and calcium. In women frequent pregnancies and prolonged breast-feeding accentuate these deficiencies. Lack of sunlight is another important factor; in the Punjab, Moslem women may live in purdah, while Hindus also receive inadequate exposure through living in overcrowded, sunless houses.

In the United Kingdom rickets and osteomalacia are now usually secondary to steatorrhoea or to renal tubular abnormalities, though osteomalacia has been described in food-faddists (Dent, 1957) and in elderly people living on inadequate diets (Gough *et al.*, 1964). A survey of Pakistanis in Glasgow, however (Dunnigan *et al.*, 1962), revealed biochemical osteomalacia in several adults, both men and women, though none had clinical or radiological evidence of the disease. Their diets contained adequate calories and protein, but there was a lack of foods containing calcium and vitamin D. Dunnigan and Smith (1965) felt that pigmentation and lack of sunlight were also important in producing late rickets in this community. Our patients did have small intakes of calcium and vitamin D, and had presumably arrived in this country with depleted reserves, though their physique was excellent. Their adherence to traditional dress further reduces their exposure to sunlight, and was probably an important aetiological factor. We excluded intestinal and renal disease.

In two patients the diagnosis was made on clinical grounds. They complained of severe pain in the back, pelvis, and legs, the bones were tender, and movements of the hips and shoulders painful. There was marked muscle weakness and fatigue. The women could not sit up for more than a few minutes unsupported and had difficulty getting in and out of bed. Their broad-based, waddling gait was characteristic and was a gross exaggeration of that normally seen in pregnancy. In the third patient the pain was localized to the sites of rib fractures, and generalized symptoms were absent. In two patients the disease had a relatively acute onset in late pregnancy, while in the other (Case 1) it had clearly been present in the previous pregnancy in a less severe form. Her symptoms had improved after delivery only to suffer an acute exacerbation early in the next pregnancy.

X-ray examination in one patient showed pseudo-fractures, which are diagnostic of osteomalacia (Albright *et al.*, 1946), and in two there was generalized demineralization. In the third patient the discovery of fractures on x-ray examination was the main diagnostic clue in the absence of the more generalized symptoms displayed by the other women. Biochemical tests were typical and grossly abnormal in two patients, but only

mildly so in the third. In the latter case the serum alkaline phosphatase was not above the normal for this stage of pregnancy (Curzen and Morris, 1965).

It is easy to disregard complaints of generalized pain in women with little command of English. This is particularly so in pregnancy, when the relaxation of pelvic ligaments results in altered posture and muscular strain. This was the reason for the delay in diagnosis in the first patient, whereas, in the second, awareness of the condition allowed a confident clinical diagnosis on her first visit to the antenatal clinic.

As extensive radiological investigations are undesirable in pregnancy, it is fortunate that simple biochemical tests can often confirm a clinical suspicion. Treatment with vitamin D (3,000–6,000 I.U. daily) and calcium results in rapid clinical response, and pain soon disappears. Other causes of osteomalacia must be excluded in Asians as well as in Europeans, particularly if there is a slow response to treatment.

Summary

Osteomalacia of dietary origin was diagnosed in three pregnant women, members of the Asian community in Birmingham. It is important to exclude this disease in immigrants who complain of skeletal pains, particularly during pregnancy.

ADDENDUM.—During the last six months three similar cases have been seen in the obstetric department of this hospital.

We wish to thank Miss A. Reynolds and Mr. G. Mitchell for allowing us to publish details of patients under their care, Mr. W. B. Yeoman for the biochemical data and advice, and Dr. A. W. Robinson for reviewing the x-ray films. Dr. H. Thompson kindly reported on the bone biopsy.

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Medical Memoranda

Quinidine-induced Paroxysmal Ventricular Fibrillation Treated with Propranolol

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Ventricular fibrillation is known as an occasional dangerous complication of quinidine therapy, and is the most likely cause of sudden death during attempts to convert atrial fibrillation to sinus rhythm with this drug (Thomson, 1956; Selzer and Wray, 1964).

This paper describes the apparently specific action of the beta-adrenergic-blocking drug propranolol (Inderal) in treating such a dysrhythmia following a course of quinidine.

CASE REPORT

A 37-year-old woman with mild asymptomatic mitral stenosis developed atrial fibrillation and cardiac failure following a pulmonary embolus after her sixth pregnancy. When her condition had been controlled with digoxin, diuretics, and anticoagulants, it was decided to attempt conversion of her arrhythmia to sinus rhythm with quinidine. At this time she was taking digoxin 0.25 mg. daily.

After a test dose of 0.3 g. quinidine on the previous day she was given 0.3 g. every two hours for seven doses. Clinical observation and repeated electrocardiograms (E.C.G.) afforded no evidence of toxicity, and the last dose of quinidine was given at 6 p.m.

At 1 a.m. the same night the patient had a brief syncopal attack from which she recovered spontaneously. At 8 a.m. she had a further syncopal attack, and an E.C.G. taken shortly afterwards showed a bigeminal rhythm in which the multiform ventricular ectopic beats had a constant coupling time. Multiple syncopal

FIG. 1.—Electrocardiogram taken during syncopal attack.

attacks, occurring between 8.30 and 9 a.m., were noted to follow runs of coupled ectopic beats, and recurrent ventricular fibrillation was shown by E.C.G. (Fig. 1). Each attack either terminated spontaneously or was terminated by external cardiac massage, but the basic dysrhythmia of coupled ventricular ectopic beats persisted.

FIG. 2.—Electrocardiogram taken before and after intravenous administration of propranolol.

Propranolol, 5 mg., was then injected slowly intravenously. By the end of the injection the E.C.G. showed no ectopic beats (Fig. 2). Whereas before the injection the patient had been suffering syncopal attacks every three to four minutes, after the propranolol one hour passed before she had a further attack. The attacks then recurred and became more frequent and prolonged. She was therefore given a further intravenous injection of 5 mg. propranolol at 12.30 p.m. and suffered no further syncopal attacks for three hours. Coupled ventricular ectopic beats then recurred, and she had one short attack of ventricular fibrillation. Propranolol, 20 mg. by mouth, was started and given six-hourly. She had no further attacks, and her atrial fibrillation was converted to sinus rhythm with one direct-current shock one week later. She was discharged home on anti-coagulants alone.

COMMENT

Until the advent of direct-current shock (Lown *et al.*, 1962 ; Oram *et al.*, 1963), quinidine was the only satisfactory way of reverting atrial fibrillation to sinus rhythm. A test dose to detect hypersensitivity and anticoagulation to prevent embolism are probably necessary precautions. Digitalis has been recommended to avoid paradoxical tachycardia (Sokolow, 1951), though some authorities think that dysrhythmias occur more commonly when the two drugs are combined, and therefore advise that digitalis should not be used (Gold, 1950).

In spite of careful observation of the patient and his E.C.G. occasional ventricular dysrhythmias can occur in an almost totally unpredictable manner. These would normally be expected to occur during, or within six to eight hours of the end of, the course of quinidine (Goodman and Gilman, 1955). However, toxic effects may appear much later (Slonim, 1961), and in our patient the maximal toxic effect was not reached until 14 hours after the last dose. This should act as a warning to prolong observation of patients having quinidine therapy until well after the last dose has been given.

Sudden collapse during quinidine therapy is now thought to be due usually to ventricular fibrillation. In a review of the literature Thomson (1956) found an overall incidence of sudden death of 3.3%, most of these deaths being presumably due to

a dysrhythmia. Rokseth and Storstein (1963) report a series of 274 patients treated without fatality, though 12 of their patients suffered syncopal attacks. Proved ventricular fibrillations as a toxic effect of quinidine therapy has been reported on numerous occasions (Davis and Sprague, 1928 ; Sokolow, 1951 ; Selzer and Wray, 1964 ; Davies, Leak, and Oram, 1965). Rainier-Pope *et al.* (1962) make the point that in their two patients, as in ours, the attacks were heralded by frequent ventricular ectopic beats.

Quinidine toxicity has been treated in a number of different ways with varying degrees of success, the aim of treatment being to tide the patient over until the quinidine has been metabolized. Molar sodium lactate (Bellet, 1963), sympathomimetics (Rokseth and Storstein, 1963 ; Linenthal and Zoll, 1963), calcium sodium versenate (Luchi *et al.*, 1963), and external massage and direct-current shock (Rainier-Pope *et al.*, 1962) are among the remedies that have been used either clinically or experimentally. In our patient the E.C.G. abnormality was closely similar to that occurring in digitalis intoxication, and may well have been due to a synergistic effect of the two drugs, in spite of the small dose of digoxin used. It was felt, therefore, that the dysrhythmia might respond to treatment with one of the adrenergic beta-receptor-blocking drugs, which have been used with good effect in digitalis intoxication (Stock and Dale, 1963 ; Vaughan Williams and Sekiya, 1963). In our patient the results of this therapy appeared to indicate that propranolol has a specific effect in the suppression of this dysrhythmia. It provides further evidence of the usefulness of beta-adrenergic blockade in the treatment of drug-induced ventricular dysrhythmias.

I wish to thank Dr. W. van't Hoff for allowing me to publish details of this case, and Dr. J. P. P. Stock for his help in the preparation of the paper.

A. SEATON, B.A., M.B., M.R.C.P.,

Medical Registrar, North Staffordshire Royal Infirmary,
Stoke-on-Trent ; present address, Royal Southern
Hospital, Liverpool.

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Unilateral Renal Vein Thrombosis with Nephrotic Syndrome

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Bilateral renal vein thrombosis, though rare, has been described as a cause of the nephrotic syndrome. However, only a few case reports of unilateral renal vein thrombosis associated with the nephrotic syndrome have been published (Ashner, 1927 ; Pollak *et al.*, 1956 ; Morris *et al.*, 1963).

This report describes such a case. The diagnosis of renal vein thrombosis was suspected from the renal histopathology and radioisotope renography and was confirmed by inferior vena cavography.

CASE REPORT

A 19-year-old youth who worked in a grain shop was referred to us for puffiness of the face and swelling of the feet of five months' duration. The onset was insidious and was not preceded by pain in the loins. There was no history of respiratory symptoms suggestive of pulmonary embolism.