ASTHMA

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Prevalence

- Very common, affects about 4-5% of the population in the United States
- Occurs at all ages but predominantly in early life
- One-half before age 10
- Another one-third before age 40
- In childhood, 2:1 male, equal after age 30

Prevalence

- Often underdiagnosed
- Increasing among the urban poor and medically underserved
- Primary care physician plays a key role in the early recognition, diagnosis, and general medical management

Definition

- Asthma is a disease of the airways characterized by increased responsiveness of the airways to a multiplicity of stimuli
- Manifested physiologically by a widespread narrowing of the air passages
- May be relieved spontaneously or with therapy

Definition

- Clinically associated with paroxysms of dyspnea, cough and wheezing
- Episodic, with acute exacerbations interspersed with disease-free intervals
- Most attacks are short-lived, lasting minutes to hours, with patient seeming to recover completely

Definition

- May have a phase where the patient experiences some degree of airflow obstruction daily
- This phase can be mild or persist for days or weeks and become severe (status asthmaticus)
- Acute attacks can be fatal
Etiology

• Heterogeneous
• Generally divided into allergic vs. idiosyncratic

Allergic Asthma

• Often associated with a personal or family history of allergic disorders such as rhinitis, urticaria, eczema
• Positive wheal-and-flare skin reactions to intradermal injections of airborne allergens
• Increased levels of IgE in the serum
• Positive response to provocation tests of inhaled antigen

“Idiosyncratic” Asthma

• Negative family and personal histories for allergies
• Normal serum IgE
• Symptoms of asthma may develop after a common cold, leading to paroxysms of wheezing and dyspnea that may last months
• Many patients won’t fit either group

Etiology

• In general, patients that develop asthma early in life tend to be “allergic,” whereas those developing it later tend to be nonallergic or to have mixed etiologies

Pathogenesis

• Common denominator is nonspecific hyperirritability of the tracheobronchial tree
• When airway reactivity is high, lung function is unstable, symptoms are severe and persistent, and the amount of therapy required is higher

Pathogenesis

• Basic mechanism appears to be airway inflammation
• Following exposure to an initiating stimulus, mediator-containing cells, such as mast cells, basophils and macrophages are activated to release a variety of inflammatory mediators which cause bronchospasm, mucus secretion, and epithelial damage
Stimuli

• The stimuli that interact with airway responsiveness and incite acute episodes of asthma can be grouped into seven categories: allergenic, pharmacologic, environmental, occupational, infectious, exercise-related, and emotional.

Allergens

• Allergic asthma is dependent on an IgE response controlled by B and T lymphocytes and activated by the interaction of antigen with mast cell-bound IgE molecules.
• Most of the allergens are airborne.
• Immunological mechanisms may cause 25-35% of asthma, and be involved with 30% more.

Allergic Asthma

• Frequently seasonal.
• Mostly seen in children and young adults.
• Nonseasonal causes include allergy to feathers, animal danders, dust mites, molds, and other antigens continuously present.

Allergic Asthma

• Exposure to the offending antigen produces an immediate response in which airway obstruction develops and then resolves.
• In 30-50% of patients, a second wave of bronchoconstriction occurs, the “late response,” which occurs 6-10 hours later.

Pharmacologic Stimuli

• Drugs implicated include aspirin, coloring agents such as tartrazine, beta blockers, and sulfiting agents.
• Aspirin triad associated with vasomotor rhinitis and polyps.
• ASA sensitivity in perhaps 10% of asthmatics (includes NSAIDs).

Air Pollution

• Asthma may be worse in heavy industrial or urban areas where atmospheric pollutants and antigens may be concentrated.
• Air pollutants known to have this effect are ozone, nitrogen dioxide, and sulfur dioxide.
Occupational Factors

- Variable airflow obstruction caused by a specific agent in the workplace
- Acute and chronic airway obstruction has been reported with a large number of compounds used in industrial processes
- The actual mechanism in many cases is unknown but many agents have allergic properties
- Examples include platinum, chrome, nickel, oak, grain, flour, castor bean, coffee beans, gums, antibiotics, toluene, persulfates, dyes, laundry detergents, animal and insect dusts, etc.

Occupational Factors: Mechanisms

- The offending agent may result in the formation of a specific IgE and cause an immunologic reaction
- The material involved may directly stimulate bronchoconstrictor release
- May "unmask" underlying asthma
- Agents divided into high molecular weight and low molecular weight compounds
- High molecular weight related to IgE and IgG antibodies

Occupational Asthma: Diagnosis

- "Stop-resume" work test
- Measurement of lung function before and after work shift
- Patient records peak flow before and after work shifts over time
- Inhalation challenge done in specially settings
- Methacholine or histamine challenge test may suffice

OA: Prognosis

- Majority fail to fully recover even several years after exposure
- May require systemic corticosteroids
- Better prognosis is associated with a shorter duration of symptoms before diagnosis, relatively normal lung function, and a lesser degree of bronchial hyperresponsiveness at the time of diagnosis
- Thus early diagnosis and removal from the offending agent are important

Evaluation

- Compensation boards use the recommendations of the AMA for evaluation of impairment/disability secondary to respiratory diseases
- The spirogram indicating the best effort is used to calculate the FEV1 and FVC
- Also document the degree of hyperreactivity in challenge testing as well as the minimal medication required to control symptoms
- Still a work in progress

Infections

- Respiratory infections are the most common type of stimuli that evoke acute exacerbations of asthma
- Respiratory viruses, rather than bacteria, are most frequently involved
- In young children--RSV and parainfluenza
- In adults--rhinovirus and influenza virus
- Increased airway reactivity may last 8 weeks after a viral infection
Exercise

- One of the most common precipitants of an asthma attack
- No long-term sequelae or change in airway reactivity
- May be the initial symptom of asthma
- Factors include the task, the temperature, and the water content of the inspired air

Emotional Stress

- A factor in at least one-half of asthmatics
- May be related to changes in vagal efferent activity and/or endorphins
- Variable effect from patient to patient and from episode to episode

Pathology

- In patients who die from asthma attacks, the most striking finding is gross overdistention of the airways, impaction of mucus, and lungs that fail to collapse when the pleural cavities are opened

Path Findings

- Numerous gelatinous plugs of exudate down to the terminal bronchiole
- Hypertrophy of bronchial smooth muscle
- Hyperplasia of submucosal vessels
- Mucosal edema
- Denudation of surface epithelium
- Thickening of basement membrane
- Eosinophilic infiltrates in the bronchial wall

Path Findings

- Many of these finding are found, at least to some extent, in the airways of asymptomatic patients
- These findings, along with consistently elevated mediator levels, have given rise to the concept that asthma is a chronic inflammatory disease

Pathophysiology

- Reduction in airway diameter
- Contraction of smooth muscle
- Vascular congestion
- Edema of the bronchial wall
- Thick tenacious secretions
### Pathophysiology
- Increased airway resistance
- Decreased forced expiratory volumes and flow rates
- Hyperinflation of the lungs and thorax
- Increased work of breathing
- Alterations in respiratory muscle function
- Changes in elastic recoil

### Pathophysiology
- Abnormal distribution of both ventilation and pulmonary blood flow with mismatched ratios
- Altered blood gases

### Pulmonary Function Abnormalities
- Forced vital capacity < 50% predicted
- FEV1 < 30% of predicted
- Residual volume may be 400% of normal
- Functional residual capacity 200% of normal

### ABG Findings
- Hypoxia in acute attacks
- Early on have decreased pCO2 (respiratory alkalosis)
- A normal or increased pCO2 may signify a severe attack
- Metabolic acidosis also may signify a severe attack

### Differential Diagnosis of Asthma
- Fictitious (glottic dysfunction)
- Upper airway obstruction or laryngeal edema
- Endobronchial disease
- Acute left ventricular failure ("cardiac asthma")
- Carcinoid tumors, recurrent pulmonary emboli, COPD

### History
- Symptoms may include coughing, wheezing, shortness of breath, chest tightness, and or sputum/production
- The pattern of symptoms may include seasonal associations, onset, duration, frequency, and day-night variation (especially nocturnal symptoms)
### History

- Must ask about factors that precipitate or aggravate the symptoms, including viral respiratory infections, environmental/occupational exposures, change in environment, drugs, food additives, climate changes, exercise, endocrine factors (pregnancy, thyroid disease) and emotions
- Age of onset, age at diagnosis
- Living situation, with consideration given to the type of heating, carpeting, humidifier, and furnishing and accessories in the patient’s bedroom (pillows, bed, floor covering, dust collectors, stuffed animals)
- Animals in the home
- Direct or sidestream exposure to smoking tobacco
- Impact of disease, including limitation on activity, number of times urgent or emergent care required, effect on lifestyle and work/school achievement
- Impact on family and assessment of family’s and patient’s perception of illness
- Family history
- Medical history
- Medication history (inhalers, steroids?)
- Hospitalizations? ventilators?
- Peak flows

### Diagnosis

- The diagnosis is made by demonstrating reversible airway obstruction
- This is defined as a 15% or more increase in FEV1 following 2 puffs of an inhaled bronchodilator
- If spirometry is normal, can do provocative tests with methacholine, histamine or cold air
Therapy

- In allergic asthma, elimination of offending agent, if possible
- Desensitization or immunotherapy have not proven to be highly effective

Drug Treatment

- Beta agonists
- Methylxanthines
- Glucocorticoids
- Mast cell stabilizing agents
- Anticholinergics

Beta Agonists

- Produce airway dilatation through stimulation of beta receptors with resultant formation of cyclic AMP
- Also decrease release of mediators and improve mucociliary transport
- Short acting, work best by inhalation
- Most commonly used are metaproterenol, albuterol, terbutaline, and salbutamol

Beta Agonists

- Except for metproterenol, these drugs are highly selective for the respiratory tract
- Allows maximal effect with few side effects, especially by inhalation
- May last longer than 6 hours
- Inhaled is the preferred route for both acute and chronic therapy

Methylxanthines

- Theophylline is a medium-potency bronchodilator working through an undefined mechanism
- Therapeutic level generally 10-20 ug/ml
- Clearance highly variable, multifactorial
- Many drug interactions
- Side effects include nervousness, nausea, vomiting, anorexia, headaches, seizures

Glucocorticoids

- Not bronchodilators
- Reduce airway inflammation
- Most beneficial in acute illness to reduce inflammation, and in chronic illness to prevent exacerbations
- Used in conjunction with beta agonists
- Various inhaled steroids are available and considered first-line therapy
Mast Cell Stabilizers

- Cromolyn sodium and nedocromil sodium
- Also, not bronchodilators
- Major effect is to inhibit the degranulation of mast cells, thereby blocking mediator release
- Most efficacious in atopic individuals with seasonal variation

Anticholinergic Agents

- Derived from atropine, which works but has lots of side effects
- Ipratropium bromide the main compound
- May have an additive effect to beta agonists
- Are slow to act, modest potency

Leukotriene Antagonists

- Accolate (Zafirlukast): 20 mg PO BID, the first, used for prophylaxis and chronic treatment
- Zyflo (Zileuton): blocks 5-lipoxygenase, can’t use with liver disease, 600 mg QID
- Singulair (Montelukast Sodium): inhibits LTC4, LTD4, and LTE4, 10 mg daily

Leukotriene Antagonists

- All are for chronic therapy
- Singulair also approved for children 6 to 14 years old
- Generally used in addition to patients regular regimen
- May be able to decrease steroid use