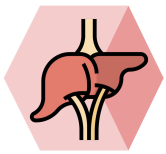
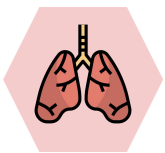
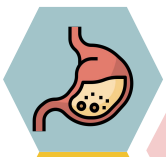
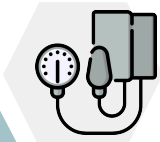
Medicine TEAM 437

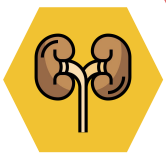
MED437 KING SAUD UNIVERSITY

Bronchial Asthma






Objectives :

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

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Resources :

- Doctor ‘s slides

Basic definition and epidemiology

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.
(Treatment targets eosinophils and T lymphocytes)

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** (Wheezing) (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

Most costs of asthma come from acute exacerbations.
A good history is key to diagnosing asthma

Saudi Arabia Figures

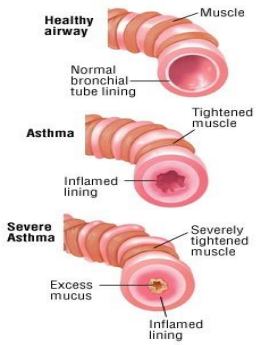
- Asthma affects >2 million Saudis
  May be up to 6 million (20% of population) a lot of them are undiagnosed
- Asthma control:
  - 5% were controlled,
  - 31% partially controlled,
  - 64% uncontrolled.

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.

What is asthma ?

- Tightening of Airways
- Airway Remodeling
- Thick Mucus Production
- Acute and Chronic Phases
  - Wheezing
  - Coughing
  - Shortness of Breath



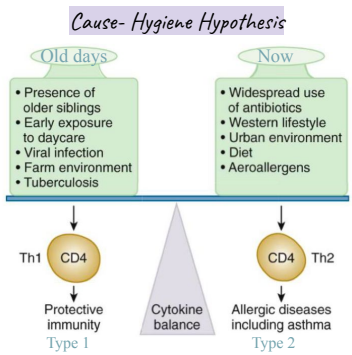
For years our concept of asthma was focused on relaxing bronchial smooth muscle (relieving airway obstruction) without dealing with the inflammation. This changed in last year!!

The outer diameter of airways remains the same, it's the diameter of the lumen inside that is severely narrowed

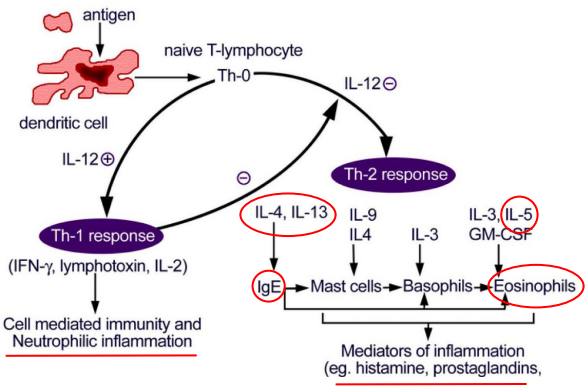
What causes Asthma ?

1. Hygiene Hypothesis
2. Atopy
3. Genetics
4. Smoking – controversial
5. Obesity – New under Investigations
   The relationship between obesity and asthma is not clear, although losing weight in obese asthmatics tends to improve their symptoms.

Th1 (Type 1) will give you the protective immunity while Th2 (Type 2) is responsible for the inflammation in asthma. Caused by an imbalance in cytokines.



Pathogenesis of Asthma



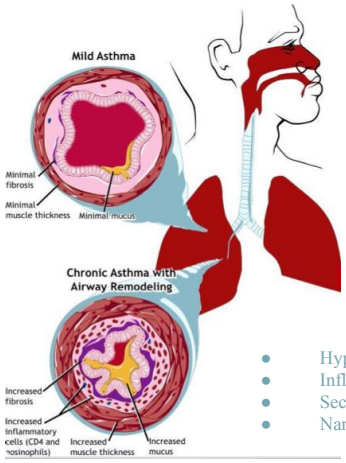
- Most abundant inflammatory cells are T lymphocytes and eosinophils.
- IL-5 produced by Th2 cells is important for eosinophils maturation in bone marrow and migration to the inflammation site.
- Remember that in asthma there is ongoing inflammation, not just bronchospasm.

Th1 and Th2 pathways explanation:

In a genetically susceptible person, an allergen entering the body will be picked by a dendritic cell and initiating the Th2 response and starting the inflammation. Th2 releases IL-4 to increase and activate IgE, which in return activates mast cells to release histamine hat cause bronchoconstriction. Also IL-5 is released to bring eosinophilia, another important mediator of inflammation.

The degree to which the Th2 response is activated is affected by the Th1 response, which tends to suppress it (protective immunity). In Asthmatics, this is lost or is very low.

Extra

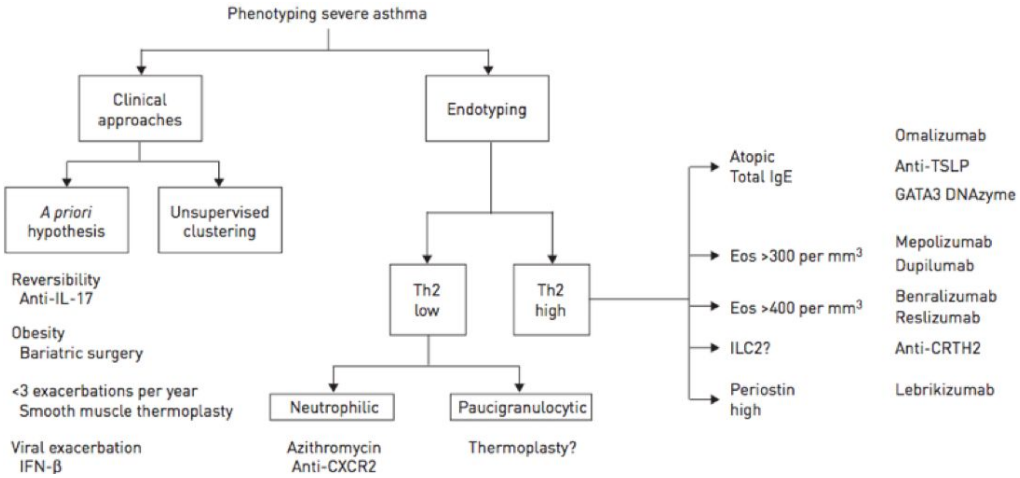


The idea is the asthma is not a disease of muscle, but inflammation going on in tha airways, this has changed the way we treat the asthma.

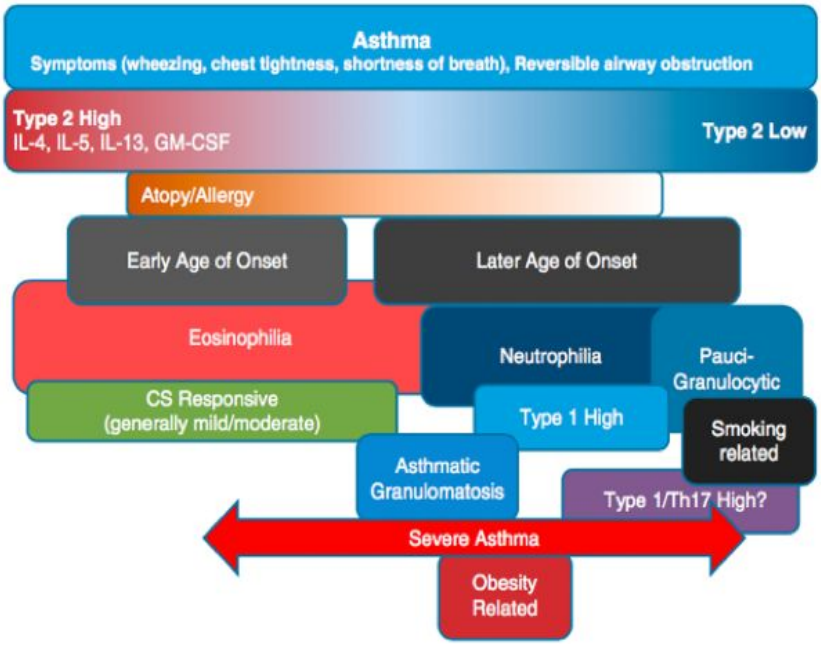
- Hypertrophy of Smooth Muscle
- Inflammation
- Secretions
- Narrowing of airways

Initially, there is minimal fibrosis and minimal secretions and no muscle hypertrophy, so no bronchoconstriction. But as the inflammation goes on and becomes a chronic process, this leads to to increased fibrosis, hyperplasia of mucous cells and smooth muscle cells, leading to hypersecretion and an increase in muscle thickness, which increases the obstruction of the airways.

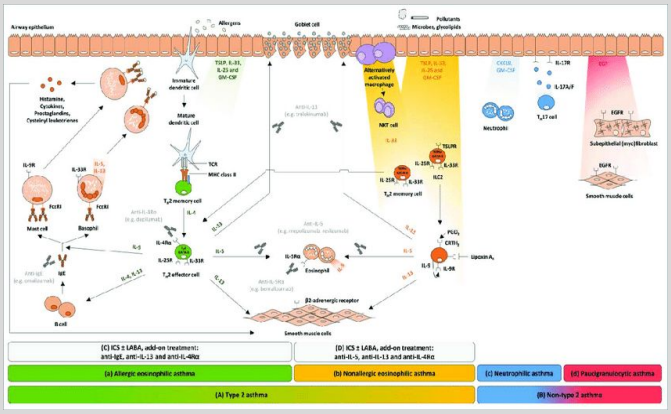
Types of Asthma

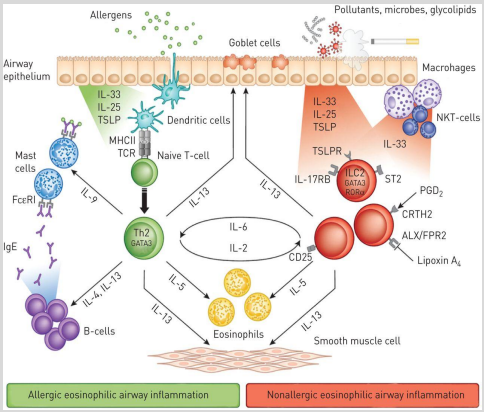


- Phenotyping means classifying asthmatics based on the characteristics you can observe by looking and taking history, young or old, history of allergies, smoker or not, obese or thin…
- While endotyping means the things you can measure by doing tests, biochemicals, genetics, etc..
- In classifying asthma, we focus more on endotyping because this will allow us to use specific treatments. For example, Anti IgE: Omalizumab, is used for atopic asthma. And Anti IL-5: Mepolizumab, is used for eosinophilic asthma.
- Remember that eosinophilic asthma (high eos) could be allergic "atopic", which means having high IgE, and it also could be non-allergic.
- Another thing we can measure in endotyping is exhaled nitric oxide from breath, which is a marker of eosinophilic inflammation. High levels of exhaled NO predicts an upcoming exacerbation even if symptoms are not present yet.



For your information





Asthma Types

Early onset (<12years)

- **Childhood-onset asthma** a relatively homogeneous group
- Allergic Asthma (Atopic) Usually a strong allergic Hx
- Family history 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

Important

History

History is **very important,** 80% of the times we can diagnose asthma from history alone.
Symptoms are very important in diagnosing asthma and for exam :)

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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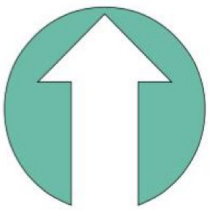
If all 4 of these symptoms (highlighted in table) are present, you are almost 100% sure of asthma diagnosis. As long as there is nothing in the history or clinical findings that would suggest an alternative diagnosis

These clinical features are important. Avoid misdiagnosing asthma

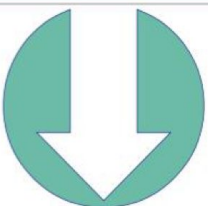
CLINICAL FEATURES THAT INCREASE THE PROBABILITY OF ASTHMA

- More than one of the following symptoms: wheeze, breathlessness, chest tightness and cough, particularly if:
  - symptoms worse at night and in the early morning (Due to chronological rhythm of smooth muscles)
  - 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*



It is **very important** to know the clinical features that **increase** the probability of asthma.

Remember the circadian levels of cortisol? Cortisol is anti-inflammatory and its levels rise in the morning but become low at night and that's why symptoms are worse at night. By early morning we mean 12AM.

Cold air triggers symptoms because it dries the airways and this induces bronchoconstriction.
Even selective beta blockers may induce symptoms because their selectivity is actually relative, also watch out for beta blockers that are used as eye drops for glaucoma, they may trigger the symptom too.

Also know the features that **decrease** the probability of asthma.

Differential Diagnosis

Other Illness with wheezing / SOB

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

In airway obstruction due to tumors or foreign bodies a monophonic wheeze is heard on auscultation as the is usually on obstruction of one airway. In asthma however, the wheeze is polyphonic as there are many small airways being obstructed.

May Coexist and complicate Dx of asthma

- GERD, OSA(obstructive sleep apnea), ABPA (allergic bronchopulmonary aspergillosis)

Some people are obese and when they exercise they get breathless because they are unfit, that is not asthma because their breathlessness will be relieved by rest.

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** high-pitched whistling sounds when breathing out
  - A lack of wheezing and a normal chest examination do not exclude asthma because it's episodic, when they are well you will not hear the wheezing.

Also in someone having an acute exacerbation of asthma, he will have a silent chest and no wheezing because not much air will be moving in and out of the lungs.

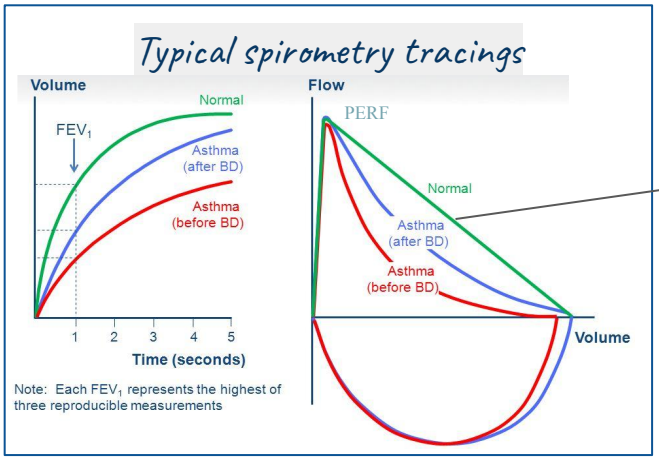
Tests

- **Spirometry** – Routine used for confirmation
- **Usually if alternate Dx considered**
  - Full Lung Functions
  - CXR / CT Chest
  - FBC full blood count / CBC
  - Airway Hyper-responsiveness tests (If spiro normal) also known as bronchial provocation test. It is where the patient is given a certain chemical to inhale (eg. histamine, methyl chlorine, mannitol) ad different doses. If the patients airways go into constriction (bronchospasm) as low doses, this suggests asthma.

Asthma Dx – variable airflow limitation

- **Confirm presence of airflow limitation**
  - Document that FEV1/FVC is reduced <0.75 (at least once)

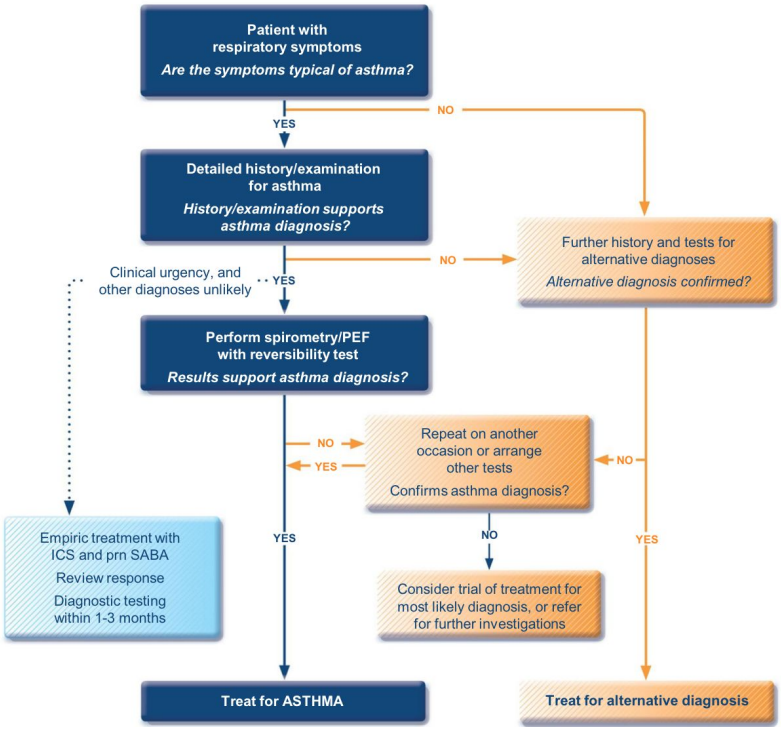
- **Confirm variation in lung function or Reversibility**
  - Excessive bronchodilator reversibility (FEV1>12% and >200mL) need both values to be significant
  - Excessive diurnal variability twice-daily PEF monitoring



If this straight green line is concave, it indicates airway narrowing

Diagnostic approach

Asthma is a very common condition, in today's lecture we will focus on the new **changes in the management of asthma** (**very important**).



Management

Components of Asthma Management:

1 Monitoring

- Symptoms
- Peak Flow (Home)
- Spirometry (Clinic)
- Novel FENO* and Sputum eosinophils
- Assess Severity and Control of asthma

2 Education

You have to educate the patients on how to use the inhalers, You should also give them plans on what to do when their symptoms gets worse.

- Compliance
- Inhalers techniques
- Asthma Action plans
- *Specific directions for daily management and for adjusting medications in response to increasing symptoms or decreasing PEFR*

*If Exhaled Nitric oxide (FENO) levels are high this indicates that there is a lot of inflammation going on in the lungs.
A raised FENO in asymptomatic patients predicts that they will become symptomatic soon

3 Control of environmental factors

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

The most important measure to prevent the attack is to avoid triggering factors.

4 Pharmacologic Management

Drugs are the last component of management

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.**

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.

GINA assessment of symptom control

A. Asthma 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/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/week?	Yes☐ No☐			
• Any activity limitation due to asthma?	Yes☐ No☐			

RED FLAGS OF ASTHMA

Independent* risk factors for exacerbations include:

- Ever intubated for asthma ICU Admission
- 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

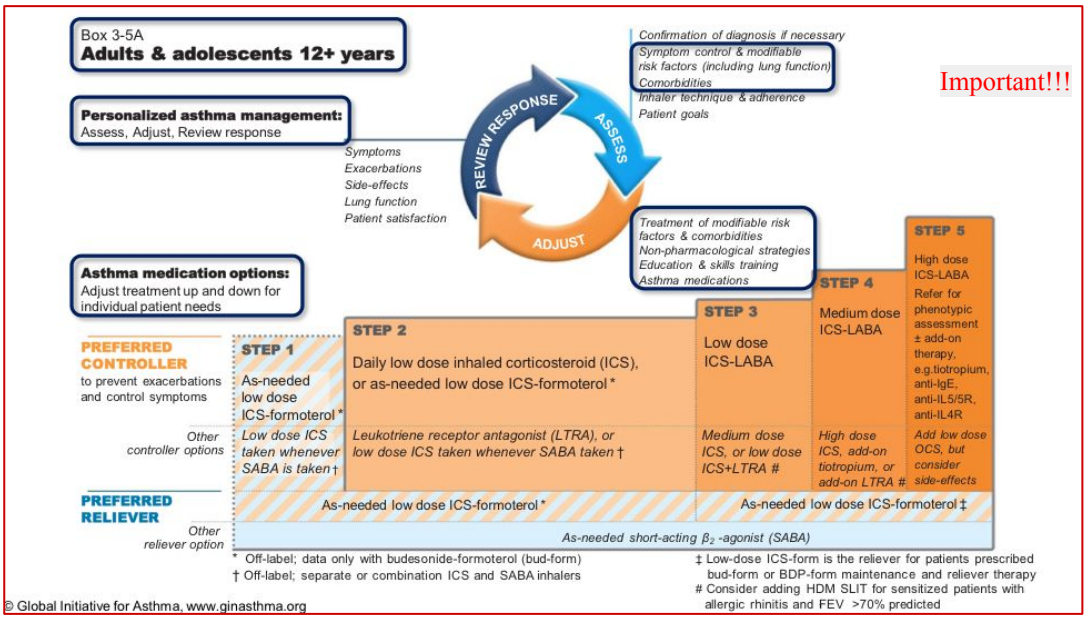
* Independent of the level of symptom control

Pharmacologic Management

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

- 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.



Important!!!

Previously, we focused more on the bronchoconstriction and we forget about the inflammation, so we used to only give SABA in step 1. Now we actually focus more on inflammation and that's why we added an inhaled corticosteroid for step 1 too.
NB: Guidelines have very recently changed. Make sure you know the new guidelines as they will be the ones asked about in the exam. The new guidelines added ICS at every step.

The following summarizes the steps of the new 2018 guidelines:

- **Step 1:** Any time any asthmatic feels the need to use their SABA (blue) inhaler they should also use a low dose ICS at the same time, someone who gets his symptoms twice or less a month.
- **Step 2:** Low dose ICS should be taken regularly. While SABA taken only as needed

An alternative that can be used in Step 1 or Step 2 is a mixture between a low dose ICS (budesonide) and formoterol, called (bud-form). Formoterol is used because it has a rapid onset and a long duration of action. Used **as needed** in either step.

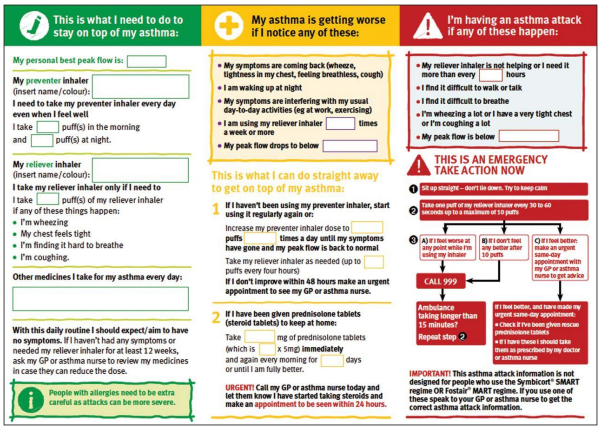
- **Step 3:** Low dose ICS and LABA
- **Step 4:** Medium dose ICS and LABA
- **Step 5:** High dose ICS and LABA (+/- Anti-IgE (Omalizumab), Anti-IL5/5R, Anti-IL4R)

In all steps, a SABA can be used **whenever needed** as a **reliever**.

SABA: Short acting beta2 agonists/
LABA: Long acting beta2 agonists/
ICS: Inhaled corticosteroids

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.



This is what I need to do to stay on top of my asthma:

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.

My asthma is getting worse if I notice any of these:

- 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.

I'm having an asthma attack if any of these happen:

- 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

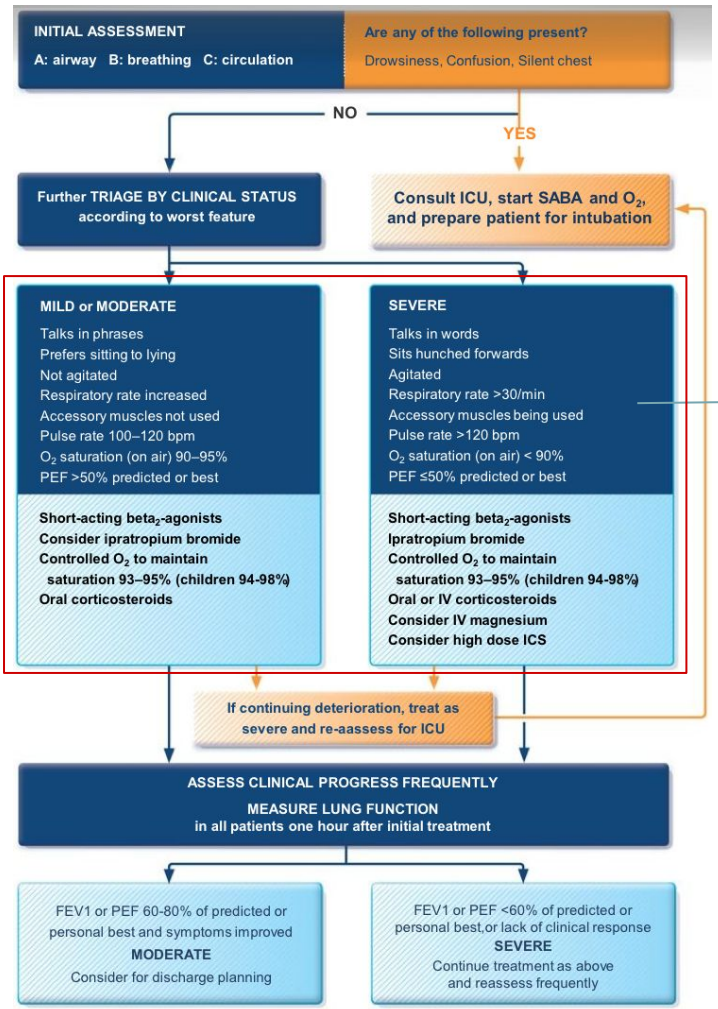
If I feel better, and have made my urgent same-day appointment:

- 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

Important



Any one of these indicates a severe asthma attack (don't need all of them)

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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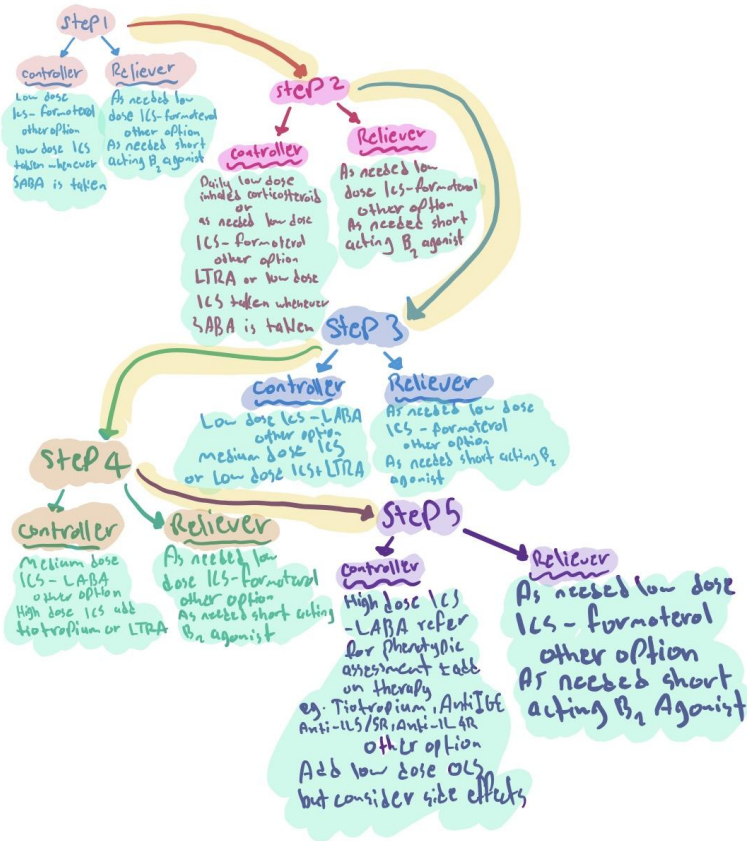
Summary

- **Diagnosis**
  - Episodic Sx
  - Triggered
  - Wheeze
  - Atopic history
- **Management**
  - Monitoring
  - Education
  - Control of environmental factors
  - Pharmacologic
  - Prevention

Clinical features that increase asthma probability	Clinical features that decrease asthma probability
Sx worsen at night and in early morning	Prominent dizziness, light-headedness, peripheral tingling
Sx in response to exercise, allergen exposure and cold air	Chronic productive cough, cough in the absence of wheeze or breathlessness
Sx after taking aspirin or beta blockers	Voice disturbance
Family Hx of asthma/atopic disorder	Sx with colds only
Otherwise unexplained peripheral blood eosinophilia	Cardiac disease
Otherwise unexplained low FEV1 or PEF	Significant Hx of smoking > 20 pack-years

Treatment



Questions

1) In Asthmatic Patient FEV1 is:

A.Increased. B. Normal. C. Reduced

2) A 30-year-old athlete presents to your office complaining of intermittent wheezing. This wheezing
shortly after running. The patient admits to smoking 1 to 2 packs of ciga
rettes per day for 5 years. What finding would be consistent with asthma?

a. Hyperinflation on chest x-ray
b. Improvement in FEV1 after bronchodilator
c. Low oxygen saturation on finger oximetry
d. Decreased FVC on PFT testing
e. Dyspnea on assuming a supine position

3) A 30-year-old athlete with asthma is also a cigarette smoker. Which of the following
is characteristic of asthma but not other obstructive lung disease?

A.Hyperinflation is present on chest x-ray
B. Airway obstruction is reversible
C.Hypoxia occurs as a consequence of ventilation-perfusion mismatch
D.The FEV1/FVC ratio is reduced

4- Which of the following doesn't indicate a poor prognostic finding in asthma?
A. Silent chest
B. Hypercapnia
C. Thoracoabdominal paradox (paradoxical respiration)
D. Pulsus paradoxus of 5 mm Hg
E. Altered mental status

5-Symptoms of asthma are:

A.productive cough
B.chest stabing
C. breatlessness
D. All

6-A 47-year-old man with a history of asthma comes to the emergency d
epartment with several days of increasing shortness of breath, cough, and sputum production. On phys
minute. He has diffuse expiratory wheezing and a prolonged expiratory pha
se.Which of the following would you use as the best indication of the s
everity of his asthma?
a. Respiratory rate
b. Use of accessory muscles
c. Pulse oximetry
d. Pulmonary function testing
e. Pulse rate

1-C 2-B 3-A 4-E 5-C 6-A