Psychosis in Systemic Lupus Erythematosus (SLE) and the Response to Cyclophosphamide

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M H, girl aged 11
Presented with tiredness and malaise and was found to have cervical lymphadenopathy and a marked retinopathy.

Investigations: Hb 7 g/100 ml, reticulocytes 8%; WBC 2,800; ESR 60 mm in 1 hour (Westergren). LE cells were demonstrated and a warm antibody was found. Treatment was begun with prednisone and the anæmia was controlled.

Two weeks later she developed an acute psychosis. This was taken to be a manifestation of the disease process and initially the steroid dosage was increased, though without effect over ten days. It was felt imperative to change the treatment and cyclophosphamide was started. Within a week her mental state was normal and the retinopathy had cleared. Treatment continued for six months, during which time her mental state remained normal.

Discussion

The psychosis may have been a manifestation of the disease process, a complication of the steroid therapy, or a combination of both factors. In our experience steroid-induced psychoses in childhood are very rare. Psychosis is a well recognized feature of SLE both in adults (Dubois & Tuffanelli 1964) and in children (Dietze & Voegele 1966). The mechanism is obscure, since the clinical features do not tally with the findings at post-mortem: patients with gross symptoms may have normal histology, whilst fibrinoid necrosis and cerebral thromboses may be found in the asymptomatic patient (O'Connor & Musher 1966).

The relevance of steroids as a precipitating factor in the psychosis of SLE has received considerable attention. Of patients with psychoses 50% have never been on steroids, the time interval for the development of a psychosis is most inconstant, and psychosis does not necessarily recur if steroids are recommenced for other reasons. The psychosis in this patient was typical of that previously described in SLE, with delusions, hallucinations, confusion, disorientation and memory defect. For these reasons we think that this child's psychosis was a manifestation of the disease process and our view was reinforced by the response to treatment, which could be observed clinically and followed objectively in the regression of the retinopathy.

The use of immunosuppressive agents in the treatment of autoimmune disorders is well established. Cyclophosphamide has been reported previously in the treatment of SLE, with variable success (Seah *et al.* 1966). The conclusion was that if high doses or prolonged courses of steroids were required for the control of the disease, or if complications of steroid therapy supervened, immunosuppressive agents might be of value.

As far as we can discover this is the first time cyclophosphamide has been reported in the treatment of SLE in childhood or of the psychosis in SLE.

REFERENCES
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Dubois E L & Tuffanelli D L
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O'Connor J F & Musher D M
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Seah C S, Wong K H, Chew A G K & Jayaratnam F J
(1966) *Brit. med. J.* i, 333

The following cases were also presented:

Nonprogressive Werdnig-Hoffman Disease
Dr J D Hardy (for Dr D N Golding)

Chemical Proctitis
Mr L Lupin (for Mr D G Young)

Meeting January 24 1969

Serious Adult Disease Arising in Childhood [*Abridged*]

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Still's Disease Followed into Adult Life

Juvenile chronic polyarthritis, often known as Still's disease or juvenile rheumatoid arthritis, is relatively uncommon and the fate of patients suffering from it is poorly documented. Chronic disease beginning in childhood can only be assessed over a long period lasting at least until the patients have reached the relatively more stable status of adults.

To try and inform ourselves on the course of this disorder children transferred for further care to the MRC Rheumatism Unit at Taplow within five years of the onset of the disease have been followed up. As there are no diagnostic tests and no universally accepted diagnostic criteria, all

patients admitted to this study fulfilled our own criteria (Ansell & Bywaters 1959). At the present time, 168 have been seen fifteen years from the onset of their disease and 84 at twenty years. This is a relatively short time but it does offer some information on prognosis. A summary of the fifteen-year follow up is now given:

There was a total of 101 females and 67 males. Seventeen, 10 females and 7 males, had died prior to the fifteen-year follow up. Infection of various types was the most common cause of death and this accounted for 7, 5 of whom were on corticosteroids; the second most common cause was renal failure due to amyloidosis, from which 6 patients died; 2 had died from unrelated causes (acute renal cortical necrosis; post-operatively following repair of congenital aortic stenosis), while another patient died of uræmia, the exact cause of which was never determined. Only one was considered to have died as a direct result of his Still's disease.

As one male and one female could not be traced a total of 90 females and 59 males were available for assessment. This included a clinical appraisal, assessment of function, urine blood and X-ray examinations. The functional capacity was designated 5 if there was no incapacity, 4 if so slight that it did not interfere with leading a normal life. Seventy of the 90 girls and 52 of the 59 boys fell into the top two categories. Twenty, 16 girls and 4 boys, were in functional status 3 and had had their lives considerably modified being severely incapacitated as a result of the disease, while a total of 5 had wheelchair/crutch existences and two were bed-fast; one of these last had an associated mental abnormality. As judged by the presence of soft tissue swelling around the joints and an ESR above 20 mm in 1 hour (Westergren), in 19 of the 90 girls and 17 of the 59 boys the disease was classed as active, whereas in the remainder it was considered inactive. Residua, either clinical or radiological, were present in 90 of the 113 inactive. Rheumatoid factor tests were positive in only 6 males and 9 females. Chronic iridocyclitis had occurred in 8 cases (4 males and 4 females) and acute iridocyclitis, often recurrent, in 4, all males. In addition to the 6 who had died from amyloidosis 7 others had been demonstrated as suffering from it. Psoriasis had developed in 3 patients and ankylosing spondylitis in 9.

Reviewing the pattern of illness, it seemed that 50 had had an acute illness, which had settled within five years; it was among these that the patients were seen without clinical or radiological residua; this always raises the question as to whether they had really suffered from Still's disease! In 37 the course had been one of recurrent bouts of activity with intervals of good health varying from months to years. Forty-four had chronic seronegative arthritis which remained active for more than five years, but many of these had become inactive at varying periods after that time. In 10 patients, 6 of whom were female, the pattern of illness had been more like that of adult rheumatoid arthritis with positive rheumatoid factor tests, the early development of erosions and occasionally nodules and vascular lesions. Eight, 6 of whom were male, had developed ankylosing spondylitis while one of the patients who had died had developed ankylosing spondylitis and psoriasis prior to death. Amyloidosis occurred in all groups but was most common among the chronic, active, seronegative cases.

To summarize, Still's disease is probably best regarded as a syndrome characterized by polyarthritis with or without systemic manifestations. The majority of such patients recover sufficiently to lead reasonably normal lives; some die from intercurrent infection but the most serious complication is amyloidosis which is usually fatal. A few patients, particularly the younger with an acute onset, settle quickly but the majority persist as a seronegative arthritis which may remit at any time leaving varying degrees of residua. Some, particularly males, may later develop ankylosing spondylitis while a few, particularly females, have a disease resembling adult rheumatoid arthritis; these last tend to persist active.

REFERENCE
Ansell B M & Bywaters E G L (1959) *Bull. rheum. Dis.* 9, 189

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Hæmophilia

Hæmophilia is a hereditary bleeding state due to deficiency or total lack of an essential blood-clotting factor called antihæmophilic globulin (AHG) or Factor VIII. The condition is inherited as a sex-linked recessive character and thus mainly affects males. Cases of female hæmophilia have arisen in the offspring of marriages between affected males and female carriers of the disease. Since the incidence of hæmophilia is very low (about 2 per 100,000 of the population) such marriages are rare. A second disease, Christmas disease, due to deficiency of another essential blood-clotting factor (Factor IX), is inherited in the same way as hæmophilia and has the same clinical features. It is distinguishable only by laboratory tests.

The clinical features characteristic of these diseases are due to the hæmorrhagic conse-