Asthma

Version 5 FINAL

Document control

Version history

Version	Date	Comments
5	29th November 2012	Signed off following review

1. Introduction

Description

Asthma has been recognised since ancient times. The term is derived from the Greek word meaning “short – drawn breath” or “panting”, and was in use in the time of Hippocrates.
The diagnosis of asthma is a clinical one; there being no standardised definition of the type, severity, frequency of symptoms, nor of the investigation findings. This may, in part, help to explain the reported variability in the prevalence or asthma.

Central to all definitions is the presence of symptoms (more than one of wheeze, breathlessness, cough or chest tightness) and variable airflow obstruction, which are potentially reversible with treatment.
Included as disease components in more recent descriptions of both childhood and adult asthma are airway hyper-responsiveness and airway inflammation. [1]

The normal diurnal variation of peak expiratory flow rate (PEFR) is increased in people with asthma. [2]

Prevalence

Asthma is a common condition, and frequently disabling. It is estimated that in the Western world 10% of children and more that 5% of adults are affected. [3]
Worldwide the estimated number of individuals with asthma is 300 million. [4]

Definition of the prevalence of asthma is complex due to factors such as disease definition, variability over time and differing interpretation and opinion.

In England a survey carried out in 2001 (Health Survey for England) gave an overall prevalence of 8.1%. This figure includes those who were symptomatic but not currently having primary care treatment, but is still regarded as giving the best evidence of asthma prevalence. [5]

Data about the extent of asthma in Britain is also available from the Quality and Outcomes Framework disease register. This is drawn from GP consultations so may produce rates which are an underestimate due to lack of uniformity across different GP practices. The data is useful for looking at doctor-diagnosed or treated asthma. [6]

A large scale study of trends in the epidemiology of asthma in England concluded that whilst the rate of new diagnoses seems to have peaked, the number of adults with a lifetime diagnosis continues to increase.
It acknowledged this may follow the introduction of incentives and guidelines on diagnosis and recording asthma, but the important public health

implication remains. [7]

In England and Wales asthma is thought to be responsible for 100,000 hospital admissions per year, and 1500 to 2000 deaths. [3]

2. Aetiology

Development of asthma is multifactorial and depends on the interactions between multiple susceptibility genes and environmental factors.

Susceptibility genes are thought to include those for T-helper 1 and 2 (T_H1 and T_H 2) cells, IgE, cytokines (IL-3, -4, -5, -9 and -13), and granulocyte-monocyte colony-stimulating factor (GM-CSF), tumour necrosis factor-α (TNF-α), and the ADAM33 gene, which may stimulate airway smooth muscle and fibroblast proliferation or regulate cytokine production. [8]

Environmental factors may include the following:

- Allergen exposure
- Diet
- Perinatal factors

Evidence clearly implicates household allergens (e.g., dust mite, cockroach, and pets) and other environmental allergens in disease development in older children and adults. Diets low in vitamins C and E and in ω–3 fatty acids have been linked to asthma, as has obesity. Asthma has also been linked to perinatal factors, such as young maternal age, poor maternal nutrition, prematurity, low birth weight, and lack of breastfeeding.

On the other hand, endotoxin exposure early in life can induce tolerance and may be protective. Air pollution is not definitively linked to disease development, though it is thought to have a part in triggering exacerbation in pre-existing asthma. [9] Current evidence indicates that exposure to cigarette smoke in childhood, and during pregnancy is associated with an increased incidence of asthma.

Genetic and environmental components may interact by determining the balance between T_H1 and T_H2 cell lineages. Infants may be born with a predisposition toward pro-allergic and pro-inflammatory T_H2 immune responses, characterized by growth and activation of eosinophils and IgE production. Early childhood exposure to bacterial and viral infections and endotoxins may shift the body to T_H1 responses, which suppresses T_H2 cells and induces tolerance. Trends in developed countries toward smaller families with fewer children, cleaner indoor environments, and early use of vaccinations and antibiotics may have the unforeseen consequence of reducing these T_H2-suppressing, tolerance-inducing infectious and environmental exposures. This may partly explain the continuous increase in asthma prevalence in developed countries (the hygiene hypothesis).

Occupational Factors

(see **Section 5** for further details about occupational asthma)

Pathophysiology

Asthma involves

- Bronchoconstriction
- Airway oedema and inflammation
- Airway hyper-reactivity
- Airway remodelling

In patients with asthma, T_H2 cells and other cell types—notably, eosinophils and mast cells, but also other CD4+ subtypes and neutrophils—form an extensive inflammatory infiltrate in the airway epithelium and smooth muscle, leading to airway remodelling (i.e. desquamation, sub-epithelial fibrosis, angiogenesis, and smooth muscle hypertrophy). Hypertrophy of smooth muscle narrows the airways and increases reactivity to allergens, infections, irritants, parasympathetic stimulation (which causes release of pro-inflammatory neuropeptides, such as substance P, neurokinin A, and calcitonin gene-related peptide), and other triggers of bronchoconstriction. Additional contributors to airway hyper-reactivity include loss of inhibitors of bronchoconstriction (epithelium-derived relaxing factor, prostaglandin E2) and loss of other substances called endopeptidases that metabolise endogenous bronchoconstrictors. Mucus plugging and peripheral blood eosinophilia are additional classic findings in asthma and may be a secondary phenomenon of airway inflammation.

Triggers:

Common triggers of an asthma attack include:

- Environmental and occupational allergens (numerous)
- Infections
- Exercise
- Cold air
- Inhaled irritants
- Emotion (stress)
- Aspirin and to a lesser extent non steroidal ant-inflammatory drugs (NSAIDs)
- Gastroesophageal reflux

Infectious triggers in young children include respiratory syncytial virus (RSV), rhinovirus, and para-influenza virus infection. In older children and adults, upper respiratory tract infections (URTIs), particularly with rhinovirus, and pneumonia are common infectious triggers.

Exercise can be a trigger, especially in cold or dry environments.

Inhaled irritants, such as air pollution, cigarette smoke, perfumes, and cleaning products, are often involved.

Emotions such as anxiety, anger, and excitement sometimes trigger attacks.

Aspirin is a trigger in up to 30% of older patients and in patients with more severe asthma. Aspirin -induced asthma is typically associated with nasal polyps with nasal and sinus congestion.

Gastro-oesophageal reflux disease (GORD) may be a trigger in some patients with asthma, possibly via oesophageal acid-induced reflex bronchoconstriction or by micro-aspiration of acid. Whilst some individual

patients seem to be helped by reflux treatment, the overall benefits in terms of asthma control have not been proven.
Allergic rhinitis often coexists with asthma. It is unclear whether the two are different manifestations of the same allergic process or whether rhinitis is a discrete asthma trigger.

Response to triggers:
In the presence of triggers, there is reversible airway narrowing and uneven lung ventilation. Relative perfusion exceeds relative ventilation in lung regions distal to narrowed airways, thus alveolar O_2 tensions fall and alveolar CO_2 tensions rise. Most patients can compensate by hyperventilating, but in severe exacerbations, diffuse bronchoconstriction causes severe air trapping, and the respiratory muscles are put at a marked mechanical disadvantage so that the work of breathing increases.
Under these conditions, and later on in exacerbations hypoxaemia worsens and $PaCO_2$ rises.
Respiratory acidosis (due to increased $PaCO_2$) and metabolic acidosis (due to decreased bicarbonate concentration in extracellular fluid) may result and, if left untreated, cause respiratory and cardiac arrest.

An individual's reaction to allergen exposure characteristically involves two phases. Inhalation of an allergen may result in an early asthmatic reaction (type I) 20 minutes after exposure, which usually resolves after an hour.
A late asthmatic response (type II) can develop after 3 hours, peaking at 6-12 hours, and persisting for 12-24 hours. This phenomenon is important because it may affect the choice of asthma treatment.
Occasionally an individual experiences a late response without the early reaction. [8]

The bronchospasm seen in asthma can arise without the presence of definable triggers.
In those who have persistent disease, there may be frequent and ongoing bronchospasm without any obvious cause.
Severe asthma can progress to respiratory arrest and death.

Asthma phenotypes

The presence of multiple pathological phenotypes of asthma is now acknowledged. This is important, because of the potential of using phenotype-guided management for the more severe cases of asthma. [10]

3. Diagnosis

Unlike many other conditions, there is no gold standard definition of asthma to refer to when making a diagnosis. This means a key element in the diagnosis of asthma will always be the clinical history.
Careful history taking should demonstrate a characteristic pattern of symptoms, but also include consideration of an alternative explanation for these.
This pattern includes more than one of the following non-specific symptoms:

- wheeze
- breathlessness
- chest tightness
- cough

An accompanying feature to these symptoms is variable airflow obstruction. In some instances, evidence for variable airflow obstruction may be difficult to obtain during exacerbations. For example in those who have well controlled asthma and normal lung function.
As treatment may be required for many years once the diagnosis has been made, it is important that confirmatory evidence (airflow obstruction varying over short time periods) is obtained if possible. This may mean repeated assessment and measurement is necessary.
Whether or not starting treatment should be delayed until there is confirmation depends on factors such as the certainty of the initial diagnosis and the severity of presenting symptoms.
The preferred test, where available, is spirometry rather than peak expiratory flow, as the results are less dependent on effort and it allows clearer identification of airflow obstruction. Some training is required to obtain reliable recordings and to interpret the results in spirometry.
Of importance is that a normal spirogram (or PEF) obtained in the absence of symptoms does not exclude a diagnosis of asthma. [1]

History

History taking for asthma in the clinical setting should be comprehensive.

Table 1: This outlines the relevant areas that may be explored in the clinical history.

Symptomatology	Impact on daily life and variability (proportion of good and bad days –highlighting different features of good and bad days). Exploration of symptoms (such as sputum production) to ensure alternative diagnoses are excluded
Pattern of the Condition	Severity of acute episodes (need for HDU, ITU or ventilation), frequency of exacerbations Frequency of use of unscheduled care such as A+E, GP, hospital admissions Presence of severity markers such as brittle disease or frequent need for oral steroids

Family and Personal History:	Asthma, eczema or hayfever
Childhood Asthma:	When asthma arises in adult life, it may reflect a re-activation of childhood asthma. The period of 'remission' may last for several years, but the tendency to develop asthma is always present.
Home environment:	Smoking and pets.
Occupation:	(See ***Section 5*** for further information about Occupational Asthma.)
Triggers:	Such as allergens, exercise and emotion (see page 6 for full list)
Response to a Trial of Treatment:	Symptoms and/or peak flow improve
Medication	Amount of medication required for asthma. Exploring possible use of other medication that may make asthma worse (such as NSAIDs, beta blockers)

Examination

Where asthma is well controlled, or reliever treatments have been taken recently clinical examination may be normal.
Even those with troublesome persistent asthma may have absence of wheeze, if examined whilst sitting quietly, particularly after having recently used reliever treatment.
In general however, in those with persistent symptomatic asthma, normal lung sounds would not be expected on examination. [3]
On observation, there may be exertional wheezing or wheezing at rest.
Accessory muscles (scalene and sternocleidomastoid in the neck) may be seen to be used to aid breathing (mainly a feature seen in an acute asthma attacks).
Auscultation may reveal diminished air entry and diffuse bilateral wheeze with a prolonged expiration phase.

Table 2: This shows clinical features in adults that influence the probability that episodic respiratory symptoms are due to asthma. [1]

Features that increase the probability of asthma

• More than one of the following symptoms: wheeze, breathlessness, chest tightness and cough, particularly if:
  ○ symptoms worse at night and in the early morning
  ○ symptoms in response to exercise, allergen exposure and cold air
  ○ symptoms 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 FEV_1 or PEF (historical or serial readings)

• Otherwise unexplained peripheral blood eosinophilia
Features that lower the probability of asthma
• Prominent dizziness, light-headedness, peripheral tingling • Chronic productive cough in the absence of wheeze or breathlessness • Repeatedly normal physical examination of chest when symptomatic • Voice disturbance • Symptoms with colds only • Significant smoking history (i.e. >20 pack-years) • Cardiac disease • Normal PEF or spirometry when symptomatic* *A normal spirogram/spirometry when not symptomatic does not exclude the diagnosis of asthma. Repeated measurements of lung function are often more informative than a single assessment.

Investigation

Whether or when investigation is carried out depends on if the person is considered to have a low, intermediate or high probability of having asthma. Those with low probability (in whom alternative diagnoses are being considered) will have investigation. In intermediate probability the preferred approach is to carry out investigation (including treatment trial). In high probability, a trial of treatment may be started and investigation reserved for those who do not respond well to this.

Pulmonary Function Tests (see Appendix A for a Glossary of Terms)

In an acute episode of asthma, the peak flow, FEV_1 and FEV_1/FVC ratio are all reduced. (They may all return to normal between episodes.)

In chronic asthma, TLC (Total Lung Capacity) may be increased by hyperinflation, and air trapping may increase RV (Residual Volume).

The Recommended Technique for Measuring Peak Flow is described in Appendix B.

The diurnal variation of peak expiratory flow rate is normally increased in asthmatics, where the lowest peak flow occurs in the early hours of the morning, 'morning dipping', and the highest is in the afternoon. Patients may be asked to keep 'Peak Flow Diaries' as an aid to diagnosis, or as part of self management plans.

Results from spirometry are also useful where the initial history and examination leave genuine uncertainty about the diagnosis. In such cases, the differential diagnosis and approach to investigation is different in patients with and without airflow obstruction (see Figure 1 and Table 3). In patients

with a normal or near-normal spirogram when symptomatic, potential differential diagnoses are mainly non-pulmonary. Such conditions do not respond to inhaled corticosteroids and bronchodilators. In contrast, in patients with an obstructive spirogram the question is less whether they will need inhaled treatment but rather exactly what form and how intensive this should be.

Other tests of airflow obstruction, airway responsiveness and airway inflammation can also provide support for the diagnosis of asthma, but to what extent the results of the tests alter the probability of a diagnosis of asthma has not been clearly established, nor is it clear when these tests are best performed. [1]

Reversibility tests

Where available, testing with spirometry is preferred to peak expiratory flow.

An increase in 400 ml of FEV_1 in response to treatment with either β_2-agonists or corticosteroids in adults strongly suggests a diagnosis of asthma.

Chronic severe asthma may not show any reversibility after bronchodilator usage. This means a failure of reversibility does not necessarily mean the diagnosis is definitely not asthma. However, a two-week trial of corticosteroid may produce an improvement in peak flow. This helps to differentiate between asthma (improvement likely), and chronic obstructive pulmonary disease (improvement less likely).

Chest X ray

This is usually normal.

Provocation tests

Exercise testing is a safe, simple and useful procedure if the diagnosis of asthma is in doubt. Spirometry should be used rather than peak expiratory flow. Measurements are taken before exercise. The patient does 6 minutes of vigorous exercise, and the test is repeated 15-20 minutes later. Those with asthma can have a greater than 5% increase in FEV_1 during exercise, and a fall of more than 10% in FEV_1 from the pre-test value after exercise. [3]

If the diagnosis is still in doubt, then the exercise test can be performed in cold dry conditions to intensify the response. Provocation with other agents such as histamine and methacholine can also be useful. Many units now use mannitol for provocation testing.

Further investigation in those with intermediate probability of asthma [1]

With airways obstruction

Tests of peak expiratory flow variability, lung volumes, gas transfer, airway hyper-responsiveness and airway inflammation are of limited value in discriminating patients with established airflow obstruction due to asthma from those whose airflow obstruction is due to other conditions. Patients

may have more than one cause of airflow obstruction, which complicates the interpretation of any test. In particular, asthma and chronic obstructive pulmonary disease (COPD) commonly coexist.

Patients with airways obstruction and intermediate probability of asthma should be offered a reversibility test and/or a trial of treatment for a specified period:

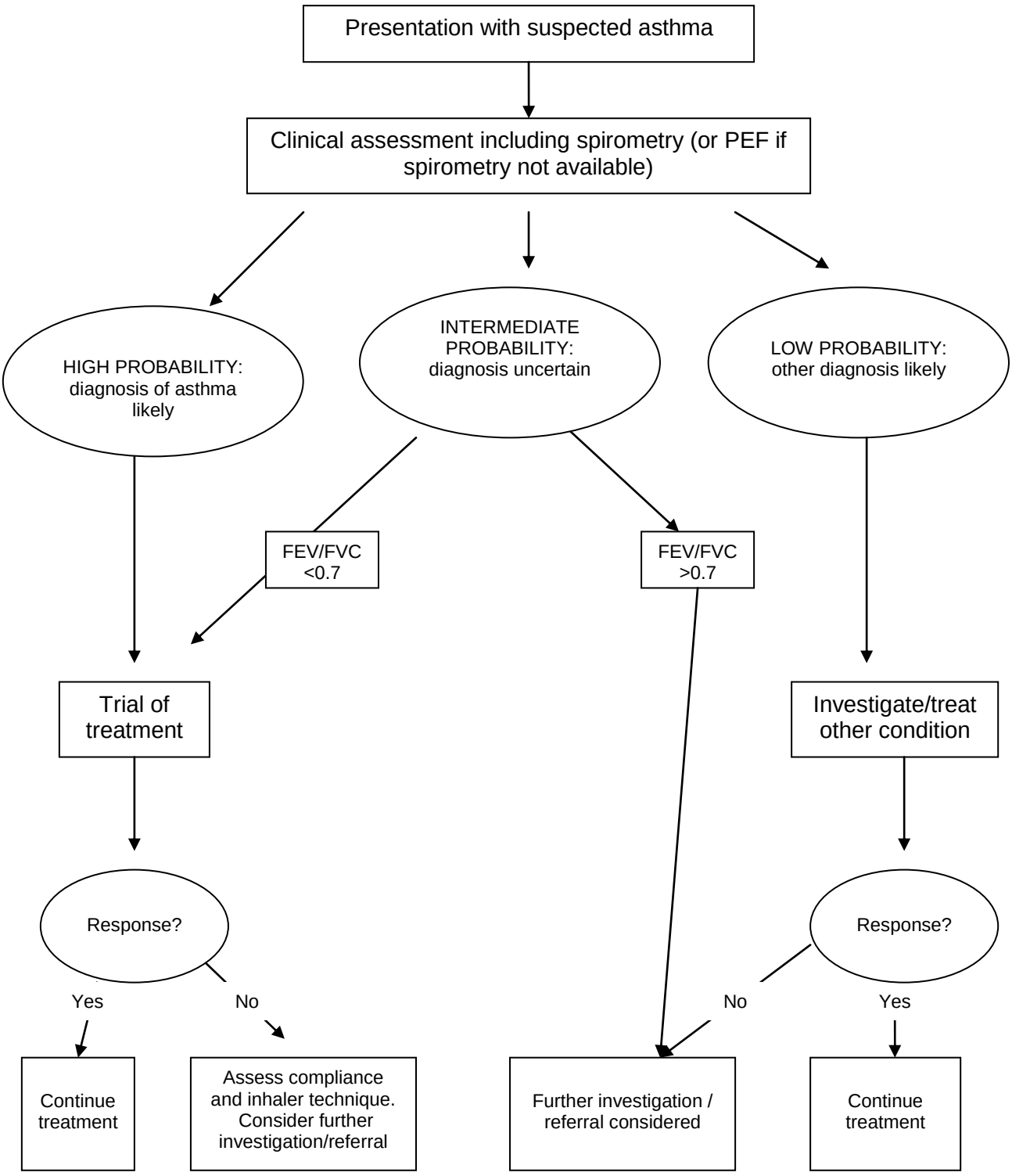
- If there is significant reversibility, or if a treatment trial is clearly beneficial treat as asthma
- If there is insignificant reversibility and a treatment trial is not beneficial, consider alternative conditions

Without airways obstruction

In patients with a normal or near-normal spirogram it is more useful to look for evidence of airway hyper-responsiveness and/or airway inflammation. These tests are sensitive so normal results provide the strongest evidence against a diagnosis of asthma.

Patients without evidence of airways obstruction and with an intermediate probability of asthma should have further investigations before commencing treatment.

Figure 1: Presentation with suspected asthma in adults. [1]



Differential diagnosis

> 'All that wheezes is not asthma, but equally all that is asthma need not wheeze.'

Table 3: Differential diagnosis of asthma in adults, according to the presence or absence of airflow obstruction (FEV1/FVC<0.7) [1]

Without airflow obstruction
• Chronic cough syndromes (e.g. associated with ACE inhibitors) • Hyperventilation syndromes • Vocal cord dysfunction • Rhinitis • Gastro-oesophageal reflux • Heart failure • Pulmonary fibrosis
With airflow obstruction
• COPD • Bronchiectasis* • Inhaled foreign body* • Obliterative bronchiolitis • Large airway stenosis • Lung cancer* • Sarcoidosis*
*May also be associated with non-obstructive spirometry

4. Treatment

Guidelines

In 1999 the British Thoracic Society (BTS) and the Scottish Intercollegiate Guidelines Network (SIGN) agreed to jointly produce a comprehensive new asthma guideline, both having previously published guidance on asthma.
The 2008 guideline considered literature published up to March 2007.
It contains:

- a completely rewritten section on diagnosis for both adults and children.
- a section on special situations which includes occupational asthma, asthma in pregnancy and the new topic of difficult asthma.
- updated sections on pharmacological and non-pharmacological management.
- amalgamated sections on patient education and compliance, and on organisation of care and audit.

Since the 2008 guidelines, there have been revisions in 2009, 2011 and 2012. The following have been added or revised:

- further updates to pharmacological management and monitoring asthma
- management of acute asthma
- asthma in pregnancy, and in adolescence [1]

Advice for asthmatics

1. Where practical, identify and then avoid precipitating factors. Evidence to support recommending controlling house dust mite in the home is lacking. [11] In spite of this, those with asthma may be keen to take measures to reduce exposure to this potential trigger.

2. Direct or passive exposure to cigarette smoke adversely affects quality of life, lung function, need for rescue medications for acute episodes of asthma and long term control with inhaled steroids. There are very few trials which have assessed smoking cessation in relation to asthma control. Two studies have demonstrated decreases in childhood asthma severity when parents were able to stop smoking. One study in adults with asthma suggested that smoking cessation improved asthma-specific quality of life, symptoms and drug requirements. Intervention to reduce smoking has had disappointing outcomes. It is likely that more intensive intervention will be required to achieve meaningful outcomes.
Uptake of smoking in teenagers increases the risks of persisting asthma. One study showed a doubling of risk for the development of asthma over six years in 14 year old children who started to smoke.
Parents with asthma should be advised about the dangers of smoking to themselves and their children with asthma and offered appropriate support to stop smoking. **[1]**

3. Weight reduction for asthmatics that are significantly overweight should be advised on the grounds of likely benefit to general health and improved asthma control.

4. Any immunisations should be administered independent of any considerations related to asthma.

5. Advice on physical exercise should follow a general approach in terms of encouraging a healthy lifestyle, with appropriate guidance on exercise induced asthma included.

Non-pharmacological management

Trials of allergen specific immunotherapy by subcutaneous injection have been shown to be of benefit in reducing symptoms, use of medication and improving bronchial-hyperactivity. To date evidence from comparisons between immunotherapy and pharmacotherapy is lacking.
The current recommended role for immunotherapy is that this treatment can be considered for those who have a clinically significant allergen that cannot be avoided. (and with prior full discussion about the potential for severe allergic reactions as mandatory) [12]
Administering immunotherapy by other routes (sublingual) is not recommended.

Studies of the Buteyko breathing technique (breathing exercises) for controlling hyperventilation (and any ensuing hypercapnia) suggest some benefit in reducing the symptoms of asthma and inhaler use, but no direct effect on lung function has been demonstrated. [1]

There is no evidence to date to support recommending alternative or complimentary medicine, use of air ionisers or dietary change such as use of probiotics or fish oil supplements.

Pharmacological management

The aim of asthma management is control of the disease. Complete control includes:

- no daytime symptoms
- no night time awakening due to asthma
- no need for rescue medication
- no exacerbations
- no limitations on activity including exercise
- normal lung function (in practical terms FEV1 and/or PEF >80% predicted or best) with minimal side effects

In practice, individuals may wish to factor in potential side effects, and the inconvenience of taking medication and aim for a balance in these respects as well as aiming for perfect control.
A stepwise approach aims to abolish symptoms as soon as possible and to optimise peak flow by starting treatment at the level most likely to achieve this. Patients should start treatment at the step most appropriate to the initial severity of their asthma. The aim is to achieve early control and to then maintain control by stepping up treatment as necessary and stepping down when control is good (see figure 2 for a summary of stepwise management in adults).

Key concept: Relievers and Preventers

"Relievers" are bronchodilator drugs. These are highly effective at temporarily relieving the symptoms of asthma.
However, with the aim of treatment being to eliminate asthma symptoms the main emphasis for most asthmatics will be the **regular** use of **"Preventer"** medication.
Inhaled steroids are the recommended preventer drug for adults and children, and regular use reduces airway inflammation and reactivity.
Preventer treatment should be started very early in the treatment of asthma, and then used aggressively to gain quick control.

A stepwise approach aims to abolish symptoms as soon as possible and to optimise peak flow by starting treatment at the level most likely to achieve this. Patients should start treatment at the step most appropriate to the initial severity of their asthma. The aim is to achieve early control and to then maintain control by stepping up treatment as necessary and stepping down when control is good (see figure 2 for a summary of stepwise management in adults).

Main treatments for chronic asthma [1] [13]

(See **Appendix C** for additional information about medication)

Relievers

1. Short Acting β_2-Agonists
   - salbutamol (Ventolin) is the most widely used example
   - terbutaline is also widely used
   - rapid onset in minutes and lasts for a few hours
   - ideal for the rapid relief of symptoms
   - use 'as required' just as effective as regular use 4 x daily [14]

2. Long Acting β_2-Agonists
   - salmeterol (Serevent) is the most widely used example
   - maximum effect after 2 hours and lasts for 12 hours
   - particularly effective for nocturnal and exercise induced symptoms
   - not suitable for immediate relief of an asthma attack
   - not prescribed without inhaled steroids

Preventers

1. Inhaled Corticosteroids ("Inhaled Steroids")
   - beclometasone, budesonide or fluticasone are widely used
   - must be taken regularly every day (usually twice daily)
   - can be taken once a day (same daily dose) if control is good
   - excellent anti-inflammatory effects

2. Oral Corticosteroids ("Oral Steroids")

- prednisolone is the drug of choice
- often used in short courses to treat exacerbations
- serious side effects are associated with regular long-term use (A last resort in outpatient management)

3. Leukotriene receptor antagonists
   - montelukast (Singulair) is an example
   - taken orally once each day
   - bronchodilator and anti-inflammatory effects

The first choice preventer drug is an inhaled steroid. Use of inhaled steroids should be considered if any of the following features are present:

- exacerbations of asthma in the last 2 years
- using inhaled β_2-agonists three times a week or more
- symptomatic three times a week or more
- waking one night a week

Other 'add-on' therapies include theophyllines and slow-release β_2-agonist tablets. Theophyllines may improve both symptoms and lung function in some patients, though their use may be limited due to side-effects. Slow-release β_2-agonist tablets are used very infrequently these days, due to their side-effect profile, and also the concern from clinicians that their use may mask important symptoms (that may indicate a need for an increase in steroid therapy).

Other treatments

These may be offered to those with severe or difficult asthma.

1. Anti IgE monoclonal antibody
   - those used include omalizumab (of use in treating severe atopic asthma with frequent exacerbations)
   - should only be initiated in specialist centres experienced in managing those with severe or difficult asthma
   - given as a subcutaneous injection every 2 to 4 weeks
   - risk of anaphylaxis means administration must be in healthcare setting under direct medical supervision

2. Immunosuppressants
   - those used include methotrexate, ciclosporin and oral gold
   - all have significant side effects and potential recipients must be counselled accordingly on risks and benefits
   - may be considered for 3 month trial if other drug treatment has been unsuccessful

3. Continuous subcutaneous terbutaline
   - reported to have been beneficial in severe asthma
   - rarely used (ideally only after placebo-controlled trial in the patient)
   - evidence from trials on efficacy and safety has yet to be assessed [1]

See **Appendix D** for information about drug delivery systems.

Monitoring and measuring asthma control [1] [15]

In primary care, the majority of this work is carried out by Practice Nurses who have received additional training and work to written guidelines.

A structured care approach has been shown to be beneficial. This includes the recording of morbidity, PEF levels, inhaler technique, and current treatment. The promotion of good self management skills is also included in this approach.
Guidelines recommend the use of validated tests such as the asthma control test (See **Appendix E**) or standard questions for monitoring purposes.
The 'Three Key Questions' compiled by the Royal College of Physicians are:

- Have you had difficulty sleeping because of your asthma symptoms (including cough)?
- Have you had your usual asthma symptoms during the day (cough, wheeze, chest tightness or breathlessness)?
- Has your asthma interfered with your usual activities e.g. housework, work/school etc?

Whilst asthma symptoms may be expected on up to three days a week, if those with mild to moderate asthma report any nocturnal wakening or activity limitation this should be considered abnormal.
Where asthma appears uncontrolled it is important to review and treat the following before increasing therapy:

- smoking behaviour
- poor inhaler technique
- compliance with regular preventative asthma therapy
- rhinitis

An asthma diary is a useful tool for assessing control, and an example is attached at **Appendix F**.

Guidelines strongly recommend the use of a written personalised action plan. These have been shown to improve outcomes. An example of such a plan is shown at **Appendix G**.

For some individuals, for example those reluctant to have regular review, it may be appropriate to consider carrying out telephone review rather than a face to face consultation. This would not apply to those with inhaler-related problems or poor asthma control.

Compliance with monitoring and treatment [1]

Compliance with regular monitoring using peak flow meters, even in clinical drug trials is poor with recorded daily use as low as 6%. The lack of evidence supporting long term peak flow monitoring, however, does not negate the use of home charting at critical times, for example, at diagnosis and initial assessment, when assessing response to changes in treatment, or as part of a personalised action plan during exacerbations.
Comparison should be with the patient's best known peak flow (not the predicted peak flow value).
Compliance can be improved through the provision of simple verbal and written instructions, and information on drug treatment.

Patients are more likely to under-use than over-use treatment and under-use should be considered when there is a failure to control asthma symptoms. Patient self reporting and health care professional assessment both over-estimate regular use of prophylactic medication.
Computer repeat-prescribing systems, widely available in general practice, provide a good indication of adherence with prescribed asthma regimens. Electronic monitoring, whilst the most accurate method, is only practical in clinical drug trials.

Treatment of difficult asthma [1] [10]

There is no universally accepted definition for 'difficult asthma'. It is generally accepted that those who are at steps 4 or 5 of the BTS/SIGN treatment guidelines who still have persistent symptoms and frequent exacerbations would be considered to have difficult asthma.
Precise data on prevalence is lacking, but is estimated at being between 5 and 10% of adults with asthma.
Of importance is that this group have disproportionately high morbidity, are at greater risk of fatal or near fatal exacerbations and may also be at increased risk of steroid related adverse effects.

The approach to management of someone with difficult asthma should include a detailed evaluation with exclusion of possible alternative causes for symptoms, treatment of co-morbidities and confirmation of compliance with treatment.

Monitoring of these patients by using questionnaires such as the asthma control test will help with assessment of level of control.
Those with severe or difficult asthma can be provided with a low-range peak flow meter rather than a standard peak flow meter to use for monitoring purposes.

In the UK, there exist a number of specialist clinics for managing those patients diagnosed with difficult asthma.

Treatment of brittle asthma [3]

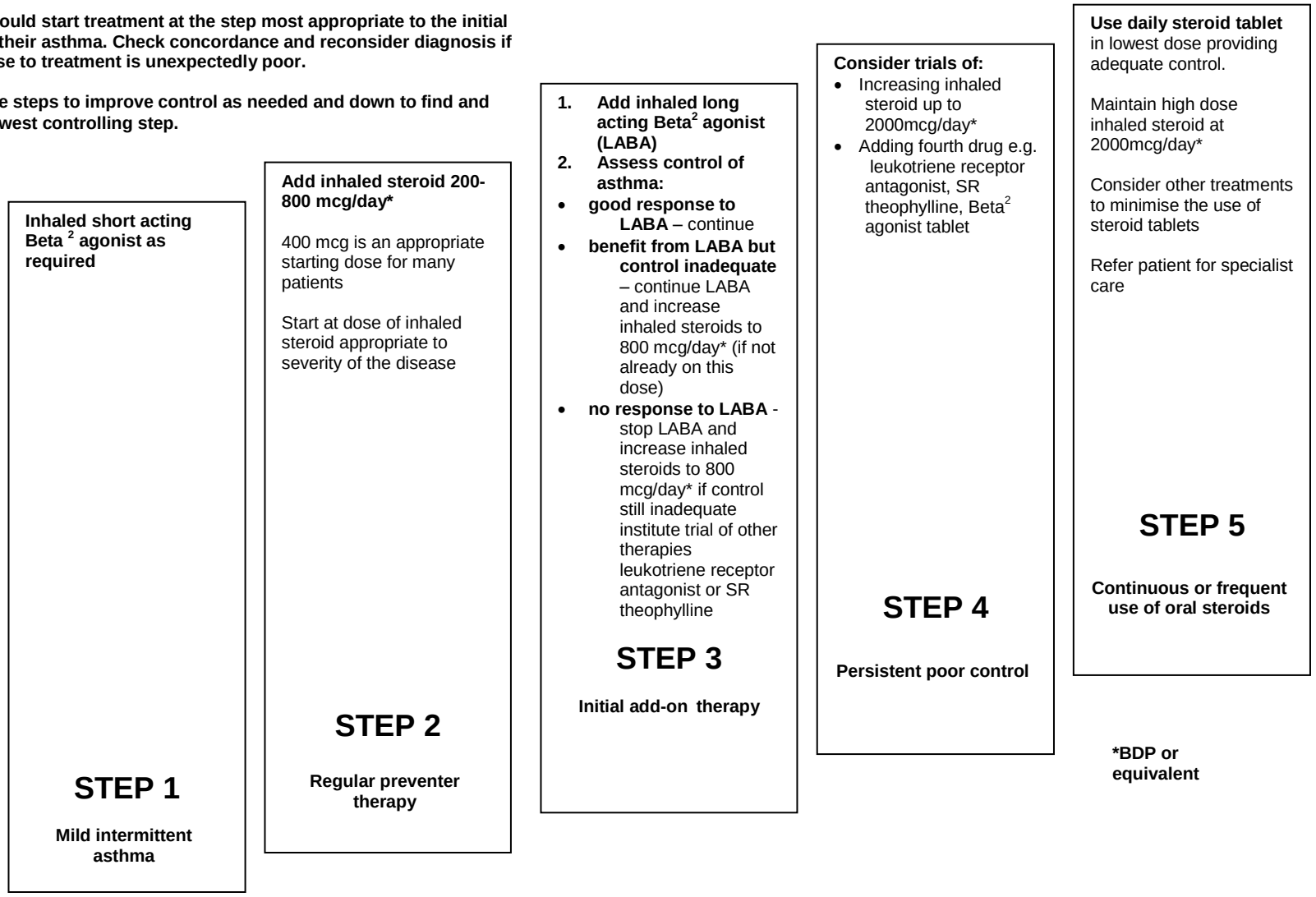
Those with brittle asthma have increased morbidity and mortality. Expert specialist assessment should be provided for this group.
In brittle asthma there may be widely varying peak flow rates, that are uncontrolled by maximum inhaled treatment.
Brittle asthma is classified into 2 types.

Type 1 – persistent chaotic daily variation. The definition includes looking at peak expiratory flow over a period of more than 150 days, with >40% diurnal variation for >50% of the time being recorded, despite intense therapy. As well as optimisation of asthma therapy with use of steroids and add-on therapies, other treatments such as sub cutaneous bricanyl administered via a pump may be considered.
Type 2 – sporadic sudden falls in PEF, on a background of asthma that is usually well controlled. Emergency treatment with injected bronchodilator may be needed urgently, and management may include the advice to carry epipen and to wear a MediAlert bracelet.

Figure 2*: Stepwise management in adults [1]*

Patients should start treatment at the step most appropriate to the initial severity of their asthma. Check concordance and reconsider diagnosis if the response to treatment is unexpectedly poor.

Move up the steps to improve control as needed and down to find and maintain lowest controlling step.



5. Occupational Asthma [16]

Asthma is one of the commonest occupational lung diseases.
About 9-15% of adult-onset asthma is considered attributable to occupational exposures. Information on incidence is available from several data sources. These include The Health and Occupation Reporting (THOR) network SWORD and OPRA schemes used by specialist physicians. Whilst acknowledging and allowing for some likely under reporting, over the past decade there is thought to have been a decrease in work-related asthma. [17] The number of new cases reported in Great Britain by specialist physicians (through the THOR-SWORD scheme) in 2010 was about 300.

Occupational asthma is defined as: asthma, which is induced by an inhaled agent at work:

- an **irritant** inhaled in toxic concentration, or
- a hypersensitivity reaction to a **sensitising agent**.

It is commonest amongst:

- paint sprayers (isocyanates)
- bakers (flour)
- plastics and chemicals workers (epoxy resins and azodicarbonamide)
- hairdressers (persulphates)

With the commonest causes being isocyanates and flour/ grain.

There are now more than 400 reported causes in the developed world with more being identified each year. Atos Healthcare's Occupational Asthma Sensitiser Information Service (OASIS) is able to give advice about identifying triggers for occupational asthma to doctors who are called upon to advise on Prescribed Disease D7 (Occupational Asthma) under the Industrial Injuries Provisions of the Social Security Contributions and Benefits Act 1982.
For Prescribed Disease D7 irritants are not included, only the respiratory sensitisers listed in the legislation, or those sensitising agents identified as triggers by OASIS.

Precautions to prevent occupational asthma are widely used. Examples include enclosure or segregation of the process, exhaust ventilation and the provision of appropriate protective devices such as respirator masks.

COSHH (Control of Substances Hazardous to Health) regulations require employers to institute health surveillance programmes where there is a risk of occupational asthma. These include symptom enquiries, measurements of lung function and reviews of sickness absence. [18]
Although they are no more likely to develop occupational asthma, it is prudent for asthmatics to avoid working in environments known to contain respiratory sensitisers. The development of occupational asthma would be more difficult to detect, and the symptoms may be more severe.

Diagnosis

A detailed, comprehensive history is one of the most crucial steps in reaching a diagnosis.

- the employment history must be obtained.
- which sensitising agent has the patient been exposed to, and to what degree?
- was there any protection available, and was it used?

The latent period must be established,

The latent period is the time between initial exposure and the onset of symptoms. This period may be days or many years, typically up to two years.

The timing of the 'first attack' may be remembered.

Typically, symptoms improve away from work, such as at weekends or during periods of holiday, and deteriorate again on return to work. It is important to remember that the patient may not have had sufficient time away from the stimulus for the inflammatory reaction to settle, before re-exposure the next day.

Symptoms and Examination

The cardinal symptoms and signs of asthma are described in the general Section 3 on Diagnosis.

Investigations

Cases of suspected occupational asthma are usually referred to a hospital specialist.

Investigations specific to occupational asthma normally include:

- A Work Place Challenge Test. The patient is removed from work for two weeks. They then return to work under clinical supervision. Several peak flow readings will have been taken before returning to work and further readings will be taken during the following three days at work.

- The Laboratory Challenge Test is the definitive test for occupational asthma. A specific agent is inhaled under laboratory conditions, and airway responsiveness is measured. The patient must be supervised for at least 8 hours.

Management

The most important aspect is:

Immediate removal from the exposure.

Removal very early in the disease process may result in complete resolution of the asthma. [19]

Delay may allow chronic asthma to develop. [19]

About 50% of those affected by occupational asthma stay with the same employer. [19]

Occupational asthma is a Prescribed Disease under the Industrial Injuries Provisions of the Social Security Contributions and Benefits Act 1982.

Differential Diagnosis (Irritant-Induced Asthma or RADS)

It is necessary to differentiate between occupational asthma and irritant-induced asthma. In the past, the more usual term for irritant-induced asthma was Reactive Airways Dysfunction Syndrome (RADS).

Indoor exposures to nitrogen oxide and volatile organic compounds are implicated in the development of irritant-induced asthma, a persistent asthma-like syndrome in people with no history of asthma. Irritant-induced asthma appears to be distinct from asthma and may be, on occasion, a form of environmental lung disease. However, irritant-induced asthma and asthma have many clinical similarities (e.g. wheezing, dyspnoea, cough), and both may respond to corticosteroids.

The diagnosis of irritant-induced asthma requires:

- the presumption of previously normal respiratory physiology, without bronchial hyperactivity.
- typical symptoms are cough, wheeze and dyspnoea.
- it follows exposure to **high** concentrations of gas, smoke, fumes, or vapour with irritant properties.
- there is no latent period, and the onset of symptoms is within 24 hours of exposure and these may persist for a period of a few days or for as long as 12 years.

Irritant-induced asthma is not a Prescribed Disease, but it can qualify as an Industrial Accident.

6. Prognosis

Chronic asthma [20]

In those with mild asthma, prognosis is good and progression to severe disease is rare. However as a group, people with asthma lose lung function faster than those without asthma, although less quickly than people without asthma who smoke.

People with chronic asthma can improve with treatment.

However, some people (possible up to 5%) have severe disease that responds poorly to treatment. These individuals are most at risk of morbidity and death from asthma.
Psychological factors may make a significant contribution to the disease burden, and also have an impact on how effectively people are able to engage with therapies and treatment services. [1]

Acute asthma [21]

About 10 – 20% of people presenting to the emergency department with asthma are admitted to hospital.
Of these fewer that 10% receive mechanical ventilation. Those who are ventilated are at a 19-fold increased risk of needing ventilation for a subsequent episode.

It is unusual for people to die unless they have suffered respiratory arrest before reaching hospital.

Independent risk factors for near-fatal or fatal asthma attacks include mental health conditions (such as significant depression or psychosis). [1]

One study of 939 people discharged from emergency care found that of those available for follow-up 17% (95% Confidence Interval of 14% - 20%) relapsed within 2 weeks.

7. Main Disabling Effects

Asthma is a chronic but variable condition. Both the baseline level of symptoms and their variability must be assessed to arrive at an accurate picture of a person's disability.
Variability can be explored in terms of good/bad days per week/month.
In this respect, some detail as to the functional differences between good and bad days should be sought.
Other fertile areas of enquiry may include asking about perceptions of their functional limitation compared with other people, or from a time prior to asthma being diagnosed. If day to day examples of functional limitation can be elicited to illustrate, this is also helpful.
History taking should include consideration of events in the past to give a representative impression of the severity of the condition. With regard to hospital admissions, considering the number of asthma admissions in the past 5 years is helpful (as considered relevant in terms or predicting outcomes). Information such as whether an asthma episode has been life-threatening with the need for ventilation is also relevant.

There is a wide range of severity in terms of disability amongst those with asthma.

Controlled asthma

Modern treatment is capable of eliminating or significantly reducing regular asthma symptoms. When asthma is well controlled activities of daily living are unlikely to be significantly restricted. Those with well controlled asthma should be able to live independently and continue with their usual interests and hobbies. Treatment and monitoring of the condition in this group is likely to be undertaken in the primary care setting.

Uncontrolled asthma

Those with poorly controlled or uncontrolled asthma are likely to have had treatment stepped up to include high doses of inhaled steroids, regular long acting ß-agonists and other treatments (beyond Step 3 of the BTS/SIGN guidelines).
Response to increased treatment will vary and symptoms may not necessarily be relieved by high doses of medication.
It should be remembered that for some individuals with severe asthma, medication doses may in fact be low if there has been a poor response to treatment, and the decision to reduce medication made. This does not mean that their compliance with treatment has been poor, but rather it reflects that their asthma is severe. This should be evident from the clinical history.
Those with severe or difficult asthma are likely to be under specialist care.
Emergency treatment through GP, Accident and Emergency department or hospital admission may have been necessary.
Respiratory symptoms such as breathlessness may be a constant feature rather than intermittent.
Lengthy or repeated hospital admissions may indicate very severe disabling asthma. (Very frequent admissions may mean personalised action plans are less useful for these individuals)

The main disabling effect of asthma is impairment of exercise tolerance. This is particularly likely to affect exertional activities such as walking and using stairs. In severe cases the ability to carry out self care tasks such as washing or dressing also becomes difficult.

Assessing asthma severity and related disability

All the available information should be considered. Documentary evidence may include client questionnaire, claim form, prescriptions, medical certificates, factual reports and previous medical examination reports.

Incorporating the following questions when taking the history will help with building up a picture of the client's disability:

- Are there any specific triggers for the asthma? (exercise, allergen exposure, respiratory infections, emotional factors, cold air etc.)
- Frequency and duration of attacks in past 2 years?
- How effective is treatment? (need for changes to treatment, courses of oral steroids, nebuliser use)
- How is their asthma monitored? (GP clinic, hospital clinic)
- Do they usually monitor peak flow themselves, or use a management plan?
- Has emergency treatment been necessary? (GP, A and E, hospital admission)
- Number of hospital admissions in the past 5 years?

The typical day approach to history taking will enable information on how asthma affects sleep pattern, mobilising, hobbies and interests and other daily tasks to be gathered.
To fully understand the variability aspect, detail on the differences between good and bad days (in terms of symptoms and function), and how these are distributed across a period of time will be valuable.

Interpreting the peak flow measurement

A peak flow measurement taken in the course of a disability examination must be interpreted in context. A 'one-off' measurement of peak flow is of limited value in assessing disability, particularly if the result is normal. A 'one-off' measurement that is low may be consistent with clinically important airflow obstruction present at the time of the test. Peak flow is much more useful in monitoring variability of airflow over a period of time.
Consideration of a 'one-off' result should include comparison with predicted peak flow, but it is probably more useful to compare the result with the individual's usual 'best' peak flow if that is known. Also useful is awareness of when a bronchodilator was last taken as this may affect the peak flow result.

Psychological and social aspects

Stress is known to be a common asthma trigger. Anxiety and depression is thought to be up to 6 times more common in those with asthma. Particularly affected in this respect are those in the 'difficult' or 'severe' groups. [14] Depression and other psychological issues are recognised as independent

risk factors for fatal or near-fatal asthma attacks. [1]

Emotions such as anxiety or denial may affect the ability to process, remember, or act upon information given. This may hinder compliance with advice and treatment, and reduce the chances of someone gaining control of their illness. [22] The successful recognition and treatment of psychological illnesses may improve quality of life and reduce disability. [23]

Research has demonstrated that the relationship between a person's symptoms and the severity of their asthma is complex. It is partly dependent on the individual's mental and physical ability to cope with the demands of the condition. [24]
Social factors such as income, marital status, alcohol consumption and housing can have an important influence on levels of physical functioning among people with chronic illnesses. [25]

There is some evidence to show that a worker with the label 'asthmatic' may face prejudicial attitudes in the workplace. [18]

Specific factors that show a link to adverse clinical outcomes, such as higher hospital admission and exacerbation rates include ethnicity (including language barriers) and poor socioeconomic status. Minority groups may be less able to engage with primary care services and have also been shown to be more likely to use emergency facilities for routine care. [1]

8. Asthma in Children and Adolescents [1]

Children

Asthma in children causes recurrent respiratory symptoms of:

- wheezing
- cough
- difficulty breathing
- chest tightness

Wheezing is one of a number of respiratory noises that occur in children. Parents often use "wheezing" as a non-specific label to describe any abnormal respiratory noise.
It is important to distinguish wheezing (a continuous, high-pitched musical sound coming from the chest) from other respiratory noises, such as stridor or rattly breathing.

There are many different causes of wheeze in childhood and different clinical patterns of wheezing can be recognised in children. In general, these patterns ("phenotypes") have been assigned retrospectively. They cannot reliably be distinguished when an individual child first presents with wheezing. In an individual child the pattern of symptoms may change as they grow older.

The commonest clinical pattern, especially in pre-school children and infants, is episodes of wheezing, cough and difficulty breathing associated with viral upper respiratory infections (colds), with no persisting symptoms. Most of these children will stop having recurrent chest symptoms by school age.

Isolated chronic cough without wheeze or breathlessness is not likely to be due to asthma. [26]

A minority of those who wheeze with viral infections in early life will go on to develop wheezing with other triggers so that they develop symptoms between acute episodes (interval symptoms) similar to older children with classical atopic asthma.

Children who have persisting or interval symptoms are most likely to benefit from therapeutic interventions.

Indications for specialist referral

These include the presence of a history of perinatal lung problem, failure to thrive, excessive vomiting or posseting, persistent wet or productive cough, severe upper respiratory tract infection or nasal polyps. Those with a family history of unusual chest disease, lack of response to conventional treatment or unexpected clinical findings should also be referred.
In some cases referral may be to clarify the diagnosis or to provide reassurance and allay parental anxiety.

Initial clinical assessment

The diagnosis of asthma in children is based on recognising a characteristic pattern of episodic respiratory symptoms and signs (see Table 1) in the absence of an alternative explanation for them (see Tables 2 and 3).

Table 1:
Clinical features that increase the probability of Asthma

More than one of the following symptoms: wheeze, cough, difficulty breathing, chest tightness, particularly if these symptoms:

- are frequent and recurrent
- are worse at night and in the early morning
- occur in response to, or are worse after, exercise or other triggers, such as exposure to pets, cold or damp air, or with emotions or laughter
- occur apart from colds

Other features include:

- personal history of atopic disorder
- family history of atopic disorder and/or asthma
- widespread wheeze heard on auscultation
- history of improvement in symptoms or lung function in response to adequate therapy

Table 2:
Clinical features that lower the probability of asthma

- Symptoms with colds only, with no interval symptoms
- Isolated cough in the absence of wheeze or difficulty breathing
- History of moist cough
- Prominent dizziness, light-headedness, peripheral tingling
- Repeatedly normal physical examination of chest when symptomatic
- Normal peak expiratory flow (PEF) or spirometry when symptomatic
- No response to a trial of asthma therapy
- Clinical features pointing to alternative diagnosis (see Table 3)

Several factors are associated with a high (or low) risk of developing persisting wheezing or asthma through childhood. The presence of these factors increases the probability that a child with respiratory symptoms will have asthma.

These factors include:

- Age at presentation
  The natural history of wheeze is dependent on age at first presentation. In general, early onset of wheeze in a child means the prognosis will be better. Cohort studies show a "break point" at around two years. Most children who present before this age become asymptomatic by mid-childhood. Co-existent atopy is a risk factor for persistence of wheeze independent of age of presentation.

- Sex
  Male sex is a risk factor for asthma in pre-pubertal children. Female sex is a risk factor for the persistence of asthma in the transition from childhood to adulthood. Boys with asthma are more likely to "grow out" of their asthma during adolescence than girls.

- Severity and frequency of previous wheezing episodes
  Frequent or severe episodes of wheezing in childhood are associated with recurrent wheeze that persists into adolescence.

- Coexistence of atopic disease
  A history of other atopic conditions such as eczema and rhinitis increases the probability of asthma. Positive tests for atopy in a wheezing child also increase the likelihood of asthma. A raised specific IgE to wheat, egg white, or inhalant allergens such as house dust mite and cat dander, predicts later childhood asthma.
  Other markers of allergic disease at presentation, such as positive skin prick tests and a raised blood eosinophil count, are related to the severity of current asthma and persistence through childhood.

- Family history of atopy
  A family history of atopy is the most clearly defined risk factor for atopy and asthma in children.
  The strongest association is with maternal atopy, which is an important risk factor for the childhood onset of asthma and for recurrent wheezing that persists throughout childhood.

- Abnormal lung function
  Persistent reductions in baseline airway function and increased airway responsiveness during childhood are associated with having asthma in adult life.

Table 3:
Clinical clues to alternative diagnoses in wheezy children (features not commonly found in children with asthma)

Perinatal and family history	**Possible diagnosis**
Symptoms present from birth or perinatal lung problem	Cystic fibrosis; chronic lung disease of prematurity; ciliary dyskinesia; developmental anomaly
Family history of unusual chest disease	Cystic fibrosis; neuromuscular disorder
Severe upper respiratory tract disease	Defect of host defence; ciliary dyskinesia
Symptom and signs	**Possible diagnosis**
Persistent moist cough	Cystic fibrosis; bronchiectasis; protracted bronchitis; recurrent aspiration; host defence disorder; ciliary dyskinesia
Excessive vomiting	Gastro oesophageal reflux (± aspiration)
Dysphagia	Swallowing problems (± aspiration)
Breathlessness with light-headedness and peripheral tingling	Hyperventilation/panic attacks

Inspiratory stridor	Tracheal or laryngeal disorder
Abnormal voice or cry	Laryngeal problem
Focal signs in chest	Developmental anomaly; post-infective syndrome; bronchiectasis; tuberculosis
Finger clubbing	Cystic fibrosis; bronchiectasis
Failure to thrive	Cystic fibrosis; host defence disorder; gastro oesophageal reflux
Investigations	**Possible diagnosis**
Focal or persistent radiological changes	Developmental anomaly; cystic fibrosis; post-infective disorder; recurrent aspiration; inhaled foreign body; bronchiectasis; tuberculosis

Case detection studies have used symptom questionnaires to screen for asthma in school-age children. A small number of questions - about current symptoms, their relation to exercise and their occurrence at night has been sufficient to detect asthma relatively efficiently. The addition of spirometry or bronchial hyper-responsiveness testing to these questionnaires adds little to making a diagnosis of asthma in children.

Most children under five years and some older children cannot perform spirometry. These children should be offered a trial of treatment for a specific period. If there is clear evidence of clinical improvement, the treatment should be continued and they should be regarded as having asthma (it may be appropriate to consider a trial of withdrawal of treatment at a later stage). If the treatment trial is not beneficial, then tests for alternative conditions should be considered and referral for specialist assessment arranged.
Between 2 - 5 years of age, many children can perform several newer lung function tests that do not rely on their cooperation or the ability to perform a forced expiratory manoeuvre.
In general, these tests have not been evaluated as diagnostic tests for asthma.

Adolescents [1]

The World Health Organisation defines adolescence as the period of growth and development between 10 and 19 years. Asthma is a common condition affecting adolescents. The under reporting of symptoms is thought to be a factor leading to under-diagnosis in adolescents.

Symptoms and signs are the same as for other age groups, but most adolescents with asthma have normal lung function despite having symptoms.

Known risk factors for developing asthma in adolescence include atopy, prematurity, wheezing in infancy, and chlorinated swimming pools. From the age of 13 -14 yrs the gender bias reverses, with more females affected than males.

9. References

[1] SIGN / British Thoracic Society Guidelines – January 2012

[2] Reddel H, Jenkins C and Woolcock A. Diurnal variability – time to change asthma guidelines. *BMJ 1999*; 319:45

[3] Asthma. Section 18.7 Oxford Textbook of Medicine Fifth Edition Oxford University Press 2010.

[4] The Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2011. www.ginaasthma.org/

[5] Lung and Asthma Information Agency. www.laia.ac.uk

[6] An Outcomes Strategy for COPD and Asthma in England. www.dh.gov.uk/en/Publicationsandstatistics

[7] Simpson CR and Sheikh A. Trends in the epidemiology of asthma in England: a national study of 333,294 patients. *J R Soc Med 2010:* 103: 98-106

[8] Merck Manual – Online – updated April 2008

[9] Bourke SJ et al. Lecture Notes in Respiratory Medicine. Blackwell Scientific 6th Edition 2003

[10] Currie GP, Douglas JG, Heaney LG. Difficult to treat asthma in adults. *BMJ* 2009;338:b494 doi:10.1136/bmj.b494

[11] Gøtzsche PC, Johansen HK. House dust mite control measures for asthma. Cochrane Database for Systematic Reviews 2008, Issue 2. Art No.:CD001187. DOI: 10.1002/14651858.CD001187.pub3.

[12] Abramson AJ, Puy RM, Weiner JM. Injection allergen immunotherapy for asthma. Cochrane Database of Systematic Reviews 2010, Issue 8. art. No.:CD001186.DOI:10.1002/14651858.CD001186.pub2

[13] www.bnf.org.uk

[14] Walters EH, Walters JAE, Gibson PG, Jones P. Inhaled short acting beta2-agonist use in chronic asthma: regular versus as needed treatment. Cochrane Database of Systematic Reviews 2003, Issue 1. Art. No.: CD001285. DOI; 10.1002/14651858.CD001285

[15] Quality Outcomes Framework guidance for GMS contract 2011/12

[16] Update on Occupational Asthma. Jan 2011 MED/S2/CMEP~0033. Medical Services

[17] http://www.hse.gov.uk/statistics/causedis/asthma. (Contains public sector

information published by the Health and Safety Executive and licensed under the Open Government license v1.0)

[18] Cox R, Edwards F, Palmer K. Fitness for Work. Oxford Medical Publications.2000

[19] Ross DJ, McDonald JC. Health and employment after a diagnosis of occupational asthma: a descriptive study. *Occupational Medicine (Oxford)* 1998; 48:219-25

[20] Dennis RJ and Solarte I. *BMJ Clinical Evidence*. Asthma in Adults (chronic). Web publication date 13 July 2011

[21] Rodrigo G. *BMJ Clinical Evidence*. Asthma in Adults (acute). Web publication date 4 April

[22] Bucknall CE, Slack R, Godley CC, Mackay TW and Wright SC. Scottish Confidential Inquiry into Asthma Deaths (SCIAD), 1994-6. *Thorax* 1999;54:978-84

[23] Lacasse Y RLMF. Prevalence of depressive symptoms and depression in patients with severe oxygen-dependent chronic obstructive pulmonary disease. *J Cardiopulm Rehabil* 2001; 21:80-6

[24] Rimington LD, Davies DH, Lowe D and Pearson MG. Relationship between anxiety, depression and morbidity in adult asthma patients. *Thorax* 2001; 56:255-71

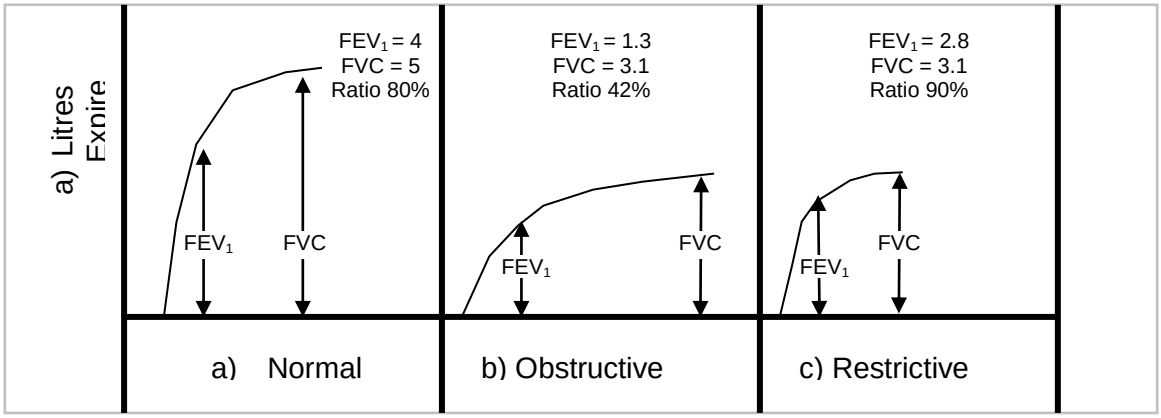
[25] Mackenbach JP, Borsboom GJ, Nusselder WJ, Looman CW and Schrijvers CT. Determinants of levels and changes of physical functioning in chronically ill persons: results from the GLOBE Study. *Journal of Epidemiology and Community Health* 2001; 55:631-8

[26] Brodie M, Graham C and McKean MC. Childhood cough. *BMJ* 2012; 344:e1177 doi: 10.1136/bmj.e1177

[27] Adapted from: www.patient.co.uk/doctor/Asthma-Action -Plans.htm

Appendix A - Glossary of Terms

Term	Meaning
Forced Expiratory Volume in the first second (FEV_1)	The amount of air that can be expelled in one second from a maximal inspiration using maximal effort.
Forced Vital Capacity (FVC)	The total amount of air expired from the lung using maximal effort from a maximal inspiration.
Peak Expiratory Flow (PEF)	A measure of lung power using a simple apparatus. Useful in monitoring asthma.
Total Lung Capacity (TLC)	Total amount of air in the lung. It can only be measured by indirect means.
Gas Transfer Factor (DL_{CO})	A measure of the ability to transfer a respiratory gas from atmosphere to blood in a given time. Useful in lung fibrosis.
Obstructive Spirometry	FEV_1 is reduced more than FVC causing a reduced FEV_1: FVC ratio. Examples: Asthma & COPD.
Restrictive Spirometry	Suggests FVC is reduced. Causes a normal or increased FEV_1: FVC ratio. Examples: chest wall abnormalities & lung fibrosis.



Appendix B - Peak Expiratory Flow Monitoring (PEF) [1]

Recommended Technique for Measuring Peak Flow

- Use equipment that functions correctly. In examination centres, report any worn-out or defective equipment so that it can be replaced.
- The type of meter used (Wright or EU) should be recorded.
- Explain the procedure and demonstrate it to the subject.
- Move the pointer to the bottom of the scale.
- The subject should be sitting up straight or standing.
- The subject should hold the peak flow meter horizontally, and the subject's fingers must not impede the movement of the pointer along the scale.
- Ask the subject to take a deep breath, seal their mouth around the mouthpiece, and blow as hard and as fast as they can. (Like blowing out a candle.) Pursed lips or air leaks will invalidate the reading.
- The result should be compared to a graph of predicted peak flow according to the subject's age, sex and height. Both the actual and the predicted peak flow should be recorded. Interpretation of the result is helpful for the Decision Maker.
- If the subject is not able to achieve good technique, then this must be noted for the benefit of the Decision Maker.

PEF should be recorded as the best of three forced expiratory blows from total lung capacity with a maximum pause of two seconds before blowing. The subject can be standing or sitting. Further blows should be done if the largest two PEF are not within 40 l/min.

PEF is best used to provide an estimate of variability of airflow from multiple measurements made over at least two weeks. Increased variability may be evident from twice daily readings. More frequent readings will result in a better estimate but the improved precision is likely to be achieved at the expense of reduced subject compliance.

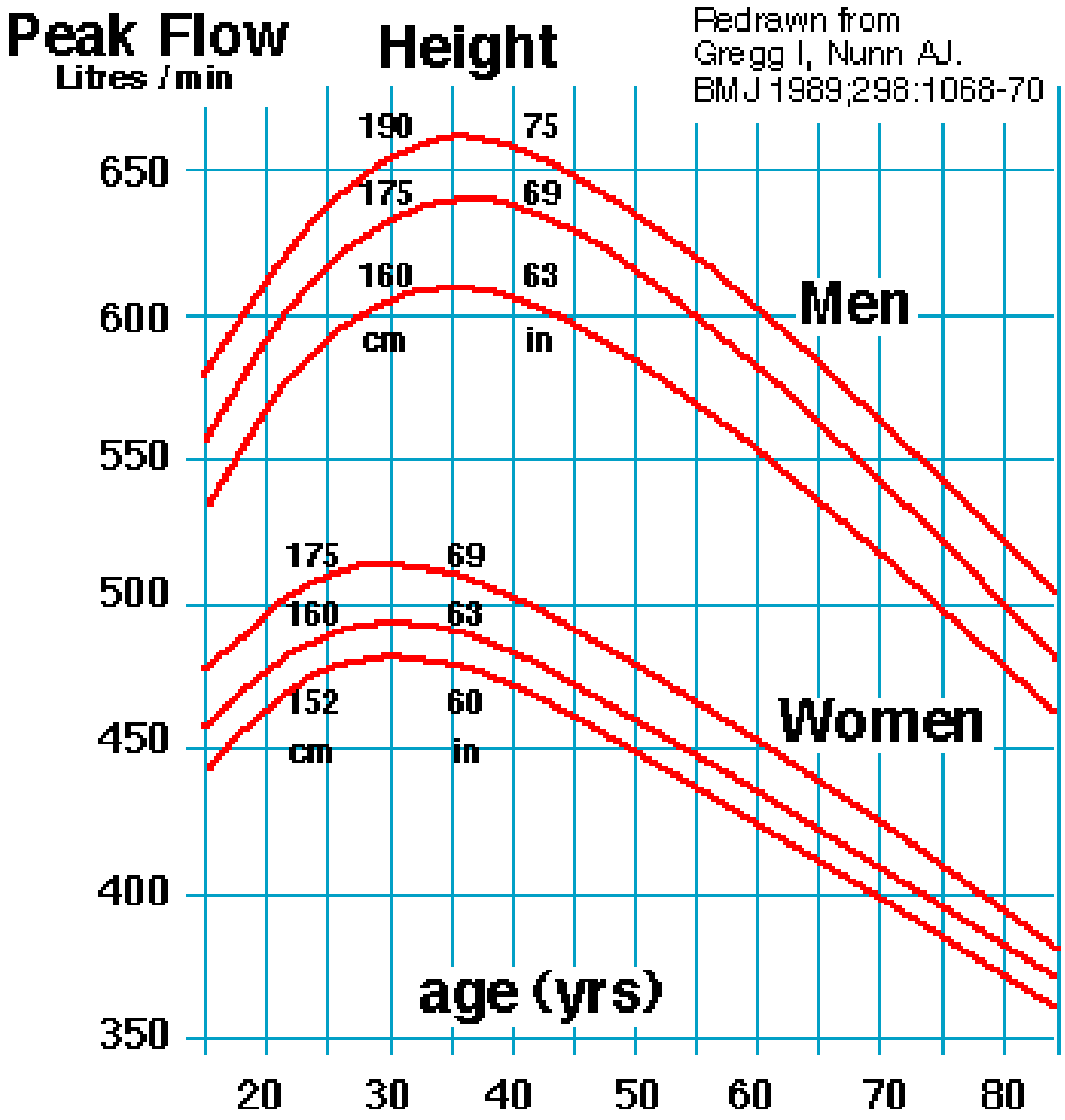
PEF variability is best calculated as the difference between the highest and lowest PEF expressed as a percentage of either the mean or highest PEF.

The upper limit of the normal range for the amplitude % highest is around 20% using four or more PEF readings per day but may be lower using twice daily readings. Epidemiological studies have shown sensitivities of between 19 and 33% for identifying physician-diagnosed asthma.

PEF variability can be increased in subjects with conditions commonly confused with asthma so the specificity of abnormal PEF variability is likely to be less in clinical practice than it is in population studies.

PEF records from frequent readings taken at work and away from work are useful when considering a diagnosis of occupational asthma.

Peak flow records should be interpreted with caution and with regard to the clinical context. They are more useful in the monitoring of patients with established asthma than in making the initial diagnosis. [1]



Appendix C - Treatments for Chronic Asthma [12]

Short Acting ß-Agonists

This group refers to the selective $ß_2$ agonists. Salbutamol (Ventolin) and Terbutaline (Bricanyl) are common examples. They are taken by inhalation, and have a rapid onset of action. (The effects begin after 15 minutes, and last about four hours). The $ß_2$ agonists cause bronchodilation, and are used as **relievers.** Possible side effects include tremor, palpitations and muscle cramps, although these are uncommon when the drugs are taken in inhaled form.

Can also be used immediately before exertion to reduce exercise–induced asthma.

Long Acting ß-Agonists

Long acting ß-agonists should always be used with inhaled corticosteroids.

Examples include salmeterol (Serevent) and eformoterol (Oxis). They achieve their maximum effect in 2 hours and this lasts for about 12 hours so is particularly effective for nocturnal symptoms. Salmeterol should not be used for the relief of acute symptoms.

Eformoterol can be used both to relieve bronchospasm, and as prophylaxis for exercise-induced asthma.

There is evidence that long acting ß-agonists given as monotherapy produce an increase in asthma related mortality. The use of inhalers which provide a combination of steroid and long acting ß-agonist increases compliance and remove any concerns about only giving long acting ß-agonists. This combination can achieve excellent symptom reduction and peak flow control.

Anticholinergic Bronchodilators

The commonest example is ipratropium bromide (Atrovent). These drugs block the cholinergic bronchoconstrictor effect of the vagus nerve. Maximum effect is achieved 30 – 60 minutes after use, and it lasts for about 4 hours. Anticholinergic bronchodilators are not as effective as ß-agonists in asthma, but can be used as an adjunct if control is incomplete, or ß-agonists are not tolerated. They are particularly suitable for very young children or older adults.

Theophyllines

These drugs are effective bronchodilators. They are taken orally as sustained release formulations. The theophyllines have a narrow therapeutic index, with considerable individual variation in the necessary dose. Therefore, it is necessary to monitor blood concentrations. For these reasons, they are used much less now that long acting ß-agonists are available. Common side effects include nausea and vomiting, abdominal

discomfort, headache, malaise, tachycardia and fits. There are numerous drug interactions with other common treatments such as erythromycin, phenytoin and cimetidine.

Sodium Cromoglicate and Nedocromil Sodium

These drugs are sometimes known as Mast Cell Stabilisers, although this may not be their main mode of action in asthma. Predicting who will benefit from their use is difficult. They block bronchoconstriction to the stimuli of exercise and antigens.They are sometimes used as first line prophylactic agents, particularly in young children, or as an addition to inhaled corticosteroids when control is poor. They are less effective than steroids in adults, and are not useful as relievers.

Inhaled Corticosteroids

Beclometasone and budesonide are the most common examples. Fluticasone is a more potent drug, and is used at half the dose. The majority of their benefits are seen at low to moderate doses, (up to 800 mcgs beclometasone equivalent), with relatively little additional benefit from higher doses. They are highly effective at reducing bronchial reactivity and inflammation and at controlling symptoms. Peak effect usually occurs 3–7 days after initiation of treatment. Side effects are dose-dependent, inhaler device-dependent, and technique-dependent. In adults, adverse effects become more likely once a daily dose of 1000 mcgs of beclometasone equivalent is reached:

- oropharyngeal candidiasis.
- dysphonia, sore throat and cough.
- purpura and thinning of the skin.
- cataracts.

Large volume spacers should be used at doses above 800 mcgs beclometasone equivalent to reduce pharyngeal deposition.
Inhaled corticosteroids should be taken regularly for the prevention of symptoms. Doubling the dose at the first sign of a respiratory infection is a frequently used tactic, and seems to reduce the risk of a severe exacerbation of asthma.
Unfortunately, commonly discussed side effects of corticosteroids, the lack of an instant improvement in symptoms, and the need to take them regularly, at least twice a day, all conspire to make poor compliance extremely common.
Current or previous smoking history both reduce the effectiveness of inhaled corticosteroids such that higher doses may be needed.

Combination inhalers

These are useful in selected patients, and may aid compliance. A combination inhaler such as symbicort (budenoside/formeterol) may be used as rescue therapy in adults with poorly controlled asthma at step 2 (if above 400 mcg BDP daily) or step 3, as well as being used for regular inhaler therapy.

Oral Corticosteroids [1]

Short courses are very valuable for controlling exacerbations of asthma. Regular long-term oral corticosteroids may be used in some people with severe asthma who are not controlled at Step 4 of the BTS/SIGN treatment guidelines.

They are used in the following situations:

- as a diagnostic test
- to gain control when starting treatment in severe cases
- when inhalers are ineffective
- during exacerbations of asthma

Patients prone to severe exacerbations of asthma often keep a supply of prednisolone tablets in reserve so that they can be used, (according to their individual management plans), should an exacerbation develop.

Regular long-term oral corticosteroids may be used in some people with severe asthma who are not controlled at Step 4 of the BTS/SIGN treatment guidelines.
Inhaled corticosteroids should be continued to keep the dose of oral steroids as low as possible.

Use of oral corticosteroids for 3 months or longer (or frequent short courses of treatment) carries the risk of systemic side effects.
The prevention of osteoporosis is particularly important for patients using long-term steroids. Treatments such as hormone replacement therapy, and bisphosphonates should be considered.
The body's immune and stress responses are blunted by regular steroid use. Patients should carry 'steroid cards', and avoid contact with chickenpox or shingles.

Leukotriene Antagonists

Leukotrienes are one of the key inflammatory mediators responsible for bronchoconstriction. Examples of leukotriene antagonists include Montelukast (Singulair) and Zafirlukast (Accolate). They are taken by mouth, once daily, and are generally very well tolerated. (So, compliance is better.) They are useful in mild asthma or in moderate asthma in addition to inhaled steroids where the two drugs together appear to have an additive effect.

Monoclonal Antibodies

Monoclonal antibodies such as omalizumab (Xolair) may be prescribed in cases of severe persistent allergic asthma, where other treatments have not achieved control. There should be proven IgE mediated sensitivity to inhaled allergens. Treatment should be initiated through a specialist centre where severe persistent asthma is managed.

Appendix D - Drug Delivery Systems

A wide variety of devices have been developed in an attempt to provide simple, efficient and cheap methods of administering inhaled drugs. Inhalation delivers the drug directly to the airways. The necessary dose is smaller than for drugs given by mouth, and the incidence of side effects is reduced.

The best choice of device for an individual is likely to be determined by factors such as ease of use and personal preference.

Metered Dose Inhaler (MDI)

This device uses compressed gas to dispense a metered dose of drug in aerosol form. MDIs are very widely used, with about 400 million prescribed annually, worldwide. Recently devices using CFC free gas have been introduced. MDIs are cheap to produce, but they are inefficient. Only 10% of the metered dose reaches the lungs (the rest is swallowed and metabolised by the liver), and about 25% of patients are unable to co-ordinate the triggering of the device with the necessary intake of breath. MDIs work more efficiently in conjunction with a spacer device such as a Volumatic, and this combination is often used for young children and the elderly. Because of the potential difficulties of using MDIs, it is particularly important to teach and then regularly check inhaler technique.

Breath Actuated Aerosol Inhalers

These inhalers do not require skilful co-ordination. Inspiration triggers the device. This makes them easier to use, especially for children.

Dry Powder Inhalers

These do not rely on co-ordination, and are easy to use. The improved efficiency of lung deposition compared with an MDI means that the use of lower doses might be possible.

Nebulisers

Nebulisers are capable of delivering a high dose of bronchodilator. These machines produce a fine mist of liquid medication that can be easily inhaled from a mask or mouthpiece. The dose is delivered over about ten minutes. However, only about 12% of it reaches the lungs, as the majority escapes into the atmosphere, or is trapped in the nebuliser tubing.

Tablets and Syrups

This route is used for the leukotriene antagonists and the theophyllines.

Subcutaneous Injection

Monoclonal antibodies are given by this route.

Appendix E - Asthma Control Test

The five questions refer to the past 4 weeks. A total score of 25 indicates perfect control, 20 – 24 indicates that asthma may be well controlled although further advice should be obtained, and a score of <20 indicates that further recommendations regarding management should be made by a doctor or nurse.

Questions	Answers	Score
Q1 - How much of the time did your asthma stop you getting as much done at work school or home?	All the time	1
	Most of the time	2
	Some of the time	3
	A little of the time	4
	None of the time	5
Q2 - How often have you had shortness of breath?	More than once a day	1
	Once a day	2
	3-6 times a week	3
	Once or twice a week	4
	Not at all	5
Q3 - How often did your asthma symptoms wake you up at night or earlier than usual in the morning?	4 nights a week or more	1
	2-3 nights a week	2
	Once a week	3
	Once or twice	4
	Not at all	5
Q4 - How often have you used your rescue inhaler or nebulised drug?	3 times a day or more	1
	1-2 times a day	2
	2-3 times a week	3
	At least once a week	4
	Not at all	5
Q 5 - How would you rate your asthma control?	Not at all controlled	1
	Poorly controlled	2
	Somewhat controlled	3
	Well controlled	4
	Completely controlled	5

Appendix F - Example Asthma Diary

Purpose: To use a diary card to keep track of a patient's daily asthma symptoms.

Citations with documentation. 01.15.02

Sriram and Svirbely 1998

enter an "x" in the appropriate column for each question (give only 1 answer per row)						
	no sleep disturbance due to asthma	awoken once during the night, for less than 1 hour, because of asthma	awoken 2 or 3 times or once for more than an hour because of asthma	awake most of the night because of asthma		
Sleep disturbance			x		Yes	2
	not present and didn't require extra bronchodilator during the night	not present but did require extra bronchodilator during the night	present			
Chest tightness on awakening			x		Yes	2
	none	occasional	frequent but not all day	most or all of the day		
Duration and frequency of daytime wheeze and breathlessness			x		Yes	2
	none	mild; not incapacitating or distressing	moderate to severe; distressing and/or had to limit activities			
Severity of daytime wheeze and breathlessness			x		Yes	2
	none	occasional	more than occasional			
Cough during the day			x		Yes	2

calculate	**result**	
data complete?	Yes	
asthma diary card score	10	out of 12
asthma severity based on score	moderate	

Appendix G - Asthma Action Plan

This is an example of how a personalised asthma action plan might look.

Patient Name	
Date of Birth	
Next of Kin Contact Numbers	
Usual doctor/ asthma nurse Contact numbers	
Best peak flow	
Asthma triggers	
Drug allergies	
Date of last update	

When my asthma is controlled:	• I have no regular daytime symptoms (cough, wheeze, chest tightness, shortness of breath) • I have no difficulty sleeping because of asthma symptoms • My asthma does not interfere with my usual activities (e.g. work, study, housework) • My peak flow is above 85% of my 'best peak flow'
What should I do?	• Continue usual treatment • See usual doctor or nurse about stepping down treatment if always in this box
My usual treatment	• My preventer/ reliever medications are:

When my asthma is getting worse	Moderate symptoms: • I have noticed the first signs of a cold (if a usual trigger) • I have mild but recurring wheeze, cough or chest tightness during the day • My sleep is disturbed by coughing, wheezing, chest tightness • I am using my reliever puffer more than once a day • My peak flow is between 70 to 85% of my 'best peak flow' Severe symptoms: • I need my reliever puffer every 3-4 hours or more often

	• I am having constant wheezing, coughing, chest tightness • I am having difficulty with normal activity • My peak flow is between 50 to 75% of my 'best peak flow'
What should I do?	• Acute treatment – bronchodilator (e.g. **salbutamol** 4 to 6 puffs) via spacer or **nebuliser**. Repeat every 10 to 20 minutes if necessary • Monitor response – symptoms and peak flow. If getting worse seek medical help. If getting better or stable, seek medical review within 48 hours • Step up usual preventative treatment (increase inhaled steroids if daily dose less than 400 micrograms or add in oral steroids as below) • If I start oral prednisolone (40 to 50 mg daily for 5 days) I should have doctor or nurse review in 24-36 hours • Once symptoms well controlled, go back to usual treatment after 3 days

How to recognise emergency asthma:	• I am having great difficulty breathing • My reliever puffer is giving little or no improvement • It is difficult to speak or walk due to severe shortness of breath • Symptoms are getting worse quickly • I am feeling frightened • My peak flow is less that 50% of my 'best peak flow'
What should I do?	• Take my reliever puffer. If there is no immediate improvement contact a doctor urgently and, if not available, call 999 for an ambulance or go straight to hospital • Sit upright and stay calm
Emergency treatment whilst waiting for doctor/ ambulance	Take one puff of salbutamol via spacer every 5 minutes or until symptoms improve