1973) and possibly shock hypotension are responsible for the acute oliguria. This may be mediated by an immune reaction, for patients on an intermittent regimen have high levels of circulating antirifampicin antibody (Aquinas *et al.*, 1972).

The patient's husband confirmed her history and we believed that it was authentic. She had been taking rifampicin and sodium aminosalicylate regularly for 16 months and suffered a severe reaction only after taking three intermittent doses of rifampicin. This is apparently the first report of combined hepatic and renal toxicity due to rifampicin, and it also seems to be the first report to incriminate rifampicin taken alone. There have been reports of immediate severe reactions with the first intermittent dose after a previous daily regimen (Kleinknecht *et al.*, 1972). Fortunately both the hepatic and renal toxic effects are re-

versible but physicians and patients need to be aware of the hazards of intermittent rifampicin therapy, even after a period of regular therapy.

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Acute Renal Failure and Rifampicin: Danger of Unsuspected Intermittent Dosage

C. T. FLYNN, D. J. RAINFORD, ELINOR HOPE

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Adverse reactions to rifampicin seem to be less common when the drug is given continuously than when it is given intermittently. Patients may not take rifampicin continuously when it is so prescribed and thus may place themselves at risk. A case of acute renal failure related to unsuspected intermittent rifampicin dosage is described.

Case Report

The patient was a married woman aged 66 years. Proven axillary and cervical tuberculous lymphadenopathy had been present for 30 years and had been treated by excision and chemotherapy since 1953. In January 1971 further axillary involvement was treated with para-aminosalicylic acid and isoniazid and, for the first time, rifampicin. The same day she developed nausea, dizziness, diarrhoea, and incontinence of urine. She took no further rifampicin but concealed this from her doctor. After an outpatient visit she took rifampicin for the second time in June 1972 and on the same day again developed nausea, dizziness, diarrhoea, and incontinence of urine. This time she was more severely affected, and she collapsed while shopping and was admitted to hospital. She was found to have fever and leucocytosis but no definitive diagnosis was made and she recovered uneventfully. The patient took rifampicin for the third time in September 1973. The same symptoms occurred as previously and she was admitted to hospital. On admission she was febrile and was tender in the right hypochondrium. Blood urea was 121 mg/100 ml, having previously been known to be normal. Serum bilirubin was 4.7 mg/100 ml. On admission her temperature was 39.5°C but was normal for the next five days. On the sixth day after admission she was given a single dose of rifampicin after which there was a solitary temperature rise to 38.5°C and she became oliguric.

The patient was transferred to the renal unit six days later for renal dialysis. On examination she was obese, the skin was dry and lax, and the hair was coarse. Clinically no jaundice, anaemia, pigmentation, or

purpura were detectable. The jugular venous pressure was raised, and there was slight ankle and sacral oedema. Blood pressure was 180/100 mm Hg but there were no hypertensive changes in the retinal vessels. Apart from a poor memory for recent events there was no abnormality of the central nervous system. Chest x-ray film and electrocardiogram showed nothing abnormal. Plain x-ray examination of the abdomen showed enlarged renal outlines. High dose intravenous pyelography produced neither a nephrogram nor a pyelogram. The diagnosis of oliguric acute renal failure was confirmed and her condition was maintained by five haemodialyses. Diuresis occurred after 10 days of oliguria. The patient made a full clinical recovery and one month later renal function was grossly normal with an uncorrected creatinine clearance of 85 ml/min.

A left renal biopsy done during the oliguric phase showed essentially normal glomeruli and tubules. There was interstitial oedema and some lymphocytes were seen in the interstitium but the appearances were not considered such as to warrant a diagnosis of interstitial nephritis. Tests for Australia antigen gave negative results. Serum and urinary levels of fibrin degradation products were not raised. Liver function test results were normal, immunoglobulin IgM, IgA, and IgG were normal, and serum complement (C3) was normal. The urine initially contained an excess of white and red blood cells but later became normal. Antibodies to rifampicin were not measured.

Discussion

The combination of fever, dizziness, nausea, diarrhoea, and incontinence of urine, while curious, was strikingly consistent after each ingestion of rifampicin. It is interesting that the symptoms occurred, albeit mildly, after the first dose. We are uncertain of the cause of the renal failure, and dehydration and transient hyperbilirubinaemia may have been contributory. There was no evidence of soluble complex disease, intravascular coagulation, or interstitial nephritis. Poole *et al.* (1971 a) showed rifampicin-dependent antibodies in patients on intermittent dosage and attributed symptoms to the interaction of high serum antibody levels with the re-introduced antigen. Other cases of acute renal failure have been described by Poole *et al.* (1971 b), Kleinknecht *et al.* (1972), and Campese *et al.* (1973).

This case illustrates the importance of ensuring that rifampicin is taken continuously and that patients are warned not to restart the drug without supervision if it has been discontinued.

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Renal Unit, Princess Mary's Royal Air Force Hospital, Halton, Aylesbury, Buckinghamshire
 C. T. FLYNN, M.R.C.P., Consultant in Medicine
 D. J. RAINFORD, M.R.C.P., Specialist in Medicine
 Tindal General Hospital, Aylesbury, Buckinghamshire
 ELINOR HOPE, M.R.C.P., Consultant Chest Physician