

unilateral tumours, one of the tumours was multifocal, and in each patient there were identical associated congenital anomalies.

Detailed family histories have not always been recorded for children with embryonal tumours and it is probable that the incidence of associated congenital anomalies is under-reported. However, the prospective epidemiological survey of families of children with Wilms's tumour which is now being carried out in this country, and also the findings of the prospective American National Wilms's Tumor Study, may give a more accurate picture of the genetic pattern of this disease.

Summary

Twin boys, both of whom had hypospadias and bilateral cryptorchidism, each developed a left-sided Wilms's tumour. The first twin was found to have an advanced multifocal tumour at the age of 15 months and died with local recurrence and pulmonary metastases. The diagnosis was made in the second twin one month later and at nephrectomy the tumour was found to be encapsulated without metastases; he is disease-free 12 years later. Although the histological appearances were similar in each twin, the tumours did not develop at the same rate and did not show the 'mirror-image' pattern suggested for embryonal tumours in identical twins.

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Serial studies of numbers of circulating T and B lymphocytes in children with acute lymphoblastic leukaemia

The effects of antileukaemia therapy on the immune response have been receiving increasing attention. Patients with acute lymphoblastic leukaemia (ALL) are given not only immunosuppressive drugs but also cranial irradiation. Serial studies of total numbers of circulating thymus-dependent (T) and bursa-equivalent (B) lymphocytes were undertaken at monthly intervals in children with ALL. Changes in total numbers of T and B lymphocytes have been related to the treatment given.

Methods

Nine children aged 3 to 9 years have been entered into the study to date. Normal ranges of T and B lymphocytes were also established in 14 children aged 1 to 14 years who had been admitted for elective surgery.

A modified version of the Acute Leukaemia Group B protocol 6801 was used (Holland and Glidewell, 1972). Remission was induced over 5 weeks with vincristine and prednisone. Maintenance therapy thereafter consisted of weekly oral methotrexate and 6-mercaptopurine with pulses of vincristine and prednisone. Intrathecal methotrexate was given weekly during induction and monthly during the first 6 months of maintenance therapy.

Between 5 and 9 weeks after starting treatment each child was given a course of cranial irradiation 2400 rads in 12 doses over 2 to 3 weeks.

Lymphocytes were obtained by centrifuging leucocyte-rich plasma from dextran-sedimented, preservative-free heparinized blood on Ficoll-Triosil (Lymphoprep, Nyegaard) gradients. A separate sample of venous blood was used for determining total and differential leucocyte counts. Relative numbers of T lymphocytes were determined by an unsensitized sheep red blood cell (Wellcome or Mercia) rosette technique. Relative numbers of B lymphocytes were determined by demonstrating the presence of surface immunoglobulin with fluorescein-conjugated, polyvalent sheep antihuman immunoglobulin (Wellcome). Total numbers of T and B lymphocytes were then calculated from the total and differential leucocyte counts.

Results

The mean numbers (± 1 SD) of T and B lymphocytes during induction and at monthly intervals thereafter are shown in the Fig. Numbers of B lymphocytes one month after the introduction of 6-mercaptopurine and methotrexate and between 1 and 2 weeks after the end of radiotherapy fell significantly (Student's 't' test, $P < 0.01$) compared with the levels during induction. By 3 months after the start of maintenance therapy this fall was even more marked (Student's 't' test $P < 0.005$).

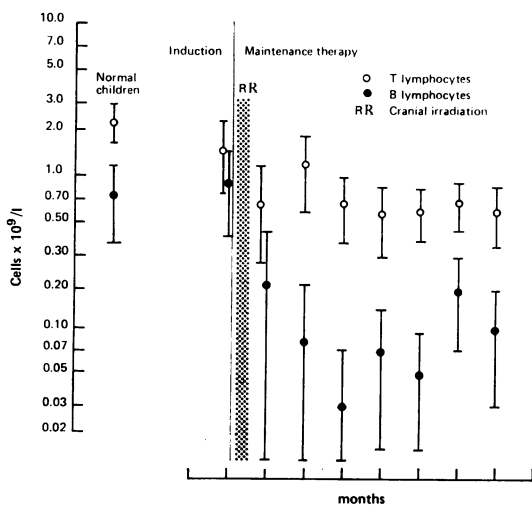


Fig. Mean numbers (± 1 SD) of circulating T and B lymphocytes at end of induction period and at monthly intervals thereafter.

Discussion

Many of the drugs used in the treatment of ALL depress lymphocyte function. Most of them depress B more than T lymphocyte function. This subject has recently been reviewed by Leventhal *et al.* (1974). The effects of radiotherapy on T and B lymphocytes are not well understood. Carlson and Lubet (1976) have shown in mice that B lymphocytes may be more radiosensitive than T lymphocytes.

Only comparatively recently has it become possible to measure routinely numbers of circulating T and B lymphocytes throughout the course of a child's treatment. Sen and Borella (1973) and Winterleitner *et al.* (1975) found a relatively greater depression of numbers of B lymphocytes than of T lymphocytes during maintenance chemotherapy in ALL, but the timing of this fall was not apparent from their reports. In spite of the small number of patients in our study there is a suggestion that the onset of a marked fall in the numbers of B lymphocytes, relatively greater than that in T lymphocytes, occurs between the end of induction therapy and the first estimation during maintenance.

These results support the findings of Sen and Borella (1973) and of Winterleitner *et al.* (1975). They also suggest that the fall in the number of B lymphocytes is not a consequence of long periods of maintenance chemotherapy but occurs early in the course of treatment and may be the result of a specific event such as radiotherapy, the introduction of 6-mercaptopurine or methotrexate, or a combination of these.

Susceptibility to infection after irradiation of the central nervous system has been noted by the Medical Research Council Working Party (1976). In the UKALL III Trial a number of patients succumbed to infection associated with profound neutropenia in the weeks immediately after irradiation. This depression of B cell numbers may be one more factor which increases the risk of infection in children undergoing treatment of ALL.

Summary

Serial studies of numbers of circulating T and B lymphocytes at monthly intervals in children with acute lymphoblastic leukaemia showed a marked fall in the number of B cells, relatively greater than that of T cells, early in the course of maintenance chemotherapy and immediately after a course of cranial irradiation. The fall in the number of B cells is not a consequence of long-term chemotherapy, and is possibly related to a specific event such as cranial irradiation.

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