It is the chameleon of pulmonology: With as many different clinical phenotypes, making a diagnosis isn’t always easy, and pathogenesis is complex. In the following article, you will find all the important information about one of the most common chronic diseases in human beings: bronchial asthma.

Definition

Bronchial asthma as an inflammatory disease of the airways

Bronchial asthma describes a chronic inflammatory disease of the airways. During the course of the inflammation, bronchial hyperreactivity occurs.

Compared to healthy people, the airways of patients with asthma react more to various stimuli. The consequence is a paroxysmal and recurring obstruction of the airways.

However, this obstruction occurs spontaneously, and with drug treatment, it is completely or partially reversible.
Epidemiology

Bronchial asthma in the population

Bronchial asthma is one of the most common chronic diseases in humans. Around 5% of adults and 10% of children and young people are affected.

With regard to sex distribution, different statements can be found in the literature. According to the World Health Organization (WHO), slightly more women than men are affected. Other sources state an approximately equal distribution.

Regardless, it is undisputed that the initial onset of the allergic type of asthma occurs mostly during childhood.

Etiology

Causes and triggering factors

Generally, 2 types of asthma can be distinguished.

1. Allergic, extrinsic asthma

Patients with allergic, extrinsic asthma develop asthma symptoms when they come into contact with environmental allergens (e.g., pollen, pet hair, house dust mites, mildew, and occupational allergens such as flour dust).

The allergic type of asthma often exists in combination with other diseases pertaining to the atopic syndrome, such as allergic rhinitis or neurodermatitis. This disease all have a polygenic predisposition for excessive production of IgE. If both parents are affected by allergic asthma, their children will have a risk of disease of around 60–80%. On the island Tristan da Cunha, 50% of the population has asthma due to hereditary transmission.
2. Non-allergic, intrinsic asthma

For non-allergic, intrinsic asthma, the following trigger factors may play a role: respiratory infection (infectious asthma), acetylsalicylic acid/NSAIDs (analgesic asthma syndrome), noxious inhaled agents, gastroesophageal reflux, as well as cold air and physical or mental stress.

Often, the 2 types cannot be rigorously distinguished especially when they occur in adult asthmatics. Only 30% of patients have purely extrinsic or intrinsic asthma; the rest display hybrid forms of both types.

Pathophysiology

The origin of bronchial asthma

In the case of allergic asthma, the production of IgE antibodies begins only a few minutes after coming into contact with a corresponding allergen. These antibodies activate mast cells, which release mediators such as leukotriene, prostaglandin, and histamine (type 1 hypersensitivity reaction). These mediators cause bronchospasms, on one hand, and attract inflammatory cells, on the other. The inflammatory cells eventually cause the long-term full picture of chronic inflammation.

For non-allergic asthma, the immunological process is similar but is without a triggering allergen. Here, infectious agents (especially viruses) are suspected to act as triggering factors.

All types of asthma have the resulting pathologic consequences in common:

- Constriction of the airways due to bronchospasm, but also due to an edematous mucosal swelling
- Hypersecretion of thick mucus
- Hyperplasia of smooth muscles (remodeling)
- Bronchial hyperreactivity and (chronic) bronchial inflammation

Symptoms

The clinical presentations of asthma can differ greatly from patient to patient.

The typical main symptoms are:

- Paroxysmal shortness of breath
- Expiratory stridor (differential diagnosis: inspiratory stridor in the event of
obstruction of the upper airways)
- Chronic cough, mostly dry and spasmodic (“cough-variant asthma”)
- Thoracic tightness

Note: Chronic cough without shortness of breath may be a sign of asthma

Most patients describe a peak of their symptoms in the second half of the night because of the low sympathetic tone (high vagal tone) during this period. If symptoms occur seasonally (e.g. during pollination), this might be a sign of allergic asthma.

In most cases, asthma appears only episodically at the beginning, and patients remain symptom-free most of the time.

Attention: During seizure-free intervals, pulmonary function often remains within normal limits. Here, a provocation test can help to confirm a diagnosis!

Diagnosis

Medical history and clinical examination of bronchial asthma

First, inquiries about possible risk factors can be made during history: Are there any other atopic medical conditions? Are there people with asthma in the family? Is the patient exposed to allergic agents at the workplace?

During clinical examination, patients often present with symptoms like dyspnea, tachypnea, orthopnea, and prolonged expiration – especially during an acute attack of asthma. When blood pressure falls by more than 10 mm Hg during inspiration, this might indicate a paradoxical pulse.

During auscultation, wheezing, humming, or whistling (especially expiratory) may be observed.

Attention: During an acute attack of asthma with marked pulmonary hyperinflation or emphysema, a patient might present with a ‘silent chest’ – the absence of any audible breath sounds!

Percussion shows a hyper resonant sound as well as a low position of the diaphragm with reduced mobility during breathing.

Pulmonary function tests in bronchial asthma

An essential part of diagnosing asthma is pulmonary function testing.

Here, an obstruction with consecutively increased airway resistance can be observed; the forced expiratory volume in 1 second (FEV1) is reduced. Given an approximately constant vital capacity, this yields a reduced Tiffeneau-Pinelli index: \( \text{FEV1} / \text{VC} < 70\% \).

A decisive factor in the differential diagnosis (e.g. in comparison to chronic obstructive pulmonary disease, COPD) is the reversibility of the obstruction, tested in a bronchodilator reversibility test. FEV1 improves significantly either directly after the administration of inhaled bronchodilator medication (e.g., 400 µg salbutamol) or in case of a lack of response, after the administration of inhaled glucocorticoids over 4 weeks.

As a rule of thumb: If FEV1 increases after a bronchodilator test by more than 15% compared to the initial value, asthma requires treatment!

If the pulmonary function testing does not show any abnormalities despite suspected
asthma, a **provocation test** (methacholine challenge test) can confirm a diagnosis. The patient inhales methacholine or histamine, and due to the hyperreactivity of the airways, this provokes bronchoconstriction, which leads to a reduced FEV1 value by at least 20% and a doubling of resistance. Subsequent inhalation of salbutamol dilates the bronchial tubes and normalization of the pulmonary function parameters should be achieved.

**Further diagnosis of bronchial asthma**

Since allergic asthma is generally the most common type of the disease, an **allergy test** should always be administered (especially intradermal or prick testing, determination of total and specific IgE).

An **ECG** can show signs of right ventricular stress.

In the **laboratory**, eosinophilia might be observed. In addition, in cases of allergic asthma, IgE is often increased; in cases of non-allergic asthma, leukocytosis, as well as increased ESR and CRP values, may be found.

In an **X-ray of the thorax**, the overinflated lung can show increased radiographic transparency, a low-positioned diaphragm, and a broadened intercostal space. The impression of a ‘barrel chest’ arises. Further, the cardiac silhouette is narrowed.
Classification of Asthma

During the initial diagnosis, the asthmatic condition is classified into different degrees of severity:

- Intermittent
- Mild persistent
- Moderate persistent
- Severe persistent

In the long run, however, more important than the severity level is the classification according to response to therapy, i.e. whether the asthma is controlled, partially controlled, or uncontrolled.

The German disease management guidelines for asthma have established the following classification:

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Controlled asthma</th>
<th>Partly controlled asthma</th>
<th>Uncontrolled asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms during the day</td>
<td>≤ 2 times/week</td>
<td>&gt; 2 times/week</td>
<td></td>
</tr>
<tr>
<td>Limitation of activities during everyday life</td>
<td>no</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Symptoms during the night</td>
<td>no</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Use of medication on demand or emergency</td>
<td>≤ 2 times/week</td>
<td>&gt; 2 times/week</td>
<td></td>
</tr>
<tr>
<td>treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary function (PEF or FEV1)</td>
<td>normal</td>
<td>&lt; 80% of the set point (FEV1) or of the personal best value (PEF)</td>
<td></td>
</tr>
<tr>
<td>Exacerbation (asthmatic attack)</td>
<td>no</td>
<td>One or more per year</td>
<td>One per week</td>
</tr>
</tbody>
</table>

Differential Diagnosis

Similar diseases such as bronchial asthma

It is not without reason that the comparison of COPD and asthma is a frequent topic in medical education as both conditions very often exhibit similar symptoms. However, their treatments and prognoses differ greatly, which is why an accurate diagnosis is crucial.

During history, there can be many signs which are more likely an indication of COPD (e.g., smoking, age > 40 years, gradual onset). The most distinctive criterion is the reversibility of airway obstruction during the bronchodilator reversibility test (see the section on diagnosis). Complete reversibility rules out COPD.

Additional important differential diagnoses are:

- **Cardiac asthma**: This occurs in patients with left-sided heart failure who have developed lung congestion with shortness of breath. Bilateral basal rales during auscultation of the lungs and a chest X-ray with signs of pulmonary congestion lead to the right diagnosis.
- **Pulmonary embolism** with shortness of breath: Here, symptoms are acute with a sudden onset. However, small pulmonary embolisms can also simulate asthma.
- **Tension pneumothorax**: Watch out for differences between the sides during auscultation.
- **Inspection:** Neck veins may be distended, with unilaterally diminished chest movement
- **Percussion:** Chest is hyper resonant on the affected side
- **Auscultation:** Decreased or absent breath sounds on the affected side
- **Palpation:** Trachea will deviate away from the affected side

  - **Obstructions with other etiology:** For instance, aspiration of foreign objects, tumor, glottal edema. Inspiratory stridor during auscultation is an indication of an obstruction of the upper airways

**Treatments**

The goal of any treatment should be to reach the controlled form of asthma (see classification). Therefore, depending on the degree of severity, PRN medication (relievers) are used for acute attacks, and if necessary, long-term therapy with so-called controllers.

This results in a gradual treatment method based on the principle: as much as necessary, as little as possible. The step to a higher level of therapy is taken when the attacks persist in spite of treatment efforts.

The current therapy recommendations according to the [guidelines of the GINA](https://ginasthma.org/) (Global initiative for asthma) is as follows:

<table>
<thead>
<tr>
<th></th>
<th>Level 1</th>
<th>Level 2</th>
<th>Level 3</th>
<th>Level 4</th>
<th>Level 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term therapy</td>
<td>Long-term therapy</td>
<td>ICS low dose</td>
<td>ICS (or LABA) low to middle dose</td>
<td>ICS middle to high dose PLUS LABA</td>
<td>ICS middle to high dose PLUS LABA PLUS OCS lowest effective dose</td>
</tr>
<tr>
<td>Long-term therapy alternative</td>
<td>ICS if necessary low dose</td>
<td>LTRA</td>
<td>ICS low dose and LTRA or theophylline</td>
<td>PLUS if necessary and LTRA and/or theophylline</td>
<td>Omalizumab if necessary (anti-IgE antibodies) for allergic asthma</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PRN medication</th>
<th>Inhaled short-acting beta-2 sympathomimetic (salbutamol, fenoterol, terbutalin)</th>
</tr>
</thead>
</table>

ICS = Inhaled corticosteroids (mostly budesonide or beclomethasone)

LABA = Long-acting beta-2 agonists (salmeterol, formoterol)

LTRA = Leukotriene receptor antagonists (mostly montelukast)

OCS = Oral corticosteroids

For asthma treatment in children, the following applies: montelukast and the mast cell stabilizer – **cromoglicic acid** are preferred to long-acting beta-2 mimetics.
The above-mentioned medications are administered by inhalation mostly using metered-dose inhalers, which are commonly known as ‘asthma sprays’. It is important to properly instruct the patient on how to use the device – only if the medication is inhaled correctly, will it work properly!

The peak flow meter helps both patient and doctor to get an objective assessment of therapeutic success.

With this small and easy-to-handle device, the patient is able to measure his/her own maximum expiratory flow in 1 sec. A decline in peak flow values is an early indication of insufficiently controlled asthma and can help to prevent an exacerbation – provided that opportune actions are taken.

Patients should also try to minimize irritations of the airways by:

- Not smoking
- Allergen avoidance
- Avoiding cold air, fog, and dust
- Infection prophylaxis and avoiding extreme physical activities

In cases of allergic asthma, allergen immunotherapy (hyposensitization) is another option.

Furthermore, additional patient education concerning the use of inhalation systems, smoking cessation, and respiratory physiotherapy can be considered.

**Acute exacerbation**

**Presentation**

- Usually known as asthma
- Lasts from minutes to a few hours
- Often preceded by a few days of poor control (e.g. increased nocturnal symptoms, using salbutamol more)
- Frequently there is an obvious trigger (e.g. upper respiratory tract infection, stress, smoke exposure)
- Acute dyspnea, wheeze, cough
On auscultation widespread polyphonic expiratory wheeze
- Fall in peak expiratory flow rate

**Signs of severe disease**

- Unable to talk in complete sentences
- High pulse (> 110) and respiratory (> 25) rates
- Pulsus paradoxicus (decrease in systolic BP on inspiration)
- Peak flow < 50% predicted/ previous best

**Signs of very severe disease requiring immediate treatment and potential intubation**

- Low and irregular pulse or respiratory rates
- Reduced blood pressure
- Reduced consciousness level
- Quiet breath sounds
- Barely recordable peak flow
- Central cyanosis
- Increased PaCO2
  - Reduced in milder attacks
  - Normal in more severe attacks
  - Raised only in severe disease

**Complications of Asthma**

**Asthma attacks**

**Asthma attack** is the **acute obstruction** of the lower airways. When it is life-threatening and treatment-refractory, we speak of ‘status asthmaticus’. This is an emergency! The patient has to be brought to the closest hospital immediately by an emergency doctor.

**Initial treatment** of an asthma attack, independent of the severity of the attack, are 2–4 inhalations of a **short-acting beta-2 sympathomimetic drug** (if necessary, to be repeated after 10 min). These drugs are considered the most effective bronchodilators!

In addition, the patient should take a supportive body position that facilitates breathing
Subsequent treatment management depends on the severity of the asthma attack:

<table>
<thead>
<tr>
<th>Severity of the attack</th>
<th>Symptoms</th>
<th>Assistance</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low to moderately severe</td>
<td>RR &lt; 25/min&lt;br&gt;HR &lt; 110/min&lt;br&gt;PEF &gt; 50% of set point</td>
<td>Wait for a response to the initial treatment</td>
<td>2–4 inhalations of a short-acting beta-2 sympathomimetic</td>
</tr>
<tr>
<td>Severe</td>
<td>Shortness of breath when speaking&lt;br&gt;RR &gt; 25/min&lt;br&gt;HR &gt; 110/min&lt;br&gt;PEF &lt; 50% of set point</td>
<td>Consider hospitalization</td>
<td>2–4 inhalations of a short-acting beta-2 sympathomimetic&lt;br&gt;Oxygen 2–4 L/min; 50-100 mg of prednisolone equivalent&lt;br&gt;Oral or IV&lt;br&gt;Inhalation of ipratropium bromide</td>
</tr>
<tr>
<td>Life-threatening</td>
<td>Silent chest*, difficult breathing, cyanosis&lt;br&gt;Hypotonia, bradycardia, exhaustion, coma&lt;br&gt;SaO₂ &lt; 92%&lt;br&gt;PEF &lt; 33% of set point</td>
<td>Immediate hospitalization accompanied by an emergency doctor</td>
<td>Immediate hospitalization accompanied by an emergency doctor</td>
</tr>
</tbody>
</table>

HR, heart rate; PEF, peak expiratory flow; RR, respiratory rate; SaO₂, oxygen saturation

**Note:** Never administer beta-blockers during an acute asthma attack!

**Prevention**

**How to prevent bronchial asthma**

In particular, exposure to smoking during childhood should be prevented. Factors like extended breastfeeding, hypoallergenic baby food, and reduction of house dust mites, are being considered as preventive measures in academic discussions. However, scientific evidence regarding these measures are currently insufficient.

**References**


