Childhood Asthma

3.0 Contact Hours

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Childhood Asthma

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Asthma is the one of the most common chronic diseases affecting children. The prevalence of asthma is increasing throughout the world both in developing and developed countries. During the past decade, the concepts about the pathophysiology and consequently the management principles of asthma have changed. Initially it was believed to be a bronchospastic disease. But now, it has been found that it is not only bronchospasm, but that also mucosal inflammation plays an important role in the pathophysiology of asthma.

Asthma is a chronic inflammatory condition of the lung airways resulting in episodic airflow obstruction. The airflow obstruction is generally reversible either spontaneously or with treatment. Worsening of symptoms occurs due to common respiratory viral infections and by inhalant allergen exposure in sensitized asthmatics. Rarely, severe sequelae such as hypoxic seizures, respiratory failure, and death can occur.

Objectives:

Upon completion of this course, the learner will be able to:

1. Define asthma
2. Discuss the etiology of childhood asthma
3. Discuss the epidemiology of childhood asthma
4. Explain the pathology and pathogenesis of childhood asthma
5. Discuss the clinical features of asthma
6. Elaborate on the various investigations to be performed
7. Discuss the treatments and outcomes of the disease

Definition

Asthma is a chronic inflammatory condition of the lung airways resulting in episodic airflow obstruction. It is characterized by recurrent attacks of breathlessness and wheezing which vary in severity and frequency from person to person. Symptoms may occur several times in a day or week in affected individuals, and for some people become worse during physical activity or at night. Asthma symptoms are usually associated with widespread but variable airflow obstruction that is generally reversible either spontaneously or with treatment.

Asthma is a reversible obstructive airway disease (ROAD) with bronchial hyper-reactivity (BHR).

Asthma = ROAD + BHR

During an asthma attack, the lining of the bronchial tubes swells, causing the airways to narrow and reducing the flow of air into and out of the lungs. Recurrent asthma symptoms frequently cause sleeplessness, daytime fatigue, reduced activity levels and school and work absenteeism. Clinical manifestations of asthma are intermittent. Dry coughing, expiratory wheezing, chest tightness, and dyspnea are commonly provoked by physical exertion and airway irritants (e.g., cold and dry air, environmental tobacco smoke).

The disease can become severe as symptoms worsen. This worsening of symptoms is generally precipitated by common respiratory viral infections and by inhalant allergen exposure in sensitized asthmatics. These exacerbations are characteristically worse at night and can progress to severe airflow obstruction, shortness of breath, and respiratory distress and insufficiency. Rarely, severe sequelae such as hypoxic seizures, respiratory failure, and death can occur.

Epidemiology

Worldwide, childhood asthma appears to be increasing in prevalence, despite considerable improvements in the management of asthma. According to World Health Organization (WHO) estimates, 300 million people suffer from asthma and 255,000 people died of asthma in 2005. Over 80% of asthma deaths occur in low and lower-

middle income countries. Asthma deaths will increase by almost 20% in the next 10 years if urgent action is not taken.

Childhood asthma in the United States is the most common cause of childhood emergency department visits, hospitalizations, and missed school days, accounting annually for 867,000 emergency department visits, 166,000 hospitalizations, and 10.1 million school days lost. In 2005, an estimated 6.5 million children under age 18 (almost 1.4 million under age 5) had asthma, 3.8 million of which had an asthma attack, and many others have undiagnosed asthma.

According to an International Study of Asthma and Allergies in Childhood performed in 56 countries, there is a 20-fold variation in asthma prevalence. Childhood asthma seems particularly common in modern metropolitan locales and is strongly linked with other allergic conditions. In contrast, children living in rural areas of developing countries and farming communities are less likely to have asthma and allergies. This striking variation in childhood asthma prevalence has led to investigations of potential environmental and lifestyle factors that may explain these differences as well as the recent rise in asthma

Etiology

Approximately 80% of asthmatics report onset of the disease before 6 years of age. Only a small percentage of children who have recurrent wheezing develop persistent asthma later in life. Though the cause of childhood asthma is not clearly known, it is believed to result from an interaction between genetic and environmental factors. More than 22 loci on 15 autosomal chromosomes have been linked to asthma. Viral infections, like respiratory syncytial virus, which produce bronchiolitis and pneumonia in the first two years of life, can precipitate asthma at any age. There are various triggers or allergens which can either precipitate an attack of asthma or worsen its symptoms. Allergen exposure, in sensitized individuals, can initiate airway inflammation and hypersensitivity to other irritant exposures as well. Eliminating the offending allergen can lead to the resolution of asthma symptoms and can sometimes "cure" asthma. Some of the common triggers are –

- Tobacco smoke

- Air pollutants (e.g., ozone, sulfur dioxide)
- Cold dry air
- Strong odors
- Indoor allergens (for example dust mites in bedding, carpets and stuffed furniture, pollution and pet dander)
- Outdoor allergens (such as pollens and moulds)
- Chemical irritants in the workplace
- Extreme emotional arousal such as anger or fear or laughter
- Physical exercise
- Medications (aspirin and other non-steroid anti-inflammatory drugs, and beta-blockers)
- Gastroesophageal reflux disease
- Fish, nuts, strawberries
- Sulfites in food (dried fruit) or beverages (wine)

There are basically two types of childhood asthma. They are –

- Recurrent wheezing precipitated by viral infections
- Chronic asthma that is associated with allergies which persist in to later childhood and adulthood.

Asthma is sometimes associated with other problems like nasal polyps. Samptar's Triad includes the presence of bronchial asthma, hyperplastic sinusitis/nasal polyposis and hypersensitivity to aspirin and non-steroidal anti-inflammatory medications (e.g., ibuprofen). Of these, the allergy associated with bronchial asthma is the most prevalent one.

Not all children who have wheezing develop persistent asthma. There are a few childhood risk factors which predisposes children to persistent asthma. Some of the factors are:

- Parental asthma
- Allergy

    - Atopic dermatitis
    - Allergic rhinitis
    - Food allergy
    - Inhalant allergen sensitization
    - Food allergen sensitization
- Severe lower respiratory tract infection
    - Pneumonia
    - Bronchiolitis requiring hospitalization
- Wheezing apart from colds
- Male gender
- Low birth weight
- Environmental tobacco smoke exposure

Pathogenesis

As stated earlier, asthma is a reversible obstructive airway disease with bronchial hyper-reactivity. The obstruction is due to bronchoconstrictrition, mucosal edema and excess mucus secretion in to the lumen, along with inflammatory infiltrate. Airway inflammation is strongly linked to hypersensitivity of the airway's smooth muscles to irritant exposures, such as cold air, dry air, strong odors, and particulate matter in smoke. The airways in asthmatics have increased inflammatory cells which include mast cells, activated eosinophils, and activated helper T lymphocytes. Helper T lymphocytes that produce proallergic, proinflammatory cytokines (e.g., IL-4, IL-5, IL-13) and chemokines (e.g., RANTES, eotaxin) mediate this inflammatory process. Persistent inflammation then leads to abnormal remodeling, causing basement membrane thickening, subepithelial collagen deposition, and smooth muscle and mucus gland hypertrophy and hyperplasia, which are responsible for the episodic manifestation of asthma.

There are two phases of airway obstruction in asthma: the early phase and the late phase. The early phase occurs within 15- 30 minutes of exposure to the allergen and consists of bronchoconstriction. The late phase occurs 4-6 hours after the allergen exposure and consists of tissue inflammation, immune cellular infiltration into the airways, airways edema and excess mucus production

Clinical features

The common symptoms of childhood asthma include breathlessness, intermittent dry coughing and wheezing. The symptoms are generally provoked by the triggers mentioned above. Respiratory symptoms are characteristically worse at night, especially during prolonged exacerbations triggered by respiratory infections or inhalant allergens.

- Cough – It is intermittent and dry. It is worse at night and during early morning. Sleep is disturbed and hence the child will have general fatigue
- Wheezing – This is a whistling sound heard during expiration. It can be heard with a stethoscope and in severe cases it is audible even without it
- Shortness of breath – The affected person says that he is not able to breathe out completely. It may be so severe that the child has difficulty in walking and talking. There may be chest tightness and an increase in the respiratory rate.

In severe cases, there may be retractions of the intercostals spaces and of other accessory muscles of respiration. In severe cases, wheezing will be absent and the child will sweat profusely and will develop cyanosis. The patient assumes a hunched over tripod like sitting position that makes it easier to breathe. Due to the strenuous use of the abdominal wall muscles and the diaphragm, the child may complain of abdominal pain.

Types of Asthma

The NAEPP guidelines classify asthma into four groups based on severity. This categorization takes into account the: frequency of daytime or nighttime symptoms, degree of airflow obstruction by spirometry, and PEF variability. The four groups are:

- Mild intermittent asthma
- Persistent asthma
    - Mild persistent asthma
    - Moderate persistent asthma
    - Severe persistent asthma

Mild intermittent asthma

The features are:

- Daytime symptoms less than three times per week
- Night time symptoms less than three times per month
- FEV_1 or PEF more than 80% of the predicted value. PEF variability is less than 20%

Mild persistent asthma

The features are:

- Daytime symptoms more than or equal to three times per week
- Night time symptoms three or four times per month
- FEV_1 or PEF more than 80% of the predicted value. PEF variability – 20% to 30%

Moderate persistent asthma

The features are :

- Daily daytime symptoms and daily use of short-acting β-agonists
- Nighttime symptoms more than once a week
- FEV_1 or PEF more than 60% and less than 80% of the predicted value. PEF variability of more than 30%

Severe persistent asthma

The features are:

- Continual daytime symptoms, limited physical activity, frequent exacerbations
- Nighttime symptoms more frequent
- FEV_1 or PEF less than 60% of the predicted value. PEF variability of more than 30%

Differential diagnosis

There are numerous other conditions which can mimic asthma. These are to be excluded before initiating treatment for asthma. Some of the common conditions which mimic asthma are:

- Foreign bodies in the airway or esophagus
- Congenital malformation of the airways, cardiovascular and gastrointestinal system
- Vocal cord dysfunction
- Bronchiolitis
- Gastroesophageal reflux
- Bronchiectasis
- Interstitial lung diseases
- Hypersensitivity pneumonitis
- Pulmonary eosinophilia
- Allergic bronchopulmonary aspergillosis
- Endobronchial tuberculosis
- Bronchial adenoma

Investigations

Among the various investigations to be performed, pulmonary function tests are the most important one. The various investigations that are performed are:

- Chest x-ray – Though a chest x-ray is not needed in all cases, they are needed to exclude other possible diagnosis and complications such as atelectasis and pneumonia. The lung markings are increased in asthma and the x-ray may show hyperinflation with flattening of the diaphragm
- Allergic skin testing – This is done to find out the specific IgE, which is useful in finding out potentially important environmental allergens.
- Pulmonary functions tests – There are four types of pulmonary function tests. They are:
    - Peak Expiratory Flow Rate (PEFR)
    - Spirometry

- Exercise test
- Histamine challenge test in asymptomatic patients

Of these four types of pulmonary function tests, Peak Expiratory Flow Rate (PEFR) is the easiest and the most commonly performed one.

Peak Expiratory Flow Rate (PEFR)

Peak Expiratory Flow Rate (PEFR) is the fastest rate at which air can move through the airways during forced expiration starting with fully inflated lungs. Peak flow is measured with the help of a peak flow meter. It is a small, portable, convenient and inexpensive device which can be used at home. Ideally, peak flow should be measured three times a day, or if this is not possible, at least twice a day - once in the morning and once at night. The peak flow varies according to age, sex and height. Normal peak flow rates are approximately 600-800 L/min for males and 400-600 L/min for females. A morning/night variation of more than 20% is suggestive of asthma. The uses of PEFR are:

- Asthma can be diagnosed
- An impending attack of asthma can be anticipated and treatment started before it produces any symptoms
- Effectiveness of treatment can be assessed

Spirometry

In spirometry, the forced expiratory volume during the first, second (FEV_1) and functional vital capacity (FVC) are measured. A ratio of the FEV_1/ FVC of less than 80% indicates airflow obstruction. Also, reversibility in the absolute value of FEV_1 by more than 20% after bronchodilator therapy indicates a significantly reversible air flow obstruction.

FEV_1 /FVC < 80% = Obstructive airway disease

Exercise test

A fall of >20% in the PEFR or FEV_1 after an exercise challenge is indicative of asthma. This test may be used in patients with a history suggestive of asthma with normal PEFR and FEV_1. Exercise precipitates an attack of asthma in these patients with a drop in the PEFR and FEV_1 of more than 20%.

Histamine challenge test

A specific inhalation challenge test can be performed on asymptomatic patients with normal lung function tests with histamine, methacholine or an allergen. This is done in the same way as the exercise test.

Treatment of asthma

The goals of childhood asthma management for children are:

- Control symptoms so as to maintain normal activity levels including exercise
- Maintain pulmonary function as close to normal levels as possible
- Avoid or control asthma triggers
- Establish plans for the prevention and management of exacerbations
- Avoid adverse effects due to asthma medications
- Educate patients to develop a partnership in asthma management
- Establish plans for chronic management and regular follow up care
- Prevent development or irreversible airway obstruction and reduce asthma deaths.

The NAEPP guidelines have been adapted for childhood asthma in a joint publication of the American Academy of Allergy, Asthma & Immunology and the U.S. National Institutes of Health's National Heart, Lung and Blood Institute and the American Academy of Pediatrics entitled Pediatric Asthma: Promoting Best Practice. These guidelines describe four components to optimal asthma management. They are:

- Regular assessment and monitoring
- Control of factors contributing to asthma severity

- Asthma pharmacotherapy
- Patient education

Regular assessment and monitoring

Children with asthma should have regular clinic visits every 2-4 weeks until good asthma control is achieved. Once good control is achieved, clinic visits 2-4 times per year should be done to maintain the control of the disease. During these visits, asthma control is assessed by asking about:

- The frequency of asthma symptoms during the day, at night, and with physical exercise
- The frequency of "rescue" short-acting β-agonist medication use and refills
- The number and severity of asthma exacerbations since the last visit
- Participation in school, sports, and other preferred activities.

Lung function testing is recommended annually and more often if asthma is inadequately controlled. The NAEPP guidelines recommend once-daily PEF monitoring, preferably in the morning.

Control of factors contributing to asthma severity

The factors that cause asthma and that have to be controlled can be divided in to two groups: environmental exposures and co-morbid conditions. In most cases asthma is precipitated by exposure to environmental allergens. Reduced exposure to allergens can decrease asthma symptoms, the need for medications, and airways hyper responsiveness. At the very least, these airways irritants should be eliminated or reduced from the homes and automobiles used by asthmatic children. Since respiratory infections are difficult to avoid, annual influenza vaccination is recommended for all asthmatic children.

Rhinitis, sinusitis, and gastro esophageal reflux commonly accompany asthma and can worsen disease severity. Effective management of these co-morbid conditions can often improve asthma symptoms and disease severity, so that less medication is needed to achieve good asthma control.

Pharmacotherapy

Based on severity, asthma is divided into four groups. It is essential to identify the persistent asthma group and initiate anti-inflammatory controller medication to prevent long term morbidity. The '3 strike rule' can be applied in the treatment of persistent asthma. If an asthmatic child has asthma symptoms, or if the child requires quick-relief medication more than three times per week, awakens at night due to asthma more than three times per month, or requires a refill for a quick-relief inhaler prescription more than three times per year, then that patient should receive daily controller therapy. Inhalation therapy is routinely used in the treatment of asthma. Spacer devices for the delivery of all medications from a metered-dose inhaler (MDI) should be used universally in all children with asthma.

The various medications used in the treatment of asthma are divided into two groups:

- Quick-relief, or "reliever" or "rescue," medications – These are used in the management of acute episodes of bronchospasm. The various drugs of this group are -
    - Short-acting inhaled β-agonists: Albuterol, levalbuterol, pirbuterol, terbutaline, metaproteronol
    - Inhaled anticholinergics: Ipratropium, atropine
    - Short-course systemic glucocorticoids: Prednisolone, methyl-prednisolone, Methylprednisolone Sodium Succinate
- Long-term-control, or "controller," medications - These are used to control inflammation and prevent long term effects. The various drugs of this group are:
    - Nonsteroidal anti-inflammatory agents: Cromolyn, Nedocromil
    - Inhaled glucocorticoids: Beclomethasone, Flunisolide, Budesonide, Fluticasone, Triamcinolone
    - Sustained-release theophylline
    - Long-acting inhaled β-agonists: Salmeterol, Formoterol
    - Leukotriene modifiers: Montelukast, Zafirlukast, Zileuton
    - Oral glucocorticoids: prednisone, methylprednisolone

The NAEPP guidelines outline a step-down approach for the treatment of asthma. The therapy is initiated at a higher level of controller therapy with measures to "step-down" therapy once good asthma control is achieved. Short-acting β-agonists are the recommended reliever medication for all asthma severity levels. They are to be used as needed for acute symptoms. The treatment outline for the various types are:

- Severe persistent asthma - High-dose inhaled glucocorticoids, a long-acting bronchodilator, and routine oral glucocorticoids if needed.
- Moderate persistent asthma - Medium-dose inhaled glucocorticoids or low-dose inhaled glucocorticoids in combination with a long-acting β-agonist or a leukotriene pathway modifier; sustained release theophylline or long-acting oral β-agonists are alternatives.
- Mild persistent asthma - Low-dose inhaled glucocorticoids, leukotriene pathway modifiers, or cromolyn/nedocromil; sustained-release theophylline is an alternative.
- Mild intermittent asthma - Short-acting inhaled β-agonists are recommended as needed for symptoms and for exercise pre-treatment for those with exercise-induced bronchospasm.

Asthma exacerbation management

Asthma exacerbations are acute or sub-acute episodes of progressively worsening symptoms associated with expiratory airflow obstruction. Asthma exacerbation severity can be quantified by the number of emergency department visits, hospitalizations, and systemic glucocorticoid courses for asthma exacerbations. Previous severe asthma exacerbations, resulting in respiratory distress, hypoxia, or respiratory failure are probably the best predictors of a future life-threatening exacerbation or fatal asthma episode.

<u>Home Management of Asthma Exacerbations</u>

All asthmatics should have a written action plan that can help guide them in recognizing and assessing their overall asthma control and the severity of acute asthma

exacerbations. Recognizing symptoms early and intensifying treatment soon after symptoms worsen can often prevent further worsening and can keep exacerbations from becoming severe. If the child develops symptoms like cough, shortness of breath, wheezing, chest tightness, use of accessory muscles, and suprasternal retractions, immediate treatment with rescue medication should be started. If there is improvement, the physician should be contacted for follow–up. If there is no improvement within 4 hours, a short course of oral glucocorticoid therapy in addition to inhaled β-agonist therapy should be instituted. The physician should also be contacted for further instructions. In case of severe exacerbations, immediate medical attention should be sought.

Hospital Management of Asthma Exacerbations

For patients with a moderate to severe asthma exacerbation that does not significantly improve within 1–2 hours after the initial treatment, associated with PEFs less than 70% or oxygen saturations less than 90–92%, admission to the hospital is warranted. Supplemental oxygen, frequently administered inhaled β-agonists, and systemic glucocorticoid therapy are the treatments of choice for children admitted to the hospital for acute asthma. Several therapies, including intravenous β-agonists, intravenous theophylline, heliox (a 70:30 helium: oxygen mixture), and intravenous magnesium sulfate have some demonstrated benefit as adjunctive therapies in severe status asthmaticus. Despite intensive therapy, some asthmatic children will remain critically ill and at risk for intubation and mechanical ventilation.

Patient education

Patient education is believed to make an important difference in the home management and adherence of families to an optimal plan of care. In initial patient visits, a basic understanding of the pathogenesis of asthma can help asthmatic children and their parents to understand the importance of recommendations aimed at reducing airways inflammation. All asthmatic children and their families can benefit from a written asthma management plan with two main components:

- A daily management plan describing regular asthma medication use and other measures to keep asthma under good control
- An action plan for asthma exacerbations, describing actions to take when asthma worsens, including what medications to take and when to contact the regular physician and/or obtain emergent or urgent medical care.

Prevention

Asthma is a reversible obstructive airway disease with bronchial hyperreactivity, and bronchial hyperreactivity due to inflammation is responsible for the long term morbidity of the disease. Early intervention with anti-inflammatory medications in young children with recurrent wheezing and persistent asthma risk factors may halt the disease's progression. According to hygiene hypothesis microbial exposure early in life will divert the immune system for getting sensitized to allergens and thus prevent asthma. In addition to these measures, avoidance of environmental tobacco smoke, prolonged breast-feeding, an active lifestyle, and a healthy diet might reduce the likelihood of asthma development.

Reference:

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