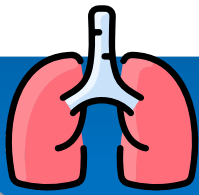




Round : Internal medicine.....

Group no : A4.....

Done By : Batool ALzubaidi.....



ASTHMA

I. PATHOPHYSIOLOGY

II. CAUSES OF ASTHMA EXACERBATIONS

- A. ALLERGENS
- B. VIRAL URTI
- C. DRUGS
- D. EXERCISE IN COLD AIR

III. CLASSIC FINDINGS OF ASTHMA

- A. DYSPNEA
- B. WHEEZING

IV. COMPLICATIONS OF ASTHMA

- A. RESPIRATORY FAILURE
- B. PNEUMOTHORAX

V. DIAGNOSTIC APPROACH TO ASTHMA

- A. WORKUP FOR DYSPNEA SUSPECTED TO BE SECONDARY TO ASTHMA
- B. ASSESS FOR THE PRESENCE OF AN OBSTRUCTIVE LUNG DISEASE LIKE ASTHMA

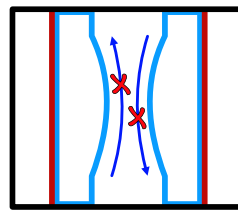
VI. TREATMENT OF ASTHMA

- A. ASSESS THE SEVERITY OF ASTHMA TO GUIDE STEPWISE TREATMENT
- B. ALTERNATIVE ASTHMA THERAPY
- C. MANAGEMENT OF ASTHMA EXACERBATION

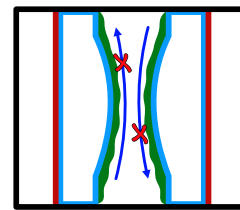
00:38

I. PATHOPHYSIOLOGY

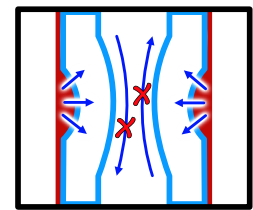
- **↑Eosinophils, ↑Histamines/Leukotrienes within the bronchioles** →
 - ↑Bronchiole wall edema and
 - ↑Bronchoconstriction →
 - Narrowing of the bronchioles →
 - ↑Resistance to airflow exiting lungs →
 - Obstruction of outgoing airflow →
 - Air trapped in alveoli →
 - Dynamic hyperinflation of lungs →
 - Difficulty with breathing** (short inspiration and prolonged expiration)



↑Wall Edema



↑Mucus

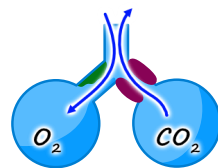


↑Bronchospasm

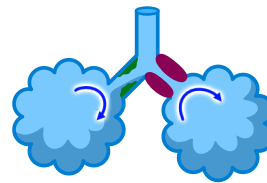
Cross section of bronchus

Bad exchange process

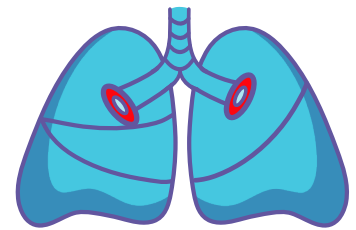
Airway Obstruction



Expiration Worse



Air Trapping



Hyperinflation

Bronchospasm = bronchoconstriction

When muscles within bronchial wall are contracting a lot this narrowing the lumen

Mucus irritates a lot of receptors within the airway precipitating inflammation which causes cough reflex

Wall edema & mucus = narrowing of airflow » 1. Difficulty in getting air in = dyspnea 2. Difficulty in getting air out = wheezing and hyper-resonance



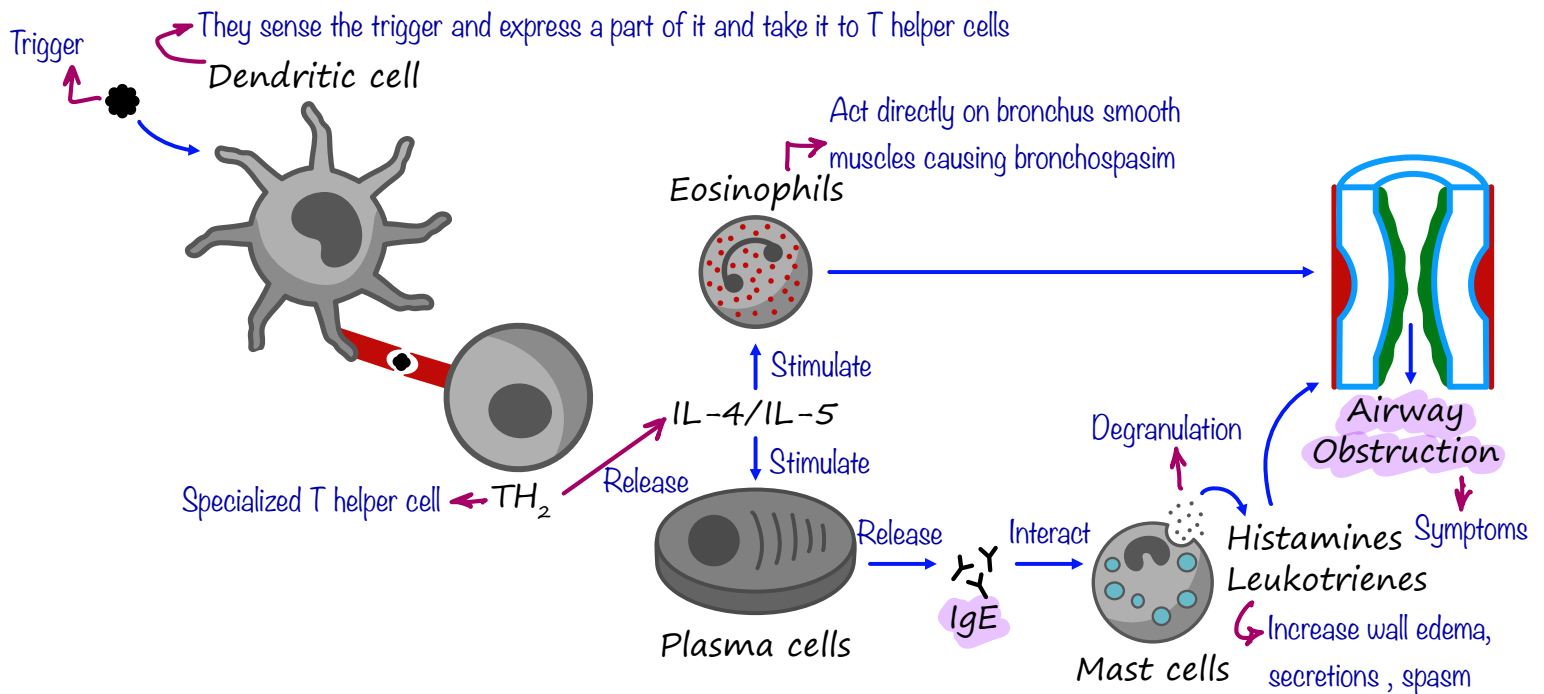
II. CAUSES OF ASTHMA EXACERBATIONS

A. ALLERGENS (E.G. POLLEN, DUST, MOLD, PET DANDER)

- Allergens → Activate **Dendritic Cells** →
Dendritic cells stimulate **TH2 cells** →
TH2 cells release of **IL-4** and **IL-5** →
This leads to stimulation of **Eosinophils** in bronchioles and also stimulates mast cells to release **Histamines** and **Leukotrienes** in bronchioles → **Bronchospasm** and **Bronchial Wall Edema**
- Assess for **Atopic Triad**:
 - Allergic Rhinitis
 - Atopic Dermatitis
 - Allergic Asthma

B. VIRAL URTI (E.G. RHINOVIRUS, INFLUENZA)

- Viruses → Activation of **Dendritic cells** →
Dendritic cells stimulate **TH2 cells** →
TH2 cells release **IL-4** and **IL-5** →
Causes stimulation of **Eosinophils** in bronchioles and stimulates mast cells to release **Histamines** and **Leukotrienes** in bronchioles → **Bronchospasm** and **Bronchial Wall Edema**
- ✦ They occur with or worsened with viral infections



C. DRUGS (E.G. BETA-BLOCKERS, ACE-I, ASPIRIN)

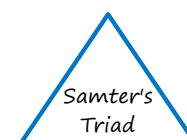
- **Beta-Blockers** → Bind to β₂-receptors on bronchioles →
Block bronchodilation → ↑Bronchoconstriction beyond normal
- **ACE-I** → ↑The production of bradykinin in bronchioles →
↑Bronchoconstriction beyond normal
- **Aspirin** → ↓Cyclo-oxygenase (COX) enzyme activity →
↓Prostaglandin and Thromboxane A₂ formation →
Results in the remaining precursors to be shunted into the Leukotriene pathway → ↑Leukotriene levels →
↑Bronchoconstriction beyond normal
- **Assess for Samter's Triad**:
 - Worsening Nasal Polyps post-aspirin use
 - Worsening Sinusitis post-aspirin use
 - Worsening Asthma post-aspirin use

Causes/Risk Factors:

↳ Allergies*



↳ Aspirin



↳ Beta Blockers

↳ Viral URTI's*

↳ Cold Air/Exercise

D. EXERCISE → ESPECIALLY IN COLD AIR

- **Exercise and Cold Air** → Dries out the airway and directly triggers ↑Bronchoconstriction beyond normal



III. CLASSIC FINDINGS OF ASTHMA

- Asthmatic patients remain **asymptomatic** with **intermittent** asthmatic **attacks or exacerbations**

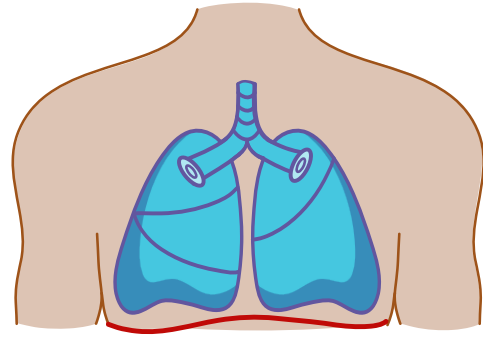
Asthmatic patients usually present with:

A. DYSPNEA

- This occurs due to an obstruction of outgoing airflow →
Air is trapped in the alveoli →
Dynamic hyperinflation of lungs →
Difficulty taking a deep breath

B. WHEEZING

- This occurs due to narrowing of the bronchioles →
↑ Resistance to airflow exiting lungs →
Obstruction of outgoing airflow →
Wheezing sound can be heard **during auscultation**



History: Dyspnea

Physical: Wheezing, Hyper-resonance

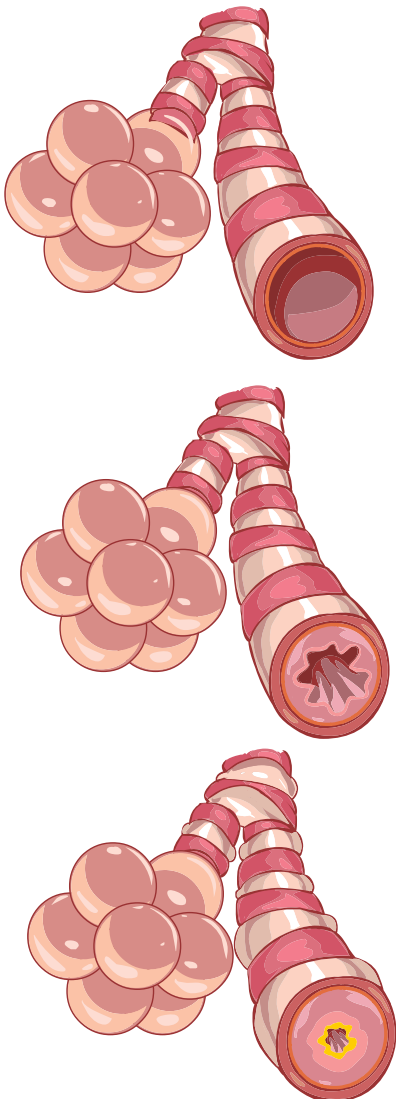
✦ Dyspnea = sensation of short breath

✦ Cough is a common clinical presentation

✦ Diurnal variation = worsening in the evening and early morning

✦ Additional symptoms » shortness of breath, chest tightness

✦ They will have a completely normal respiratory exam when they're symptom free



IV. COMPLICATIONS OF ASTHMA

A. RESPIRATORY FAILURE (E.G. STATUS ASTHMATICUS)

11:28

- **Pathophysiology:** ➔ Getting air out is much more difficult

- Asthma exacerbations triggered by allergens or viral URTI → Lead to **increased bronchiole wall edema** and **bronchoconstriction** → **Narrowing** of bronchioles, increased **resistance** to airflow during exhalation, and subsequent **obstruction** of outgoing air → Consequently, air becomes **trapped** in the alveoli, causing **dynamic lung hyperinflation** → This **impedes the ability to inhale deeply** and leads to **alveolar hypoventilation** → There is a marked **reduction in CO₂ clearance** and a slight **impairment in O₂ diffusion**. In severe cases, this can progress to markedly **elevated pCO₂** and **decreased paO₂** → Resulting in **Hypercapnic and Hypoxic Respiratory Failure** ➔ They will take short inspirations

- **Presentation:**

- Worsening dyspnea which very long expiration
- Tachypnea and ↑ Work of breathing (WOB)
- Severe wheezing or silent chest (suggests no air movement)
- **Pulsus Paradoxus:**
 - In patients with an asthma exacerbation, hyperinflation of the lungs leads to a significant **decrease in intrathoracic pressure during inspiration** → This increased negative pressure allows a **greater volume of blood to enter the RV** during ventricular filling → This results in a **right-to-left shift of the septum**, causing it to bow into the LV, which compromises LV filling → Consequently, there is a noticeable **decrease in SBP during inspiration**, characterized by a **drop of > 10 mmHg in SBP**

- **ABG to Reveal Variable Findings:**

- **Respiratory Alkalosis:**

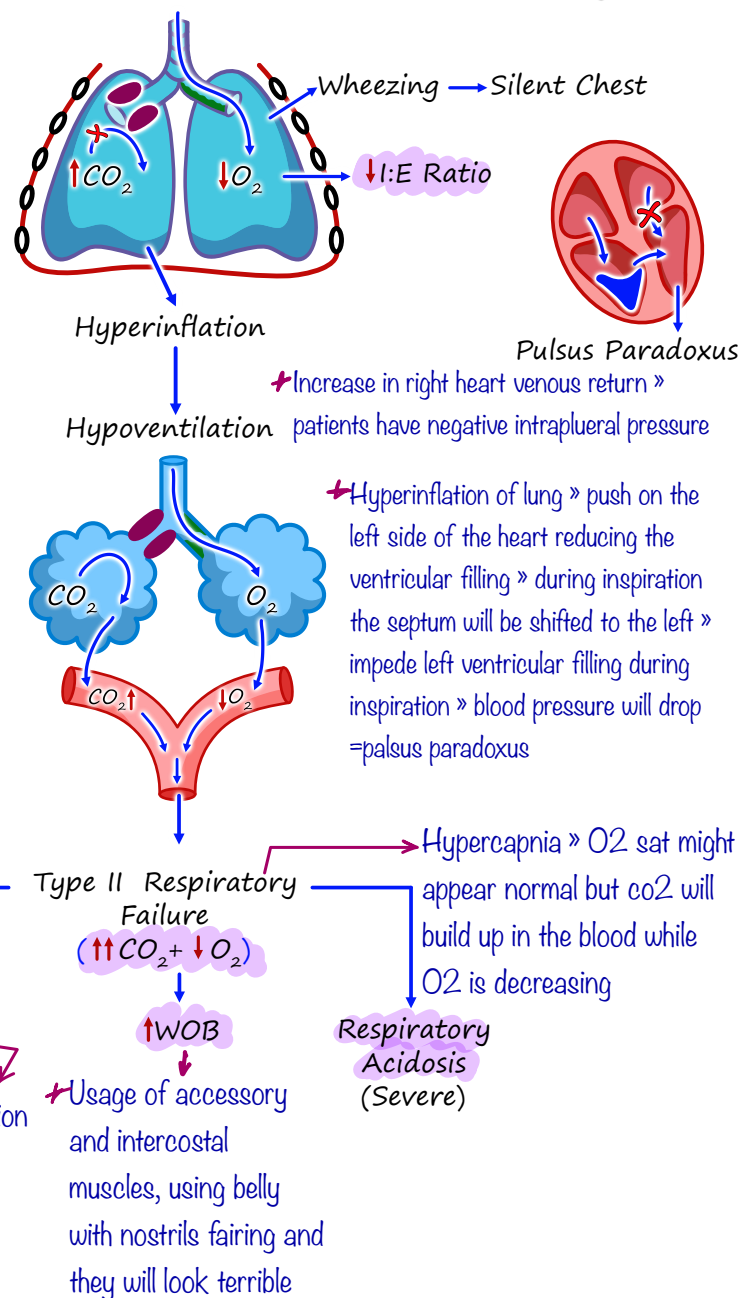
- This indicates a **less severe asthma exacerbation**, as evidenced by **effective CO₂ clearance** resulting in alkalosis → The alkalosis is due to **tachypnea from dynamic hyperinflation**, which enables the patient to expel excess CO₂

- **Normal ABG:**

- This indicates a **moderate asthma exacerbation**: CO₂ clearance is compromised, despite the presence of tachypnea, suggesting increased CO₂ retention → Consequently, there is a **pseudonormal pH**, resulting from the patient's increased respiratory effort to expel CO₂ due to dynamic hyperinflation, and the gradual increase in CO₂ levels caused by airway obstruction and respiratory muscle fatigue

- **Respiratory Acidosis:**

- This indicates a **severe asthma exacerbation** → Despite tachypnea, the patient is **not eliminating CO₂ effectively**. This likely results in **CO₂ trapping**, leading to a **reduced pH** due to **CO₂ retention from airway obstruction and respiratory muscle fatigue**



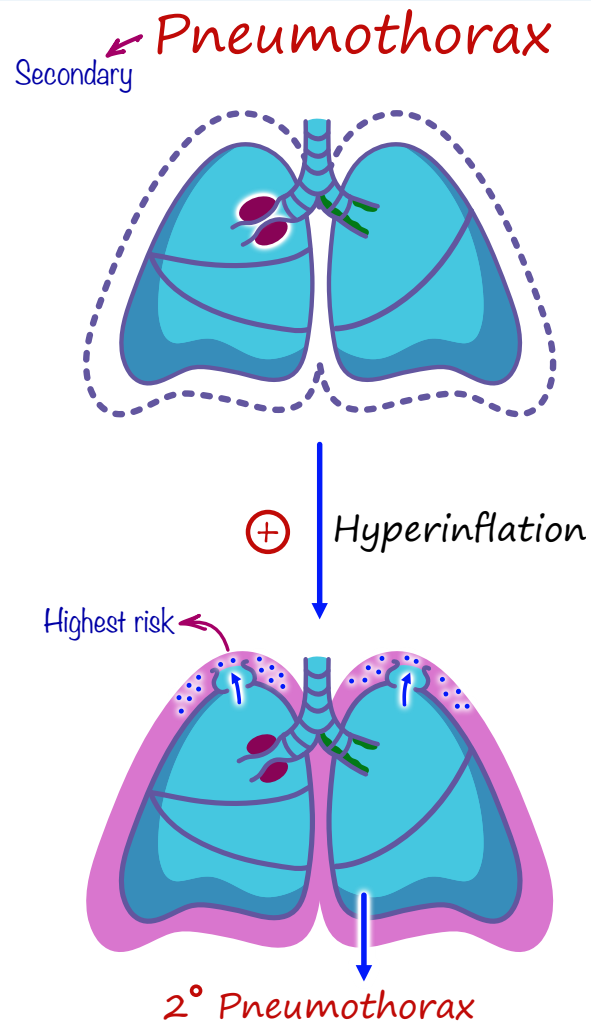
- **Pathophysiology:**

- Obstruction of the outflow of air leads to air becoming trapped within the alveoli → Resulting in dynamic hyperinflation of the lungs → The subsequent increase in intrapulmonary pressure can trigger barotrauma, causing alveolar rupture → Air then leaks into the pleural cavity, raising intrapleural pressure and compressing the lung
 - Alveolar rupture often results from multiple factors → During an asthma exacerbation, the need for mechanical ventilation can lead to abnormally high airway pressures → This, in turn, may cause barotrauma that leads to the rupture of the alveoli

- **Presentation:**

- Pleuritic Chest pain
- ↓ Tactile fremitus
- Hyper-resonance to percussion
- Absent or ↓ Breath sounds on the affected side

✚ Tracheal deviation

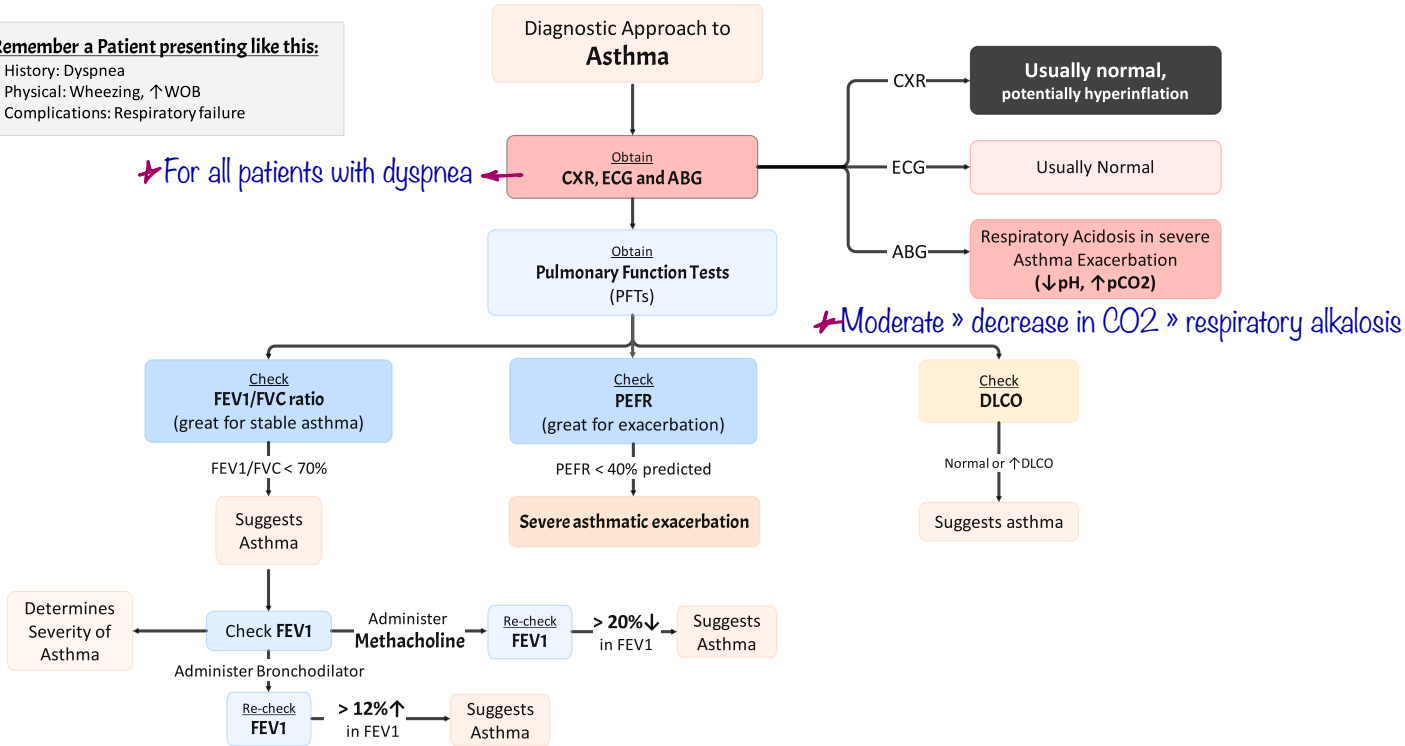


V. DIAGNOSTIC APPROACH TO ASTHMA

Remember a Patient presenting like this:

- History: Dyspnea
- Physical: Wheezing, ↑WOB
- Complications: Respiratory failure

✚ For all patients with dyspnea



A. WORKUP FOR DYSPNEA SUSPECTED TO BE SECONDARY TO ASTHMA

1. Obtain CXR

- Indications:**
 - Rule out other pulmonary causes of dyspnea (e.g. PNA, Pulmonary edema, Pleural effusions, Pneumothorax)
- Findings Supportive of Asthma Exacerbation:**
 - Asthma usually will present with a **normal CXR**
 - If **severe exacerbation** → Can lead to **hyperinflation of the lungs** causing hyperlucency and flattening of the diaphragm (not common)

2. Obtain 12 Lead ECG

- Indications:**
 - Rule out cardiac causes of dyspnea (e.g. Acute Myocardial Infarction)
- Findings Supportive of Asthma Exacerbation:**
 - Asthma usually will present with a **normal ECG**
 - If **severe exacerbation** → Can lead to pulmonary HTN causing **right heart strain** which would be evident by:
 - Right axis deviation
 - RBBB

3. Obtain ABG

- Indications:**
 - Respiratory failure
 - May help with differentiating a primary Type I (hypoxic) from Type 2 (hypercapnic) respiratory failure
 - Determine the severity of asthma
- Findings Supportive of Asthma Exacerbation:**
 - Respiratory Alkalosis:**
 - This indicates a **less severe asthma exacerbation**, as evidenced by the clearance of CO₂ leading to alkalosis. The alkalosis arises from tachypnea, which is a result of dynamic hyperinflation, allowing the patient to exhale more CO₂ than normal
 - Normal ABG:**
 - This indicates a **moderate asthma exacerbation**. Although CO₂ is being eliminated, it is not as effective as it should be since the patient is tachypneic. They are likely retaining more CO₂ than usual, leading to a pseudonormal pH. This is due to the patient's attempts to expel excess CO₂ caused by dynamic hyperinflation, combined with a gradual increase in CO₂ retention from airway obstruction and muscle fatigue
 - Respiratory Acidosis:**
 - This indicates a **severe asthma exacerbation**, a late-stage finding characterized by the inadequate clearance of CO₂ despite being tachypneic. The patient is likely retaining a significant amount of CO₂, leading to a decreased pH. This acidosis is a consequence of CO₂ retention caused by airway obstruction and muscle fatigue



B. ASSESS FOR THE PRESENCE OF AN OBSTRUCTIVE LUNG DISEASE LIKE ASTHMA

1. Obtain Pulmonary Function Tests (PFTs)

- **Parameters of PFTs:**

- FEV₁/FVC ratio
- FEV₁ post Bronchodilator administration
- FEV₁ Post Methacholine administration
- Diffusion limitation of carbon monoxide (DLCO)
- Peak Expiratory Flow Rate (PEFR)

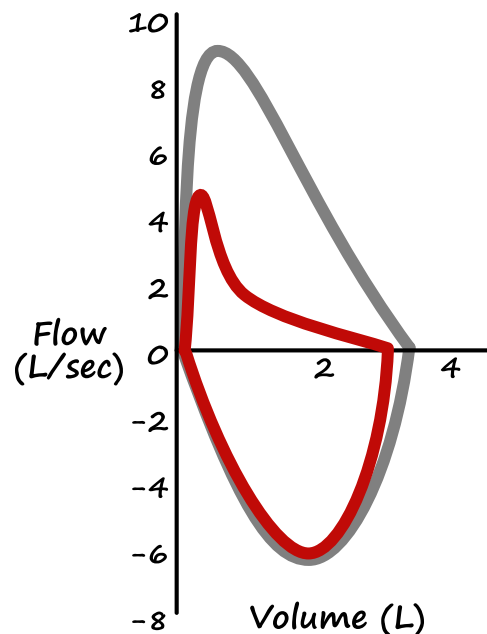
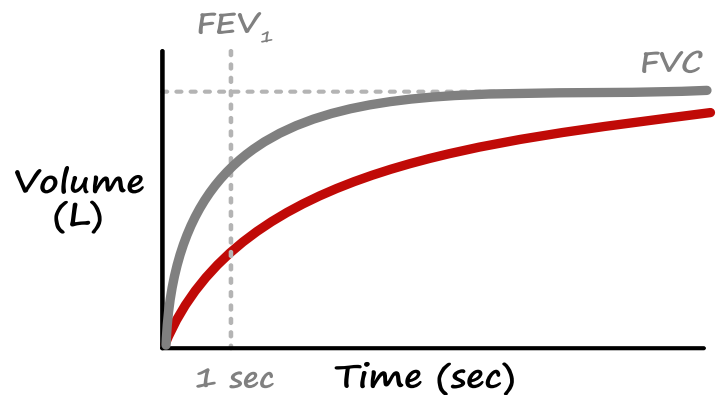
- **Indications:**

- Determine if the patient has an obstructive vs restrictive lung disease

- **Findings Supportive of Asthma:**

- **Obstructive Lung Disease Pattern that is Reversible:**

- **FEV₁/FVC ratio < 70%** suggests obstructive lung disease
 - FEV₁ helps to determine the severity of asthma
 - ↓↓↓ FEV₁ → Suggests ↑↑↑ the severity of asthma
- **↑↑ in FEV₁ of > 12% from baseline after bronchodilator**
Suggests a **reversible obstructive lung disease like asthma**
 - Bronchodilators (e.g. albuterol) reduce resistance to expiratory flow
- **↓↓ in FEV₁ of > 20% from baseline after Methacholine**
Suggests an **inducible obstructive lung disease like asthma**
 - Methacholine is a transient bronchoconstrictor that increases resistance to expiratory flow
 - This test is not commonly performed, but it may be considered when the results from the FEV₁/FVC ratio and the FEV₁ response to bronchodilators are inconclusive, yet there is a strong suspicion of asthma
- **DLCO** is a less useful parameter as it can be normal or increased
- **PEFR is best utilized during asthma exacerbations** to identify the severity of an asthma exacerbation and monitor/trend those values during treatment to assess for improvement or deterioration
 - **PEFR < 40% predicted** → Suggests a **severe exacerbation** and should be admitted for close monitoring

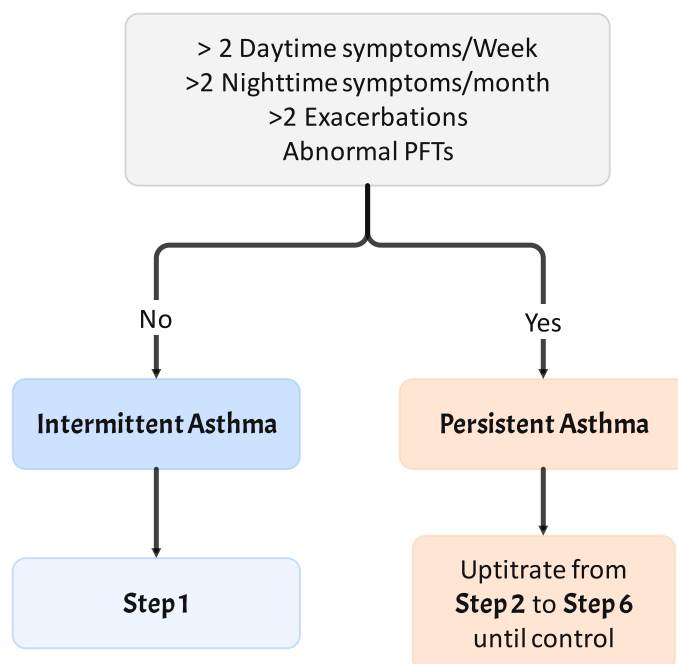


VI. TREATMENT OF ASTHMA

A. ASSESS THE SEVERITY OF ASTHMA TO GUIDE STEPWISE TREATMENT

Type of Asthma

Class	Symptoms	PFTs	Exacerbations
<i>Intermittent</i>	< 2 daytime symptoms/wk < 2 nighttime symptoms/month	FEV1 > 80% (normal)	< 2/yr
<i>Mild Persistent</i>	> 2 daytime symptoms/wk > 2 nighttime symptoms/month		> 2/yr
<i>Moderate Persistent</i>		FEV1 60-80%	
<i>Severe Persistent</i>		FEV1 < 60%	



1. Management of Intermittent Asthma

- **Treatment:**
 - Start Short-acting beta-2 agonist (SABA) → Albuterol PRN
- **Purpose:**
 - SABA → Promotes bronchodilation → Improves expiratory airflow
- **Monitoring:**
 - Improvement in wheezing and dyspnea

2. Management of Mild Persistent Asthma

- **Treatment:**
 - Continue SABA PRN
 - Add a low dose Inhaled corticosteroid (ICS) such as Budesonide daily
- **Purpose:**
 - SABA → Promotes bronchodilation → Improves expiratory airflow
 - ICS → Promotes reduction in airway inflammation → Reduces bronchial edema and bronchoconstriction → Improves expiratory airflow
- **Monitoring:**
 - Improvement in wheezing and dyspnea

3. Management of Moderate Persistent Asthma

- **Treatment:**
 - Continue SABA PRN
 - Plus one of the two options:
 - Add a Long-acting beta-2 agonist (LABA) daily such as formoterol or Salmeterol and Continue the low-dose ICS daily
 - This is the preferred regimen given the ease of escalating the dose of the ICS if poor response
- **Purpose:**
 - SABA → promotes bronchodilation → improves expiratory airflow
 - ICS → Promotes reduction in airway inflammation → Reduces bronchial edema and bronchoconstriction → Improves expiratory airflow
 - LABA → Promotes longer-acting bronchodilation → Improves expiratory airflow
- **Monitoring:**
 - Improvement in wheezing and dyspnea
 - If no improvement → Escalate therapy given the patient is likely in between moderate and severe persistent asthma:
 - Continue SABA PRN
 - Continue LABA
 - Increase Low-dose ICS to Medium-dose ICS

4. Management of Severe Persistent Asthma

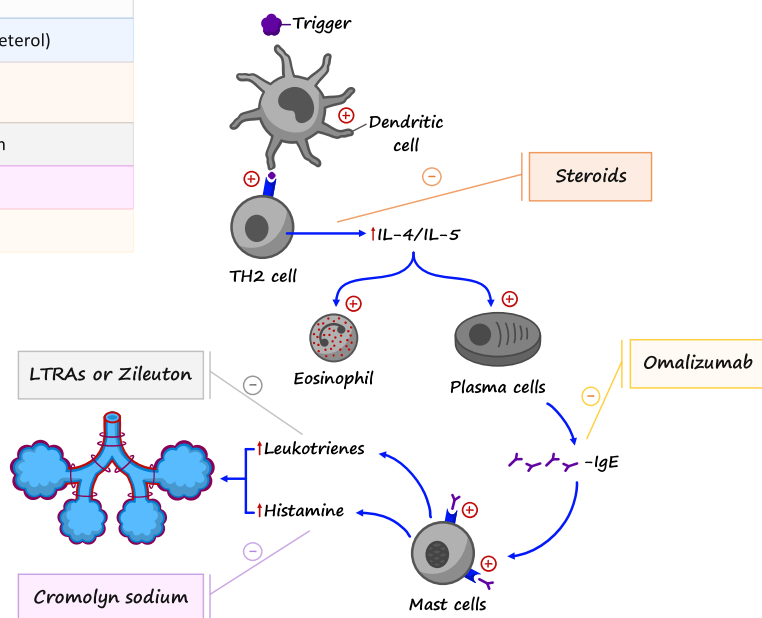
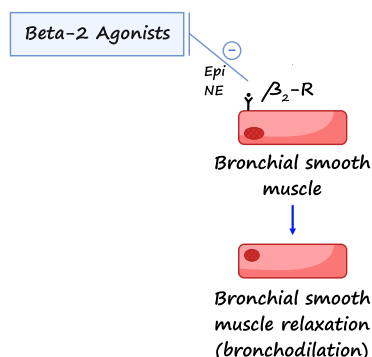
- **Treatment:**
 - Continue SABA PRN → Continue LABA
 - Increase Medium-dose ICS to High dose ICS
 - If poor response to low dose ICS → Up titrate to medium dose in moderate persistent asthma that is beginning to bridge into severe persistent asthma
- **Purpose:**
 - SABA → Promotes bronchodilation → Improves expiratory airflow
 - ICS → Promote reduction in airway inflammation → Reduces bronchial edema and bronchoconstriction → Improves expiratory airflow
 - LABA → Promotes longer-acting bronchodilation → Improves expiratory airflow
- **Monitoring:**
 - Improvement in wheezing and dyspnea
 - If no improvement escalate therapy given the patient is likely in the most severe form of persistent asthma:
 - Continue SABA PRN
 - Continue LABA
 - Continue High-dose ICS
 - Add Oral steroids and consider adding a Biologic such as Omalizumab

Step	Treatment
Step1	SABA prn
Step2	Add low dose ICS
Step3	Medium dose ICS or Add LABA + keep low dose ICS
Step4	LABA + medium dose ICS
Step5	LABA + high dose ICS
Step6	Add PO steroids + LABA + high dose ICS

- Consider LTRAs (ASA induced asthma & allergic asthma)
- Consider Zileuton (cold & exercise induced asthma)
- Consider Omalizumab (allergic asthma or ↑ IgE)



Mechanism of Treatment	Treatment
Beta-2 Agonists (bronchodilation)	SABA (albuterol), LABA (Salmeterol)
↓ Inflammatory mediators & T-Cell activity	Corticosteroids (Budesonide)
↓ Leukotriene	LTRAs (Montelukast), Zileuton
↓ Histamine	Cromolyn sodium
↓ IgE activity	Omalizumab



B. ALTERNATIVE ASTHMA THERAPY

1. Leukotriene Receptor Antagonists (LTRAs) (e.g. Montelukast)

- **Indications:**
 - Allergic asthma
 - Aspirin-induced asthma
- **Purpose:**
 - Allergies and Asthma → ↑ Leukotrienes
 - LTRAs → ↓ Leukotrienes → Reduces bronchial edema and bronchoconstriction → Improves expiratory airflow
- **Monitoring:**
 - Improvement in wheezing and dyspnea

2. Zileuton

- **Indications:**
 - Prophylaxis for cold and exercise-induced asthma
- **Purpose:**
 - Blocks the effects of leukotrienes → Reduces bronchial edema and bronchoconstriction → Improves expiratory airflow
- **Monitoring:**
 - Improvement in wheezing and dyspnea

3. Mast Cell Stabilizers (e.g. Cromolyn sodium)

- **Indications:**
 - Allergic asthma
 - Aspirin-induced asthma
- **Purpose:**
 - Prevents mast cell degranulation → Prevents release of histamine and leukotrienes → Reduces bronchial edema and bronchoconstriction → Improves expiratory airflow
- **Monitoring:**
 - Improvement in wheezing and dyspnea

4. Omalizumab

- **Indications:**
 - Severe persistent asthma not responsive to LABA-ICS-SABA with ↑ IgE and positive skin test for allergens
- **Purpose:**
 - This is a monoclonal antibody that blocks the IgE antibody from attaching to mast cells → Leads to a reduction in histamine and leukotriene production → Reduces bronchial edema and bronchoconstriction → Improves expiratory airflow
- **Monitoring:**
 - Improvement in wheezing and dyspnea
 - Reduction in exacerbations/year providing sparing of steroid use



C. MANAGEMENT OF ASTHMA EXACERBATION

Mechanism of Treatment	Treatment
Bronchodilation	SABA (albuterol) + SAMA (ipratropium) IV magnesium
↓ Inflammatory mediators & T-Cell activity	IV or PO Corticosteroids (Methylprednisolone or Prednisone)
↓ Work of breathing (↓ respiratory distress)	BIPAP Intubation (last resort)
↓ Anxiety	Ketamine (also a bronchodilator)

1. Bronchodilators

- **Treatment:**
 - Combination of **SABA** (e.g. albuterol) and **SAMA** (ipratropium)
 - These are referred to as “**Duonebs**” and are often dosed every 6 hours
 - Use of **IV magnesium sulfate** → One/two doses
- **Indications:**
 - First-line therapy in an asthma exacerbation
- **Purpose:**
 - To promote bronchodilation and assist in expiratory airflow and resolution in air trapping
- **Monitoring:**
 - Improvement in wheezing, dyspnea, RR and WOB
 - Improvement in PEFR from baseline/pre-treatment

2. Reduce Airway Inflammation

- **Treatment:**
 - **Systemic Corticosteroids:**
 - If able to swallow pills use **Oral Prednisone** usually 40-60mg (depending on severity) daily x 5-7 days
 - If unable to swallow pills given respiratory distress use **IV Methylprednisolone** usually 40-125 mg (depending on severity) every 6 hrs x 5-7 days
- **Indications:**
 - Asthma exacerbation that is not improving with bronchodilator therapy
- **Purpose:**

Systemic Corticosteroids → Achieve higher than normal serum steroid levels → Promote massive reduction in airway inflammation → Massively reduces bronchial edema and bronchoconstriction → **Massively improves expiratory airflow**
- **Monitoring:**
 - Improvement in wheezing, dyspnea, RR and WOB
 - Improvement in PEFR from baseline/pre-treatment

3. Reduce Work of Breathing

- **Treatment:**
 - Noninvasive Positive Pressure Ventilation (e.g. BIPAP)
 - Given the discomfort of BIPAP, a patient is given **Ketamine** which provides a dual function:
 - Anxiolysis
 - Bronchodilation
 - Invasive Positive Pressure Mechanical ventilation (e.g. intubation)
- **Indications:**
 - Severe tachypnea, wheezing or silent chest, and ↑WOB
 - ↑↑PCO₂ (Hypercapnia) → Suggests severe obstruction and poor CO₂ clearance
 - Hypercapnia can also lead to severe lethargy and sometimes comatose states which can impair the protection of the airway
- **Purpose:**
 - Positive Pressure ventilation (e.g. BiPAP or intubation) → Maintains bronchioles open due to higher airway pressure delivery → Allows air to escape the lungs more easily → Enables the lungs to deflate properly → Makes it easier for the patient to take a deep breath → Facilitates CO₂ removal and results in improvement of tachypnea and WOB
- **Monitoring:**
 - Improvement in tachypnea, dyspnea, and WOB
 - Improvement in PCO₂ on serial ABGs
 - Improvement in mental status if severely hypercapnic

