Ministry of Defence

Synopsis of Causation

Bronchial Asthma

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Disclaimer

This synopsis has been completed by medical practitioners. It is based on a literature search at the standard of a textbook of medicine and generalist review articles. It is not intended to be a meta-analysis of the literature on the condition specified.

Every effort has been taken to ensure that the information contained in the synopsis is accurate and consistent with current knowledge and practice and to do this the synopsis has been subject to an external validation process by consultants in a relevant specialty nominated by the Royal Society of Medicine.

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1. Definition

1.1. **Bronchial asthma** is an inflammatory condition of the bronchial airways of the lung characterised by reversible airways obstruction and hyperresponsiveness of the air passages to a variety of stimuli that would not produce an effect in normal circumstances.

1.2. It was originally considered to be due only to the effects of reactive spasm of the smooth muscle lining the bronchial airways. When this muscle layer contracts it constricts the lumen of the tubular airways which become narrower and impede the rate of airflow.

1.3. It is now understood that the condition is essentially inflammatory with swelling and congestion of the epithelial lining of the bronchi as well as contraction of the smooth muscle layer producing the effect of constriction of the diameter of the air passage.[1] The original description of 'acute bronchospasm' to describe the onset of an attack is now not considered accurate although the term may well be used still by some to describe an acute episode.

1.4. The condition is typified by episodes of reversible airways obstruction and respiratory impairment. Symptoms improve between attacks although in chronic or inadequately treated asthma a variable degree of airways obstruction may persist. In severe or chronic disease there may not be measurable reversal of airways obstruction due to the effect of airway wall remodelling (see section.4.9).

1.5. Synonyms are:

- Asthma
- Allergic asthma
- Reversible obstructive airways disease

1.6. Bronchial asthma usually starts in early childhood, more often before age 5 years, and affects 20% of children. It also affects 7-10% of adults in the United Kingdom, some of whom have asthma persisting from childhood and others who develop it afresh without a previous history in early life. Some individuals with childhood onset asthma improve in adolescence but relapse in later life. Prevalence has been increasing over the past twenty years.[2] It is more common in boys than girls up to the age of 15 years. After this females predominate, especially in the case of more severe disease.[3]

1.7. It has been estimated that 5.1 million people suffer from asthma in the UK. It is responsible for around 40,000 adult and 30,000 child admissions to hospital per annum and around 1400 deaths each year.[4,5]

2. Clinical Features

2.1. The typical attack is of sudden onset of wheezing, caused by the air being forced through the narrowed air passages, and breathlessness due to inadequate ventilation of the lung resulting in reduced oxygenation of the blood. Hyperventilation at the onset of the attack may produce hypocapnia. The attack can resolve spontaneously after several hours or can persist or progress to severe respiratory failure and possible death. In a severe attack hypercapnia develops due to inadequate clearing of carbon dioxide from the lungs and is an indication of ventilatory failure needing artificial support of ventilation.

2.2. In the acute attack, wheezing is of high-pitched musical nature (sibilant wheezing) typifying obstruction of the smaller air passages or bronchioles. The patient looks anxious, describes a 'tightness' of the chest and sits in a hunched posture, arms braced to aid use of the accessory respiratory muscles to assist ventilation which requires greater effort against the obstructed airflow. The onset of the attack may be accompanied by a dry non-productive cough whilst the conclusion is often associated with the expectoration of a large amount of frothy white sputum. Expiration is prolonged due to the greater effort needed for expiration than inspiration. Speech may be difficult with sentences needing to be shortened or interrupted to accommodate shorter expiration.

2.2.1. In severe acute attacks, wheezing may be absent, representing the markedly reduced airflow through the small bronchioles – the so-called 'silent chest' which is an indication of respiratory failure.

2.3. In chronic asthma, there may be persistent low grade wheezing between acute attacks with continuing breathlessness and restriction of effort tolerance.

2.4. In some cases the only manifestation may be chronic cough, particularly at night. In childhood this can disturb sleep, with the child repeatedly being awakened by episodes of dry irritating cough, sometimes with wheezing.

2.5. The underlying abnormality in allergic bronchial asthma is a chronic eosinophilic inflammation of the bronchial mucosa. Histology of the mucosa shows infiltration by eosinophils and mast cells suggesting an allergic type response. This tends to be persistent even between acute attacks and most authorities now believe that this supports the need to continue specific anti-inflammatory treatment despite there being no symptoms. The cause of symptoms and acute bronchoconstriction is due to a combination of several factors resulting from this inflammatory process as outlined below:[6]

- Oedema with swelling of the mucous lining of the bronchial airways reducing lumen size
- Active constrictive spasm of the smooth muscle layer of the bronchial wall, especially of the small airways
- Increased secretion from the mucosal glands and goblet cells blocking the lumen, with associated reduction in ciliary action and blockage from mucous plugs
- Mucous metaplasia spreading down to involve smaller airways

2.6. Associated with the inflammatory process is the condition of bronchial hyperresponsiveness which results in episodes of bronchoconstriction in response to provocation by stimuli that would not normally cause a reaction. Bronchial hyperresponsiveness is an almost universal finding in asthma.

2.7. **Diagnosis.** Apart from the typical clinical picture in an acute episode, diagnosis depends largely on establishing airways obstruction using spirometry, including home measurement of peak expiratory flow, and demonstrating reversibility of the spirometric abnormality. In acute attacks and in chronic severe asthma, other abnormalities of lung function measured by blood gas analysis may show typical changes of low relative oxygen saturation of the circulating blood. Evidence of carbon dioxide retention in the blood may be found in severe attacks and would indicate incipient respiratory failure. Blood tests may show an eosinophilia as a manifestation of an allergic component. Sputum samples may also show a high eosinophil content.

2.7.1. **Radiology.** Plain chest x-ray does not usually show any specific abnormality although the signs of hyperinflation of the lung due to obstructive retention of air in the lung tissue may be evident in the acute or chronic phase. Some thickening of the walls of the bronchi may be evident on CT scan but this is not a reliable diagnostic indicator.[1]

2.7.2. **Spirometry.** This procedure measures the volume of air that moves in and out of the lungs during the respiratory cycle and also relates this volume to time. Several parameters can be measured but the most important for estimating severity of obstruction are the forced expiratory volume in one second (FEV_1), forced vital capacity (FVC) and the peak expiratory flow (PEF). The definitions and relevance of these are given at Appendix A.

2.7.3. Home PEF monitoring is especially valuable in identifying asthma. Reversibility of airways obstruction is a characteristic feature of asthma and can be demonstrated by an improvement of FEV_1 following inhalation of a β2-adrenergic agonist drug such as salbutamol. An improvement of at least 20% following inhalation would demonstrate reversibility although in some cases of long-term asthma and severe disease the airways obstruction may be so well established that reversibility may not be apparent.

2.7.4. **Challenge tests** to the airway using inhalation of histamine or methacholine which give a dose-related response of airways narrowing are useful in confirming bronchial hyperresponsiveness and the diagnosis of asthma. However, these investigations are not without risk and needed in only a few difficult cases. Challenge with specific allergens can also be used in controlled conditions where the specific cause needs to be identified. Other indicators of bronchial hyperresponsiveness include the response to exercise, cold air, fog and atmospheric pollutants such as sulphur dioxide.

2.7.5. **Exercise.** Airways narrowing provoked by exercise is a common feature of asthma and exercise testing in a respiratory laboratory should give valid and reproducible results in confirming the condition.

2.7.6. **Skin testing** using common allergens, usually those relating to pollens, house dust mite or animal dander may establish a specific allergy. Allergy may be

identified in up to 40% of the populations but in only a proportion of these does it become manifest as asthma.

2.8. The frequency and severity of symptoms can vary considerably from person to person and from time to time in the same individual. Some have recurrent but infrequent symptoms that are mild and short lived, some have continuous cough and wheezing with periods of marked worsening and others have chronic persistent symptoms with little improvement over time. Acute worsening can occur in all of these types on exposure to known precipitating factors. One classification which allows assessment of the severity of asthma in a particular case describes: [7]

- **Mild intermittent asthma** – symptoms no more than twice a week with no symptoms and normal PEF between attacks; FEV_1 80% or more of predicted, PEF variability <20%
- **Mild persistent asthma** – symptoms more than twice a week but not daily; FEV_1 80% or more of predicted, PEF variability 20-30%
- **Moderate persistent asthma** – daily symptoms, regular use of reliever medication; FEV_1 60-80% predicted, PEF variability >30%
- **Severe persistent asthma** – continual symptoms, limited effort tolerance; FEV_1 <60% predicted, PEF variability >30%

2.9. Whatever the particular severity in an individual, it is possible for all to experience severe acute exacerbations or status asthmaticus that may be life threatening.

3. Aetiology

3.1. The cause of asthma is not known but it is considered to be due to a combination of genetic and environmental factors. Asthma occurs when an individual with a genetic predisposition encounters an environmental factor that induces airways inflammation.

3.2. Asthma has been classified as '**extrinsic**' where onset is usually at a young age, with a strong family history of allergy, specific allergic triggers and raised IgE levels, and '**intrinsic**' where there is adult onset, no family history, perennial symptoms and attacks which often follow respiratory infections. The intrinsic form is often of later onset, more resistant to treatment and there may be no allergic component. A third group includes those who have developed sensitisation to specific allergens encountered at work.[8]

3.3. **Genetic factors.** Children of parents who suffer from asthma or allergies are more likely to develop these conditions. Children with one parent who has asthma are 14% more likely to develop asthma and if both parents are affected the likelihood is increased to 29%. Frequency of asthma and allergies is greater in family members than the population as a whole. There is a greater incidence in identical than non-identical twins. Although this link is well established, the specific reason is uncertain and is probably the result of multiple interacting genetic influences.[1]

3.4. **Environmental factors** that precipitate asthma can be divided into two types; those that induce the underlying inflammatory condition ("inducers") and those that provoke acute bronchoconstriction ("provokers"). Sometimes the boundaries between these can become blurred but individual factors are well recognised. The part played by hyperresponsiveness of the airways is crucial but whether this is a function of the underlying inflammation or the effects of provocation is less clear. The term "airway responsiveness" indicates the ease with which acute airway constriction occurs following a variety of stimuli, and can be defined as the level of fall in FEV_1 against the concentration or degree of the provoking factor. For example the dose of histamine that provokes a fall of 20% in FEV_1 can be used as a standard measure.[1]

3.5. **Inducers.** Asthma inducers cause the underlying inflammatory process and tend to increase the magnitude of hyperresponsiveness with effects lasting days or weeks. The main factors that induce asthma are:

3.5.1. **Allergy.** Most childhood asthmatics display sensitisation to common airborne allergens such as pollen, house dust mite, animal dander, fungi and some foods. Although it is difficult to measure or estimate past allergen exposure retrospectively it has long been held that high exposure to allergens in childhood is likely to induce asthma in predisposed individuals. This relationship is not straightforward and some authorities suggest that very high levels of exposure in childhood can give an effect of increasing tolerance of an individual to potential sensitisers. Whatever the mechanism the relationship between allergy and asthma is generally accepted.

3.5.2. **Infection.** Many children with asthma appear to have developed the condition following a severe respiratory tract infection in childhood. Likewise adults who develop asthma for the first time often identify an episode of bronchitis as the precipitating factor. Conversely there is a hypothesis (the hygiene hypothesis) which suggests that reduced exposure to infection in childhood from better

living conditions leads to increased risk of allergic disease.[6] The apparent protective influence of larger sibling groups and birth order also suggest that those from small families have less exposure to infection in infancy and this increases the risk of later development of asthma.

3.5.3. **Atopy.** This is a condition that is caused by a hereditary tendency to react to certain allergens, such as occurs in hay fever, some skin irritations, and asthma. It results from production within the body of a specific immunoglobulin (IgE) which acts as a specific antibody to common inhaled antigens such as pollen, house dust mite and animal dander. The tendency to overproduction of this antibody is hereditary and the risk of developing asthma is increased in atopic individuals. It is said that 40% of individuals in the UK are atopic with symptoms varying from eczema to hay fever and asthma. In a sensitised atopic individual, the allergen acts as a provoking agent (see below) although the underlying cause has been induced through the hereditary tendency to react abnormally to potential allergens.

3.6. **Provokers.** These are physical or psychological factors that precipitate an attack of bronchoconstriction in an asthmatic person.

3.6.1. **Cold air and air pollutants.** Sudden change in the ambient temperature particularly exposure to cold air is well known to provoke an acute attack of bronchoconstriction in susceptible asthmatics. Exposure to air pollutants such as ozone, sulphur dioxide and environmental tobacco smoke can also precipitate an attack. Regular exposure to such changes due to lifestyle factors can lead to more persistent symptoms but the effects are often short lived with return to the normal state.

3.6.2. **Exercise.** In an individual with bronchial hyperresponsiveness exercise frequently provokes an acute attack. The cause is not fully understood but drying of the mucosa from evaporation due to movement of a large volume of air through the lungs is thought to be responsible. The drying effect results in mast cell production and stimulates peripheral nerve endings, causing vasodilatation in the mucosa and spasm of the bronchial wall muscles. Athletes can suffer exercise-induced asthma (EIA), particularly elite athletes and those involved in skiing or other winter sports. In the latter it seems that the combined effects of strenuous exercise and a cold environment are responsible. Some individuals appear to have a measurable fall in FEV_1 after extreme training. This may last for several hours and can also recur on repetition of the exercise.[9] This response is thought to be a provocation of existing asthma which may even occur in a person who has been symptom-free since childhood. Current opinion suggests that exercise may provoke asthma in an individual with innate bronchial hyperresponsiveness but does not induce asthma as a fresh condition. It has been found in studies of one group of Olympic athletes that up to 14% had a diagnosis of asthma and 50% of cyclists had a previous diagnosis of asthma or had been using asthma medication at some time. Elite ski athletes may develop asthma due to airways remodelling following repeated breathing of unconditioned cold air.[10,11,12]

3.6.3. **Nocturnal asthma.** This is often a feature of asthma both as part of persistent asthma or in some cases as the main manifestation of the condition. The

mechanism is not fully understood but it is thought to be due to a combination of factors such as circadian variation in lung function, increased release of inflammatory mediators, sleep posture, allergens in bedding and sleep related changes in cerebral respiratory drive.[13] Nocturnal or early morning asthma is a strong indication of disease severity and indicates poor control.

3.6.4. **Allergens.** In patients sensitised to an allergen, exposure to that allergen can precipitate an acute asthmatic attack. Seasonal asthma follows the pattern of worsening at the time when tree and grass pollens or fungal spores such as those of *Aspergillus* or *Alternaria* are released. It may worsen in spring, summer or autumn depending on the particular allergen which is prevalent at the time. Allergy to house dust mites tends to be perennial but can worsen in the autumn when mites proliferate. Specific allergies to animals tend to occur sporadically with individual exposure although in some cases there may be sensitisation to a variety of airborne allergens making avoidance difficult.

3.6.5. **Infection.** Upper respiratory infections, particularly those due to common respiratory viruses, are frequently responsible for provoking exacerbations of asthma. As has already been noted, infection in childhood can also act as a significant factor in inducing the asthmatic state (see section 3.5.2). It has been shown recently that epithelial cells from the airways of asthmatics show a deficiency in production of interferon-β with reduced protection of the bronchial mucosa from infection by common cold or rhinoviruses. This may lead to innovative methods of treatment or prevention of virus-induced asthma with interferon-β.[14]

3.6.6. **Psychological factors.** While anxiety or stress does not induce the underlying condition both can provoke the onset of symptoms in susceptible asthmatic individuals. The mechanism for this is unclear but emotional factors and anxiety, particularly due to stressful life events, can worsen the condition.

3.6.7. **Gastro-intestinal reflux.** Irritation of the lower oesophagus (gullet) by acid from the stomach can induce bronchoconstriction probably due to stimulation of the vagus nerve which is also associated with control of bronchial muscle tone.

3.6.8. **Drugs.** Certain drugs can provoke asthma, the most commonly recognised being aspirin, non-steroidal anti-inflammatory drugs (NSAIDs) and non selective β-adrenergic blocking agents. The effects of these are well known but are specific to the individual. Not all asthmatic patients are affected by aspirin and some react more to some NSAIDs than others. Early non-selective β-adrenergic blocking agents tend to have a more widespread effect on the autonomic nervous system but the newer selective types may not worsen asthma.

3.7. **Occupational asthma.** It has long been recognised that the work environment can both induce and provoke asthma. The term “occupational asthma” tends to be used to indicate asthma that has been induced by an allergen encountered at work. The term “work related asthma” more correctly covers all causes of asthma related to work including those where the inflammatory condition is induced by factors encountered at work and those where symptoms are provoked by something in the work environment.

3.7.1. **Allergic work-induced asthma.** A wide variety of occupations has been associated with allergens from products or processes encountered in the daily working environment. These include low molecular weight chemicals and animal or vegetable material. "Occupational asthma" is prescribed under the UK Industrial Injuries Disablement Benefit scheme and recognises specific allergens such as:

- isocyanates
- epoxy resin hardeners
- platinum salts
- soldering flux
- flour dust
- animal dander
- hardwood dusts

The regulations also allow consideration of a wide variety of other agents that have been associated with development of allergic asthma, and around three hundred substances used in industry are accepted as likely sensitisers. As long as other factors have been excluded, a direct causal link would be accepted if typical symptoms occurred following exposure to known sensitisers at work. Investigation and prevention of asthma due to these substances involves active management by occupational health services.

3.7.2. **Work-exacerbated asthma.** A wide variety of non-allergenic irritants can provoke an acute attack in someone with underlying airway hyperresponsiveness. These may be non-allergenic dusts or vapours and although they do not cause asthma they can represent a significant problem of prolonged provocation for an asthmatic whose job involves contact with such substances.

3.7.3. **RADS.** Very high exposure to a non-allergenic irritant such as acid vapours or halogens can produce a severe reaction in the airways that is physiologically indistinguishable from asthma. This is described as "reactive airways dysfunction syndrome" (RADS). This appears to be able to produce a chronic hyperresponsiveness of the airways even with a short exposure and may represents irritant induced asthma in someone who was previously unaffected. The possibility that irritant-induced asthma may result from long-term, low dose exposure remains speculative and is yet to be generally accepted.[6]

3.7.4. **Smoking.** Tobacco smoke from personal habit or from passive smoking can act as an irritant provoking agent in an asthmatic and may precipitate an acute attack or worsen chronic symptoms. There is evolving evidence that smoking is a factor in inducing the inflammatory process of asthma in adults who have no previous history of the disorder. There is also an increased risk of developing asthma for the offspring of mothers who smoke.[15]

3.8. **The hygiene hypothesis.** Over recent years there has been an increase in incidence of asthma particularly in developed countries.[16] Various reasons for this have been postulated including increases in atmospheric pollution, changes in the home environment, increase in use of chemicals in domestic products and differences in rates of childhood infection and immunisation. Changes in definition for diagnosis of asthma

and greater awareness of the condition may have led to an increase in diagnosis of the condition but, even excluding this as a possible factor, the increased incidence appears to have been substantiated. A concurrent increase in hay fever and atopic eczema has also occurred. The reasons for this increase have been widely investigated but the 'hygiene hypothesis' relates the increased incidence to a reduction in episodes of respiratory infection in childhood in developed countries and a consequent increase in the tendency to develop atopic states.[6] However, other factors such as a possible increase in the number of potential allergens and atmospheric pollution have been investigated with no consensus conclusion on their contribution to the increase in asthma.

4. Prognosis

4.1. Asthma tends to be a chronic long-term condition with the underlying abnormality of airway hyperresponsiveness persisting throughout life. Symptoms and severity may be variable and some individuals are apparently completely symptom-free between attacks. Patients with mild intermittent asthma can have severe acute attacks whereas those with moderate persistent asthma can have effective control of symptoms with little functional disability.

4.2. Sensitisation to allergens is usually permanent. Allergy to common environmental agents such as house dust mite is likely to cause persistent symptoms but in occupational sensitisation, removal from the specific allergen may result in permanent improvement in symptoms unless incidental re-exposure precipitates a further attack.

4.3. Asthma that develops in childhood has a variable prognosis. Various studies have shown that more than half of children with asthma before age seven years were symptom free after age 14 years. However, many of these may have had virus associated wheeze and may not have had asthma in the first place. Persistence of asthma is related to the frequency of wheezing, particularly between ages 7-14 years. Children who had infrequent wheezing in this age group were least likely to have symptoms persisting into adult life.[1]

4.4. Studies have also shown that asthma may recur in adult life following a period of remission in adolescence. More than half of patients in the UK who reported asthma at age 33 years had had a period of at least seven years free of symptoms following childhood wheezing. Many of the cases of apparent adult-onset asthma have a history of wheezing in childhood.[1] Adult-onset asthma, especially if non-allergic, tends to be more refractory to treatment.[8]

4.5. Treatment of asthma is aimed at prevention of troublesome symptoms, enabling levels of activity and lifestyle that are as normal as possible, maintaining the best possible level of lung function and preventing recurring attacks, in particular those that are severe or life threatening.

4.6. Treatment strategy is complex and includes procedures for avoidance of allergens or environmental provocation of attacks, and drug treatment with a variety of therapeutic agents.

4.7. **Drug treatment.** This involves the use of several types of drugs by varying methods of delivery. Evolving research has regularly produced new preparations over recent years.

4.7.1. The mainstay of treatment that is responsible for more than 90% of prescriptions for asthma is the use of inhaled β2-adrenoreceptor agonists, which mimic the bronchodilator action of adrenaline, and inhaled corticosteroids, which reduce the inflammatory response in the bronchial mucosa. These are used either separately or in combined preparations. The inhaled β2-agonists generally are used intermittently as "relievers" to abort an acute attack whereas inhaled corticosteroids are used regularly in the longer term for prevention. Inhalation therapy is given by a variety of methods using aerosol, dry powder or nebulisation. The use of "spacer" devices can facilitate delivery of aerosol

preparations. Longer acting β2-agonists such as salmeterol and formaterol are now available to enhance control but these drugs should be used separately.

4.7.2. Oral β2-agonists may be used in more difficult cases and oral corticosteroids may be used to resolve a more severe attack. Long-term use of oral corticosteroids is avoided in most cases because of the potentially serious systemic side effects.

4.7.3. Other bronchodilator drugs such as the methylxanthines (e.g. theophylline and its derivatives) may be used. Several other substances such as sodium cromoglycate, nedocromil sodium, ipratropium, and more recently leukotriene receptor antagonists have been added to the armamentarium for managing difficult asthma.

4.7.4. The British Thoracic Society has produced a set of guidelines for the management of asthma which describe five steps of drug treatment depending on severity and individual response to treatment. Severity is based on a generally accepted scale which is broadly similar to that quoted at section 2.8.[17] The five steps are:

- **Step 1 -** mild intermittent asthma. Short acting β2-agonist inhalers needed less than once a day
- **Step 2** - mild persistent asthma. Regular anti-inflammatory treatment such as inhaled corticosteroids, sodium cromoglycate or nedocromil
- **Step 3** - moderate persistent asthma that has failed to be controlled at step 2. The addition of long-acting β2-agonist combined with inhaled low dose corticosteroid
- **Step 4** - severe persistent asthma. The combination of treatment at step 3 with high dose inhaled steroid and the addition of theophylline or leukotriene receptor antagonist
- **Step 5** - severe persistent asthma not controlled at step 4. The addition of oral corticosteroids

4.8. Most patients treated in the community are at step 1-2 while those needing steps 3-5 represent less than 5% of patients. Approximately 1.2 million people in the UK suffer regular restriction of activity.[5] The step of treatment needed for control in an individual can be a useful guide to the severity of asthma, although some who are well controlled at a higher step may be less disabled than others who need a lower step but who comply poorly with treatment.

4.9. **Airways remodelling.** Chronic long-term asthma, particularly where treatment has been inadequate or compliance poor can result in permanent change in the structure of the air passages, which may lead to permanent loss of lung function with loss of the normal feature of reversibility. Airways remodelling may also contribute to the bronchial hyperresponsiveness seen in more severe asthma despite treatment with corticosteroids.

4.10. Management of asthma must involve active support of the patient with advice and information as well as surveillance of the clinical state and adjustment of treatment. An understanding of the aims of the treatment regime is essential to maintain compliance, particularly at times when symptomatically improved.

5. Summary

5.1. Asthma is a chronic inflammatory disease of the lining of the conducting airways of the lung with hyperresponsiveness to stimuli that would not normally cause a reaction. The resulting bronchoconstriction causes the sensation of tightness in the chest, wheezing and breathlessness. The symptoms are essentially reversible with lung function improving or returning to normal between attacks.

5.2. The cause of asthma is due to a complex interaction between genetic constitutional factors and environmental insult from allergens, viruses, diet and plants. Asthma is a heterogeneous disorder varying from having a strong allergic component on one hand to no evidence of allergy on the other. In the range of cases, the response to corticosteroids may vary between excellent to negligible and airways obstruction from easily reversible to irreversible. It commonly arises in childhood but can present in adult life, although many adult presentations are a manifestation of a dormant state from childhood or from specific sensitisation by factors encountered at work.

5.3. Factors relating to causation of asthma fall into three broad categories: those which induce the underlying inflammatory reaction; those which induce an acute episode of bronchoconstriction; and those which lead to airway wall remodelling.

5.4. Asthma tends to be a long-term condition with disability dependent on the frequency and severity of attacks and the response of the patient to treatment. Treatment is based on a combination of control of environmental factors and effective ‘controller’ and ‘reliever’ therapy.

5.5. Management with drug therapy uses a stepwise approach with a combination of drugs to relieve symptoms and control the inflammatory process, and treatment is aimed at reducing the frequency and risk of acute attacks, maintaining lung function and enabling a full and active life for the patient.

Appendix A - Spirometry

Spirometry is carried out using one of a variety of instruments that measure the volume of air blown out and in some instances breathed in. Some of these form part of a lung function laboratory but there are many portable versions that can be used in clinics. They give a print out of the results, usually both in numeric and graphical form and have the facility to calculate percentage volumes and ratios using programmed reference values.

The commonly used parameters for assessing airways obstruction in asthma are as follows:

- **Forced vital capacity (FVC)** is the volume of air that can be exhaled from a full inspiration to full expiration using maximum effort.
- **Forced expiratory volume in one second (FEV_1)** is the volume of air exhaled in the first second of expiration using maximum effort.
- **Peak expiratory flow (PEF)** is the maximum flow in litres per second achieved during expiration at maximum effort.

The graphical tracings are of the expiratory volume-time curve and the flow-volume loop, which shows the rate of flow throughout the inspiratory/expiratory cycle. The shape of the spirometric tracings of both the volume-time curve and the flow-volume loop show typical patterns in obstructive disease, and can help to distinguish obstruction at different levels within the bronchial tree.

The normal expiratory volume-time curve shows a rapid rise in the first second of expiration reaching the maximum level within three seconds when it remains at a plateau level for the rest of expiration. In the typical obstruction of asthma the pattern is of a slower initial rise which continues as a gradual, almost linear rise throughout expiration, with a plateau level not being reached. The expiratory part of the flow-volume loop shows a typically concave sag in the normally linear fall in flow as expiration progresses.

All of these parameters vary depending on age, height, gender and ethnic origin, and a series of normograms have been developed that indicate the normal expected ranges. Assessment of spirometric results depends on comparing the readings obtained with the predicted level for the individual. Results are usually given as a percentage of the predicted level.

FVC is often not reduced in asthma as the lung volume is not restricted, but it takes longer to exhale the total volume. In some cases, FVC is reduced because of obstructive air trapping in the lung on forced expiration.

Seventy five per cent of the forced vital capacity is normally exhaled in the first second of expiration giving a normal ratio of FEV_1/ FVC of 75%. This ratio is reduced in obstructive airways disease because of the longer time taken moving air out of the lungs against obstruction. The level of the FEV_1/FVC ratio gives a reliable measure of the severity of obstruction and allows estimation of reversibility.

PEF is proportionally reduced in airways obstruction and can be measured with a simple flow meter as well as a spirometer. It is a useful method for measuring daily variation and progress of treatment that can be used by the patient to monitor progress.

6. Related synopses

Chronic Obstructive Pulmonary Disease

7. Glossary

allergen	A substance that produces an allergic reaction in the body.
autonomic nervous system	Part of the nervous system that controls functions automatically without voluntary control, such as control of heartbeat, gland secretions or, in this context, the bronchial smooth muscle controlling airway diameter.
β2-adrenergic agonists	Drugs that act to trigger a response by stimulating nerve receptors in the sympathetic nervous system. In this context, they cause dilatation of smooth muscle and relax smooth muscle spasm.
bronchoconstriction	Narrowing of the lumen (*q.v.*) of the bronchial tubes due to spasm of the circular muscle and swelling of the tissue lining.
ciliary	Pertaining to the cilia, which are fine hair-like structures protruding from cells ling the bronchial tubes. They facilitate removal of debris from the bronchial system.
circadian	Relating to a 24-hour cycle. Used to describe a pattern that is repeatable through a 24-hour period.
dander	Minute particles or scales that are shed from the feathers, hair, or skin of various animals.
eosinophil	A white blood cell that plays a part in allergic reactions and the body's response to parasites and fungi. Hence *eosinophilia*; an excess of these cells above the normal.
epithelial	The covering of surface tissue that forms a thin protective layer lining the internal cavities of the body.
goblet cells	Cells which produce secretion of mucus in the epithelial lining of the airways of the lung.
heterogeneous	Pertaining to differences in items within a group. In this instance, having a wide range of presentation and cause.
histamine	An amine compound released by cells of the body's immune system in allergic reactions.
histology	The study of microscopic cell structure.
hypercapnia	An increased level of carbon dioxide circulating in the blood.

hypocapnia	A decreased level of carbon dioxide circulating in the blood.
IgE	Abbreviation for “immunoglobulin E”, a class of immunoglobulin associated with immediate type hypersensitivity reactions.
interferon-β	One of a family of glycoproteins derived from human cells which normally has a role in fighting viral infections by preventing virus multiplication in cells.
lumen	The space within a tubular structure in the body such as an artery, vein or bronchial tube.
mast cells	A large connective tissue cell that can release histamine (*q.v.*) in allergic reactions.
methacholine	A drug that mimics the effect of the parasympathetic nervous system which stimulates spasm of bronchial smooth muscle.
mucous metaplasia	Excessive development of the glands which produce mucus secretion.
nebulisation	Use of an instrument to produce a fine spray of liquid to propel drug solutions into the lungs.
non-selective β-adrenergic blocking agents	Drugs that block the effect of adrenaline at receptors in the autonomic nervous system (*q.v.*). Commonly referred to as “β blockers”. Used to treat a variety of conditions, particularly blood pressure and angina but can cause unwanted bronchoconstriction in the lungs.
oedema	An abnormal build up of fluid between tissue cells in the body.
reversible	Capable of being restored to normality: in this context, by means of therapeutic drugs. Hence: *reversibility*.
spirometry	The measurement of lung capacity using an instrument to measure volumes of air breathed in and out.
status asthmaticus	A prolonged severe asthma attack that does not respond to standard treatment.

8. References

[1] Newman Taylor AJ. Asthma. In: Warrell D, Cox TM, Firth JD, Benz EJ, editors. Textbook of medicine. 4th ed. Oxford, UK: Oxford University Press; 2004. para 17.12.

[2] Yunginger JW, Reed CE, O'Connell EJ et al. A community based study of the epidemiology of asthma. Incidence rates, 1964-1983. Am Rev Respir Dis 1992;146:888-94.

[3] Preston-Clark P, Primatesta P (editors). Health Survey for England 1995. London: The Stationery Office; 1997.

[4] Hoare J, Bruce M. Prevalence of treated asthma and its management in general practice in England and Wales, 1994-98. National Statistics. Health Statistics Quarterly 2003;17(Spring):15-22.

[5] National Asthma Campaign Asthma Audit (2001). Out in the open: a true picture of asthma in the United Kingdom today. Asthma J 2001;6(3):S1-14

[6] Cullinan P, Newman Taylor A. Asthma: environmental and occupational factors. Br Med Bull 2003;68:227-42.

[7] National Asthma Education and Prevention Program [NAEPP]. Guidelines for the diagnosis and management of asthma. Expert panel report 2. NIH publication No. 97-4051. Bethesda, MD: National Institutes of Health, National Heart Lung and Blood Institute; 1997.

[8] Boushey Jr HA, Corry DB, Fahy JV. Asthma. In: Murray JF, Nadel JA, editors. Textbook of respiratory medicine. 3rd ed. Philadelphia, PA: WB Saunders; 2000.

[9] Rundell KW. Jenkinson DM. Exercise-induced bronchospasm in the elite athlete. Sports Med 2002;32(9):583-600.

[10] Weiler JM, Layton T, Hunt M. Asthma in United States Olympic athletes who participated in the 1996 Summer Games. J Allergy Clin Immunol 1998;102(5):722-6.

[11] Helenius I. Haahtela T. Allergy and asthma in elite summer sport athletes. J Allergy Clin Immunol 2000;106(3):444-52.

[12] Karjalainen EM, Laitinen A, Sue-Chu M et al. Evidence of airway inflammation and remodelling in ski athletes with and without bronchial hyperresponsiveness to methacholine. Am J Respir Crit Care Med 2000;161(6):2086-91.

[13] Sharma G. Asthma. [Online]. 2004 [cited 2004 Oct 25]. Available from: URL:http://www.emedicine.com/

[14] Wark PA, Johnston SL, Bucchieri F et al. Asthmatic bronchial epithelial cells have a different innate immune response to infection with rhinovirus. J Exp Med 2005;201(6):937-47.

[15] Jaakkola MS. Piipari R. Jaakkola N. Jaakkola JJ. Environmental tobacco smoke and adult-onset asthma: a population-based incident case-control study. Am J Public Health 2003;93(12):2055-60.

[16] The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis and atopic eczema: ISAAC. Lancet 1998;351:1225-32.

[17] British Thoracic Society. The British guidelines on asthma management. Thorax 1997;52(Suppl1);1-21.