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somewhat different

Inhalers provide rapid relief of asthma symptoms.

# Bronchial asthma

## Epidemiology and disease characteristics

Asthma affects up to 300 million people worldwide. It resulted in approximately 418,000 deaths globally in 2016 or 0.7% of the total. The overall age-standardised incidence rate decreased from 1990 to approximately 2005 but has now rebounded and is approaching 1990 levels, resulting in a U-shaped pattern. This pattern has held for most socioeconomic groups. The exception is the highest sociodemographic category, where the current rates have remained at or below those seen in early 2000's.[1-3]

Asthma is a chronic disorder in which various stimuli result in airway hyperactivity, leading to a reversible airflow obstruction. The airflow obstruction is due to a combination of spasm of the bronchial smooth muscle, edema and congestion of the airway walls, and increased secretion of mucus. In the past, spasm of the airways was thought to be the major contributor to obstruction. More recently, the data supports the view that chronic asthma is really an inflammatory disease; and, the more severe the inflammation, the more hyper-responsive are the airways.[1, 4, 5]

Asthma may develop at any age but onset is more common in children and young adults. Children with onset of asthma generally fall into one of two groups. The first has intermittent symptoms, often related to viral illnesses, and frequently outgrow the condition as they get older. The second tends to have an onset at older age with more regular symptoms that persist over time. This second group is more likely to have multiple allergies, more severe disease and a maternal history of asthma. Adults with the disease are less likely to have resolution over time. New onset adult disease is more likely to occur in women, especially those in the perimenopausal period. In general, the more severe the condition, the more likely it is to be persistent over time.[6]

Risk factors for the onset of asthma include: a positive family history, exposure to environmental tobacco smoke or pollution, viral respiratory infections in the first 3 years of life and socioeconomic factors such as low income level, reduced access to medical care and exposure to cockroach and rodent antigens.[4]

## Pathology

Asthma is considered either atopic (allergic) or nonatopic. Atopic asthma is more common in children, is caused by external allergens and is associated with allergic rhinitis, conjunctivitis, atopic dermatitis, urticaria and food allergies. Nonatopic asthma is not related to known allergens. It is more common in adults and is triggered by various nonimmune causes, such as aspirin, respiratory tract infections, inhaled irritants, stress, exercise and cold temperatures.[4]

Reversibility of the airways obstruction to normal or near-normal pulmonary function between acute attacks is characteristic of asthma. The definition of reversibility is an increase of 200 ml or 12 percent or greater in the forced

expiratory volume in one second (FEV1) following two puffs of a bronchodilator.[4]

## Symptoms

The classic asthma attack lasts up to several hours, followed by a return to normal respiratory function. The symptoms of an asthma attack are:[1, 4]

- Wheezing
- Coughing
- Sputum production
- Shortness of breath/respiratory failure
- Chest tightness
- Air hunger
- Tachypnea
- Tachycardia

## Classification of severity

A combination of factors defines the severity of asthma. These include the frequency of daytime symptoms, nighttime awakenings due to symptoms, frequency of use of short-acting beta agonist medications (rescue inhalers), interference with normal activities, measures of lung function (FEV1 and the ratio of the FEV1 to the forced vital capacity or FVC (FEV1/FVC ratio)) and the number of exacerbations requiring oral systemic steroids. The severity categories are intermittent, mild persistent, moderate persistent and severe persistent. (Table 1) The most severe symptom or factor in a class defines the severity category.[4, 7-9]

Status asthmaticus is the most severe form of asthma in which the acute attack persists for days or even weeks. This often necessitates the use of mechanical ventilation. Pulmonary function testing helps assess both the severity of an acute asthmatic attack and whether chronic obstructive pulmonary disease (COPD) has developed in those with recurrent symptoms. A persistently abnormal FVC and FEV1 is compatible with the onset of COPD. Individuals with COPD who contract COVID-19 are more likely to get severely ill or die from the infection.[10-12]

**Table 1**

| Criteria | Intermittent | Persistent | | |
|---|---|---|---|---|
| | | Mild | Moderate | Severe |
| **Symptoms** | 2 days or less per week | 2+ days per week; not daily | Daily | Multiple times per day |
| **Nighttime awakenings** | 2 or less per month | 3 to 4 per month | > 1 per week; not daily | Multiple per week to daily |
| **Short-acting beta-agonist use** | 2 days per week or less | 3+ days per week; not daily | Daily | Several times per day |
| **Interference with normal activity** | None | Minor limitation | Moderate limitation | Extremely limited |
| **FEV1** | > 80% | > 80% | 60–79% | < 60% |
| **FEV1/FVC** | Normal | Normal | Reduced ≤ 5% | Reduced > 5% |
| **Exacerbations requiring oral** | 0 to 1 per Year | ≥ 2 per year | ≥ 2 per year | ≥ 2 per year |

## Treatment

Basic therapies for asthma include avoidance of known allergens or precipitating irritants or behaviors, allergy desensitisation, routine influenza, pneumonia and COVID-19 vaccinations and home monitoring with a peak flow meter. The goal of this monitoring is to initiate therapy as soon as possible after the detection of a deterioration in clinical status.

Treatment of asthma with medication generally occurs in a stepwise fashion and depends on the severity of the disease. These drugs include short-acting beta-adrenergic agonist (SABA) inhalers, which provide rapid relief of symptoms and are frequently used as "rescue" inhalers as needed for control of acute exacerbations. Termination of an acute episode often requires the use of a short course (5-10 days) of oral steroids. Thus, these short bursts of glucocorticoids are a marker for exacerbations but not a reliable indicator for severity of disease.

Persistent asthma requires medication designed for long-term control. Inhaled glucocorticoids, which reduce inflammation, is the principle one of these agents. Others include long-acting beta agonist (LABA) inhalers, the leukotriene-receptor antagonists (LTRA), cromolyn, zileuton and theophylline. The use of chronic oral glucocorticoids and/or biologic agents indicates the presence of severe disease. The biologic agents are active against immunoglobulin E (IgE), interleukin-5 (IL-5) leading to a reduction of eosinophils or the interleukin-4 receptor alpha subunit. These drugs may be effective in severe asthma that is unresponsive to other treatments. They include omalizumab (anti-IgE), mepolizumab, reslizumab, benralizumab (anti-IL5) and dupilumab (anti-IL-4 alpha subunit).[1, 4, 8, 9, 13]

## Prognosis

With the appropriate use of medications, most individuals with asthma will never require emergency room (ER) or hospital treatment. In particular, the use of inhaled steroids has significantly decreased the frequency of severe exacerbations and death rates in recent years. However, compliance with recommended regimens is critical for long-term success.

Nevertheless, asthma may be associated with an increase in mortality in a subset of those affected. Individuals who die of asthma appear to have one of two patterns. With the first, the person has an extended period of deterioration with an exacerbation of symptoms that fails to clear. This is what happens with a majority of fatal episodes. The second pattern is less common. In this case, the affected individual has a sudden deterioration of their clinical condition and death may occur before they can reach medical help. Many in this latter group have a poor ability to recognise a worsening of their condition before it is too late to reverse it.[10]

A number of factors have been found to be associated with fatal or near fatal asthma.[10, 14-22] These should be taken into account in evaluating the risk associated with the disease and include the following[10]:

- A past history of sudden onset severe asthmatic episodes
- A history of prior intensive care unit admission for asthma
- A prior history of endotracheal intubation for an asthma exacerbation
- Two or more hospitalisations for asthma in the past year
- Three or more ER visits for asthma in the past year
- A hospitalisation or ER visit within the past month
- Reduced awareness on the part of the individual of airflow obstruction and its severity
- The presence of significant comorbid cardiovascular disease or COPD
- Serious psychiatric illness which may affect asthma in several ways (see below)
- Poor compliance with treatment of moderate to severe disease
- Frequent use (more than 2 canisters per month) of short-acting beta agonists
- Current use of or recent withdrawal from oral steroids
- A history of substance abuse

Asthma may develop at any age but onset is more common in children and young adults.

Of note, asthma is associated with a greater likelihood of mental illness, especially anxiety and depression. In addition, severe mental illness is associated with worsened outcomes including fatal and near fatal episodes. Several factors related to psychiatric illness lead to these worsened outcomes. These include precipitation of acute attacks by psychological distress, altered perception of the severity of disease or exacerbations and the direct physiological effects of anxiety and depression such as increased inflammation and autonomic nervous system dysfunction. In addition, poor compliance with recommended treatment is more common in the presence of mental disorders.[16, 23, 24]

In summary, asthma is a common condition that affects individuals of all ages. With use of modern therapies, it is a benign illness with little risk for mortality or serious morbidity in a significant majority of those affected. Nevertheless, it remains a serious illness for a subgroup of those with the disease, where it carries a significant risk for physical limitation and premature mortality. The challenge for underwriters is to find those high-risk applicants and price them appropriately.

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