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.

In an advanced stage of the disease, primary pulmonary hypertension could be distinguished in the arteriogram from thromboembolic hypertension, but pathologically only with difficulty, even using quantitative methods.

PHYSICS OF GAS FLOW IN THE TRACHEOBRONCHIAL TREE

R. C. SCHROTER Flow patterns obtained in inspiration and expiration are described. The effect of the physical properties of the gas mixture (density and viscosity) on the flow patterns and distribution of resistance are discussed and related to obstructive and restrictive lung disease.

LUNG TRANSPLANTATION

Immunological Control in Lung Transplant

M. BEWICK There are many tests of lymphocyte activity available but the majority of them are of little clinical importance because of the time taken to produce a result. If rejection is occurring then it has progressed for 24 to 48 hours before therapy, based on these results, can be instigated.

The Rosette inhibition test may be an exception to this, in that it can produce an estimate of lymphocyte activity within four hours of taking a relatively small sample of peripheral blood. Clinical evaluation of this test has been studied in renal transplantation and is now used as one of the major adjuncts to management of a renal transplantation in our unit. In the lung transplant performed at King's College Hospital the Rosette results seem to correlate with other retrospective immunological investigations and the clinical picture.

Functional Problems of Lung Transplantation

A. GUZ This review attempts to show the relevance of animal experimental work in lung autotransplantation to the problem of transplantation in man. There is now good evidence in both dog and primate that, provided the surgical anastomoses of pulmonary artery, vein, and bronchus are adequate, a lung will function as a gas exchanger *in the long term*. Thus disruption of the bronchial circulation, lymphatic drainage, nervous supply, and ciliary clearance mechanism does not seem to matter very much. Bilateral autotransplantation in animals results in *slow* breathing, often inadequate to maintain adequate ventilation. This is due to abolition of the important Hering-Breuer reflexes. This is *unlikely* to happen in man where these reflexes do not modulate breathing within the eupnoeic range. Denervation of the lungs is likely to have its most serious effect as a result of abolition of the cough; the degree of abolition will depend on whether the major bronchi of the recipient can be left intact.

The problem of matching perfusion to ventilation becomes very serious when one lung is transplanted and the other diseased lung is untouched.

Operative Technique for Lung Transplantation

A. M. MACARTHUR Two surgeons were in adjacent operating rooms. Through a right posterolateral thoracotomy a dissection pneumonectomy was started but because of gross arterial hypoxaemia a right atriofemoral bypass had to be instituted before the lung could be resected. Meanwhile the donor lung was removed, the timing of this being arranged to reduce the period of ischaemia to a minimum. End-to-end anastomosis of the pulmonary artery and veins was carried out first, followed by the bronchial anastomosis. The technical points of these anastomoses are discussed, in particular the difficulties due to disproportion between the donor and recipient structures.

Postoperative haemorrhage necessitated a second thoracotomy for the evacuation of clot on the first postoperative day.

Lung Postoperative Care

P. A. CULLUM Major obstacles to human lung transplantation have included pulmonary infection, the absence of simple tests to detect impending rejection, and the inability to distinguish infection from rejection in an ill patient.

This report concerns the clinical, radiographic, and immunological findings following lung transplantation in a man of 40 with terminal fibrosing alveolitis. One episode of pulmonary sepsis was successfully treated. Four episodes of rejection, indicated by changes in the Rosette inhibition test, were usually associated with clinical deterioration either immediately or within two to three days. Radiological changes were noncontributory. Detection of circulating lung-binding antibody possibly indicated incipient rejection about 72 hours before other changes on two occasions. Each rejection episode responded to an increase in immunosuppressive therapy so that the patient lost his dependence to oxygen, became ambulant, and was able to leave the hospital for limited periods.

These preliminary findings indicate that pulmonary sepsis can be controlled after human lung transplantation, and infection can be distinguished from rejection, and that the latter can be diagnosed within a few hours by simple laboratory tests, even before clinical deterioration occurs.

Pathological Findings following Lung Transplantation

KEITH SHILKIN and LYNNE REID The pathological findings in a patient who underwent right lung transplantation seven weeks before death are described. The pulmonary artery system in the resected right lung was injected: at necropsy material was obtained for electron microscopy.

The pathological findings were important to establish the cause of death and to investigate the changes that developed in the donor lung during the period of survival—changes either of rejection or of the disease from which the patient suffered.

Another problem in transplantation, necrosis of the stump of the donor bronchus, is also illustrated.