ASTHMA IN PREGNANCY

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INTERNAL MEDICINE, PULMONARY, CRITICAL CARE

NO FINANCIAL DISCLOSURES.

1. WHAT IS ASTHMA?

2. DO MATERNAL FACTORS AFFECT ASTHMA RISK IN THE CHILD?

3. DOES PREGNANCY AFFECT ASTHMA?

4. HOW DO YOU TREAT ASTHMA IN PREGNANCY?

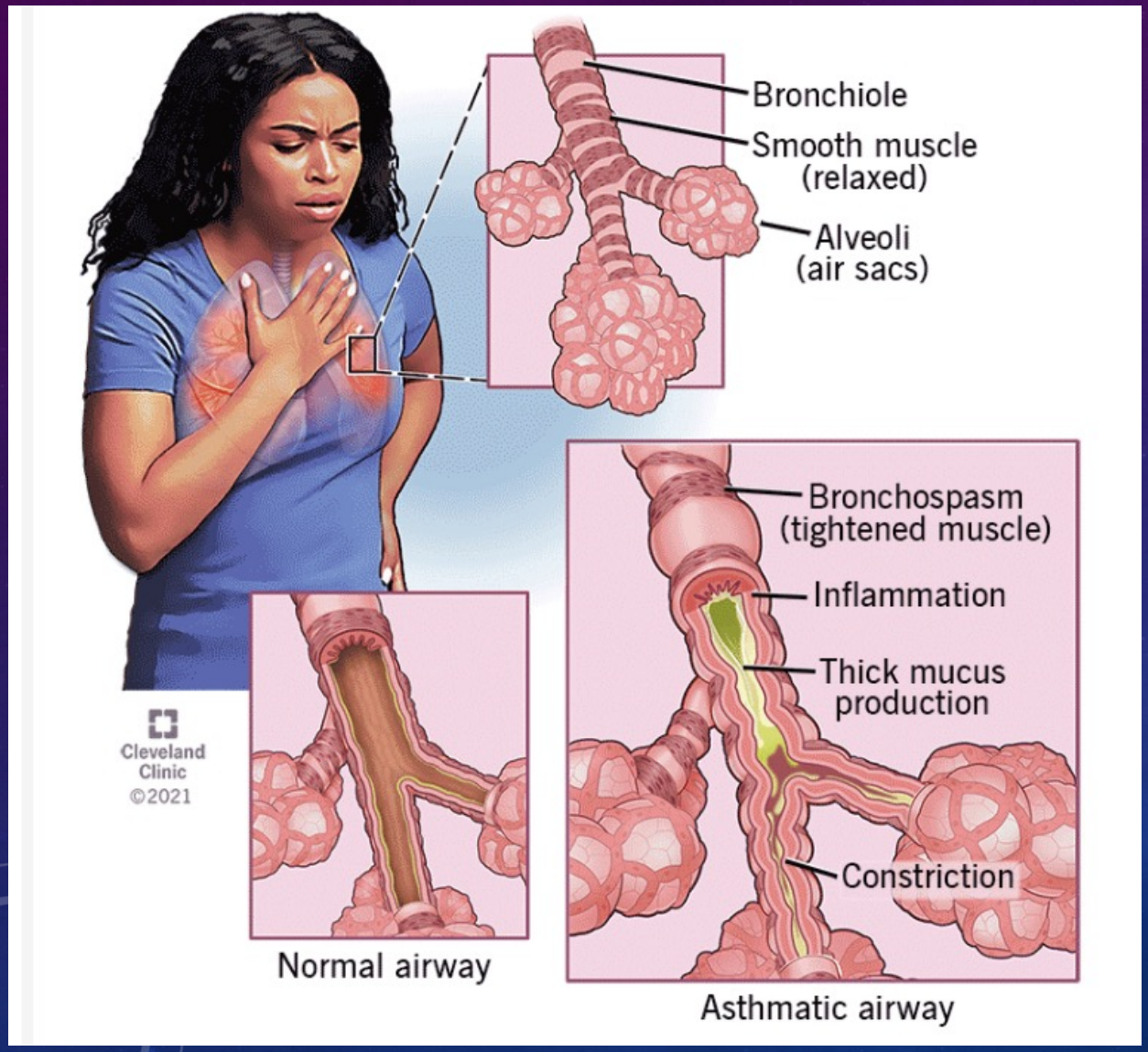
WHAT IS ASTHMA?

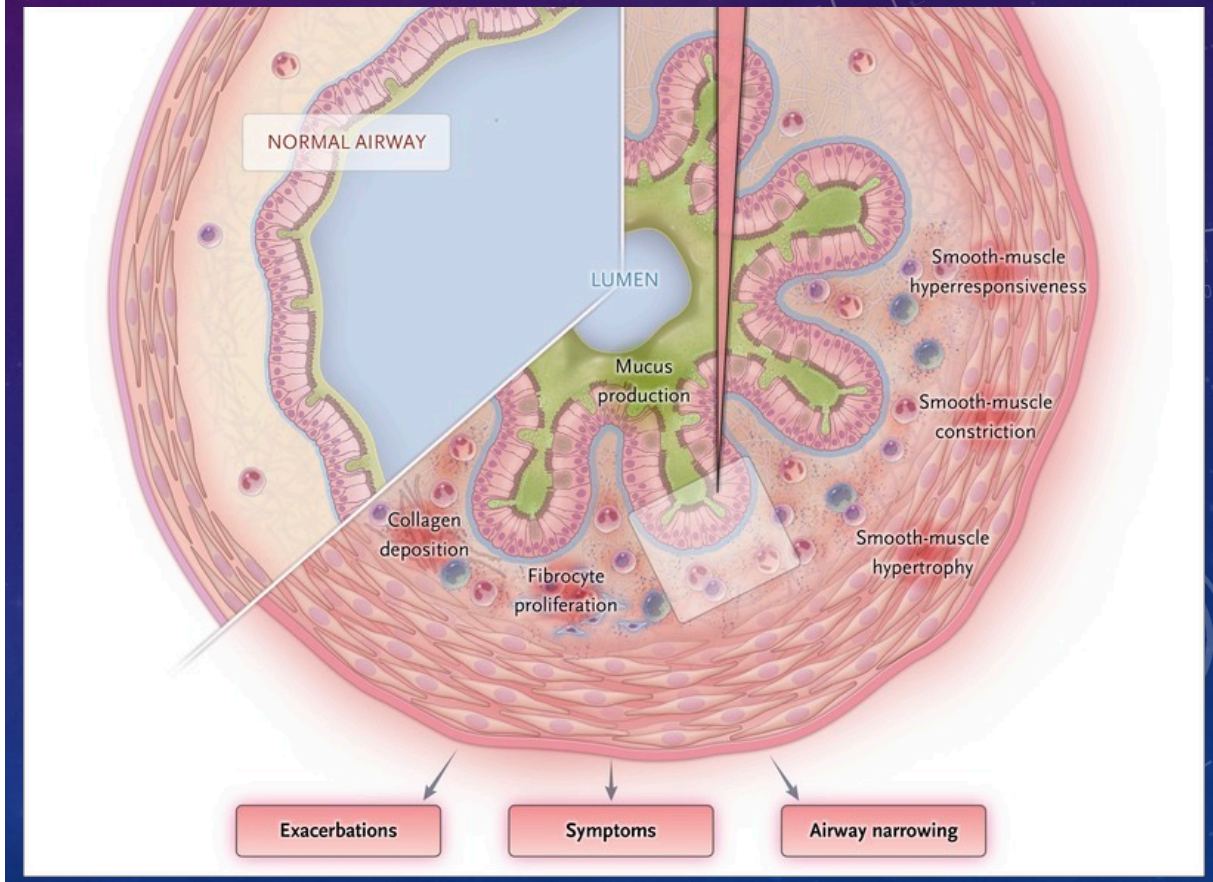
- A disorder of the airways, characterized by chronic (long standing) inflammation, variable and recurring symptoms (shortness of breath, cough, wheezing, chest tightness), airflow obstruction, and bronchial hyperresponsiveness.

National Asthma Education and Prevention Program (NAEPP). National Heart, Lung, and Blood Institute. Guidelines for the Diagnosis and Management of Asthma 2007 (EPR-3). 2012.

Global Initiative for Asthma (GINA). Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. www.ginasthma.org

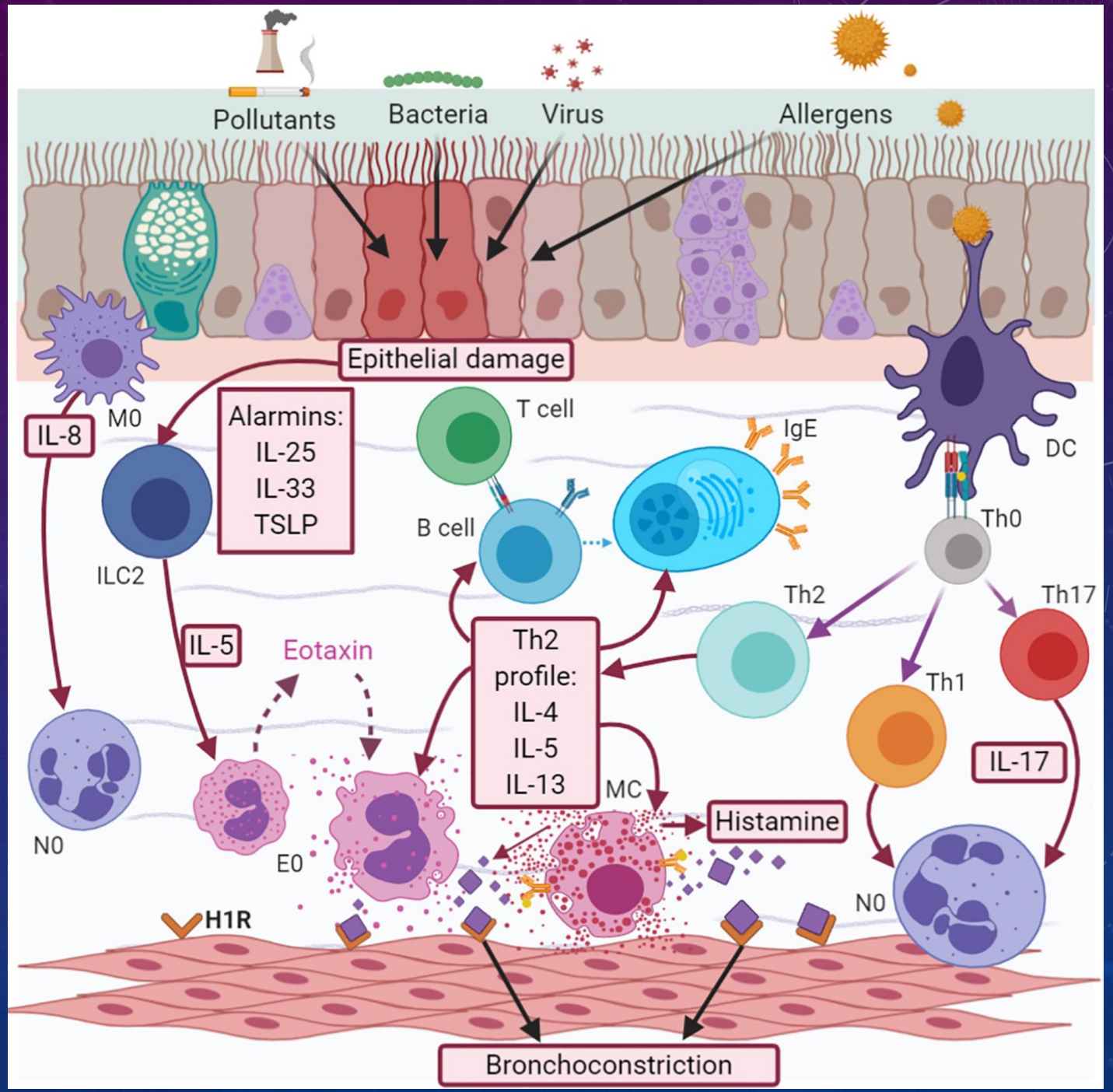
WHAT IS ASTHMA?



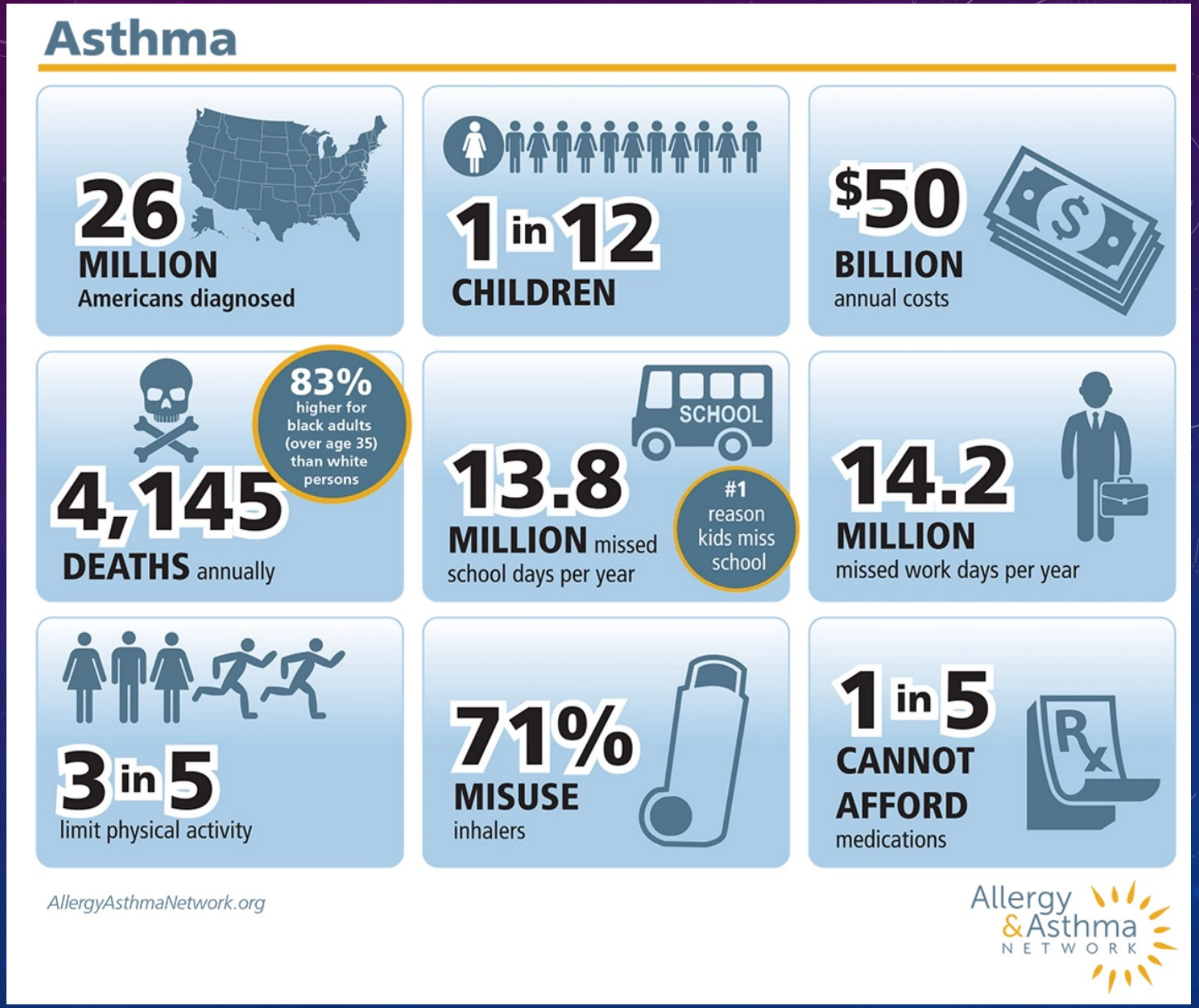


WHAT IS ASTHMA?

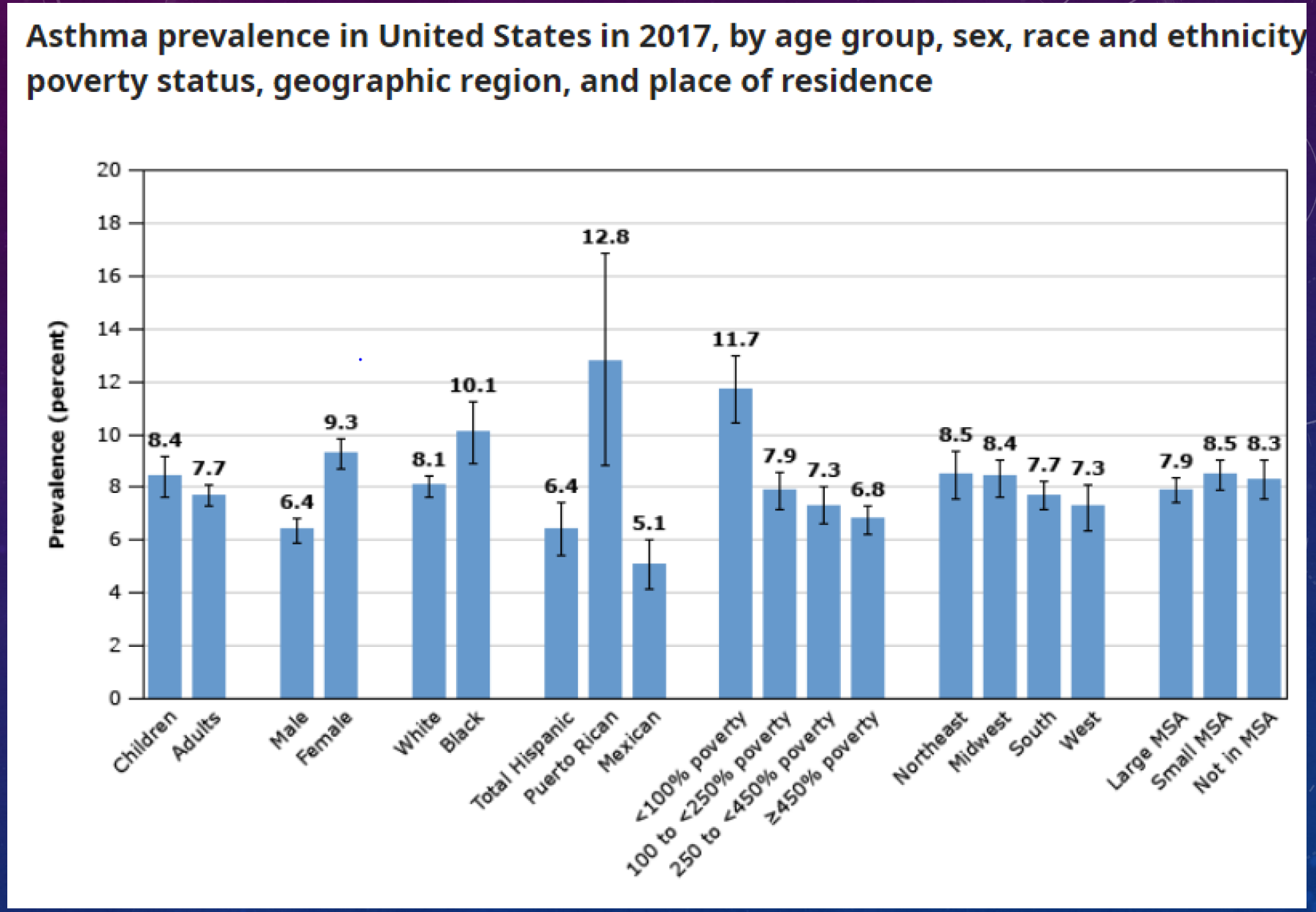
Neuroimmune Pathophysiology of Asthma. Front. Cell Dev. Biol., 13 May 2021



WHAT IS ASTHMA?



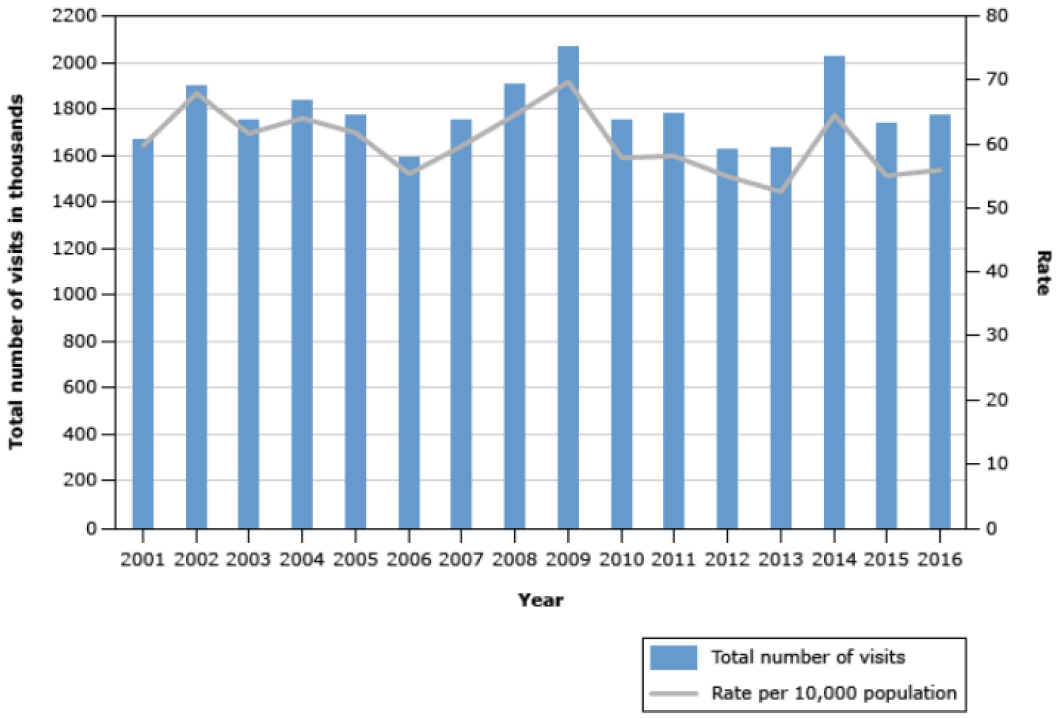
WHAT IS ASTHMA?



www.cdc.gov. Data from 2020. MSA –Metropolitan Statistical Data

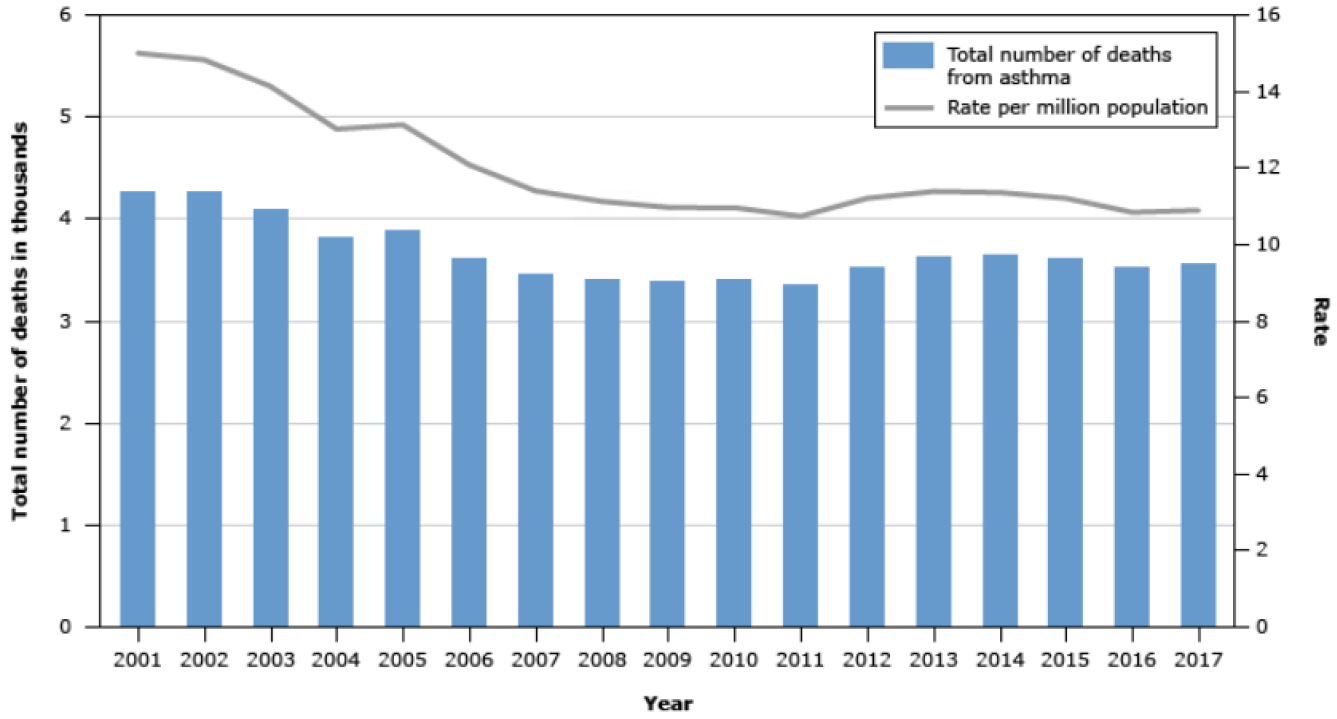
WHAT IS ASTHMA?

Asthma-related emergency department visits in the United States, 2001 to 2016



The bars represent the total number of visits, and the line represents the rate per 10,000 population. The rate of asthma-related emergency department visits did not change significantly from 2001 to 2016.

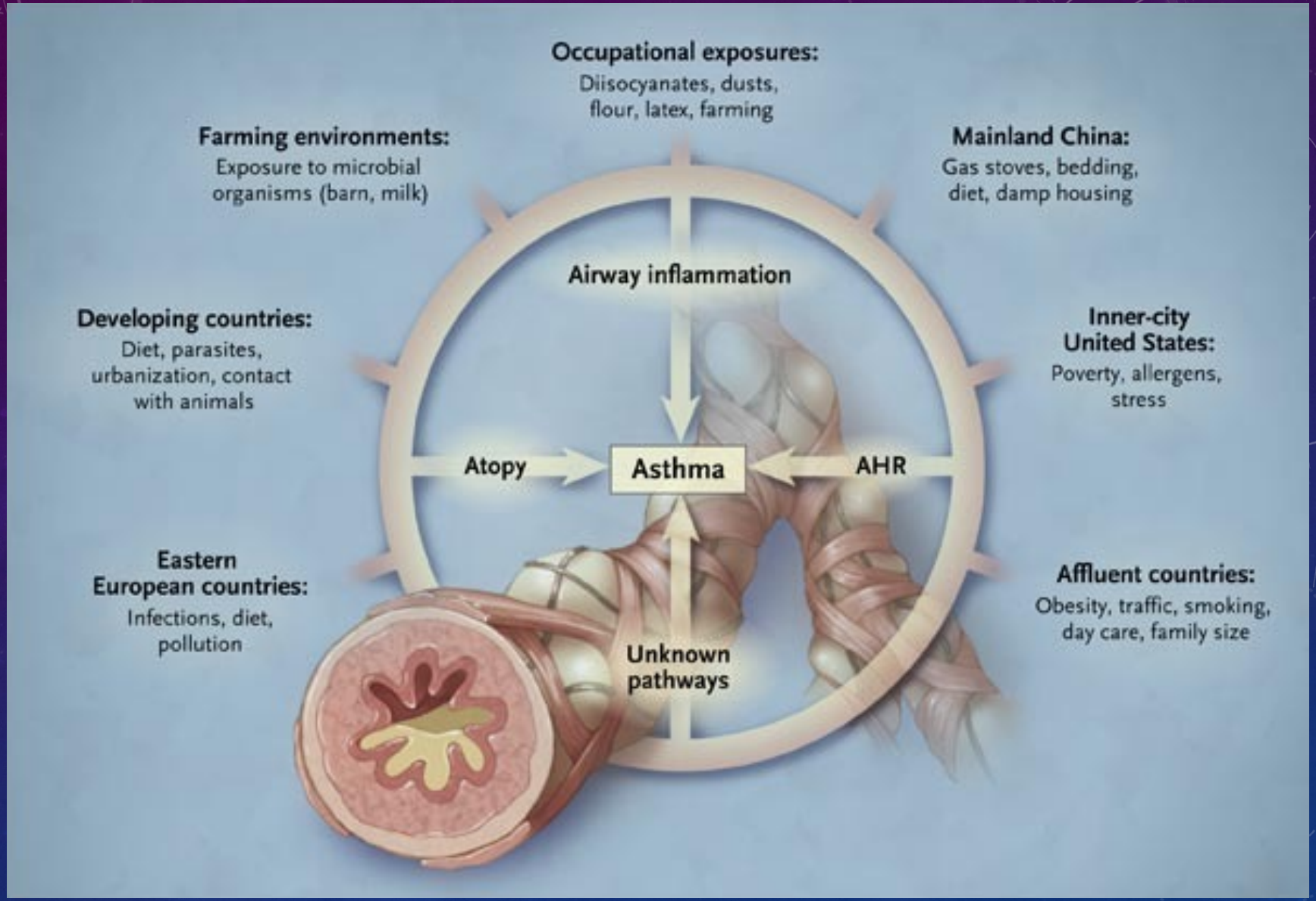
Mortality from asthma in the United States, 2001 to 2017



The bars represent the total number of deaths from asthma; the line represents the rate per million population. The rate of asthma deaths declined from 15 per million population in 2001 to 11.2 deaths per million population in 2008, and then remained stable through 2017.

www.cdc.gov. Data from 2020. MSA –Metropolitan Statistical Data

WHAT CAUSES ASTHMA?



The Asthma Epidemic. N Engl J Med 2006; 355:2226-2235

DIAGNOSIS….

- Bronchodilator responsiveness: an improvement in 12% and 200 ml in either FEV1 or FVC.
- Bronchoprovocation testing: A >=20% drop in FEV1 with <=200 mcg or 8 mg/ml methacholine dilution.

DO MATERNAL FACTORS AFFECT ASTHMA IN THE CHILD?

RISK FACTORS FOR THE CHILD

- Increasing maternal age at delivery (>30 years) is associated with LOWER risk for asthma in the offspring.

Gómez Real et al. Maternal age at delivery, lung function and asthma in offspring: a population-based survey. Eur Respir J. 2018;51(6) Epub 2018 Jun 7.

RISK FACTORS FOR THE CHILD

- Asthma can be GENETICALLY INHERITED, although not by simple Mendelian pattern.
- The ORMDL3/GSDMB locus in chromosome 17q12–q21 had one of the strongest associations for asthma in the EVE Consortium.
- Association of the interleukin-33 (IL33) and ST2 (IL1R1) genes with asthma also identified.
- Association with the susceptibility locus for thymic stromal lymphopoietin (TSLP) has already been translated into therapy – an anti TSLP monoclonal antibody, Tezepelumab.

Torgerson DG et al. Meta-analysis of genome-wide association studies of asthma in ethnically diverse North American populations. Nat Genet. 2011;43(9):887. Epub 2011 Jul 31.

RISK FACTORS FOR THE CHILD

- Vitamin D deficiency in the mother (colder climates, sunscreen use, affluency in Western countries affording indoor living) has been associated with INCREASE risk of asthma in the offspring

- High-dose maternal vitamin D supplementation during pregnancy might reduce the risk of early life asthma/wheeze in the offspring.

- For pregnant patients with high risk of asthma in offspring (one or both parents have asthma), extra Vitamin D3 supplementation (2000-4000 IU/day) in addition to the RDA of 600 IU/day is suggested.

Devereux G et al. Diet as a risk factor for atopy and asthma. J Allergy Clin Immunol. 2005;115(6):1109.
Litonjua AA et al. Effect of Prenatal Supplementation With Vitamin D on Asthma or Recurrent Wheezing in Offspring by Age 3 Years: The VDAART Randomized Clinical Trial.
JAMA. 2016 Jan;315(4):362-70.

RISK FACTORS FOR THE CHILD

- American diet with increased intake of omega-6 polyunsaturated fatty acids may potentially be associated with increased risk of asthma in offspring, compared to a diet rich in omega-3 PUFAs.

Bisgaard H et al. Fish Oil-Derived Fatty Acids in Pregnancy and Wheeze and Asthma in Offspring.
N Engl J Med. 2016;375(26):2530.

RISK FACTORS FOR THE OFFSPRING

- Higher Vitamin E intake during pregnancy is associated with reduced risk for asthma in the offspring.

- Vitamin C supplementation (500 mg/day) can reduce the chances of infant asthma if the mother is a smoker.

Allan KM et al. Maternal vitamin D and E intakes during pregnancy are associated with asthma in children. Eur Respir J. 2015;45(4):1027. Epub 2014 Oct 30.
McEvoy CT, et al. Vitamin C to Pregnant Smokers Persistently Improves Infant Airway Function to 12 Months of Age: A Randomised Trial. Eur Respir J. 2020

RISK FACTORS FOR THE CHILD

- The likelihood of childhood atopic asthma increases with high sugar consumption in the mother.

- There is an increased prevalence of asthma in women with obesity and also children with obesity

- Bédard A et al. Maternal intake of sugar during pregnancy and childhood respiratory and atopic outcomes. Eur Respir J. 2017;50(1) Epub 2017 Jul 5.
- Peters U et al. Obesity and asthma. J Allergy Clin Immunol. 2018;141(4):1169
- Lang JE et al. Being Overweight or Obese and the Development of Asthma. Pediatrics. 2018;142(6)

RISK FACTORS FOR THE CHILD

- MATERNAL SMOKING both prepartum and postpartum INCREASES THE RISK OF CHILDHOOD ASTHMA.

- Burke H et al. Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis.Pediatrics. 2012;129(4):735. Epub 2012 Mar 19.

RISK FACTORS FOR THE CHILD

- Acetaminophen taken by the mother MIGHT (NOT SURE) increase the rate of asthma in the child.

- Acid suppressive medications taken by the mother MIGHT (not sure) increase the rate of asthma in the child.

- Sordillo JE et al. Prenatal and infant exposure to acetaminophen and ibuprofen and the risk for wheeze and asthma in children. J Allergy Clin Immunol. 2015;135(2):441. Epub 2014 Oct 28. .
- Brew BK et al. Acid Suppressant Use in Pregnancy and Asthma in Offspring: Should We Be Worried?
- Pediatrics. 2018;141(2) Epub 2018 Jan 11.

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- Pediatrics. 2018;141(2) Epub 2018 Jan 11.

RISK FACTORS FOR THE CHILD

- Maternal asthma increases the risk of pre-eclampsia. Also, pre-eclampsia in the mother is a risk factor for increased risk of asthma for the child.

- Premature delivery is also a risk factor for asthma in the child.

- Children born by caesarean section have a higher risk of asthma than those born by vaginal delivery, particularly children of allergic parents. Possible explanation is the “hygiene hypothesis”.

- Stokholm J et al. Preeclampsia Associates with Asthma, Allergy, and Eczema in Childhood. Am J Respir Crit Care Med. 2017;195(5):614.
- Leps C et al. Gestational age at birth and wheezing trajectories at 3-11 years. Arch Dis Child. 2018;103(12):1138. Epub 2018 Jun 2.
- Roduit C, et al. Asthma at 8 years of age in children born by caesarean section. Thorax. 2009;64(2):107.

RISK FACTORS FOR THE CHILD

- Breastfeeding is associated with lower risk of wheezing in the first 2 years of life, possibly due to improved immunity against respiratory viral infections.

- Longer versus shorter duration of breastfeeding was associated with a decreased risk of asthma in children 5 to 18 years of age.

- Dogaru CM et al. Breastfeeding and childhood asthma: systematic review and meta-analysis. Am J Epidemiol. 2014 May;179(10):1153-67. Epub 2014 Apr 11.
- Lodge CJ et al. Breastfeeding and asthma and allergies: a systematic review and meta-analysis.Acta Paediatr. 2015;104(467):38.

DOES PREGNANCY AFFECT ASTHMA?

PREGNANCY AND ASTHMA

- In pregnant patients who have asthma, the asthma gets worse in 1/3 patients, stays stable in 1/3 and gets worse in 1/3 patients.

- Asthma exacerbations occur in 20-45% pregnant asthmatic patients, with severe exacerbations in 10%

- Asthma control prior to pregnancy is a good indicator of asthma control during pregnancy.

- Schatz M et al. The course of asthma during pregnancy, post partum, and with successive pregnancies: a prospective analysis. J Allergy Clin Immunol. 1988;81(3):509.

RISK FACTORS FOR ASTHMA EXACERBATION

- Maternal obesity
- 1st trimester weight gain
- History of exacerbation in the 12 months prior to pregnancy
- Smoking during pregnancy
- Anxiety during pregnancy

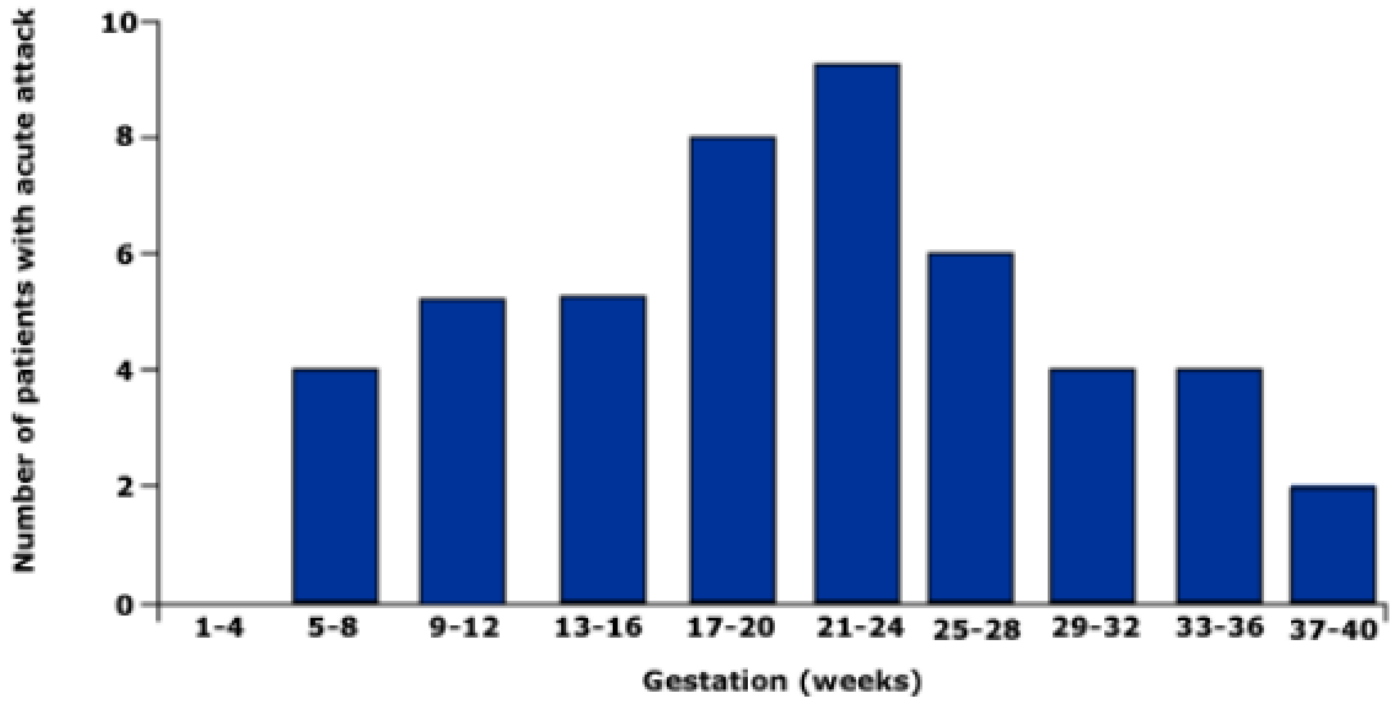
- Bokern MP. Factors Associated with Asthma Exacerbations During Pregnancy. J Allergy Clin Immunol Pract. 2021;9(12):4343. Epub 2021 Aug 14.

PREGNANCY AND ASTHMA

- Acute asthma exacerbations are most common during weeks 17 to 24 of pregnancy.
- Pregnant patients often initially quit using their inhalers, which can cause early exacerbations.

Schatz M et al. The course of asthma during pregnancy, post partum, and with successive pregnancies: a prospective analysis. J Allergy Clin Immunol. 1988;81(3):509.

Frequency distribution of acute attacks during pregnancy



Asthma attacks during pregnancy were seen most frequently between weeks 17 and 24 of gestation.

PREGNANCY AND ASTHMA

- Asthma during pregnancy is associated with 15-20% increased risk of….
  - Perinatal mortality
  - Spontaneous abortion
  - Uterine hemorrhage
  - Pre-eclampsia
  - Neonatal mortality
  - Prematurity and low birth weight infants
- The possible cause is increased hypoxia….

- Friedman AM et al. Trends in and Maternal Outcomes of Delivery Hospitalizations of Patients With an Asthma Diagnosis. Obstet Gynecol. 2022;139(1):52.

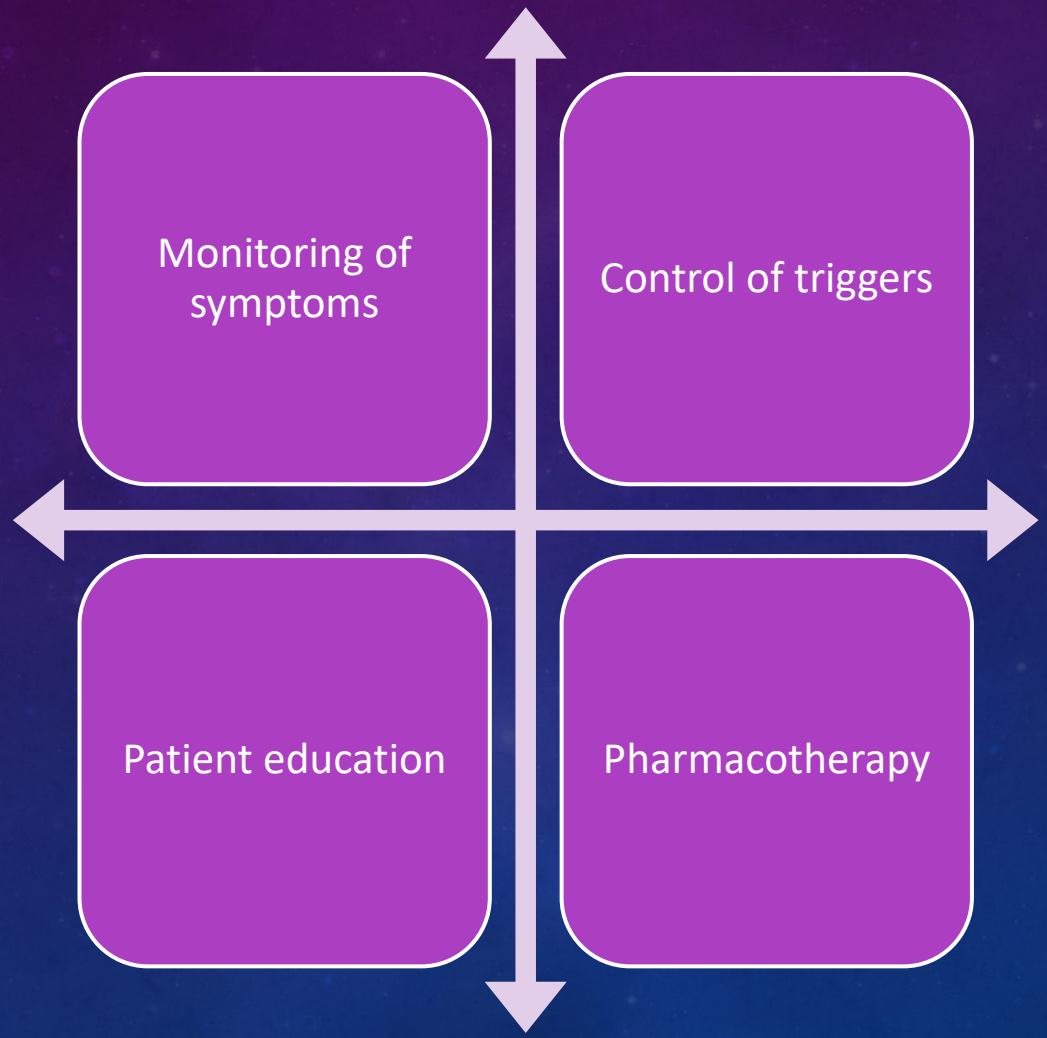
PREGNANCY AND ASTHMA

- Spirometry parameters such as FEV1, FVC, FEV1/FVC ratio and Peak Expiratory Flow remain stable to slightly *increased* in pregnancy.
- TLC may decline in the 3rd trimester. DLCO measurement is NOT contra-indicated, although not needed for asthma diagnosis.
- ABG shows mild respiratory alkalosis with lower PCO2, normal to higher PO2
- PaCO2 > 35 (instead of 40) and PaO2 < 70 (instead of 60) may represent severe asthma exacerbation in a pregnant patient.

DIAGNOSIS OF ASTHMA IN PREGNANCY

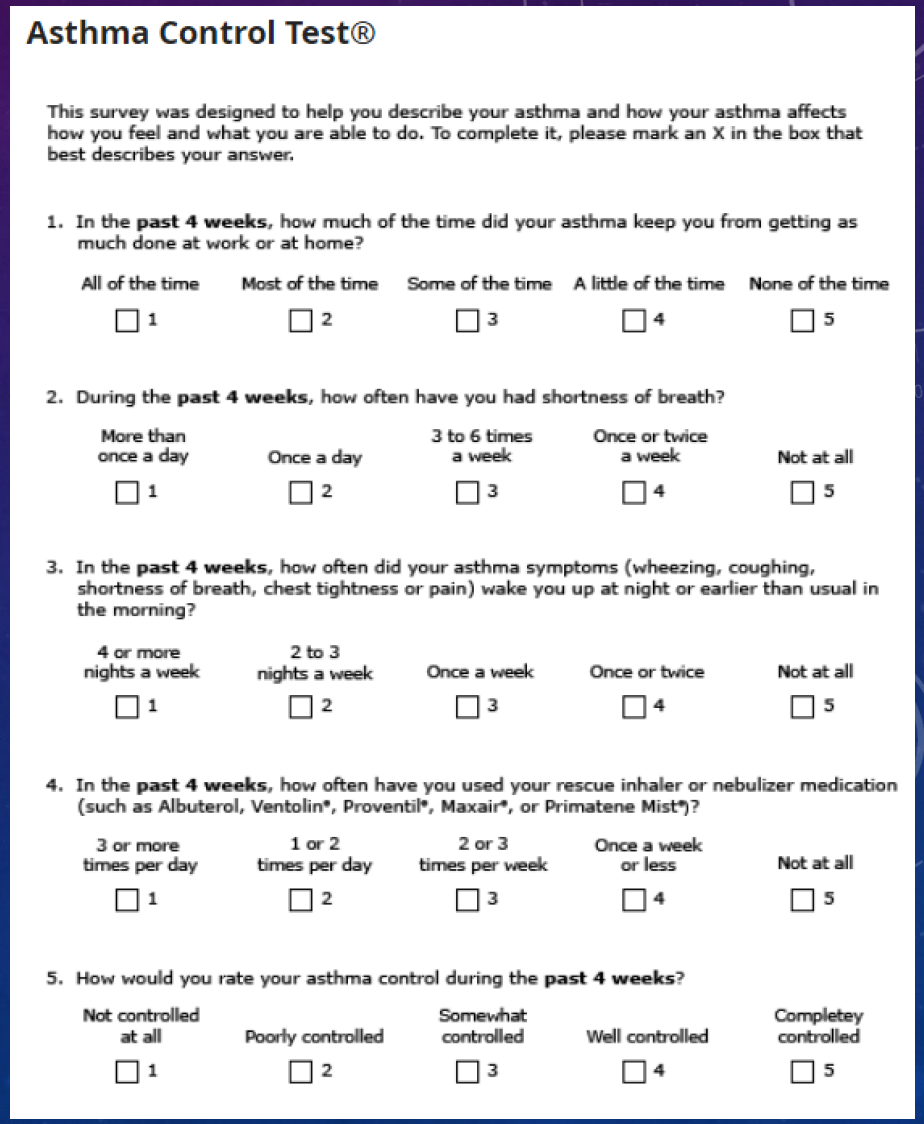
- Spirometry with bronchodilator response can be done to diagnose asthma during pregnancy.
- Bronchoprovocation testing (eg methacholine challenge) is contra-indicated in pregnancy.

TREATMENT


Monitoring of symptoms
Control of triggers
Patient education
Pharmacotherapy

MONITORING OF SYMPTOMS

- Asthma Control Test



Asthma Control Test®

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®)?

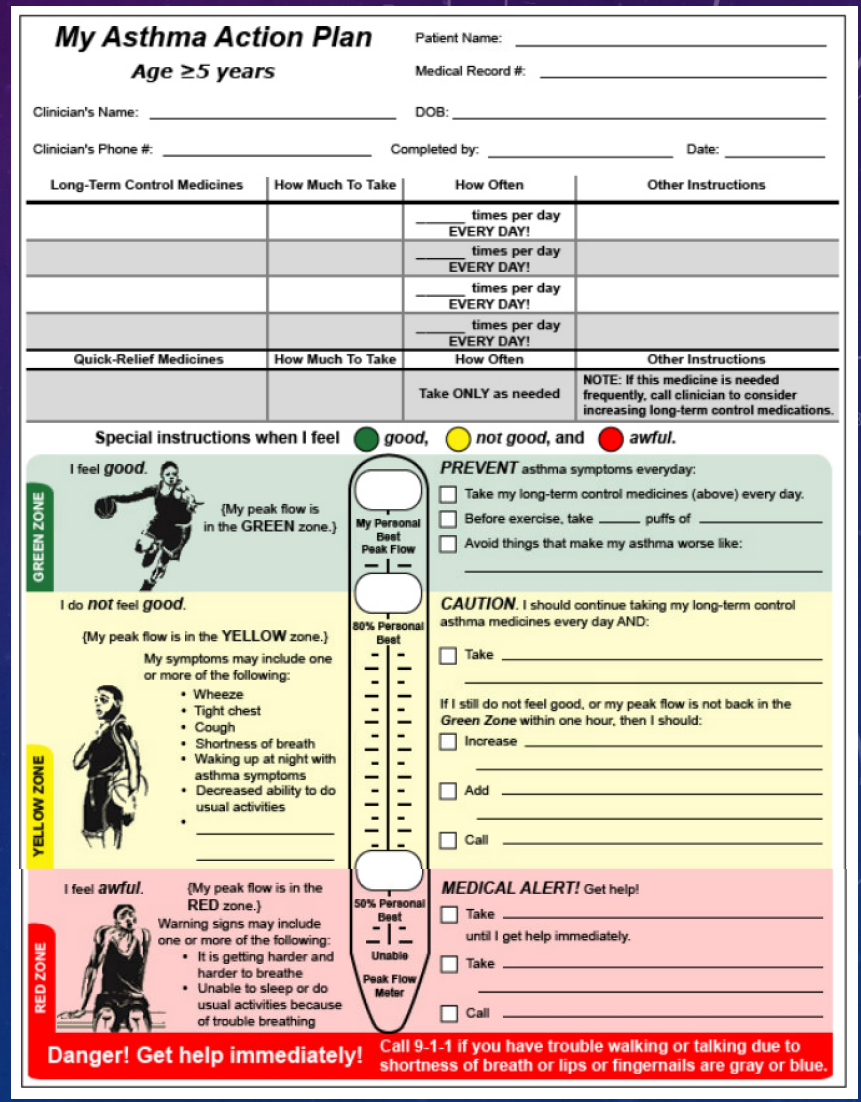
3 or more times per day	1 or 2 times per day	2 or 3 times per week	Once a week or less	Not at all
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

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

MONITORING OF SYMPTOMS

Peak Expiratory Flow monitoring



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.}

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
- _____

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 _____

My Personal Best Peak Flow

80% Personal Best

50% Personal Best

Unable

Peak Flow Meter

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

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.

CONTROL OF TRIGGERS

- Smoking cessation and also avoiding second hand smoke inhalation
- Allergen avoidance: dust, environmental allergens, pollutants, pets, etc.
- ALSO: measures to reduce chances of asthma in the child…Vitamin C and D supplements, healthy diet, avoidance of excess sugars etc.

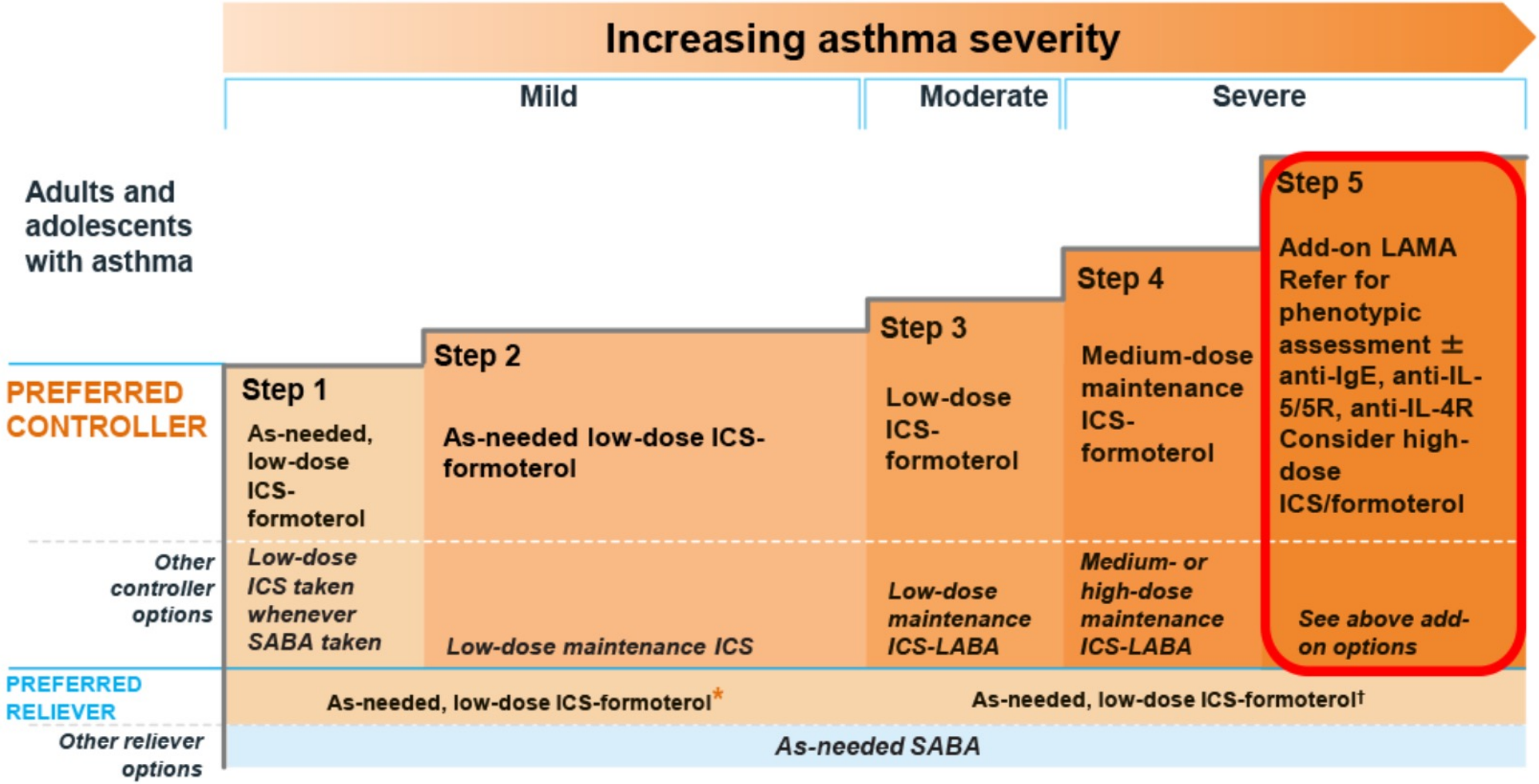
PATIENT EDUCATION

- Asthma and COPD management program, Lee Health.
- Education on inhaler techniques.
- Education about disease process.
- Co-ordination of care – PCP, Ob/Gyn, Pulmonologist

PHARMACOTHERAPY

- The general principles of asthma treatment remain the same in pregnant patients as in non pregnant patients.

GINA 2021: Stepwise Treatment Approach



FDA = US Food and Drug Administration; ICS = inhaled corticosteroid; Ig = immunoglobulin; IL = interleukin; □LABA = long-acting β2-agonist; LTRA = leukotriene receptor antagonist; OCS = oral corticosteroid; SABA = short-acting β2-agonist.

Adapted from GINA. Global Strategy for Asthma Management and Prevention. Updated 2021 (https://ginasthma.org/wp-content/uploads/2021/05/GINA-Main-Report-2021-V2-WMS.pdf). Accessed 7/25/21.

PHARMACOTHERAPY

- All patients should have a short acting beta agonist (SABA) rescue inhaler eg. albuterol.

PHARMACOTHERAPY

- Inhaled corticosteroids (ICS) reduce asthma exacerbations in pregnancy.
- Budesonide has the most amount of published data, Fluticasone and Beclomethasone are OK also.

PHARMACOTHERAPY

- Salmeterol is the preferred long acting beta agonist (LABA), not expected to increase the risk of congenital abnormalities. Formeterol also has reassuring safety data.

- LABA should NOT be used without concurrent ICS.

PHARMACOTHERAPY

- Tiotropium is the preferred Long Acting Muscarinic Agent (LAMA) in pregnancy.
- The other available LAMA eg . aclidinium, glycopyrrolate and umeclidinium do not have adequate data.

PHARMACOTHERAPY

- Montelukast and Zafirlukast (leukotriene receptor antagonists) can be used in pregnancy, data so far is reassuring.

- Allergy immunotherapy should not be started during pregnancy, but can be continued if the patient was tolerating it prior to pregnancy.

PHARMACOTHERAPY

- Systemic glucocorticoids may increase the risk of congenital malformations (primarily cleft palate), pre-eclampsia, gestational diabetes, low birth weight, and neonatal adrenal insufficiency.

- However, systemic steroids have been used for asthma exacerbations in pregnancy very extensively, and the benefits of controlling the asthma exacerbation and reducing maternal / fetal mortality exceed the risks .

PHARMACOTHERAPY

- Omalizumab (anti-immunoglobulin E monoclonal antibody) should not be started in pregnancy, but can be continued, and does cross the placenta.
- There is some human data which is reassuring.

- Namazy JA et al. Pregnancy outcomes in the omalizumab pregnancy registry and a disease-matched comparator cohort. J Allergy Clin Immunol. 2020;145(2):528. Epub 2019 May 27.

PHARMACOTHERAPY

- Anti-interleukin (IL)-5 antibody preparations, benralizumab, mepolizumab and reslizumab, for patients with severe eosinophilic asthma also cross the placenta. There is limited animal safety data and no human safety data in pregnancy.
-
- Dupilumab binds to the IL-4 receptor alpha subunit, which is also part of the IL-13 receptor. Tezepelumab is an antithymic stromal lymphopoietin (anti TSLP) inhibitor. Both have some animal data but no human safety data in pregnancy.

PHARMACOTHERAPY

- For acute asthma exacerbations, the treatment in pregnancy is the same as in non pregnant patients. (NAEPP Expert Panel III guidelines.)

Pharmacologic management of acute asthma exacerbations during pregnancy

1. Beta$_2$-agonist bronchodilator (nebulized or metered-dose inhaler)
Albuterol by MDI 4 to 8 puffs every 20 minutes up to 1 hour, then every 1 to 4 hours, as needed
Albuterol by nebulizer 0.083 percent (2.5 mg/3 mL), 2.5 to 5 mg every 20 minutes for 3 doses and then 2.5 to 5 mg every 1 to 4 hours, as needed
Albuterol by continuous nebulization, administering 10 to 15 mg per hour
2. Ipratropium
By nebulizer, 500 mcg every 20 minutes for 3 doses, then as needed. Can be given simultaneously with beta$_2$-agonist.
By MDI, 4 to 8 inhalations every 20 minutes for 3 doses, then as needed
3. Systemic glucocorticoids (for those with a poor response to treatment after one hour, or with initial therapy for patients on chronic oral glucocorticoids)
For patients who can be managed at home: prednisone 40 to 60 mg per day in a single or divided dose
For patients who require hospitalization: prednisone 40 to 80 mg daily in a single or divided dose (or the equivalent dose of methylprednisolone* intravenously) until peak flow reaches 70 percent of predicted or personal best, and then taper as patient improves
For patients who have a life-threatening exacerbation, a higher initial dose of methylprednisolone*, 60 to 80 mg every 6 to 12 hours, may be given intravenously, and then tapered as the patient improves, as above
4. For patients not responding to above therapies, consider adjunct therapies
Intravenous magnesium sulfate 2 g infused over 20 minutes, in absence of renal insufficiency¶
Subcutaneous terbutaline 0.25 mg every 20 minutes for up to 3 doses

MDI: metered dose inhaler.

* A conversion calculator is available in UpToDate. Refer to the calculator on corticosteroid medication dosing conversions (glucocorticoid effect).

¶ For patients with renal insufficiency, a baseline serum magnesium level is assessed. The decision to use intravenous magnesium requires consideration of the potential benefit in terms of asthma and the anticipated risk of hypermagnesemia based on the degree of renal insufficiency and baseline serum magnesium level.

QUESTIONS?

THANK YOU.