FIG. 2—Postoperative x-ray film one year after mitral valve replacement by Starr-Edwards prosthesis.

strengthened in this concept by the experience of Bennet and Oakley (1968), who reported a fatal termination for both mother and child following caesarean section at 30½ weeks in a woman who had undergone mitral valve replacement two and a half years previously. At necropsy the valve was found to be immobilized by thrombus, and they concluded that for the present the insertion of a mitral valve prosthesis precludes future pregnancy. Hedstrand and Cullhed (1968), however, reported a successful outcome for both mother and fetus in three patients with valve prostheses inserted two years previously, the control of anticoagulant therapy and management of the confinement being identical with ours. They reviewed an additional nine successful deliveries in whom five mothers had had aortic and four mitral prostheses.

Encouraged by these more favourable results, we felt it reasonable to recommend pregnancy in our patient, as she was very anxious to embark on this. Four and a half years had elapsed since valve replacement, and there is strong evidence

from several sources (Starr, Herr, and Wood, 1967; Reid, Barclay, Welsh, Stevenson, and McSwan, 1970) that the most dangerous period for thromboembolism is the first 36 months after operation. Hirsh, Cade, and O'Sullivan (1970) described their clinical experience with anticoagulant therapy during pregnancy in 14 patients, three of whom had prosthetic heart valves. The regimen to which they adhered to avoid both maternal and fetal haemorrhage was heparin for the first 12 weeks, oral anticoagulants from the 13th to 37th week, and finally reverting to heparin until term. On further reflection they concluded that it was unnecessary to recommend heparin during the initial trimester as there was no evidence that oral anticoagulants were detrimental to either mother or fetus.

Manifestly the question of pregnancy in women with valve prostheses will remain a subject of controversy for some time. In older and parous women further pregnancy is probably inadvisable. In younger women with no children our contention is that provided a minimum period of three years has elapsed since valve insertion, and on the proviso that strict anticoagulant control is maintained, a single pregnancy is justifiable if the woman appreciates the additional hazards. The administration of prophylactic antibiotic therapy is mandatory in the puerperium to prevent the possibility of endocarditis and valve infection originating from local sepsis in perineal tears or episiotomies (Littler, 1970).

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Renal Failure and Glucocorticoid Therapy

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Renal failure resulting in death may occur in patients with collagen diseases who are being treated with glucocorticoid drugs. In such cases progressive impairment of renal function is usually attributed to involvement of the kidneys by the collagen disease process, and this may be treated by increasing the dose of glucocorticoids.

The following report shows how renal failure complicated the management of a patient with polyarteritis nodosa who was treated with large doses of prednisone. Kidney function

showed a slow but definite improvement when prednisone was gradually withdrawn under cover of immunosuppressive therapy. It is proposed that renal failure complicating collagen diseases may occasionally be related to administration of glucocorticoid drugs. The mechanism of renal failure under these circumstances is discussed.

Case Report

A 20-year-old woman was admitted to the referring hospital with a two-month history of pain and tenderness of the left shin. On examination the tibial area of the left leg was swollen, hot, and tender. Radiographic examination showed incompletely ossified new bone along the anterior border of the left tibia, and bone biopsy of the radiographically abnormal area showed severe inflammation and fibrosis with evidence of vasculitis. Bone pain improved after a course of tetracycline, but one month later it recurred in the left lower leg and the left wrist became swollen and painful.

On examination she was pyrexial and had lost 9 lb (4 kg) in weight. There were firm raised tender skin lesions, 0.5 cm in diameter, involving both legs. The left wrist was swollen and tender. The pulse rate was 120 and there was mild abdominal tenderness.

Investigations.—Hb 11.0 g/100 ml; E.S.R. 60 mm/hour; blood urea 26 mg/100 ml; plasma potassium 3.4 mEq/l; plasma sodium 124 mEq/l; HCO₃ 24 mEq/l; serum aspartate aminotransferase

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10 units; serum alanine aminotransferase 8 units; serum bilirubin 0.3 mg/100 ml; antinuclear protein factor negative; L.E. cells negative; plasma albumin 2.9 g/100 ml; protein electrophoresis normal; blood cultures negative. Midstream specimen of urine showed no proteinuria, casts, or cells.

Biopsy of a skin nodule showed necrotizing arteriolitis affecting vessels in the most superficial part of the subcutaneous tissue. The features were consistent with a diagnosis of polyarteritis nodosa. Treatment with prednisone 40 mg daily was begun and the patient remained symptomless for four months. She then complained of abdominal pain and was readmitted.

On examination she had a Cushingoid appearance and was pyrexial. The abdomen was very tender and radiographic examination showed gaseous distension and fluid levels suggestive of subacute bowel obstruction.

Investigations.—Hb 6.9 g/100 ml; W.B.C. 17,400 cells/mm³; serum amylase 200 units/100 ml; plasma sodium 124 mEq/l; plasma potassium 4.3 mEq/l; blood urea 23 mg/100 ml.

She was treated conservatively with intravenous fluids and gastric suction. Prednisone dosage was increased in stages to 100 mg/day and there was a steady improvement in her condition. A

occurred when the dosage of prednisone reached 75 mg daily, was accompanied by a fall in creatinine clearance and a rise in blood urea. The creatinine clearance reached its lowest value at the height of the hypercalciuria, but the blood urea fell at the eighth month because of protein restriction, which was discontinued at the end of that month. Azathioprine therapy had no effect on hypercalciuria, but gradual reduction of prednisone dosage resulted in a fall in urinary calcium and blood urea and a rise in creatinine clearance. Plasma calcium remained normal throughout the illness.

Comment

Hypercalciuria in spontaneous and induced Cushing's syndrome has been shown (Albright and Reifenstein, 1948; Pechet *et al.*, 1959; Geschwind, 1961; Bentzel *et al.* 1964; Eisenberg, 1966), but there are no reports of renal failure under these circumstances. Rapidly progressive renal failure is often associated with hypercalcaemia accompanied by hypercalciuria, but it is controversial whether hypercalciuria in the presence of normocalcaemia will cause renal failure (Relman and Schwartz, 1967). Kidney biopsy was not performed in the above case, so renal involvement by polyarteritis nodosa cannot definitely be excluded. Involvement of the kidneys by this disorder, however, appears improbable, as there was no evidence of proteinuria until the sixth month of steroid therapy, when hypercalciuria developed. Furthermore, proteinuria decreased and eventually disappeared when the urinary calcium fell to normal.

The precise mechanism by which hypercalciuria damages the kidneys is unknown, but concomitant hypercalcaemia and hypercalciuria result in necrosis and calcification of the epithelial cells of the distal renal tubule. Calcific casts are formed (Carone *et al.*, 1960), and these result in intratubular obstruction which probably accounts for the development of azotaemia.

Monitoring of urinary calcium in all patients given large doses of glucocorticoids may be particularly important following renal transplantation or if there is impaired renal function.

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Treatment and results during 12 months.

barium meal and follow-through examination of the gut two weeks later showed nothing abnormal apart from some widening and flattening of the jejunal mucosal folds.

The urinary calcium, creatinine clearances, and blood urea values over a year are given in the Chart. Hypercalciuria, which