Asthma

Version 4 Final

Document control

Version history

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Changes since last version

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 is no standardised definition of the type, severity, frequency of symptoms, nor of the findings on investigation. This may, in part, account for the reported variability in the prevalence of asthma.

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

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

Prevalence

Comprehensive information on asthma prevalence in the UK is not available[3].

- Asthma prevalence is usually estimated from survey data.
  In children and young adults, wheezing is most commonly used as an indicator of asthma although estimates based on wheezing will include trivial illness. Estimates based on wheezing alone are unreliable in older adults.

- 12-15% of children suffer episodes of wheezing characteristic of asthma. Less than 5% suffer persistent or repeated attacks.

- The prevalence of asthma in children increased by about half between the early 1970s and mid 1980s but recent trends are less clear cut.
  The proportion of children diagnosed as having asthma increased over the last decade. Childhood asthma is more common in boys. Following puberty females are more often affected.

- 15-20% of adults experience wheezing, but probably less than 5% suffer night time breathlessness or reversible air flow limitation characteristic of asthma.

Aetiology[4]

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 (TH1 and TH2) cells, IgE, cytokines (IL-3, -4, -5, -9, and -13), 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.

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 may trigger exacerbations. The role of childhood exposure to cigarette smoke is controversial, with some studies finding a contributory and some a protective effect.

Genetic and environmental components may interact by determining the balance between Th1 and Th2 cell lineages. Infants may be born with a predisposition toward pro-allergic and pro-inflammatory Th2 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 Th1 responses, which suppresses Th2 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 deprive children of these Th2-suppressing, tolerance-inducing exposures and may partly explain the continuous increase in asthma prevalence in developed countries (the hygiene hypothesis).

Occupational Factors

(See ***Section 3*** for further details about Occupational Asthma.)

Pathophysiology[4]

Asthma involves

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

In patients with asthma, Th2 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
- Inhaled irritants
- Emotion
- Aspirin and to lesser extent 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) is a common exacerbating factor in some patients with asthma, possibly via oesophageal acid-induced reflex bronchoconstriction or by micro-aspiration of acid.
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:
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 O2 tensions fall and alveolar CO2 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, 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.

Diagnosis

The diagnosis of asthma is based on the recognition of a characteristic pattern of symptoms and the absence of an alternative explanation for them (see Table 1). The key is to take a careful clinical history. In many cases this will allow a reasonably certain diagnosis of asthma, or an alternative diagnosis, to be made.
If asthma does appear likely, the history should also explore possible causes, particularly occupational.

In view of the potential requirement for treatment over many years, it is important even in relatively clear cut cases, to try to obtain objective support for the diagnosis. Whether or not this should happen before starting treatment depends on the certainty of the initial diagnosis and the severity of presenting symptoms. Repeated assessment and measurement may be necessary before confirmatory evidence is acquired.

Confirmation hinges on demonstration of airflow obstruction varying over short periods of time. Spirometry, which is now becoming more widely available, is preferable to measurement of peak expiratory flow because it allows clearer identification of airflow obstruction, and the results are less dependent on effort. It should be the preferred test where available (although some training is required to obtain reliable recordings and to interpret the results). It is important to note that a normal spirogram (or PEF) obtained when the patient is not symptomatic does not exclude the diagnosis of asthma[1].

History

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 6*** for further information about Occupational Asthma.)
Triggers:	Cold Air, Exercise and Emotion
Response to a Trial of Treatment:	Symptoms and/or Peak Flow Improve

Examination

Subjects with mild intermittent asthma frequently have no signs or symptoms.

Observation may indicate exertional wheezing or wheezing at rest.

Pigeon Chest is a feature of chronic severe asthma. (Hyper-inflated.)

Accessory muscles (scalene and sternocleidomastoid muscles in the neck) may be seen to be used to aid breathing.

Auscultation may reveal diminished air entry and diffuse bilateral wheeze with a prolonged expiratory phase.

Table 1[1] Clinical features in adults that influence the probability that episodic respiratory symptoms are due to asthma

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.

Pulmonary Function Tests (See *Appendix F* 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 A.

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 are often asked to keep 'Peak Flow Diaries' as an aid to diagnosis and assessing the effectiveness of treatment.

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 2). 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

The best of three peak flow readings is recorded. A bronchodilator is given, and the peak flow readings are repeated 15-20 minutes later.
An improvement of at least 15% (or 200 mls) is suggestive of asthma.

Chronic severe asthma may not show any reversibility after bronchodilator usage. However, a two-week trial of corticosteroid may produce an improvement in peak flow. This helps to differentiate between asthma (improvement likely), and COPD (improvement less likely).

Provocation tests

Exercise testing is a safe, simple and useful procedure if the diagnosis of asthma is in doubt. Peak flow is measured before exercise. The patient

does 6 minutes of vigorous exercise, and the peak flow is repeated 15-20 minutes later. A fall of 10-20% is highly suggestive of asthma.[5] [6]

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 metacholine can also be useful.

Chest X Ray

This is usually normal.

Further investigation of patients with an intermediate probability of asthma

Patients with airways obstruction[1]

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:

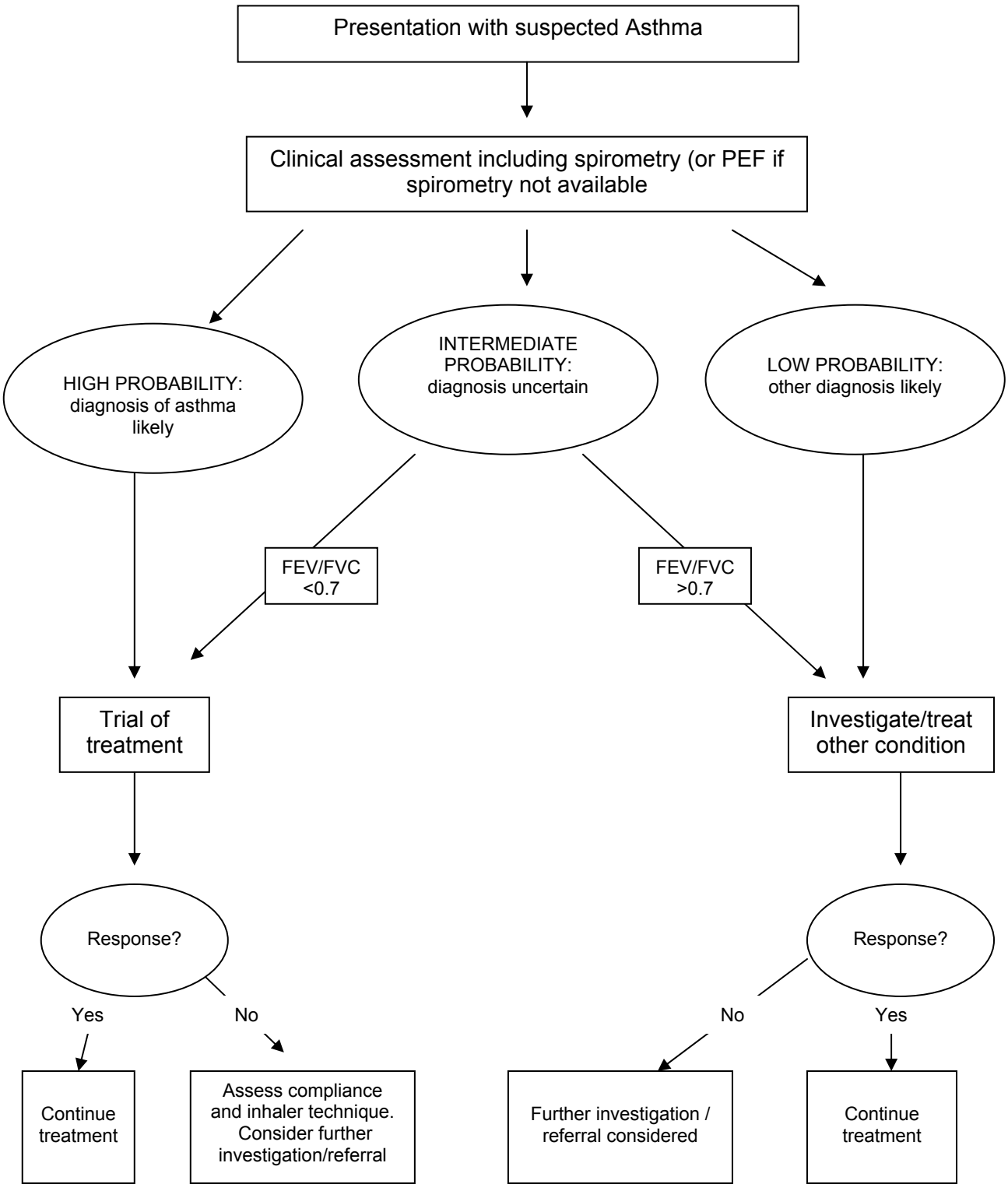
- If there is significant reversibility, or if a treatment trial is clearly beneficial treat as asthma
- If there is insignificant reversibility and a treatment trial is not beneficial, consider alternative conditions.

Patients without airways obstruction[1]

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 2: 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

Occupational Asthma[7] [8]

Asthma is one of the commonest occupational lung diseases.[8]
About 9-15% of adult-onset asthma is considered attributable to occupational exposures. [9] [10] There is no indication that this figure has changed over the past decade.
Approximately 1160 new cases were reported in the UK in 1999[11] [12].

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)

There are over 200 known respiratory sensitisers and more are 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.

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[13].

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[13].

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' is usually well 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 ***Sections 5.2*** and ***5.3***.

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[14].

Delay may allow chronic asthma to develop[14].

About 50% of those affected by occupational asthma stay with the same employer[14]

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

Differential Diagnosis (RADS)[7] [15]

It is necessary to differentiate between Occupational Asthma and Reactive Airways Dysfunction Syndrome (RADS).

Indoor exposures to nitrogen oxide and volatile organic compounds are implicated in the development of RADS, a persistent asthma-like syndrome in people with no history of asthma. RADS appears to be distinct from asthma and may be, on occasion, a form of environmental lung disease. However, RADS and asthma have many clinical similarities (e.g. wheezing, dyspnoea, cough), and both may respond to corticosteroids.[4]

The diagnosis of RADS 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. The onset of symptoms is within 24 hours of exposure and they may persist for a period of a few days or for as long as 12 years.

RADS is not a Prescribed Disease, but it can qualify as an Industrial Accident.

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 new 2008 guideline has 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.[1]

Advice for Asthmatics

1. Where practical, identify and then avoid precipitating factors. (Not possible with widespread allergens e.g. house dust mite and pollen.)
   However, evidence that reducing allergen exposure can reduce morbidity and/or mortality in asthma is tenuous. In uncontrolled studies, children and adults have derived benefit from removal to a low allergen environment such as occurs at high altitude, although the benefits seen are not necessarily attributable to allergen avoidance alone.[16]

2. Stopping Smoking
   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. Annual influenza vaccination is recommended.[17]

4. Regular exercise.[18] [19] [20] (Sport, exercise and pulmonary rehabilitation improve respiratory function and quality of life.)

Pharmacological management [1, 21]

The aim of asthma management is control of the disease. Control of asthma is defined as:

- 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 clinical practice patients may have different goals and may wish to balance the aims of asthma management against the potential side effects or inconvenience of taking medication necessary to achieve 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 maintain control by stepping up treatment as necessary and stepping down when control is good (see figure 2 for summary of stepwise management in adults*).* [21]

Key Concept: Relievers and Preventers

Bronchodilator drugs are highly effective at temporarily relieving the symptoms of asthma, ***"Relievers."***

However, the aim of treatment is to eliminate asthma symptoms, so the main emphasis for most asthmatics should be the **regular** use of ***"Preventer"*** medication.
Regular use of inhaled corticosteroids reduces airway inflammation and reactivity. It is anticipated that this will prevent airway damage, which would otherwise lead to irreversible chronic airway obstruction. Preventer treatment should be started very early in the treatment of asthma, and then used aggressively to gain quick control.

The Main Treatments for Chronic Asthma

(See ***Appendix B*** for additional details and information about less widely used drugs.)

Relievers

1. Short Acting β_2-Agonists [22]
   - Salbutamol (Ventolin) is the most widely used example.
   - Rapid onset in minutes and lasts for a few hours.
   - Ideal for the rapid relief of symptoms.

2. Long Acting β_2-Agonists. [23]
   - 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.

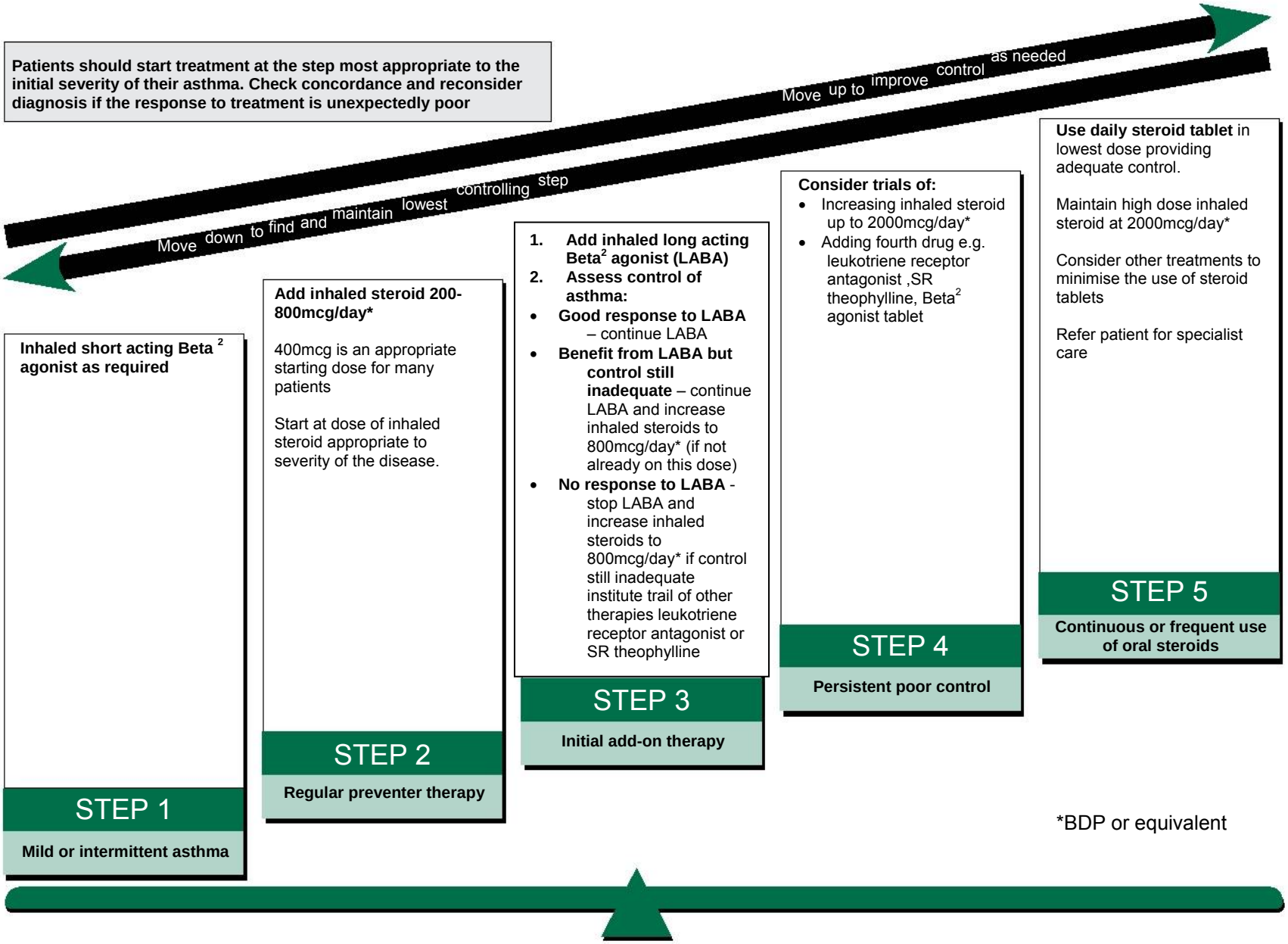
Preventers

1. Inhaled Corticosteroids. ("Inhaled Steroids.") [24]
   - Beclomethasone is the most widely used example [25]
   - Must be taken regularly every day.
   - 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.

Figure 2: Stepwise management in adults [1]



Monitoring and Measuring Asthma Control

In General Practice, the majority of this work is performed by Practice Nurses who have received additional training and work to written guidelines. The following information is valuable for assessing the success of asthma treatment, and it should be checked at each asthma review [26] [27] [28]

- Frequency of daytime symptoms.
  (Ideally, these should be no more common than once a fortnight.)

- Frequency of nocturnal symptoms.
  (If these are present at all, the asthma is poorly controlled.)

- Patient's Peak Flow Diary.
  (Diurnal variation of peak flow >20% indicates poor control.)

- Inhaler Technique.
  (This is critical, as it is often sub-optimal, and may prevent a useful therapeutic effect.)

- Education and Understanding [29]

  The success of asthma treatment depends on this. Patients often have misconceptions about their condition and its treatment. The provision of written information and written individual management plans is effective for improving compliance and symptom control.[30]

  (An example is provided in Appendix C.)

An asthma diary is a useful tool for assessing control, and an example is attached at Appendix D.[31]

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).

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.

Prognosis

Chronic asthma[32].

In people 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 (possibly up to 5%) have severe disease that responds poorly to treatment. These people are most at risk of morbidity and death from asthma.

Acute asthma.[32]

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

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

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.

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 a true picture of a claimant's disability.

Assessing the Claimant

The assessment should be made using all the information available. This includes information from the claimant's file, informal observations, medical history, activities of daily living, and examination.

To take account of the variability of asthma, it is important to ask about the claimant's illness over time. Considering events in the last 2 years will give a representative impression. There is a wide range of severity amongst claimants with asthma:

Controlled Asthma

Modern asthma treatment is capable of eliminating or significantly reducing regular asthma symptoms. 'Activities of Daily Living' are unlikely to be significantly restricted. The asthmatic should be able to live independently and continue with their usual interests and hobbies. The claimant's asthma will probably be monitored and treated in primary care.

Poorly controlled/Uncontrolled Asthma

Poorly controlled asthmatics are likely to require high doses of inhaled and/or regular oral steroids, regular long acting ß-agonists, and one or more of: theophylline, leukotriene antagonist, cromoglycate, nedocromil or anticholinergic bronchodilator.

Poorly controlled/Uncontrolled asthmatics are likely to experience frequent or severe exacerbations that require additional treatment such as high dose oral steroids, nebulised bronchodilators or courses of antibiotics. Some may have required emergency treatment from their GP or at an Accident and Emergency unit, and the most severe may have experienced hospital admission. Their asthma may be under the supervision of a Consultant.

The main effect of asthma is to impair exercise tolerance. This is particularly likely to affect the activities of walking and climbing stairs. In the most severe cases, even washing and dressing may become difficult.

Considering Exemption from the IB-PCA

Exemption from the assessment should be considered if effort tolerance is severely limited, or they have had to adapt their home, for example by installing a stair lift or converting a room downstairs for their bedroom.

Helpful Questions for Assessing Asthma Severity and Related Disability

- Are there any specific triggers for the asthma?
  - (Exercise, cold air, respiratory infections, allergen exposure, drugs, emotional factors.)
- What has been the frequency and duration of attacks over the last 2 years?
- 'Bad Days' – what, in terms of daily activities, makes them different, and how often do they occur?
- Does their asthma interfere with hobbies and interests?
- How do they get around, for instance for shopping or taking the children to school? (Walking, car, bicycle or public transport.)
- Does their asthma cause any difficulty sleeping? Where do they sleep?
- What is the claimant doing about their asthma?
  - Do they attend their GP's asthma clinic?
  - Do they do monitor their peak flow?
  - Do they have a management plan for their asthma?
- How effective is their treatment?
  - Have there been any changes to medication in the last 2 years and why were the changes made?
  - How many courses of oral steroids and antibiotics have they needed in the last 2 years?
  - Have they required the use of a nebuliser in the last 2 years?
- Do they attend a hospital outpatient clinic because of their asthma? Have they required emergency asthma treatment from their GP or at Casualty?
  Have they been admitted to hospital because of their asthma in the last 2 years?

Interpreting the Peak Flow Measurement

A peak flow measurement taken in the course of a disability examination is only a snapshot, and may not reflect the typical experience of the claimant. However, it does provide an objective piece of information that can be weighed with all the other data obtained from the claimant's medical history, treatment, examination findings and Typical Day. All this information must be used to build up a picture of their asthma and any disability it may cause.

Aids to Grading the Disabling Effects of Asthma

The Medical Research Council Breathlessness Scale[33]

Grade	Degree of breathlessness related to activities
1	Not troubled by breathlessness except on strenuous exercise
2	Short of breath when hurrying or walking up a slight hill
3	Walks slower than contemporaries on level ground because of breathlessness, or has to stop for breath when walking at own pace
4	Stops for breath after walking about 100m or after a few minutes on level ground
5	Too breathless to leave the house, or breathless when dressing or undressing

Percentage of Predicted Peak Flow

The percentage of predicted peak flow is one way of assessing the severity of asthma. It is important to remember that there is considerable variability between individuals, and measures of lung function do not always correlate with functional ability.
The following table describes broad categories of functional impairment:
NB. The table is for guidance only. [7]

% Predicted Peak Flow	Description of Severity	Range of Functional Effects	
>75%	Mild	Nil	
50-75%	Moderate	**From**	Breathlessness on heavy exertion.
		To	Breathlessness walking at normal pace on the flat.
33-49%	Severe	**From**	Breathlessness on walking 100m.
		To	Breathlessness on climbing one flight of stairs without stopping.
<33%	Very Severe	**From**	Cannot climb one flight of stairs without stopping.
		To	Bed-bound or chair-bound.

Psychological and Social Aspects

When a person is suffering from a chronic illness such as asthma, psychological problems may result. Emotions such as anxiety or denial may affect their ability to process, remember, or act upon the information they are given. This may hinder their compliance with advice and treatment, and reduce their chances of gaining control of their illness.[34] The successful recognition and treatment of psychological illnesses may improve quality of life and reduce disability. [35]

Research has demonstrated that the relationship between a person's symptoms and the severity of their asthma is complex. It partly depends on the individual's mental and physical ability to cope with the demands of the condition.[36]

Social factors such as income, marital status, alcohol consumption and housing have an important influence on levels of physical functioning among people with chronic illnesses.[37]

There is some evidence to show that a worker with the label 'asthmatic' may face prejudicial attitudes in the workplace.[38]

Asthma in children[1]

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.

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.

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
- 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.15,20 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, the earlier the onset of wheeze, the better the prognosis. 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

Table 3: ***Clinical clues to alternative diagnoses in wheezy children (features not commonly found in children with asthma)***	
Symptom and signs	
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	
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.

Appendix A Peak Expiratory Flow Monitoring (PEF)[1]

Recommended Technique for Measuring Peak Flow[39]

- Use equipment that functions correctly. In examination centres, report worn-out or defective equipment to the Medical Examination Assistant (MEA) 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 with a brief explanation to help the Decision Maker to interpret the result.
- 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.[1]

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.[1]

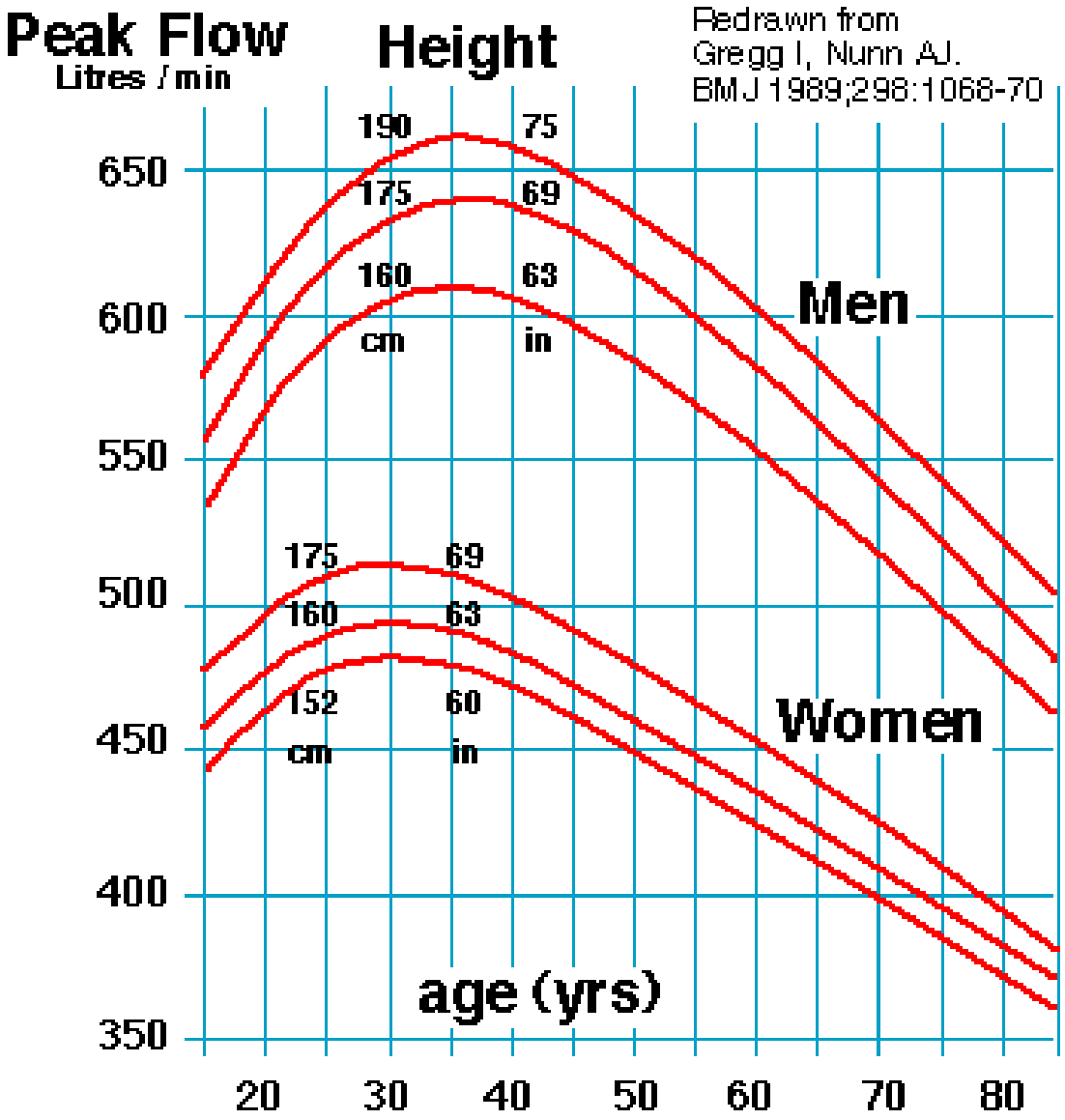
PEF variability is best calculated as the difference between the highest and lowest PEF expressed as a percentage of either the mean or highest PEF.[1]

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.[1]

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.[1]

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 B Treatments for Chronic Asthma [21]

Short Acting ß-Agonists [22]

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.

Long Acting ß-Agonists [23]

Examples include Salmeterol (Serevent) and Eformoterol (Oxis). They achieve their maximum effect in 2 hours and last for about 12 hours. Thus, they are particularly effective for nocturnal symptoms, but they should not be used for the relief of acute symptoms. The long acting ß-agonists do not suppress inflammation, so they should always be used with inhaled corticosteroids. Indeed there is evidence that given as monotherapy there is an increase in asthma related mortality. Inhalers which provide a combination of steroid and Long Acting ß-Agonist increase 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 [23]

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 Cromoglycate and Nedocromil Sodium

These drugs are sometimes known as Mast Cell Stabilisers, although this may not be their main mode of action in asthma. 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 [24 25 40 41]

Beclomethasone 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), with relatively little additional benefit from high 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 beclomethasone 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 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.

Oral Corticosteroids

Regular long-term oral corticosteroids are the last resort in the out-patient management of asthma treatment. However, short courses are very valuable for controlling exacerbations of asthma.

Short courses of oral steroids are used in the following situations:

1. As a diagnostic test.
2. To gain control when starting treatment in severe cases.
3. When inhalers are ineffective.
4. 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.
In long-term use, a regime of alternate daily dosing is preferable. Inhaled corticosteroids should be continued to keep the dose of oral steroids as low as possible.

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. The leukotriene antagonists are an exciting and relatively new class of treatment for asthma. Examples 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. (They are too new to feature in the BTS guidelines, but they are often considered for use as an alternative to long acting ß-agonists at step 3.)

Desensitisation and Avoidance of Allergens [42]

Trials of these treatments have been disappointing, except where a patient has an obvious precipitating factor. More common are asthmatics who are sensitive to a variety of ubiquitous allergens such as pollen, house dust mite, and fungal spores. Unfortunately, it is impractical to entirely avoid these.

Appendix C Management Plan

Example of an Individual Management Plan for an Adult Asthmatic

NB: This is only an example: medication and peak flow are individual to each patient.

Preventers

- Take **one** puff of the becloforte in the morning and evening **every day.**
- If you get a cold, or your peak flow drops below 300, take **two** doses morning and evening.

Relievers

- Take **two** puffs of ventolin when you need it.
- If you need it more than **five** times a day, arrange an appointment at the surgery.

Actions

- If your peak flow is less than 250, take **six** prednisolone tablets a day, and get an appointment at the surgery within 48 hours.
- If your peak flow is less than 200, take **six** prednisolone tablets, **four** puffs of ventolin, and ring the surgery immediately

Appendix D 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 E 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.

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

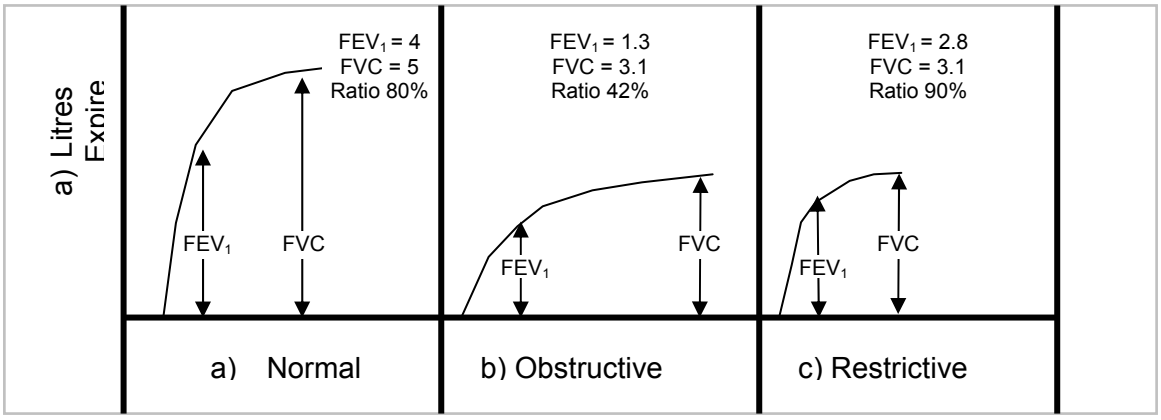
Nebulisers are capable of delivering a high dose of bronchodilator. These machines produce a fine mist of liquid medication that can be easily inhaled from a mask or mouthpiece. The dose is delivered over about ten minutes. However, only about 12% of it reaches the lungs, as the majority escapes into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

Tablets and Syrups

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

Appendix F 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 lungpower 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.



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