

DR CARSON: I accept the sense of that, but I'm also concerned about the intellectual side. Doctors are meant to be learned professional men. If you're going to look after somebody who's had a heart attack you're meant to know about heart attacks. You're saying you don't need to know.

DR HAMPTON: You can find out next day. As long as you've excluded the things you must do something about like a perforated peptic ulcer than I don't think it matters if you don't turn up the diagnosis until the following day.

DR CARSON: But if I was lying in bed and my GP came round to say that he didn't know much about it but he thought I ought to stay put, then I would say, "Well, let's have somebody who does know something about it."

### Reference

<sup>1</sup> Tunstall-Pedoe, H, *et al*, *Lancet*, 1975, 2, 833.

## Today's Treatment

# Diseases of the respiratory system

## Asthma

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Asthma is a common condition that most doctors can recognise easily in most cases, yet it defies exact and agreed definition. For practical purposes, however, asthma may be regarded as variable airways obstruction, which presents clinically as wheezing dyspnoea. Just how variable is "variable" is debatable, but most people would agree that a 20% change in either direction in some index of resistance to airflow constitutes variability and hence asthma, as opposed to chronic irreversible airways obstruction as found in chronic bronchitis and emphysema.

### Diagnosis

Given the above description of asthma, how is the condition to be recognised in practice? Often the history alone is sufficient, particularly in the case of classic episodic asthma, in which symptoms may be accurately described as wheezing dyspnoea with obvious and pronounced variability in severity. Sometimes the pattern of breathing even in episodic dyspnoea cannot be defined by the patient, and the diagnosis may then be confirmed by the finding of rhonchi on examination of the chest. Examination is often unrevealing, however, the patient being in remission when visiting the surgery or outpatient clinic, though severe airways obstruction may have occurred during the night. Thus the finding of a normal chest does not preclude the diagnosis, though positive findings may support it.

The next step in diagnosis is some simple test of pulmonary function, such as the peak flow rate (PFR), or spirometry, with measurement of the forced expiratory volume in one second (FEV<sub>1</sub>) and the forced vital capacity (FVC). The latter values are often expressed as the ratio FEV<sub>1</sub>/FVC, and an arbitrary level of 65% or 75% is taken as the lower limit of normal. Again, a normal result on a single occasion cannot exclude asthma and

neither can a low value distinguish asthma from other forms of airways obstruction. Variability in airflow obstruction is most easily shown by repeating the test after using a bronchodilator such as salbutamol aerosol, but a failure to improve by 20% may be because the patient was in remission at the time of testing, with no room for further improvement in pulmonary function. In this case confirming the diagnosis by provocation tests such as exercise or inhalation of dilute histamine may be justified, since one of the characteristics of the asthmatic patient is increased bronchoconstrictor reactivity of the airways in response to non-specific stimuli. These tests are specialised procedures, which should be carried out only under experienced supervision, since they can occasionally provoke severe wheezing.

### Types of asthma

After diagnosis it is useful to characterise the type of asthma more fully to assess prognosis and management. The present broad classification into extrinsic (allergic) and intrinsic (or late-onset) asthma is certainly an oversimplification, and there are many intermediate or mixed forms, but it still forms a useful basis for management in many cases (see table).

### Assessment of asthma

Assessment of asthma with a view to treatment can be approached in several ways, more than one of which is generally used in any individual patient. Firstly, causative factors such as

TABLE—Types of asthma

Extrinsic	Intrinsic
Onset in childhood Usually external allergic "trigger" Sometimes caused by infection	Onset in adult life None Commonly caused by infection
Atopic features: hay fever, eczema Positive family history Episodic, many improve	None Often none Often becomes chronic; prognosis less good Commonly needs steroids
Occasionally needs steroids	

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specific allergy, industrial pollutants, exercise, or infection have to be considered and avoided or counteracted if possible. Secondly, the frequency and severity of attacks should be ascertained since the approach to the occasional mild attack is clearly going to differ from that to repeated bad attacks. Thirdly, the seasonal and temporal patterns of attacks are important, and recent work from the Brompton Hospital has emphasised several clinical patterns such as the "morning dipper" and the "brittle asthmatic," which need careful choice and timing of treatment for the best effect.<sup>1</sup> Fourthly, other practical considerations such as psychological factors and the patient's ability or willingness to manipulate an inhaler will influence the type of treatment suggested. The management of every asthmatic patient thus becomes an individual matter, but there remain certain broad guidelines that form the basis of standard treatment.

## Management

### TRIGGER MECHANISMS

Trigger mechanisms may be divided into three groups.

#### *Allergic factors*

Allergic factors are commonly important in the young extrinsic asthmatic patient, and the best guide is a history of wheezing in response to a specific allergen, such as pollen or animal fur. This may be confirmed by simple skin prick tests, but these commonly show multiple sensitivities, and positive skin test results in the absence of a suggestive history are of doubtful importance. If specific allergy is confirmed avoidance of the allergen is the best course, but this may be impossible—for instance, with grass pollen—and in this case hyposensitisation may be considered. This is a large and controversial topic and results have generally been poor in controlling asthma, except with specific grass-pollen sensitivity. It is particularly disappointing that controlled trials have shown little or no benefit from hyposensitisation to the house-dust mite, *Dermatophagoides pteronyssinus*, a common and widespread allergen.

An important and growing group of allergic agents are those encountered in industry, such as soldering flux fumes and epoxy resins. Bronchial provocation tests with these should be performed only under strictly controlled hospital conditions by investigators with experience, but they may be useful in confirming a suggestive history since skin tests are often unavailable.

If avoidance or hyposensitisation are impracticable allergic bronchoconstriction may be helped by disodium cromoglycate. Exposure to an antigen to which the patient has been sensitised is thought to lead to the release of bronchoconstrictor mediators, such as histamine, from mast cells in the bronchial walls. Disodium cromoglycate appears to work partly by stabilising mast cell walls and partly by preventing the release of these mediators, though its full mode of action is not understood. It is particularly effective in extrinsic asthma and in the experimental prevention of exercise-induced bronchoconstriction. It acts prophylactically, and patients should be warned not to expect symptomatic relief, such as they get from bronchodilator aerosols. Disodium cromoglycate is sometimes combined with powdered isoprenaline to prevent any irritant bronchoconstriction caused by the inhaled powder, but this may lead to misusing the preparation for symptomatic relief, rather than prophylaxis, and is generally best avoided. The search for a useful oral form of cromoglycate continues unabated and is as yet unsuccessful.

#### *Infection*

Infection is another important trigger factor, mainly in intrinsic asthma, but its role in extrinsic asthma is probably small, despite the common use of antibiotics for the latter. The

apparently purulent sputum is commonly due to the presence of eosinophils rather than polymorphonuclear leucocytes. In intrinsic asthma associated with infection, broad-spectrum antibiotics such as tetracycline, co-trimoxazole, and ampicillin (or amoxycillin) are the drugs of choice, and they should be started early, if possible before the asthmatic response is fully established.

#### *Non-specific factors*

Non-allergic trigger factors such as exercise and physical stimuli, including cold air, deep breathing, and inhaled irritants may also be important in a few asthmatic patients. Avoidance is again the best protection, but cromoglycate or anti-cholinergic agents, such as atropine methonitrate given by inhalation, may help some patients.

### MEDIATORS

It is widely held, as suggested above, that after exposure to the appropriate "trigger", bronchoconstrictor chemical mediators are released in the lung, at least partly from the mast cells, and narrow the bronchi through contraction of bronchial smooth muscle and through oedema and inflammation of the bronchial walls. The most familiar of these agents is histamine, which is a known bronchoconstrictor and is released in human allergic reactions. Treatment of asthma with antihistamines, however, is generally unsuccessful, and the occasional benefit claimed in children may well be caused by the drugs' sedative and anti-cholinergic effects rather than to their antihistaminic properties. Other potential mediators of asthma include slow-reacting substance of anaphylaxis (SRS-A) and prostaglandin  $F_{2\alpha}$ , but no selective antagonists of these substances are available, and attempts to interfere with the action of possible chemical mediators have been disappointing in managing asthma.

### BRONCHOCONSTRICTION

Bronchoconstriction is the final common pathway, at least in acute asthma, and most drug treatment is aimed at causing bronchodilatation through relaxation of bronchial smooth muscle. The latter is contracted by the cholinergic parasympathetic division of the autonomic nervous system (vagus nerve) and relaxed by the adrenergic sympathetic division.

#### *Anticholinergics*

One of the earliest treatments of asthma was smoking atropine-like alkaloids as described in Indian texts, and stramonium cigarettes were introduced into England in the nineteenth century. Because of the side effects of dry mouth and tachycardia, anticholinergics have to be inhaled, and they fell from popularity with the development of sympathomimetic agents such as ephedrine. Nevertheless, many inhalant mixtures still include atropine methonitrate, and a pure pressurised aerosol, ipratropium bromide, has recently been introduced.

Although there are good theoretical and experimental grounds for using anticholinergic agents in asthma, these are generally less effective than sympathomimetics, and their main role may be as an alternative treatment in chronic obstructive bronchitis.

#### *Sympathomimetics*

Sympathomimetics are now the main treatment for asthma and have undergone considerable refinement in specificity and duration of action.

Adrenaline was one of the first to be used but had the theor-

etical drawback of stimulating both dilator beta-sympathetic receptors and potentially constrictor alpha-receptors. In practice the beta-receptors predominate in the airways to the extent that agents with mixed actions act as bronchodilators, and alpha-adrenergic blockers have not proved useful in treating asthma. After adrenaline the pure beta-stimulant isoprenaline was introduced, followed by the very similar but longer-acting orciprenaline. These remain useful bronchodilator drugs, particularly when inhaled, but are apt to cause tachycardia since they are non-selective and stimulate cardiac beta-1 receptors as well as bronchial beta-2 receptors. The more recent selective beta-2 stimulants have less direct effect on the heart, but still cause muscular tremor when taken by mouth, and may cause reflex tachycardia through peripheral vasodilatation and hypotension. The number of these agents is increasing fast, and among the more familiar are salbutamol, terbutaline, isoetharine, fenoterol, and rimiterol. With the exception of rimiterol, which is shorter acting, differences between these agents seem to be small,<sup>2</sup> though fenoterol may have a rather longer duration of action than terbutaline or salbutamol.<sup>3</sup>

### *Xanthine derivatives*

Xanthine derivatives are widely used in treating asthma and are thought to act on the same biochemical pathway as the beta-sympathomimetics, increasing intracellular cyclic adenosine monophosphate through inhibition of the enzyme phosphodiesterase, which normally breaks it down. Oral preparations often cause gastric irritation, and blood concentrations are unpredictable, probably due to differences in metabolism. Ideally, the dose should be adjusted according to blood concentrations, but this is not possible in most cases and the value of the drugs is consequently limited. They are effective in some patients, however, and may also be given rectally to avoid the gastric problems associated with oral administration. Aminophylline given intravenously remains useful in the emergency treatment of severe asthma.

### *Corticosteroids*

Corticosteroids are one of the most important lines of treatment in severe asthma, but should be used with caution in view of their familiar side effects of gastrointestinal haemorrhage and osteoporosis. Prednisone (or prednisolone) is the usual oral form, and there is no advantage in using other preparations, while hydrocortisone itself is most commonly used intravenously in the emergency treatment of severe asthma.

## **Practical guidelines**

### MILD-MODERATE ASTHMA

Mild-moderate asthma is most satisfactorily treated with beta-adrenergic stimulants, preferably given by aerosol to minimise side effects. Current selective beta-2 stimulants such as salbutamol, terbutaline, and fenoterol have theoretical and possibly practical advantages over non-selective agents. They are usually given symptomatically, particularly in mild asthma, but regular inhalation three or four times a day may be better in more severe cases. Careful explanation and demonstration of aerosol techniques are more important than the exact drug used, and a short time spent on this aspect of treatment with each new asthmatic patient is a good investment.

Beta-adrenergic stimulants are also widely taken by mouth, and this route, though less immediately effective, is essential for those patients unable or unwilling to master a pressurised aerosol. Side effects, mainly somatic tremor that may occur in up to 20% of patients taking salbutamol or terbutaline four times daily, limit dosage, but these single drugs are preferable to the

numerous compound proprietary tablets, usually containing suboptimal doses of a non-selective beta stimulant, a xanthine, and a barbiturate sedative.

There is rarely any indication for starting treatment with such products today, but a patient who has confidence in a particular preparation should be weaned off it cautiously.

If attacks remain frequent or exercise-induced bronchoconstriction is prominent one spincap of disodium cromoglycate should be inhaled four times a day. The efficacy of this drug should be assessed carefully in each patient, if possible by means of diary cards supplemented by simple objective tests of pulmonary function. This is a counsel of perfection, rarely achieved in specialised chest clinics let alone general practice, but it is important to curb the tendency to continue prescribing ineffectual and expensive, if harmless, drugs.

If the patient fails to improve while taking disodium cromoglycate or has typical late-onset asthma, inhaled corticosteroids, such as beclomethasone or betamethasone, may help. These have become widely used over the past few years and often produce useful symptomatic relief and allow the dose of oral steroids to be reduced or stopped.<sup>1</sup> They seem to be free from side effects apart from occasional oropharyngeal thrush, which can usually be controlled by nystatin mouthwashes, and they have made an important contribution to the managing mild-to-moderate asthma. Like disodium cromoglycate, inhaled steroids are used prophylactically and the usual dose is two puffs four times a day, which can be reduced as the patient improves.

### SEVERE ASTHMA

When attacks of asthma are severe or frequent, or when the condition becomes more-or-less chronic, as it often does in the late-onset group, oral corticosteroids may be essential, though they should obviously be used sparingly because of their side effects of obesity, susceptibility to infection, gastroduodenal bleeding, and osteoporosis. It is usual to begin with intermittent treatment in a reducing dosage, starting with about 30 mg daily of prednisone and tailing off over a week, but to prevent relapse it is often more satisfactory to maintain the high dose for a few days, until there is definite symptomatic or objective improvement, before reducing. If asthma with this regimen keeps recurring continuous prednisone should be used in the smallest daily dose needed to give adequate symptomatic relief, and beclomethasone should generally be given at the same time for its steroid-sparing effect. There is no advantage in preparations other than prednisone (or prednisolone) except occasionally corticotrophins in growing children or adults unable to swallow tablets.

### STATUS ASTHMATICUS

Status asthmaticus is a loose term, used here to describe a prolonged, severe attack of asthma needing vigorous treatment and usually hospital admission. It is impossible to cover all the details of management, which are described in standard textbooks of medical emergencies, but the principles consist of rehydration with intravenous fluids to help loosen bronchial secretions; bronchodilatation with aminophylline or salbutamol given intravenously, either as a bolus or as a continuing infusion<sup>5</sup> (at rough rates of 1mg and 10 µg/minute, respectively); and intravenous hydrocortisone together with oral prednisone. The intravenous route is used to ensure absorption of bronchodilators and their distribution to the bronchial smooth muscle, which they may fail to reach if given by inhalation in the presence of severe bronchoconstriction. It has recently been suggested, however, that aerosols remain effective, provided they are given by continuous nebulisation rather than as a metered aerosol.<sup>6</sup> There is often a delay of several hours before response to treatment occurs, and if during that time the patient becomes exhausted and develops ventilatory failure with a rising arterial

PCO<sub>2</sub>, artificial ventilation should be considered, though it presents considerable practical difficulties. If infection is thought to be playing an important part, broad-spectrum antibiotics such as amoxycillin or co-trimoxazole should be given. With this regimen there is usually considerable improvement in 48 to 72 hours, after which the drip can be discontinued and the patient maintained on inhaled and oral bronchodilators, with a reducing dose of oral prednisone.

### Conclusions

Asthma remains a challenging problem to the general practitioner, the general physician, and the chest physician alike. As in certain other common and incurable conditions such as hypertension, the final physiological pathway—variable narrowing of the airways—is well established, but the underlying pathogenesis remains obscure and the subject of continuing research. Meanwhile, several effective symptomatic remedies have been evolved, and the lives of many asthmatic patients can

be transformed by careful immunological and physiological assessment, followed by the proper use of bronchodilators and corticosteroids. The available drugs are now widely familiar, but they are often misused and continuing education of doctors is an essential step towards better management of asthma.<sup>7</sup>

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## Letter from . . . Zurich

# Paediatric surgery in Europe: the first five years of EUPSA

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The European Union of Paediatric Surgical Associations (EUPSA) is, as its name suggests, a union of 17 national associations of paediatric surgery. It is not a scientific society and does not hold scientific meetings. Its aims are professional and educational: to support and co-ordinate the practice of paediatric surgery in each country; to promote its recognition as a surgical specialty; and to unify training by co-ordinating nationally recognised hospitals and training programmes, laying down criteria for training, and promoting the exchange of trainees between member countries.

### A separate specialty

EUPSA met for the first time in Rotterdam in February 1973 with representatives from 14 western-European nations. Spain and Portugal joined a little later, and the Greek Paediatric Surgical Association, which joined in 1977, is the most recent member. Several resolutions were passed at the Rotterdam meeting defining the specialty of paediatric surgery and laying down standards for its practice.

Firstly, it was decided that paediatric surgery by definition must include neonatal surgery and the surgery of congenital malformations and tumours in childhood (with subspecialisations

if appropriate). Children with surgical conditions should be treated in large paediatric centres, preferably in children's hospitals, by a paediatric surgical team with full clinical responsibility. Secondly, an area with a population of one million should have at least one centre of about 50-60 beds with at least two fully qualified paediatric surgeons apart from those in training. Thirdly, the maximum age of paediatric surgical patients should be the same as that of medical paediatric patients according to local customs. Fourthly, the total period of postgraduate training should be at least six years, with three of those years being spent in paediatric surgery. Training should be in recognised hospitals and should be full-time.

### Progress

In October 1972, before EUPSA was formed, questionnaires were sent to all future members asking about the state of paediatric surgical practice in their countries. After five years (in October 1977) the member associations again filled in a questionnaire; the answers were compared with their earlier ones to see whether any progress had been made towards fulfilling EUPSA's aims. Some of the figures from Spain and Portugal were not available for five years ago, as they did not join until later, and Greece has been excluded from the following tables.

### NUMBERS OF PAEDIATRIC SURGEONS

The number of paediatric surgeons has increased noticeably in most countries (table I). In western Europe as a whole the increase is over 50%, and there is now one paediatric surgeon for every million inhabitants. But the surgeons are very

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