Bronchial Asthma

3rd year Medical Students

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Objectives

- Definition
- Epidemiology
- Pathophysiology
- Types
- Diagnosis
- Management
- Summary

Asthma

- Word “**asthma**” is derived from the ancient Greek word for “**panting**.”

- Although asthma is a clearly recognized clinical entity, agreement on a **precise definition** of asthma has proved elusive.

- Asthma has been more often **described than defined**.

Definition

*Asthma is a **chronic** inflammatory disorder of the airways in which many cells play a role: in particular, mast cells, **eosinophils**, neutrophils.*

***T lymphocytes**, macrophages, and epithelial cells.*

*In susceptible individuals, this inflammation causes **recurrent episodes** of **coughing**, **wheezing, breathlessness,** and chest tightness.*

*These episodes are usually associated with widespread but **variable airflow obstruction** (airway hyper-responsiveness) that is often **reversible** either spontaneously or with treatment.*

Epidemiology

- Any age, 75% Dx age <7
- Remission around puberty
- **Prevalence** on the rise. likely Multifactorial
- Wide geographical variation (4-25%)
- Females 40% higher prevalence
- **Severe asthma** 10 % but morbidity / costs

Saudi Arabia Figures

- Asthma affects >2 million Saudis
- Asthma control: 5% were controlled, 31% partially controlled, 64% uncontrolled.

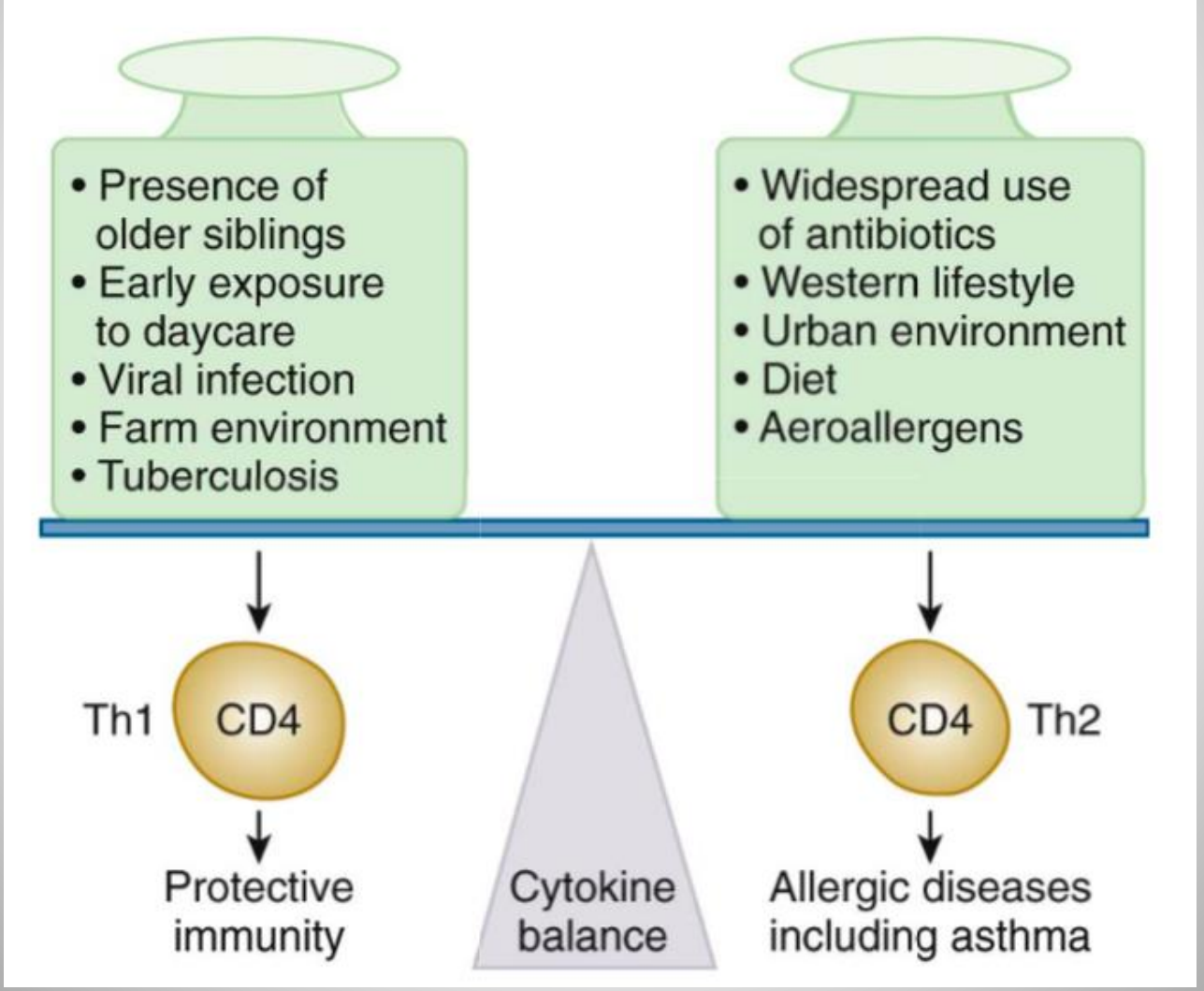
Etiology

Although asthma is **multifactorial** in origin, **inflammation** is believed to be the cornerstone of the disease and is thought to result from **inappropriate immune responses** to a variety of **antigens** in genetically susceptible individuals.

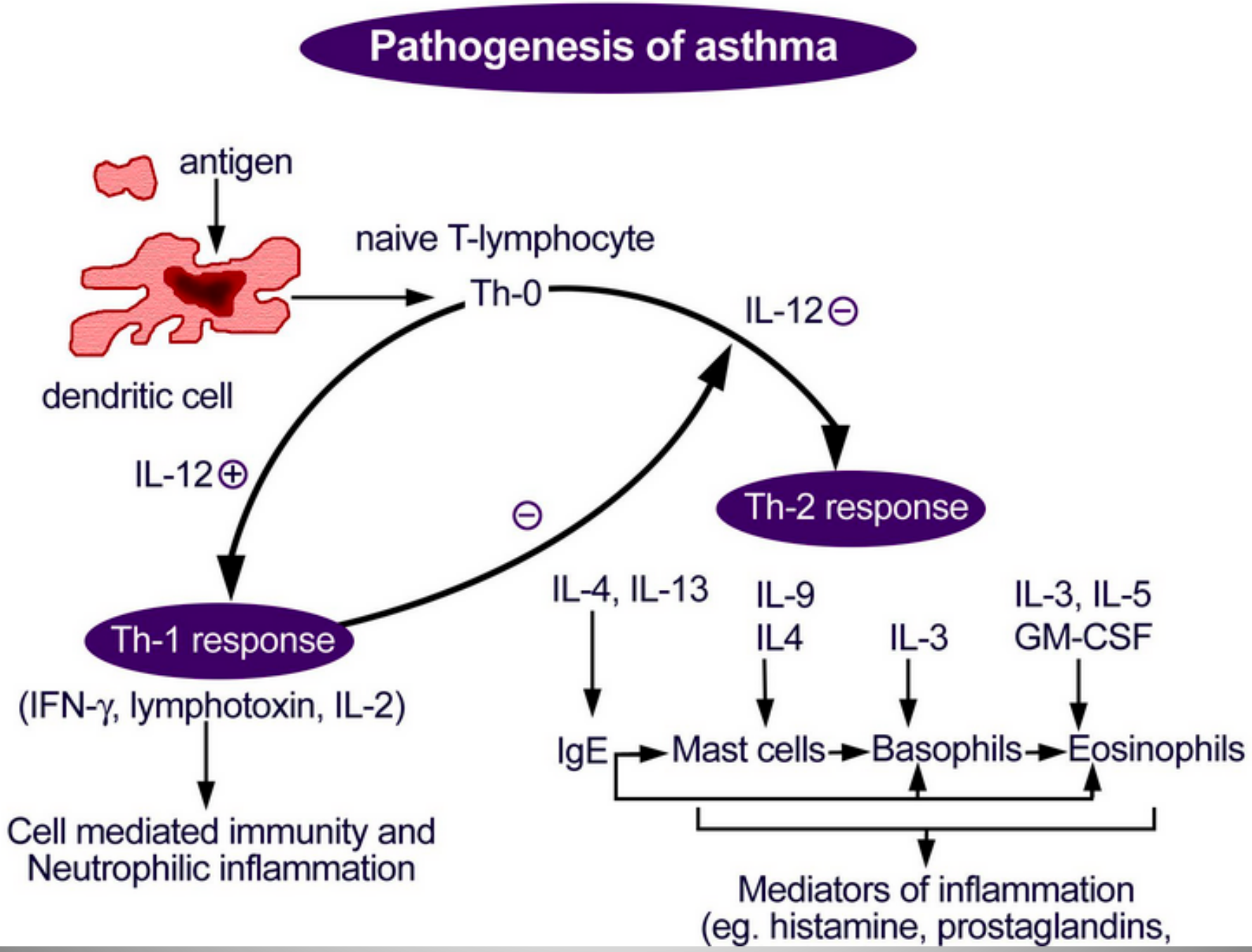
Causes

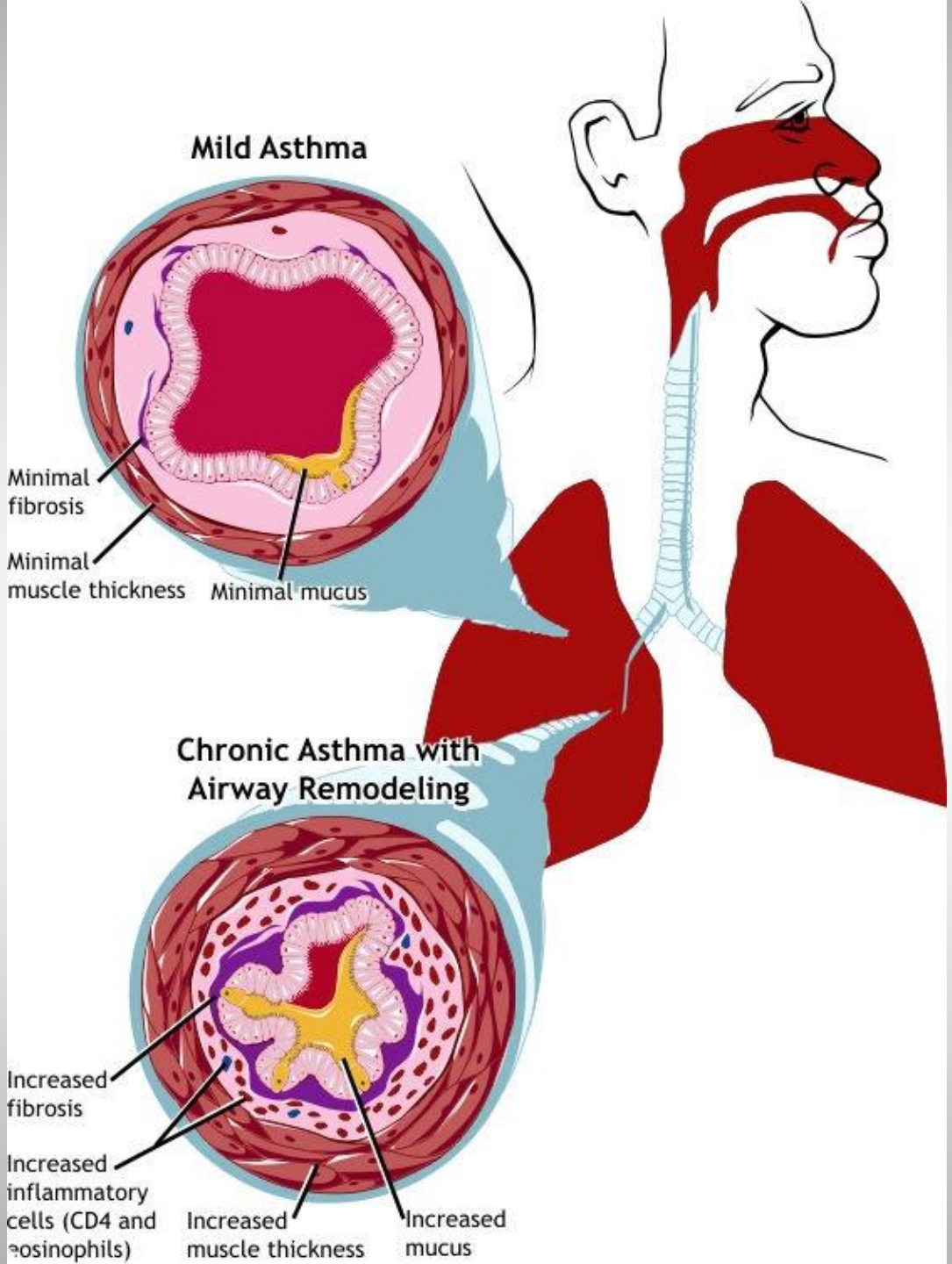
- Hygiene Hypothesis
- Atopy
- Genetics
- Smoking – controversial
- Obesity – New under Ix

Cause - Hygiene Hypothesis



Pathogenesis of asthma



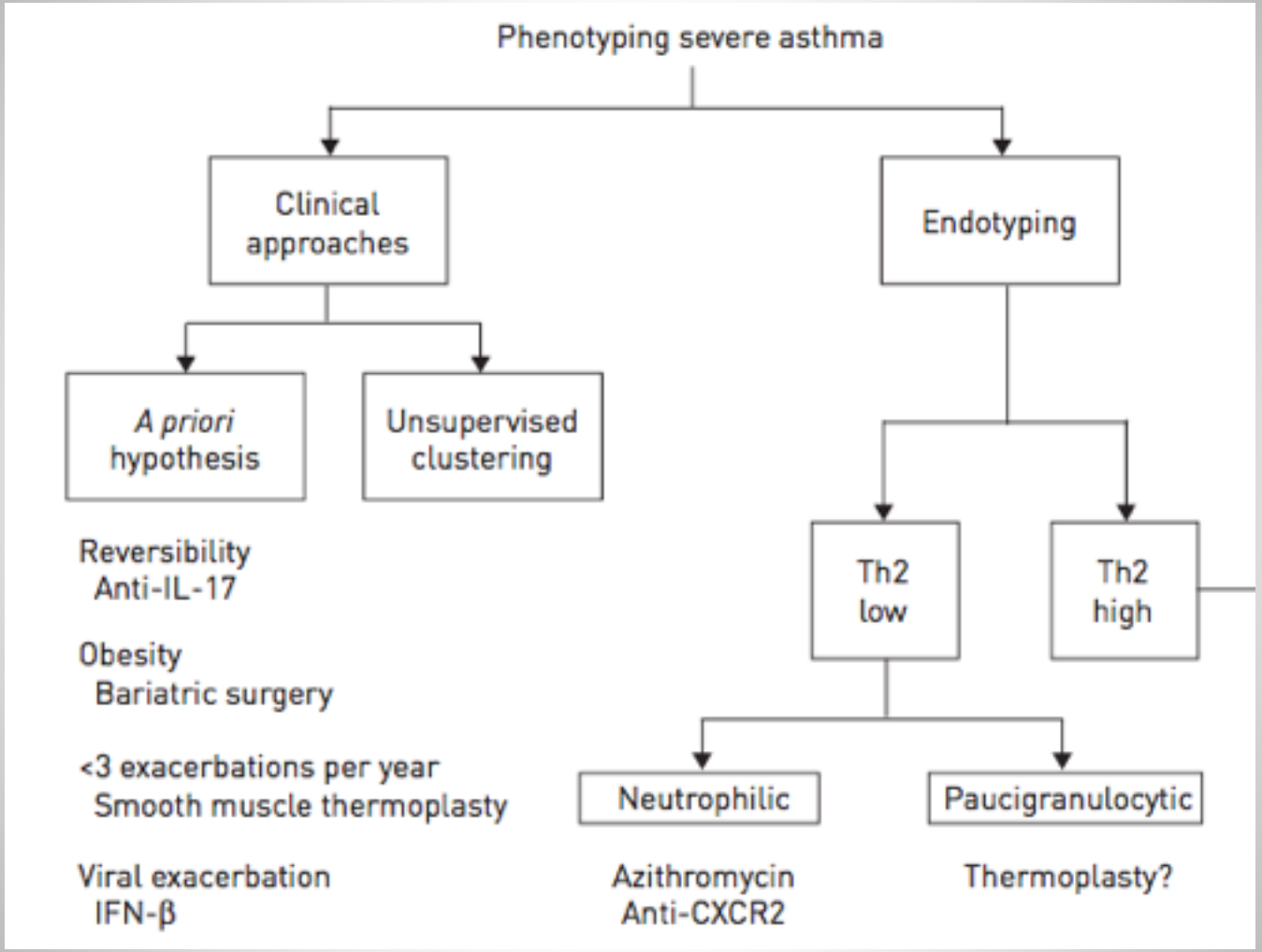

Mild Asthma
Minimal fibrosis
Minimal muscle thickness
Minimal mucus
Chronic Asthma with Airway Remodeling
Increased fibrosis
Increased inflammatory cells (CD4 and eosinophils)
Increased muscle thickness
Increased mucus

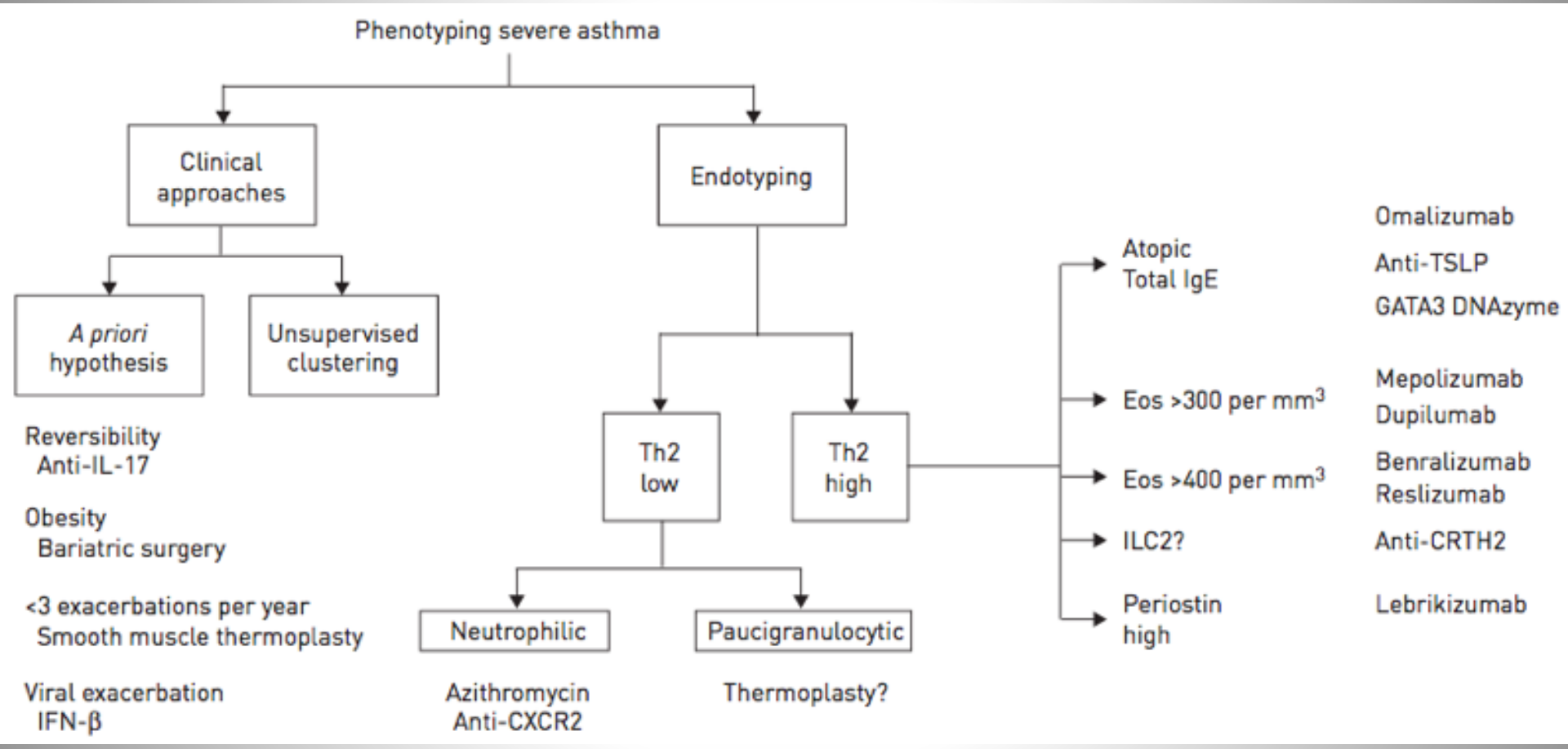
Asthma Types

Types

- Phenotypes
- Endotypes

- Mixed or overlapping features


Phenotyping severe asthma
Clinical approaches
Endotyping
A priori hypothesis
Unsupervised clustering
Th2 low
Th2 high
Neutrophilic
Paucigranulocytic
Reversibility
Anti-IL-17
Obesity
Bariatric surgery
<3 exacerbations per year
Smooth muscle thermoplasty
Viral exacerbation
IFN-β
Azithromycin
Anti-CXCR2
Thermoplasty?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Th2 low
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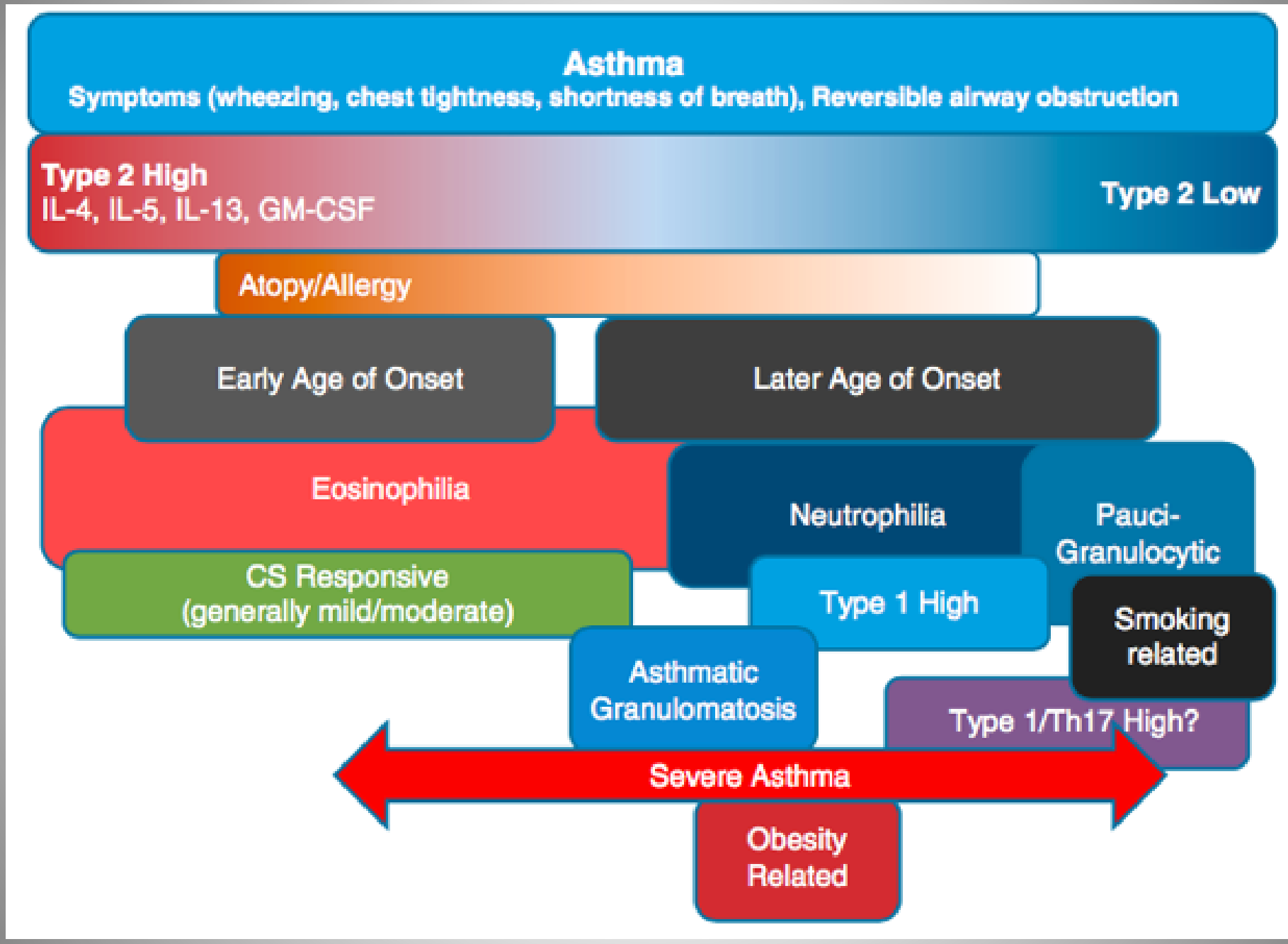
Paucigranulocytic
Azithromycin
Anti-CXCR2
Thermoplasty?
Atopic
Total IgE
Eos >300 per mm3
Eos >400 per mm3
ILC2?
Periostin high
Omalizumab
Anti-TSLP
GATA3 DNAzyme
Mepolizumab
Dupilumab
Benralizumab
Reslizumab
Anti-CRTH2
Lebrikizumab


Asthma
Symptoms (wheezing, chest tightness, shortness of breath), Reversible airway obstruction
Type 2 High
IL-4, IL-5, IL-13, GM-CSF
Type 2 Low
Atopy/Allergy
Early Age of Onset
Later Age of Onset
Eosinophilia
Neutrophilia
Pauci-Granulocytic
CS Responsive (generally mild/moderate)
Type 1 High
Smoking related
Asthmatic Granulomatosis
Type 1/Th17 High?
Severe Asthma
Obesity Related

Asthma Types

- **Early onset** (<12years)
  - **Childhood-onset asthma** a relatively **homogeneous** group
  - **Allergic Asthma** (Atopic) Usually a strong allergic Hx
  - **FH** of asthma.

- **Late onset** (>12years)
  - **Adult-onset asthmatics** are a very mixed group **Heterogeneous**
  - Late onset – **Atopic** (**34**%) have less severe disease. Those with severe disease are less likely to be **atopic**
  - **Non Atopic** (52%) have mild-to-moderate **persistent** asthma
  - Late onset eosinophilic asthma
  - AERD Aspirin Exacerbated Respiratory Disease

Diagnosis

- History
- Examination
- Test

History

DIAGNOSIS

INITIAL STRUCTURED CLINICAL ASSESSMENT

The predictive value of individual symptoms or signs is poor, and a structured clinical assessment including all information available from the history, examination and historical records should be undertaken. Factors to consider in an initial structured clinical assessment include:

Episodic symptoms

More than one of the symptoms of wheeze, breathlessness, chest tightness and cough occurring in episodes with periods of no (or minimal) symptoms between episodes. Note that this excludes cough as an isolated symptom in children. For example:

- a documented history of acute attacks of wheeze, with symptomatic and objective improvement with treatment
- recurrent intermittent episodes of symptoms triggered by allergen exposure as well as viral infections and exacerbated by exercise and cold air, and emotion or laughter in children
- in adults, symptoms triggered by taking non-steroidal anti-inflammatory medication or beta blockers.

An historical record of significantly lower FEV_1 or PEF during symptomatic episodes compared to asymptomatic periods provides objective confirmation of obstructive nature of the episodic symptoms.

Wheeze confirmed by a healthcare professional on auscultation

- It is important to distinguish wheezing from other respiratory noises, such as stridor or rattly breathing.
- Repeatedly normal examination of chest when symptomatic reduces the probability of asthma.

Evidence of diurnal variability

Symptoms which are worse at night or in the early morning.

Atopic history

Personal history of an atopic disorder (ie, eczema or allergic rhinitis) or a family history of asthma and/or atopic disorders, potentially corroborated by a previous record of raised allergen-specific IgE levels, positive skin-prick tests to aeroallergens or blood eosinophilia.

Absence of symptoms, signs or clinical history to suggest alternative diagnoses (including but not limited to COPD, dysfunctional breathing, obesity).

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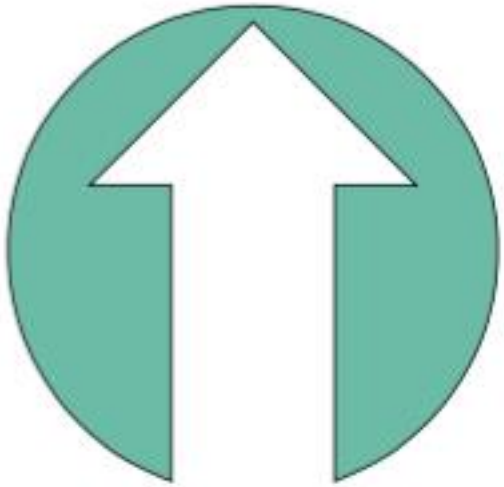
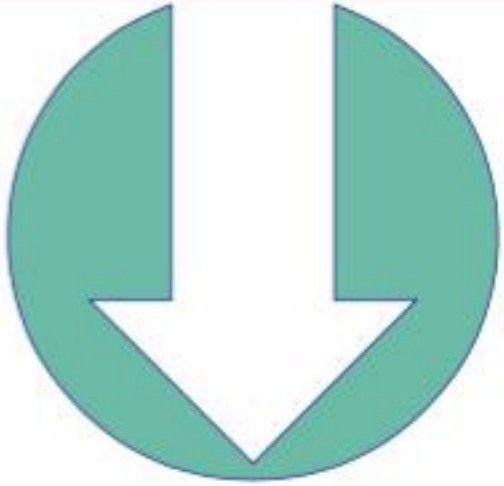
CLINICAL FEATURES THAT INCREASE THE PROBABILITY OF ASTHMA

- More than one of the following symptoms: wheeze, breathlessness, chest tightness and cough, particularly if:
  - symptoms worse at night and in the early morning
  - symptoms in response to exercise, allergen exposure and cold air
  - symptoms after taking aspirin or beta blockers
- History of atopic disorder
- Family history of asthma and/or atopic disorder
- Widespread wheeze heard on auscultation of the chest
- Otherwise unexplained low FEV_1 or PEF (historical or serial readings)
- Otherwise unexplained peripheral blood eosinophilia



CLINICAL FEATURES THAT LOWER THE PROBABILITY OF ASTHMA

- Prominent dizziness, light-headedness, peripheral tingling
- Chronic productive cough in the absence of wheeze or breathlessness
- Repeatedly normal physical examination of chest when symptomatic
- Voice disturbance
- Symptoms with colds only
- Significant smoking history (ie > 20 pack-years)
- Cardiac disease
- Normal PEF or spirometry when symptomatic*



Differential Diagnosis

Other Illness with wheezing / SOB

- COPD (Smoker)
- Heart failure
- Airway obstruction (Tumors, FB)
- Vocal cord dysfunction

May Coexist and complicate Dx of asthma

- GERD, OSA, ABPA

Examination

Examination

- **Upper respiratory tract** (nasal secretion, mucosal swelling, nasal polyp)
- **Chest** (**Wheezing** or prolonged phase of forced exhalation, Chest hyper-expansion, accessory muscles)
- **Skin** (atopic dermatitis, eczema)

Wheezing

- **Wheezing**—high-pitched whistling sounds when breathing out
- A lack of wheezing and a normal chest examination do not exclude asthma

Wheeze

Investigations

Tests

- **Spirometry** – Routine

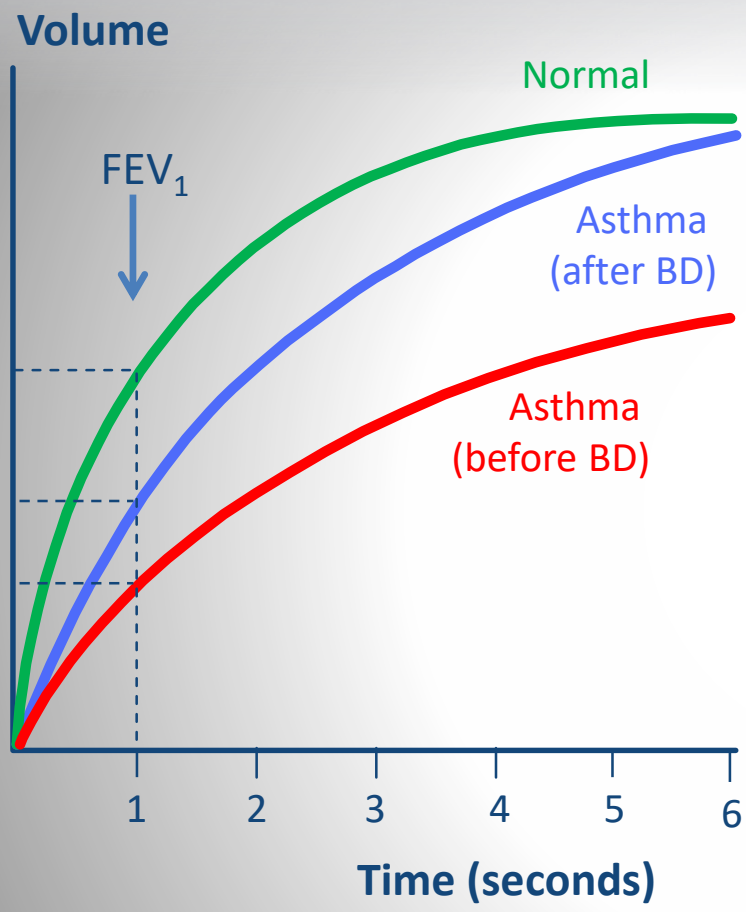
Usually if alternate Dx considered

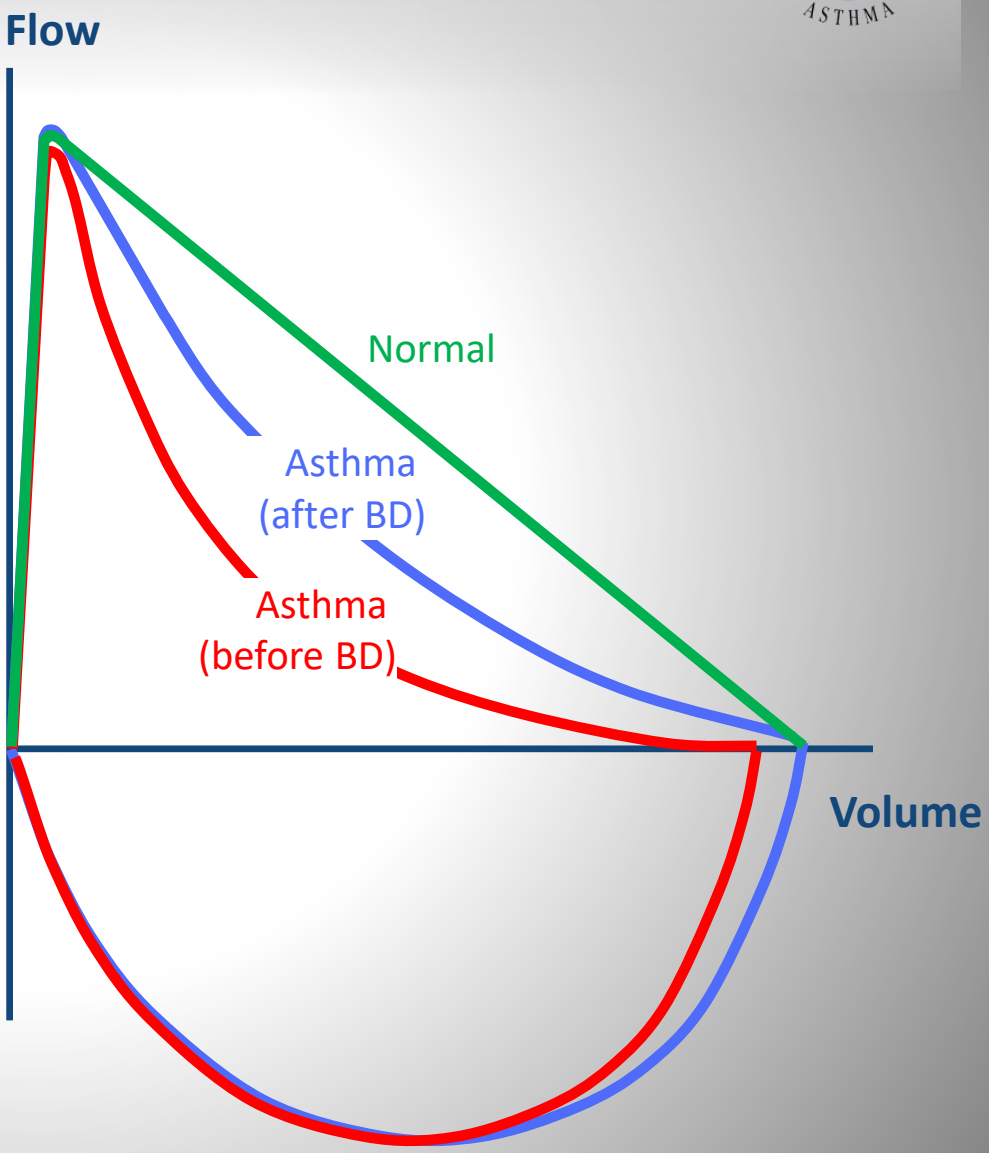
- Full Lung Functions
- CXR / CT Chest
- FBC
- Airway Hyper-responsiveness tests (If spiro normal)

Asthma Dx – variable airflow limitation

- **Confirm presence of airflow limitation**
  - Document that FEV_1/FVC is reduced <0.75 (at least once)
- **Confirm variation in lung function or Reversibility**
  - Excessive bronchodilator reversibility (FEV_1 >12% and >200mL)
  - Excessive diurnal variability twice-daily PEF monitoring

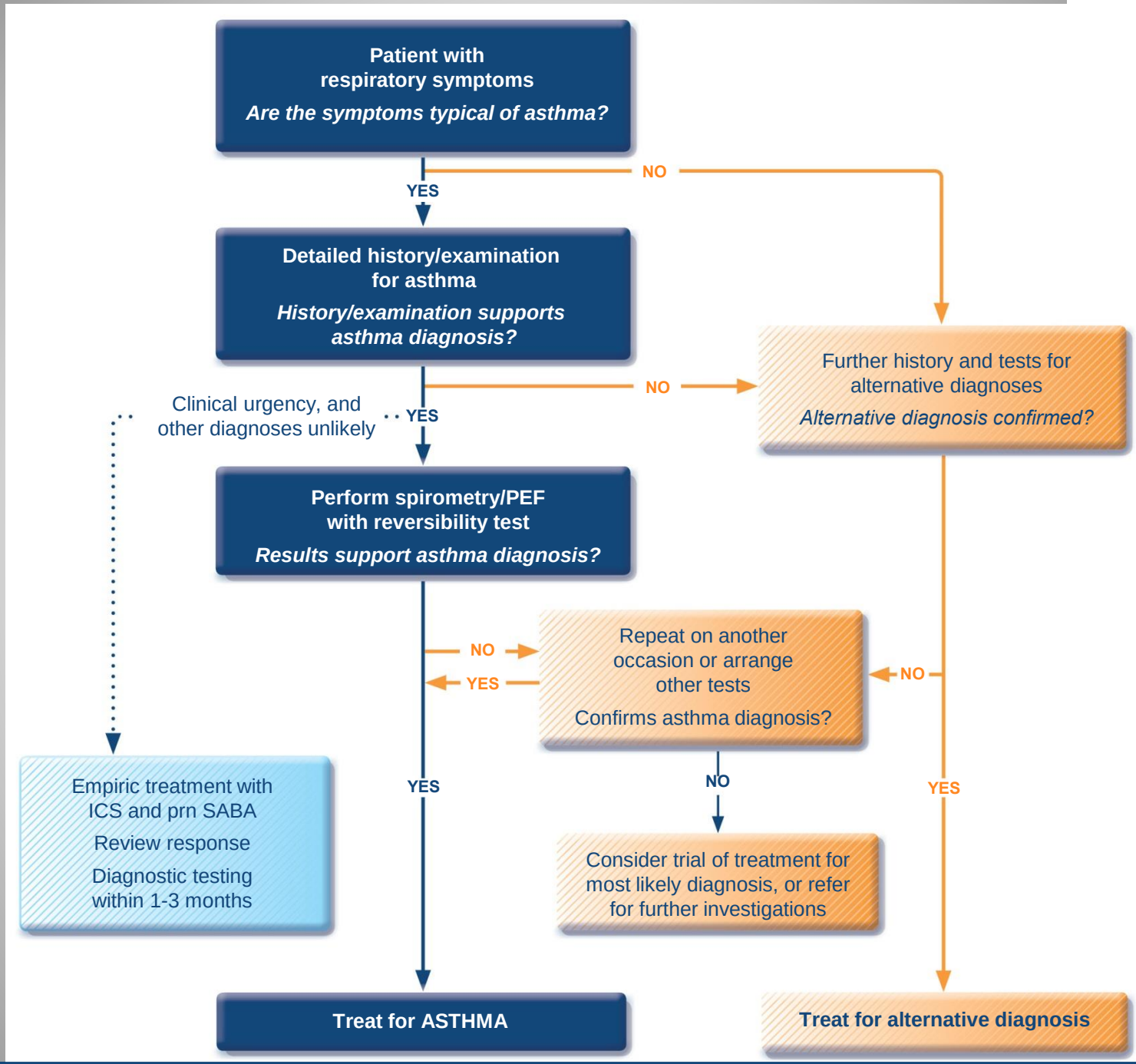
Typical spirometric tracings





Note: Each FEV_1 represents the highest of three reproducible measurements

Diagnostic Approach



Management

Components of Asthma Management

- Monitoring
- Education
- Control of environmental factors
- Pharmacologic Rx

Monitoring

- Symptoms
- Peak Flow (Home)
- Spirometry (Clinic)
- Novel FENO and Sputum eosinophils

- Assess **Severity and Control** of asthma

Education

- Compliance
- Inhalers techniques
- Asthma Action plans

Specific directions for daily management and for adjusting medications in response to increasing symptoms or decreasing PEFR

Environmental Factors

- **Triggers** (Aeroallergens, Irritants)
- **Co-morbid conditions** (Obesity, GERD, Rhinitis, ABPA, VCD, stress)
- **Medications** (Aspirin, Beta Blockers)
- **Infections** (Vaccinations)

Pharmacologic Management

Aims

The aim of asthma management is control of the disease. Complete control is defined as:

- no daytime symptoms
- no night time awakening due to asthma
- no need for rescue medication
- no asthma attacks
- no limitations on activity including exercise
- normal lung function (in practical terms FEV_1 and/or PEF >80% predicted or best)
- minimal side effects from medication.

GINA assessment of symptom control

A. Symptom control		Level of asthma symptom control		
In the past 4 weeks, has the patient had:		**Well-controlled**	**Partly controlled**	**Uncontrolled**
• Daytime asthma symptoms more than twice a week?	Yes ❑ No ❑	None of these	1-2 of these	3-4 of these
• Any night waking due to asthma?	Yes ❑ No ❑			
• Reliever needed for symptoms* more than twice a week?	Yes ❑ No ❑			
• Any activity limitation due to asthma?	Yes ❑ No ❑			

*Excludes reliever taken before exercise, because many people take this routinely

Assessment of risk factors for poor asthma outcomes

Independent* risk factors for exacerbations include:

- Ever intubated for asthma
- Uncontrolled asthma symptoms
- Having ≥1 exacerbation in last 12 months
- Low FEV_1 (measure lung function at start of treatment, at 3-6 months to assess personal best, and periodically thereafter)
- Incorrect inhaler technique and/or poor adherence
- Smoking
- Elevated FeNO in adults with allergic asthma
- Obesity, pregnancy, blood eosinophilia

UPDATED 2017

* Independent of the level of symptom control

Approach

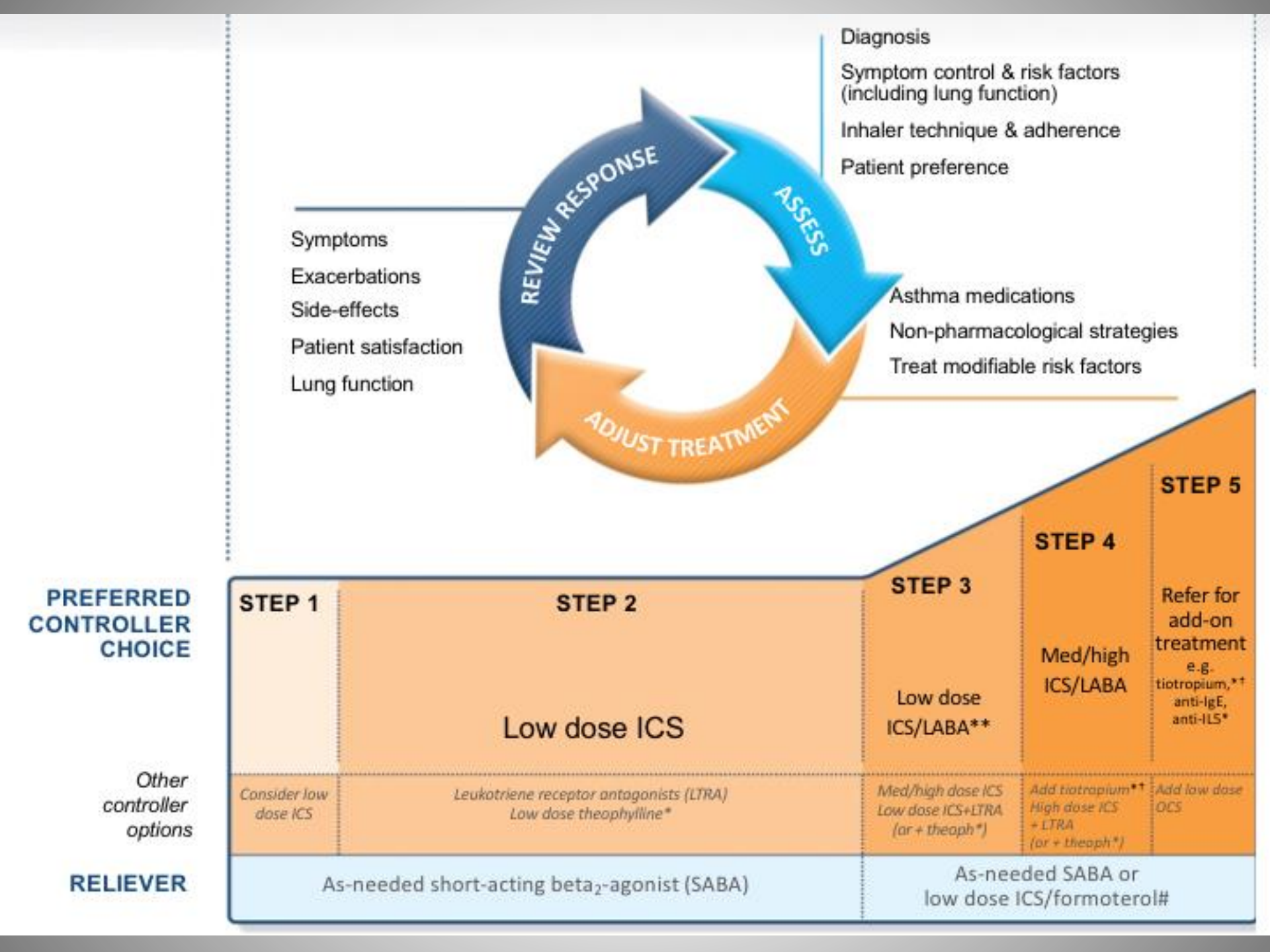
APPROACH TO MANAGEMENT

1. Start treatment at the level most appropriate to initial severity.
2. Achieve early control.
3. Maintain control by:
   - increasing treatment as necessary
   - decreasing treatment when control is good.

✓ Before initiating a new drug therapy practitioners should check adherence with existing therapies, check inhaler technique and eliminate trigger factors.

Pharmacologic Treatment

- **Relievers**
  - Short Acting Beta agonist
- **Preventer**
  - **Steroids**
  - Long acting Beta Agonist and LAMA
  - Leukotriene's receptors Antagonist
  - Theophylline
- **Personalized Medicine**
  - eg Anti IgE or Anti IL5


Diagnosis
Symptom control & risk factors (including lung function)
Inhaler technique & adherence
Patient preference
ASSESS
Asthma medications
Non-pharmacological strategies
Treat modifiable risk factors
ADJUST TREATMENT
Symptoms
Exacerbations
Side-effects
Patient satisfaction
Lung function
REVIEW RESPONSE
PREFERRED CONTROLLER CHOICE
STEP 1
STEP 2
Low dose ICS
STEP 3
Low dose ICS/LABA**
STEP 4
Med/high ICS/LABA
STEP 5
Refer for add-on treatment e.g. tiotropium,*† anti-IgE, anti-IL5*
Other controller options
Consider low dose ICS
Leukotriene receptor antagonists (LTRA)
Low dose theophylline*
Med/high dose ICS
Low dose ICS+LTRA
(or + theoph*)
Add tiotropium*†
High dose ICS + LTRA
(or + theoph*)
Add low dose OCS
RELIEVER
As-needed short-acting beta2-agonist (SABA)
As-needed SABA or low dose ICS/formoterol#

- Provide guided self-management education (self-monitoring + written action plan + regular review)
- Treat modifiable risk factors and comorbidities, e.g. smoking, obesity, anxiety
- Advise about non-pharmacological therapies and strategies, e.g. physical activity, weight loss, avoidance of sensitizers where appropriate
- Consider stepping up if … uncontrolled symptoms, exacerbations or risks, but check diagnosis, inhaler technique and adherence first
- Consider adding SLIT in adult HDM-sensitive patients with allergic rhinitis who have exacerbations despite ICS treatment, provided FEV1 is >70% predicted
- Consider stepping down if … symptoms controlled for 3 months + low risk for exacerbations. Ceasing ICS is not advised.

Asthma Self Management

- Communicate and educate patient

- A **written asthma action plan** includes all the information you need to look after your asthma well, so you'll have fewer symptoms and significantly cut your risk of an asthma attack.

Every day asthma care:

My personal best peak flow is: ____

My preventer inhaler
(insert name/colour): ____

I need to take my preventer inhaler every day even when I feel well

I take ____ puff(s) in the morning
and ____ puff(s) at night.

My reliever inhaler
(insert name/colour): ____

I take my reliever inhaler only if I need to

I take ____ puff(s) of my reliever inhaler if any of these things happen:

- I'm wheezing
- My chest feels tight
- I'm finding it hard to breathe
- I'm coughing.

Other medicines I take for my asthma every day:

With this daily routine I should expect/aim to have no symptoms. If I haven't had any symptoms or needed my reliever inhaler for at least 12 weeks, ask my GP or asthma nurse to review my medicines in case they can reduce the dose.

People with allergies need to be extra careful as attacks can be more severe.

When I feel worse:

- **My symptoms are coming back (wheeze, tightness in my chest, feeling breathless, cough)**
- **I am waking up at night**
- **My symptoms are interfering with my usual day-to-day activities (eg at work, exercising)**
- **I am using my reliever inhaler ____ times a week or more**
- **My peak flow drops to below ____**

This is what I can do straight away to get on top of my asthma:

1 **If I haven't been using my preventer inhaler, start using it regularly again or:**

Increase my preventer inhaler dose to ____ **puffs** ____ **times a day until my symptoms have gone and my peak flow is back to normal**

Take my reliever inhaler as needed (up to ____ puffs every four hours)

If I don't improve within 48 hours make an urgent appointment to see my GP or asthma nurse.

2 **If I have been given prednisolone tablets (steroid tablets) to keep at home:**

Take ____ mg of prednisolone tablets (which is ____ x 5mg) **immediately** and again every morning for ____ days or until I am fully better.

URGENT! Call my GP or asthma nurse today and let them know I have started taking steroids and make an appointment to be seen within 24 hours.

In an asthma attack:

- **My reliever inhaler is not helping or I need it more than every ____ hours**
- **I find it difficult to walk or talk**
- **I find it difficult to breathe**
- **I'm wheezing a lot or I have a very tight chest or I'm coughing a lot**
- **My peak flow is below ____**

THIS IS AN EMERGENCY TAKE ACTION NOW

1. Sit up straight – don't lie down. Try to keep calm
2. Take one puff of my reliever inhaler every 30 to 60 seconds up to a maximum of 10 puffs
3. A) If I feel worse at any point while I'm using my inhaler
   B) If I don't feel any better after 10 puffs
   C) If I feel better: make an urgent same-day appointment with my GP or asthma nurse to get advice

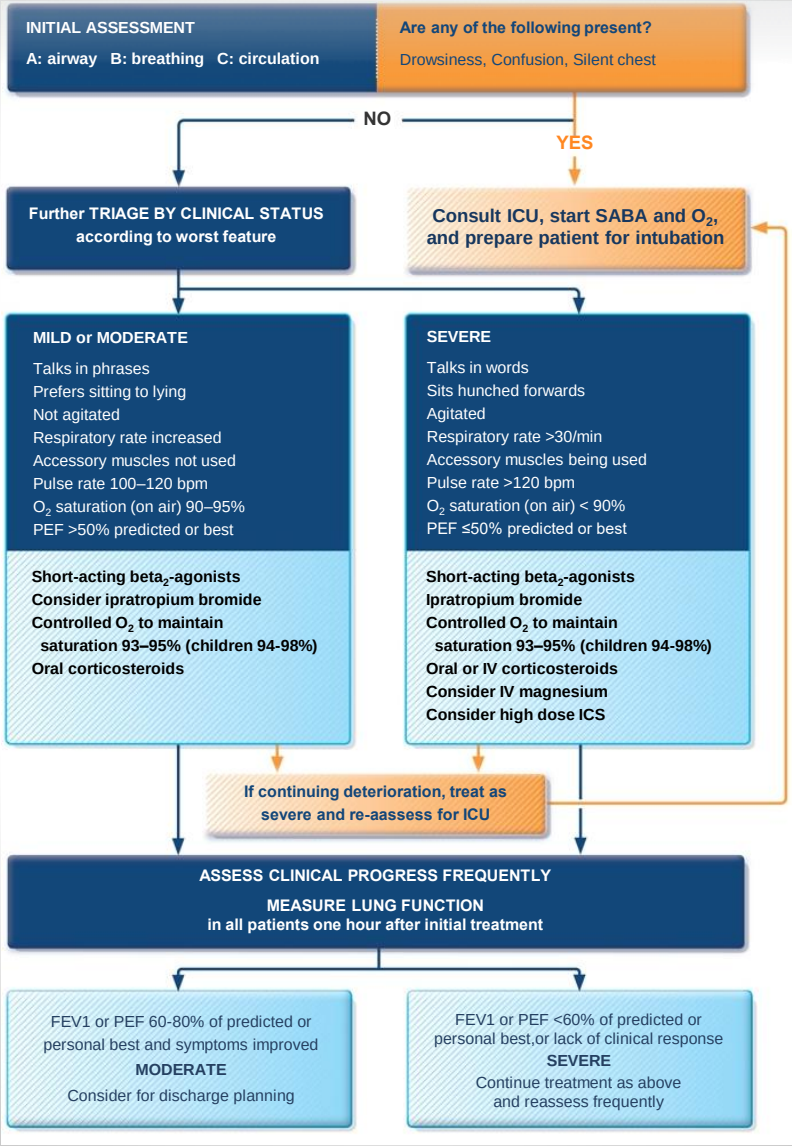
CALL 999

Ambulance taking longer than 15 minutes?
Repeat step 2

If I feel better, and have made my urgent same-day appointment:
- Check if I've been given rescue prednisolone tablets
- If I have these I should take them as prescribed by my doctor or asthma nurse

IMPORTANT! This asthma attack information is not designed for people who use the Symbicort® SMART regime OR Fostair® MART regime. If you use one of these speak to your GP or asthma nurse to get the correct asthma attack information.

Managing exacerbations in acute care settings



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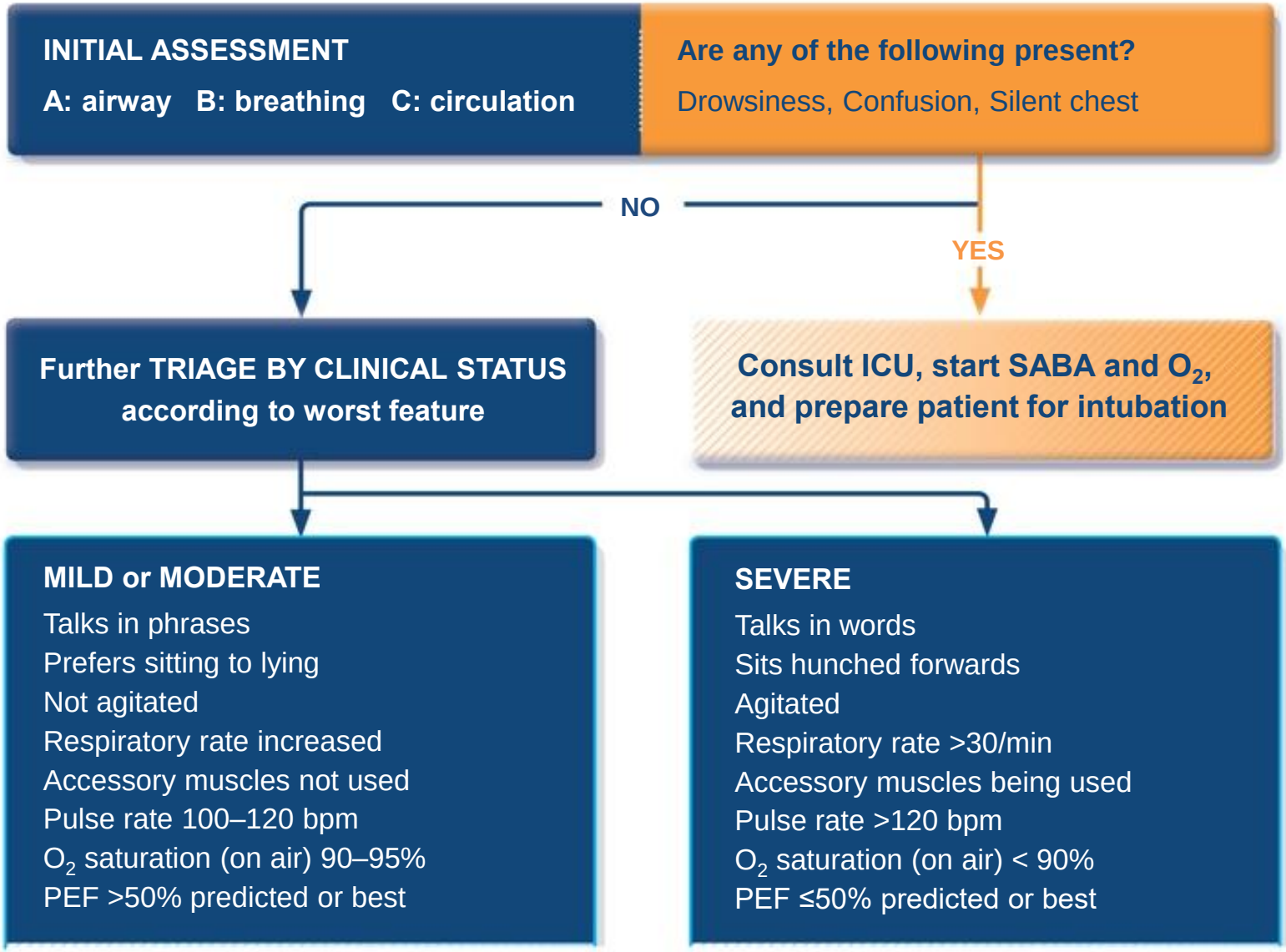


MILD or MODERATE

Talks in phrases
Prefers sitting to lying
Not agitated
Respiratory rate increased
Accessory muscles not used
Pulse rate 100–120 bpm
O_2 saturation (on air) 90–95%
PEF >50% predicted or best

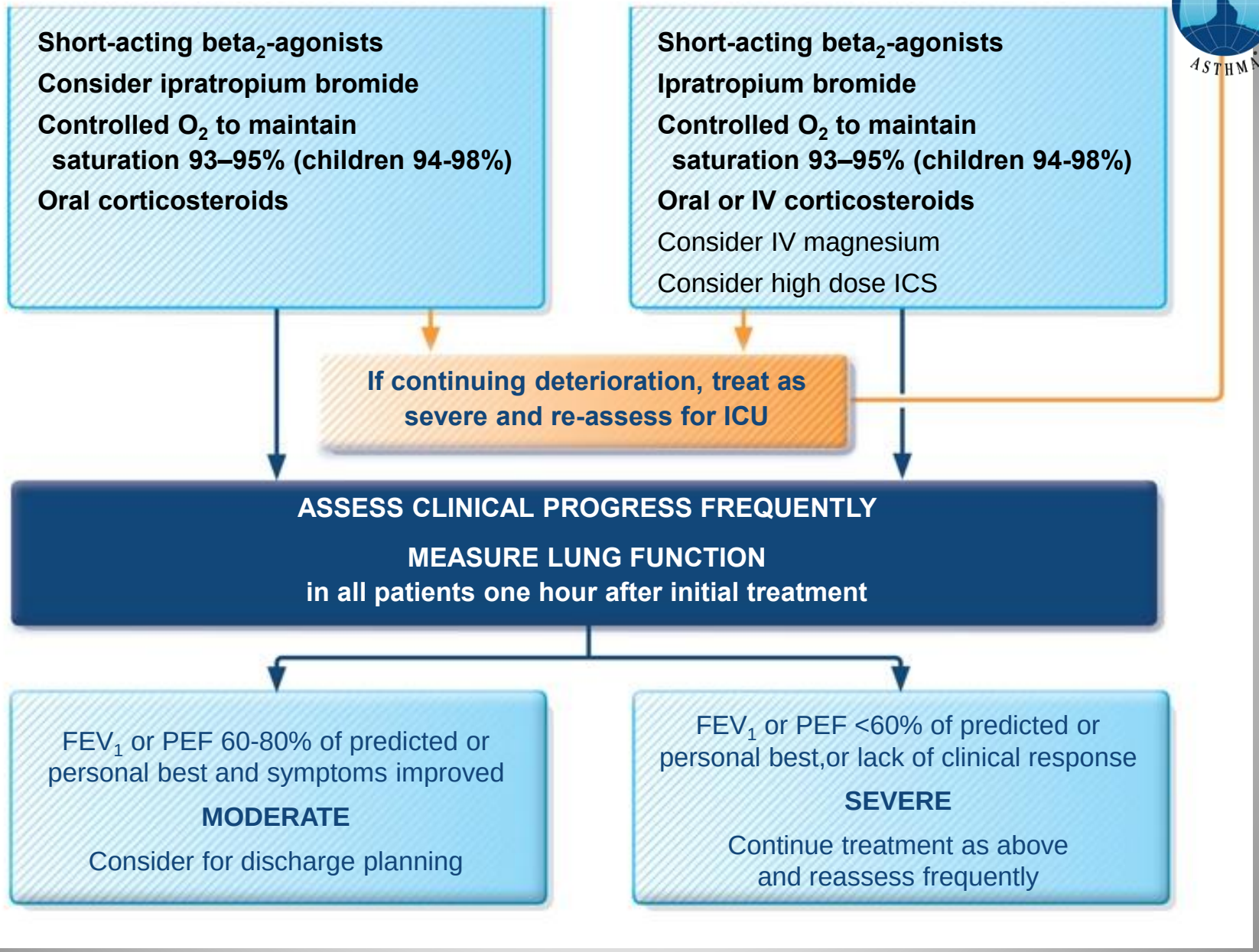
Short-acting beta$_2$-agonists
Consider ipratropium bromide
Controlled O_2 to maintain saturation 93–95% (children 94-98%)
Oral corticosteroids

SEVERE

Talks in words
Sits hunched forwards
Agitated
Respiratory rate >30/min
Accessory muscles being used
Pulse rate >120 bpm
O_2 saturation (on air) < 90%
PEF ≤50% predicted or best

Short-acting beta$_2$-agonists
Ipratropium bromide
Controlled O_2 to maintain saturation 93–95% (children 94-98%)
Oral or IV corticosteroids
Consider IV magnesium
Consider high dose ICS

GINA 2017, Box 4-4 (3/4)



Key Messages

Asthma is a chronic inflammatory condition associated with significant morbidity and mortality which is preventable and manageable with appropriate treatment and effective patient communication

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References

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