PATTERNS OF AIRFLOW IN UPPER AIRWAYS OBSTRUCTION

D. EMPEY The forced expiratory volume in one second (FEV_1) and peak expiratory flow rate (PEFR) were measured in normal subjects both with and without resistances in the form of orifices of decreasing diameter.

The ratio $\frac{FEV_1 \text{ as } \% \text{ of predicted normal}}{PEFR \text{ as } \% \text{ of predicted normal}}$ was calculated and found to be approximately 1·10 without added resistance. The addition of increasing resistances led to a rise in this ratio, e.g., 1·60 with an orifice 8 mm in diameter and 3·10 with an orifice 4 mm in diameter. Groups of patients were then studied. These included 24 patients with obstruction of the upper airways (tracheal stenosis, bilateral vocal cord paresis, etc.); 42 patients with lower airways obstruction (asthma and bronchitis); and 19 with fibrosing alveolitis.

It was found that the ratio $\frac{FEV_1 \text{ predicted } \%}{PEFR \text{ predicted } \%}$ exceeded 1·60 only in those cases with obstruction of the upper airways (above the carina). Those patients with the highest ratios had the most severe degrees of obstruction. Some patients were also investigated by more complex techniques such as flow-volume curves and derived flow rates. Consideration of these, and further studies, provide an explanation for the alteration in $\frac{FEV_1 \text{ predicted } \%}{PEFR \text{ predicted } \%}$ ratio and a theoretical justification for its use. The measurement of this ratio by means of simple standard equipment appears to be useful in the diagnosis and assessment of upper airways obstruction.

LUNG FIBROSIS IN ANKYLOSING SPONDYLITIS

D. DAVIES In recent years it has become recognized that some patients with ankylosing spondylitis develop progressive upper lobe fibrosis, often with cavitation. The condition can easily be mistaken for tuberculosis. It usually develops several years after the onset of joint symptoms and begins as unilateral or bilateral apical consolidation and fibrosis. The rate of progression is variable and it may extend to involve the upper half of both lungs. The cavities frequently become colonized by *Aspergillus fumigatus* with the formation of fungus balls. This occurs more commonly than in most tuberculosis cavities.

The condition is illustrated by a selection from 11 cases recognized in recent years.

There is no evidence that bacterial infection or radiotherapy are causal factors. There are good reasons for accepting this as another extra-articular manifestation of ankylosing spondylitis.

INCLINED FRONTAL PLANE TOMOGRAPHY

M. MEREDITH BROWN In several hundred patients frontal plane tomograms have been made with a Massiot-Philips radiotome with which both the patient and the film are rotated so that the plane of the tomograms is parallel to that of the trachea and main bronchi.

In the normal patient, the trachea, main bronchi, and principal branches are shown on a single cut, including the angle of the carina and the thickness of the right wall of the trachea. Narrowing or distortion of these air passages can be demonstrated more accurately than by other radiographic methods, except perhaps bronchography. Lesions of the smaller bronchi, such as the middle lobe bronchus or the segmental branches, cannot be demonstrated as they do not lie in the plane of the tomograms. Vascular abnormalities can sometimes be recognized, and the technique is particularly valuable in demonstrating enlarged lymph nodes.

In clinical practice these tomograms have been found useful in demonstrating lesions of the trachea and main bronchi; in confirming suspected lymph node enlargement of hilar and paratracheal groups; and in helping to elucidate the hilar structures in patients with bronchial neoplasms. In this way the technique is an aid to diagnosis and to the planning of treatment. The accuracy is such that negative findings can be confidently accepted.

BRONCHODILATATION

Pharmacology of the Bronchi

G. STERLING Recent research into the pharmacology of the contraction of bronchial smooth muscle has emphasized both neural and humoral factors.

Of the former there is now no doubt that the cholinergic parasympathetic system causes bronchoconstriction and that atropine may be of diagnostic and therapeutic value in bronchial asthma. Current research is concentrated more on the role of the adrenergic system: partly on the question of whether alpha-adrenergic receptors, which appear to cause bronchoconstriction when stimulated, are likely to be important clinically; partly on the effects of beta-adrenoceptive blockade in asthma and the possibility of catecholamine metabolites causing beta-blockade.

With regard to humoral factors, interest has been concentrated on the mode of action of disodium cromoglycate in alleviating allergen and exercise-induced asthma and in reducing the hyperreactivity to histamine shown by asthmatic subjects. Recent evidence suggests that disodium cromoglycate *in vivo* may have an antihistaminic action as well as preventing the breakdown of mast cells, though this observation needs to be confirmed. Of the potential humoral mediators of bronchoconstriction and bronchodilatation the prostaglandins have been investigated most intensively recently, following the discovery that they occur naturally in the human lung and have potent constrictor and dilator effects on the bronchus.

Side Effects of Beta-adrenergic Receptor Stimulant Bronchodilator Drugs

J. W. PATERSON The side effects of this group of drugs may be divided into three classes:

1. *Expected*: These are side effects which may be predicted from a knowledge of the pharmacology of the drug. Thus stimulation of beta-receptors in sites

other than bronchial smooth muscle results in effects such as cardiac stimulation. Side effects of this type have been reduced by the introduction of so-called 'selective' beta-stimulant drugs. Selectivity can be achieved by altering the mode of administration, and this is referred to as 'therapeutic selectivity'.

2. *'Semi'-expected*: These are side effects which may not be immediately obvious from a consideration of pharmacology, such as effects on oxygen tension and the development of tolerance to beta-stimulants.

3. *Unexpected*: These will include all the rare reactions that may occur with any drug, such as bone marrow damage, etc., but with beta-stimulant bronchodilator drugs particular interest is focussed on the possible toxic effects of the fluorocarbons used as propellent gases in aerosols.

Prostaglandins and Bronchial Smooth Muscle

M. F. CUTHBERT Prostaglandins are naturally occurring fatty acids which are widely distributed in human tissues; prostaglandins E_2 (PGE_2) and $F_{2\alpha}$ ($PGF_{2\alpha}$) have been isolated from the lungs and bronchi. Among their many physiological properties prostaglandins have powerful effects on bronchial smooth muscle, those of the E series causing bronchodilatation while those of the F series cause bronchoconstriction.

Prostaglandin E_1 and isoprenaline have similar bronchodilator effects in anaesthetized guinea-pigs when given intravenously, but when given by aerosol PGE_1 is 10 to 100 times more active than isoprenaline[1]. The high activity and lack of cardiovascular effects when prostaglandins are given by aerosol may be related to their rapid metabolism within the lung[2].

Isolated human bronchial muscle is contracted by $PGF_{2\alpha}$ and relaxed by PGE_1[3]. Aerosols of prostaglandins E_1 and E_2 have no effect in normal volunteers but in asthmatic subjects inhalation of 55 μg PGE_1 and PGE_2 has a bronchodilator effect, as measured by changes in FEV_1, of similar degree and duration to that of 550 μg isoprenaline[4,5]. These results have recently been confirmed in studies in which inhalation of PGE_1 and PGE_2 caused a marked decrease in airways resistance and an increase in specific conductance in asthmatics. Inhalation of the natural E prostaglandins, however, can be associated with irritation of the upper respiratory tract.

The current use of intravenous prostaglandins in the induction of labour and therapeutic abortion may lead to an increase in airways resistance. In normal women this is not sufficient to cause symptoms but may represent a hazard in asthmatics[6].

The possibility of the therapeutic use of prostaglandins and prostaglandin antagonists in reversible obstructive airways disease will be considered in the light of speculations concerning the relationship of the prostaglandins to the function of bronchial smooth muscle.

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Respiratory Assessment of Bronchodilator Drugs

P. L. KAMBUROFF In assessing a bronchodilator drug in the laboratory it is usual to measure the speed with which it takes effect, the magnitude of that effect, and its duration as well as the occurrence and severity of any side effects it produces.

Difficulties encountered in carrying out trials arise from two sources: the day-to-day variability in the response of the individual subjects to whom the drug is given and the choice of appropriate methods of measuring the response.

Statistical methods can be applied which will minimize the differences in responses obtained from individual patients. These should make due allowance for day-to-day variations in the degree of airways obstruction as well as the changes which can occur naturally during the course of a single day. These difficulties cannot be completely eliminated.

Spirometric tests depend not only on airways resistance but also on the properties of the lung tissue and the chest wall. The body plethysmograph can be used to measure accurately and specifically airways resistance but this measurement applies mainly to resistance in the larger airways in which gas flow is fairly rapid. Valuable information may be obtained from flow-volume curves to supplement plethysmographic data. The effects of the drug on the distal airways may also be assessed by estimating the frequency dependence of compliance. The latter is beset with technical difficulty and is not easy to apply to patients.

It is a good custom to compare the effects of a new drug with those of one of established potency such as isoprenaline. For such a comparison to be valid, it is necessary to study the responses of each patient to different doses of the two drugs.

COMPARISON OF PRIMARY AND THROMBOEMBOLIC PULMONARY HYPERTENSION

LYNNE REID, GERALD ANDERSON AND GEORGE SIMON The clinical features of 46 patients with either primary or thromboembolic pulmonary hypertension are described. An analysis of the changes in the chest radiograph has been made, and, on the basis of these, six patterns of abnormality were found and used as a basis for grouping the patients. The clinical features were related to each group.

Methods of injection and quantitation of the pulmonary artery circulation are described, and the criteria of normality are defined for both pre- and intra-acinar arteries. In a small series of 46 patients studied, detailed pathological studies of the lung were made in a similar manner. These revealed new features, particularly in early primary pulmonary hypertension.