ASTHMA

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Definition

- It is a chronic inflammatory disorder (chronic Lower Respiratory Tract Disease).
- characterized by:
    - **Reversible airway obstruction**.
    - **Increased bronchial reactivity**, once there is stimulating antigen there is abnormal response of the bronchial tree which leads to narrowing of the airways.
    - **Airway inflammation**, that's why we give anti-inflammatory either in prophylaxis or in acute treatment.

Pathophysiology

- Airways narrowing is the main visible pathology in asthma that related to 3 events:
    - Inflammation and mucosal Oedema with thickened basement membrane.
    - Bronchial Smooth Muscle Spasm and Hypertrophy.
    - Mucous plugging.
- The pathophysiology is very complex:
    i. We have local causes (allergens, irritants)
    ii. Then inflammatory cells involvement: Mast cells, eosinophils and epithelial cells.
    iii. Which lead to **tissue destruction, Sub-epithelial proliferation** of myofibroblasts, **neural elements (sensory C-fibers)**, **multiple interleukins involvement**, also we have **increased mucous secretion** then **decreased mucous transport.**
    iv. All of them finally lead to **bronchospasm**.
- In longstanding asthma, there will be structural changes (Airway remodeling).
- Unfortunately even with drug antagonists, sometimes we still can't control asthma. So if we have inadequate treatment there is a possibility of lung tissue damage or even death.

Clinical Presentation

Symptoms

1. COUGH:
    - After exertion
    - After breathing cold air
    - At night
    - Paroxysmal
2. WHEEZING:
    - Variable or intermittent
    - After exertion

- At night

***Always cough causes wheezes at night and wheeze always considered LRTI.**

***In children there is no single test to diagnose asthma.**

Signs of Silent Asthma

- "Silent Asthma" = no wheezing is heard
- **Signs:**
  - Persistent cough at night
  - Cough with exercise
  - Cough with laughter
  - Cough when consuming cold foods or drinks
  - Prolonged cough following or accompanying cold
  - Feeling of "tight chest"
  - Difficulty breathing

Soft Signs Indicating that Asthma is Out of Control

- Frequent wheezing episodes
- Increasing frequency of using rescue medications (i.e. acute use of albuterol)
- A previously stable asthmatic, now having signs of "silent asthma"
- Reduction or termination of activities
- Patient who had exposure to known trigger
- Persistent cough following bronchitis or pneumonia

- There are many presentations of asthma. **The most recognizable form is the acute episode** in which the patient presents with **acute shortness of breath.**
- Depending on the underlying degree of inflammatory damage of the airways, the episode may have been festering with persistent cough and occasional bouts of shortness of breath for weeks.
- Failure to attend to these soft signs of "asthma in transition" may lead to an acute case of status asthmaticus. Hence, paying attention to signs of "silent asthma", can prevent costly and life threatening consequences.
- Asthma may appear solely as an event associated with work or exercise. Most asthma in childhood occurs as a result of encounters with respiratory viruses.
- If the asthmatic is already unstable because of a poor maintenance regimen of the existing chronic asthma, the acute phase will begin simultaneously with the first signs of "cold".
- If the asthma is managed well, then the cough and wheezing may occur several days after cold symptoms. Hence, early recognition of "asthma in transition" is a major point of cooperation involving the physician and patient.
- So the clinical picture is usually as the following:
  - History: episodic symptoms of airway obstruction
  - Physical examination: wheeze and hyperinflation

- Laboratory: exhaled nitric oxide (eNO)
- NOT EVERY WHEEZE IS ASTHMA AND NOT EVERY ASTHMA HAS WHEEZE.
- Around 10% of children they present with cough only, without a history of wheeze.

Etiology

- The most important are HERITABLE and ENVIROMENTAL factors, they contribute to its pathogenesis.
- Also there are at least 20 distinct chromosomal regions with linkage to asthma and asthma related traits have been identified.

Triggering Factors

1. Infections:
   - **URTI** is the most common triggering factor in the 1st year of life.
   - Most of the time children have long history of cough but suddenly they have acute attack or acute exacerbation of symptoms.
2. Pollens:
   - Common in spring season (April), this is related to different pollens like flowers or olives especially in Jordan, that's why sometimes prophylactic treatment is initiated.
3. House dust mites:
   - Present in every house and its hard to get rid of them, because they found on corners, pillows, beds... etc.
4. Noxious agents:
   - like air-refreshers and perfumes.
5. Smoking.
6. Exercise: almost in older children.
7. Crying and Laughing.

***Diurnal variation: There is more narrowing in asthmatics airway compared to normal person between day and night. Explained by the diurnal rhythm of hormones, mainly corticosteroids.**

- Risk Factors for persistent wheezing and predisposing to asthma:
  i. Frequent wheezing in 1st year of life.
  ii. Maternal history of asthma or smoking.
  iii. Eczema.
  iv. High IgE levels.

Diagnosis

- In order to diagnose asthma in young children there is certain criteria:
  - **> 4 episodes/yr of wheezing lasting more than 1 day affecting sleep in a child** with **one MAJOR** or **two MINOR** criteria.
  - **MAJOR CRITERIA:**
    - Parents with asthma
    - Physician diagnosed atopic dermatitis (eczema)

- **MINOR CRITERIA:**
  - Physician diagnosed allergic rhinitis
  - Eosinophilia (> 4%)
  - Wheezing apart from colds

Investigations

- **CBC**
- **ABG with moderate to severe RD**
- **Pulmonary Function Test**

Asthmatics patients have tachypnea (co2 washing out) and finally alkalosis which indicates good respiratory muscles function, but this is not in all patients some of them as he gets exhausted and the CO2 rises he will have respiratory acidosis then inadequate perfusion and oxygenation resulting in hypoxia and metabolic acidosis together with respiratory acidosis.

- So ABG is indicated in:
  - Patients with moderate to severe respiratory distress.
  - Patients not responding to therapy.

Differential diagnosis

1. Bronchiolitis:
   - Age of 2-3 years.
   - Patient present with crackles, hyperinflation, Rhonchi.
   - Mainly diagnosed by nasopharyngeal aspirate.
   - Treated by supportive treatment.
2. Cystic fibrosis:
   - Common in developed countries.
3. Foreign body aspiration:
   - Usually preceded by choking.
   - Mainly in ages between 1-3 years.
4. Gastroesophageal Reflux:
   - especially in 1st year of life.
   - Associated with multiple aspirations.
5. Immotile cilia syndrome:
   - Definite diagnosis is done by taking a biopsy from the epithelium.
6. Vascular ring:
   - Double aortic arch that rings around the esophagus and trachea.
   - We do barium swallow to find indentations in the esophagus.
   - Or by using MRI, or an ECHO.
7. Psychogenic cough: which disappears during sleep.

- **An acute asthma exacerbation is a biphasic process:**

- The first phase was described as the **immediate (bronchospastic) phase** and the second phase as the **late phase (inflammatory response)**.

a. **In the early phase** of allergic inflammation, preformed mediators such as histamine and rapidly formed mediators such as leukotrienes are released and cause bronchospasm.

b. **In the late phase** inflammatory cells (e.g. eosinophils) recruit other cells such as epithelial cells to participate in the resultant inflammatory damage of the airways and sub-epithelial structures.
   - These events eventually result in extensive restructuring of the normal histology of the airways. This damage is not restored by beta-2 bronchodilators.

- An important immunologic occurrence is the activation of the T helper 2 cell, which is important in the progression of the **allergic immunologic process**. The other helper designated Th1 cell does not enhance the allergic inflammatory process.
- **Acute exacerbations** are treated with quick relief (or rescue) medications, which is most commonly **prn albuterol** and optional short bursts of systemic corticosteroids.
- **The inflammatory process** of asthma starts within 4 to 8 hours following allergen exposure, wheezing would occur when there is no response (or less responsive) to beta agonists, but it is ablated by **cromolyn and corticosteroids**.
- However, beta agonists could easily neutralize the immediate reaction, occurring within minutes of the allergen exposure. This created a picture of a biphasic reaction to allergen (or infection) induced wheezing.

Recognition and Assessment of Severe Acute Asthma

- History:
  - In history ask if the child was in NICU or any previous admissions
- Physical Exam:
  - The general appearance of the child is very important
  - If he can't talk or speak
  - Vital signs
  - Signs of dehydration
  - Wheezing which is usually an expiratory sound
  - Tachypnea: which is >40 in children under 2 yrs
  - Tachycardia: in general any HR >140
  - Hypoxia: O2 saturation <90%
  - A pCO2 of 40 or greater on a blood gas
  - Silent chest: late sign of severe asthma indicates very low air entry
  - Persistent respiratory distress despite aggressive beta-2 agonists
  - Barrel chest shape: bad sign in uncontrolled asthma
  - Pulsus paradoxes: which is a drop in the systolic pressure during inspiration>20mmHg
  - Pneumothorax: indicates severe asthma
  - All asthmatics have hyperinflation and horizontal ribs in CXR.

Management of Acute Attack

- Asthma management plans depend on the severity of the asthmatic.

- Higher severity levels warrant greater use of corticosteroids and prophylactic medications such as leukotriene inhibitors and inhaled corticosteroids.
- The NIH guidelines categorizes severity levels into "steps" as follows:
    - **Step 1 (mild intermittent)**: Day symptoms two days per week or less **and** night symptoms two nights per month or less. **Chronic peak flow (PEF) is 80% of expected or higher**. This step requires no daily medications. ALL of the other categories (any category with the word "persistent"), requires a chronic controller (anti-inflammatory medication).
    - **Step 2 (mild persistent):** Day symptoms greater than two times per week, but less than once per day **or** night symptoms greater than two nights per month. **Chronic peak flow is still 80% of expected or higher**. This step recommends a low dose inhaled corticosteroid. Alternatively, a cromolyn medication or a leukotriene receptor antagonist may be used. Theophylline is another option, but only in children older than 5 years.
    - **Step 3 (moderate persistent):** Day symptoms occur daily **or** night symptoms occur more than once per week. **Chronic peak flow is 60% to 80% of expected value.** This step recommends a low dose inhaled corticosteroid plus a long acting beta-2 agonist (salmeterol or formoterol). Three other alternatives exist: 1) A medium dose inhaled corticosteroid 2) A low dose inhaled corticosteroid plus an LTRA 3) A low dose inhaled corticosteroid plus theophylline.
    - **Step 4 (severe persistent):** Continues day symptoms **or** frequent night symptoms. **Chronic peak flow is less than or equal to 60% of expected value**. This step recommends a high dose inhaled corticosteroid, plus a long-acting beta-2 agonist.

- Oxygen:
    - Any patient with acute attack we give him O2 by mask 8-10 L/min to keep the saturation above 95%.
    - It can lead to Retinopathy, Prematurity, Bronchopulmonary dysplasia. That's why in NICU, O2 is monitored and not allowed to increase >98%.
    - Don't forget that prolonged 100% O2 can cause lung tissue damage.

- Nebulizer Salbutamol:
    - Is a beta-2 agonist, given after O2 in acute attack at least 8 L/min given by mask.
    - The large volume and high gas flow through the nebulizer produce a small aerosol particle size, maximizing deposition of the drug in small airways.
    - Side effects: hypokalemia, hyperglycemia, tachycardia, palpitation and tremor.

- Corticosteroids:
    - Prednisolone – Oral
    - Methyl prednisolone - Oral, IV
    - Dexamethasone - Oral, IV
    - Most important drug in asthma, it takes long time to work 4-6 hrs.
    - Reduce the severity of acute severe asthma.

- Reduce the inflammation in bronchial mucous.
- Potentiate the relaxation of bronchial smooth muscle by beta-2 agonists.
- Reduce mucous production.
- Decrease recruitment and activation of inflammatory cells.
- Decrease microvascular permeability.
- Up regulates B2 receptors.

***The above 3 drugs should always be given in any acute asthma. But if there is no response we give:**

- Ipratropium Bromide:
  - Anti-cholinergic bronchodilator with no systemic atropine like effects and no inhibition of mucociliary clearance.
  - Has a good synergy with beta-2 agonist and can be mixed with salbutamol in nebulizer.

Also if there is no response we give:

- Aminophyllineas:
  - The use of this drug is controversial, because the therapeutic levels are narrow as it causes many side effects like convulsions.
  - So plasma levels should be monitored.
- IV Salbutamol:
  - unfortunately this drug is not found in Jordan.
- Magnesium Sulfate:
  - is a bronchodilator with unclear MOA but maybe due to: 1- inhibition of Ca++ mediated smooth muscle contraction 2- Direct inhibition of smooth muscle contraction.
  - Can be given IV or Nebulized.
- Ketamine:
  - It is sedative and analgesic drug can be used in asthma.
  - Has sympathomimetic action.
  - Side effects: arrhythmia, laryngospasm, increased secretions.
  - Contraindicated in pts with neurological problems and hyperkalemia.

In very rare cases there are no response and we put patients on:

- Mechanical Ventilators:
  - 10-33% of all PICU admissions for status asthmaticus require MV.
  - Mortality rates for those pts requiring MV up to 5%.
- IV fluids:
  - Because most of the patients are dehydrated due to:

1. Increase insensible loss.
2. Increase metabolism.
3. Decrease intake.
4. Vomiting.

- Non-Conventional interventions:
  - Manual chest compression.
  - Inhaled anesthetics.

- Nitric Oxide: it is a strong bronchodilator.
- Bronchoscopy: if there is severe collapse.
- Heliox: O2 and Helium.
- ECMO: extracorporeal membrane oxygenation (artificial lung). only if the cause is reversible like infection.
- CPAP (continuous positive airway pressure).

- Controller Medications:
  a. Inhaled corticosteroids.
  b. Leukotriene modifiers.
  c. Long acting inhaled beta-2 agonists.
  d. Theophylline: long acting (slow release).
  e. Cromolyn: useless in children.
  f. Long acting oral beta-2 agonist.
  g. Systemic glucocorticosteroids.

- The type of medication used to treat asthma reflects the mechanism of airway obstruction:
  - Bronchospasm versus inflammation.
  - The logic for appropriate use of individual medications for asthma can be understood by recalling the biphasic reaction.
  - Now it is possible to create an asthma treatment program:
    i. Genetics aside, elimination of triggers and aggravators of asthma such as allergens, cigarette smoke, and environmental and industrial pollutants, can prevent acute exacerbations of asthma and serve as the first line of defense.
    ii. Conditions such as weather changes and respiratory infections fall outside of the readily controllable factors.
- Co-morbid conditions such as allergic rhinitis, sinusitis, eczema, and gastroesophageal reflux have profound influence on asthma. Their presence makes asthma extremely difficult to control.
- The main goal is to keep the patient functional and free of side effects from medications. With this approach, asthmatics have been able to participate in a normal life style.

Prevalence

- It varies from country to another, in Jordan around 10% of the population suffered from one event of asthma.
- It is more common in males.
- There is familial tendency, if one of the parents has asthma it will increase the incidence in the siblings.
- There is no definite mode of inheritance it is a multifactorial.

Real Facts About Asthma in Childhood

- It is number one of chronic illness causing school absence.
- Affects around 5 million children <18 years in US.

- 658,000 emergency department visits for asthma in US children <15 years in 1999.

Natural History of Asthma

- 27% never reported wheezing.
- 21% reported wheezing at only one assessment.
- 10% had intermittent wheezing
- 14% had wheezing that persisted throughout the study.
- 15% had remission during adolescence and no further wheezing.
- 12% had remission with subsequent relapse.

Asthma Education

Self managed education associated with:

- Improvement in air flow.
- Improvement in self efficacy scales.
- Reduction in school absence.
- Reduction in emergency room visits.