of disease patterns. Through his and other work done in New Guinea, our understanding of the aetiology of neurological disease has been potentially transformed.

Relevance of New Guinea

Many have questioned the point of my elective in New Guinea and its relevance to what I will be doing in England. New Guinea offers a perspective about the limitations of medicine today, and yet highlights the progress that has been and may still be made. It is only the absence of expected standards that makes you appreciate the measures required to attain them. Though physically far away, Papua New Guinea will remain close in my mind for many years to come. As I sat waiting for

my finals medicine viva, I pondered unlearned lists of relevant diseases, but my contemplation was arrested by the ringing of the entrance bell. "Right, well the last student didn't know much about this, let's see what you know . . . about malaria."

Finally, my happy memories of Madang have been marred by news of the tragic death of my supervisor there, Dr Helena Vbrova. She is a great loss to medicine in New Guinea and to world malariology. She will be remembered particularly for her spirit and devotion to work.

I thank Dr Alpers and Dr Heywood of the Institute of Medical Research for allowing me to join them and their research team. I also thank the Medical Research Council for its support in the project.

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Lesson of the Week

Nebulised salbutamol and angina

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Nebulised solutions of beta₂-adrenergic stimulants are very effective in the treatment of airflow obstruction in patients with asthma, chronic bronchitis, and emphysema^{1 2} and are often prescribed in large doses to both inpatients and outpatients. We report on three patients who developed evidence of cardiac ischaemia with this treatment. The possible aggravation of angina by nebulised salbutamol should be considered before patients with a history of ischaemic heart disease are given this treatment, and the dose of nebulised beta stimulant should be adjusted to each patient's requirements.

Case reports

Case 1—A 59-year-old retired welder was admitted to the coronary care unit after five episodes of angina over the previous four days. The last episode had lasted for one hour. He had smoked heavily until aged 56 years and had symptoms of chronic bronchitis with airflow obstruction. He had suffered from ischaemic heart disease for many years and had to retire from work aged 48 on account of angina. His medication included oral salbutamol 4 mg three times daily.

On admission there were no abnormal cardiovascular signs, but he had widespread inspiratory and expiratory wheezes. The initial electrocardiographic tracing showed no acute ischaemic changes. The airflow obstruction was treated with salbutamol respirator solution 5 mg diluted to 5 ml with saline and nebulised with oxygen. During the first administration of this treatment

Nebulised solutions of salbutamol may aggravate angina

he developed severe chest pain and the ECG monitor showed an acute rise in ST segment. The pain was rapidly relieved by stopping the nebulised salbutamol and giving sublingual glyceryl trinitrate. The change in the ST segment reverted to normal. He subsequently developed further episodes of angina that proved refractory to medical management. He underwent coronary arteriography and coronary artery grafting but developed intractable ventricular fibrillation immediately after surgery and died.

Case 2—A 73-year-old retired civil servant who was severely disabled by airflow obstruction was admitted to hospital for assessment of his airways disease, intensive treatment with bronchodilators, and treatment with steroids. He had had an inferior myocardial infarction. He had an angina attack about once a month, and these attacks were adequately controlled by sublingual glyceryl trinitrate as necessary. His electrocardiographic tracing showed the old inferior infarct and minor ST segment depression in leads V4-6.

On admission treatment was started with nebulised salbutamol, 10 mg in 5 ml saline four times per day. Immediately after the third dose of salbutamol he developed severe prolonged central chest pain at rest. He then admitted to also having had angina attacks during the two previous doses of nebulised salbutamol. The electrocardiographic tracing showed gross acute ST segment depression in leads V2 and V3 (figure), which slowly resolved over the next week. The creatinephosphokinase concentration rose to 683 IU/l (normal < 175 IU/l), and a sub-endocardial myocardial infarction was diagnosed. The salbutamol was continued in a reduced dose of 1 mg in 5 ml saline four times a day, and he had no further chest pain in hospital.

Case 3—A 49-year-old taxi driver was diagnosed as having asthma at the time of an anterior myocardial infarction in May

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1980. There was no history of angina after the infarct. In 1981 he presented with increased breathlessness and attacks of diarrhoea and flushing after eating. Carcinoid syndrome was confirmed by a 24-hour urinary HIAA estimation of 928 mmol (normal 10-73) and a technetium liver scan showed multiple metastases. His asthma became increasingly difficult to control, and he required admission to hospital. He was prescribed nebulised salbutamol 5 mg in 5 ml saline but developed typical attacks of angina on two occasions immediately after this treatment. The dose of salbutamol was reduced to 1 mg with no further episodes of angina.

Case 2. Electrocardiogram leads V1 to V3 on admission and after salbutamol nebuliser during episode of chest pain.

Discussion

Some patients with severe airflow obstruction fail to respond to β_2 -adrenergic stimulants given from a conventional pressurised aerosol but improve when the same drug is given by nebuliser. It is often unclear whether this response is due to the use of large doses or to the means of administration. In a dose-response study of nebulised salbutamol in asthma Ruffin and colleagues³ found no appreciable differences between 1.0, 2.5, and 5.0 mg of salbutamol solution, whereas Walters *et al*⁴

confirmed a good response with a dose of 1.5 mg but also showed further improvement with 3 mg and 7.5 mg. They suggested that 3 mg salbutamol respirator solution might be the optimal dose for asthmatic patients. The dose of salbutamol inhaled from a conventional pressurised aerosol or capsule of dry powder is 200 or 400 μ g. A dose of even 1 mg, therefore, represents an appreciable increase though what dose reaches the patient's airway is uncertain.

Salbutamol is an adrenergic agonist whose principle effect is stimulation of β_2 -receptors with resultant bronchodilatation and peripheral vasodilatation. In large doses, however, salbutamol may cause palpitations and tachycardia.⁵ Tachycardia shortens diastole and hence reduces the time for coronary artery perfusion. When coronary arteries are diseased this may lead to angina or even myocardial infarction, as in our second patient. Although β_2 stimulants may produce slight reductions in arterial oxygenation⁶ this was not relevant to the patients reported here, as in each case the nebuliser was driven by the hospital oxygen supply at 6-8 l/min.

We suspect that this association of angina with nebulised salbutamol may often be unrecognised, as only one other such patient has been reported to the Committee on Safety of Medicines (personal communication). We therefore recommend caution in the use of nebulised salbutamol in older patients and those with known or suspected coronary artery disease. We suggest that in such patients the initial dose of salbutamol should be no more than 1 mg, with subsequent increase if necessary to the lowest dose which produces adequate bronchodilatation.

We thank Dr Douglas S Reid for permission to report details of a patient under his care.

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