BRONCHIAL ASTHMA

Lecturer: Professor Vladimir Babadzhan
Asthma is a chronic inflammatory disorder of the airways causes recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or in the early morning.

These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment.
ASTHMA
A lung disease characterized by
1. airways obstruction that is reversible, either spontaneously or with treatment,
2. airways inflammation, and
3. increased airways responsiveness to a variety of stimuli.
Asthma

Affects 5-10% of the population in industrialized countries

Is a recurrent and reversible (in the short term) obstruction to the airways in response to substances (or stimuli) that:

- are not necessarily noxious
- normally do not affect non-asthmatic subjects

Causes of attacks are numerous:

- allergens (in atopic individuals)
- exercise (cold, dry air)
- respiratory infections (e.g. viral)
- smoke, dust, environmental pollutants etc.

Acute severe asthma (status asthmaticus) is a medical emergency and can be fatal (~2000 deaths per annum in the U.K.)
Pathogenesis of asthma

- **Allergens** *Allergic asthma* is frequently seasonal. A nonseasonal form may result from allergy to feathers, animal danders a.s.

- **Pharmacologic Stimuli** - aspirin, coloring agents such as tartrazine, beta-adrenergic antagonists. The typical *aspirin-sensitive respiratory syndrome* – a perennial vasomotor rhinitis, a hyperplastic rhinosinusitis, nasal polyps and asthma.

- **Environment And Air Pollution.**

- **Occupational Factors** *Occupation-related asthma* can result from working with *metal salts* (platinum, chrome, nickel), *wood and vegetable dusts* (oak, grain, flour, green coffee bean), *pharmaceutical agents* (antibiotics, piperazine, cimetidine), *industrial chemicals and plastics* (persulfates, ethylenediamine), *biologic enzymes* (laundry detergents), and *animal and insect dusts, serums, and secretions.*

- **Infections** - respiratory viruses.
Asthma - intermittent attacks of bronchoconstriction cause:
- cough
- wheezing
- difficulty in breathing

Chronic asthma involves pathological changes to the bronchioles that result from long standing inflammation (\( \bullet = \text{inflammatory cells} \))

1. increased mass of smooth muscle
2. accumulation of interstitial fluid (oedema)
3. increased secretion of mucus
4. epithelial damage (exposing sensory nerve endings)

Airway narrowing by inflammation and bronchoconstriction increase airway resistance decreasing FEV\(_1\) and PEFR
Initial presentation of an antigen (e.g. dust mite protein or pollen) initiates an adaptive immune response.
IgE antibodies (immunoglobulin)

DEVELOPMENT OF ALLERGIC ASTHMA (2)

Effector phase

Storage granule

Mast cells in airway tissue (express IgE receptors in response to IL-4 and IL-13 released from Th2 cells)

Eosinophils (differentiate and activate in response to IL-5 released from Th2 cells)

IL-4

Th2

B

P

B

P

IgE

IgE receptor (Fcε)

+
Subsequent presentation of antigen

Cross links IgE receptors

Stimulates calcium entry into mast cells evoking:

- release of secretory granules containing histamine and the production and release of other agents (e.g., leukotrienes $\text{LTC}_4$ and $\text{LTD}_4$) that cause airway smooth muscle contraction

- release of substances (e.g., $\text{LTB}_4$) that attract cells causing inflammation (e.g., eosinophils) into the area
Early phase

- Antigen
- IgE
- IgE Receptor
- Ca$^{2+}$ Channel
- Storage granule
- Spasmogens (e.g., Histamine, Leukotrienes)
- Chemotaxins (e.g., LTB$_4$)

Delayed phase

- Infiltration
- Eosinophils, Th2 cells, and monocytes
- Spasmogens (LTC$_4$, LTD$_4$)
- Proteins causing epithelial damage (airway irritation)

Smooth muscle contraction - bronchoconstriction

DEVELOPMENT OF ALLERGIC ASTHMA (4)
In many individuals, an asthma attack comprises immediate (mainly bronchospasm) and delayed (inflammatory reaction) phases.
PATHOLOGY

In a patient who has died of acute asthma, the most striking feature of the lungs at necropsy is their gross overdistention and failure to collapse when the pleural cavities are opened. When the lungs are cut, numerous gelatinous plugs of exudate are found in most of the bronchial branches down to the terminal bronchioles.

Histologic examination shows hypertrophy of the bronchial smooth muscle, hyperplasia of mucosal and submucosal vessels, mucosal edema, denudation of the surface epithelium.
History of Asthma

• Symptoms: cough, wheezing, shortness of breath, chest tightness, sputum production.
• Symptom patterns:
  - Perennial versus seasonal;
  - Continual versus episodic;
  - Duration, severity, and frequency;
  - Diurnal variations (nocturnal and early-morning awakenings).
• Precipitating or aggravating factors: allergens, occupation, medications, exercise.
• Disease development: age at onset, history of injury early in life due to infection or passive smoke exposure, progress of disease, current response to management, comorbid conditions, the profile of exacerbation.
• Family history: asthma, allergy, sinusitis, rhinitis.
• Social history: home characteristics, smoking, workplace or school characteristics, educational level, employment, social support.
Physical examination

• General: respiratory distress (increased respiratory and cardiac rates, diaphoresis, and use of accessory muscles of respiration); weight loss or wasting (indicate emphysema); pulsus paradoxus (occur during an acute asthma exacerbation), depressed sensorium (during a severe asthma exacerbation with impending respiratory failure).

• Chest examination: end-expiratory wheezing or a prolonged expiratory phase is found; diminished breath sounds and chest hyperinflation (during exacerbations).

• Upper airway: look for the presence of polyps from sinusitis, allergic rhinitis, or upper respiratory infection.

• Skin: Observe for the presence of atopic dermatitis, eczema, or other manifestations of allergic skin conditions.
Causes (factors that can contribute to asthma)

- Environmental allergens, pollutants, tobacco smoke
- Viral respiratory infections
- Exercise; hyperventilation
- Gastroesophageal reflux disease
- Chronic sinusitis or rhinitis
- Aspirin or NSAID-hypersensitivity, sulfite sensitivity
- Beta-blockers
- Occupational exposure, emotional factors
- Irritants (household sprays and paint fumes).

Factors that contribute to EIA symptoms include:

- Exposure to cold or dry air
- Environmental pollutants (e.g., sulfur, ozone)
- Level of bronchial hyperreactivity
- Chronicity of asthma and symptomatic control
- Duration and intensity of exercise
- Allergen exposure in atopic individuals
- Coexisting respiratory infection
Laboratory Findings

Eosinophilia (> 250 to 400 cells/μL);

Sputum:

*Grossly*, it is tenacious, rubbery, and whitish; in the presence of infection it may be yellowish.

*Microscopically:*

- eosinophils;
- histiocytes and polymorphonuclear leukocytes.
- Eosinophilic granules from disrupted cells *(Creola bodies)*.
- Elongated dipyramidal crystals *(Charcot-Leyden)* originating from eosinophils.
- bronchitic elements, polymorphonuclear leukocytes and bacteria.
Lab Studies

Eosinophilia greater than 4% or 300-400/μL supports the diagnosis of asthma.

Total serum immunoglobulin E levels greater than 100 IU are observed in patients experiencing allergic reactions.
Mucous Cast of Small Airway in Sputum
Charcot-Leyden Crystals
Creola Body
Eosinophils
Imaging Studies

Chest radiography. In most patients, chest radiography findings are normal or indicate hyperinflation. Findings may help determine other pulmonary diseases such as chronic bronchitis (emphysema, pneumosclerosis, increase pulmonary roots), pneumonia.

Sinus CT scan may be useful to determine acute or chronic sinusitis as a contributing factor.

Other Tests:

Allergy skin testing is a useful adjunct in individuals with atopy. Results help guide indoor allergen mitigation or help diagnose allergic rhinitis symptoms.

In patients with reflux symptoms and asthma, 24-hour pH monitoring or FGDS can help determine if gastroesophageal reflux disease is a contributing factor.
Pulmonary function testing (spirometry)

Perform spirometry measurements before and after inhalation of a short-acting bronchodilator in all patients in whom the diagnosis of asthma is considered.

Spirometry measures the forced vital capacity, the maximal amount of air expired from the point of maximal inhalation, and the FEV₁.

A reduced ratio of FEV₁ to forced vital capacity, when compared with predicted values, demonstrates the presence of airway obstruction.

Reversibility is demonstrated by an increase of 12% or 200 mL after administration of a short-acting bronchodilator.
Diagnostics
Determination of severity
Determination of prognosis
Monitoring of disease progression

Basic indexes of spirometry
FEV$_1$ – the Force expiratory volume for the first second;
FVC – the Force vital capacity;
FEV$_1$/FVC (%) - the relation shown in percents
OVERVIEW OF DRUGS USED IN THE TREATMENT OF ASTHMA

Symptomatic (bronchodilators)

First line
- β2-Adrenoceptor agonists

Second line
- Muscarinic ACh receptor antagonists
- Cysteinyi leukotriene receptor antagonists
- Xanthines

Prophylactic (prevent inflammation)

First line
- Glucocorticosteroids

Second line
- Xanthines
- Cromoglycates

Anti-inflammatory (resolve inflammation)

- Glucocorticosteroids
DRUGS USED IN THE TREATMENT OF ASTHMA
Bronchodilators (1 continued)

β2-Adrenoceptor agonists – short acting agents (e.g. salbutamol)

- are first line treatment for mild, intermittent, asthma
- are ‘relievers’ taken as needed
- are usually administered by inhalation via metered dose/dry powder devices (lessens systemic effects) - oral and i.v. administration are also sometimes used
- act rapidly (often within 5 minutes) to relax bronchial smooth muscle - relaxation persists for 4-6 hours
- increase mucus clearance and decrease mediator release from mast cells and neutrophils
- have few adverse effects (due to systemic absorption) when administered by the inhalational route, tremor being the most common
DRUGS USED IN THE TREATMENT OF ASTHMA
Bronchodilators (2 continued)

β2-Adrenoceptor agonists – longer acting agents (e.g. salmeterol)

- are not recommended for acute relief of bronchospasm (can be relatively slow to act)
- are useful in nocturnal asthma
- can be used as add-on therapy in asthma inadequately controlled by other drugs (e.g. glucocorticosteroids)

NOTE!

1. The use of selective β2-adrenoceptor agonists reduces potentially harmful stimulation of cardiac β1-adrenoceptors. Non-selective agonists (e.g. isoprenaline) are redundant
2. The use of non-selective β-adrenoceptor antagonists (e.g. propranolol) in asthmatic patients is contraindicated – risk of bronchospasm
CYSTEINYL LEUKOTRIENE (CysLT) RECEPTOR ANTAGONISTS - act as competitive antagonists at the CysLT receptor. Cysteinyl leukotrienes ($\text{LTC}_4$ and $\text{LTD}_4$) released from mast cells and infiltrating eosinophils cause smooth muscle contraction, mucus secretion and oedema.
CysLT receptor antagonists (e.g. Montelukast & Zafirlukast)

- are effective as add on therapy in mild persistent asthma and in combination with other medications in more severe conditions
- are effective against antigen-induced and exercise-induced bronchospasm
- relax bronchial smooth muscle in response to LTC$_4$ & LTD$_4$,
- are delivered by the oral route
- are not recommended for relief of acute severe asthma (bronchodilator activity < salbutamol)
- are generally well tolerated
DRUGS USED IN THE TREATMENT OF ASTHMA
Bronchodilators (4 continued)

Non-selective muscarinic ACh receptor antagonists (e.g. ipratropium)

- are delivered by the inhalational route
- have a delayed (>30 min) onset of action
- are second line drugs – used as an adjunct to β2-adrenoceptor agonists and glucocorticosteroids
- relax bronchospasm caused by irritant stimuli (irritants initiate a vagal reflex that liberates ACh)
- decrease mucus secretion
- have no effect on the late inflammatory stage
- have few adverse effects

More effective agents (e.g. tiotropium) with selectivity for M3 muscarinic receptors have recently been introduced.
DRUGS USED IN THE TREATMENT OF ASTHMA
Bronchodilators (5)

XANTHINES (e.g. Theophylline and Aminophylline)

- are present in coffee, tea and chocolate-containing beverages
- have an uncertain molecular mechanism of action - might involve inhibition of isoforms of phosphodiesterases that inactivate cAMP and cGMP (second messengers that relax smooth muscle)
- combine bronchodilator and anti-inflammatory actions (relax bronchial smooth muscle, inhibit mediator release from mast cells, increase mucus clearance)
- are second line drugs used in combination with $\beta_2$-adrenoceptor agonists and glucocorticosteroids
- are delivered by the oral route as sustained release preparations
- have several adverse effects at therapeutic concentrations including: nausea, vomiting abdominal discomfort and headache – problematic because of numerous drug interactions – mandates monitoring serum concentrations
Classification of severity and treatment options of BA

Step 1 – Intermittent bronchial asthma

• Intermittent symptoms occurring less than once a week
• Brief exacerbations
• Nocturnal symptoms occurring less than twice a month
• Asymptomatic with normal lung function between exacerbations
• No daily medication needed
• Occasional use of inhaled short acting beta2-adrenoceptor agonist bronchodilators (salbutamol 100 mcg 3-4 times daily).

• FEV1 or PEF rate greater than 80%, with less than 20% variability
Classification of severity and treatment options of BA

Step 2 - Mild persistent bronchial asthma. Symptoms occurring more than once a week but less than once a day
- Exacerbations affect activity and sleep
- Nocturnal symptoms occurring more than twice a month
- **Regular inhaled anti-inflammatory agents.**
- Inhaled short acting beta2-adrenoceptor agonists
  - as required **plus** an inhaled low dose of steroid range 250-500 mcg daily (budesonide 100 mcg or fluticasone 125 mcg 1-2 puffs q12h),
  - or long-acting bronchodilator, especially for nighttime symptoms, long-acting beta2-agonist salmeterole 25 mcg 1-2 puffs q12h, formoterol 4.5 mcg 1-2 puffs q12h.
  - combine inhaler: **symbicort** (budesonide 160 mcg+formoterole 4.5 mcg) 1 puff q12h; **seretid** (salmeterol 25 mcg+fluticasone125 mcg) 25/125 or 50/250 mcg 1 puff q12h.
  - Alternatively sodium cromoglycate 20 mcg or nedocromil sodium 2-4 puffs bid/qid.
- FEV1 or PEF rate greater than 80% predicted, with variability 3f 20-30%.
Classification of severity and treatment options of BA

Step 3 - Moderate persistent bronchial asthma

Daily symptoms
- Exacerbations affect activity and sleep
- Nocturnal symptoms occurring more than once a week
- **Medium dose inhaled steroids**, the dose range 500-1000 mcg daily (beclomethasone 250 mcg, budesonide 200 mcg or fluticasone 250 mcg 1-2 puffs q12h).
- **plus long-acting bronchodilator**, especially for nighttime symptoms (salmeterole 25 mcg 1-2 puffs q12h, formoterol 4.5 mcg 1-2 puffs q12h.).
- combine inhaler: **seretid** (salmeterol 25 mcg+fluticasone 250 mcg) 25/250 or 50/250 mcg), **symbicort** (budesonide 160 mcg+formoterole 4.5 mcg) 1-2 puffs q12h.
- sustained-release theophylline 150 mg q12h.

$\text{FEV}_{1}$ rate 60-80% of predicted, with variability greater than 30%.
Classification of severity and treatment options of BA

Step 4 - Severe persistent bronchial asthma

Continuous symptoms
• Frequent exacerbations
• Frequent nocturnal asthma symptoms
• Physical activities limited by asthma symptoms

• **High dose inhaled steroids** (1000-2000 mcg daily)
  • and regular inhaled long-acting beta2-adrenoceptor agonist (salmeterole 50 mcg or formoterole 12 mcg) 2 puffs q12h.
  • **seretid** (salmeterol 25 mcg+fluticasone 500 mcg) 25/500 50/500 mcg) 1-2 puffs q12h.
  • sustained-release theophylline 150 mg q12h and
  • inhaled ipratropium bromide 25 mcg 1 puff q12h or oxitropium bromide, long acting oral beta2-adrenoceptor agonist (sustained release salbutamole or terbutaline preparations), FEV1 or PEF rate less than 60%, with variability greater than 30%.
Classification of severity and treatment options of BA
Step 5 - Severe persistent (steroid-dependent) bronchial asthma
Addition of regular oral steroid therapy.
• Inhaled short acting beta$_2$-adrenoceptor agonists as required with an inhaled steroid in high dose (800-2000 mcg) with nebulizer (budesonide 400 mcg or fluticasone propionate 1000 mcg)
• one or more of the long acting bronchodilators
• regular prednisolone (medrol) 5-15 mg (or mometasone 4-16 mcg, hydrocortisone5-15 mg) tablets in the lowest dose necessary to control symptoms in a single daily dose.
Short Course Oral Steroid Treatments

For adults 30-60 mg of prednisolone can be given initially and the same dose continued in single daily doses each morning until 2 days after control has been re-established. Indications for 'rescue' courses of prednisolone include:
- symptoms and peak expiratory flow (PEF) progressively worsening day by day
- fall of PEF below 60% of the patient's best known recording
- onset or worsening of sleep disturbance by asthma
- persistence of morning symptoms until midday
- progressively diminishing response to an inhaled bronchodilator
- symptoms severe enough to require treatment with nebulised or injected bronchodilators.
# Treatment of Asthma (1)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose and Route</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Selective beta$_2$-agonists</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol (Ventolin, Proventil)</td>
<td>100 mcg 1-2 puffs q4-6h; not to exceed 12 puffs/d; may use 2-4 puffs q20min for 3 doses to treat an acute exacerbation. Nebulizer: Dilute 0.5 mL (2.5 mg) 0.5% inhalation solution in 1-2.5 mL of NS; administer 2.5-5 mg q4-6h, diluted in 2-5 mL sterile saline or water</td>
<td>Selective beta$_2$ agonist; beta$_1$ (cardiac) effects at higher doses (inhalation preferred route)</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>25 and 50 mcg 2 puffs (42 mcg) bid. Diskus: 1 puff (50 mcg) bid</td>
<td>Selective beta$_2$ agonist; long-acting agent for maintenance therapy</td>
</tr>
</tbody>
</table>
# Treatment of Asthma (2)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose and Route</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methylxanthines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Theophylline (Slo-bid, Theo-Dur, Uniphyl)</td>
<td>150 – 300 mg td PO, IV twice per day or once daily 0.5 mg/kg</td>
<td>Nervousness, nausea, vomiting, anorexia, and headache.</td>
</tr>
<tr>
<td>Aminophylline</td>
<td>5 – 10 ml 2,5 % IV 1 – 2 d, 5-6 mg/kg toad 0.3-0.6 mg/kg maint. infusion</td>
<td>Side-effects common. Therapeutic level 10-20μg/ml</td>
</tr>
<tr>
<td><strong>Anticholinergic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipatropium bromide (Atrovent)</td>
<td>Nebulizer: 1-dose vial (500 mcg) q2h for acute exacerbations MDI: 2 puffs qid; not to exceed 12 puffs/d</td>
<td>60 to 90 min may be required before peak bronchodilation is achieved.</td>
</tr>
</tbody>
</table>
## Treatment of Asthma (3)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose and Route</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Topical corticosteroids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluticasone (Flovent)</td>
<td>44-mcg MDI: 2 puffs bid for mild persistent asthma</td>
<td>Onset of action 2 hours</td>
</tr>
<tr>
<td></td>
<td>125 - 250-mcg MDI: 2 puffs bid for moderate-to-severe persistent asthma</td>
<td></td>
</tr>
<tr>
<td>Triamcinolone (Azmacort)</td>
<td>180 mcg 2 puffs tid/qid or 4 puffs bid; not to exceed 4 puffs qid for mild</td>
<td>Onset of action 6 hours</td>
</tr>
<tr>
<td></td>
<td>persistent or easily controlled moderately severe asthma</td>
<td></td>
</tr>
<tr>
<td>Beclomethasone (Vanceril,</td>
<td>250 mcg, 2 puffs tid/qid; Severe asthma: 12-16 puffs (1000-1500 mcg)/d;</td>
<td>thrush (Oropharyngeal candidiasis) and dysphonia</td>
</tr>
<tr>
<td>Beclovent, QVAR)</td>
<td>adjust dose downward to response</td>
<td></td>
</tr>
</tbody>
</table>
## Treatment of Asthma (4)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose and Route</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Corticosteroids</strong></td>
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</tr>
<tr>
<td>Methyl-prednisolone (Solu-Medrol)</td>
<td>IV 1-2 mg/kg q6-12h</td>
<td>Onset of action 6 hours</td>
</tr>
<tr>
<td>Prednisone</td>
<td>PO 60-120 mg q12h</td>
<td>Onset of action 6 hours</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>PO, IV 30 to 40 mg once daily</td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>IV 4 mg/kg q6h</td>
<td></td>
</tr>
<tr>
<td>Beclomethasone dipropionate</td>
<td>2 puffs 3 to 4 times daily for adults</td>
<td>thrush (Oropharyngeal candidiasis) and dysphonia</td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>------</td>
<td></td>
</tr>
<tr>
<td>Flunisolide</td>
<td>2 puffs twice daily</td>
<td></td>
</tr>
</tbody>
</table>
### Treatment of Asthma (5)

<table>
<thead>
<tr>
<th>Mast cell-stabilizing agents</th>
<th>Cromolyn sodium (Intal)</th>
<th>20 mg, 2 puffs 4 times daily for 4 to 6 weeks</th>
<th>for maintenance therapy only and has no place in treatment of the acute attack</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nedocromil sodium (Tilade)</td>
<td>7 mg, 2 puffs qid (14 mg/d)</td>
<td></td>
</tr>
</tbody>
</table>

**Antibiotics for treatment infective-dependent exasorbtion**

<table>
<thead>
<tr>
<th>Levofloxacin (Loxof)</th>
<th>PO, IV infusion 400 mg d</th>
<th>Used only with clinical evidence of bacterial infection.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spiramicin (Rovamycin)</td>
<td>PO 3000000 IU q12h</td>
<td></td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>IV, IM 750 mg q8h</td>
<td></td>
</tr>
</tbody>
</table>
General Principles of the Drugs Use in exacerbation of asthma:

1) Bronchodilators should be used in orderly progression, with the patient under close observation during initial therapy.

2) Inhalation of nebulized bronchodilators (ventolin) and steroids (pulmicort or flixotide).

3) Parenteral steroids – prednisolon 60 mg IV drops 1-2 times daily, dexametason 8 mg IV drops 1-2 times daily.

4) Sodium bicarbonate 5% 100-200 ml IV drops ones daily.

5) Myotrop concentrix: nospa 2% 4 ml IV drops 1-2 times daily.

6) Antibiotics ceftriaxon 1 g IV drops 2 times daily + levofloxsaxin 500 mg IV drops ones daily.
An Acute Attack of Asthma

The symptoms of asthma consist of a triad of dyspnea, cough, and wheezing. Respiration becomes audibly harsh, wheezing in both phases of respiration becomes prominent, expiration becomes prolonged, and patients frequently have tachypnea, tachycardia, and mild systolic hypertension. The patient prefers to sit upright or even leans forward, uses accessory muscles of respiration, is anxious, and may appear to struggle for air. Chest examination shows a prolonged expiratory phase with relatively high-pitched wheezes throughout inspiration and most of expiration. They have "squared off" thorax. Although coarse rhonchi may accompany the wheezes, fine crackles are not heard unless pneumonia, atelectasis, or cardiac decompensation is also present. The cough during an acute attack sounds "tight" and is generally nonproductive of mucus. Tenacious mucoid sputum is produced as the attack subsides.
## Staging Of The Severity Of An Acute Asthma Attack

<table>
<thead>
<tr>
<th>Stage</th>
<th>Symptoms and Signs</th>
<th>FEV&lt;sub&gt;1&lt;/sub&gt; or FVC</th>
<th>pH</th>
<th>PaCO&lt;sub&gt;2&lt;/sub&gt;</th>
<th>PaO&lt;sub&gt;2&lt;/sub&gt; (Room air)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (mild)</td>
<td>Mild dyspnea, diffuse wheezes, adequate air exchange</td>
<td>50-80% of N</td>
<td>N or ↑</td>
<td>N or ↑</td>
<td>N or ↓</td>
</tr>
<tr>
<td>II (moderate)</td>
<td>Respiratory distress at rest.  hyperpnea, use of accessory muscles. marked wheezes, air exchange N or ↓</td>
<td>50% N</td>
<td>N or ↑</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>III (severe)</td>
<td>Marked respiratory distress, cyanosis, use of accessory muscles, marked wheezes or absent breath sounds; check for pulsus paradoxus 20-30 mm Hg</td>
<td>25% N</td>
<td>↓</td>
<td>N or ↑</td>
<td>↓↓</td>
</tr>
<tr>
<td>IV (respiratory failure)</td>
<td>Severe respiratory distress, lethargy, confusion, prominent pulsus paradoxus 30-50 mm Hg, use of accessory muscles</td>
<td>10% N</td>
<td>↓↓</td>
<td>↑↑</td>
<td>↓↓↓</td>
</tr>
</tbody>
</table>
Complications During an Acute Attack of Asthma

- **Spontaneous pneumothorax** may present as a sudden worsening of respiratory distress, accompanied by sharp chest pains and, on physical examination, a shift of the mediastinum. X-ray examination confirms the diagnosis.

- **Mediastinal and subcutaneous emphysema** due to alveolar rupture and dissection of air along vessels is occasionally observed.

- **Atelectasis**, usually involving the right middle lobe or even an entire lung, is more common.

- **Bronchiectasis** is rare.

- While evidence of acute **cor pulmonale** can occasionally be noted on an ECG, chronic cor pulmonale secondary to asthma is rare.
Immediate Assessment Of Acute Severe Asthma

Features of severity
- Pulse rate >120 per mm
- Pulsus paradoxus
- Unable to speak in sentences
- Peak flow < 50% of expected

Life-threatening features
- Can't speak
- Central cyanosis
- Exhaustion, confusion, reduced conscious level
- Bradycardia
- 'Silent chest'
- Unrecordable peak flow

Arterial blood gases in life-threatening asthma
- A normal (5-6 kPa) or high CO₂ tension
- Severe hypoxaemia (< 8 kPa) especially if being treated with oxygen
- A low pH or high [H⁺]
Treatment of the acute attack of asthma

• Stage I or II - high doses of aerosolized beta2 agonists (salbutamol 200 – 400 mcg or phormoterol 5 – 10 mcg) for nebulization or with a spacers every 20 min for three doses. Thereafter, to every 2 h until the attack has subsided. Aminophyllline should be given IV 250 mg (2,5% 10 ml).

• Stage III - an ABC determination should be obtained immediately and IV aminophylline started. Criteria for hospitalization are (1) failure to improve, (2) relapse after repeated adrenergic therapy and aminophylline, and (3) significant decrease in PaO2 (< 50 mm Hg) or increase in PaCO2 (> 50 mm Hg), indicating progression to respiratory failure. IV infusion of prednisolone 90 mg or dexametasone 8 mg.

• Stage IV patient should immediately be given methyl-prednisolone 1 to 2 mg/kg IV q 4 to 6 h or hydrocortisone sodium succinate 4 mg/kg IV q 2 to 4 h. IV, prednisolone 60 mg or dexametasone 8 mg q 4 to 6 h.
**Status asthmaticus** occurs the severe attack, especially if it has been prolonged (> 12 h), or severe obstruction persisting for days or weeks.

Fatigue and severe distress are evident in rapid, shallow, ineffectual respiratory movements.

There may be a loss of adventitial breath sounds, and wheezing becomes very high pitched. Further, the accessory muscles become visibly active, and a paradoxical pulse often develops.

Cyanosis becomes evident as the attack worsens.

The end of an episode is frequently marked by a cough that produces thick, stringy mucus, which often takes the form of casts of the distal airways (Curschmann's spirals).
**Status asthmaticus**

- **O₂ therapy** is indicated and may be given with nasal prongs or, if tolerated, a Venturi mask with low Flo₂ (2 to 4 L/min).

- **Adrenocortical steroids:** *methylprednisolone* (or *prednisolon*)
  1 to 2 mg/kg (90-120mg) IV q 4 to 6 h or hydrocortisone 4 mg/kg (125-250 mg) IV q 2 to 4 h.

- **Beta₂-adrenergic agonists:** salbutamol 200-400 mcg once or twice in 20 to 30 min, Inhalation every 2-4 h. Ipratropium bromide 0.5 mg should be added.

- **Alkaline solutions** (sodium bicarbonate) in the IV fluid should be limited to maintain the pH between 7.2 and 7.3.

- **Patients** who show no favorable response to aggressive bronchodilator and anti-inflammatory therapy and who evidence fatigue and progressive deterioration in ABCs and pH should be considered candidates for endotracheal intubation and respiratory assistance and should be hospitalized in an ICU.
Indications for Assisted Ventilation in Acute Severe Asthma

1. Coma
2. Respiratory arrest
3. Exhaustion, confusion, drowsiness
4. Deterioration of arterial blood gas tensions despite optimal therapy:
   - $PaO_2 < 8$ kPa and falling
   - $PaCO_2 > 6$ kPa and rising
   - $pH < 7.3$ and falling