MANAGEMENT OF CHRONIC ASTHMA – A PERSONAL VIEW

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DEFINITION

The word ASTHMA is of Greek origin, meaning "breathless" or "to breathe with open mouth", and was originally applied to breathlessness of any cause. An accurate and comprehensive definition has proved far more elusive than expected, but from a clinician's viewpoint the currently most acceptable is that asthma is a disease characterised by wide variations over short periods of time in resistance to flow in intrapulmonary airways[1]. The definition implies objective measurement and 15-20% variation is a significant level.

This vague definition avoids the problem of dividing patients absolutely into categories of asthma and chronic bronchitis and then debating whether patients with chronic bronchitis have reversible airways disease. Even if symptoms suggest bronchitis, the finding of significant variation in resistance to airflow means that asthma co-exists and patients should be regarded as having "chronic bronchitis with asthmatic features."

Difficulties with regard to definition make accurate assessment of the prevalence of the disease impossible and there are wide variations in the results of surveys in general practice. However, this is a common disease with a cumulative prevalence of up to about 5% in the United Kingdom.

Differences between Chronic Bronchitis and Chronic Asthma

Bronchitis	Asthma
Rare or unknown in children	Common in children
Almost all smoke	Few smoke
Good night's sleep	Symptoms disturb sleep
Worse in morning	Worse at night
Cough and sputum in all	Cough and sputum in some
Cough on going to bed	Cough during night
Wheeze in some	Wheeze in all
Exercise causes breathlessness	Exercise causes wheeze
Few respond to cortico-steroids	Most respond to cortico-steroids
Few have good broncho/ dilator reversibility	Most have good broncho/ dilator reversibility

TABLE 1

DIAGNOSIS

Asthma should be suspected at an early stage in young adults since it is the only common cause in this group of recurrent breathlessness, cough or wheeze. In practice, however, it is still often labelled as wheezy bronchitis and may then be treated inappropriately. A recent study[2] in adults showed that patients correctly labelled as having asthma were prescribed bronchodilator drugs three times more often than those labelled as having chronic bronchitis and twelve times more often than those without a diagnostic label.

Difficulty often occurs in differentiating asthma from chronic bronchitis (Table 1). Particularly important discriminating features are that patients with asthma have troublesome symptoms at night and rarely smoke during acute exacerbations when symptoms are usually made worse by a smoky atmosphere.

The diagnosis may be less apparent when asthma presents as a cough alone or as nocturnal breathlessness in an elderly patient. Upper airways obstruction due to a tumour or external compression (fig 1) can be mistaken for asthma but should be indicated by rapid deterioration, stridor and poor response to bronchodilator therapy.

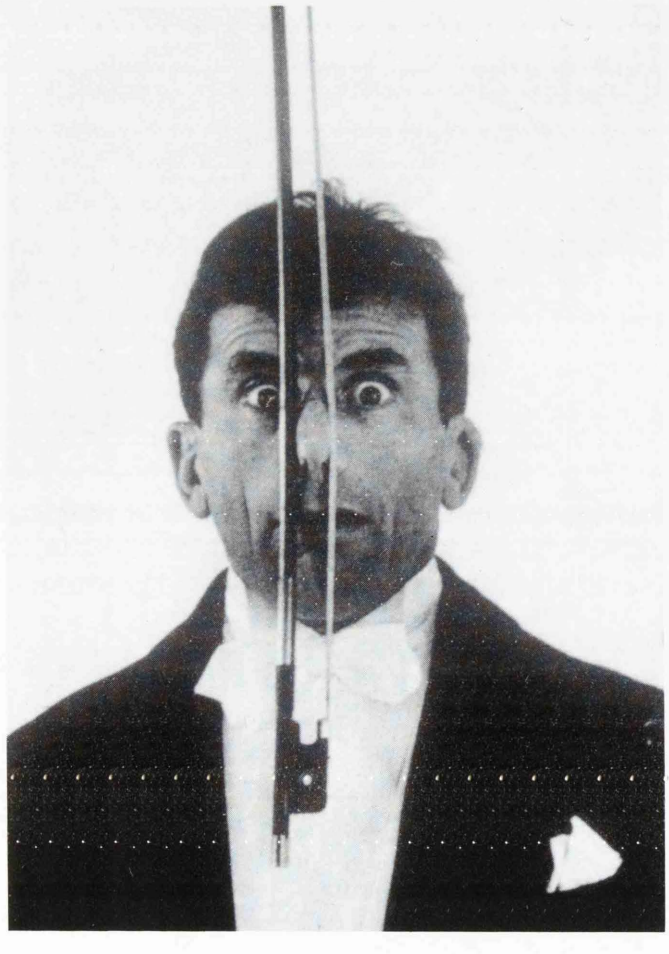

Fig 1 – Upper airways obstruction

INVESTIGATION

The aims of investigation are summarised in Table 2.

Aims of Investigation

1. Establish diagnosis of asthma
2. Identify precipitating causes
3. Identify possible complications
4. Establish a target for treatment

TABLE 2

1. Establish the Diagnosis of Asthma Asthma is usually easily diagnosed in most patients by the demonstration of reversible airway obstruction using a bronchodilator, e.g. by performing peak expiratory flow rates (PEFR) or forced expiratory volume in one second (FEV_1) before and after salbutamol by inhaler or by nebulizer. Difficulty may occur if initial breathing tests are normal when serial PEFR may be of value and rarely exercise tests and bronchial challenge tests may be required. Occasionally patients with long-standing severe chronic asthma fail to respond to an initial bronchodilator test and reversibility is only confirmed by a full corticosteroid assessment.

2. Identify Precipitating Causes: History Non-specific provoking factors can often be identified by careful history-taking. Upper respiratory tract infections mainly of viral origin are implicated in one third of asthmatic attacks in adults[3]. Exercise-induced asthma occurs in 70-85% of adults and atmospheric factors such as cold dry air, cigarette smoke and sulphur dioxide can exacerbate asthma. All too often therapy for other diseases can exacerbate or even cause asthma (Table 3) and particular note should be made of concomitant treatment with beta-adrenergic antagonist drugs which may even induce asthma when given topically as eye drops. 2% of patients give a history of aspirin-induced asthma but 19% may show broncho-constriction with formal provocation tests. One third of women have menstrual or pre-menstrual exacerbations of asthma and symptoms may worsen or improve during pregnancy. Emotional stress may exacerbate asthma but there is no evidence that it causes the disease, as was previously believed.

Drugs causing Asthma

Penicillin and other antibiotics
Beta adrenergic antagonists
Aspirin and other non-steroidal anti-inflammatory drugs
Mono-amine oxidase inhibitors
Antisera and some vaccines
Allergen extracts for hyposensitisation
Blood and blood products
Intravenous contrast media

TABLE 3

Allergy Tests. Positive skin prick tests indicate atopy but a reaction to any particular allergen does not mean that it is necessarily responsible for symptoms. Radioallergosorbent (RAST) tests for specific IgE levels are more expensive and still lack sensitivity. Bronchial provocation tests are much more accurate indices of hypersensitivity but nonetheless rarely result in the identification of a troublesome avoidable allergen of which the patient was not already aware. Most clinicians therefore have abandoned skin prick tests completely, RAST tests almost completely and reserve bronchial provocation tests for special situations or research purposes.

Serial Peak Flow Monitoring. Serial peak flow monitoring is useful in the diagnosis of occupational asthma. Although patterns of reaction can be very complicated, typically there is a fall in PEFR 10-60 minutes following exposure to the allergen and PEFR tends to be lower on days at work than at weekends or during holidays. Some agents, especially isocyanates, can induce asthma which may be troublesome for years after exposure has ended.

Endoscopy. Gastro-oesophageal reflux may provoke wheeze as well as the more familiar symptoms and early investigation of mild symptoms is therefore indicated in patients who have asthma.

3. Identify Possible Complications

Chest X-ray is of little benefit in uncomplicated chronic asthma, showing hyperinflation only. Since repeated "silent'" pulmonary opacities are the hallmark of asthmatic bronchopulmonary eosinophilia, one chest x-ray should be undertaken on all new patients, with further x-rays if there are factors suggestive of allergic bronchopulmonary eosinophilia, or to exclude reactivation of tuberculosis in patients on long-term corticosteroid therapy.

Eosinophilia. An eosinophil count above 5% of the total white cell count may help to differentiate asthma from chronic bronchitis. A higher, more persistent level may be useful in the early identification of bronchopulmonary eosinophilia.

Aspergillus and Candida Precipitins. About 60% of bronchopulmonary eosinophilia is due to sensitivity to Aspergillus fumigatus or Candida albicans and these precipitins are therefore routinely checked in new patients.

4. Establish a Target for Treatment

Many adults with moderate or severe chronic asthma have an irreversible component to their airway obstruction despite maximal therapy. It is valuable to assess this at the start of treatment so that maintenance treatment is not repeatedly increased with no possibility of further response. FEV1 and forced vital capacity (FVC) are therefore measured before and after maximal doses of a bronchodilator given via nebuliser at the patient's first visit and after a course of prednisolone, 20-30mgs for 7-21 days, depending on the severity of symptoms and the degree of reduction in pulmonary function tests. Indeed all wheeze should be regarded as asthma until this has been excluded by failure to respond to these reversibility tests, even if the presenting symptoms suggest chronic bronchitis or emphysema.

MANAGEMENT

PATIENT EDUCATION

Asthma, like many other diseases, is incurable. Patients are often frightened by the diagnosis and only respond to advice and treatment if they understand the nature and natural history of asthma and how drug therapy can modify them. The lack of immediate response to preventative drugs often results in poor compliance and treatment failure. Many patients need instruction and regular supervision of inhaled therapy if they are to obtain therapeutic benefit. Careful explanation is time-consuming and needs reinforcement later, but it improves management and saves time in the long run. The Asthma Society (12 Pembridge Square, London W2

4EH) produces pamphlets, books and a newspaper for patient education. Local branches arrange meetings for further education as well as supporting social events.

IRRITANT AND ALLERGEN AVOIDANCE

Patients should be strongly advised to stop smoking and obtain prompt treatment for bronchial infection. In the small minority where a specific allergen is responsible for symptoms, avoidance or reduction of exposure can result in improvement. Unfortunately this is rarely successful since the commonest allergens are ubiquitous, e.g. house dust mite, grass pollens and some fungi. Elaborate attempts to avoid exposure have therefore largely been abandoned as effective, safe treatment regimens have been developed.

HYPOSENSITISATION

Hyposensitisation has caused little or no relief of asthma symptoms and is not justified on present evidence since any benefit has to be balanced against the occasional severe or even fatal adverse reaction[5].

DRUG THERAPY

Therapy of asthma has improved dramatically in the last 30 years, enabling good control of symptoms to be achieved in the majority with few side effects. Wherever possible, therapy should be by the inhaled route, thus minimising side effects and avoiding tachyphyllaxis. Since many patients are unable to use a pressurised inhaler properly, the prescriber must regularly check technique and where necessary find an appropriate alternative such as a dry powder inhaler or spacer attachment. Breath-activated devices may soon solve most of these problems, but will only be of full value when corticosteroids can also be given by this method.

Treatment of asthma can conveniently be divided into the use of four types of drugs – antihistamines, bronchodilators, preventatives and systemic steroids.

Antihistamines In general antihistamines are of no value in the treatment of asthma. For all practical purposes ketotifen can be regarded as nothing more than an antihistamine.

Bronchodilators

Beta-Adrenergic Receptor Stimulants are the first line of treatment and should be used in all patients. Many $beta_2$ selective drugs are available (eg salbutamol, terbutaline, fenoterol, pirbuterol) and have replaced the less selective drugs isoprenaline and orciprenaline. There is nothing to choose between them in terms of efficacy, speed and duration of action or acceptability. Cost and personal preference are adequate reasons for making a decision. Very occasional patients who require treatment infrequently may complain of troublesome tremor. This can be minimised by using rimiterol, which causes less tremor but its value is limited by its much shorter duration of action[6]. Treatment should be taken as frequently as necessary to relieve symptoms and also before exercise or allergen exposure. It is illogical to set an arbitrary limit on the maximum dosage permitted per day, since there is such a wide safe therapeutic range. Patients should, however, be advised how to react to changing requirements for, and response to treatment (Table 4).

Large doses by nebuliser are rarely required in routine management of chronic asthma, being mainly of benefit to those who have corticosteroid-resistant disease, but good bronchodilator reversibility.

Oral administration in slow-release form is occasionally of value in treatment of those who have nocturnal symptoms despite good daytime control with inhaled bronchodilators and steroids in full dosage. Oral treatment may well be totally superceded by the introduction in the near future of two new, long-acting inhaled preparations, salmeterol and formoterol. These appear to have at least a 12-hour duration of action and may have significant prophylactic, as well as bronchodilator properties. They may well prove to be the next "revolution" in asthma therapy.

Ipratropium Bromide This anti-parasympathetic drug may have some marginal advantages over beta-agonists in patients with non-asthmatic airflow obstruction, but in asthma effects appear to be additive rather than synergistic. It is therefore better to rely on larger doses of beta-agonists than to confuse patients by the addition of another inhaler.

Methyl Xanthines. The common occurrence of minor side effects, especially nausea and epigastric pain and the occasional occurrence of severe toxic effects of convulsion, life-threatening dysrhythmias and even death results in these drugs being used only in those patients who still have disabling symptoms despite maximal doses of beta-agonists and preventative treatment. Probably their role will also be superceded by long-acting inhaled bronchodilators.

PREVENTATIVE THERAPY

Sodium Cromoglycate (SCG) remarkably rarely causes side effects[7], but is only effective in up to 50% of patients. Since inhaled steroids have also proved remarkably safe SCG has been almost abandoned in the treatment of adult asthma. It is occasionally of use in preventing exercise-induced asthma.

Nedocromil undoubtedly has a preventative action but there is still no good reason to select it in preference to inhaled steroids or SCG. Addition of nedocromil to treatment of patients with persisting symptoms despite maximal doses of inhaled steroids has been very disappointing.

Inhaled Corticosteroids. The introduction, nearly 20 years ago, of inhaled corticosteroids has proved to be one of the major therapeutic advances in respiratory medicine. Treatment is as effective when given twice daily as four times daily and is equivalent to 7 to 10mgs. of prednisolone daily. Topical treatment avoids the many systemic side effects of oral treatment, but adrenal suppression and systemic effects occur with more than 2mgs of beclomethasone daily. Other side effects include oropharyngeal candidiasis which occurs in about 5% of patients[8], virtually never requiring withdrawal of treatment. Problems can be minimised by twice rather than four times daily treatment, addition of a spacer attachment to the inhaler, washing the mouth immediately following treatment and the occasional or even regular administration of anti-fungal therapy. Recently there have been reports of a possible association with posterior sub-capsular cataract[9] and particular care will be needed in patients on high-dose treatment.

Systemic-Corticosteroids. A few patients with severe chronic asthma require small doses of oral prednisolone as well as inhaled corticosteroids, but this treatment should only be added after careful consideration and under close supervision. Alternate-day therapy minimises the risk of side effects and is possible in most patients. Intermittent injections of triamcinolone acetonide (Kenalog)[10] is now rarely justified since the drug is ten times more potent than first believed and an 80mg. injection is equivalent to about 35mgs. of prednisolone daily for one month.

Most patients can be taught when to take a short course of prednisolone, usually 20 to 30mgs. daily for 7 days to prevent a severe exacerbation of asthma. This should in most cases be available at home for early use as symptoms deteriorate (Table 4). There is usually no need to tail off treatment if it is administered for less than three weeks. Patients taking oral steroids for a long period will develop adrenal suppression and should be issued with a "steroid card".

Indications for a Short Course of Prednisolone

1. Increasing requirement for inhaled bronchodilators
2. Shorter duration of benefit from inhaled bronchodilators
3. Lack of response to repeated inhaled bronchodilators
4. Recurrence, or increase in frequency, of nocturnal symptoms

TABLE 4

PLAN OF TREATMENT

Patients with minimal symptoms may require no more than intermittent doses of inhaled bronchodilators. If baseline pulmonary function tests are below normal, or if treatment is needed more than two to three times daily, or if sleep is interrupted by symptoms, a steroid assessment should be undertaken. If there is a response, early addition of inhaled steroid therapy is indicated. It is usually better to err on the side of over-treatment, to gain early relief of symptoms, but it is essential to reduce the dose subsequently to the minimum effective level. There is no value in increasing the dose of inhaled corticosteroid therapy during an acute exacerbation, when oral prednisolone will be required. On the other hand inhaled therapy should be continued during an acute exacerbation since it remains equivalent to an additional 7 to 10mgs. of prednisolone. Frequent exacerbations may indicate the need for long-term increase in the inhaled dose.

If symptoms persist despite maximum doses of inhaled steroids (usually 1.5mgs. of beclomethasone daily), then a nocturnal dose of oral long-acting beta-agonist or methyl xanthine should be added to prevent nocturnal symptoms. An additional morning dose of methyl xanthines may be needed to reduce daytime symptoms. Long-term oral steroids are finally added if severe disability persists, or to prevent frequent severe exacerbations, but only after reversibility to steroids has been demonstrated.

MONITORING OF DISEASE AND TREATMENT

The aim of treatment is to allow patients to lead as normal a life as possible, on as small and simple a treatment regimen as possible, with as few side effects as possible. Asthma is by definition a variable disease and uncontrolled symptoms can lead to irreversible airflow limitation, severe attacks and death. Regular monitoring is therefore essential in all patients except those with minimal symptoms, i.e., in all patients requiring more than intermittent inhaled bronchodilator therapy. The essential factors which require regular monitoring are summarised in Table 5.

Factors requiring Regular Monitoring in Chronic Asthma

1. Measurement in pulmonary function – PEFR or FEV and FVC
2. Check inhaler technique
3. Assess compliance with therapy – especially prophylactic agents
4. Check patient understands principles of asthma management
5. Assess frequency and appropriateness of short course steroid therapy
6. Assess complications of asthma, e.g. pulmonary eosinophilia
7. Assess side effects of therapy, especially with systemic steroids
8. Check the need for dosage adjustment
9. Check the requirements for additional drug therapy.

TABLE 5

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