Bronchial asthma

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• chronic inflammatory disease of the airways, characterized by recurrent respiratory symptoms:
  • dyspnea, wheezing, chest tightness and/or cough
  • almost always associated with reversible airflow limitation
Patient’s point of view...
Asthma prevalence worldwide

Proportion of population (%)

- ≥10.1
- 7.6-10.0
- 5.1-7.5
- 2.6-5.0
- 0-2.5
- No standardised data available
Asthma prevalence increase

Country (prevalence %)

- Costa Rica (27.4)
- Australia (27.0)
- New Zealand (26.9)
- United Kingdom (24.8)
- Japan (20.6)
- Panama (19.8)
- Barbados (18.8)
- Singapore (17.0)
- Canada (15.1)
- Taiwan (13.5)
- Chile (11.6)
- Malaysia (11.3)
- Malta (11.2)
- Sultanate of Oman (10.5)
- Portugal (9.8)
- South Korea (9.1)
- Spain (8.8)
- Italy (8.6)
Asthma prevalence in USA by race, 1980–1994

Hospitalization rates for asthma in USA

**Global Initiative for Asthma (GINA).** WHO/NHLBI, 1995
• exaggerated responsiveness of the airways to various stimuli

• rather specific inflammation of the airways (CD4+ T-cells, eosinophils and metachromatic cells in the mucosa, increased thickness of the reticular layer of the epithelial basement membrane
Pathological changes in asthma

Normal airway

- Epithelium
- Basement membrane
- Smooth muscle
- Mucus glands
- Mucus plug

Constricted airway in asthma

Robbins Pathologic Basis of Disease. 6th ed. WB Saunders, 1999
Pathological changes in asthma

- Mucous plug
- PAS-positive matrix
- Polymorphonuclear neutrophils
- Eosinophils
- Charcot-Leyden crystals
- Curschmann's spirals
- Cluster of epithelial cells (creola body)
- Bacteria and/or viruses
- Epithelial denudation
- Hyaline thickening of basement membrane
- Hypertrophy of smooth muscle, mucous glands, and goblet cells
- Inflammatory exudate with eosinophils and oedema
- Engorged blood vessels

Microscopic Definition

Epidemiology

Pathogenesis

Diagnosis

Differential diagnosis

Treatment
Airway modulation due to chronic inflammation

Pathophysiology of asthma

Macrophage

Antigen etc.

Mast cell

T-lymphocyte

Mucus plug

Vasodilation

New vessels

Plasma leak

Oedema

Eosinophil

Subepithelial fibrosis

Sensory nerve

Efferent nerve

Airway constriction and smooth muscle hypertrophy/hyperplasia

### Triggers

#### Inducers
- allergens
- viral infections
- occupational

Enhance inflammatory response

#### Provokers
- exercise
- irritants
- emotions
- aspirin

Activate bronchospasm

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Adapted from Busse WW. J Allergy Clin Immunol 1998
Risk factors

- familial predisposition
- atopy
- exposure to allergens and sensitising agents
Classification

- allergic asthma
- adult-onset asthma (usually non-allergic)
- occupational asthma
- asthma in smokers
- asthma in obese
Minimum requirements for the diagnosis

- clinical history + lung function test
## Symptoms

- wheezing
- chest tightness
- episodic shortness of breath

\[ \text{90\% of patients} \]

- chronic cough

all symptoms are non-specific!
Physical examination

• normal in stable condition
• during attacks:
  – general signs:
    • use of accessory muscles
    • intercostal recession
    • anxiety
    • cyanosis
    • drowsiness, confusion
    • tachycardia
  – on chest:
    • signs of acute hyperinflation:
      – barrel-chest, hypersonorous percutoric sound, low diaphragmatic position, poor diaphragmatic excursion
    • signs of airway obstruction
      – vesicular breathing, prolonged expiration, expiratory wheezing, rhonchi
Lung function test

- obstructive ventilatory disorder
- hyperinflation of the lung
- reversibility of the obstruction
- diurnal variability of the obstruction
- airway hyperresponsiveness
- increased lung diffusion capacity
- increased FENO
Obstructive ventilatory disorder
Hyperinflation of the lung

**Definition**

**Epidemiology**

**Pathogenesis**

**Diagnosis**

**Differential diagnosis**

**Treatment**
Reversibility of the obstruction to bronchodilators

- \((\text{FEV1 after} - \text{FEV1 before})/\text{FEV1 before} \times 100\)
- \(\Delta \text{FEV1}>12\% \text{ and } >200 \text{ ml} = \text{asthma}\)
Diurnal variability of the obstruction

Definition
Epidemiology
Pathogenesis
Diagnosis
Differential diagnosis
Treatment
Diurnal variability of the obstruction

- \[
\frac{(\text{PEF}_{\text{max}} - \text{PEF}_{\text{min}})}{((\text{PEF}_{\text{max}} + \text{PEF}_{\text{min}})^2)} \times 100
\]

- variability >20% = asthma
Airway hyperresponsiveness

- $\Delta$FEV1>20% RV
Lung function test

- obstructive ventilatory disorder
- hyperinflation of the lung
- reversibility of the obstruction
- diurnal variability of the obstruction
- airway hyperresponsiveness
- increased lung diffusion capacity
- increased FENO
• Allergy tests

• Skin tests
• Specific IgE
• Total IgE level – no diagnostic value
Differential diagnosis

- Foreign body
- Endobronchial tumor
- Vocal cord dysfunction
- COPD
- Eosinophilic bronchitis
- Postinfectious airways hyperresponsiveness

- Churg-Strauss sy.
- Left ventricular failure
- Carcinoid
- ABPA
- GERD
- Drugs (IACE, beta-blockers)
### Asthma or COPD?

<table>
<thead>
<tr>
<th>Feature</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>earlier</td>
<td>later</td>
</tr>
<tr>
<td>Smoking</td>
<td>?</td>
<td>+++</td>
</tr>
<tr>
<td>Attacks</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Nocturnal attacks</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>History of allergy</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Family history</td>
<td>+++</td>
<td>?</td>
</tr>
<tr>
<td>PEF variability</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Airway hyperresponsiveness</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Response to bronchodilators</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Effect of corticosteroids</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>DLCO</td>
<td>normal or ↑↓</td>
<td></td>
</tr>
<tr>
<td>FENO</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Sputum</td>
<td>Eosinophilia</td>
<td>Neutrophilia</td>
</tr>
<tr>
<td>Allergy tests</td>
<td>+++</td>
<td>-</td>
</tr>
</tbody>
</table>
## Drugs in asthma treatment

**Relievers:**
- SABA (salbutamol, fenoterol...)
- Anticholinergic agents (ipratropium)

**Controllers:**
- ICS (beclomethasone, budesonide, fluticasone, flunisolide...)
- LABA (salmeterol, formoterol, indacaterol)
- Cromoglycate (nedocromil)
- Leukotriene modifying agents (zfirlucast, montelucaet)
- Systemic corticosteroids
- Anti-IgE monoclonal antibodies (omalizumab)
- Theophyllines
How it works?

- Virus?
- Adenosine
- Exercise
- Fog
- Antigen
- Macrophage
- Eosinophil
- Virus?
- T-lymphocyte
- ICS
- Mast cell
- Bronchoconstriction
- Plasma leak
- Sensory nerve activation
- Airway hyper-responsiveness

Definition
Epidemiology
Pathogenesis
Diagnosis
Differential diagnosis
Treatment
# Steps in the asthma treatment

<table>
<thead>
<tr>
<th>SABA as-needed</th>
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<th>SABA as-needed</th>
<th>SABA as-needed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low-dose ICS</strong></td>
<td><strong>Medium or high-dose ICS</strong></td>
<td><strong>Medium or high-dose ICS+LABA</strong></td>
<td><strong>Medium or high-dose ICS+LABA+leukotriene modifier</strong></td>
<td><strong>Medium or high-dose ICS+LABA+leukotriene modifier+SR theophylline</strong></td>
</tr>
<tr>
<td><strong>leukotriene modifier</strong></td>
<td><strong>Low-dose ICS+leukotriene modifier</strong></td>
<td><strong>Low-dose ICS+LABA+leukotriene modifier</strong></td>
<td><strong>Low-dose ICS+LABA+leukotriene modifier+SR theophylline</strong></td>
<td><strong>Low-dose ICS+LABA+leukotriene modifier+SR theophylline+oral CS</strong></td>
</tr>
<tr>
<td><strong>Education, environmental control</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Asthma control

<table>
<thead>
<tr>
<th></th>
<th>controlled (all of following)</th>
<th>partly controlled (any)</th>
<th>uncontrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>daytime symptoms</strong></td>
<td>&lt;3 times per week</td>
<td>&gt;twice per week</td>
<td>&gt;2 features of partly controlled asthma</td>
</tr>
<tr>
<td><strong>limitations of activities</strong></td>
<td>none</td>
<td>any</td>
<td></td>
</tr>
<tr>
<td><strong>nocturnal symptoms</strong></td>
<td>none</td>
<td>any</td>
<td></td>
</tr>
<tr>
<td><strong>need for reliever</strong></td>
<td>&lt;3 times per week</td>
<td>&gt;twice per week</td>
<td></td>
</tr>
<tr>
<td><strong>lung function</strong></td>
<td>normal</td>
<td>&lt;80% PV</td>
<td></td>
</tr>
<tr>
<td><strong>exacerbations</strong></td>
<td>none</td>
<td>&gt;=1 per year</td>
<td>1 per week</td>
</tr>
</tbody>
</table>
Patient education

- check the inhalation technique
- instruct in drugs dosage adaptation
- individual written plan
Controlled: Maintain and find lowest controlling step.
Partly controlled: Consider stepping up to gain control.
Uncontrolled: Step up until controlled.