Asthma

Asthma is characterised by paroxysmal and reversible obstruction of the airways. It is increasingly understood as an inflammatory condition combined with bronchial hyper-responsiveness. Acute asthma involves:

- Bronchospasm (smooth muscle spasm narrowing airways).
- Excessive production of secretions (plugging airways).

Triggers unleash an inflammatory cascade within the bronchial tree, leading to the typical symptoms of asthma - eg, wheeze, shortness of breath, chest tightness, cough.

With treatment, persistent inflammation only occurs in patients with under-treated asthma. If their inflammation is appropriately treated there will not be any evidence of ongoing inflammation. Patients with under-treated asthma who continue to have chronic low levels of inflammation may then undergo remodelling of the airways and develop fixed airways disease, which no longer responds as well or even at all to bronchodilator therapy.

Acute severe asthma (status asthmaticus) can be life-threatening and the disease causes significant morbidity, so it is imperative to treat it energetically. The bulk of asthma management has taken place within primary care.

Epidemiology

- Undoubtedly, asthma is a very common condition and, according to Asthma UK:
  - 5.4 million people in the UK receive treatment for asthma: 1 in 11 children and 1 in 12 adults.
  - It is the most common chronic medical condition in children.
  - The cost of asthma to the NHS runs at about a billion pounds per year.

- The sharp increase in asthma and other allergic diseases between the early 1960s and late 1980s is perceived to be a consequence of an intense migration from rural to urban regions, from poor developing countries to rich but heavily industrialised regions of Europe, Asia and Americas.
- Adult-onset asthma differs from childhood asthma in that it is more often non-atopic and severe and has a lower remission rate.
- Although asthma has a relatively low mortality in younger adults, it is associated with substantial morbidity and mortality in the elderly.

The numbers within an individual practice, based on an age/sex/disease register, tend to overestimate true prevalence significantly, as many outgrow asthma without the removal of the diagnosis. It should be changed to past history of asthma when a patient is no longer receiving treatment for the condition.

Risk factors

There is a long list of possible risk factors which includes:

- Personal history of atopy.
- Family history of asthma or atopy.
- Inner city environment; socio-economic deprivation.
- Obesity.
- Prematurity and low birth weight.
- Viral infections in early childhood.
- Smoking.
- Maternal smoking.
- Early exposure to broad-spectrum antibiotics.

Possible protective factors include:

- Breast-feeding.
- Vaginal birth - observational studies suggest that caesarean delivery might be associated with a greater risk of asthma.
- Increasing sibship.
- Farming environment.

Presentation

Features that increase the probability of asthma in adults include:

- More than one of the following symptoms: wheeze, breathlessness, chest tightness and cough, particularly if:
• Symptoms are worse at night and in the early morning.
• Symptoms are present in response to exercise, allergen exposure and cold air.
• Symptoms are present after taking aspirin or beta-blockers.
• History of atopic disorder.
• Family history of asthma and/or atopic disorder.
• Widespread wheeze heard on auscultation of the chest.
• Otherwise unexplained low forced expiratory volume in one second (FEV1) or peak expiratory flow (historical or serial readings).
• Otherwise unexplained peripheral blood eosinophilia.

For children, see separate Diagnosing Childhood Asthma in Primary Care article.

History
The history is extremely important, as patients may present between acute attacks when examination and investigation may be completely normal. The paroxysmal nature of the condition is important.

Wheeze or rhonchi may be seen as the cardinal feature but this can be misleading. Ensure that the patient or their parent/carer’s understanding of ‘wheeze’ is the same as yours - whistling, squeaking or gasping sounds, or a different style, rate or timbre of breathing are all sometimes described as ‘wheeze’, so it is important to clarify. Also, wheeze can be absent in severe asthma when there is insufficient air flow to cause wheeze - beware the silent chest.

Ask what happens in an attack. There are a number of possibilities, including wheeze (common but not invariable), cough, shortness of breath and chest tightness.

Ask if there is an obvious precipitating or aggravating factor for attacks:

• Cold symptoms - upper respiratory tract infection (URTI) - frequently trigger exacerbations.
• Cold air - if this causes chest pain in an adult, it may be angina.
• Exercise - symptoms may occur during exercise but more classically after exercise. Running tends to be worse than cycling.
• Pollution - especially cigarette smoke.
• Allergens - exacerbations may occur seasonally around pollen exposure or following exposure to animals such as cats, dogs or horses.
• Time of day - there is a natural dip in peak flow overnight and in a vulnerable person this may precipitate or aggravate symptoms. It may cause nocturnal waking or simply being rather short of breath or wheezy in the morning.
• Work-related - if symptoms are better at home/during holidays, asthma may be related to occupation. This has significant implications and it is sensible to refer the person to a chest physician or an occupational physician. See separate Occupational Asthma article. Adults with a new diagnosis of asthma should be assessed for occupational asthma.

Past, present and family history
• Atopic eczema, asthma and hay fever tend to run together in individuals and in families.
• Ask about medication - the patient may have been started on a beta-blocker recently (including drops for glaucoma) or taken anti-inflammatory drugs. The association between non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin, and the precipitation of asthma is well documented but, in reality, it is not often seen.
• Ask about smoking, including passive smoking.

Examination
See separate Respiratory System History and Examination article. The chest should be examined but this may be normal between attacks:

• Before examining the chest, check the pulse rate. This may be artificially elevated by excessive use of beta_2 agonists but, nevertheless, tachycardia is a significant feature. Respiratory rates above 25 breaths per minute and heart rate above 110 beats per minute are regarded as significant signs in adults[^7]. Where available, also check oxygen saturations in acute attacks (saturations of <92% indicate a more severe subgroup of patients who may require admission).
• Look at the patient’s breathing:
  • Is it fast?
  • Is it laboured?
  • Do they appear anxious?
  • Can they speak in full sentences?
  • Are accessory muscles of respiration employed?
  • Is there pursed lip breathing?
  • Is there cyanosis?

• Note the ratio between the inspiratory and expiratory phase. Usually this can be assessed by counting one on the way in and one, two on the way out. This 2:1 ratio of expiratory to inspiratory phase is normal. The longer the expiratory phase compared with the inspiratory phase, the more severe the obstruction.
• The chest may appear hyperinflated.
• With chronic asthma, there may be chest deformity - eg, Harrison's sulci.
• In a small child, there may be intercostal recession with respiratory distress.
• Check that there is no deviation of the trachea or any abnormality on percussion to suggest pneumonia, pulmonary collapse or pneumothorax.
• There may be diffuse expiratory rhonchi. If they are not diffuse and particularly if asymmetrical in a child, be suspicious of inhaled foreign body. There may be inspiratory rhonchi too. Where rhonchi are predominantly inspiratory and the inspiratory phase is prolonged, this suggests that airway obstruction is outside the chest.

**Diagnosis**

**Undertake a structured clinical assessment to assess the initial probability of asthma.** This should be based on:

- History of recurrent episodes (attacks) of symptoms, ideally corroborated by variable peak flow when symptomatic and asymptomatic.
- Symptoms of wheeze, cough, breathlessness and chest tightness that vary over time.
- Recorded observation of wheeze heard by a healthcare professional.
- Personal/family history of other atopic conditions (particularly atopic eczema/dermatitis, allergic rhinitis).
- No symptoms/signs to suggest alternative diagnoses.

**Compare the results of diagnostic tests undertaken whilst a patient is asymptomatic with those undertaken when a patient is symptomatic to detect variation over time.**

**Carry out spirometry using the lower limit of normal to demonstrate airway obstruction, provide a baseline for assessing response to initiation of treatment and exclude alternative diagnoses.** Obstructive spirometry with positive bronchodilator reversibility increases the probability of asthma. Normal spirometry in an asymptomatic patient does not rule out the diagnosis of asthma.

**In patients with a high probability of asthma:**

- Record the patient as likely to have asthma and commence a carefully monitored initiation of treatment (typically six weeks of inhaled corticosteroids).
- Assess the patient's status with a validated symptom questionnaire, ideally corroborated by lung function tests (FEV1 at clinic visits or by domiciliary serial peak flows).
- With a good symptomatic and objective response to treatment, confirm the diagnosis of asthma and record the basis on which the diagnosis was made.
- If the response is poor or equivocal, check inhaler technique and adherence, arrange further tests and consider alternative diagnoses.

In years to come it may be possible to identify patients with asymptomatic asthma and hence underlying inflammation by using more sensitive tests (eg impulse oscillometry or challenge testing) as equipment becomes available in a clinical setting rather than just in a pure research setting.

**Editor’s Note**

November 2017 - Dr Hayley Willacy draws your attention to the newly released NICE guideline dealing with asthma diagnosis, monitoring and management[^8]. In contrast to the existing SIGN/BTS 2016 Guidance, NICE is now recommending objective testing with spirometry and FeNO for most people with suspected asthma. (FeNO tests measure the levels of nitric oxide in the breath. Increased levels are thought to be related to lung inflammation and asthma.) This is a significant change to current practice, which will take the NHS some time to implement, with additional infrastructure and training needed in primary care. This may involve establishing diagnostic hubs to make testing efficient and affordable. In the meantime, primary care is advised to implement what they can from the guidance, using currently available methods of diagnosis until the infrastructure for objective testing is in place. It is hoped that the recommendations will help tackle inappropriate diagnosis and ensure that if a diagnosis is given, the person is monitored to ensure their symptoms still indicate asthma.

**Differential diagnosis**

Asthma is a very common condition but there are many other diagnoses that must be considered: ‘not all asthma wheezes and all that wheezes is not asthma’. See separate Wheezing in Children article.

**Children**

- **Bronchiolitis** - be aware of the dangers of making a definitive diagnosis of asthma in a very young child.
- Especially if the problem appears to have been present since birth, consider cystic fibrosis. It may also cause severe infections and a persistent cough.
- Other congenital problems may present from birth or early in infancy - eg, laryngeal or tracheal structural abnormalities, congenital heart disease.
- Vocal cord dysfunction mimics steroid refractory asthma[^9].
- Vomiting and aspiration in babies suggests gastro-oesophageal reflux which can cause a cough on lying down.
- Inhalation of a foreign body can occur at all ages from the orally curious infant to the performing, older child catching peanuts or grapes in their mouth. Peanuts tend to go straight down to the right main bronchus and cause considerable inflammation, and obstruct the right lower lobe. The choking episode may not have been observed by an adult or may have occurred sufficiently long ago for the family to have forgotten it.
- Postnasal drip causes a cough, which is worse at night.
- Inspiratory stridor and wheeze suggest a laryngeal disorder including croup.
- Focal signs may suggest bronchiectasis or tuberculosis. The latter is very important if the child is from a high-risk family.
Adults

- COPD (see also separate Diagnosing COPD article):
  - Reversibility distinguishes asthma from COPD, although the reversibility is relative rather than absolute.
  - People with severe asthma may never achieve completely normal parameters for lung function and COPD is rarely totally refractory to medication.
  - People with asthma who have been undertreated or non-compliant (not necessarily with severe asthma) may develop remodelling of the airways due to chronic inflammation and therefore may not show significant reversibility.
  - Almost all patients with COPD do smoke or have smoked in the past. People with asthma can also develop COPD. Whether or not this reflects disease progression or comorbidity is debatable.

- Asthma-COPD overlap syndrome is characterised by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD\(^\text{[10]}\).

- Heart failure can cause nocturnal cough and cardiac asthma.
- Coronary heart disease - chest tightness or pain, especially on meeting a stiff wind on a cold morning - may be asthma or angina.
- Malignancy is important to remember, especially in smokers. Look for clubbing which also occurs in bronchiectasis. Malignancy is not just lung cancer but may be in the upper airways.
- Gastro-oesophageal reflux can cause nocturnal cough and a postnasal drip may cause more coughing when lying down.
- Vocal cord dysfunction mimics steroid refractory asthma\(^\text{[9]}\).
- Other less common causes of chronic cough, wheeze or breathlessness include pulmonary fibrosis, interstitial lung disease, recurrent pulmonary embolism and tuberculosis.

Distinguish wheezing from shortness of breath on exertion - this can be due to heart failure, severe anaemia and obesity, often aggravated by lack of physical fitness.

Investigations

Peak flow

Measurement of peak expiratory flow rate (PEFR) is the simplest and most basic test. Every GP should have a mini Wright's peak flow meter with disposable mouthpieces, and a smaller, low-reading one is often useful for children and for more severe obstruction. Caution should be used when diagnosing asthma based on peak flow readings but it has an important role in the management of established asthma.

Lung function tests, whether peak flow or spirometry, are unreliable below the age of 5 years and even among some older children and adults who lack comprehension or co-ordination for the task. As well as obstruction of airways, poor effort or neuromuscular disease will limit performance. In those able to use a peak flow meter reliably, it is often helpful to prescribe a peak flow meter for home use to encourage self-monitoring and adjustment of treatment in line with a self-management plan.

Technique

- Advise the patient to take in a deep breath and expel it as rapidly and as forcefully as possible into the meter.
- The very first part is all that matters for this test and it is not necessary to empty the lungs completely.
- Record the best of three tests. Continue blows if the two largest are not within 40 L/minute, as the patient is still acquiring the technique.

Interpretation

- Charts of 'normal values' are available. There are different charts for males and females, as males tend to have higher peak flows than females, all other parameters being equal. Expected PEFR increases with increasing height and it varies with age, reaching a peak in the early 20s and then gradually declining. Current normative charts are criticised for being outdated and not encompassing ethnic diversity.
- A patient's peak flow can be compared with that listed normal for their age, sex and height. However, it is often more helpful in a patient with asthma to compare changes with an individual's best peak flow, recorded in a clinically stable period on optimal treatment. Thus, a patient with asthma may have a 'predicted' PEFR of 500 L/minute but know that a peak flow of 400 L/minute indicates reasonable control and that, where it falls to 300 L/minute, appropriate action is required.
- Patients are frequently asked to record a peak flow diary (recording PEFR several times a day over a couple of weeks). It is normal for peak flow to fall slightly overnight and these 'nocturnal dips' may be accentuated in asthma. A marked diurnal variation in peak flow (>20%) is significant. There may be significant day-to-day variation and the patient may be able to demonstrate that testing PEFR after certain aggravating activities causes measurable dips. PEFR is best recorded on a chart which provides graphical illustration of this variability. Peak flow variability is not specific to asthma and so its diagnostic value is debatable\(^\text{[7]}\).
- Reversibility testing can be performed with PEFR testing in subjects with pre-existing obstruction of the airways and is demonstrated by an increase of >60 L/minute.
- Peak flow diaries may also be helpful for patients with moderate or severe asthma. They can provide an objective warning of clinical deterioration.
**Spirometry**
- **Spirometry** is now preferred over peak flow measurement for initial confirmation of obstruction of airways in the diagnosis of asthma, as it is felt to offer clearer identification of airway obstruction, to be less effort-dependent and more repeatable.[7] Spirometry measures the whole volume that may be expelled in one breath (vital capacity). It also permits calculation of the percentage exhaled in the first second - the FEV1. However, as with peak flow, some (particularly young children) may not be able to undertake it reliably.
- Spirometry may be normal in individuals currently asymptomatic and does not exclude asthma, and should be repeated, ideally when symptomatic. However, a normal spirogram when symptomatic does make asthma an unlikely diagnosis.
- It also offers good confirmation of reversibility in subjects with pre-existing obstruction of the airways where a change of >400 mL in FEV1 is found after short-term bronchodilator/longer-term corticosteroid therapy are trialled.

**CXR**
CXR is remarkably normal, even in very severe asthma. It should not be used routinely in the assessment of asthma but consider CXR in any patient presenting with an atypical history or with atypical findings on examination[7].

**Assessment and review[7]**

See separate *Acute Severe Asthma and Status Asthmaticus* article.

All patients with asthma in primary care should be reviewed at least annually and reviews should include:

- Symptomatic control assessment using a directed question-based tool. The ‘three questions’ approach of the Royal College of Physicians has been widely used and valued for its simplicity, although it is poorly validated:
  - Have you had any difficulty sleeping because of your asthma symptoms, including cough?
  - Have you had your usual asthma symptoms during the day (cough, wheeze, chest tightness of breathlessness)?
  - Has your asthma interfered with your usual activities (housework, work, school, etc)?

- Alternatives include the Asthma Control Questionnaire, Asthma Control Test and Mini Asthma Quality of Life Questionnaire.
- Measurement and recording of lung function with peak flow or spirometry.
- Review of exacerbations in the previous year, use of oral corticosteroids and time off school or work.
- Check inhaler technique.
- Check patient adherence and bronchodilator reliance. Review medication use - the use of more than two canisters of reliever per month or 10-12 puffs per day is associated with poorly controlled and higher-risk asthma.
- Check patient ownership and use of an asthma action plan.

**Management[7]**

**The stepwise approach**

See separate *Management of Adult Asthma* and *Management of Childhood Asthma* articles. The National Institute for Health and Care Excellence (NICE) has defined Quality Standards for asthma care[11]. These evidence-based standards cover all aspects of diagnosis and management.

As management is discussed in detail elsewhere, this section will be confined to general principles. The management of asthma is based on four principles:

- Control symptoms, including nocturnal symptoms and those related to exercise.
- Prevent exacerbations and need for rescue medication.
- Achieve the best possible lung function (practically, FEV1 and/or PEFR >80% predicted or best).
- Minimise side-effects.

To achieve this:

- Start at the appropriate step according to the severity of the presenting condition.
- Achieve early control.
- Step up or down the medication to enable optimum control without excessive medication. Maintain patients on the lowest possible dose of inhaled steroid. Reduce slowly, with reductions of 25-50%, every three months.
- Always check compliance with current medication, and inhaler technique, and exclude triggers as far as possible before starting a new drug.
- Patient education and access to a written personalised action plan are considered critical.

It is very important to consider the upper respiratory tract when treating asthma. It is much more difficult to treat asthma successfully if co-existing allergic rhinitis is not adequately controlled.
Devices
Delivery of drugs to the lungs is a very efficient method in terms of both swiftness of action and limitation of systemic side-effects. However, it is essential to ascertain that the patient is competent at using the inhaler. Simply giving a prescription for a metered dose inhaler (MDI) is inadequate; steps must be taken to teach the patient to use the device and to check technique. There are many types of inhaler and they can be used by even the very young. The choice is discussed in the separate Which Device in Asthma? article. The value of spacers is also discussed, as not only the young have poor co-ordination; spacers may be just as important for adults and the elderly who have difficulties. See separate Nebulisers in General Practice article.

Drug treatment
Current UK guidelines advocate the following, stepwise drug management for adults[7]:

- **Step 1** - for those with very mild, intermittent asthma, the occasional use of a beta2-agonist inhaler may be all that is required but all patients with asthma should be prescribed this for short-term relief of symptoms as required.
- **Step 2** - start regular inhaled steroid at an appropriate dose for the severity of disease (200-800 micrograms/day beclometasone diproprionate or equivalent). Triggers for starting inhaled corticosteroids should be:
  - An exacerbation in the previous two years.
  - Use of a beta2-agonist inhaler more than three times per week.
  - Symptomatic of asthma more than three times per week.
  - Waking due to asthma more than once per week.
- **Step 3** - initial add-on therapy involves the addition of a long-acting beta2 agonist (LABA). These should not be used without the concurrent use of inhaled steroid. Where control is good, continue but, where there is no response, stop and increase the dose of inhaled corticosteroid (up to 800 micrograms/day beclometasone diproprionate or equivalent). With partial benefit, continue the LABA but also increase the inhaled corticosteroid dose. If this fails to provide control, trial a leukotriene receptor antagonist or sustained release (SR) theophylline.
- **Step 4** - with persistent poor control, increase inhaled steroid up to 2,000 micrograms/day beclometasone diproprionate or equivalent and/or add a fourth drug (leukotriene receptor antagonist, SR theophylline or beta2-agonist tablet).
- **Step 5** - continuous or frequent use of oral steroids, maintaining high-dose inhaled steroids.

Referral to a respiratory physician would be normal at Step 4-5 depending on expertise.

**Editor’s Note**
November 2017 - Dr Hayley Willacy draws your attention to the recently published NICE guideline[8]. This recommends people take a leukotriene receptor antagonist tablet before treatment with a long-acting beta2 agonist (LABA), as in Step 3. LABA is often given in a combination inhaler, or in two separate devices. NICE states that this change could save the NHS an estimated £2 million a year for every 10,000 people who are managed this way.

**Omalizumab[13]**
NICE recommends omalizumab as an option for treating severe persistent confirmed allergic IgE-mediated asthma as an add-on to optimised standard therapy in people aged 6 years and older who need continuous or frequent treatment with oral corticosteroids (defined as four or more courses in the previous year). Omalizumab should only be initiated by a specialist.

Optimised standard therapy is defined as a full trial of and, if tolerated, documented compliance with inhaled high-dose corticosteroids, LABAs, leukotriene receptor antagonists, theophyllines, oral corticosteroids and smoking cessation if clinically appropriate.

**Exercise-induced asthma**
For most, exercise-induced asthma indicates poorly controlled asthma and will require regular inhaled steroid treatment beyond the anticipatory use of a bronchodilator when preparing for sport. Where exercise poses a particular problem and patients are already on inhaled corticosteroids, consider the addition of LABAs, leukotriene inhibitors, chromones, oral beta2 agonists or theophyllines.

**Complications**
Inadequate control of asthma leads to much morbidity and poor quality of life, with a high rate of working days lost and emergency hospital admissions. Complications mostly relate to acute exacerbations:

- Pneumonia.
- Pneumothorax.
- Pneumomediastinum.
- Respiratory failure and arrest.

Individuals continue to die from asthma (approximately 1,167 deaths in the UK from asthma in 2011)[2]. A common feature of deaths from asthma is that the patient and/or the medical staff have underestimated the severity of the attack. Patients frequently have adverse psychosocial factors that interact with the ability to judge or manage their disease, leading to late presentation. At-risk asthma registers in primary care do not reduce numbers of exacerbations but do improve management and numbers of hospitalisations for high-risk patients[14].
Prognosis

Many children will wheeze early in life (about 30% of those aged under 3 years) in response to respiratory tract infections but most appear to grow out of it by the time they go to school\[15\]. A few will continue to wheeze and develop persistent or interval symptoms, similar to older children with atopic asthma. Predictors for continued wheezing include\[7\]:

- Presentation after the age of 2 years.
- Male sex in prepubertal children.
- Frequent or severe episodes of wheezing.
- Personal or family history of atopy.
- Abnormal lung function.

Some children present with asthma later in childhood and they appear to be less likely to have markers of atopy early in life compared with the persistent early wheezers\[16\].

Prevention

The ‘hygiene hypothesis’ is currently popular. It suggests that decreased exposure to childhood infections, endotoxin and bacteria increases the risk of developing atopy\[17\].

Current guidelines suggest the promotion of breast-feeding (for its other benefits and possible preventative effect) and smoking cessation amongst parents; however, evidence for other strategies (eg, modifying maternal diet during pregnancy, weaning strategies or early aeroallergen avoidance) is lacking\[7\].

Further reading & references

- Global Initiative for Asthma (GINA)
- Annual Asthma survey 2016 report; Asthma UK, 2016
- Aedema facts and statistics; Asthma UK
- British Guideline on the management of asthma; Scottish Intercollegiate Guidelines Network - SIGN (2016)
- Asthma: diagnosis, monitoring and chronic asthma management; NICE Guideline (Nov 2017)
- Asthma; NICE Quality Standard, February 2013
- Omalizumab for treating severe persistent allergic asthma (review of technology appraisal guidance 133 and 201); NICE Technology Appraisal Guidance, April 2013

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