This patient was transplanted before the diagnosis of leprosy was made. Recrudescence of leprosy two years after transplantation was presumably associated with suspension of anti-leprosy treatment on the patient's part, and a lepra reaction became manifest as a result of reducing the dosage of immunosuppressive drugs. He was treated with clofazimine, a riminophenazine dye which combines an anti-leprosy action as effective as that of dapsone with an anti-inflammatory effect which is valuable in suppressing lepra reactions. Control of his leprosy assessed clinically and by the fall in morphological index was good.

Patients with lepromatous leprosy have a specific loss of cell-mediated immune response against *Mycobacterium leprae* and also a diminution in the ability to show other aspects of cell-mediated immune response—for example, contact sensitivity and skin homograft rejection (Hart and Rees, 1967; Bullock, 1968; Turk, 1970; Han *et al.*, 1971).

As the lepra reaction is an antigen-antibody reaction, immunosuppressive agents such as steroids and azathioprine which suppress antibody-mediated cellular immunity as well as antibody production would be expected to benefit the lepra reaction of lepromatous leprosy as well as the renal allograft.

At necropsy all the changes on histology of the renal graft could be readily explained on the basis of immune rejection and its consequences. There was no evidence to suggest involvement of the graft by the renal complications of leprosy.

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Mononeuritis Multiplex Occurring in a Diabetic Patient with Hb C Disease

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Mononeuritis multiplex is a well recognized complication of diabetes mellitus. It is seen in elderly patients but is not a feature in young diabetics (Raff and Asbury, 1968).

We report the case of a youth with homozygous Hb C disease who developed mononeuritis multiplex after hyperosmolar diabetic coma complicated by acute renal failure.

Case History

A previously healthy 14-year-old Negro from Barbados was admitted to hospital comatose on 4 January 1972 with a two-week history of increasing thirst, polydipsia, and polyuria. He was dehydrated and hypotensive (B.P. 70/0 mm Hg). The urine contained sugar and a trace of acetone. The blood sugar was 1,000 mg/100 ml, plasma bicarbonate 26.5 mEq/l., and the blood urea 186 mg/100 ml. He was treated with intravenous fluids and soluble insulin. Over the next three days plasma sodium concentration rose from 144 to 174 mEq/l., he became oliguric, and the blood urea level rose to 330 mg/100 ml. Plasma osmolality was not measured but the calculated osmolality ranged from 360 to 380 mOsm/l. On 7 January he was transferred to St. Leonard's Hospital hypotensive (B.P. 90/0 mm Hg), oliguric, and uraemic. Haemoglobin was 8.0 g/100 ml, packed cell volume 20%, mean corpuscular haemoglobin concentration 40%, reticulocytes 3%, white blood count 24,900/mm³ (polymorphs 93%), platelets 120,000/mm³. A single band with the mobility of Hb C was noted on haemoglobin electro-

phoresis. The presence of the disease was confirmed by observing the characteristic crystals of Hb C in 3% sodium chloride. There was no evidence of intravascular coagulation apart from the moderate thrombocytopenia.

Acute tubular necrosis secondary to hypovolaemia and hypotension was suspected. High dose excretion urography, however, did not show the typical findings associated with acute tubular necrosis but those observed with severe glomerular disease (Fry and Cattell, 1972). Peritoneal dialysis was begun, and after two weeks a diuresis occurred. Creatinine clearance returned to normal after eight weeks. The diabetes was treated by carbohydrate restriction (180 g/day) and soluble insulin (24-36 units/day). After recovering consciousness the patient remained apathetic for 10 days and his limbs were noticed to adopt unusual postures. The cerebrospinal fluid was normal. As his mental state improved, it became clear that he had bilateral wrist and foot drop. On the right there was a radial palsy distal to the branch to brachioradialis, and a median palsy distal to the origin of the branch to flexor digitorum. On the left there was a patchy and incomplete radial palsy. In the right leg there was a complete lateral popliteal and a posterior tibial palsy, accompanied by sensory loss in the distribution of these nerves. In the left leg there was a complete lateral popliteal palsy. The tendon reflexes were normal. Five weeks later the right posterior tibial palsy had recovered and there was some return of power to the forearm radial muscles on each side. The other neurological signs were unchanged. Electromyography of the right tibialis anterior at this time showed profuse fibrillation without units under voluntary control. Evidence of partial denervation was found in the right abductor pollicis brevis, and areas of extensor carpi radialis were completely denervated. The right median and ulnar sensory action potentials were normal.

Comment

The development of mononeuritis multiplex in a young, acute onset, diabetic is extremely unusual. This prompts consideration of the possible role of the associated haemoglobinopathy in the pathogenesis of the neuropathy.

Isolated lesions of peripheral nerves have been observed in sickle cell disease (Konotey-Ahulu, 1972), but we are not aware of any published report of such lesions in homozygous Hb C disease. The finding that the pathological change in mononeuritis multiplex complicating polyarteritis nodosa (Lovshin and Kernohan, 1948) and diabetes mellitus (Raff *et al.*, 1968) is localized infarction of the affected nerves suggested that the neuropathy in this case might be due to occlusion of vasa nervorum. Red cells from patients with homo-

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zygous Hb C disease show abnormal physical properties in vitro—their viscosity is higher than that of normal cells and they appear to be more rigid. These differences are exaggerated when the osmolality of the suspending solution is increased (Charache *et al.*, 1967). Given these in-vitro observations, it may be postulated that alterations in the physical properties of the red cells of this patient produced by the hyperosmolar state may have resulted both in ischaemic mononeuritis multiplex due to occlusion of vasa nervorum and acute renal failure due to intravascular damage or sludging within the renal glomeruli.

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Massive Haemolysis Caused by Rifampicin

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Rifampicin has been shown to be a highly effective anti-tuberculosis drug and is now being used in initial therapy as well as in retreatment regimens (Favez *et al.*, 1972). The serious side effects with daily therapy have been minimal and have mainly consisted of hepatotoxic reactions (Lees *et al.*, 1970). A higher incidence of adverse reactions has been reported with high dose intermittent rifampicin (Poole *et al.*, 1971, Aquinas *et al.*, 1972). These reactions—thrombocytopenia and febrile episodes—were associated with rifampicin-dependent antibodies in the serum (Poole *et al.*, 1972). Although these antibodies fix complement to red blood cells, haemolytic reactions have been reported in two instances only (Hasse *et al.*, 1971, Sors *et al.*, 1972). This paper reports a case of near fatal massive haemolysis caused by rifampicin.

Case Report

A 54-year-old woman was admitted to Colorado General Hospital on 8 May 1972 after an overdose of glutethimide and alcohol for which she had been treated at another hospital for five days with supportive care and assisted ventilation. At the time of admission she was conscious and had a tracheostomy tube in position.

Pulmonary tuberculosis was first diagnosed in 1930 and recurred in 1942; both episodes were treated with bed rest. In 1962 sputum cultures for *Mycobacterium tuberculosis* were positive and she received a six-month course of isoniazid and streptomycin. Her sputum was again positive by culture in March 1970, and she was treated with isoniazid, pyrazinamide, and ethambutol. She then developed migratory arthritis secondary to isoniazid and this drug was discontinued. While still receiving pyrazinamide and ethambutol she had a positive culture for *Myco. tuberculosis* in May 1971. Based on in-vitro susceptibility studies and previous drug therapy, she was given rifampicin 600 mg/day, ethionamide 500 mg/day, and kanamycin 1 g/day. After three months the kanamycin was discontinued and she was discharged from the hospital in September 1971. By her own admission, she took

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rifampicin irregularly and discontinued the ethionamide in December 1971 because of gastrointestinal intolerance. After her drug overdose, rifampicin alone was resumed on 5 May 1972 but was again discontinued on 8 May, when she was admitted to this hospital.

On 14 May, rifampicin and ethambutol were resumed. Two hours after receiving the drugs the patient was found to be hypotensive and unresponsive. She was transferred to the intensive care unit, where a diagnosis of severe haemolysis was established on the basis of a serum haemoglobin of 510 mg/100 ml, absent serum haptoglobins, a fall in the packed cell volume of 20 volumes %, raised indirect serum bilirubin, and haemoglobinuria. The platelet count was 155,000/mm³ compared to 350,000/mm³ six days earlier. Other liver function tests showed no abnormality and the serum total haemolytic complement levels were consistently less than 20 CH₅₀ units/ml (50% haemolytic unit of complement) for three days (normal 33-61 CH₅₀ units/ml). Blood cultures were sterile on several occasions. The patient became anuric after this haemolytic episode and required haemodialysis on four occasions, with subsequent recovery of her renal function. During the haemolytic episode her direct Coombs test was strongly positive with a negative indirect test.

After her recovery, as the aetiology of her haemolytic episode was not established and because of the desirability for further antituberculosis therapy, the patient was challenged with increasing doses of rifampicin while following her closely for evidence of haemolysis. She was given 10, 20, 50, 100, 200, and 300 mg of rifampicin on successive days with daily monitoring of packed cell volume, reticulocyte count, platelets, serum bilirubin, plasma haemoglobin, and urinary haemoglobin levels. Two hours after a dose of 300 mg her temperature rose from 36.5 to 38.2°C orally and she developed a shaking chill. Her serum bilirubin and plasma haemoglobin levels were raised from baseline values. Her packed cell volume fell by 6 volumes % and her serum haptoglobin fell by 79 mg/100 ml. The platelet count fell from 260,000 to 208,000/mm³; urinary haemoglobin was also detected (table I). Her blood pressure was stable. At the time of the trial doses of rifampicin she was not receiving any other medication.

TABLE I—Results after Challenge with 300 mg Rifampicin

	P.C.V.	Serum Bili-rubin Total/Direct (mg/100 ml)	Serum Hapto-globins (mg/100 ml)	Urinary Haemo-globin	Platelet Count/mm ³	Plasma Haemo-globin (mg/100 ml)	Temp-erature (°C)
Baseline values	29%	0.7/0.2	128	—	260,000	<1 mg	36.5
Two hours after 300 mg rifampicin	23%	3.2/0.5	49	+	208,000	21 mg	38.2

At the time of writing she was not on antituberculosis drugs as her sputum had remained consistently negative for mycobacteria on culture.

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