The Evolution of Asthma & Update of Asthma

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Conflicts

I have no financial disclosures.

Objectives

- Upon completion participants will be familiar with the heterogeneity of asthma and asthma phenotypes.
- Participants will become familiar with changes in the asthma guidelines.
- Upon completion participants will know the pathophysiology and triggers of asthma.
- Participants will become familiar with the biologic options available for the treatment of moderate to severe asthma.

Asthma

Complex, heterogeneous disease characterized by inflammation.

Variety of clinical phenotypes.

Symptoms; wheezing, shortness of breath, chest tightness and cough.

Symptoms vary over time in occurrence, frequency and intensity.

Variable expiratory airflow

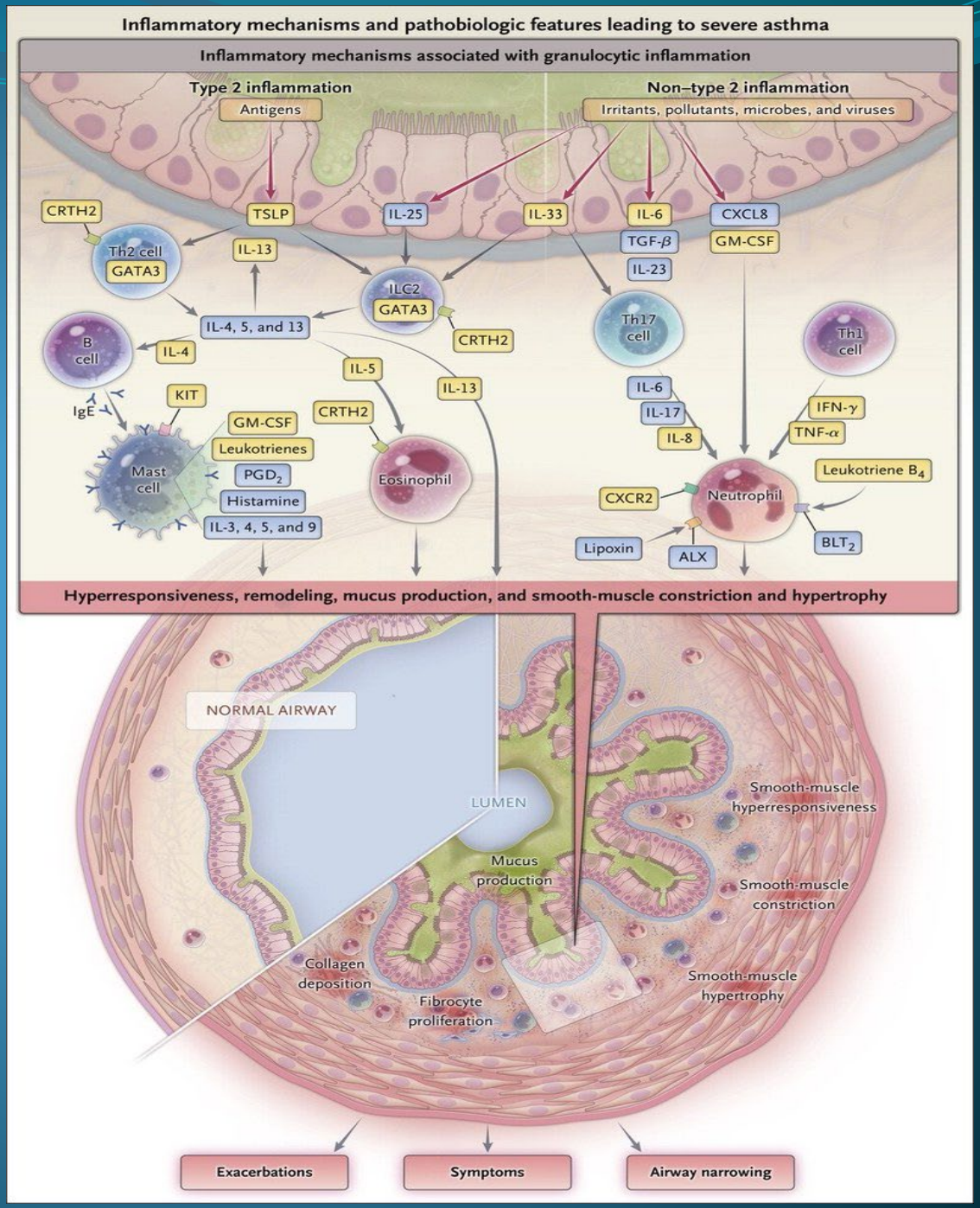
- Bronchoconstriction (airway narrowing)
- Airway wall thickening
- Increased mucus

Burden of Asthma

- 300 million people have asthma worldwide.
- Increase in global prevalence, morbidity ,mortality and economically over past 40 years especially in children.
- In North America 8-10% have asthma (20.2 million adults, 4.6 million children).
- Estimated economic cost $50 billion annually.
- 3,500 people die of asthma each year, **nearly a third of whom are age 65 or older.**
- 50% have at least one asthma attack each year, adults (39.6%) children (38.7 %). OCS
- The burden of asthma in the United States falls disproportionately on people with low-income, senior adults, and Black, Hispanic, and American Indian/Alaska Native people.

CDC-U.S. Department of Health & Human Services & AAFA

Patho-physiology of an Asthma Exacerbation



Ehttps://img.grepmed.com/uploads/407/pathophysiology-inflammatory-leukotriene-immunologic-mechanism-original.jpegxacerbation

Asthma is a Complex Heterogeneous Disease With Clinical Variability

Severity of symptoms.

Natural history
- Age of onset
- Disease progression

Risk of adverse asthma outcomes.

Physiologic characteristics.

Response to therapy.

1.National Ashma Education and Prevention Program, National Heart, Lung, and Blood Institute, National Institutes of Health. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Full Report 2007. Bethesda, MD: US Department of Health and Human Services: August 2007. NIH publication 07-4051.
2.Busse WW, Lemanske RF Jr. Asthma. N Engl J Med. 2001;344:350–362.
3.Weiss ST. Epidemiology and heterogeneity of asthma. Ann Allergy Asthma Immunol. 2001;87(suppl):5–8.
4.Luskin AT. What the asthma end points we know and love do and do not tell us. J Allergy Clin Immunol. 2005;115(4 suppl):S539–S545.
5.Holgate S, Polosa R. The mechanisms, diagnosis, and management of severe asthma. Lancet. 2006;368:

Asthma Phenotypes - Definition

- observable characteristics that result from a combination of environmental and hereditary influences.
- clinical, demographic, and pathological characteristics, such as lung function and inflammation.
- phenotypes can help inform diagnoses and disease.

Examples of Asthma Phenotypes

Allergic asthma

Eosinophilic asthma

Exercise-induced asthma

Aspirin exacerbated respiratory disease (AERD)

Microbes

Growing up on a farm or close to livestock

low prevalence of asthma.

VonMutius E. Microbial Environment and its influence on asthma prevention in early life. JACI 2016:137:680-689

Hygiene hypothesis – Increased vaccination and antibiotics directly related to asthma and allergic disease.

Reducing exposure to Bacteria skews toward TH2-High Response Liu A H. Hygiene Theory and Allergy and Prevention. Paediat Perinat Epidemole. 2007;21:2-7

Decreased stool flora diversity (age 1 month) predictive of atopic disease at age 2 and 6 .

Burbank AJ.Sood AK, Hernandez MI. Environmental Determinants of Allergy and Asthma. JACI. 2017; 140:1-12.
Abrahamssom T R, Jenmalm M C. Low diversity of the gut microbiota in infants with atopic eczema. J JACI. 2012; 129:434- 440. el-2.

Asthma : The Hygiene Hypothesis

Clean environments fail to provide the necessary exposure to germs required to "educate" the immune system : to launch its defense responses to infectious organisms.

Defense responses end up being so inadequate that they actually contribute to the development of asthma.

Before birth, the fetal immune system's "default setting" is suppressed to prevent it from rejecting maternal tissue.

Allergic diseases and asthma are more likely to occur when the incidence and levels of endotoxin (bacterial lipopolysaccharide, or LPS) in the home are low.

LPS is a bacterial molecule that stimulates and educates the immune system by triggering signals through a molecular "switch" called TLR4, which is found on certain immune system cells.

FDA-U.S. Food and Drug Content 3-23-2018

Revising the Hygiene Hypothesis

- Early exposure to a diverse range of good bacteria "commensals", not infectious pathogens at an early age: (train the human immune system to react appropriately to stimuli).
- Processed food doesn't have the normal components of a healthy microbiome.
- C/S prevent exposure or "seeding" of mother's healthy bacteria.
- Exposure to the fecal material of animals.

Caitlin Rivers, PhD, MPH, is a senior scholar at the Johns Hopkins Center for Health Security and an assistant professor in Environmental Health and Engineering at the Johns Hopkins Bloomberg School of Public Health.News Feature: Cleaning up the hygiene hypothesis
Megan Scudellari
PNAS February 14, 2017 114 (7) 1433-1436; https://doi.org/10.1073/pnas.1700688114

Triggers of Allergic Asthma

What Am I?

Two million of us sleep with you every night

I thrive in humid conditions, especially 65% humidity

I eat your (human) shed skin cells

My protein is found in my body and in my waste

I don't survive in hot water, especially temperatures greater than 130°F

I don't like zip covers on mattresses or pillows

What Am I?

I am attracted to water sources such as leaky faucets and pipes.

I enter your home through small openings.

I thrive in houses with open food, open garbage cans, and lots of crumbs and your pets' food/water bowls.

Food sources include your recyclables that are not rinsed.

Exterminators destroy our families.

Cockroach

3,000 different types of cockroaches.

Three main types of cockroaches in homes in the U.S.:

German, Oriental, American.

German

Oriental

IgE Mediated Asthma Triggers

IgE

Pollen

Dust mites

Mold

Pets

Pests

Food

What am I?

I am the third most common cause of cough (non smoker).

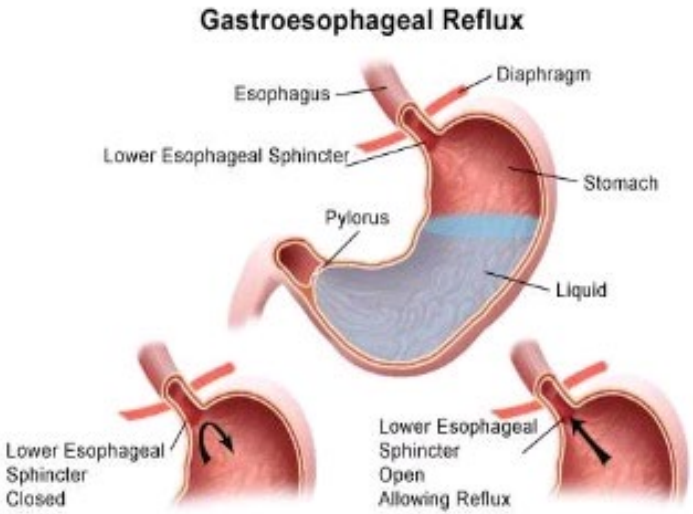
I can be controlled with medication, surgery, or lifestyle changes.

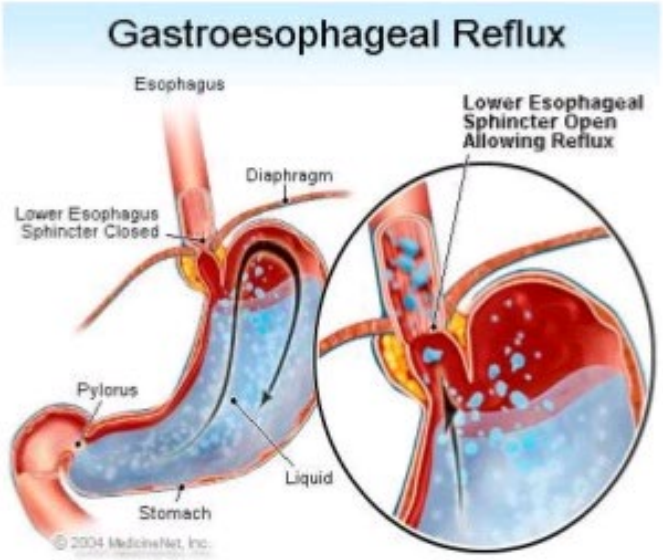
Elevating the head of the bed decreases symptoms.

I cause night asthma, belching and heartburn.

GERD

Gastro esophageal reflux disease (GERD)





GERD Precautions

- Elevate head of bed
- Avoid evening snacks
- H2 antagonists i.e. Pepcid, Zantac, Tagamet
- Proton pump inhibitors (PPI's) i.e. Prilosec, Prevacid, Nexium, Protonix, etc
- Minimize stress
- Avoid caffeine, theophylline, spices, fatty foods, ethanol, etc.

What am I?

I release substances that irritate the moist lining of the airways.

I damage respiratory cilia and increase mucus production.

I release carcinogens that cause lung cancer.

I can cause lung and sinus infections with indirect exposure.

Environmental Tobacco Precautions

Avoid smoking home or car.

Counsel individuals smoking around children.

Avoid public places that permit smoking.

Smoking during pregnancy – Ten fold increase in asthma development.

Indirect exposure triggers asthma symptoms.

Tobacco Cessation

Set quit date.

Discard all cigarettes, lighters, and ashtrays.

Avoid all situations that trigger desire to smoke.

For urges to smoke, take a deep breath/ hold it for five to ten seconds.

No smoking in your home.

Keep finger foods, like carrot sticks, handy.

Stay active to keep your mind off smoking

Join a support group or smoking cessation class.

Nicotine replacement aids.

Non-IgE Mediated Asthma Triggers

Non IgE

Infections

Temperature Changes

High Emotion

Cold Air

GERD

Hormones (pregnancy)

Medications

Irritants

Exercise

Obesity

- Difficult to treat/severe asthma
- Pathophysiology poorly understood
- Decreased quality of life and increased utilization of resources.

- Mosen DM, Schatz M, Magid DJ, Camargo CA., Jr The relationship between obesity and asthma severity and control in adults. J Allergy Clin Immunol 2008; 122: 507–11.e6. [PubMed]

- Risk factor for asthma - multiple demographic groups

- An official American Thoracic Society Workshop report: obesity and asthma.
- Dixon AE, Holguin F, Sood A, Salome CM, Pratley RE, Beuther DA, Celedón JC, Shore SA, ATS Ad Hoc Subcommittee on Obesity and Lung Disease. Proc Am Thorac Soc. 2010 Sep; 7(5):325-35.

- **Decreased response to ICS, and ICS plus LABA**

- Peters U, Obesity and asthma JACI. 2018:141:1169-1179.Boulet L P. Influence of obesity on response to fluticasone with or without salmeterol in moderate asthma. Respir Med. 2007;101:2240-2247.

- Four to six-fold increase in hospitalization

- Peters U, Obesity and asthma JACI. 2018:141:1169-1179.Holquin F, Busse W W, et al. Obesity and asthma; in association modified by age of asthma onset. JACI 2011;127:1486-1493. e2.

Obesity Treatment

- Dietary changes
  - Avoid sugar
  - Limit processed foods
- Exercise and activity
- Behaviorial change
  - Support groups
  - Counselling
- Prescription weight-loss medications
- Weight-loss surgery

Criteria for Asthma Diagnosis

- Characteristic symptom patterns
- Variable airflow limitation- **reversibility from bronchodilator (12% and 200ml improvement in FEV1 post bronchodilation) or other medications**.
- Characteristic airway inflammation and hyperresponsiveness.

https://ginasthma.org/

Asthma Diagnosis-Symptoms

Increased Probability of Asthma

- ≥ 1 type of symptom (wheeze, shortness of breath, cough, chest tightness)
- Symptoms worse at night/early morning
- Symptoms vary over time and in intensity
- Symptoms triggered by viral infections, exercise, allergen exposure, changes in weather, laughter, irritants such as car exhaust fumes, smoke, or strong smells

https://ginasthma.org/

Evolution of Asthma Guidelines

NIH/NHLBI/NAEPP/EPR and GINA

EPR-1 1991, EPR-2 1997 Focus on classification by severity. Shift from opinion to evidenced based management.

EPR-2 2002 Continued focus on severity with new focus on control: 2 domains: 1. impairment 2. risk

EPR-3 2007

GINA 1995

GINA 2006

EPR-4 2020

GINA 2022

Update GINA and EPR Guidelines AIR MART/SMART

- Anti-inflammatory Reliever AIR
  - ICS-formoterol or ICS-SABA
  - Takes ICS-formoterol as needed for sx.

- Maintenance and Reliever Therapy MART
- Single Maintenance Deliver Therapy SMART
  - ICS and LABA
- Budesonide or mometasone -formoterol

EPR-Asthma Management ≥ 12 year olds

ASTHMA MANAGEMENT—YOUTHS ≥12 YEARS OF AGE & ADULTS (part 1 of 2)

Classifying Asthma Severity and Initiating Treatment in Youths ≥12 Years of Age and Adults

Assessing severity and initiating treatment for patients who are not currently taking long-term control medications

Components of Severity		Classification of Asthma Severity (≥12 Years of Age)			
			Persistent		
		Intermittent	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	≤2×/month	3–4×/month	>1×/week but not nightly	Often 7×/week
	Short-acting β_2-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week 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 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	≥2/year →		
		← 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
		In 2 to 6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			

EIB = exercise-induced bronchospasm; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity.

Adapted from National Asthma Education and Prevention Program. *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma 2007*. U.S. Department of Health and Human Services. Available at: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed on: September 21, 2007.

Asthma Management ≥ 12 year olds Adjusting Therapy

ASTHMA MANAGEMENT—YOUTHS ≥12 YEARS OF AGE & ADULTS (part 2 of 2)

Assessing Asthma Control and Adjusting Therapy in Youths ≥12 Years of Age and Adults

Components of Control		Classification of Asthma Control (≥12 Years of Age)		
		Well Controlled	**Not Well Controlled**	**Very Poorly Controlled**
Impairment	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	≤2×/month	1–3×/week	≥4×/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting β_2-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day
	FEV_1 or peak flow	>80% predicted/ personal best	60%–80% predicted/ personal best	<60% predicted/ personal best
	Validated questionnaires* ATAQ ACQ ACT	0 ≤0.75† ≥20	1–2 ≥1.5 16–19	3–4 N/A ≤15
Risk	**Exacerbations requiring oral systemic corticosteroids**	**0–1/year**	**≥2/year**	
		Consider severity and interval since last exacerbation		
	Progressive loss of lung function	Evaluation requires long-term follow-up care		
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		
Recommended Action for Treatment		• Maintain current step • Regular follow-ups every 1 to 6 months to maintain control • Consider step down if well controlled for at least 3 months	• Step up 1 step and • Reevaluate in 2 to 6 weeks • For side effects, consider alternative treatment options	• Consider short course of oral systemic corticosteroids • Step up 1 to 2 steps and • Reevaluate in 2 weeks • For side effects, consider alternative treatment options

ACQ = Asthma Control Questionnaire©; ACT = Asthma Control Test™; ATAQ = Asthma Therapy Assessment Questionnaire©; EIB = exercise-induced bronchospasm; FEV_1 = forced expiratory volume in 1 second.

*Questionnaires do not assess lung function or the risk domain.

†ACQ values of 0.76–1.4 are indeterminate regarding well-controlled asthma.

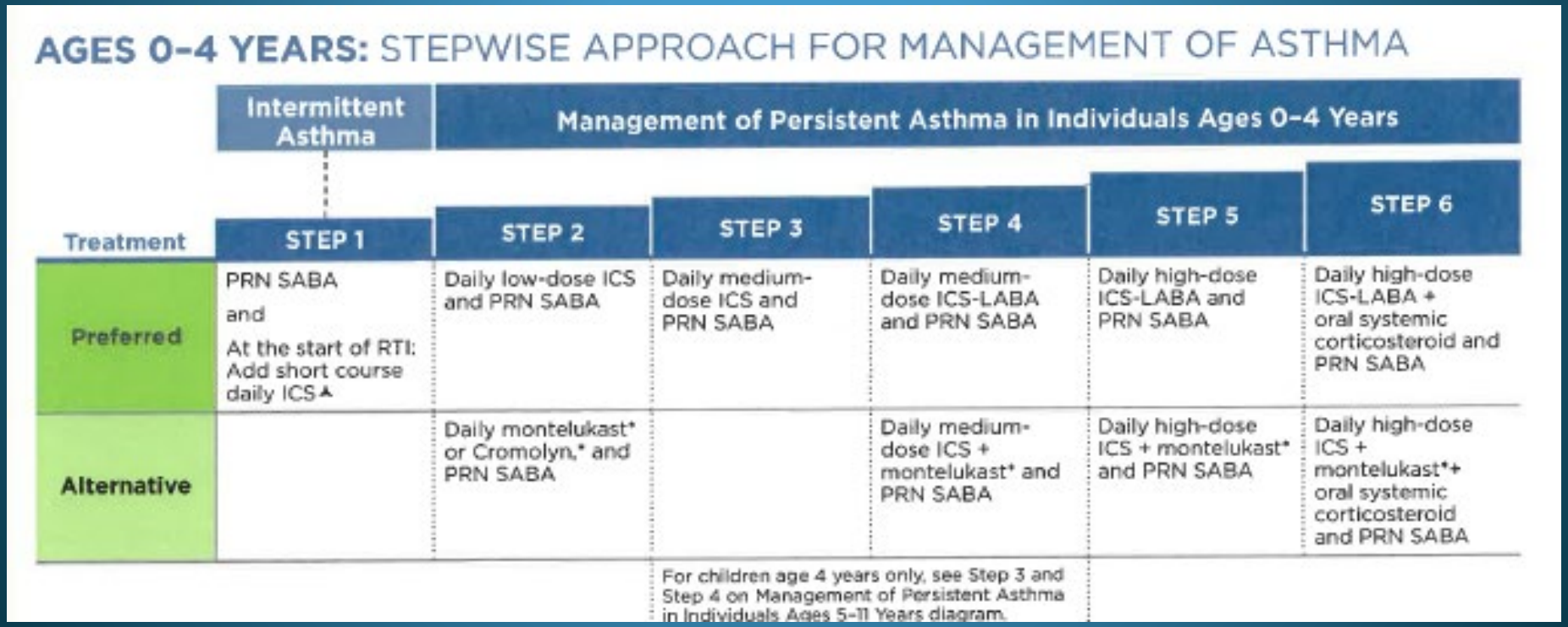
Adapted from National Asthma Education and Prevention Program. *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma 2007.* U.S. Department of Health and Human Services. Available at: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed on: September 21, 2007.

EPR-4 Asthma Guidelines Update

Children 0-4 years

- Intermittent use of steroids-ICS (7-10 days) wheeze only at the time of a URI.
- Daily ICS with SABA as quick relief and ICS and a short-acting bronchodilator as rescue medication as needed in adolescents and adults with mild to persistent asthma.
- AirSupra NOT indicated for individuals < 18 years old

Asthma Management Children 0-4 years old



AGES 0–4 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

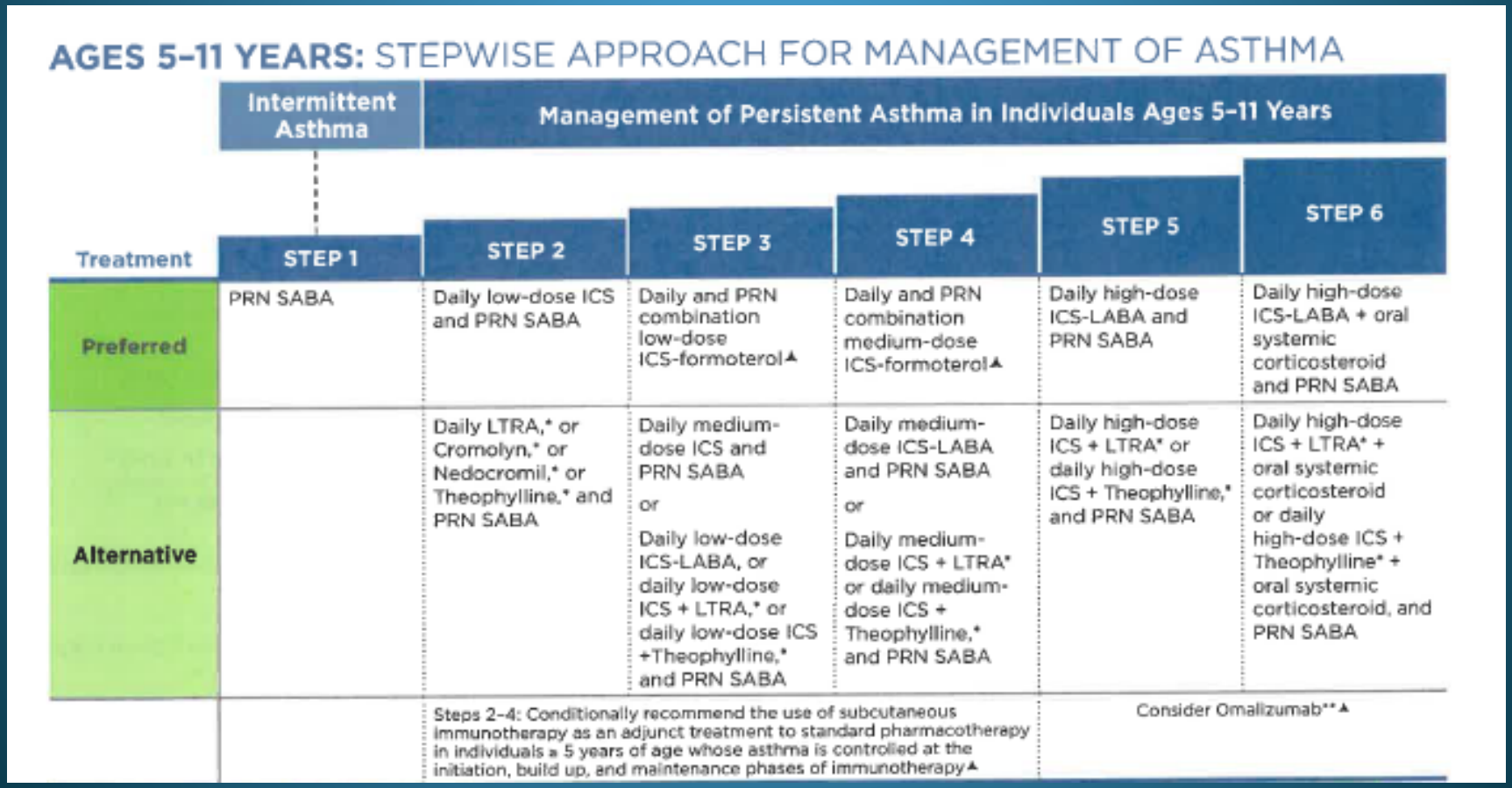
	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 0–4 Years				
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA and At the start of RTI: Add short course daily ICS▲	Daily low-dose ICS and PRN SABA	Daily medium-dose ICS and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily montelukast* or Cromolyn,* and PRN SABA		Daily medium-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast*+ oral systemic corticosteroid and PRN SABA
			For children age 4 years only, see Step 3 and Step 4 on Management of Persistent Asthma in Individuals Ages 5–11 Years diagram.			

EPR-4 Asthma Guidelines Update

Individuals ≥ 4 years with mod. to severe asthma

- ICS - formoterol or SMART.
- Both for daily and prn therapy.
- Short term increase in ICS for exacerbation NOT recommended.

Asthma Management Children 5-11 years old



AGES 5–11 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

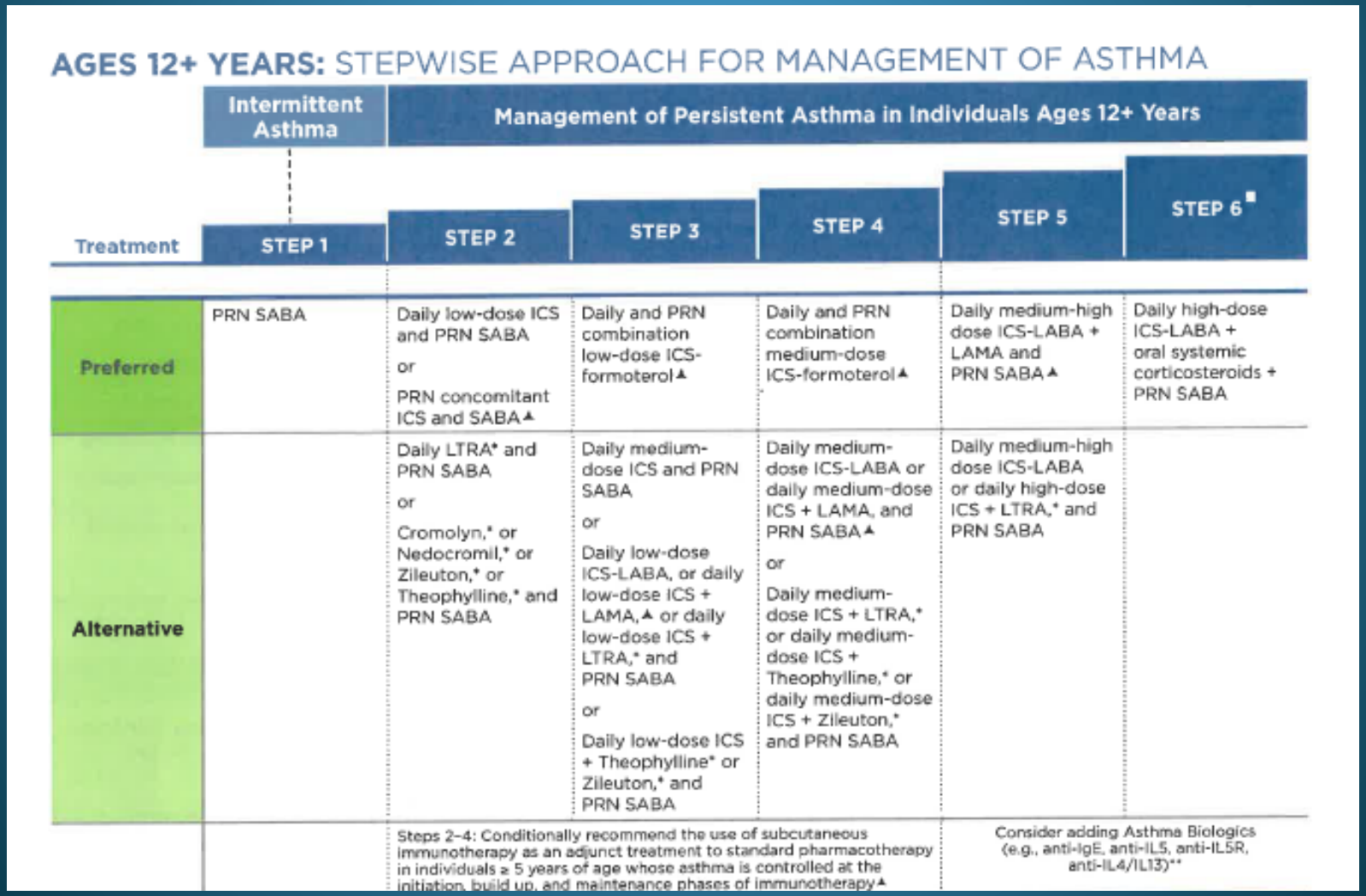
	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 5–11 Years				
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily LTRA,* or Cromolyn,* or Nedocromil,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LTRA,* or daily low-dose ICS +Theophylline,* and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA or Daily medium-dose ICS + LTRA* or daily medium-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* or daily high-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* + oral systemic corticosteroid or daily high-dose ICS + Theophylline* + oral systemic corticosteroid, and PRN SABA
		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider Omalizumab**▲	

EPR-4 Asthma Guidelines Update

Individuals ≥ 12 years

- If on ICS, add LABA >LAMA.
- Both for daily and prn therapy.
- If taking ICS/LABA, add LAMA

EPR 4
Asthma Management ≥ 12 years old



AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

Treatment	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years				
	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6 ■
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA▲	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily medium-high dose ICS-LABA + LAMA and PRN SABA▲	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA,▲ or daily low-dose ICS + LTRA,* and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton,* and PRN SABA	Daily medium-dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA▲ or Daily medium-dose ICS + LTRA,* or daily medium-dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,* and PRN SABA	
		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**	

Asthma Guidelines
EPR-3/4

Inhaled corticosteroids most effective long term.
Management of persistent asthma.

Written asthma action plan.

Initial assessment of asthma severity.

Review the level of asthma control (impairment and risk) at all follow up visits.

Periodic, follow up visits (every 6 months).

Assessment of exposure and sensitivity to allergens and irritants.

EPR-4 Asthma Guidelines Update

Indoor Allergen Mitigation

Intermittent Inhaled Corticosteroids

Long-Acting Muscarinic Antagonists

Fractional Exhaled Nitric Oxide Testing

Immunotherapy in the Treatment of Allergic Asthma

Bronchial Thermoplasty

GINA guidelines Update

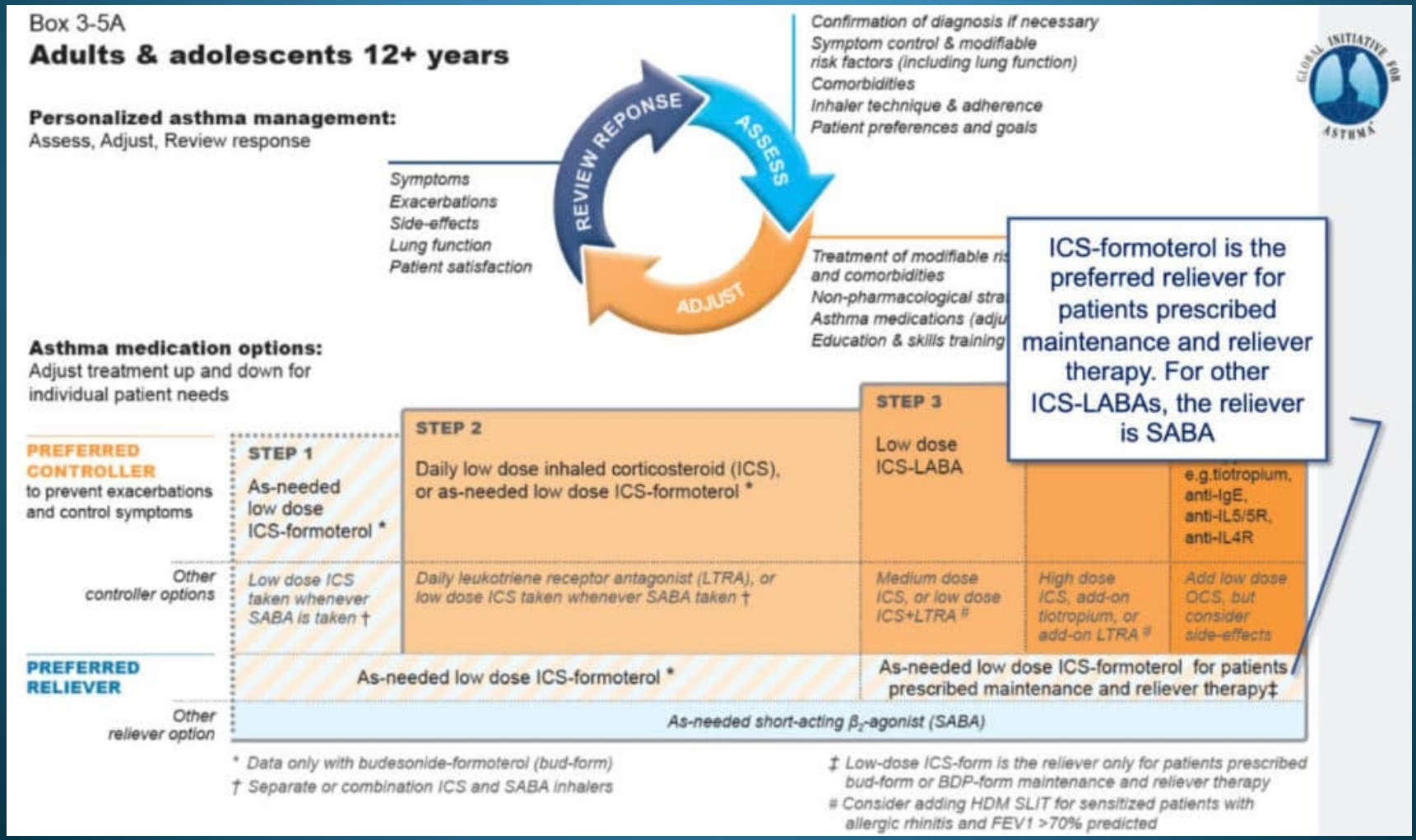
Adults and adolescents divided into two tracks.

Track 1 (preferred) has low-dose ICS-formoterol as the reliever at all steps: as-needed only in Steps 1-2 (mild asthma), and with daily maintenance ICS-formoterol (maintenance-and-reliever therapy, MART) in Steps 3-5.

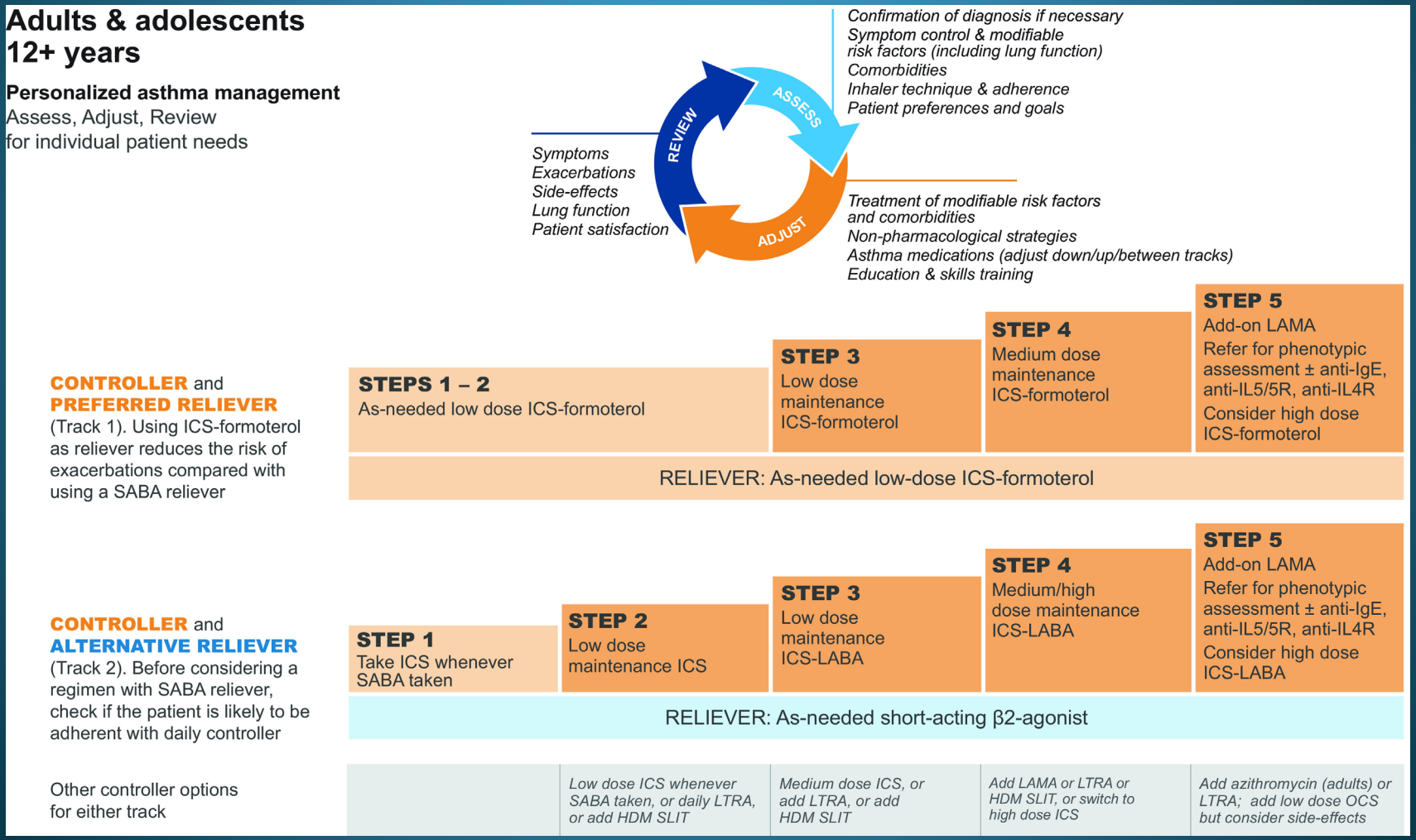
Track 2 (alternative) has as-needed SABA across all steps, plus regular ICS (Step 2) or ICS-long-acting beta2-agonist (LABA) (Steps 3-5).

For adults with moderate-to-severe asthma, GINA makes additional recommendations in Step 5 for add-on long-acting muscarinic antagonists and azithromycin, with add-on biologic therapies for severe asthma.

GINA
Asthma Management ≥ 12 years old



GINA- Guidelines - 2 tracks

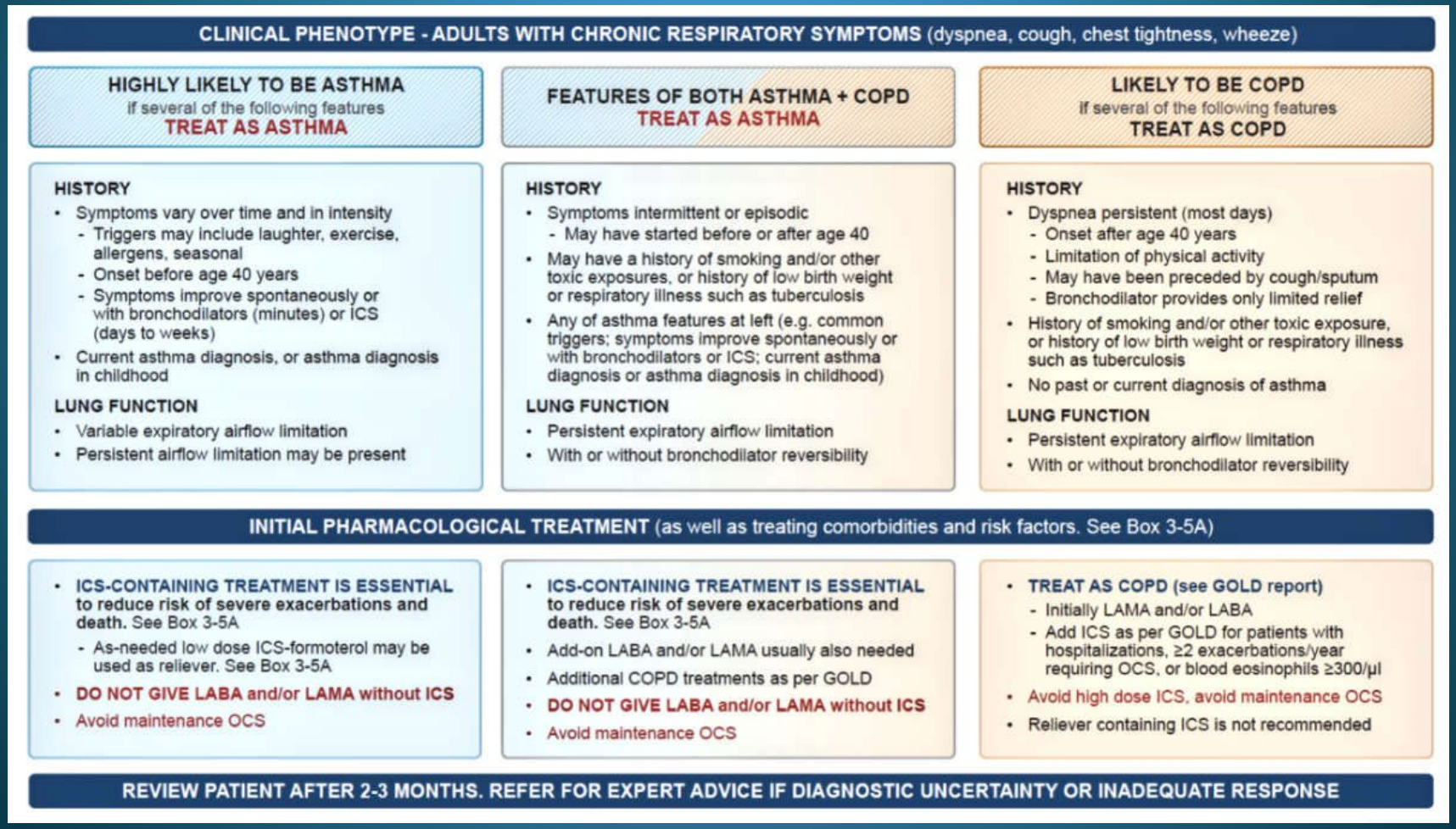


GINA Guidelines update-2022

- Screening patients on maintenance OCS or high dose ICS-LABA for adrenal insufficiency
- For patients with eosinophils ≥300/µl, investigate non-asthma causes before starting biologics.
- If patients have hypereosinophilia, check for other conditions, such as EGPA
- Assess for the inflammatory phenotype
- Updated treatment options for those without evidence of Type 2 inflammation.

OCS should only be used as a last resort option. For patients with hypereosinophilia, e.g. ≥1500/µl, investigate for conditions such as EGPA

Patients with Features of Asthma and COPD



AIRSUPRA- Astra Zeneca

Approved by FDA January 2023

Airsupra- dual inhaler: albuterol and budesonide.

Indicated for the as-needed treatment or prevention of bronchoconstriction and to reduce the risk of exacerbations in patients with asthma 18 years of age and older.

Voluntary Price Caps on Inhalers

- Drug companies **Boehringer Ingelheim**, **AstraZeneca** and **GSK** have announced they are capping out-of-pocket costs for their inhaler products at $35 per month.

- Price caps for Boehringer Ingelheim and AstraZeneca inhalers go into effect on June 1, 2024. GSK says it will implement its price caps no later than January 1, 2025.

Voluntary Price Caps on Inhalers

Boehringer Ingelheim inhalers affected by the price cap include:

- Atrovent® HFA (ipratropium bromide HFA) Inhalation Aerosol
- Combivent® Respimat® (ipratropium bromide and albuterol) Inhalation Spray
- Spiriva® HandiHaler® (tiotropium bromide inhalation powder)
- Spiriva® Respimat® 1.25 mcg (tiotropium bromide) Inhalation Spray
- Spiriva® Respimat® 2.5 mcg (tiotropium bromide) Inhalation Spray
- Stiolto® Respimat® (tiotropium bromide and olodaterol) Inhalation Spray
- Striverdi® Respimat® (olodaterol) Inhalation Spray
- AstraZeneca inhalers affected by the price cap include:
- AIRSUPRA® (albuterol and budesonide)
- Bevespi Aerosphere® (glycopyrrolate and formoterol fumarate) Inhalation Aerosol
- Breztri Aerosphere® (budesonide, glycopyrrolate, and formoterol fumarate) Inhalation Aerosol
- Symbicort® (budesonide and formoterol fumarate dihydrate) Inhalation Aerosol
- AstraZeneca also says it substantially reduced the list price for Symbicort starting Jan. 1, 2024.
- GSK inhalers affected by the price cap include:
- Advair Diskus (fluticasone propionate and salmeterol inhalation powder)
- Advair HFA (fluticasone propionate and salmeterol inhalation aerosol)
- Anoro Ellipta (umeclidinium and vilanterol inhalation powder)
- Arnuity Ellipta (fluticasone furoate inhalation powder)
- Breo Ellipta (fluticasone furoate and vilanterol inhalation powder)
- Incruse Ellipta (umeclidinium inhalation powder)
- Serevent Diskus (salmeterol xinafoate inhalation powder)
- Trelegy Ellipta (fluticasone furoate, umeclidinium, and vilanterol inhalation powder)
- Ventolin HFA (albuterol sulfate inhalation aerosol)
- The price caps will apply at retail pharmacies. They should be particularly helpful for people who are uninsured or underinsured.

What are biologics?

- A medication made from the cells of a living organism, such as bacteria or mice.
- Modified to target specific molecules in humans.

Biologics for asthma

- targets antibodies (IgE), inflammatory molecules (IL4,5,TSLP), or cell receptors.
- biologics work to disrupt the pathways that lead to inflammation that causes asthma symptoms.

Asthma Biologics

Xolair - omalizumab

Cinqair - reslizumab

Nucala - mepolizumab

Fasenra - benralizumab

Dupixent - dupilumab

Tezspire - tezepelumab

Xolair - Omalizumab – Genentech/Novartis

Asthma

Chronic Spontaneous Urticaria

Chronic Rhinosinusitis with Nasal Polyps

Food allergy

Xolair - Omalizumab – Genentech/Novartis

Asthma

- Mod/Severe Asthma
- Age ≥ 6 years
- Elevated IgE
- Positive reactivity to perennial allergen
- Adults ≥ 30-700
- 6-18 year olds ≥ 30-1300
- Doing dependent on IgE level and weight

Xolair - Omalizumab – Genentech/Novartis

Chronic Idiopathic Urticaria

- Age ≥ 12 years.
- Doing NOT dependent on IgE level and weight.
- 150mg-300mg sc injection every 4 weeks.

Xolair - Omalizumab – Genentech/Novartis

Chronic Rhinosinusitis with Nasal Polyps

- Age ≥ 18 years.
- Doing NOT dependent on IgE level and weight.
- 100mg sc injection every 4 weeks.

Xolair - Omalizumab – Genentech/Novartis

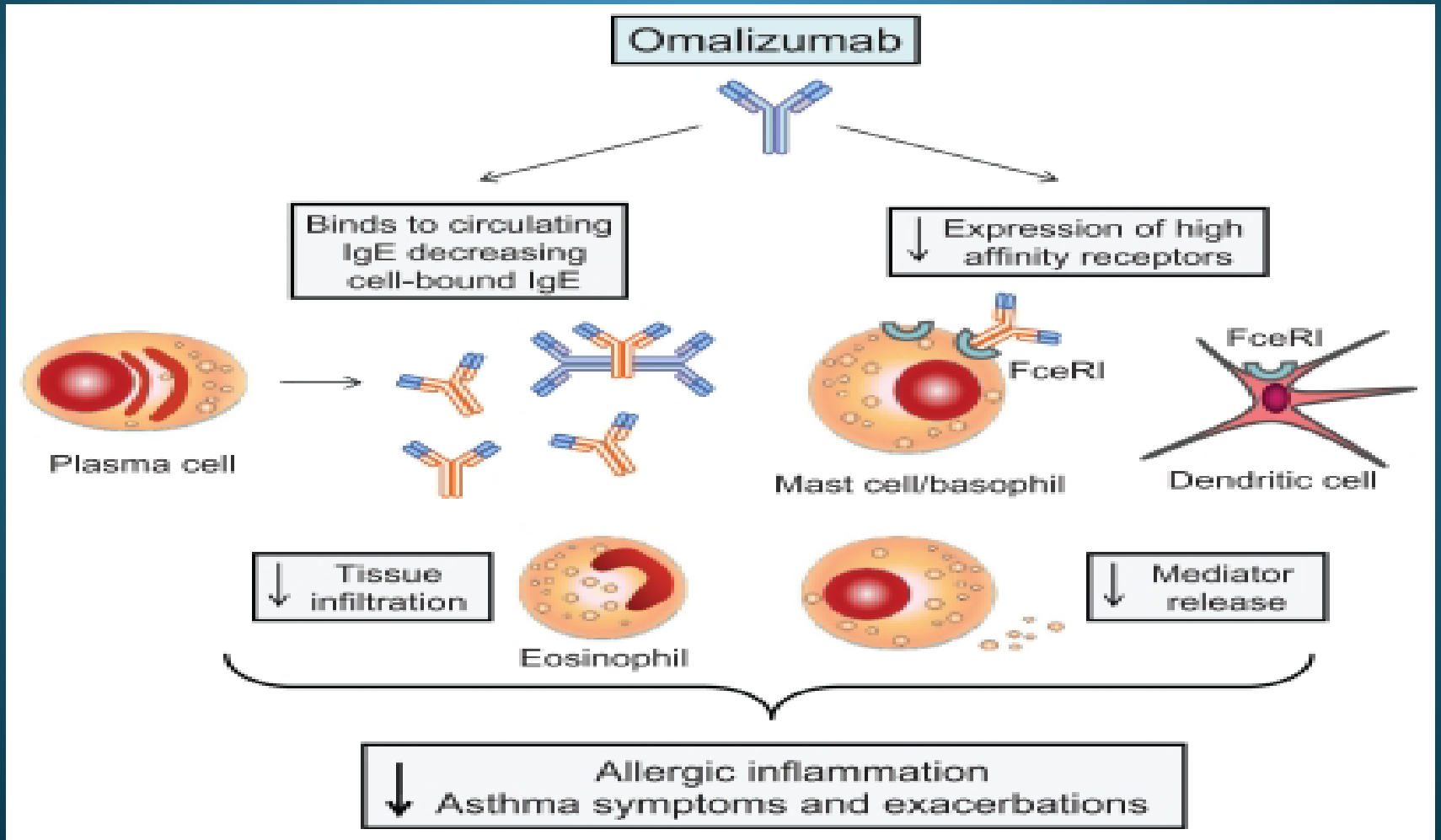
Food Allergy

- Age ≥ 1 years.
- Reduce food allergic reactions, including anaphylaxis, following accidental exposure to one or more foods.
- Dosing dependent on IgE level and weight.
- 75-600mg sc injection every 2 or 4 weeks.

Xolair - Omalizumab – Genentech/Novartis Anaphylaxis Warning

- Injection site Reactions
- Anaphylaxis
- Malignancy
- Fever, Arthralgia, Rash
- Parasitic Infections

MOA-omalizumab (Xolair)



Cinqair - add on maintenance treatment of Severe Eosinophilic Asthma

Reslizumab - Teva

Age ≥ 18 years

Severe eosinophilic asthma.

Eosinophil count ≥ 400.

3 mg/kg every 4 weeks Iv infusion.

May adjust dose for weight.

Nucala - Mepolizumab – GSK

Severe Eosinophilic Asthma (SEA).

Eosinophilic Granulomatosis with Polyangitis.

Chronic Rhinosinusitis with Nasal Polyps.

Hypereosinophilic Syndrome.

Nucala-add on maintenance treatment of Severe Asthma

Mepolizumab – GSK

Severe eosinophilic asthma

≥ 6-11 years 40mg sc every 4 weeks

> 12 years 100 mg sc every 4 weeks

Eosinophil count > 150

Nucala-Eosinophilic granulomatosis with polyangitis (Churg-Strauss)

Nucala - mepolizumab Genentech/Novartis

Chronic Rhinosinusitis with Nasal Polyps

- Age ≥ 18 years.
- Doing NOT dependent on IgE level and weight.
- 100mg sc injection every 4 weeks.

Nucala-Hypereosinophilic Syndrome (HES)

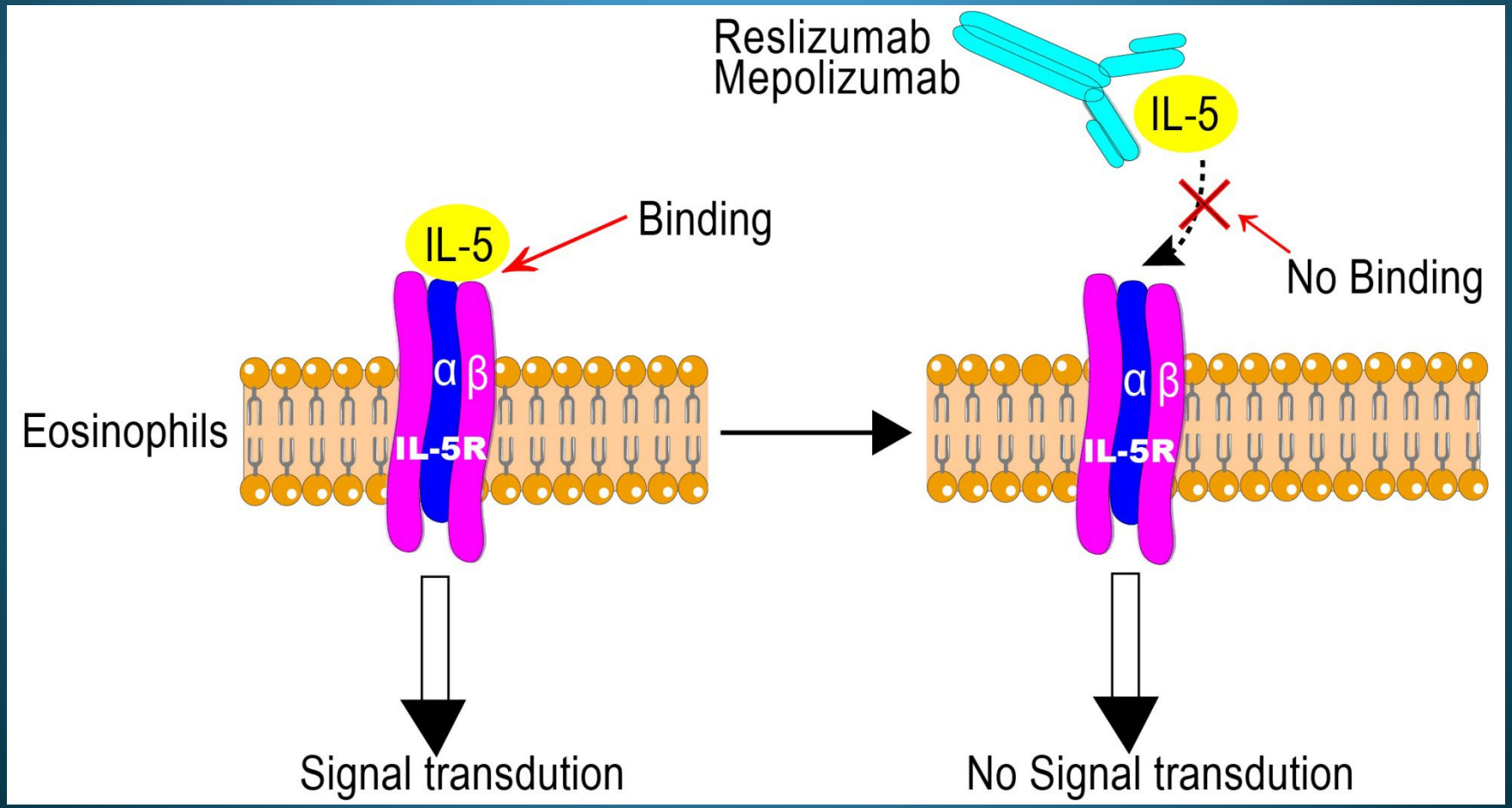
Mepolizumab – GSK.

Age ≥ 12 years old.

Age ≥ 6 months old without identifiable non-hematologic secondary cause.

Three separate 100 mg sc injections every 4 weeks.

MOA for reslizumab (Cinqair) & mepolizumab (Nucala)



Fesenra-add on maintenance treatment of Severe Eosinophilic Asthma

Benralizumab – Astra Zeneca

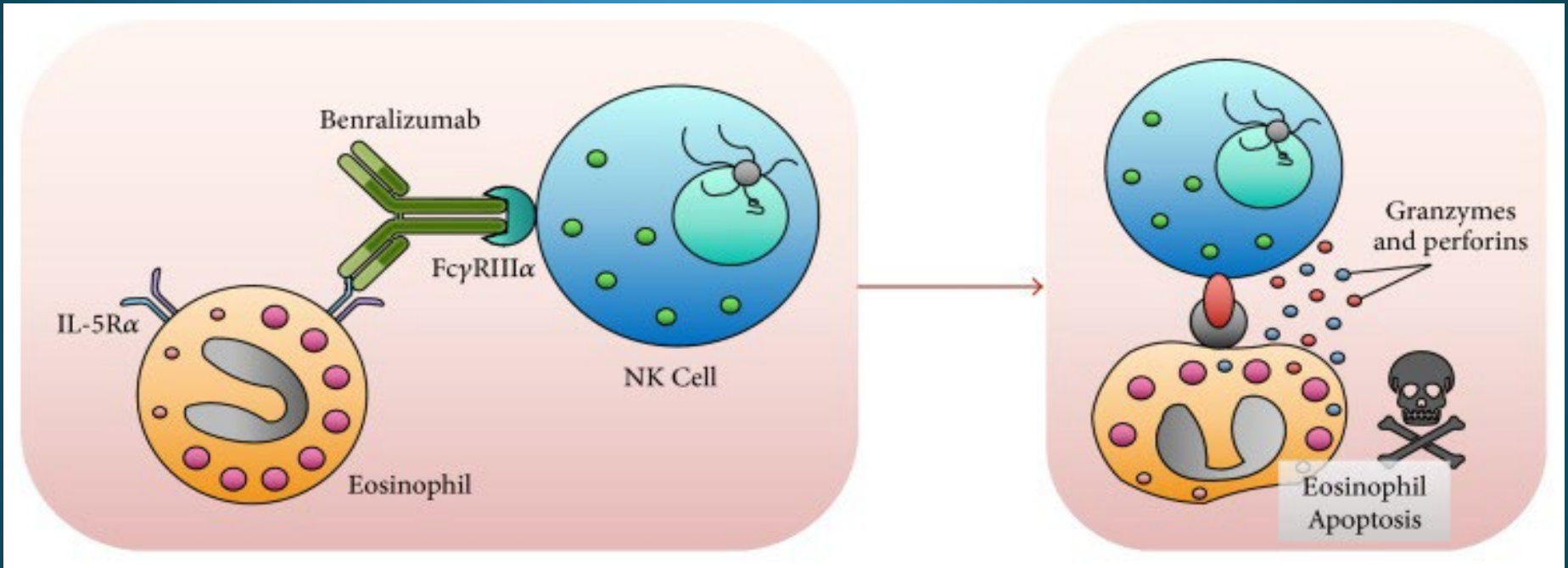
Age ≥ 6 years.

Severe eosinophilic asthma.

No specific eosinophil count; however, most health insurance organizations will not approve unless eosinophil count of 150-200.

30 mg sc .every 4 weeks x 3 doses, then every 8 weeks.

Mechanism of Action: benralizumab-Fesenra



Benralizumab binds to IL-5Rα -blocks IL-5 and its receptor. Benralizumab binds to the FcγIIIRa- induces eosinophil apoptosis.

Biomed Res Int. 2018; 2018: 4839230. Published online 2018 May 10. doi: 10.1155/2018/4839230

Dupixent- Regeneron/Sanofi Genzyme

Eosinophilic Asthma

Dermatitis

Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP).
Eosinophilic Esophagitis

Prurigo Nodularis

Dupixent

Dupilumab – Sanofi Genzyme - Regeneron

Age ≥ 6 years.

Moderate to severe asthma with eosinophils or corticosteroid dependent asthma.

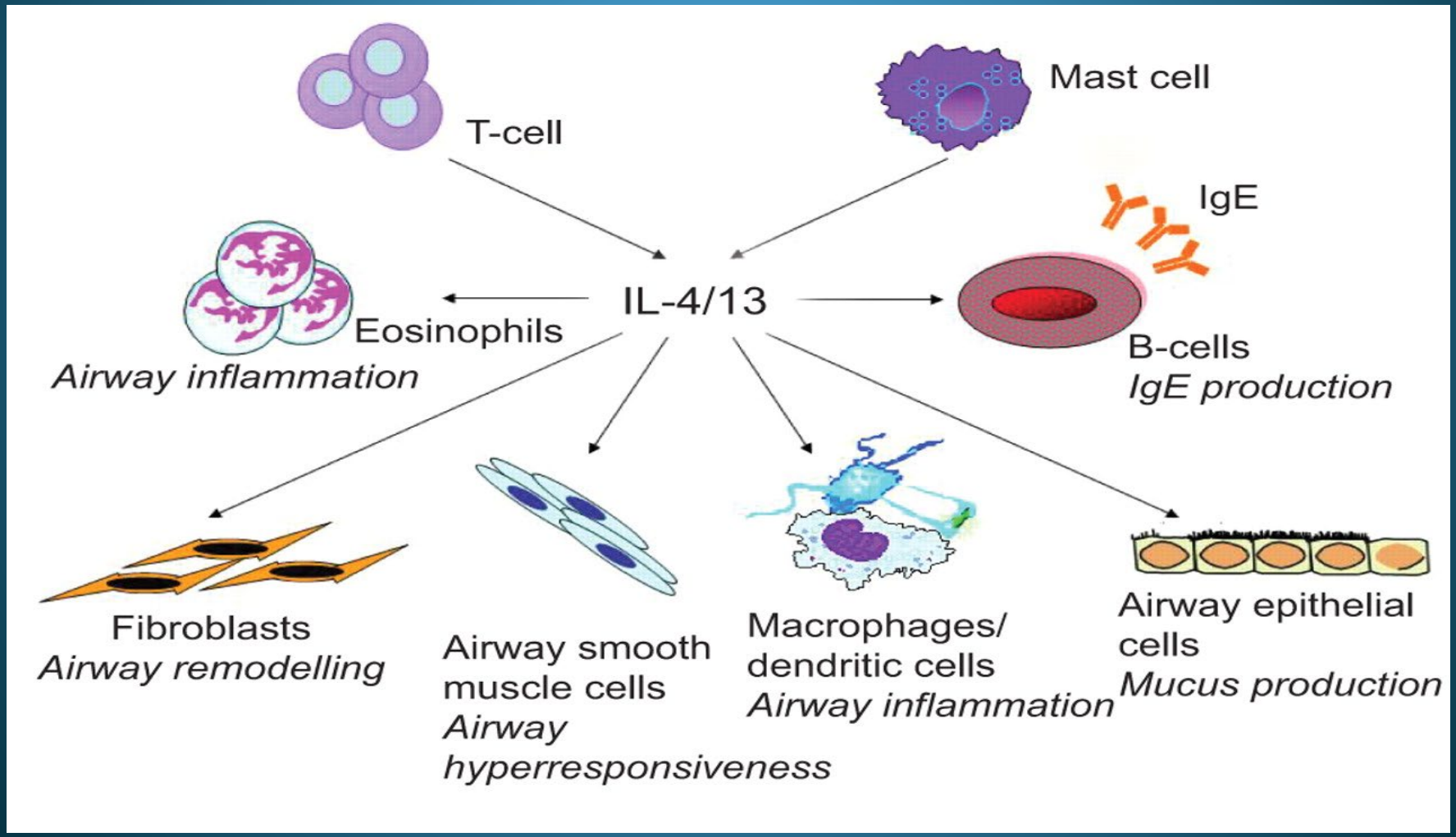
Subcutaneous administration.

Individuals ≥ 12 years 400 mg LD followed by 200 mg every 2 weeks or 600 mg LD followed by 300 mg every 2 weeks.

Individuals 6-11 years old based on body weight.

- 15-30kg 300mg q 4 weeks.
- ≥ 30kg 200mg q 2 weeks.

Mechanism of Action for dupilumab (Dupixent)



Tezspire-tezelepumab add on maintenance treatment of pediatric and adults with Severe Asthma

Tezelepumab- ekko Amgen/Astra Zeneca

Age ≥ 12 years.

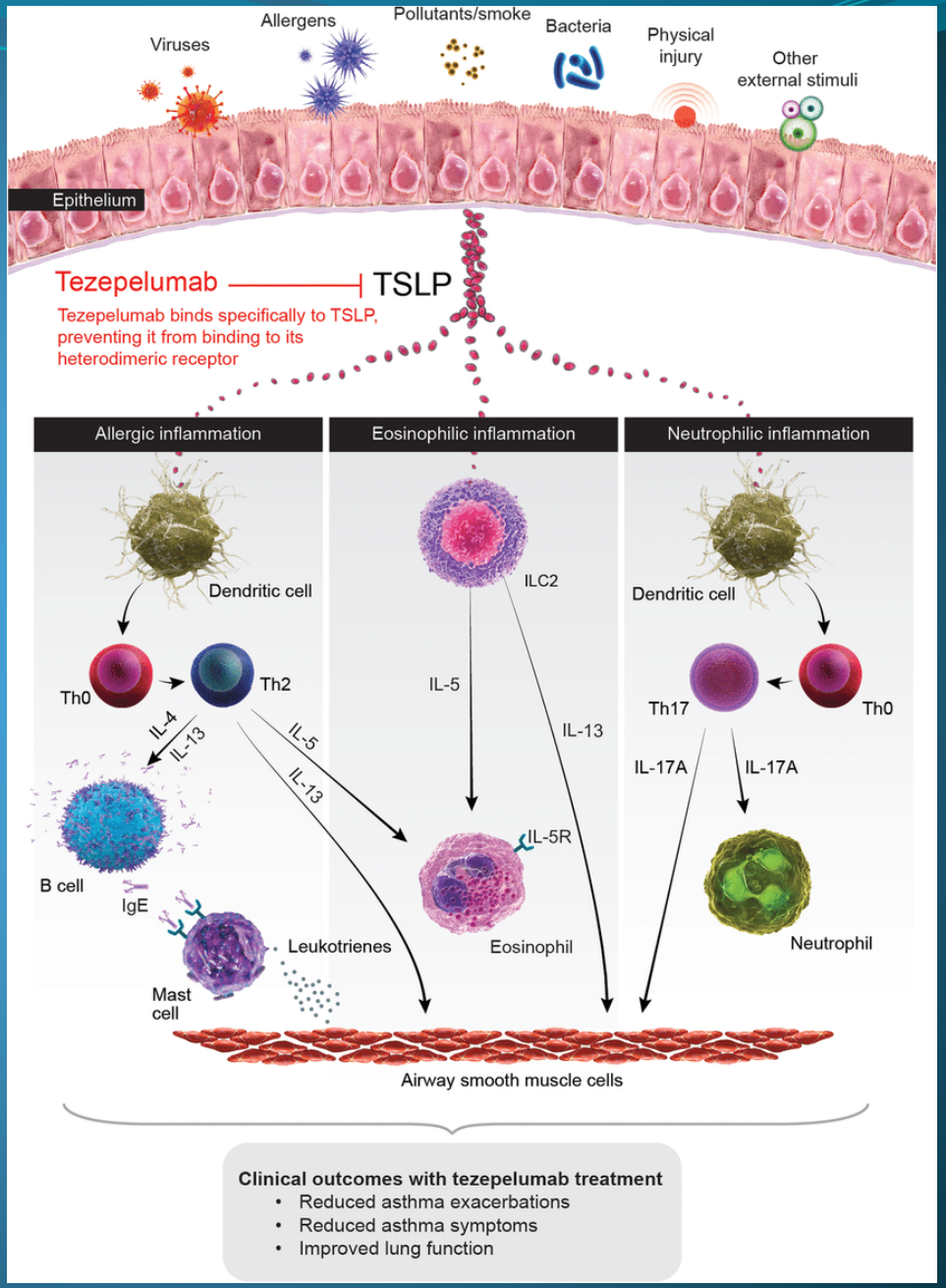
Severe asthma.

Subcutaneous administration.

210 mg sc every 4 weeks.

NO biomarkers needed.

Tezspire MOA



Referral to Asthma Specialist
NHLBI Guidelines

Life-threatening asthma exacerbation.

Unmet goals of asthma therapy after 3–6 months of treatment.

Signs and symptoms are atypical.

Associated complicating conditions or diagnoses :sinusitis, nasal polyps, aspergillosis, severe rhinitis, VCD, GERD, COPD).

Diagnostic testing is indicated (e.g., allergy skin testing, rhinoscopy, complete pulmonary function studies, provocative challenge, bronchoscopy).

Referral to Asthma Specialist NHLBI Guidelines cont'd

Education and guidance on complications of therapy, adherence, or allergen avoidance.

Allergen immunotherapy.

Patient requires step 4 care or higher (step 3 for children 0–4 years of age). Consider referral if patient requires step 3 care (step 2 for children 0–4 years of age).

More than two bursts of oral corticosteroids in 1 year or has an exacerbation requiring hospitalization.

Identification of an occupational or environmental inhalant or ingestant.

Depending on the complexities of diagnosis, treatment, or the intervention required in the work environment, co-manage with specialist.

Summary

Asthma is a heterogeneous lung disease.

Asthma has variable phenotypes.

Identification and understanding asthma phenotypes leads to targeted and effective management.

Optimal asthma management includes following ERP-4/GINA guidelines: routine spirometry, selection of appropriate medications, allergen desensitization.

The use of asthma biologics has improved asthma outcomes.

Personalized precision medicine including biologics is the future.