Rider, 1963; Schjeide *et al.*, 1966), and demyelination after high-dose x-irradiation has been found in animals and man (Innes and Carstan 1961; Rider, 1963). The development of transient radiation myelopathy in some patients after cervical cord irradiation (Jones, 1964) is an important analogous syndrome. These patients may complain of an electric-shock-like sensation in the limbs and down the back on flexing the neck, eight to 12 weeks after irradiation of the neck including the cervical spinal cord ("Lhermitte's sign of electrical paraesthesiae"), which may persist for several months. Jones (1964) postulated that irradiation inhibits the synthesis of myelin by the oligodendroglia and that the latent period reflects an absence of effect on preformed myelin; the symptomatic phase reflects relative demyelination, with clinical recovery after increased myelin synthesis. This sequence of events is equally applicable to the cerebral syndrome. Clinicopathological verification of this concept within this dose range is lacking in man but there is experimental evidence in animals that myelin synthesis is suppressed by radiation.

The E.E.G. abnormalities during somnolence support the concept of a diffuse cerebral disturbance, with improvement noted after clinical recovery. E.E.G. studies before and at appropriate stages during treatment are still in progress and may help to clarify the significance of these abnormalities.

The development of this somnolence syndrome after prophylactic cranial irradiation has been noted by other workers using identical radiotherapeutic techniques both in Britain and elsewhere (Ward, 1973; Lampert, 1973). The remarkably high incidence of this syndrome reported here may be partly explained by our increased awareness of it, with specific inquiry for symptoms at the appropriate time. The unexpected development of somnolence in these children will inevitably cause much anxiety in parents and may lead to hospital admission and unnecessary investigation in an attempt to find a viral or bacterial cause for this encephalopathy. If additional clinical features are present appropriate investigations will be required. We now, therefore, advise all parents of this syn-

drome before C.N.S. prophylaxis is begun, stressing its transient nature and complete recovery. This syndrome should be regarded as a minor and relatively unimportant complication of cranial irradiation in these children, just as the development of transient radiation myelopathy is regarded as an acceptable side effect of curative wide-field irradiation in Hodgkin's disease. It is a small price to pay for the proved efficacy of C.N.S. prophylaxis (Aur *et al.*, 1972; Medical Research Council, 1973) in greatly reducing the incidence of meningeal leukaemia and improving the prognosis of acute lymphoblastic leukaemia.

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MEDICAL MEMORANDA

Haemolysis in Infectious Mononucleosis: Inapparent Congenital Spherocytosis

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Haemolysis in infectious mononucleosis sufficient to be an important feature of the clinical illness remains an infrequent occurrence. Usually the picture is of the autoimmune type, with spherocytosis, increased osmotic fragility, a positive result in the antiglobulin test, or the presence of cold agglu-

tinins. Typically such haemolytic episodes are transitory, being followed by complete recovery within a few weeks (Dacie, 1963; Wintrobe, 1967). Three recent cases have been observed in which haemolysis during glandular fever did not conform to this pattern and investigation showed previously inapparent congenital spherocytosis.

Case 1

An 18-year-old woman developed malaise, fever, sore throat, and cervical adenopathy and a few days later became jaundiced. Haemoglobin was 10.8 g/100 ml and the W.B.C. 6,400/mm³ (neutrophils 1,900, lymphocytes 4,300, and monocytes 200/mm³). The blood film showed a number of atypical lymphoid cells compatible with those seen in infectious mononucleosis; rare spherocytes and 8% reticulocytes were present. Serum bilirubin was 4.2 mg/100 ml. Results of direct antiglobulin tests were negative but the Paul-Bunnell test gave a titre of 320. Osmotic fragility was greatly increased, confirming spherocytosis. Autohaemolysis at 24 hours was 5.4% without glucose, 3.1% with glucose, and 4.5% with adenosine triphosphate.

At that stage it became known that other members of the family had been investigated, and it was possible to construct a family tree showing her to have hereditary spherocytosis. Complete recovery followed without treatment in three weeks.

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Case 2

A 15-year-old boy had been ill for a week with malaise, fever, loss of appetite, and mild cervical adenopathy. A probable diagnosis of infectious hepatitis seemed confirmed with the onset of jaundice. He remained ill, however, and was thought to be pale. Investigations confirmed anaemia (haemoglobin 9.6 g/100 ml). The W.B.C. was 8,400/mm³ (neutrophils 2,900, lymphocytes 3,600, monocytes 450, and atypical lymphoid cells 1,450/mm³). Many spherocytes and polychromatic cells were present, and the reticulocyte count was 10.2%. The Paul-Bunnell test gave a titre of 160. Results of the direct antiglobulin test and test for cold agglutinins were negative. The degree of osmotic fragility was compatible with spherocytosis. Autohaemolysis at 24 hours was 3.8% without glucose, 1.8% with glucose, and 4.1% with adenosine triphosphate. Two brothers, the mother, and an aunt also showed increased fragility, reticulocytosis (5.1%, 4.8%, 8.1%, and 5.3% respectively), and scanty spherocytes in their peripheral blood. The patient recovered rapidly over the next 10 days.

Case 3

A 10-year-old girl presented with cervical adenopathy, sore throat, and pallor. Leukaemia had been considered until the onset of jaundice that morning. The peripheral blood showed haemoglobin 10 g/100 ml, and the W.B.C. was 4,600/mm³ (neutrophils 1,100, lymphocytes 3,200, and monocytes 300/mm³); rare atypical lymphoid cells were present. Only occasional spherocytes were seen but polychromatic cells were plentiful, and the reticulocyte count was 9%. The Paul-Bunnell test gave a titre of 80. Results of direct antiglobulin tests and tests for cold agglutinins were negative. The degree of osmotic fragility confirmed spherocytosis. Autohaemolysis at 24 hours was 6.1% without glucose, 5.3% with glucose, and 5.8% with adenosine triphosphate. Family studies showed pre-existing evidence; the father had had a splenectomy and a brother showed spherocytes in the peripheral blood.

The patient recovered without specific treatment.

Comment

It is generally accepted that congenital spherocytosis may be aggravated by infective episodes, leading to increased haemolysis or transitory hypoplasia.

In view of mounting evidence relating infectious mono-

nucleosis to E.B. virus infection and the increasing frequency with which infectious mononucleosis is being diagnosed the coincidence of infectious mononucleosis and congenital spherocytosis should become more widely recognized. Though there is a definite relation between agglutinability of red cells in hereditary spherocytosis and anti-i (Giblett and Crookston, 1964), and in some previous examples of haemolytic episodes in hereditary spherocytosis complicated by infectious mononucleosis anti-i has been found in the sera (Young *et al.*, 1951; Bean, 1957; DeNardo and Ray, 1963), anti-i was not detected in the present cases.

Aplastic episodes are well recognized in hereditary haemolytic disorders and may be induced experimentally by viral infection. Some degree of erythroid depression during an attack of infectious mononucleosis may thus allow recognition of previously inapparent congenital spherocytosis by reducing the compensatory power of the bone marrow. In all three cases described here a reticulocytosis was present, and it must therefore be assumed that any such impaired marrow function had occurred at a stage before clinical presentation.

Initially case 2 was thought to be suffering from infectious hepatitis, a well recognized diagnostic dilemma. Since infectious hepatitis itself may be complicated by more or less florid degrees of haemolysis this difficulty may be enhanced unless the possibility of coexistent disease is borne in mind. In two earlier cases sulphonamides had been ingested (Dameshek 1943; Gehlbach and Cooper, 1970), and an unusual reaction to drugs might, in those cases, have been a causal factor. Previous drug therapy had not been given in any of the three present cases.

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Myopathy associated with Anticonvulsant Osteomalacia

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Myopathy has been described in association with all forms of osteomalacia except the sex-linked form of type 1 hypophosphatemia.

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phataemic rickets (Smith and Stern, 1967, 1968). So far as we are aware myopathy in association with anticonvulsant osteomalacia, has not been reported previously, apart from a reference to proximal weakness in one of the four cases (Case 2) of anticonvulsant osteomalacia described by Dent *et al.* (1970).

Case Report

A 36-year-old Irish housewife was admitted to hospital for investigation in June 1972.

She had been mentally retarded since birth, and her full scale I.Q. (W.A.I.S.) was 68. Grand mal seizures began at the age of 11, since when she had been treated with varying doses of phenobarbitone and diphenylhydantoin. On admission she was taking phenobarbitone 200 mg daily, diphenylhydantoin 300 mg daily, sulthiame 600 mg daily, and amitriptyline 150 mg daily.

In 1964 she twice took an overdose of anticonvulsant tablets. During 1966 she first complained of back pain which was attributed to depression, and she improved after two courses of electroconvulsive therapy. From 1968 onwards she became progressively disabled by weakness and pain. The weakness was proximal in distribution, affecting legs more than arms. As a result she had increasing difficulty in rising from a bed or chair, in climbing stairs, and in lifting heavy objects or raising her arms to comb her hair. The pain was experienced in the back, left shoulder, and hip. By 1970 she was housebound and by the time of her admission