

chapter 7

Asthma

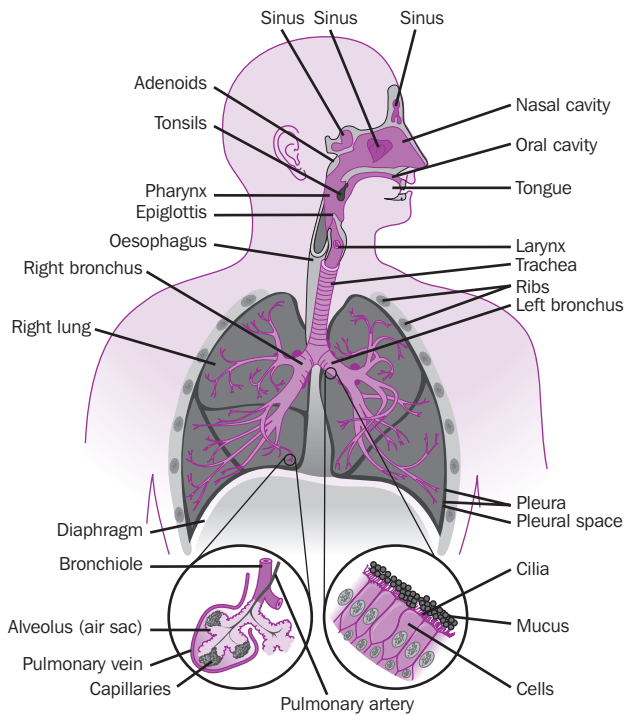


Figure 7.1 The respiratory system.

Overview

- Asthma is a chronic condition with a pattern of acute episodes separated by periods with few symptoms.
- It is managed using a stepwise approach.
- Management is mainly through the use of inhaled therapies.
- Patients can have a significant role in self-management.
- Ensuring patients know how to use their inhaler devices appropriately is a key factor in management.
- Acute episodes are potentially life-threatening events.

Tip

Although NSAIDs are generally considered to be contraindicated in asthmatic patients, a carefully taken drug history can often reveal that patients have taken over-the-counter preparations containing NSAIDs without any problem.

Aetiology

- The disease process results from hypersensitivity of the lungs to one or more stimuli (Table 7.1).
- The body reacts to stimuli to produce chronic bronchoconstriction.
- Allergens act on macrophages, T-lymphocytes, epithelial cells and eosinophils. Each produces inflammation through direct or neural mechanisms.
- Mast cells release histamine, leukotrienes and prostaglandins to induce bronchospasm.
- The immune response leads to marked hypertrophy and hyperplasia of bronchial smooth muscle, resulting in narrowing of the small airways.
- Bronchial gland and goblet cell hypertrophy results in excessive mucus production, often more viscous than usual. This can plug the airways in conjunction with epithelial and inflammatory cell debris.
- Airways become oedematous and mucociliary clearance is decreased.
- In the long term, the airways can become more responsive to triggers and acute bronchoconstriction can occur, leading to acute severe episodes.

Table 7.1 Common triggers in asthmatic patients

Trigger type	Examples
Allergens	Pollen, house dust mites, moulds, pets
Chemicals	Paints, cleaning products, aerosols, aluminium
Foods	Dairy products, food dyes, nuts, seafood
Industrial	Wood dust, colophony, cotton, smoke, sulphur dioxide
Medications	NSAIDs, beta-blockers
Others	Stress, exercise, cold air, viral infections, emotions

Epidemiology

- Prevalence is difficult to determine as there is an overlap with other respiratory conditions, such as chronic obstructive pulmonary disease (COPD), difficulty in diagnosis in children and variation in the classification of airway restriction.
- It is thought that there are 5.2 million people in the UK are being treated for asthma, of whom 1.1 million are children.

- It is estimated that one in five households in the UK has a person suffering from asthma.
- Prevalence in children is thought to be approximately 5–10%, with 30–70% becoming asymptomatic by adulthood.
- Asthma is vastly more prevalent in the developed world than in the developing world, owing to increased exposure to environmental triggers, diet and stress.

Signs and symptoms

Patients can present with a range of symptoms; however, certain characteristics can help to diagnose, or exclude, asthma. Patients often describe fluctuating severity of symptoms, with varying time periods that may be symptom free. The most common symptoms indicative of asthma are:

- wheeze
- breathlessness
- chest tightness
- chronic cough.

Patients also have a history of atopic disorders such as eczema, family history of asthma or atopy, unexplained peripheral blood eosinophilia and widespread wheeze of auscultation of chest.

Symptoms and factors that may indicate an alternative disease state include a significant smoking history (i.e. greater than 20 pack-years), symptoms only with viral infections, voice disturbance, normal chest examination when symptomatic, dizziness, chronic productive cough in absence of wheeze and breathlessness.

Investigations

Initial diagnosis is made using the presence of clinical signs and symptoms but requires further tests to confirm.

Lung function tests

- A spirometer is used to determine the patients forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC). FEV_1 is a measure of the volume of air expelled in the first second of breathing out. FVC is a measure of the maximum volume of air it is possible for the patient to breathe out after taking maximal inspiration.
- The FEV_1/FVC ratio is used to determine the severity of airway obstruction. A patient with normal airways should have a value of approximately 0.75. In asthmatic patients, it is usually 0.7.
- Peak expiratory flow rate (PEFR) can be measured by the patient using a peak flow meter.
- Variability in readings of greater than 20% and at least 60 mL on 3 days of a week is highly suggestive of asthma.

- A peak flow meter can also allow patients to monitor their condition on a daily basis, particularly when they feel an increase in their symptoms.

Management

The management of asthma is split into two phases, chronic and acute. Acute asthma is an emergency.

Chronic management

The aim of treatment in the chronic phase is to control the disease. Control is defined as:

- no daytime symptoms
- no acute episodes
- no night-time awakening
- no need of rescue medication
- no limitations on activity owing to asthma
- normal lung function, defined as FEV₁ and/or PEF_R 80% predicted or best
- minimal adverse effects.

A stepwise approach is utilised in the chronic management of asthma. There are five steps to therapy and treatment should be initiated at the most appropriate step for the patient's symptoms (Table 7.2).

- Treatment should be reviewed regularly and stepped up if control is inadequate or down if control is good.
- Patients should also be educated to avoid their known trigger factors where possible.
- The majority of treatments are administered via inhalation in order to minimise side-effects and maximise delivery to the target site.
- Patient's inhaler technique should be assessed at every review and counselling to improve should be provided or a change to the inhaler device considered if technique is not adequate.
- All asthmatic patients should receive "reliever" inhalers for the relief of symptoms and those at stages 2 to 5 (Table 7.2) should receive "preventer" inhalers.

Reliever medication

- *Beta-adrenoceptor agonists* are the basis of asthma therapy. Examples are salbutamol and terbutaline.
- They act on β_2 -adrenoceptors to produce bronchodilation. They have some effect on β_2 -adrenoceptors in cardiac tissue to produce tachycardia.
- Inhaled anticholinergic agents (e.g. ipratropium) have a slower onset but longer duration of action than the β_2 -adrenoceptor agonist.

Table 7.2 Treatment steps in the chronic management of asthma in adults^a

Treatment	
Step 1 ↓	Occasion relief with bronchodilator Inhaled short-acting β_2 -agonist, e.g. salbutamol, when required Move to step 2 if required more than twice weekly, significant night time symptoms once weekly, or exacerbation within last 2 years requiring systemic steroids or nebulised bronchodilators
Step 2 ↓	Inhaled short-acting β_2 -agonist when required Plus, standard dose inhaled corticosteroid regularly, e.g. beclometasone dipropionate 100–400 μg twice daily or equivalent
Step 3 ↓	Inhaled short-acting β_2 -agonist when required Plus, standard dose inhaled corticosteroid regularly Plus, trial of inhaled long-acting β_2 -agonist regularly, e.g. salmeterol or formeterol, to be stopped if no apparent benefit If asthma not controlled, ensure corticosteroid dose is at higher end of dose range and consider adding leukotriene receptor antagonist, theophylline or oral β_2 -agonist
Step 4 ↓	Inhaled short-acting β_2 -agonist when required Plus, high-dose inhaled corticosteroid regularly, e.g. beclometasone dipropionate 400–1000 μg twice daily or equivalent Plus, inhaled long-acting β_2 -agonist regularly Plus, a 6 week trial of one or more of leukotriene receptor antagonist, theophylline or oral β_2 -agonist
Step 5 ↓	Inhaled short-acting β_2 -agonist when required Plus, high-dose inhaled corticosteroid regularly Plus, one or more long-acting bronchodilators Plus, regular oral prednisolone

^aPatients can move up and down the steps as dictated by assessments.

- Inhaled anticholinergic agents are normally only used in acute severe asthma or in patients with mixed asthma and COPD.
- Inhaled *corticosteroids* are the most common agents used for the long-term control of asthma. The dose used should be the lowest effective dose for the patient and should be reviewed regularly.
- When corticosteroid dose reductions are felt to be appropriate, they should be done in increments of approximately 25–50% of the total dose every 3 months.
- Doses of inhaled corticosteroids are expressed as the equivalent dose of beclometasone given via CFC-containing metered dose inhaler (MDI). It is important to bear in mind the equivalence of the corticosteroid used to beclometasone when switching from one to another.
- Corticosteroids are usually initiated in patients who have had an exacerbation within the last 2 years while using inhaled β_2 -adrenoceptor agonists three or more times per week, who have experienced symptoms three times a week, or who are awakened one night a week.
- Adrenal suppression is unlikely but is more likely to occur at doses of 2 mg per day.

- Inhaled corticosteroids can cause candidiasis and vocal harshness. This can be minimised with the use of large-volume spacer devices and rinsing the mouth after use.
- Long-acting β_2 -adrenoceptor agonists (LABA) are added to patient's therapy when low-dose inhaled corticosteroids have had an inadequate response. Examples are salmeterol and formoterol.
- The long-acting β_2 -adrenoceptor agonists should be trialed for 4 to 6 weeks and discontinued if there is no response.
- The long-acting β_2 -adrenoceptor agonists are unsuitable for use as relievers and should not be used without inhaled corticosteroids.
- *Theophylline* or *aminophylline* are oral bronchodilators. They have a narrow therapeutic window, so patients require individual dosing regimens optimised using therapeutic drug monitoring.
- Toxicity with theophylline or aminophylline may present as vomiting, insomnia, fitting, arrhythmia, hyperglycaemia and hypotension.
- *Leukotriene antagonists*, such as montelukast, are oral agents useful for patients with difficulty in controlling asthma. They are especially useful in those with aspirin-induced asthma.
- Anti-IgE monoclonal antibodies are a new class of asthma treatment. The first agent in the class is omalizumab. Their use is restricted to those with severe persistent allergic asthma failing to respond to other agents. They are a very costly therapy and are currently rarely used.
- Long-term oral corticosteroids are only used in chronic management when other options have failed to adequately achieve treatment goals.
- Long courses of oral corticosteroids are associated with adrenal suppression, osteoporosis, skin thinning, peptic ulceration, bruising and many other adverse effects.
- In those requiring long-term oral steroids, agents such as oral gold, methotrexate and ciclosporin have been used with varying success. They should only be prescribed by specialists and their use must be closely monitored.

Tip

Salbutamol overdose is virtually impossible to achieve, so patients with acute severe asthma should use as much as they feel they require.

Acute management

Acute asthma is a life-threatening emergency. Patients should be reviewed and managed as soon as possible. The severity of the episode must be assessed and treated accordingly. It is classified into three types according to the results of the assessment:

- *moderate exacerbation*
 - increasing symptoms

- PEFR 50–75% of best or predicted
- no features of acute severe asthma
- *acute severe asthma*: any one of PEFR 33–50% of best or predicted, respiratory rate 25 breaths/min, heart rate 110 beats/min or inability to complete sentences
- *life-threatening asthma*: the presence of any one of:
 - PEFR 33% of best or predicted
 - SpO₂ 92% (peripheral oxygen saturation measured by pulse oximetry)
 - PaO₂ 8 kPa (arterial oxygen tension)
 - normal PaCO₂ (arterial carbon dioxide tension)
 - silent chest
 - cyanosis
 - feeble respiratory effort
 - bradycardia, arrhythmia, hypotension
 - exhaustion, confusion, coma.

Patients should be admitted if they have life-threatening asthma or acute severe asthma that fails to respond to initial treatment.

In those not requiring admission, treatment with increased doses of β_2 -adrenoceptor agonists and a short course of corticosteroids (e.g. prednisolone 40–50 mg daily for 1 week) is normally sufficient.

In those requiring admission, further treatment is required.

- High-flow oxygen.
- Nebulised, high-dose β_2 -adrenoceptor agonists.
- Nebulised ipratropium may be added if required.
- Oral corticosteroids, as above; IV hydrocortisone can be given in patients unable to tolerate oral therapy.
- A single dose of IV magnesium sulphate 1.2–2 g can be given to patients with acute severe asthma without a good response to inhaled bronchodilator therapy or with life-threatening asthma.
- IV aminophylline may be administered to those without adequate response to other therapies. It is given as an initial bolus of 250 μ g, followed by an infusion of 500 μ g/kg per hour. The bolus dose is omitted in those already taking aminophylline or theophylline therapy.
- Antibiotics are only necessary when there are clear clinical signs of infection.

Monitoring parameters

- Many patients can self-monitor their asthma using a peak flow meter and symptom diary.
- All patients should be reviewed by their medical team at appropriate intervals, at least

Tip

Inhalers are available in a wide range of devices. Pharmacists should be familiar with which drugs are available in each device and how each device is used.

annually for stable patients and more often for those with a history of acute severe episodes or inadequate control.

- Patient's treatment should be stepped up and down whenever appropriate.
- Monitoring should include an assessment of their symptoms, their objective lung function data and frequency of acute episodes.
- The presence of any side-effects to drug therapy should be ascertained.

Counselling

- Patients should have a firm knowledge of the actions and side-effects of the drugs they are taking.
- The most appropriate inhaler devices should be utilised and patients should receive regular counselling on their use.
- Patients should be told to seek prompt medical advice if there are any signs of acute severe asthma or gradual worsening of symptoms with a loss of response to inhaled β_2 -adrenoceptor agonists.

Multiple choice questions

1. Which of the following is *not* a sign of asthma?
 - a. Shortness of breath
 - b. Chronic cough
 - c. Dizziness
 - d. Chest tightness
 - e. Wheeze

2. Are the following statements regarding asthma true or false?
 - a. Lung function tests are carried out to aid diagnosis.
 - b. There are six steps to asthma therapy.
 - c. Salbutamol is a beta-agonist.
 - d. Overdose with salbutamol is common in patients with asthma.

Useful websites

www.sign.ac.uk
www.brit-thoracic.org.uk
www.asthma.org.uk