021??

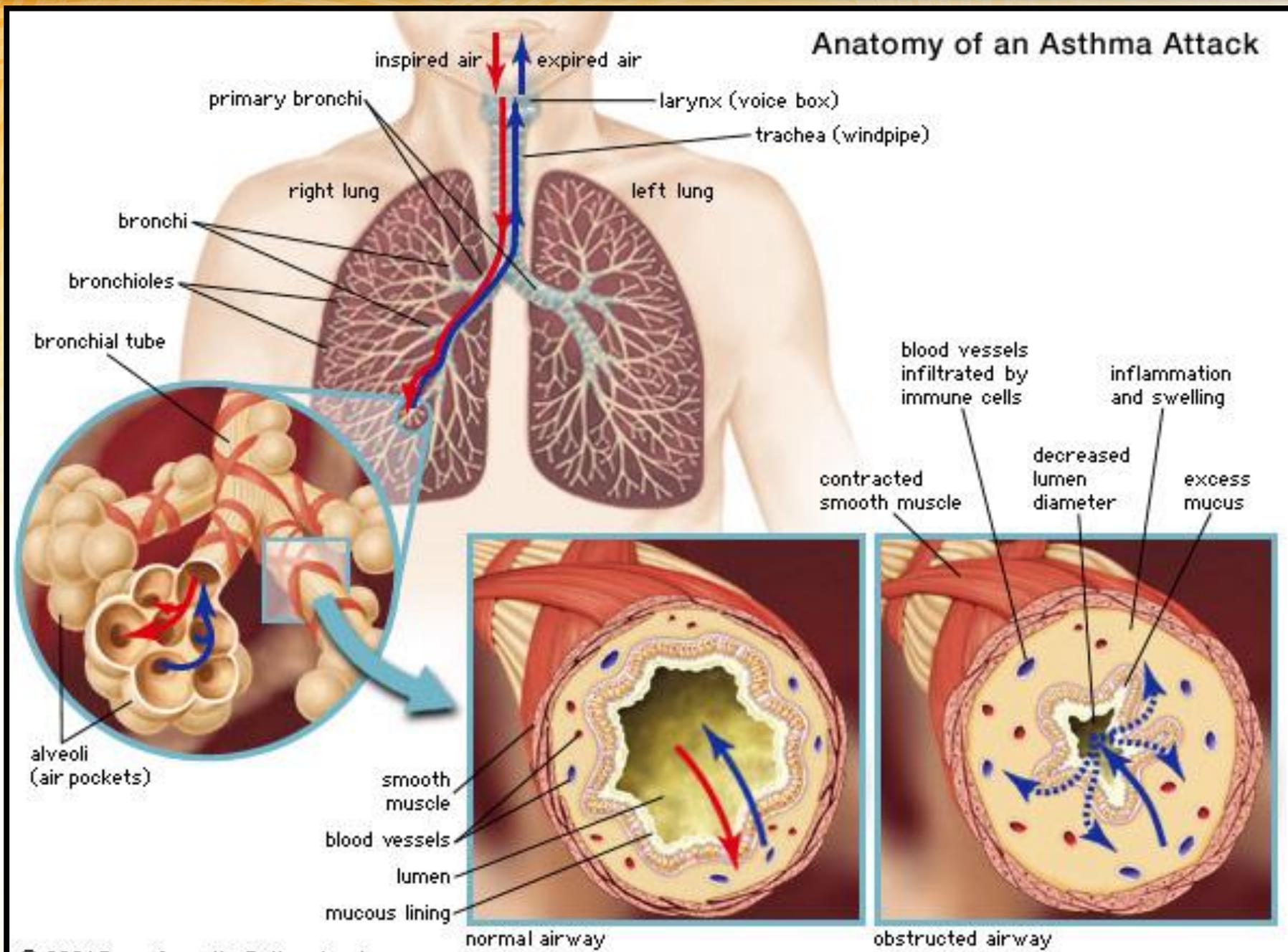
- **Asthma** is a chronic (long-lasting) inflammatory disease of the airways.
- In those susceptible to asthma, this inflammation causes the airways to spasm and swell periodically so that the airways narrow. The individual then must wheeze or gasp for air.
- Obstruction to air flow either resolves spontaneously or responds to a wide range of treatments, but continuing inflammation makes the airways hyper-responsive to stimuli such as cold air, exercise, dust mites, pollutants in the air, and even stress and anxiety.

Asthma Pathophysiology

- Airway inflammation (always present)
- Airway hyperresponsiveness
- Airway obstruction



Anatomy of an Asthma Attack

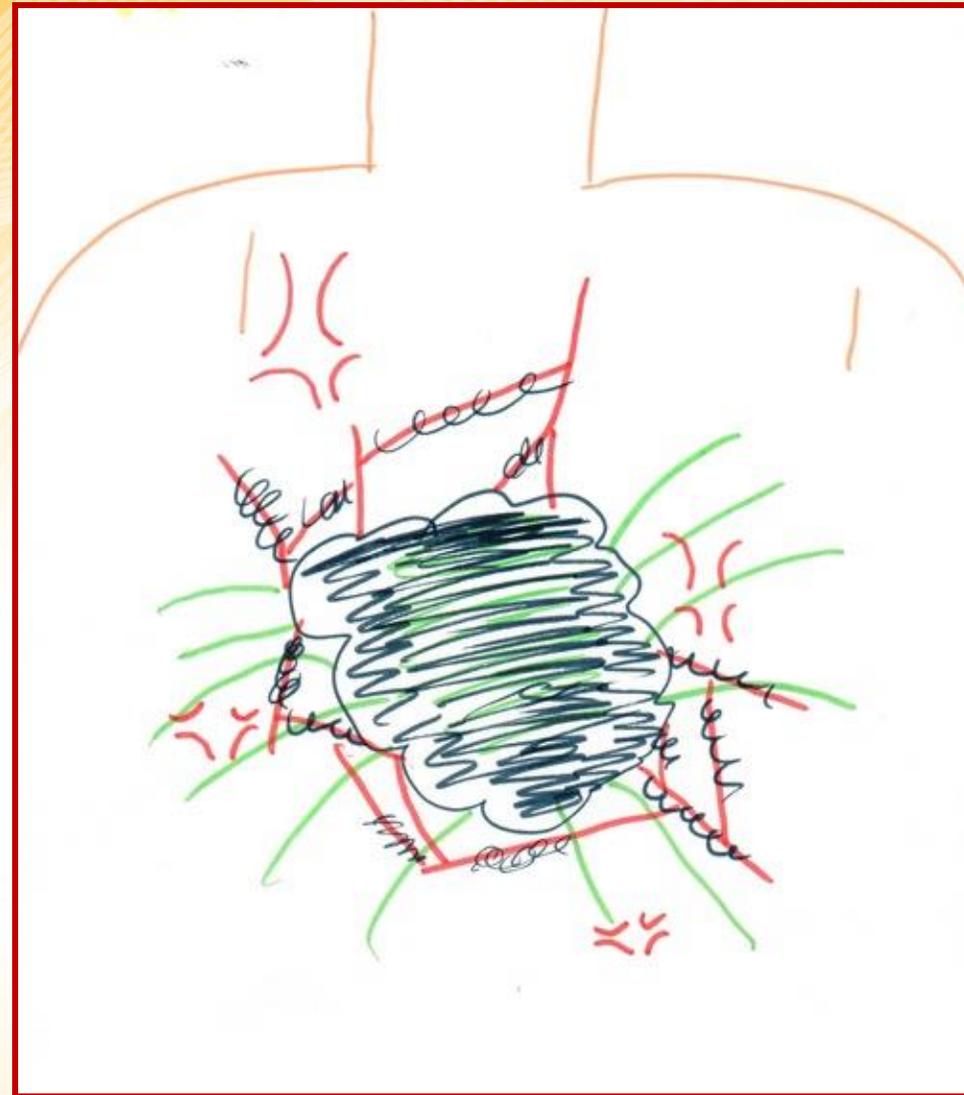


Mucus Plugging in Asthma



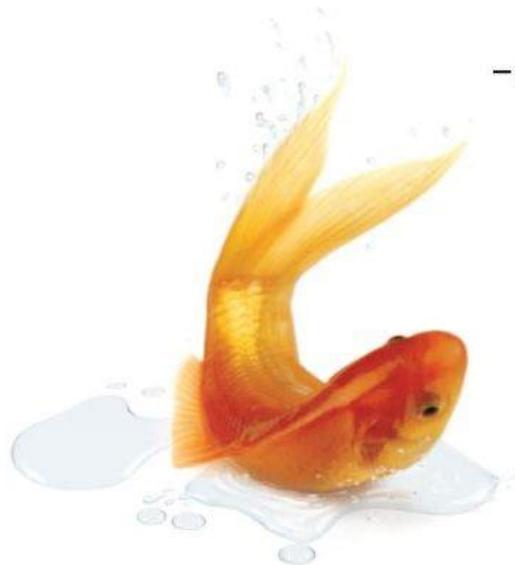
Child's View of Asthma





**“WHEN I HAVE AN
ASTHMA ATTACK
I FEEL LIKE A FISH
WITH NO WATER.”**

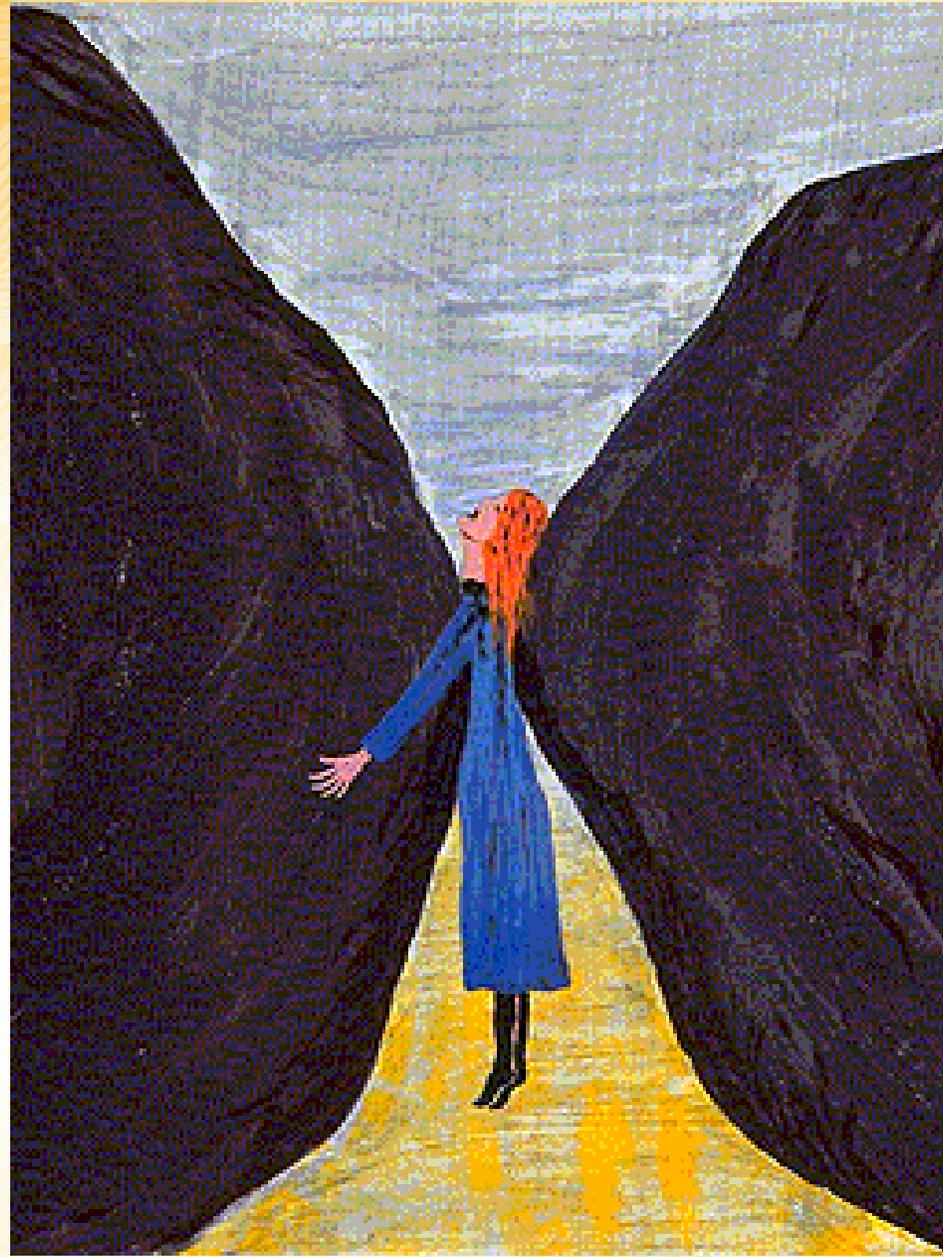
-JESSE, AGE 5

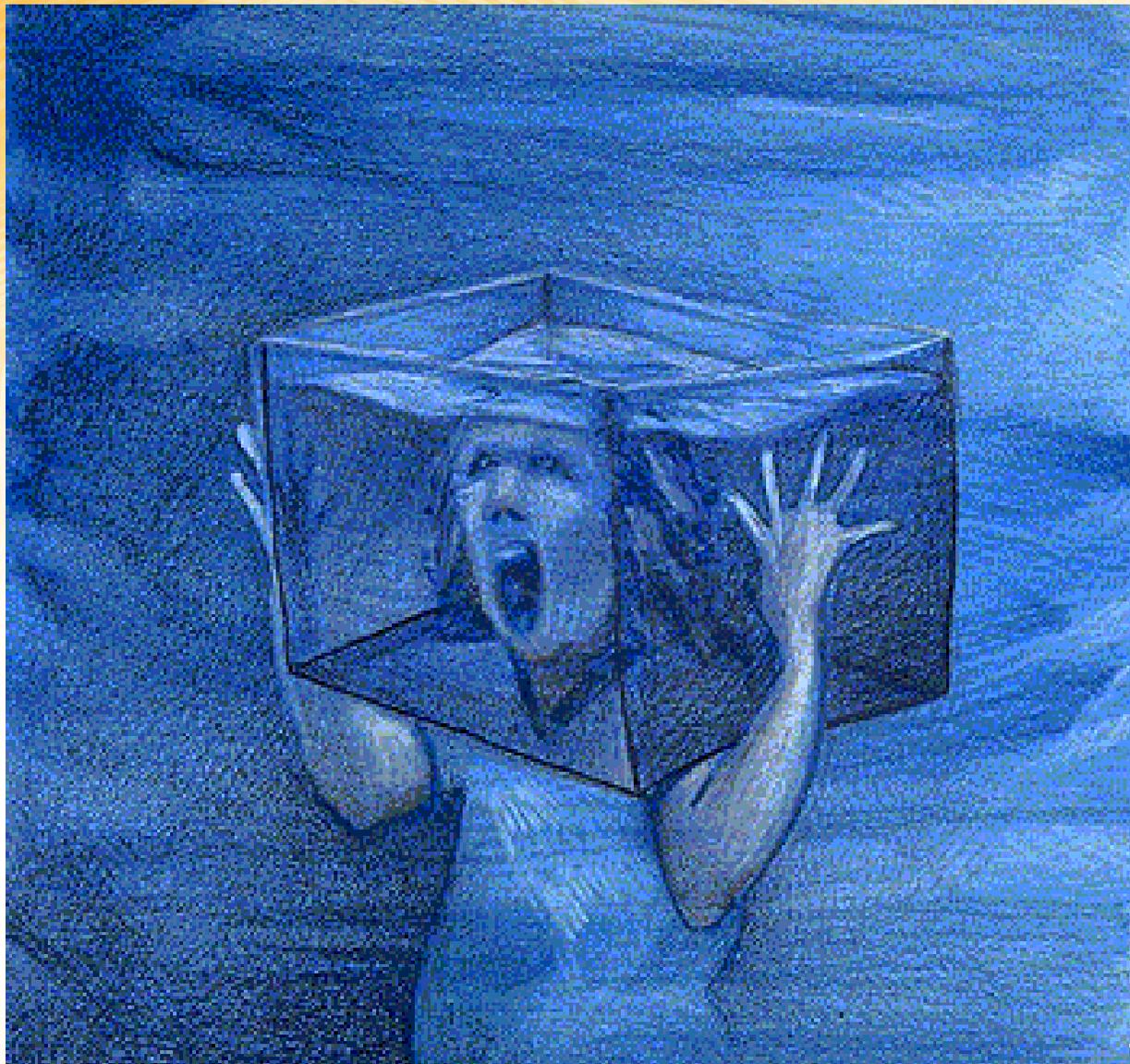


**ATTACK ASTHMA. ACT NOW.
1-866-NO-ATTACKS
WWW.NOATTACKS.ORG**



**Teenager's view
Of Asthma**





Asthma Epidemiology

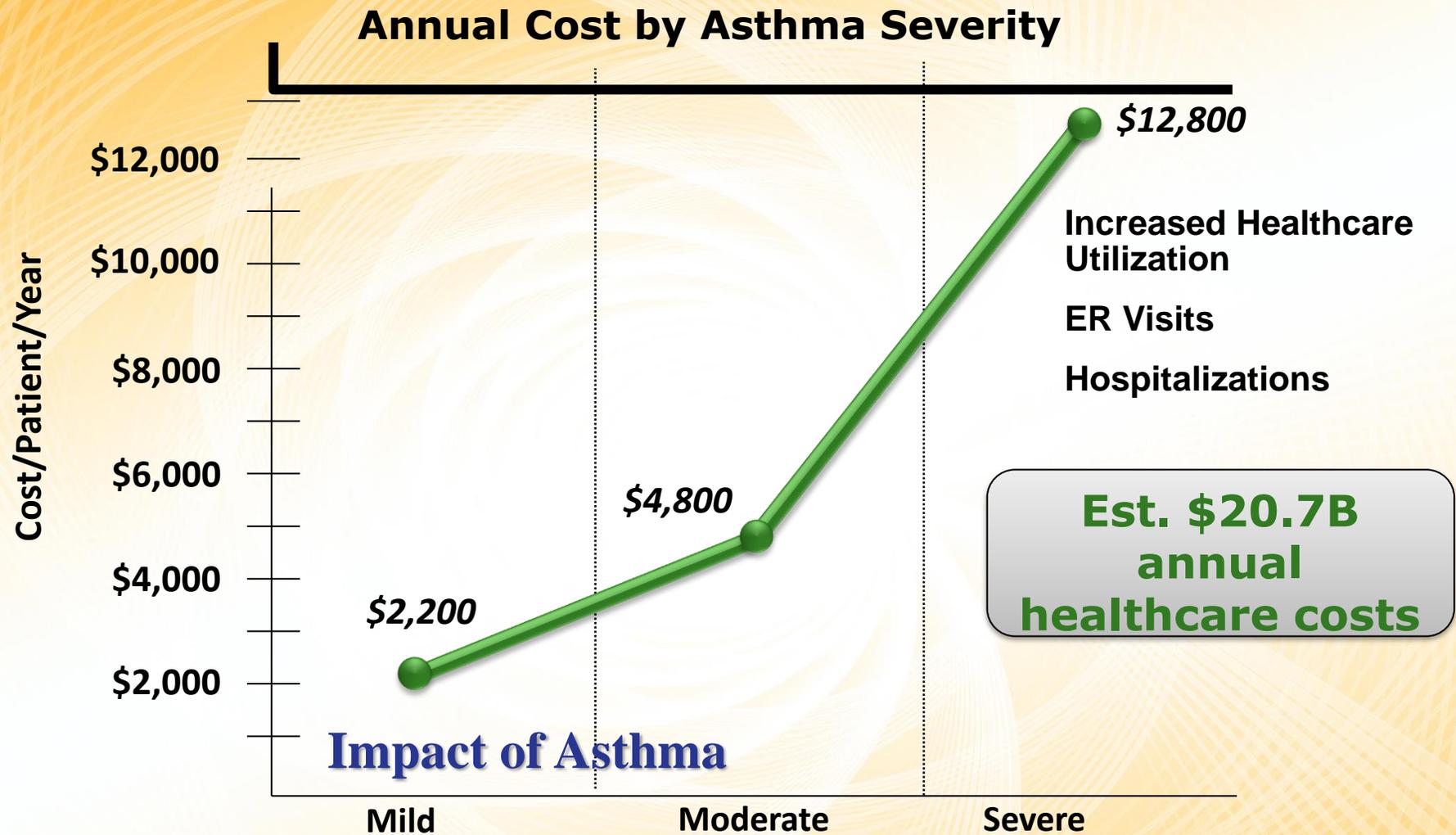
- Prevalent in 10% of the world's population
- Increase noted by 20-30% over the last two decades
- More common in males, but **more lethal** in females
- Approximately **3,500 death per year in the United States**
- Death rates higher in patients >55 years old
- Admission and death rates higher in lower social-economic groups

Asthma Overview: Prevalence, Morbidity and Mortality in the USA

- 24.6 million
People diagnosed with asthma
- 12.8 million
People experience asthma attacks
- 1.8 million
Emergency room visits
- 456,000
Hospitalizations
- 3,447
Asthma-related deaths

Annual incidence, based on 2018 data

Approximately 9 People Die From Asthma Each Day in the U.S.



Is Asthma an Social-Economic or Race Disease?



Table 1. Prevalence, Mortality, and Health Care Utilization Among Adults With Asthma in the United States

Measure	Value
Prevalence, %^a	
Overall prevalence	7.4
Sex	
Male	5.1
Female	9.6
Race/ethnicity	
White non-Hispanic	7.6
Black non-Hispanic	8.7
Hispanic	5.8
Others	6.8
Hispanic of Puerto Rican origin	13.3
Hispanic of Mexican origin	4.9
Asthma-Specific Mortality (Deaths per Million per Year)^b	
Overall	14.1
Race/ethnicity	
White non-Hispanic	8.8
Black non-Hispanic	25.4
Hispanic	7.7
Others	9.9
Health Care Utilization	
Inpatient discharges (rate per 10 000 per year)^c	
Overall	13.0
Race	
White	8.7
Black	29.9
Other	12.6
Emergency department visits (in millions per year) ^d	1.8
Physician office visits (in millions per year) ^e	10.5
Hospital outpatient department visits (in millions per year) ^f	1.3

^a Asthma prevalence by age, sex, and race/ethnicity as reported in 2014 National Health Interview Survey.

^b Asthma mortality (deaths per million) as reported in 2014 National Centers for Health Statistics surveys. Death rates by age are age-adjusted to 2000 US Standard Population.

^c Inpatient discharges as reported in the 2010 National Hospital Discharge Survey.

^d Emergency department visits as reported in the 2013 National Ambulatory Medical Care Survey.

^e Physician office visits as reported in the 2012 National Ambulatory Medical Care Survey.

^f Hospital outpatient department visits as reported in the 2010 National Hospital Ambulatory Medical Care Survey.

Questions?

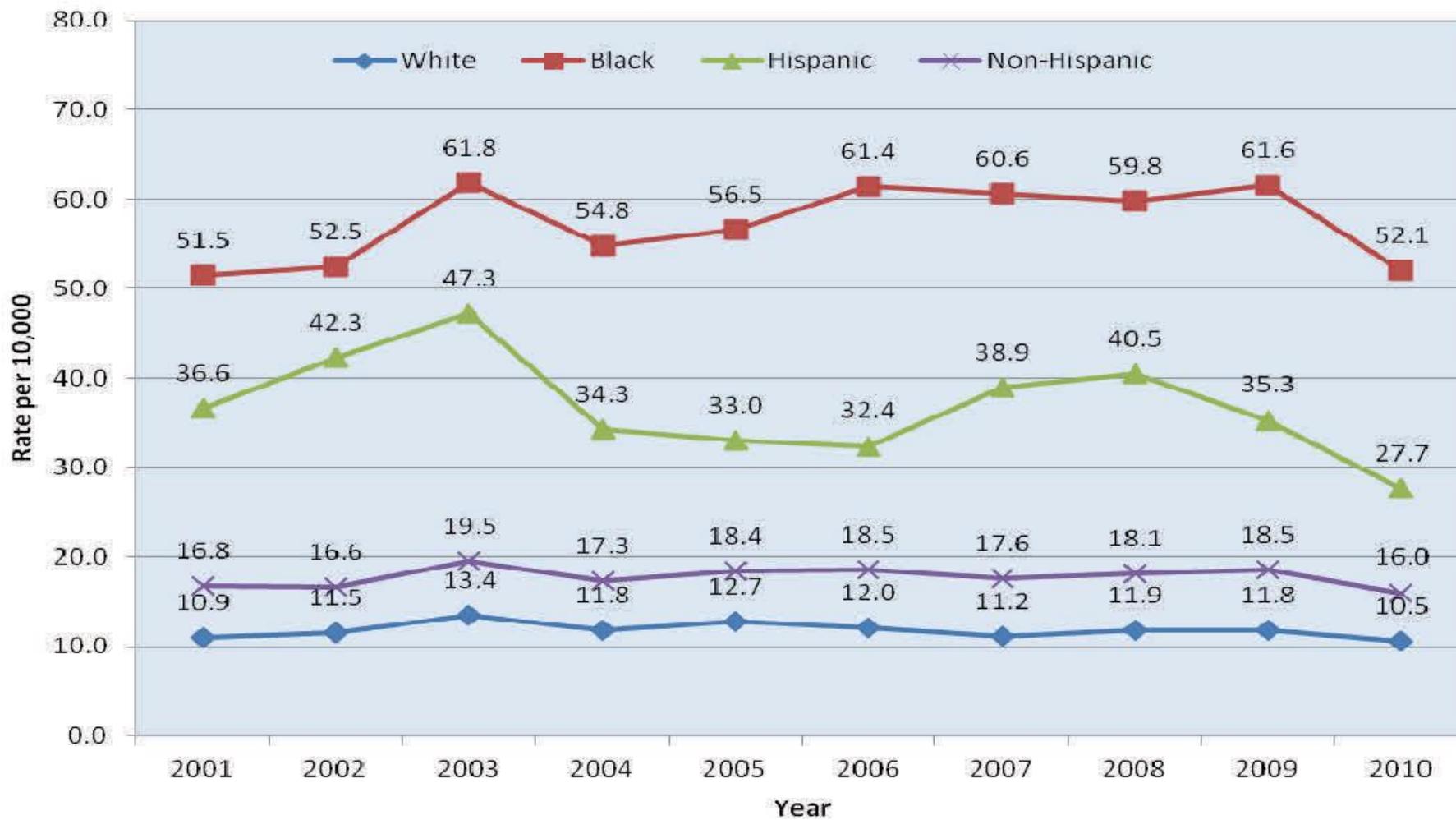
What Causes Higher Asthma Rates in African Americans?

Genetics

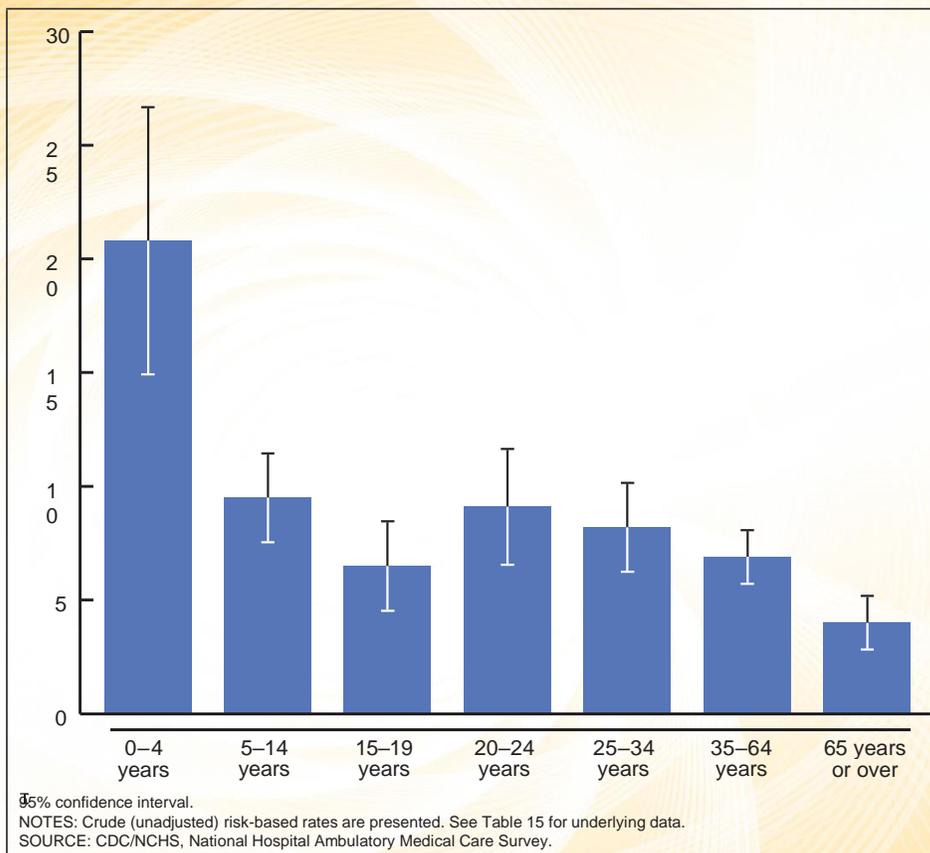
- **Although there is evidence to suggest that social determinants and inequities in healthcare play a role, certain biological factors also appear to be associated with the disparities outlined above.**
- For example, differences in genes that make someone more susceptible to developing asthma or increase the severity of their asthma symptoms may also explain the higher rates of asthma in African American populations.
- A study in the *[American Journal of Respiratory and Critical Care Medicine](#)* examined some possible differences in people's responses to respiratory medications. The researchers used a cohort of 1,441 African American, Puerto Rican, and Mexican American participants.
- The researchers found both common — that is, those that affected all populations — and rare genetic variants **associated with a decreased response to albuterol.**
- Albuterol is a bronchodilator that doctors frequently prescribe to treat asthma. Although research continues, genetic mutations such as these may provide some explanation for the disparities in asthma rates in different racial groups

- **Healthcare inequalities:** Inequities in healthcare occur for various reasons, including systemic racism and policies that discriminate against African American populations. Discrimination and racism affect economic stability and, in turn, access to healthcare. A lack of accessible healthcare may lead to a person having poorly managed asthma.
- **Social determinants:** Social determinants include factors such as a person's physical environment and socioeconomic status. For example, having poor housing conditions and a low income may result in increased exposure to asthma triggers such as mold or higher levels of air pollution.

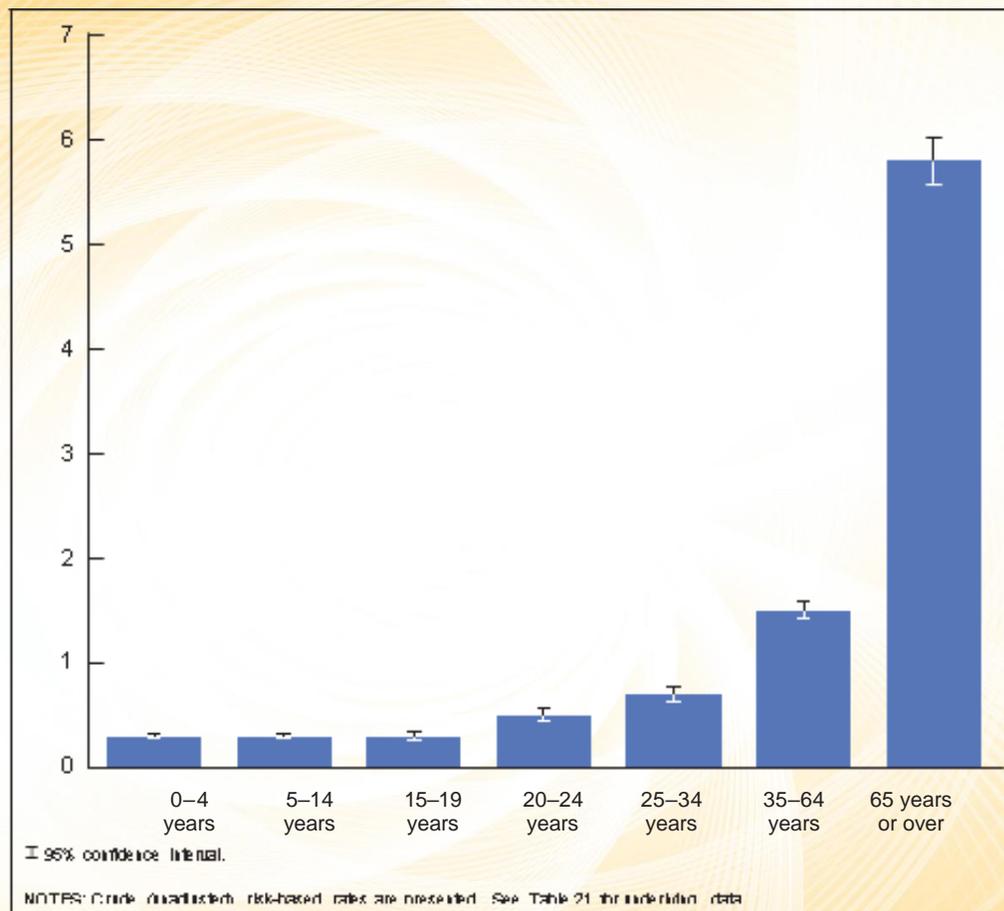
PA Asthma Partnership 2005-2010



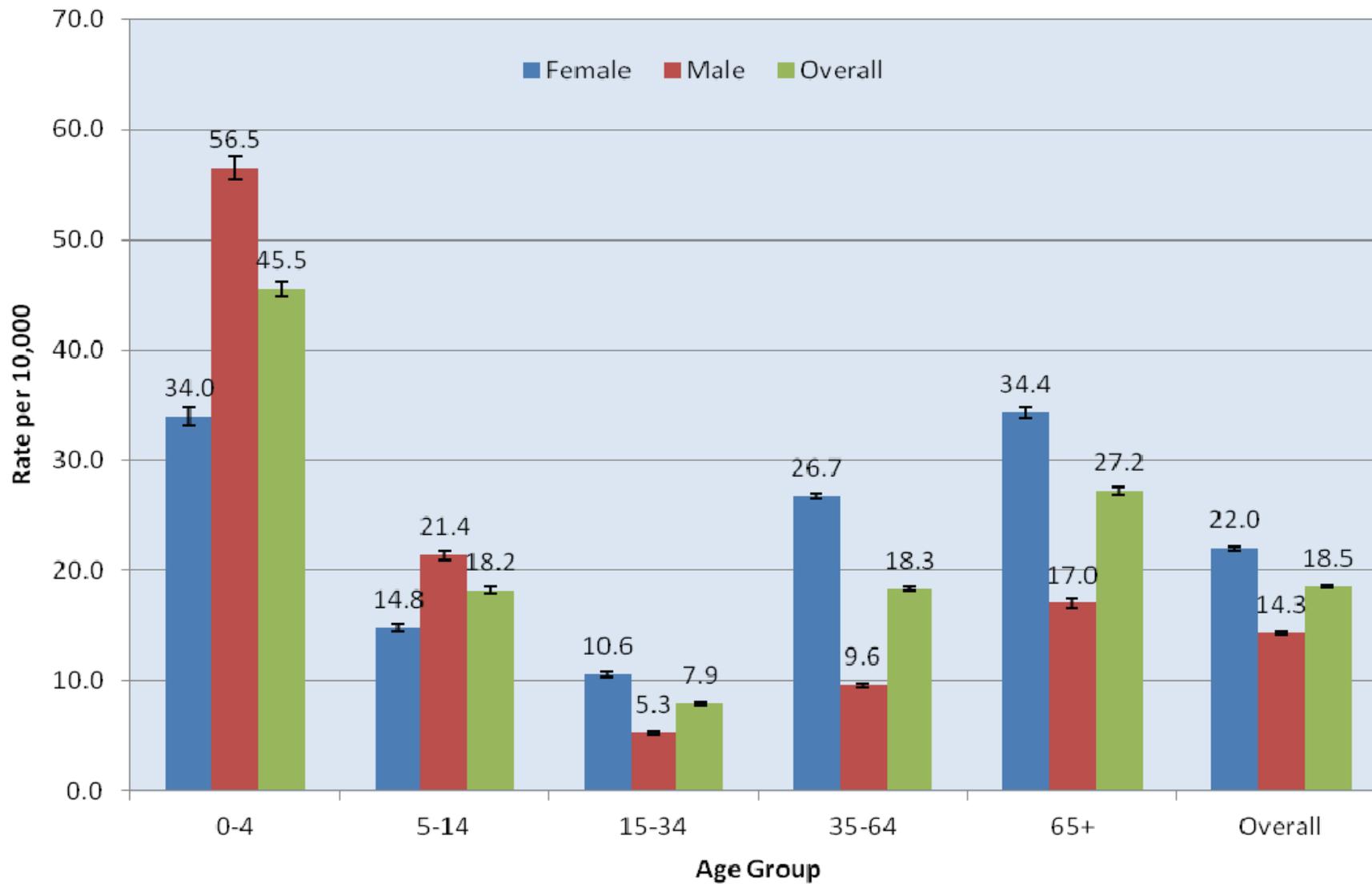
ED Visits by Age Group



Deaths by Age

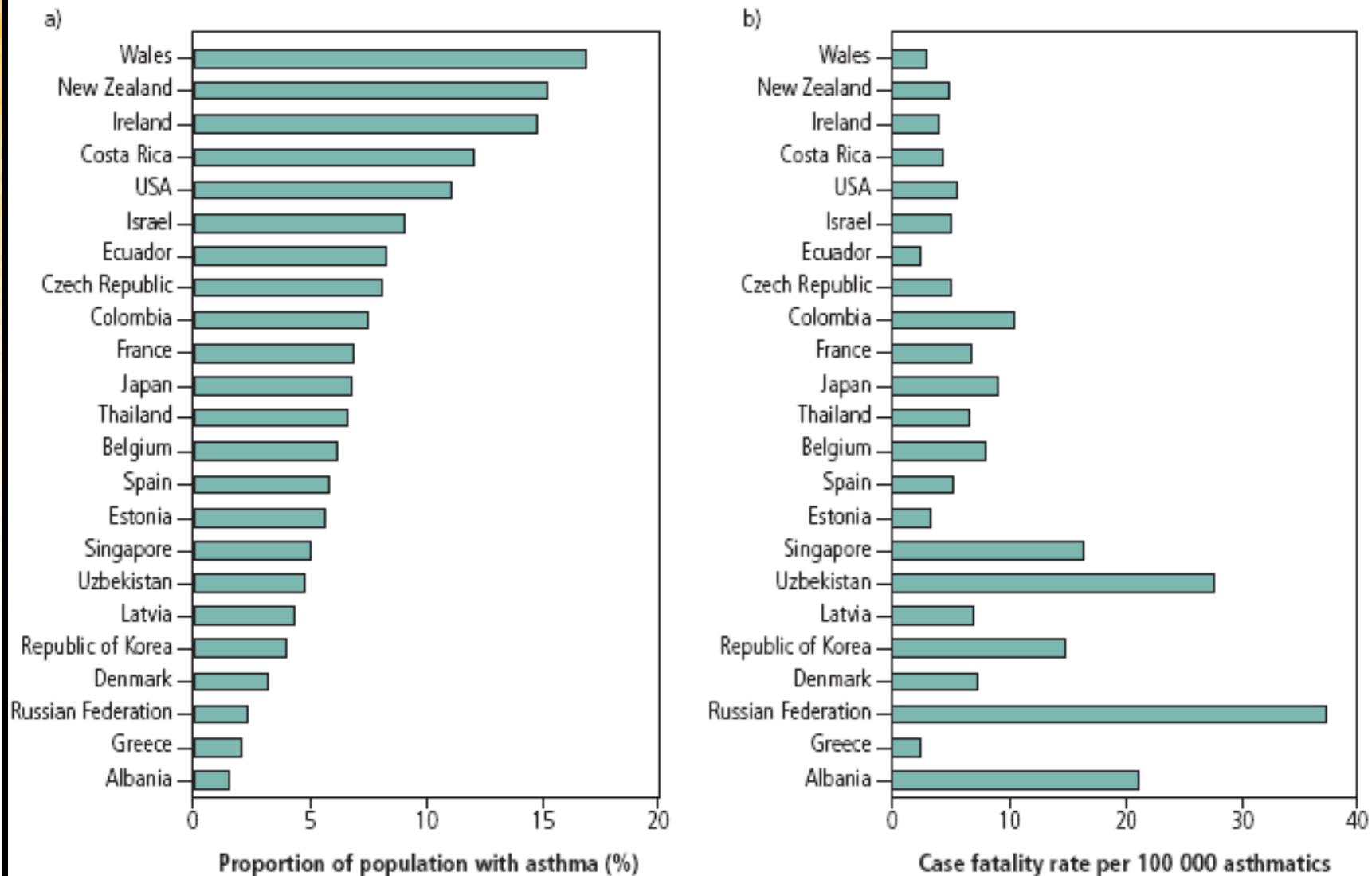


PA Asthma Partnership 2010-2015



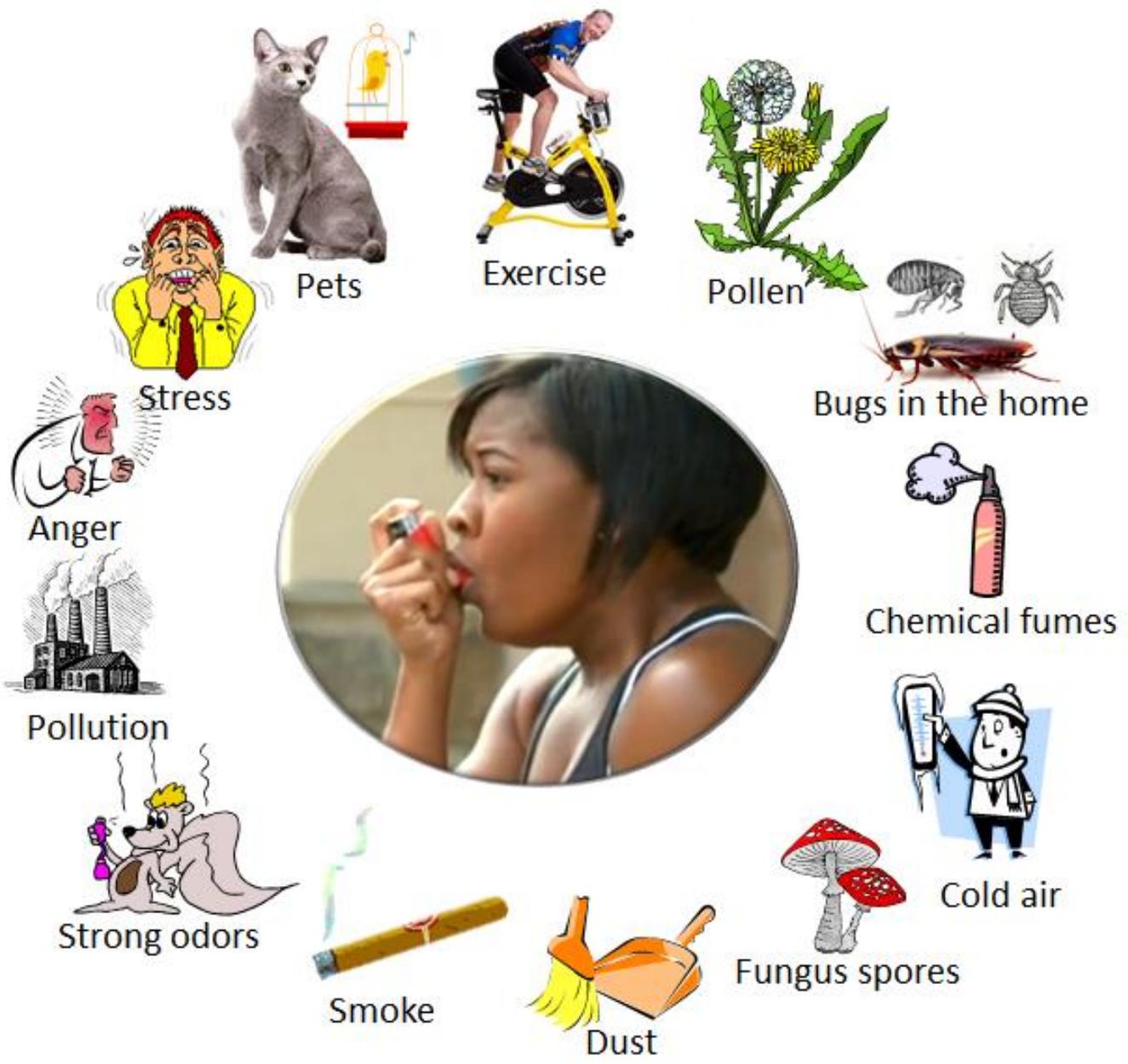
ns?

Fig. 1. Prevalence and mortality from asthma



Adapted from Masoli et al. (6).

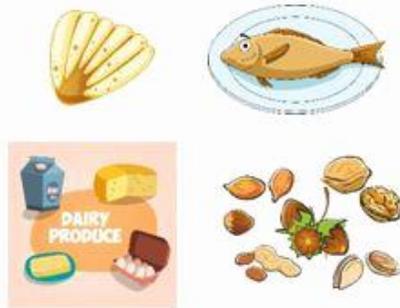
Asthma Triggers



Asthma Triggers

Common Triggers

Foods



Colds/Infections



Air Pollution



Smoking

House-Dust Mite



Weather



Emotions



Pollen, Moulds, Fungi



Medicines



Hormones

Exercise



Animals



Role of Pollution in Asthma



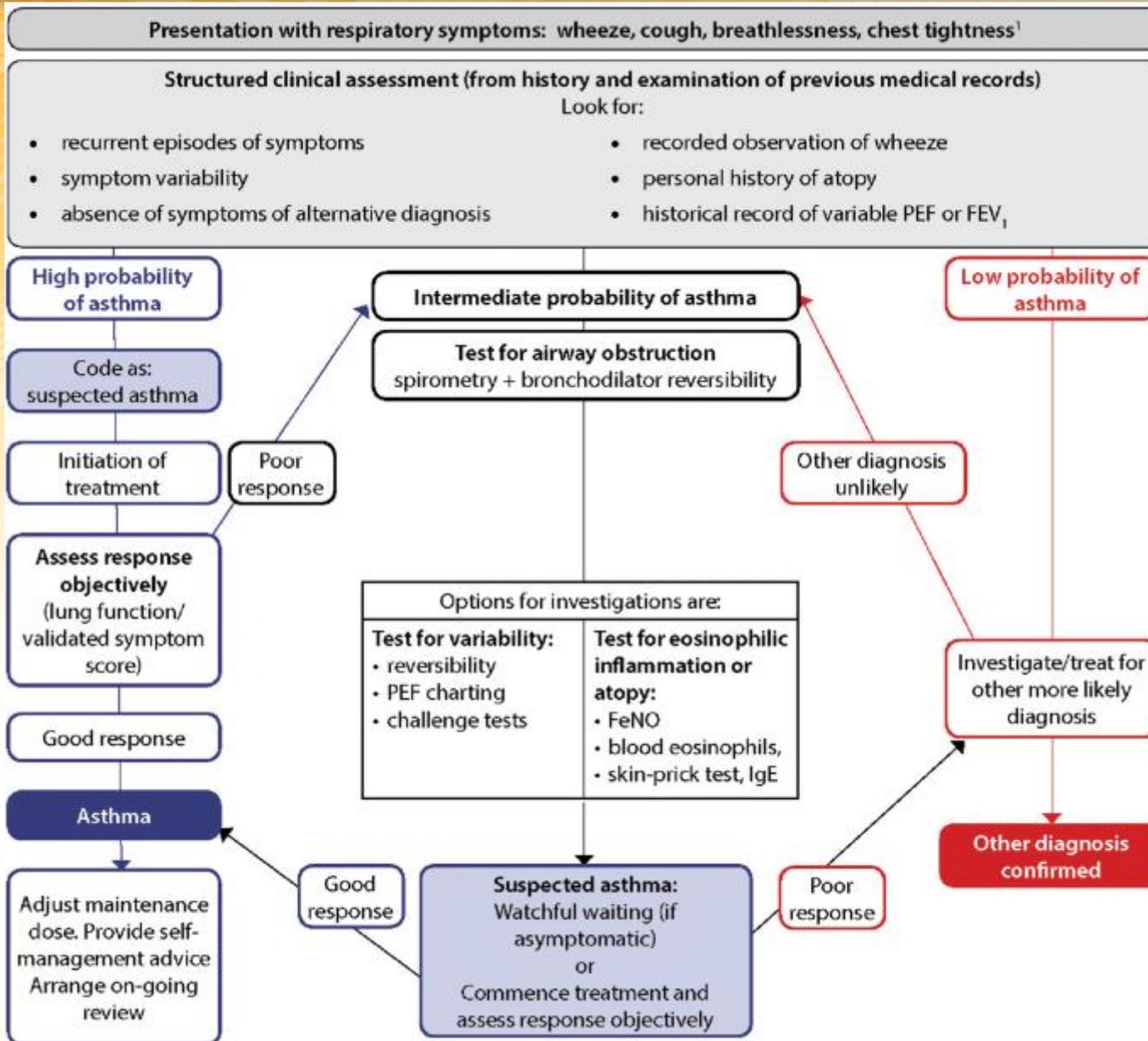
Air Quality and Outdoor Activities: Recommendations for Schools

Air Quality Index (AQI) Chart for Ozone (8-hr standard)

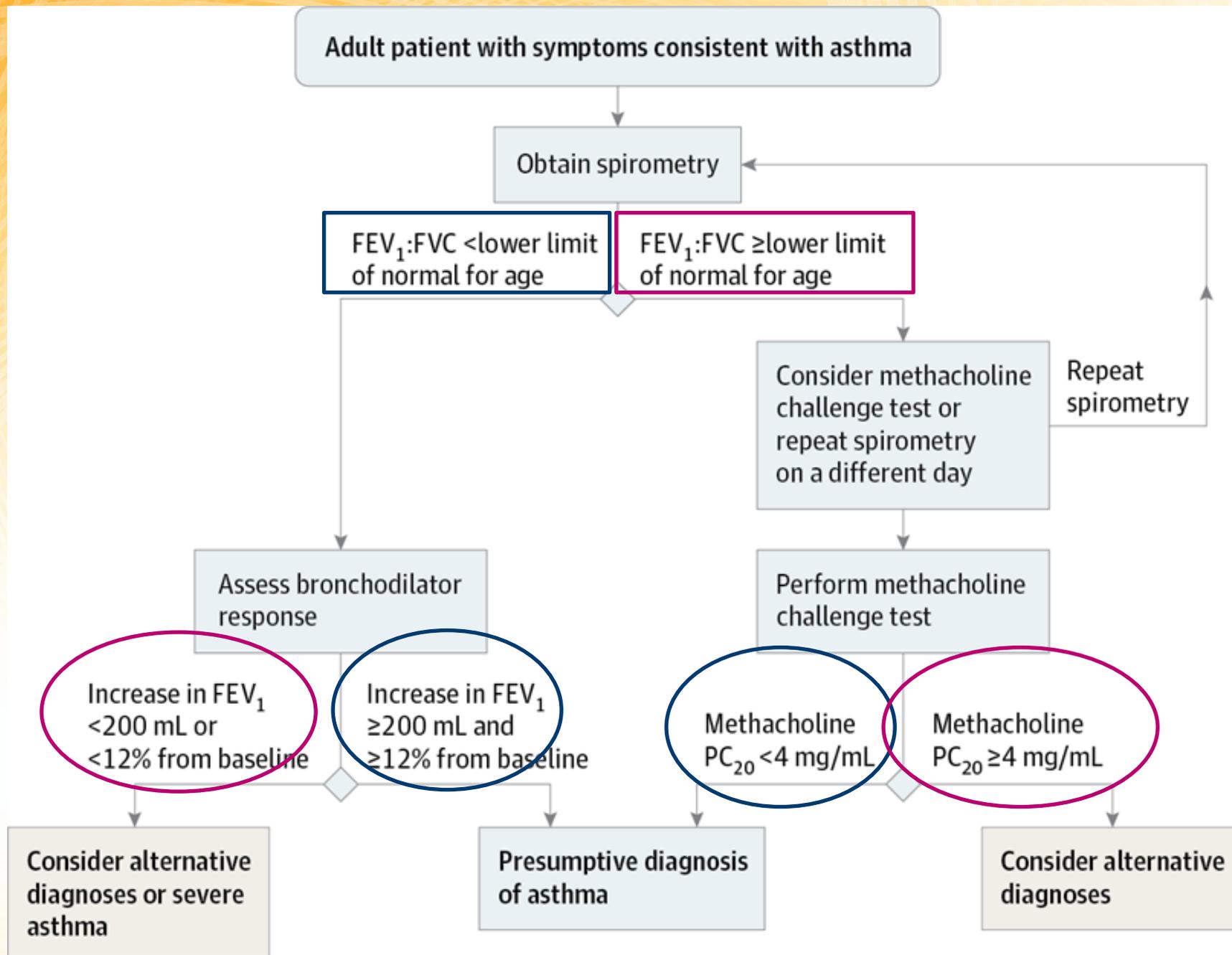
ACTIVITY	0 to 50 GOOD	51 to 100 MODERATE	101 to 150 UNHEALTHY FOR SENSITIVE GROUPS	151 to 200 UNHEALTHY	201 to 300 VERY UNHEALTHY
Recess (15 min)	No Restrictions	No Restrictions	Make indoor space available for children with asthma or other respiratory problems.	Any child who complains of difficulty breathing, or who has asthma or other respiratory problems, should be allowed to play indoors.	Restrict outdoor activities to light to moderate exercise.
P.E. (1 hr)	No Restrictions	No Restrictions	Make indoor space available for children with asthma or other respiratory problems.	Any child who complains of difficulty breathing, or who has asthma or other respiratory problems, should be allowed to play indoors.	Restrict outdoor activities to light to moderate exercise not to exceed one hour.
Scheduled Sporting Events	No Restrictions	Individuals who are unusually sensitive to ground-level ozone should limit intense activities.	Individuals with asthma or other respiratory or cardiovascular illness should increase rest periods and reduce activities to lower breathing rates.	Consideration should be given to rescheduling or relocating event.	Event should be rescheduled or relocated indoors.
Athletic Practice and Training (2 to 4 hrs)	No Restrictions	Individuals who are unusually sensitive to ground-level ozone should limit intense activities.	Individuals with asthma or other respiratory or cardiovascular illness should increase rest periods and reduce activities to lower breathing rates.	Activities over 2 hours should decrease intensity and duration. Add rest breaks or substitutions to lower breathing rates.	Sustained rigorous exercise for more than one hour must be rescheduled, moved indoors or discontinued.

**=120
Days
>100
Lehigh
Valley
2018**

How Do We Diagnosis Asthma?



¹ In children under 5 years and others unable to undertake spirometry in whom there is a high or intermediate probability of asthma, the options are monitored initiation of treatment or watchful waiting according to the assessed probability of asthma.



Classification of Asthma 2018

Components of severity		Classification of asthma severity (age ≥12 y)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment	Symptoms	≤2 d/wk	>2 d/wk but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2× mo	3-4× mo	>1× wk but not nightly	Often 7× wk
	Short-acting β ₂ -agonist use for symptom control (not prevention of EIB)	≤2 d/wk	>2 d/wk but not daily, and not more than 1× on any day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function Normal FEV ₁ : FVC ratio 20-39 y 80% 40-59 y 75% 60-80 y 70%	<ul style="list-style-type: none"> • Normal FEV₁, between exacerbations • FEV₁, >80% predicted • FEV₁: FVC normal 	<ul style="list-style-type: none"> • FEV₁, >80% predicted • FEV₁:FVC normal 	<ul style="list-style-type: none"> • FEV₁, >60% but <80% predicted • FEV₁:FVC normal 	<ul style="list-style-type: none"> • FEV₁, <60% predicted • FEV₁:FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0-1/y	≥2/y	≥2/y	≥2/y
		Consider severity and interval since last exacerbation Frequency and severity may fluctuate over time for patients in any severity category Relative annual risk of exacerbation may be related to FEV ₁			
Recommended step for initiating treatment (see Figure 3 for treatment steps)		Step 1	Step 2	Step 3	Step 4 or 5
		and consider short course of oral systemic corticosteroids			
In 2-6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly					

Questions?

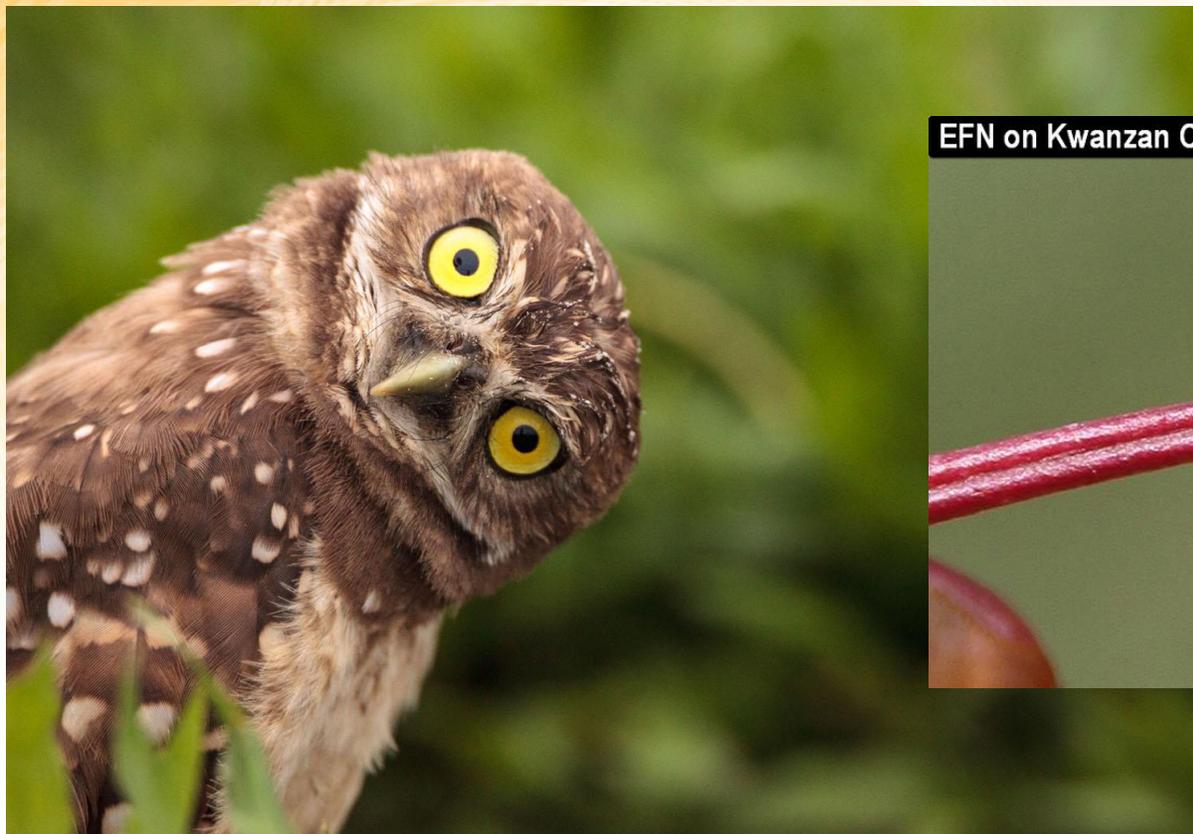
**How Do We
Treat Asthma???**
Past and Now

Early Treatment ?



In ancient times, "Album graecum" – or more colloquially known as dog poo – was a popular treatment for a Asthma. In these days, feces was usually mixed with honey and misted into the airways to treat airway redness

Owl's Blood Mixed With Tree Nectars



EFN on Kwanzan Cherry



Joe Boggs, OSU Extension©



Asthma Cigarettes That contains Medicines Or herbs

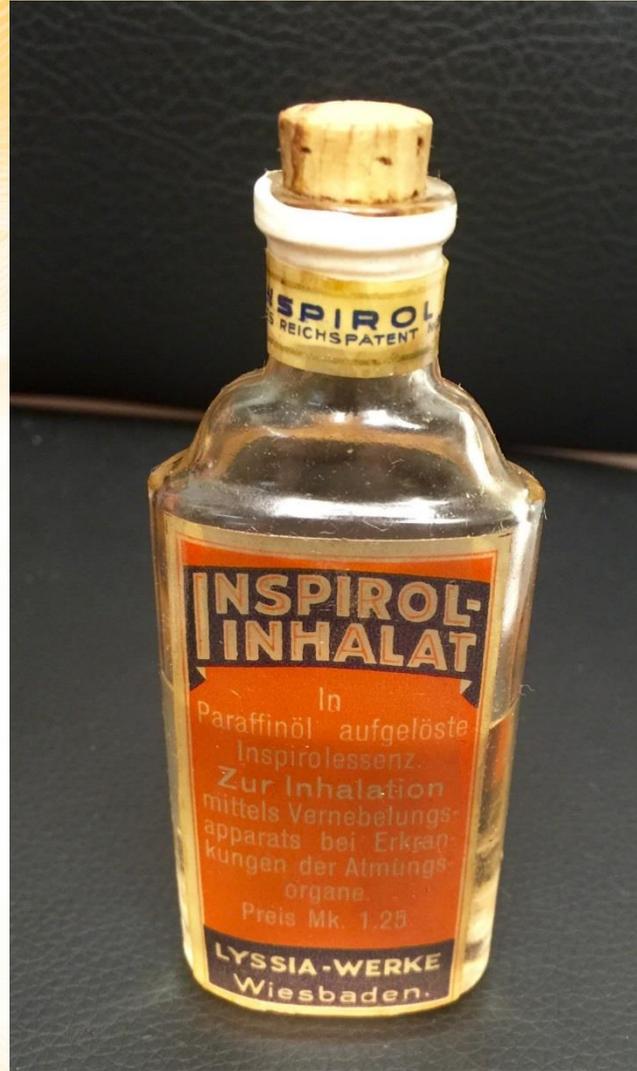
CIGARETTES de **JOY**
(JOY'S CIGARETTES)

CURE **ASTHMA**

JOY'S CIGARETTES afford immediate relief in cases of **ASTHMA, WHEEZING, AND WINTER COUGH,** and a little perseverance will effect a permanent cure. Universally recommended by the most eminent physicians and medical authors. Agreeable to use, certain in their effects, and harmless in their action, they may be safely smoked by ladies and children.

All Chemists and Stores, box of 35, 2s. 6d., or post free from **WILCOX & Co., 239, OXFORD STREET, LONDON, W.**

Asthma Nectar





Early atomizer

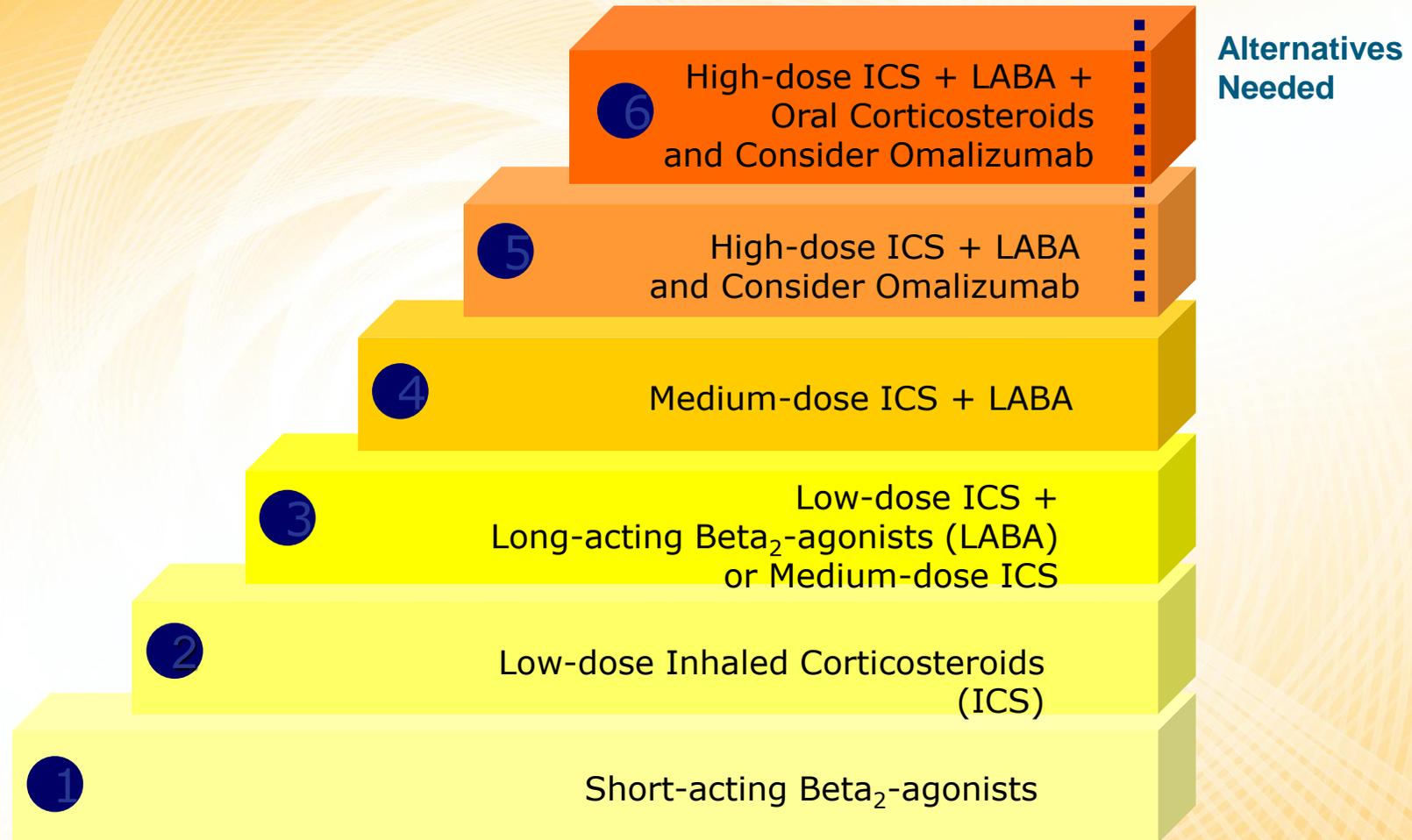


Early
nebulizer

Photo with permission: Felix Kudish.

**Global Initiative for Asthma
(GINA)
Global Strategy for Asthma
Management and Prevention**

2018 Stepwise Approach for Managing Asthma



- Asthma is the most common chronic non-communicable disease, affecting over 260 million people globally in 2019.
- Asthma is characterized by variable respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough, and variable expiratory airflow limitation. It is usually associated with airway inflammation.
- People with asthma often have periods of worsening symptoms and worsening airway obstruction, called exacerbations (also called attacks or flare-ups), that can be fatal.
- Most of the morbidity and mortality associated with asthma is preventable, particularly with use of inhaled corticosteroids.

GINA 2019 – landmark Changes in Asthma Management

- For safety, GINA no longer recommends SABA-only treatment for Step 1 in adults and adolescents
- This decision was based on evidence that SABA-only treatment increases the risk of severe exacerbations, and that adding any ICS significantly reduces the risk. n GINA now recommends that all adults and adolescents with asthma should receive ICS-containing controller treatment, to reduce the risk of serious exacerbations § The ICS can be delivered by regular daily treatment or, in mild asthma, by as-needed low dose ICS-formoterol. This is a population-level risk reduction strategy
- The aim is to reduce the probability of serious adverse outcomes at a population level
-

GINA 2021 – Mild Asthma

- There are many definitions of mild asthma
- Current definition: Asthma that is able to be well-controlled with reliever alone or low dose ICS; but severity cannot be assessed until the patient has been on treatment for several months
- In research studies, mild asthma is often defined by treatment with SABA alone or low dose ICS (but patients may be being under- or over-treated) § Patients and clinicians often consider ‘mild asthma’ to mean infrequent or mild symptoms n GINA does not distinguish between ‘intermittent’ and ‘mild persistent’ asthma
- Historically, this was an arbitrary distinction, based on an assumption that patients with symptoms twice a week or less would not benefit from ICS
- Patients with so-called ‘intermittent’ asthma are still at risk of severe exacerbations n GINA is planning to review the definition of mild asthma during 2021

“Mild Asthma”

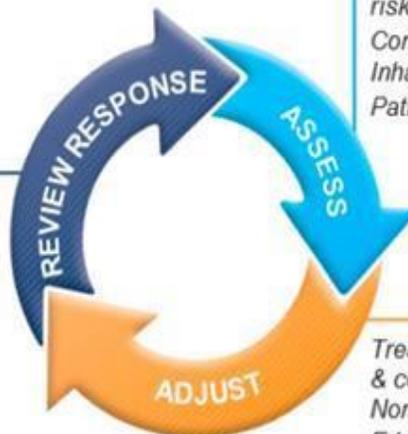
- Patients with apparently mild asthma are still at risk of serious adverse events.
 - 30–37% of adults with acute asthma.
 - 16% of patients with near-fatal asthma
 - 15–20% of adults dying of asthma.
- Exacerbation triggers are unpredictable (viruses, pollens, pollution, poor adherence)
Inhaled SABA has been first-line treatment for asthma for 50 years § Dating from an era when asthma was thought to be a disease of bronchoconstriction.
- Its role has been reinforced by rapid relief of symptoms and low cost.
- Starting treatment with SABA trains the patient to regard it as their primary asthma treatment

Adults & adolescents 12+ years

Personalized asthma management:

Assess, Adjust, Review response

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (including lung function)
Comorbidities
Inhaler technique & adherence
Patient goals

Treatment of modifiable risk factors & comorbidities
Non-pharmacological strategies
Education & skills training
Asthma medications

Asthma medication options:

Adjust treatment up and down for individual patient needs

PREFERRED CONTROLLER

to prevent exacerbations and control symptoms

Other controller options

STEP 1

As-needed low dose ICS-formoterol*

Low dose ICS taken whenever SABA is taken †

STEP 2

Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol*

Leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken †

STEP 3

Low dose ICS-LABA

Medium dose ICS, or low dose ICS+LTRA#

STEP 4

Medium dose ICS-LABA

High dose ICS, add-on tiotropium, or add-on LTRA#

STEP 5

High dose ICS-LABA

Refer for phenotypic assessment ± add-on therapy, e.g. tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R

Add low dose OCS, but consider side-effects

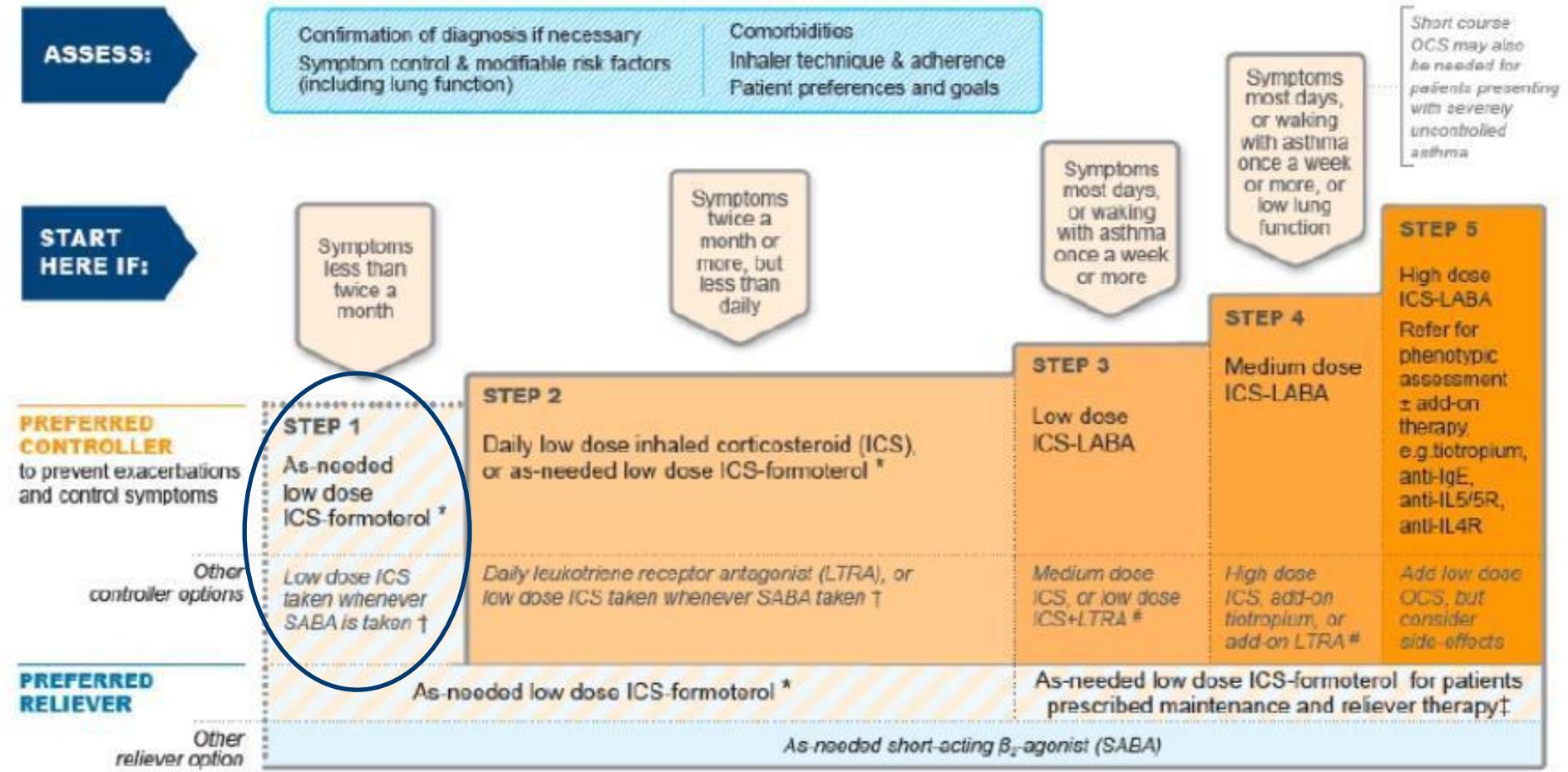
As-needed low dose ICS-formoterol*

As-needed low dose ICS-formoterol for patients prescribed maintenance and reliever therapy

PREFERRED RELIEVER

Box 7B. Initial treatment: adult or adolescents with a diagnosis of asthma

SELECTING INITIAL CONTROLLER TREATMENT IN ADULTS AND ADOLESCENTS WITH A DIAGNOSIS OF ASTHMA



* Data only with budesonide-formoterol (bud-form)

† Low-dose ICS-form is the reliever only for patients prescribed

ASTHMA ACTION PLAN



Name:	Date:
Doctor:	Medical Record #:
Doctor's Phone #: Day	Night/Weekend
Emergency Contact:	
Doctor's Signature:	

The colors of a traffic light will help you use your asthma medicines.



- GREEN means Go Zone!**
Use preventive medicine.
- YELLOW means Caution Zone!**
Add quick-relief medicine.
- RED means Danger Zone!**
Get help from a doctor.

Personal Best Peak Flow: _____

GO		Use these daily preventive anti-inflammatory medicines:		
<p>You have <i>all</i> of these:</p> <ul style="list-style-type: none"> Breathing is good No cough or wheeze Sleep through the night Can work & play 	<p>Peak flow: from _____ to _____</p>	MEDICINE	HOW MUCH	HOW OFTEN/WHEN
		For asthma with exercise, take:		
CAUTION		Continue with green zone medicine and add:		
<p>You have <i>any</i> of these:</p> <ul style="list-style-type: none"> First signs of a cold Exposure to known trigger Cough Mild wheeze Tight chest Coughing at night 	<p>Peak flow: from _____ to _____</p>	MEDICINE	HOW MUCH	HOW OFTEN/ WHEN
		CALL YOUR PRIMARY CARE PROVIDER.		
DANGER		Take these medicines and call your doctor now.		
<p>Your asthma is getting worse fast:</p> <ul style="list-style-type: none"> Medicine is not helping Breathing is hard & fast Nose opens wide Ribs show Can't talk well 	<p>Peak flow: reading below _____</p>	MEDICINE	HOW MUCH	HOW OFTEN/WHEN

GET HELP FROM A DOCTOR NOW! Do not be afraid of causing a fuss. Your doctor will want to see you right away. It's important! If you cannot contact your doctor, go directly to the emergency room. DO NOT WAIT. Make an appointment with your primary care provider within two days of an ER visit or hospitalization.

Category	Examples	Usual Dosing	Treatment Effect	Adverse Effects	Notes
Standard Therapies					
Relievers					
Short-acting β_2 -agonists (SABAs)	Albuterol Levalbuterol Pirbuterol	2 puffs every 4-6 h	Bronchodilation (7%-15% increase in FEV ₁ , dose dependent)	Nervousness, tremor, bronchospasm, tachycardia, headache, pharyngitis	
Short-acting muscarinic antagonists (SAMAs)	Ipratropium	2-3 puffs every 6 h	Bronchodilation (7%-15% increase in FEV ₁ , dose dependent)	Bronchitis, COPD exacerbation, dyspnea, headache	
Controllers					
Inhaled corticosteroids (ICSs)	Fluticasone	2 puffs twice daily	Decreased daytime and nocturnal symptoms	Upper respiratory tract infection, throat irritation, sinusitis, dysphonia, candidiasis, cough, bronchitis, headache	Comparisons for low, moderate, and high doses of ICSs are detailed elsewhere ^{12,13}
	Budesonide	2-4 puffs twice daily	Reduced exacerbations and death		
	Mometasone	Varies by device	Improved FEV ₁ (improvement in symptoms, exacerbations, death, and FEV ₁ are all dose dependent ^{18,19})		
	Ciclesonide	160-320 μ g twice daily			
Leukotriene receptor antagonists (LTRAs)	Montelukast	10 mg daily	Decreased daytime and nocturnal symptoms	Headache, fatigue, abdominal pain, dyspepsia, mood changes	
	Zafirlukast	20 mg twice daily	Improved FEV ₁ ²⁰		
Leukotriene synthesis inhibitor	Zileuton	600 mg 4 times daily	Improved FEV ₁ ²¹	Headache, pain, abdominal pain, dyspepsia, nausea, myalgia, increased alanine aminotransferase	Requires monitoring of hepatic enzymes Drug interactions are common
Long-acting β_2 -agonists (LABAs)	Salmeterol	2 puffs twice daily	Improved FEV ₁ ²²	Headache, rhinitis, bronchitis, influenza, dizziness	These agents should not be used without a simultaneous ICS agent
	Formoterol	2 puffs twice daily			
	Vilanterol	NA			
Long-acting muscarinic antagonist (LAMA)	Tiotropium	2 inhalations once daily	Improved FEV ₁ ²³	Dry mouth, upper respiratory tract infection, pharyngitis, sinusitis, chest pain	
Combined ICSs/LABAs	Fluticasone/salmeterol inhaler	1 puff twice daily	Benefits of both ICSs and LABAs ²⁴	Nasopharyngitis, URI, headache, sinusitis, influenza, back pain	
	Fluticasone/salmeterol HFA	2 puffs twice daily			
	Budesonide/formoterol	2 puffs twice daily			
	Fluticasone/vilanterol	1 puff daily			
Other Therapies					
Oral corticosteroids	Prednisone	5-20 mg/d		Hypertension, increased appetite, weight gain, insomnia, mood changes, gastritis, skin atrophy, osteoporosis, adrenal suppression, avascular necrosis of bone	Doses listed are for chronic maintenance, not for exacerbations Daily use of oral corticosteroids is not recommended unless other options are ineffective; consult with an asthma specialist
	Methylprednisolone	4-16 mg/d			
Biologics					
Anti-IgE	Omalizumab	Varies by weight	Reduced asthma exacerbations Variable benefit in FEV ₁ ²⁵	Injection site reaction, viral infections, URI, sinusitis, headache, pharyngitis, anaphylaxis	Used primarily by asthma specialists
Anti-IL-5	Mepolizumab	100 mg subcutaneously monthly	Reduced asthma exacerbations	Headache, injection site reaction, back pain, fatigue, oropharyngeal pain	Used primarily by asthma specialists
	Reslizumab	Varies by weight, IV administration	Small improvement in FEV ₁ ²⁶⁻²⁹		
Bronchial thermoplasty		3 Bronchoscopic treatments, once monthly for 3 mo	Reduced asthma exacerbations, emergency department visits through at least 1 y ³⁰	Short-term worsening of asthma symptoms, cough, wheezing, chest pain, URI, infection	Specialty treatment Durability of benefit is controversial

Abbreviations: COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in first second of expiration; URI, upper respiratory infection.



Respiratory Treatments

2019

AllergyAsthmaNetwork.org
800.878.4403



Allergy & Asthma Network is a national nonprofit organization dedicated to ending needless death and suffering due to asthma, allergies and related conditions through outreach, education, advocacy and research.



1123 = DOSE INDICATOR G = GENERIC AVAILABLE DISEASE STATES: A = ASTHMA C = COPD

SHORT-ACTING BETA₂-AGONIST BRONCHODILATORS

relax tight muscles in airways and offer quick relief of symptoms such as coughing, wheezing and shortness of breath for 3-6 hours

ProAir® HFA albuterol sulfate 1123 A		ProAir® RespiClick® albuterol sulfate inhalation powder 1123 A		Proventil® HFA albuterol sulfate A		Ventolin® HFA albuterol sulfate 1123 A		Xopenex® HFA levalbuterol tartrate A G	
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LONG-ACTING BETA₂-AGONIST BRONCHODILATORS

relax tight muscles in airways and offer lasting relief of symptoms such as coughing, wheezing and shortness of breath for at least 12 hours

Arcapta™ Neohaler™ indacaterol inhalation powder C		Serevent® Diskus® salmeterol xinafoate inhalation powder 1123 A G		Striverdi® RespiMat® olodaterol hydrochloride 1123 C	
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INHALED CORTICOSTEROIDS

reduce and prevent swelling of airway tissue; they do not relieve sudden symptoms of coughing, wheezing or shortness of breath

Alvesco® HFA 80 mcg, 160 mcg ciclesonide 1123 A		ArmonAir™ RespiClick® 55 mg, 113 mg, 232 mg fluticasone propionate inhalation powder 1123 A		Arnuity® Ellipta® 100 mcg, 200 mcg fluticasone furoate inhalation powder 1123 A		Asmanex® HFA mometasone furoate 1123 A		Asmanex® Twisthaler® 110 mcg, 220 mcg mometasone furoate inhalation powder 1123 A		Flovent® Diskus® 50 mcg, 100 mcg, 250 mcg fluticasone propionate inhalation powder 1123 A		Flovent® HFA 44 mcg, 110 mcg, 220 mcg fluticasone propionate 1123 A		Pulmicort Flexhaler® 90 mcg, 180 mcg budesonide inhalation powder 1123 A		QVAR® Redihaler™ 40 mcg, 80 mcg beclomethasone dipropionate 1123 A	
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COMBINATION MEDICATIONS

contain both inhaled corticosteroid and long-acting beta₂-agonist (LABA)

Advair Diskus® 100/50, 250/50, 500/50 fluticasone propionate and salmeterol inhalation powder 1123 A C		Advair® HFA 45/21, 115/21, 230/21 fluticasone propionate and salmeterol xinafoate A G		AirDuo™ RespiClick® 55/14 mcg, 113/14 mcg, 232/14 mcg fluticasone propionate and salmeterol inhalation powder 1123 A G		Breo® Ellipta® 100/25 mcg, 200/25 mcg fluticasone furoate and vilanterol inhalation powder 1123 A C		Dulera® 100/5, 200/5 mometasone furoate and formoterol fumarate dihydrate 1123 A		Symbicort® (HFA) 80/4.5, 160/4.5 budesonide and formoterol fumarate dihydrate 1123 A C	
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contain both long-acting beta₂-agonist (LABA) and long-acting muscarinic antagonist (LAMA)

Anoro® Ellipta® 62.5 mcg/25 mcg umecidinium and vilanterol inhalation powder 1123 C		Bevespi Aerosphere® 9 mcg/4.8mcg glycopyrrate and formoterol fumarate 1123 C		Stiolto™ RespiMat® 2.5 mcg/2.5 mcg tiotropium bromide and olodaterol 1123 C		Utibron™ Neohaler® 27.5 mcg/15.6 mcg indacaterol and glycopyrrate inhalation powder C		Trelegy® Ellipta® 100 mcg/62.5 mcg/25 mcg fluticasone furoate, umecidinium and vilanterol inhalation powder 1123 C	
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MUSCARINIC ANTAGONIST (ANTICHOLINERGIC)

relieve cough, sputum production, wheeze and chest tightness associated with chronic lung diseases

Short-acting Atrovent® HFA ipratropium bromide 1123 C		Long-acting Seebri™ Neohaler® glycopyrrate inhalation powder C		Incruse® Ellipta® umecidinium inhalation powder 1123 C		Spiriva® HandiHaler® tiotropium bromide inhalation powder C		Spiriva® RespiMat® tiotropium bromide 1123 A C		Tudorza™ Pressair™ acridinium bromide inhalation powder 1123 C	
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COMBINATION

muscarinic antagonist and beta₂-agonist

Short-acting Combivent® RespiMat® ipratropium bromide and albuterol 1123 C	
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BIOLOGICS

Cinqair® reslizumab A		Dupixent® 200 mg, 300 mg dupilumab A		Fasenra® benralizumab A		Nucala® mepolizumab A		Xolair® omalizumab A	
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BRONCHIAL THERMOPLASTY

A minimally invasive procedure that uses mild heat to reduce airway smooth muscle, leading to fewer severe asthma flares, ER visits, and days lost from activities.
www.bfrazma.com

PDE4 INHIBITORS

Daliresp® 250 mcg/500 mcg roflumilast C	
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Beta-agonist Therapy

Types of Beta-2 Agonists:

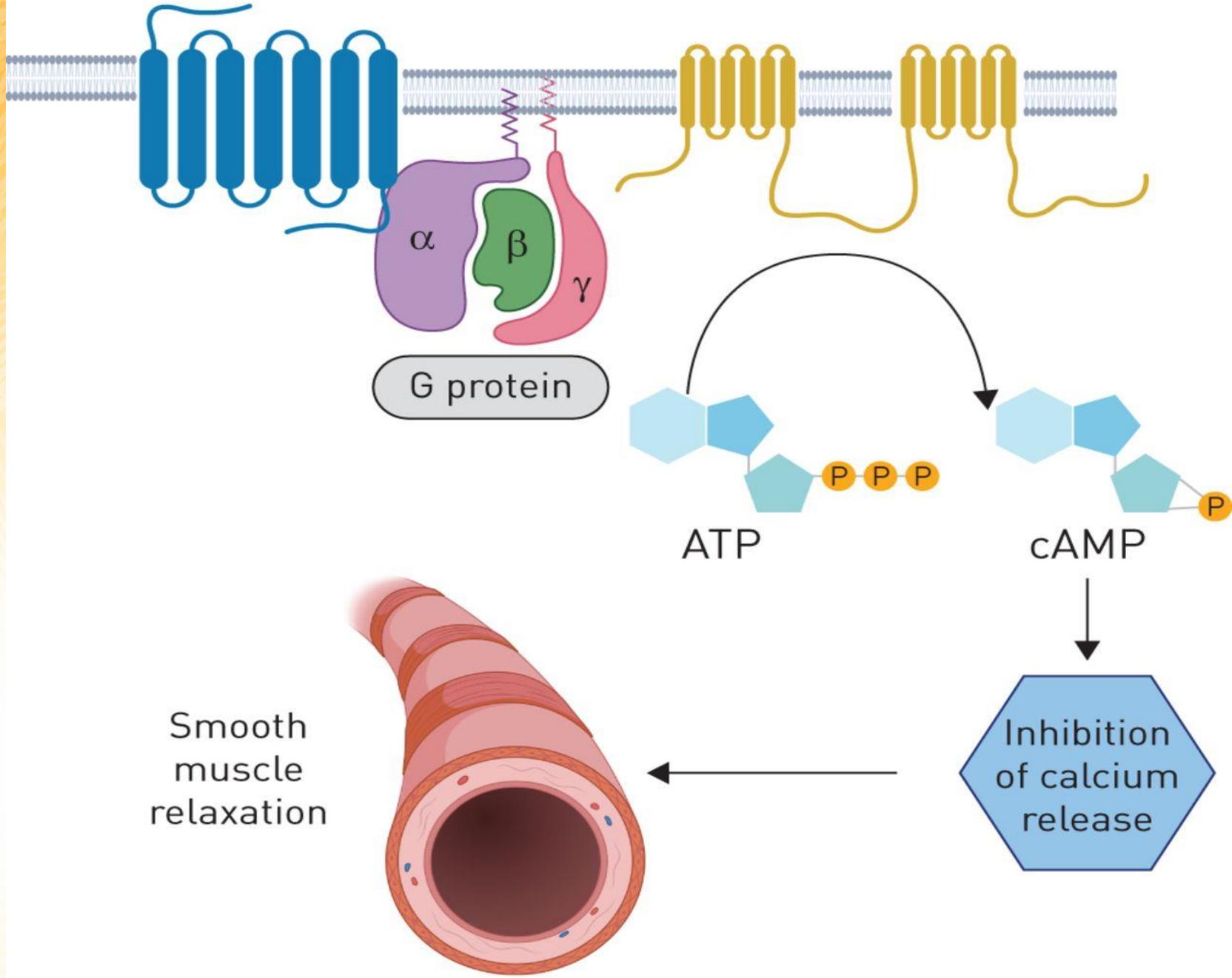


1. Short-Acting Beta-2 Agonists
2. Long-Acting Beta-2 Agonists
3. Ultra-Long-Acting Beta-2 Agonists



β_2 -receptor

Adenylyl cyclase



Smooth muscle relaxation

Inhibition of calcium release

Taking an asthma controller medication twice a day?

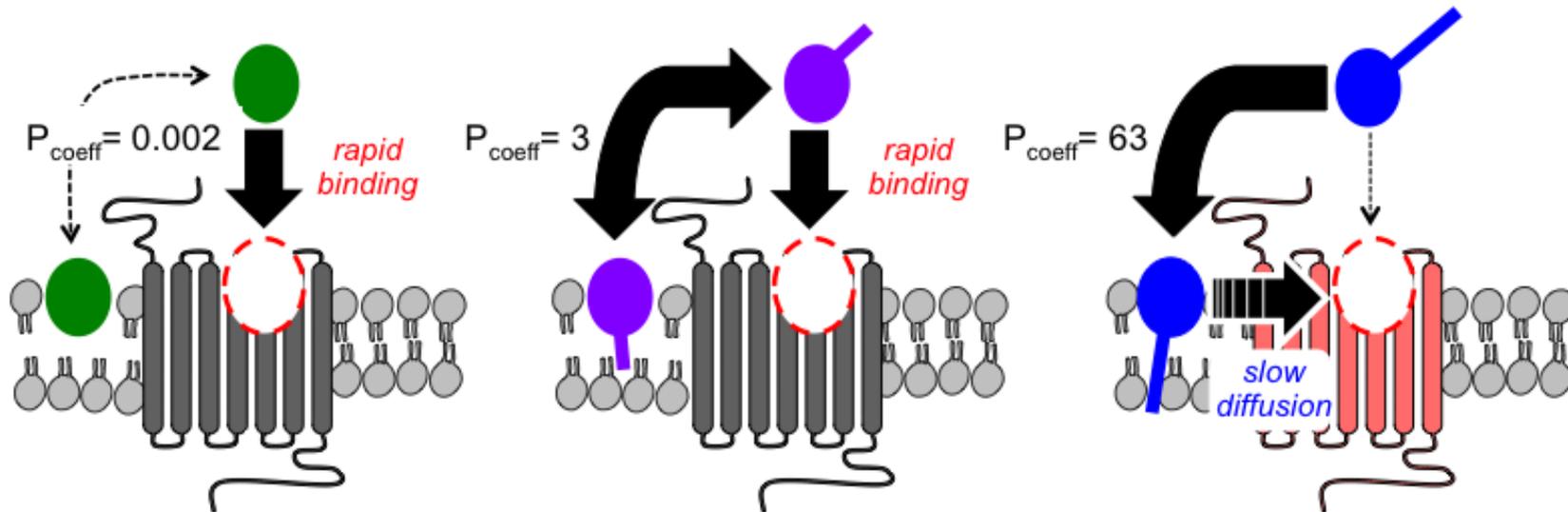
*Ask your doctor if **once-daily BREO** could be right for you.*

With just one inhalation once a day, BREO works for a full 24 hours and prevents asthma symptoms.



Beta₂ Agonist Kinetics

Based on Anderson et al, 1994



Albuterol

- Hydrophilic
- Short duration (not stored in lipid)
- Rapid onset

Formoterol*

- Amphiphilic
- Long duration (retained by lipid)
- Rapid onset

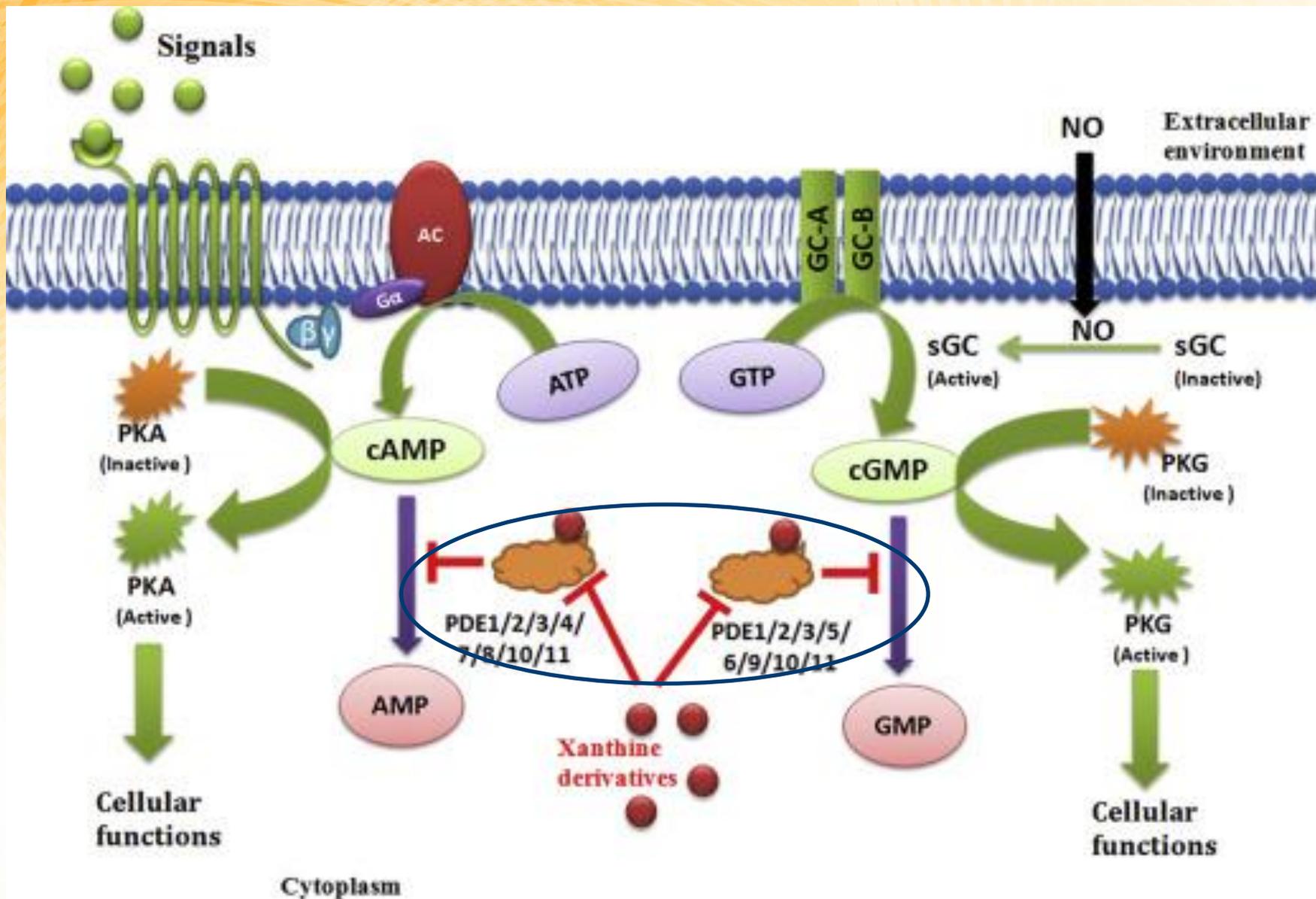
Salmeterol*

- Lipophilic
- Long duration (retained by lipid)
- Slow onset (slow lipid diffusion to β_{2R})

While the mechanisms of action of Theophylline are not totally known with certainty, studies in animals suggest that bronchodilation is mediated by the inhibition of two isozymes of **phosphodiesterase** (PDE III and, to a lesser extent, PDE IV

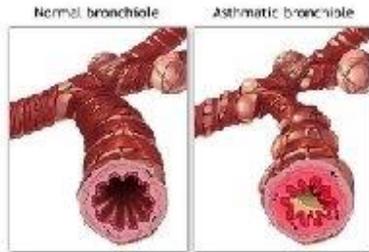
Theophylline





Leukotriene Inhibitors

Leukotriene Modifiers



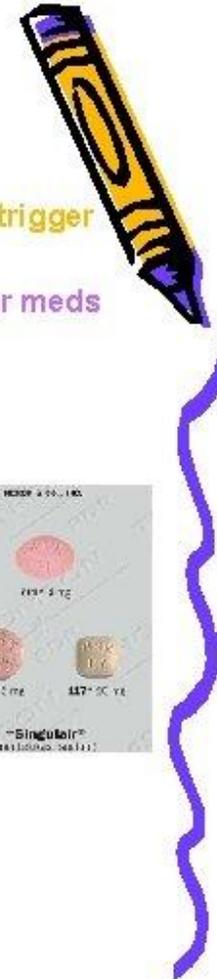
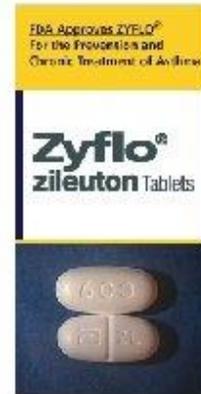
Prevent episodes by interfering with actions that trigger inflammation and muscle tightening

Used for mild asthma or in combination with other meds

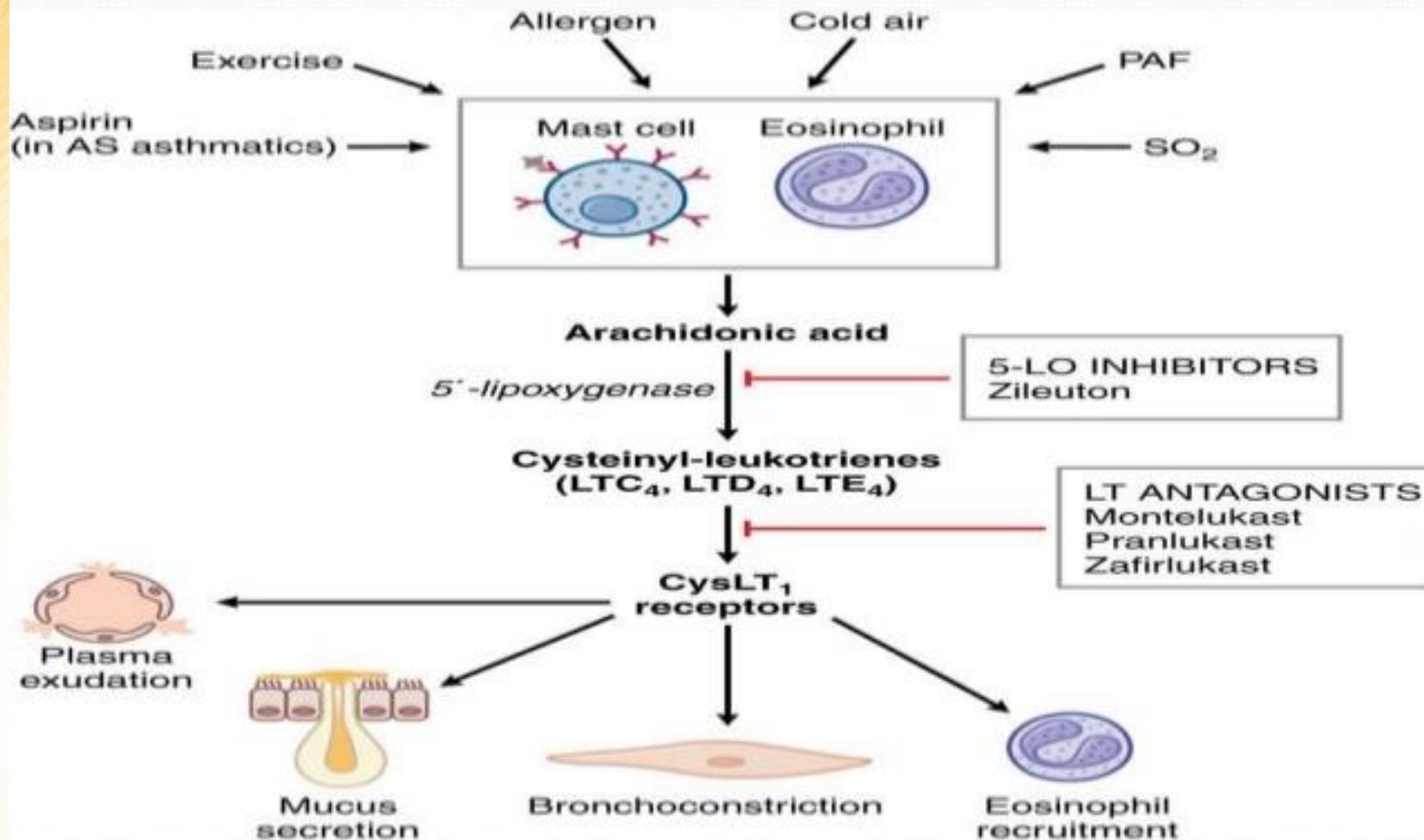
Must take daily

DOES NOT GIVE QUICK RELIEF!

©ADAM



Mechanism of Action



COVID-19 and Asthma

- Are people with asthma at increased risk of COVID-19, or severe COVID-19?
 - People with asthma do not appear to be at increased risk of acquiring COVID-19, and systematic reviews have not shown an increased risk of severe COVID-19 in people with well-controlled, mild-to-moderate asthma.
- Are people with asthma at increased risk of COVID-19-related death? §
 - Overall, people with well-controlled asthma are not at increased risk of COVID-19-related death (Williamson, Nature 2020; Liu et al JACI IP 2021) § However, the risk of COVID-19 death was increased in people who had recently needed oral corticosteroids (OCS) for their asthma (Williamson, Nature 2020) and in hospitalized patients with severe asthma (Bloom, Lancet Respir Med 2021).
- What are the implications for asthma management?
 - It is important to continue good asthma management (as described in the GINA report), with strategies to maintain good symptom control, reduce the risk of severe exacerbations and minimize the need for OCS.
- Have there been more asthma exacerbations during the pandemic?
 - No. In 2020, many countries saw a reduction in asthma exacerbations and influenza-related illness. The reasons are not precisely known, but may be due to handwashing, masks and social/physical distancing that reduced the incidence of other respiratory infections, including influenza.

Treatment of Refractory Asthma



Challenges in Managing Severe Asthma

- Prevalence of severe asthma (NAEPP) = 5-10%
- Many patients remain symptomatic despite standard of care medications
- Medications are limited, require adherence, and can have serious side effects
- **Additional therapeutic treatment options are needed...**

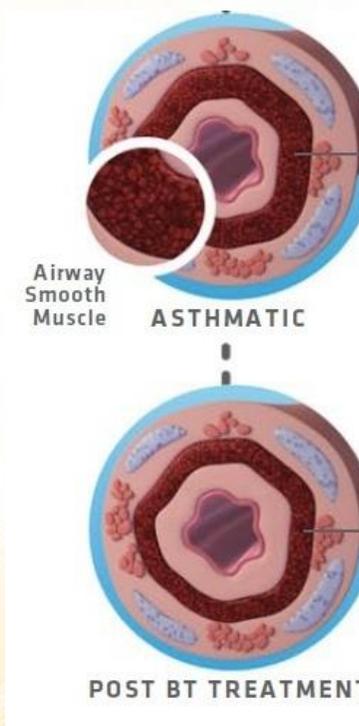
Bronchial Thermoplasty – Reduces ASM

Reduce Airway Smooth Muscle (ASM)

Reduce Bronchoconstriction

Reduce Asthma Exacerbations

Improve Asthma Quality of Life



What is Bronchial Thermoplasty?

- **Safe, outpatient bronchoscopic procedure:**
 - Delivers controlled energy to the airway walls in the lungs
 - Reduces excess airway smooth muscle, which limits the muscle's ability to constrict the airways (asthma exacerbations)
- Demonstrated to **increase asthma control and improve asthma-related quality of life** in patients with severe asthma
- **Complementary treatment** to current asthma reliever and controller medications - not a cure or replacement for current asthma medications

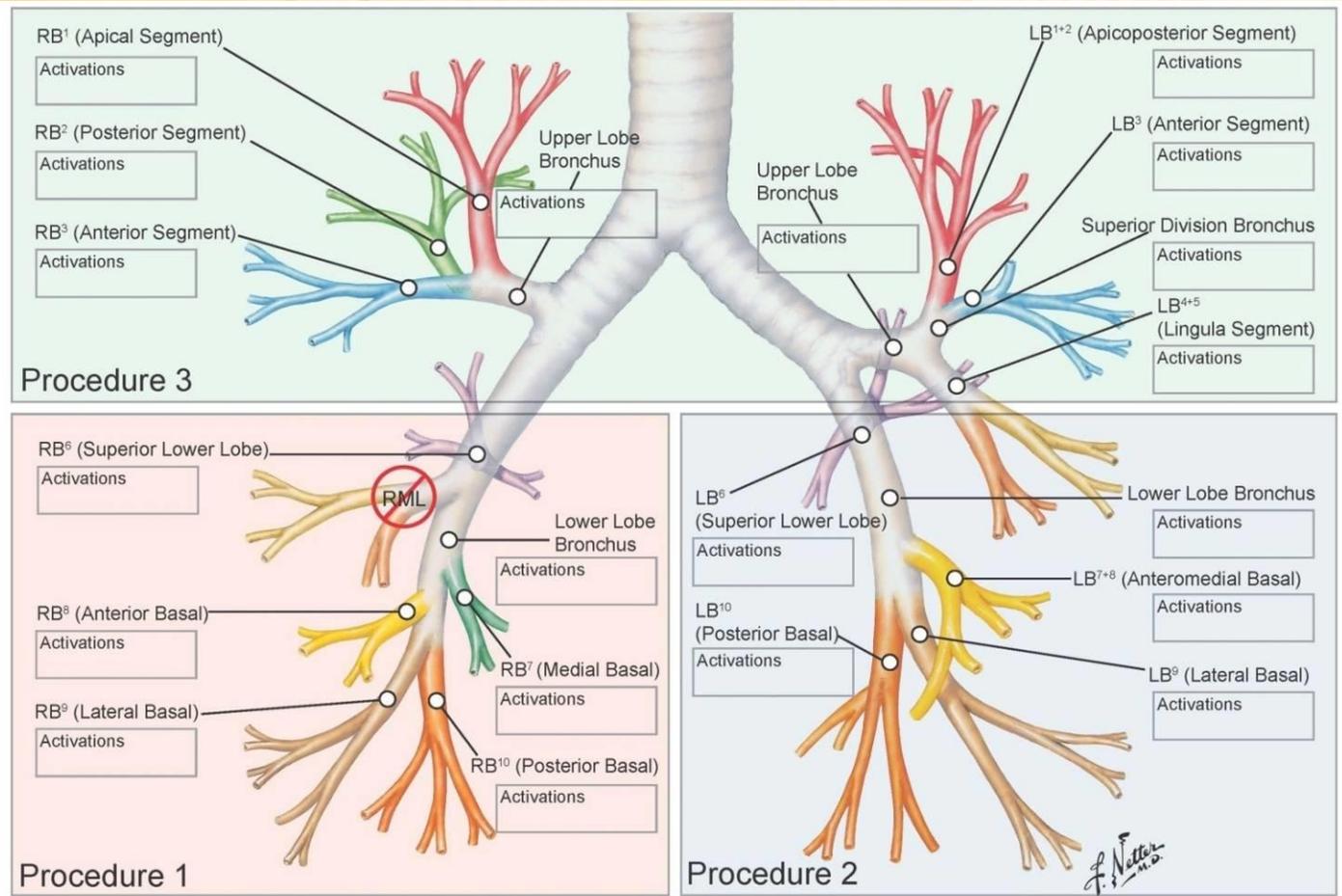
The Alair[®] Bronchial Thermoplasty System

- **Alair Catheter** – a flexible tube with an expandable wire array at the tip (introduced into the lungs through a standard bronchoscope)
- **Alair Radiofrequency (RF) Controller** – supplies energy via the Catheter to the airway wall



Application of RF Energy

- Temperature controlled energy (**65^o C-180F**) is delivered to airway wall for 10 seconds per activation – no permanent damage to epithelium



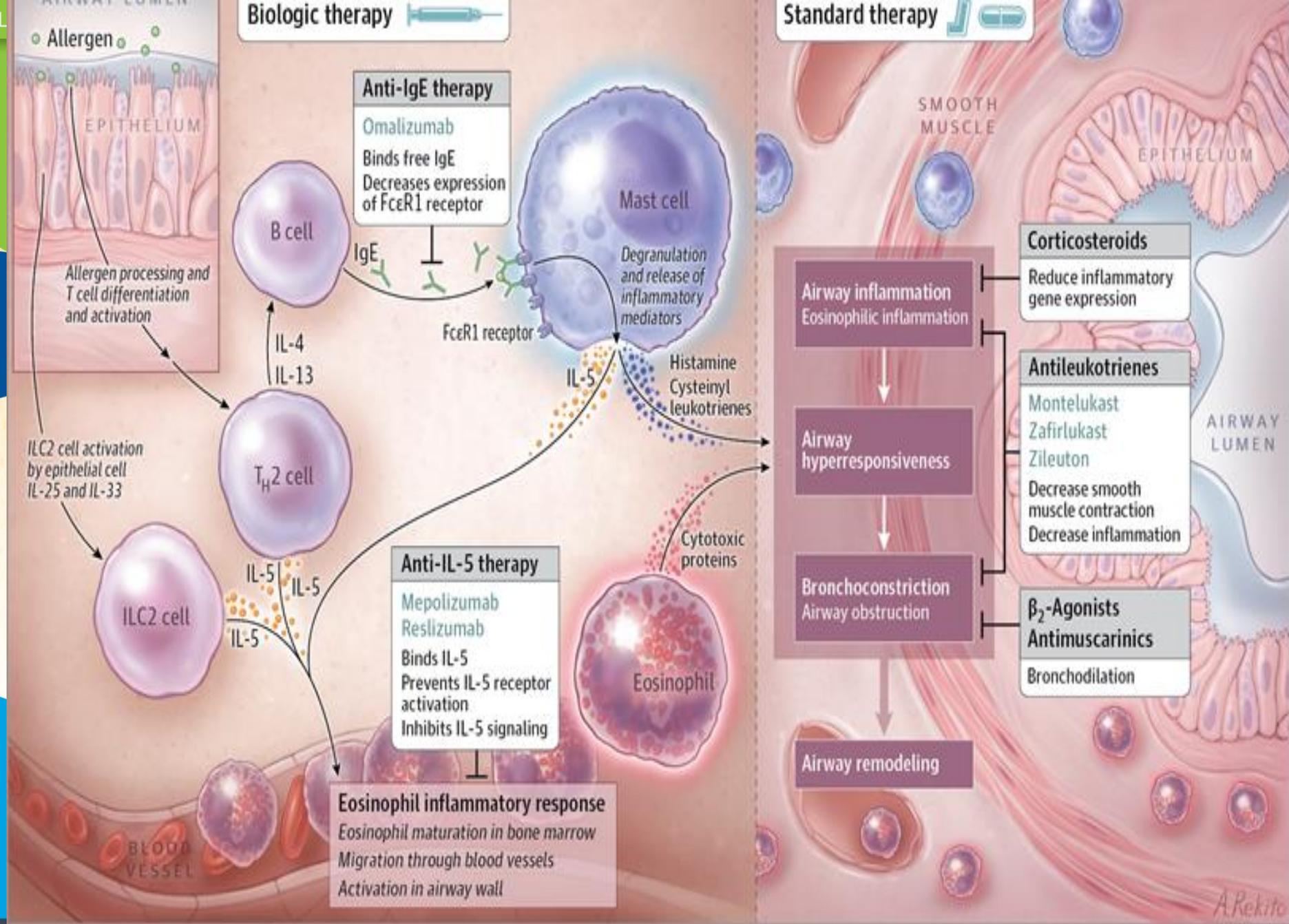
Bronchial thermoplasty is performed in 3 separate treatment sessions each scheduled approximately 3 weeks apart

Airway Responsiveness to Local Methacholine Challenge



Canine Model: Airway on left treated with bronchial thermoplasty. Airway on right was not treated.

Biologicals in Asthma Management



As?

Omalizumab (Xolair, Genentech)

***Is a recombinant humanized IgG1 monoclonal anti-IgE antibody that binds to the IgE molecule**

Omalizumab binds to circulating IgE, regardless of allergen specificity, forming small, biologically inert IgE–anti-IgE complexes without activating the complement cascade thus causing edema.

*Omalizumab is administered subcutaneously once every 2 or 4 weeks.

*For each patient, the dosing schedule (2 vs 4 weeks between injections; and the amount of omalizumab, in milligrams, for each injection) is determined according to the serum IgE level and the body weight of the patient.

*The product label of Xolair initially approved by FDA covers patients with serum IgE in the range of 30 to about 700 IU/ml (international units per milliliter).¹ A clinical development effort is on-going to expand the coverage of patients with serum IgE up to 1500 IU/ml.

Administration Of Xolair

Cost of Xolair

A one-month supply of Xolair will cost patients between **\$541** and **\$2,706**, depending on the dosage. This price is much higher than the cost of conventional treatments for asthma.

Side Effects of Xolair

- itching, mild rash;
- joint pain, bone fractures;
- arm or leg pain;
- nausea;
- dizziness, tired feeling;
- ear pain; or.
- cold symptoms such as stuffy nose, sneezing, sinus pain, cough, sore throat.

New Drug Shows Promise Against Tough-to-Manage Asthma

- This new drug, tezepelumab, is yet another monoclonal antibody, but it targets an inflammatory protein thought to play an early role in many different types of asthma
- Tezepelumab blocks a protein called thymic stromal lymphopoietin (TSLP) that promotes multiple inflammatory processes that have all been linked to asthma attacks
- After a year's treatment, patients on tezepelumab experienced fewer asthma attacks and better lung function, asthma control, and health-related quality of life than those on placebo, the researchers reported

During PATHWAY Trial, and in ongoing phase 3 trials, **tezepelumab** has been **administered** in the clinic via subcutaneous (SC) injection, drawn from a vial and **injected** via a syringe

FDA OKs Tezspire for Severe Asthma

- The FDA approved AstraZeneca and Amgen's medication, tezepelumab-ekko (brand name Tezspire), to treat severe asthma for patients aged 12 years and older
- *Tezspire* is a first-in-class biologic for severe asthma that acts at the top of the inflammatory cascade by targeting thymic stromal lymphopoietin (TSLP), an epithelial cytokine.²⁻⁵ It is the first and only biologic to consistently and significantly reduce asthma exacerbations across Phase II and III clinical trials which included a broad population of severe asthma patients irrespective of key biomarkers, including blood eosinophil counts, allergic status and fractional exhaled nitric oxide (FeNO). *Tezspire* is the only biologic approved for severe asthma with no phenotype (e.g. eosinophilic or allergic) or biomarker limitation within its approved label.
- In clinical studies, the most common adverse reactions in patients who received *Tezspire* were pharyngitis, arthralgia and back pain

High Flow Oxygen in Acute Asthma

- Nasal high-flow therapy may decrease the degree of dyspnea more than the use of conventional oxygen therapy in patients with acute severe asthma and hypoxemia in the ED setting.
- This was demonstrated by the significant improvements in the mean modified Borg scale, mean numeric rating scale, mean dyspnea scale score, and the mean respiratory rate.

Therefore, nasal high flow may be beneficial to respiratory support and oxygenation in patients with acute severe asthma and hypoxemia in the ED.

Conclusion

- Historically asthma has been problematic
- There are a plethora of asthma triggers
- Currently there is an array of asthma medications available to treat and prevent asthma symptoms

References

- Global Asthma Network. *Global Asthma Report 2018*. Accessed October 14, 2020. <http://www.globalasthmanetwork.org>
- Expert Panel Working Group of the National Heart, Lung, and Blood Institute. Focused updates to the asthma management guidelines: a report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group. *J Allergy Clin Immunol*. 2020;146:1217-1270.
- Lin SY, Azar A, Suarez-Cuervo C, et al. *The Role of Immunotherapy in the Treatment of Asthma*. Comparative Effectiveness Review No. 196. Rockville, MD: Agency for Healthcare Research and Quality; March 2018:22-23. Accessed October 11, 2020. <https://effectivehealthcare.ahrq.gov/products/asthma-immunotherapy/research/>
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