More than 2,000 years ago, Hippocrates used the word asthma to describe episodic shortness of breath — ie, panting. Now that more is known about the nature of the condition, asthma is defined as "a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation causes an associated increase in airway hyper-responsiveness that leads to 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."1

The UK has one of the highest rates of asthma in the world.2 The charity Asthma UK estimates that there are 5.4 million people in the UK currently receiving treatment for the condition. Of these, 1.1 million are children, giving asthma a prevalence in children of approximately 10%. In the UK, one person every eight hours dies from asthma — in 2008 there were approximately 1,200 deaths among people with asthma, of whom 29 were children aged 14 years or under.3 These are frightening statistics, especially because as much as 90% of these deaths are preventable.

In 2008–09, there were nearly 80,000 emergency admissions to hospital for asthma, with around 75% being preventable. These and other aspects of asthma care cost the NHS around £1bn each year.3 As well as this economic burden, there are physical, emotional, and social effects, leading to a reduced quality of life for patients and their families.4 Around half of patients with asthma do not have an acceptable level of asthma control, characterised by the presence of disease symptoms and reduced quality of life. Patients often tolerate their poorly controlled asthma. The "Asthma control and expectations" (ACE) survey found that almost 70% of asthma patients interviewed agreed with the statement: "I have to accept there are things I cannot do because of my asthma."5

Classification

Asthma is a heterogeneous disease. Over the years, there have been numerous ways of classifying asthma. In the early 20th century, Rackemann6 proposed classifying asthma as "extrinsic" (where an external trigger can be identified) or "intrinsic" (where no causative agent can be found) — a concept that remains widely used. Additional asthma phenotypes, based on causation (eg, allergic, non-allergic, aspirin-sensitive, occupational asthma), severity and physiological parameters (eg, type I brittle, type II brittle) have been subsequently identified. More recently, classification of asthma according to the nature of the
underlying airway inflammation has been suggested — namely “eosinophilic” or “non-eosinophilic” disease. New evidence is emerging to suggest that the identification of such inflammatory phenotypes could help to guide the management of asthma for individual patients.

**Pathophysiology**

In most cases, asthma is an allergic disorder mediated, in part, by immunoglobulin E (IgE)-dependent mechanisms. The likelihood of having asthma has been shown to increase with increasing serum IgE concentrations. IgE is formed in response to an allergen such as pollen, house dust mite or animal dander. On first exposure, the body becomes sensitised, storing information about the allergen and producing allergen-specific IgE. On re-exposure, the allergen (or trigger) binds to a specific IgE molecule on the surface of mast cells (see Figure 1) releasing inflammatory mediators, such as histamine, prostaglandins, leukotrienes and thromboxane, a process known as degranulation. Such mediator release causes the bronchospasm associated with the early or acute phase of an asthma attack (exacerbation).

If early phase asthma remains untreated, patients’ airways become infiltrated by eosinophils, T-lymphocytes, mast cells and, sometimes, neutrophils. Goblet cells are increased in number and are stimulated, generating plugs of mucus. T-lymphocytes release cytokines that, in turn, recruit other pro-inflammatory cells, causing the inflammatory late phase of an asthma attack. The effect of inflammation is to increase basal airway tone and airway responsiveness so that patients’ airways narrow too easily and too much to a wide range of triggers, and hence the attack is exacerbated further (see Box 1, p206). Autopsy studies show that patients who have died from asthma have hyperinflated lungs, with both their large and small airways blocked by plugs of mucus, proteins, inflammatory cells and cell debris (see Figure 2).

If asthma is poorly controlled over a period of many years, structural changes to airways occur. Chronic inflammation causes bronchial smooth-muscle hypertrophy and hyperplasia, new vessel formation, interstitial collagen deposition (resulting in basement membrane thickening) and airway wall remodelling. These changes can eventually result in some persistent airflow obstruction (despite treatment) similar to that observed in people with chronic obstructive pulmonary disease (COPD).

**Causes**

Asthma can occur at any time in life, although it most commonly develops in infancy and childhood. There is no single known cause of asthma, but there are several genetic and environmental factors that may contribute to the condition. These include:

- Having a family history of asthma (in particular, a parent or sibling with asthma), or of other atopic conditions, such as eczema or allergic rhinitis
- Having had bronchiolitis as a child
- Being exposed to tobacco smoke as a child, particularly when his or her mother also smoked during pregnancy
- Being born prematurely
- Being born with a low birth weight

**Signs and symptoms**

Classic symptoms of asthma are wheezing (i.e., a high-pitched whistling sound), shortness of breath, coughing (particularly at night and early in the morning) and chest tightness. Wheezing is usually heard on expiration, but may also be heard on inspiration, and results from airway constriction. It is important to note that the absence of wheezing is not sufficient to preclude a diagnosis of asthma — in an exacerbation, some patients may have such severe obstruction of their airways that wheezing may not be noticeable. Such patients, however, usually have other signs of respiratory obstruction, such as difficulty in speaking, cyanosis, drowsiness and chest hyperinflation. Chest tightness (dyspnoea) is the sensation that patients often experience because of the increased
work needed to breathe when the airways are constricted. Coughing probably results from stimulation of sensory nerves in the airways.

During exacerbations of asthma, patients will often wheeze and have reduced lung function but, outside these acute episodes, there may be no objective signs of asthma. It is important to remember that people with asthma may have a variety of non-specific respiratory symptoms. The hallmark of asthma is that these symptoms tend to be variable, intermittent, worse at night and provoked by triggers (see Box 2).

### Diagnosis

A careful medical history, physical examination, lung function tests (preferably using spirometry) and monitoring the clinical response to a trial of treatments provide the information needed to diagnose most cases of asthma. However, diagnosis is not always straightforward.

#### Box 1: Phases of an asthma attack

<table>
<thead>
<tr>
<th>Acute or early phase response</th>
<th>Acute bronchospasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure to allergens results in bronchospasm and wheezing within minutes</td>
<td></td>
</tr>
<tr>
<td>Maximal effect reached within 15 to 20 minutes</td>
<td></td>
</tr>
<tr>
<td>Effect subsides after one to three hours</td>
<td></td>
</tr>
<tr>
<td>Early phase may then progress to late phase reaction</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Late phase response</th>
<th>Inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Develops about four hours after the initial acute phase and may last typically for a further six to eight hours</td>
<td></td>
</tr>
<tr>
<td>Characterised by eosinophilia in the mucous membrane, mucosal oedema and increased smooth muscle excitability (hyper-responsiveness)</td>
<td></td>
</tr>
<tr>
<td>Airways obstruction with cough and sputum production</td>
<td></td>
</tr>
</tbody>
</table>

### Box 2: Triggers

The following can act as possible triggers for asthma:

- Airborne irritants, such as cigarette smoke, chemical fumes and atmospheric pollution
- Allergens, such as pollen, dust mites and animal dander or feathers
- Infections of the respiratory tract
- Weather conditions, such as cold air
- Foods containing sulphites (food and drink high in sulphites include beer, wine, shrimp and many processed or “pre-cooked” meals)
- Emotional factors, such as stress or laughter
- Medicines, such as non-steroidal anti-inflammatory drugs and beta-blockers (including eye drops)
- Exercise

### Box 3: Reversibility testing

The following options can be used with spirometry (pictured) for reversibility testing in patients whose FEV₁/FVC ratio is <0.7:

- Record FEV₁
- Give 400μg of inhaled salbutamol by metered dose inhaler and a spacer device or 2.5mg salbutamol by nebuliser
- Await dose response (20–30min)
- Record FEV₁
- If increased by 400ml or more, this is a positive response

OR

- Record FEV₁
- Give oral corticosteroid (eg, prednisolone 30mg daily for 14 days) or at least 400μg inhaled beclometasone (or equivalent) daily for 6–8 weeks
- Record FEV₁
- If increased by 400ml or more, this is a positive response

FEV₁ = Forced expiratory volume in one second, FVC = Forced vital capacity
As an obstructive lung disease, asthma is characterised by a decrease in PEF and FEV<sub>1</sub>. For a patient with asthma, these measurements can appear normal, especially when asymptomatic. If measurements are repeatedly normal in the presence of symptoms, then a diagnosis of asthma is doubtful. If obstruction is found, a patient should be tested again to establish that the obstruction is reversible — i.e., that lung function increases after administration of an effective dose of inhaled bronchodilator or a trial of inhaled or oral corticosteroids (see Box 3, p206).

Where diagnostic doubt remains, it is important that patients are referred for further specialist investigations so that they are not given an inaccurate diagnosis and exposed to ineffective treatments. Currently available advanced diagnostic techniques include assessing airway hyper-responsiveness (often using inhaled methacholine or histamine) and testing for eosinophilic airways inflammation using exhaled nitric oxide monitors or induced sputum.

Although there are many shared features in the diagnosis of asthma in adults and in children, there are also important differences, for example the differential diagnoses, the ability to perform spirometry and other tests are all influenced by age.

**Differential diagnosis**

A correct diagnosis of asthma is essential if appropriate drug therapy is to be given. Although there are many features of asthma that are common to other diseases, there are also important differences. The differential diagnosis of patients with suspected asthma differs according to age groups.

Particularly challenging is the differential diagnosis between asthma and COPD (Box 4). One survey reported that, of 776 GPs completing an online questionnaire, 80% between asthma and COPD (Box 4). One survey reported suspected asthma differs according to age groups. Although there are many features of asthma that are common to other diseases, there are also important differences. The differential diagnosis of patients with suspected asthma differs according to age groups.

**Particularly challenging is the differential diagnosis between asthma and COPD.** (Box 4). One survey reported that, of 776 GPs completing an online questionnaire, 80% found distinguishing asthma from COPD "quite or very challenging". A further survey by the British Lung Foundation, found that 39% of 654 COPD patients had been told that they had both asthma and COPD. Given that the rate of co-existing asthma and COPD in the UK has been estimated as 15%, it is likely that asthma has been diagnosed in patients who do not actually have the condition. Failure to distinguish between asthma and COPD can lead to distress among patients and to inappropriate and ineffective treatments being given.

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