

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 propellant 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 E₂ (PGE₂) and F_{2a} (PGF_{2a}) 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 E₁ and isoprenaline have similar bronchodilator effects in anaesthetized guinea-pigs when given intravenously, but when given by aerosol PGE₁ is 10 to 100 times more active than isoprenaline¹. The high activity and lack of cardiovascular effects when prostaglandins are given by aerosol may be related to their rapid metabolism within the lung².

Isolated human bronchial muscle is contracted by PGF_{2a} and relaxed by PGE₁³. Aerosols of prostaglandins E₁ and E₂ have no effect in normal volunteers but in asthmatic subjects inhalation of 55 µg PGE₁ and PGE₂ has a bronchodilator effect, as measured by changes in FEV₁, 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 PGE₁ and PGE₂ 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 asthmatics⁶.

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.

REFERENCES

1. Large, B. J., Leswell, P. F., and Maxwell, D. R. (1969). *Nature*, **224**, 78.

2. Piper, P. J., Vane, J. R., and Wyllie, J. H. (1970). *Nature*, **225**, 600.
 3. Sweatnam, W. J. F., and Collier, H. O. J. (1968). *Nature*, **217**, 69.
 4. Cuthbert, M. F. (1969). *Brit. Med. J.*, **4**, 723.
 5. Cuthbert, M. F. (1971). *Proc. Roy. Soc. Med.*, **64**, 15.
 6. Smith, A. P. (1972). Unpublished observations.

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 intracinar 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.