high (Kass, 1960 ; Turner, 1961 ; Kincaid-Smith *et al.*, 1964). Repeated or persistent infection is held to be the major factor in the development of chronic pyelonephritis (Brumfitt and Percival, 1964), and it is hoped that by the detection and treatment of acute or unsuspected infections the incidence of chronic renal failure may be reduced.

This study of a group of non-pregnant women has shown that the incidence of unsuspected infection (5.3%) is similar to that found in pregnant women. The detection of these infections is relatively simple, and the screening of all women attending gynaecological outpatient departments and the treatment of those infected may be of value. Though some variation in incidence was found in differing gynaecological conditions, infections were present in all groups. The incidence among women whose prime complaint was infertility was higher than that found in pregnancy and similar to the incidence of 8% mentioned by Sleight *et al.* (1964).

The organisms causing the infections were similar to those in bacteriuria of pregnancy, with *E. coli* predominating. A higher incidence of pyuria was present, however, among gynaecological patients than in pregnancy bacteriurias (Williams *et al.*, 1965).

In the majority of cases a short course of a sulphonamide was sufficient to clear the infection, and ampicillin cured many of those failing to respond to sulphonamides. Only 12 (18%) of the 66 patients closely followed up proved resistant to treatment, and eight of these had abnormal pyelograms. Among

those who responded to simple therapy, abnormalities were also found on pyelography, but they were usually of minor importance, and it was among the more resistant infections that the major disease, such as the presence of calculus, was found. The short courses of treatment given in this study helped us to discover those patients whose severe underlying renal disease failed to respond to the simpler measures.

The role which asymptomatic infection plays in the development of progressive renal damage is not clear, but the presence of infection, often associated with hypertension, is a pointer to existing renal disease needing treatment.

Though treatment is easy to administer the follow-up of these patients is difficult within the resources of gynaecological clinics. The amount of occult renal disease found in this survey, however, suggests that consideration be given to the provision of facilities for urine screening and adequate follow-up.

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Effect of Salbutamol on Spirometry and Blood-gas Tensions in Bronchial Asthma

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Summary: A new bronchodilator drug, salbutamol, reduced airway obstruction in 37 patients with bronchial asthma but did not lead to a significant fall in lowered arterial oxygen tension. This drug, unlike other bronchodilators, appears to have little or no effect on the cardiovascular system, and it is suggested that it does not therefore lead to an intensification of the ventilation/perfusion disturbance in the lung leading to a worsening of hypoxaemia.

Introduction

Sympathomimetic drugs are much used to reverse or decrease the widespread small airway obstruction which characterizes attacks of bronchial asthma. However, deaths from asthma have risen progressively during the past decade, and the increase in the use of pressurized aerosols, most often containing isoprenaline, correlates closely with the increase in asthma mortality in Britain (Speizer *et al.*, 1968). Isoprenaline is a powerful stimulant of β -adrenergic receptors in both bronchial and cardiac muscle, so that in addition to relaxing the smooth muscle of the bronchi it increases cardiac output and dilates the pulmonary vasculature (Aviado and Schmidt, 1957). Probably as a direct consequence of its action on the cardio-

vascular system, even though airway obstruction is diminished, there may be no increase in lowered arterial oxygen tensions, and indeed in many instances the degree of hypoxaemia may become worse afterwards (Knudson and Constantine, 1967 ; Field, 1967 ; Palmer and Diamant, 1967). The decrease in arterial oxygen saturation in patients already hypoxaemic as a result of the asthma attack is clearly undesirable ; moreover, it has been suggested that the stimulant effect of isoprenaline on the hypoxaemic myocardium may lead to ventricular irritability and fatal arrhythmia (Speizer *et al.*, 1968).

We report here the effect, when given by aerosol inhalation, of a new selective β -adrenergic stimulant (salbutamol) on spirometric and blood-gas tension measurements in asthmatic subjects. This drug is a potent and long-lasting stimulator of β -adrenergic receptors in bronchial muscle, but has relatively little effect on the cardiovascular system (Brittain *et al.*, 1968), and might therefore be expected to reduce increased airway resistance without a concomitant fall in PaO_2 .

Patients and Methods

Thirty-seven patients were investigated. Their mean age was 45.6 years (± 14.0). They had been admitted to hospital in status asthmaticus and had a long history of attacks of acute airway obstruction with little or no disability between attacks. All had either blood or sputum eosinophilia, and the majority had both. Blood samples were obtained in a heparin-lubricated

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Effect of Control and Salbutamol Aerosol Inhalation on Blood-gas Tensions and Spirometry in Bronchial Asthma (37 Patients)

Measurement	Before Control Inhalation	After Control Inhalation	Difference	After Salbutamol	Difference
F.V.C. (l. A.T.P.S.) ..	2.71 (± 1.21)	2.70 (± 1.20)	-0.01 (N.S.)	3.13 (± 1.20)	+0.43 (P < 0.001)
F.E.V. ₁ (l. A.T.P.S.) ..	1.48 (± 0.77)	1.49 (± 0.81)	+0.01 (N.S.)	1.83 (± 0.86)	+0.34 (P < 0.001)
F.E.V. ₁ (%) ..	53.3 (± 9.2)	53.1 (± 10.3)	-0.2 (N.S.)	56.6 (± 11.1)	+3.5 (P < 0.001)
Pao ₂ (mm.Hg) ..	82.5 (± 12.5)	—	—	80.6 (± 12.6)	-1.9 (N.S.)
Paco ₂ (mm.Hg) ..	41.2 (± 8.2)	—	—	40.5 (± 7.9)	-0.7 (N.S.)

syringe from the brachial artery when the patient was breathing air at the start of the experiment and five minutes after the aerosol inhalation of 200 mg. of salbutamol (which is equivalent to 0.8 mg. of isoprenaline sulphate), and Pao₂ and Paco₂ were measured in duplicate by means of electrodes manufactured by Radiometer, Copenhagen. The standard deviation of a single measurement with these electrodes in our hands was 1.7 mm. Hg for the oxygen electrode and 1.2 mm. Hg for the carbon dioxide electrode. Forced expiratory spirometry (F.E.S.) were obtained before and five minutes after a control inhalation of an aerosol containing only the propellant gas and again five minutes after the aerosol inhalation of 200 mg. of salbutamol. In each case the aerosol was released by the investigator from residual volume. From the spirometry the forced vital capacity (F.V.C.), the forced expiratory volume in 1 second (F.E.V.₁), and the F.E.V.₁ as a percentage of the F.V.C. (F.E.V.₁%) were calculated. The measurements were recorded in litres at A.T.P.S. (ambient temperature and pressure saturated with water vapour).

Results

Results of the spirometric and blood-gas tension measurements are shown in the Table. At the beginning of the experiment the F.V.C., F.E.V.₁, and F.E.V.₁% were all much reduced, and there was hypoxaemia without hypercapnia—changes which are characteristic of an asthma attack of moderate severity. Following the control inhalation there was no change in the spirometric measurements, but after salbutamol there was a significant increase in F.V.C., F.E.V.₁, and F.E.V.₁%. After salbutamol there were insignificant falls of 1.9 mm. Hg in Pao₂ and 0.7 mm. Hg in Paco₂ respectively.

Discussion

These asthmatic subjects had asthma of moderate severity. There was no change in the F.E.S. following the control inhalation, but there were highly significant changes in F.V.C., F.E.V.₁, and F.E.V.₁% after salbutamol, indicating a reduction in airway obstruction and lung hyperinflation. However, in spite of this improvement in ventilation there was no significant intensification of the hypoxaemia, the fall in Pao₂ being only 1.9 mm. Hg, whereas mean falls of 8.7 mm. Hg (Knudson and Constantine, 1967) have been reported in comparable

asthmatic subjects after aerosol isoprenaline. The fall in Pao₂ after isoprenaline is attributed to an intensification of ventilation/perfusion disturbance in the lung due to increased pulmonary blood flow consequent on the increase in cardiac output, and possibly in addition to reversal of hypoxic-induced pulmonary vasoconstriction.

In the experimental animal the stimulant effect of salbutamol on the cardiovascular system was 2,000 times less than that of isoprenaline, and its vasodilator action was only about 1/10 that of isoprenaline (Brittain *et al.*, 1968). It seems likely, therefore, that because salbutamol has a minimal effect on the cardiovascular system compared with isoprenaline undesirable lowering of Pao₂, even though airway obstruction is much reduced, does not occur. Nevertheless, though Pao₂ did not fall after the drug, it did not rise even though ventilatory function was much improved. We have suggested that after aerosol isoprenaline it is only when there is a considerable reduction in the degree of hyperinflation of the lung, as shown by an increase in F.V.C. of greater than 20%, that any improvement in Pao₂ can be expected (Palmer and Diamant, 1968). In this study the rise in F.V.C. after salbutamol was 15.9%, so presumably these subjects did not improve sufficiently in this respect to allow for a rise in the Pao₂.

We conclude that salbutamol is a useful bronchodilator drug, which because it appears to have little or no effect on the cardiovascular system may have advantages over isoprenaline. However, because of the known variability of asthmatic patients' response to bronchodilator drugs this could be best established by a comparison between isoprenaline and salbutamol in the same patient.

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