

# 1

## What is asthma?

### → Key points

- ◆ Asthma is a long-term disease that affects the breathing tubes that carry air in and out of the lungs
- ◆ Childhood allergic asthma is more common in boys than in girls
- ◆ Around one in ten cases of asthma in adults is due to occupational exposure to allergens
- ◆ Estimates vary, but aspirin sensitivity may occur in 5–10% of asthmatics

Asthma is a common disease that affects approximately 300 million children and adults worldwide. It is so common that it is now regarded as a serious public health problem. Asthma may be mild, in which case it does not cause a great deal of concern. However, in other situations, it may be a serious and even life-threatening condition. Caring for people with asthma is time-consuming and expensive. The global burden of asthma is increasing, particularly in children, leading to increasing healthcare costs, reductions in quality of life, and increased take-up of hospital beds for management of asthma attacks. How asthma is managed depends upon the individual's understanding of asthma, which determines the level of control, the need for emergency visits, and the number of school/work days lost. A better understanding of asthma by patients and parents is paramount in improving the quality of life and in reducing hospital admissions by recognizing the early warning signs of worsening asthma.

## What is asthma?

Asthma is a chronic disease that affects the breathing tubes that carry air in and out of the lungs. The airways are inflamed (swollen) in asthma, and this makes them very twitchy and sensitive. A sensitive airway reacts to various different irritants causing narrowing, leading to reduced airflow through the lungs. The narrowing of the airways is due to a combination of increased secretions within the airways as a consequence of inflammation and to the constriction of the muscles around the airways (Figure 1.1). This manifests as:

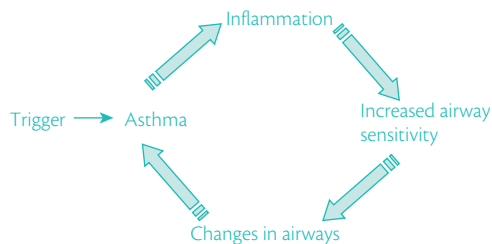
- ◆ wheezing (a whistling noise while breathing);
- ◆ chest tightness;
- ◆ cough;
- ◆ breathing difficulties.

These symptoms are more common during the night and early morning. Wheezing is the sound that is heard when air tries to escape from the narrowed breathing tubes. Symptoms are variable from individual to individual, but do get worse during an asthma attack, which is usually caused by an infection, exposure to allergens, or other factors leading to an inability to expel air from the lungs.

The factors or triggers for asthma vary from individual to individual. A trigger is anything that sets off an asthma attack. Common triggers for asthma are shown in Table 1.1.

## Types of asthma

Previously, it was thought that asthma has two main subtypes, i.e. allergic (also called extrinsic) asthma and non-allergic (also called intrinsic) asthma.



**Figure 1.1** The asthma cycle.

**Table 1.1** Asthma triggers

Trigger	Examples
Allergen	House dust mite, animals (cat and dog), cockroaches, pollen, trees, mould
Infection	Virus infections such as coughs and colds
Pollutants	Cigarette smoke (active or passive), sulphur dioxide
Occupational agents	Flour, certain chemicals
Foods	Seafood, nuts, food additives such as sulphites
Drugs	Heart drugs (atenolol, propranolol, bisoprolol), pain killers (ibuprofen, voltarol)
Psychological factors	Stress, anxiety, intense emotions
Cold air	
Exercise	
Hyperventilation	
Others	Chemical agents, perfumes, etc.

However, there are various types of asthma with considerable overlap between these two categories. In fact, asthma is best regarded not as one disease, but as a multifaceted condition, where one or more aspects, often in varying combinations, are evident in any one individual. This will become apparent as we read more about asthma types in the following sections.

### Allergic asthma

Individuals whose asthma symptoms are brought about by exposure to one or more allergens are said to have allergic asthma. Overall, this is the commonest form and is particularly common in children (60–70% of asthma in children is allergic asthma). This is also called atopic asthma. Atopy is an inherited tendency in some individuals to produce a particular type of antibody called immunoglobulin E or IgE for short. These antibodies are produced when someone is exposed to a new allergen for the first time or the first few times in life (called the initial exposure). Once these antibodies have been produced, they have the ability to react on subsequent exposures to the same allergen.



## Asthma · the facts

The reaction that ensues in the body following these subsequent exposures may produce the symptoms of asthma. It is possible to identify what these individuals with allergic asthma might react to by doing an allergy skin test. When a suspected allergen is injected under their skin, these individuals react with localized itching, swelling, and redness. Those with a hereditary tendency towards this type of allergy are likely to have allergic asthma, but in addition may develop a number of other related allergic conditions such as hay fever, runny nose (rhinitis), eczema, hives, and skin rashes.

### Fact!

Childhood allergic asthma is more common in boys than in girls.

Avoidance of specific allergens (for example, those identified by an allergy skin test) and other precipitating factors is helpful in the management of asthma.

## Non-allergic asthma

In a subgroup of asthmatics, allergens do not play a significant role in causing asthma symptoms or asthma attacks. These are patients who often develop asthma in adulthood, and an allergy skin test or blood test cannot identify a specific allergen. The allergy antibody (IgE) levels are low in these groups. What causes asthma in these individuals remains a mystery and it is difficult to identify a triggering agent. Nonetheless, inhalation of chemicals and cigarette smoke, exposure to cold air, laughter, food additives, and a myriad of other factors are implicated and may act as an irritant in the bronchial tubes.

In common with patients with allergic asthma, these people have twitchy airways and manifest symptoms such as wheezing, chest tightness, and cough. This group does not need to worry about avoidance of allergens such as dust mites or furry animals. However, avoidance of irritant triggers such as cigarette smoke, perfumes, and cold air should be possible and does help.

## Exercise-induced asthma

Physical exertion is an important cause of symptoms in many patients with asthma. For some people, exercise is the only cause of their asthma symptoms. These subjects do not usually have any symptoms until they exercise, when symptoms of breathing difficulty, a sense of tightness in the chest, and wheezing (a whistling sound) develop. Symptoms rarely occur during exercise; they more typically develop 5–10 minutes after completing the exercise. Symptoms vary in



severity and in most cases resolve within 30–45 minutes. Children with exercise-induced asthma are not able to keep up with their peers in games and thus avoid participation in physical activities. Exercise-induced asthma is more common in younger people, and it is believed that the airways of these patients are sensitive to changes in the temperature and humidity of the air.

In cold, dry weather, the effect of exercise is exaggerated. When at rest, we breathe through the nose, which warms and humidifies the air making it more like the air in the lungs, but while exercising, we breathe through our mouth, making the air delivered to the lungs colder and dryer. This difference between the warm air in the lungs and the cold, dry inhaled air can trigger asthmatic symptoms. Once triggered, the muscles around the bronchial tubes constrict and the lining of the breathing tubes swells, leading to narrowing and asthma symptoms.

Some forms of exercise such as running are more likely to precipitate asthma symptoms. Sports and games that require more continuous activity and those that are played in cold weather are more likely to precipitate exercise-induced asthma. These include:

- ◆ long-distance running;
- ◆ basketball;
- ◆ ice and field hockey;
- ◆ football;
- ◆ cross-country skiing.

Activities that are less likely to trigger asthma symptoms include:

- ◆ walking;
- ◆ swimming;
- ◆ track and field events;
- ◆ golf;
- ◆ volleyball;
- ◆ wrestling;
- ◆ gymnastics;
- ◆ hiking.

The severity of symptoms depends upon the individual's sensitivity, how cold or dry the ambient air is (the colder and drier the air, the more severe the symptoms), if the exercise is continuous or intermittent (the symptoms are more severe with continuous exercise), and how strenuous the exercise is (the more strenuous it is, the greater the need to breathe more heavily and therefore the more severe the symptoms). Taking prophylactic medications can prevent the onset of symptoms, and allow children to participate in games and healthy physical activities.

### Cough-variant asthma

In some individuals with asthma, chronic (long-term) cough is the principal, if not the only, symptom of asthma. This is more common in children and the symptoms are more pronounced at night. The cough is usually dry or non-productive. These patients usually do not have the typical symptoms of wheezing, chest tightness, or shortness of breath. However, they may have hypersensitivity of the airways as in patients with typical asthma and they may react to triggers such as exercise, exposure to allergens, and irritants. Cough-variant asthma should not be considered as a different entity because there is inflammation of the airways in this group similar to that of typical asthma. However, when these patients present with cough as the only symptom, it is important to consider other causes of chronic cough.

The diagnosis of cough-variant asthma is difficult. These patients do not have typical asthma symptoms such as wheezing or difficulty breathing, and often have normal lung function. Apart from excluding other causes of chronic cough, it is important to make a positive diagnosis of asthma. This can be done with certain tests. These patients may manifest hypersensitivity of the airways, which can be demonstrated using specialized breathing tests. A treatment response may also be of help. For example, administration of bronchodilators or steroid-containing inhalers may improve the symptoms, indicating the presence of an underlying tendency towards asthma. Once the diagnosis is made, it is important to treat this group of patients, because 30% of patients with cough-variant asthma eventually develop classical asthma.

### Nocturnal asthma

Nocturnal asthma is a term used to describe the asthma of patients whose symptoms get worse at night. It is still being debated whether nocturnal asthma is a separate type of asthma or is only a symptom of severe asthma. The majority of these patients—almost 75%—experience increased symptoms at night, and frequent night-time wakening due to asthma implies poor asthma control. The breathing problems associated with nocturnal asthma often cause patients to awaken during the night.

Disruption of the amount or quality of sleep can result in daytime sleepiness, and may affect the ability to learn and perform tasks. Therefore, treatment for nocturnal asthma can improve the quality of life for these patients. The signs and symptoms of nocturnal asthma are similar to classical asthma, but are often under-reported because they occur at night. This indicates that nocturnal asthma may merely reflect poor control of asthma, and this is perhaps the case in the majority of people with prominent asthma symptoms at night. However, some patients do not have severe asthma and have hardly any symptoms during the daytime, but are bothered by symptoms, often chronic cough, at night. These patients may be suffering from a variant form of asthma.

### Fact!

The majority of nocturnal asthma symptoms occur between midnight and 8 a.m., peaking at 4 a.m.

It is at this time of night that the lung functions are at their lowest levels. This is mainly due to normal variations in the body functions that facilitate changes according to the time of day (or night), something called circadian rhythm. It is partly explained by the level of certain hormones such as adrenalin and cortisol, which are at their lowest levels during the early morning hours. These hormones are protective against asthma, as their natural effect is to widen the airways and suppress inflammation.

Other factors may also explain the occurrence of nocturnal symptoms in asthma. Some argue that exposure to the house dust mite may be an explanation in those who are sensitized to this allergen. House dust mite allergen is found in abundance in mattresses and pillows, and even minor disturbances of this reserve as we sleep increases the level of allergen in the air that we breath during the night.

Other factors such as reduced levels of asthma medication in the body system at night and a decrease in room temperature may also play a part. Another factor in some people may be acid reflux (heartburn), which can make asthma worse at night. In the lying position, stomach acids may trickle back into the throat and then into our breathing tubes or airways. The lining of the airways is very sensitive, and even the tiniest amount of acid irritates and burns the lining, initiating a cough response; this may become persistent if this acid trickling occurs every night or on a regular basis. It can then lead to chronic inflammation seen in the more typical forms of asthma (as opposed to nocturnal cough only). Successful treatment of the heartburn can sometimes improve asthma symptoms. Nocturnal asthma appears more often in patients who are obese. The reason for this is not entirely clear, but may be related to increase acid reflux or hormonal effects.

## Occupational asthma

Occupational asthma is defined as asthma caused by exposure to an agent encountered in the work environment. Over 300 substances have been associated with occupational asthma. These include:

- ◆ small molecules such as isocyanates;
- ◆ irritants;
- ◆ platinum salts;
- ◆ animal biological products;
- ◆ plant products.

These are all capable of provoking the immune system to produce allergic antibody (IgE). Occupational asthma generally affects adults of working age as they become exposed to sensitizing chemicals at their work place.

### Fact!

Around one in ten cases of asthma in adults is due to occupational exposure to allergens.

Individuals working in certain types of work or industry are at higher risk. These include:

- ◆ farming and agricultural work;
- ◆ painting (including spray painting);
- ◆ cleaning work;
- ◆ plastic manufacturing.

Soldering is a procedure that is used commonly in many industries, particularly in the electronic industry. Certain resins used as flux in soldering may give rise to vapours of a substance called colophony, which is an important cause of occupational asthma. Substances of biological origin, such as flour, wood dust, and animal dander, are also important causes of both occupational asthma and occupational rhinitis.

**Table 1.2** Suspected causes of occupational asthma

Substance	Industry/occupation at risk
Isocyanates	Polyurethane: insulators, laminators; plastics: roofers, painters, chemists, rubber workers
Anhydrides	Chemical workers, paint and plastic workers, those working with epoxy resins
Metals	Chrome platers, welders, platinum refiners, nickel platers, tool grinders, diamond polishers
Drugs	Pharmaceuticals, laboratory workers, farm workers, fumigators, pesticide formulators
Formaldehyde	Embalmers, laboratory workers, insulators, textile workers
Glutaraldehyde	Hospital staff
Ethylenediamine	Photographic processors, rubber workers
Persulfate salts	Beauticians, chemical workers
Ammonium thioglycolate	Beauticians
Hexamethylenamine	Pesticide industry
Polyvinyl chloride	Meat wrappers
Pyrethrin	Fumigators
Animals	Farmers, veterinarians, meat processing, poultry breeders, bird fanciers, laboratory workers, oyster farmers, prawn and crab processors, silk sericulturers
Plants	Farmers, grain handlers, bakers, brewers, millers, textile workers, cigarette manufacturers, spice processors, coffee and castor bean workers
Vegetable gums	Printing, food processing
Wood dusts	Woodworkers
Dyes	Fabric and fur dyeing, cosmetics, dye manufacturers
Fluxes (Colophony)	Solderers, electronic workers
Enzymes	Pharmaceutical workers, detergent manufacturers, food processors, plastic and rubber workers

People working in these environments do not become asthmatic as soon as they start work and are exposed to these chemical or biological substances. Indeed, it is not uncommon for asthma to appear months or even years after the onset of exposure to the sensitizing substance. Why some people develop occupational asthma whilst others, working in the same environment, do not is not entirely clear. However, it may depend on their genetic risk in combination with other environmental exposures. For example, individuals with an inherited allergic tendency (atopy) are at higher risk. Similarly, those who smoke run a higher risk of becoming sensitized to these occupational substances and developing asthma.

Workers may be unaware of the possible relationship between their symptoms and their work. Even if they do suspect a link, they may still be reluctant to present their concerns to their doctor, fearing adverse consequences for their employment. The indicators of occupational asthma include development or worsening of asthma-type symptoms at work or after work, with disturbance of sleep and an improvement in symptoms when away from work (for example, over the weekend or while on holiday). The symptoms are the same as those of more typical forms of asthma, including wheezing, chest tightness, cough, chest pain, shortness of breath, and fatigue. These symptoms may or may not be associated with rhinitis (hay fever)-type symptoms such as sneezing, a stuffy runny nose, and itchy eyes indicating the presence of occupational rhinitis, or itchy red skin (indicating occupational eczema).

Once a diagnosis of occupational asthma has been established, complete avoidance of the sensitizer is paramount in the management of this condition.

If diagnosis and avoidance of the sensitizer is carried out early enough, it is likely that asthma symptoms will improve quickly and may even disappear. However, if exposure to the substance had continued for some time, the disease may persist for several years, even after removal from exposure of the causative agent. Continued exposure may lead to increasingly severe and potentially fatal asthma exacerbations. Some of the occupations that can lead to occupational asthma are listed in Table 1.2.

### Aspirin-sensitive asthma

Most people with asthma do not have any problems with aspirin. However, some subjects with asthma develop symptoms if they consume aspirin or other related painkillers (non-steroidal anti-inflammatory drugs).

Estimates vary, but aspirin sensitivity may occur in 5–10% of asthmatics.

Often, patients with asthma are advised by their physicians to avoid aspirin in case they have aspirin sensitivity. This is because there is no simple test to confirm or refute this possibility. If asthma symptoms clearly get worse or someone has an exacerbation after taking aspirin, then aspirin and non-steroidal anti-inflammatory drugs should be avoided. If there is any doubt, an inhalation test (called an aspirin-lysine bronchial challenge) can be organized by an asthma specialist.

### Case study

#### Asthma and sensitivity to aspirin

A 24-year-old man developed nettle rash after taking aspirin for a headache. The rash and swelling subsided over the next few hours, but a couple of weeks later he had another similar episode after taking aspirin. He avoided aspirin, but over the next few weeks, he gradually developed an intermittent rash and the respiratory symptoms of cough, wheezing, shortness of breath, and chest tightness. He could not identify any specific triggers for these symptoms. He made an appointment with his GP who, after assessment, told him that he had developed asthma and needed treatment with inhalers. With regular use of a preventative inhaler, he improved, but some wheezing and rash persisted. He was referred to an asthma specialist who, after assessment, made a diagnosis of aspirin sensitivity causing asthma and recurrent urticaria (rash) was made. He was put on a diet that excluded food containing small quantities of salicylate for four weeks. His symptoms improved significantly, and his requirement for the rescue inhaler was reduced. He was then asked to reintroduce salicylate, and, within a week, his rash and asthma symptoms returned, confirming the diagnosis.

### Refractory asthma

In characterizing the severity of asthma, various factors need to be considered including:

- ◆ the level of symptoms and medication use;
- ◆ pulmonary function;
- ◆ the degree of sensitivity of the airways;
- ◆ the type and severity of airway inflammation;
- ◆ the need for hospitalization;



## Asthma · the facts

- ◆ the frequency and severity of exacerbations;
- ◆ the response to treatment;
- ◆ the impact on health and well-being.

Refractory asthma is defined as asthma with persistent symptoms and/or frequent or serious exacerbations accompanied by serious airway obstruction that requires high doses of steroids to control.

Other equivalent designations are severe or difficult-to-control asthma. This is only a small proportion (5–10%) of the total number of asthmatics, but they account for the majority of hospital admissions and hospital visits for asthma worsening. These patients do have certain features peculiar to this form of asthma, such as a specific type of inflammation in the airways. Nonetheless, it is not clear whether this is a distinct form of asthma or simply typical asthma that is very severe. The important aspect of labelling someone with refractory asthma is that these individuals should be managed by a specialist. It is also imperative that they adhere to their prescribed medications, avoid smoking, and are aware of the early symptoms of asthma worsening for early intervention.

## Steroid-resistant asthma

A prominent feature of asthma is the presence of inflammation in the airways. This inflammation almost always responds to treatment with steroids, usually given in inhaled form, but occasionally as tablets or injections, e.g. during an attack or for those with severe asthma. A minority of those with severe asthma do not respond adequately even to oral steroids. These patients are regarded as having steroid-resistant asthma. Whether this lack of response to steroids is simply a manifestation of the severity of asthma or is indeed a separate entity is not clear.

## Does smoking cause asthma?

The answer to the question of whether asthma can be caused by smoking is not straightforward. Smoking usually causes chronic bronchitis and emphysema, which are different diseases. However, some people with chronic bronchitis and emphysema do behave like asthmatics. Moreover, some people with asthma, when they smoke, develop a mixed type of disease with features of both asthma and bronchitis/emphysema. There is also evidence that smoking may increase the risk of asthma developing in the first place.

Research has revealed that people whose partners smoke are nearly five times more likely to develop asthma than those who are not exposed to passive smoking.



It is also believed that children of mothers who smoked during pregnancy are more likely to have respiratory problems and are much more likely to develop asthma. Children are especially at risk because their lungs are smaller and still developing. Exposure to second-hand smoke can lead to decreased lung function and symptoms of airway inflammation. These people are also more likely to develop lung and sinus infections. These infections can make asthma symptoms worse and more difficult to control.

There is no doubt that exposure to cigarette smoke makes asthma symptoms worse, whether it is active (by the asthmatic subject) or passive (by those around them). Because the airways of asthmatics are more sensitive than non-asthmatic subjects, smoking irritates the airways of asthmatic subjects even more, making them inflamed, swollen, narrow, and full of mucus. This leads to worsening symptoms of asthma such as cough, wheezing, and shortness of breath. These symptoms are similar to those during an asthma flare-up. In other words, smoking can lead to frequent asthma flare-ups, which may be more severe and more difficult to control, even with medication.

Studies have shown that asthma control is significantly worse in asthmatics who smoke compared with those who have never smoked, with all symptoms related to asthma control uniformly worse in smokers, even in those with relatively good lung function. Furthermore, smoking can reduce the effect of any controlling medications being taken for asthma and can increase the use of rescue medications. Inhaled steroids are the mainstay of treatment in asthma acting as preventers of symptoms. Smoking confers a degree of steroid resistance in asthma, thereby making the drugs less efficacious. In addition, the long-term effect of smoking in asthmatics is to cause permanent damage to their lungs and airways.

Quitting smoking and avoiding second-hand smoke therefore:

- ◆ improves asthma control;
- ◆ improves asthma flare-ups;
- ◆ decreases the number of emergency visits to hospital;
- ◆ improves the response to medications, both preventative and rescue;
- ◆ reduces the likelihood of developing asthma in adulthood;
- ◆ decreases the likelihood of asthma persisting in adulthood.

There is evidence to suggest that by the sixth week after ceasing smoking, there is considerable improvement in lung function and a reduction in the inflammation of the airways compared with individuals who continue to smoke, highlighting the importance of smoking cessation in asthma patients.

## Classification of asthma severity

Asthma is classified into various categories based primarily on the level and frequency of symptoms, i.e. whether symptoms are mild, moderate, or severe, and if these symptoms are intermittent or persistent.

The four categories of asthma are mild intermittent, mild persistent, moderate persistent, and severe persistent.

The degree of impairment of lung function is also taken into account (Table 1.3).

The classification of asthma is useful for decision-making in asthma management. This classification of asthma according to severity reflects not only the severity of the underlying disease, but also the responsiveness to treatment and is subject to change. For example, on initial presentation, an individual could be classified as having severe persistent asthma, but could respond well to treatment and then be reclassified as having moderate persistent asthma.

**Table 1.3** Classification of asthma

Category	Symptoms
Intermittent	Symptoms less than once a week Occasional, mild, and short-lasting exacerbations Night-time symptoms less than twice a month Good lung function, as indicated by: ◆ FEV <sub>1</sub> or PEF more than 80% of normal or expected ◆ variation in FEV <sub>1</sub> or PEF of less than 20%
Mild persistent	Symptoms more than once a week, but less than once a day Exacerbations may affect sleep and activities Night-time symptoms more than twice a month Average lung function, as indicated by: ◆ FEV <sub>1</sub> or PEF more than 80% of normal or expected ◆ variation in FEV <sub>1</sub> or PEF of 20–30%
Moderate persistent	Daily symptoms Exacerbations may affect sleep and activities Night-time symptoms more than once a week

(continued)

**Table 1.3** Classification of asthma (*continued*)

Category	Symptoms
	<ul style="list-style-type: none"> <li>◆ FEV<sub>1</sub> or PEF 60–80% of normal or expected</li> <li>◆ variation in FEV<sub>1</sub> or PEF of more than 30%</li> </ul>
Severe persistent	Daily symptoms Frequent exacerbations Frequent night-time symptoms Limitations of physical activity Poor lung function, as indicated by: <ul style="list-style-type: none"> <li>◆ FEV<sub>1</sub> or PEF of less than 60% of normal or expected</li> <li>◆ variation in FEV<sub>1</sub> or PEF of more than 30%</li> </ul>

PEF, peak expiratory flow; FEV<sub>1</sub>, forced expiratory volume in one second

Lung function tests or pulmonary function tests evaluate how well the lungs work. The simplest breathing test is called peak expiratory flow (PEF), which is a measure of how rapidly the patient can blow out air. This is directly related to the size of the bronchial tubes, which tend to narrow in asthma. A variation in the size of bronchial tubes causing changes in peak flow is one of the main features of asthma and helps in the diagnosis. Spirometry is also a basic lung function test. It measures how much and how quickly a person can move air out of the lungs. For this test, after a deep breath, the person is asked to breathe forcefully into a mouthpiece attached to a recording device (spirometer), and various volumes of air are recorded and can be printed. The most useful is FEV<sub>1</sub> (forced expiratory volume in one second), i.e. the amount of air that comes out in the first second of a forceful breathing effort. Other parameters are also sometimes measured to assess detailed lung function, severity of airway narrowing, and the twitchiness of the airways. These will be dealt with in subsequent chapters.

