and the functional residual volume (F.R.C.) and residual volume (R.V.) of the lung steadily decreased. Thus measuring changes in lung volume in addition to those in $F.E.V._1$ may increase the value of the tests.

A more sensitive measure of airways obstruction may be obtained using a body plethysmograph, which also has the advantage that the thoracic gas volume may be measured simultaneously, so that values comparable to a combined $F.E.V._1$ and F.R.C. measurement may be made. For example, such measurements using a body plethysmograph, together with measurements of lung volumes, $Pco_2$, and other indices were made in another trial of disodium cromoglycate.[49] In addition the patients measured their own peak expiratory flow with a Wright's meter twice daily and recorded their own subjective assessment of themselves each day. Though there were changes in the expected direction in the specific conductance, lung volumes, and some other tests, these were not always great and were proportionally less than those the patients recorded themselves on their peak flow meters. Thus the more complicated tests had failed to add much to the study, and these findings emphasize the value of frequent measurements of airways obstruction, however simple the methods used.[50] This was confirmed in another study[51] in which daily peak flow readings done by outpatients on themselves were used to show the beneficial effect of steroid therapy on their asthma. Thus to assess the severity of a patient's asthma and the effect of therapy we should not be content to rely on "spot" measurements made in a clinic or a surgery once a month, or even once a week, but should make more frequent observations ourselves if the patient is in hospital or encourage him to make his own at home.

Finally, the part played by psychological factors should not be forgotten.[52] Patients may complain of breathlessness disproportionate to any abnormality that can be shown by any objective pulmonary function tests. In at least some of these patients the dyspnoea is of psychogenic origin.

Despite these difficulties, however, pulmonary function tests are valuable in both the diagnosis and management of asthma today. By using them we may be able to establish the diagnosis and even detect the aetiology. Repeated measurements add greatly to the assessment, especially when trying to determine the effects of treatment. The $F.E.V._1$ and peak flow rate are the most useful tests, and the latter can be carried out by patients themselves. It is important that the objective evidence these tests give should always be considered together with the symptoms and signs of the patients and not in isolation.

# Treatment

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There have been two important advances in the drug therapy of asthma in the last few years—firstly, the introduction of a completely new prophylactic agent, disodium cromoglycate, and, secondly, the development of sympathomimetic bronchodilators with a relatively selective action on bronchial receptors. Some developments in the management of long-term corticosteroid therapy and in the treatment of respiratory failure in severe asthma will also be discussed briefly.

## Disodium Cromoglycate

*Disodium cromoglycate* has no immediate bronchodilator action but is remarkably effective in inhibiting the experimentally induced bronchial reaction to specific inhaled allergens. Protection from allergen challenge can be shown within 10 minutes of a single dose of cromoglycate, and it begins to decline after four hours. In clinical use, however, it has been suggested that benefit may not be seen for some days after initiating treatment and may persist for some days after withdrawal.

The experimental findings suggest that cromoglycate should be most effective in the prophylaxis of "extrinsic" asthma with identified allergens. Most trials confirm that this is usually the case, and, in particular, children appear to respond best. Nevertheless, some patients with late onset asthma of the "intrinsic" (i.e., no identified allergen) type have been improved.

Cromoglycate is poorly absorbed from the gastrointestinal tract and has to be administered as a dry powder, which is inhaled into the lungs from a special capsule and inhaler. As the inhalation of a dry dust can cause transient bronchoconstriction, the manufacturers have combined 0·1 mg. isoprenaline with 20 mg. cromoglycate in the one capsule (Intal Co.). The standard dose is four capsules a day, but in acute episodes this has been increased to one capsule every three hours. Apart from local throat and tracheal irritation, cromoglycate has so far proved to be remarkably free of side-effects.

The full place of cromoglycate in the management of asthma is not yet clear. Particular points that need to be established are the proportion of adult patients with asthma that are likely to be helped and the extent of the improvement to be expected. As the drug is expensive and relatively cumbersome to administer, trials of cromoglycate in an individual patient should be carefully assessed. In most adults who have been helped by cromoglycate the changes may be termed "useful" rather than "dramatic," and such changes are notoriously difficult to assess in a condition as variable as asthma. Early studies suggested that subjective improvement did not correlate well with simple spirometric tests of airways obstruction, but this discrepancy has not been so pronounced in recent studies. Ideally the patient should keep a diary card of symptoms and treatment taken and supplement this with frequent measurements of a simple test of airways obstruction, such as peak expiratory flow. A fuller review of this drug was published in this journal last year.[53]

## Sympathomimetic Bronchodilators

These drugs produce bronchodilatation by stimulating $\beta$-adrenergic receptors in bronchial smooth muscle. The most used of these drugs in recent years has been *isoprenaline*, which is a very effective bronchodilator but has a relatively short duration of action. In the doses used for bronchodilatation isoprenaline also stimulates $\beta$-adrenergic receptors in the heart and blood vessels and may cause a rise in pulse rate, systolic blood pressure, and cardiac output.

*Orciprenaline* and *salbutamol* are more recently developed drugs, which have structures very similar to that of isoprenaline and are also effective bronchodilators. They differ from iso-

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prenaline in having a bronchodilator action which lasts for several hours, less effect on β-receptors in cardiac muscle, and possibly less tendency to cause a fall in arterial $PO_2$. There is no evidence that either orciprenaline or salbutamol will cause bronchodilatation in patients in whom isoprenaline has failed. Differences between salbutamol and orciprenaline in acute experiments are relatively small, but probably salbutamol has a somewhat greater bronchodilator effect and a smaller effect on the cardiovascular system than orciprenaline.[54 55] Neither orciprenaline nor salbutamol is entirely free from cardiovascular effects, and overdosage could have serious effects because of their long duration of action.

Sympathomimetic bronchodilators are extremely useful when there is a moderate degree of airways obstruction. When asthma becomes more severe, however, the improvement after adrenergic drugs often becomes much less, even in a patient who on other occasions has shown an excellent response to the same drug. Once it is established that there is no response to the normal therapeutic dose then it is useless and may be dangerous to persist, since there is now good evidence that over-dosage of bronchodilator aerosols has been associated with the recent rise and fall in deaths from asthma. It is not certain whether the association with overuse reflects a catastrophic effect on the cardiovascular system or unwise persistence with an ineffective bronchodilating agent in the face of increasingly severe airways obstruction. The most effective precaution in using these drugs is to make sure that the patient has strict instructions about the dose and that he understands that a lack of his normal response is an indication to seek medical advice and not an indication to increase his dose. If overdose is avoided choice of the actual bronchodilator to use is probably of less importance. The more selective and sustained action of orciprenaline and salbutamol gives them some advantage over isoprenaline for routine use. Salbutamol is somewhat the more effective of the two newer drugs in acute experiments, but as yet little is known about its relative effectiveness in longer-term use.

## Long-term Corticosteroid Treatment

The complications of long-term corticosteroid treatment can be reduced by various regimens of intermittent therapy, such as giving steroids for four or five consecutive days each week, or giving a single dose on alternate days. Such intermittent treatment can control asthmatic symptoms adequately in a high proportion of steroid-dependent patients.[56] Alternatively the risks may be reduced by giving injections of corticotrophin (A.C.T.H.) gel instead of corticosteroids ; this course is particularly indicated in children, in whom it has been shown that there is less retardation of growth during treatment with A.C.T.H. than with continuous oral corticosteroids.[57] A trial of the new synthetic depot-tetracosactrin has given promising results in asthmatic patients who are hypersensitive to animal A.C.T.H.[58]

## Respiratory Failure in Severe Asthma

Moderate degrees of hypoxaemia are invariably present in severe asthma, and the arterial $PO_2$ can be below 40 mm. Hg even when there is no rise in arterial $PCO_2$.[59] Hypoxaemia can be improved by giving 24% or 28% oxygen by Ventimask. In adult asthmatics the risk of oxygen inducing a severe rise in $PCO_2$ appears to be relatively small,[59] but in children $CO_2$ narcosis has been found to be a serious hazard.[60] Until further information is available it would seem best to give only controlled $O_2$ therapy and to monitor the resulting changes in $PO_2$ and $PCO_2$ carefully.

In most patients with hypoxaemia the arterial $PCO_2$ is normal or reduced ; a rise in the $PCO_2$ indicates that the patient's situation is dangerous and that he may require mechanical ventilation. It is not possible to lay down an absolute figure at which mechanical ventilation is indicated ; this will be influenced by the adequacy of previous medical treatment, particularly with corticosteroids, and by the facilities and experience available, since there are considerable problems in ventilating asthmatic patients who have a well-prepared respiratory drive and a high airways resistance.[61] In general, however, ventilation will be required at a lower $PCO_2$ than in patients with chronic obstructive bronchitis. Certainly any patient whose arterial $PCO_2$ is greater than 60 mm. Hg needs to be monitored very carefully and a high proportion of such patients will need assistance. Some workers believe that mechanical ventilation is necessary in all such patients and also in patients in whom the arterial $PCO_2$ is still more than 50 mm. Hg after eight hours of intensive medical therapy.[59] In addition, assisted ventilation is indicated in some severely exhausted patients even although they still maintain a normal $PCO_2$.

In completely intractable status asthmaticus the airways obstruction may be so severe that it is not possible to achieve adequate ventilation even with a mechanical respirator. In these desperate circumstances correction of the accompanying acidaemia by intravenous sodium bicarbonate has been reported to restore responsiveness to bronchodilator drugs.[62] An alternative approach is to try to remove some of the more accessible mucus plugs from the airways by extended bronchial lavage under general anaesthesia. Good results have been reported to follow this treatment in individual patients, but overall it is not established that the benefits from this demanding procedure outweigh the undoubted risk of further impairing ventilation and gas exchange.

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# CONFERENCES AND MEETINGS

## Health Service Administration

[FROM A SPECIAL CORRESPONDENT]

A symposium on the organization and structure of health services, sponsored by the Science of Science Foundation Ltd., was held at the National Institute for Medical Research, London, on 22 October.

### Universal Trends in Europe

Professor T. E. CHESTER (Manchester), outlining the common causes of dissatisfaction, within both the health service administrations and the public sector, emphasized the universality of these problems to Europe as a whole. In Europe the average cost of providing health services had increased annually by 6 to 8%. In Britain the average annual proportion of the gross national product spent on medical services over the last few years was 4½ to 5%. Furthermore, the increase in the aged population (10 to 15% of the total population were in the over-65 age groups), the rising morbidity rates in contrast to mortality, the changing character and incidence of disease (heart disease, cancer, and road accidents being the three commonest causes of death) had accentuated the disequilibrium between supply and demand. In Britain wages and salaries for medical staff amounted to about 60 to 70% of the total cost of the health service, while the cost of medical engineering and equipment amounted to 40% of the major hospital costs. Throughout Europe the traditional patterns of delivery of medical care, particularly in the field of general practice, and the role of politics in medicine were being questioned.

### Health Care in the U.S.A.

Professor O. W. ANDERSON (Chicago, U.S.A.) continued the seminar by outlining the development of health care in the U.S.A. from the late 19th century to the present day. Up until 1920 two-thirds of hospital income had been provided by the private individual, while one-third had come from philanthropic sources. After the economic depression of the 1930s, the role of private insurance on a non-profit basis had grown, until in 1952 voluntary health insurance covered 65% of the total population. In 1946 hospital building was subsidized by Federal Government grants, which amounted to 25% of the total cost of the hospital expansion programme. Today "Medicaid" provided for those people whose earnings fell below a given income level, voluntary health insurance schemes covered the self-supporting, and "Medicare" provided for the elderly. In the last 20 years the picture was one of diversity of funds, growing accumulation of data, no centralization of power, and little obvious health care policy.

### Health Service Structures in Europe

In examining the structure of the health service in Western Germany Professor CHESTER considered it typical of Western Europe as a whole. For a population of 60 million people, 3,600 hospitals provided 600,000 beds. A system of compulsory insurance was the basis of the service. For the 87% of the population insured under the State scheme (as opposed to private insurance schemes) the premium was shared equally by employer and employee. In the case of the unemployed the premium was paid by the State; and, for the elderly, retirement pension funds covered the cost. Hospital care was therefore financed directly by the insurance schemes on a "per diem" basis, regardless of the treatment given. Since this method of payment resulted in vast deficits for the hospitals every year it had been proposed that the patient should contribute directly to the total cost of hospital care.

### Sweden

Continuing, Professor Chester briefly outlined the role of the Board of Health and Welfare in Sweden. This had direct responsibility to the Minister of Social Affairs. Each of the 25 county councils covered a catchment area of about 250,000 people, and was responsible for providing general medical services, including mental health care and general-practitioner services; the appointment of district medical officers, and the control of area finance. Since the yield of patients in each area for any one specialty was too low, the 25 areas were grouped together into seven regions for the purpose of providing specialist units.

### Czechoslovakia

Finally, an account of the growth of one of the first unified national health systems created since the end of the second world war was given by Dr. E. COUFALIK (Prague, Czechoslovakia). The important aspects of the Czechoslovakian service were the close co-ordination of scientific research and clinical practice, the wide scope of preventive medicine, particularly with regard to venereal disease and gynaecological disorders; the provisions for the expectant mother, both financially and at work; the reduced rents for families of one child or more; the provision of sickness benefits and wage-related pension schemes; and the major role of the general practitioner in area community health.