

cal adenoma, demonstrated by x-ray, was surgically removed. Oestrogen levels fell immediately. 3 years later the boy shows complete regression of the gynecomastia and no signs of recurrence.

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Wilms's tumour, hypospadias, and cryptorchidism in twins

The familial incidence of embryonal tumours of childhood is extremely low, with the exception of retinoblastoma, in which the bilateral form of the disease is usually hereditary (Sorsby, 1972). Wilms's tumour may occasionally occur in 2 or more sibs (Maslow, 1940), or in more than one generation of

the same family (Brown *et al.*, 1972), but has rarely been reported in twins.

Various congenital anomalies, including abnormalities of the urogenital tract, occur with increased frequency in patients with Wilms's tumour (Miller *et al.*, 1964). These anomalies may be found in association with each other as well as with Wilms's tumour, sometimes in members of the same family (Meadows *et al.*, 1974).

The survey of 335 families of children diagnosed as having Wilms's tumour between 1962 and 1966 in England and Wales (Ledlie *et al.*, 1970) showed only 2 cases of familial involvement; one of these was in a mother and daughter and one was in twin boys (Hewitt *et al.*, 1966). The latter case is of particular interest because of the presence of other identical anomalies in each twin, known to be associated with Wilms's tumour. This family is described in detail.

Case reports

Twin boys were born to unrelated parents. The mother was aged 22 years and had been x-rayed at 8 months' gestation; she had also been treated for hypertension during the last month of pregnancy. Delivery was uncomplicated and a common placenta found. Both twins were found to have hypospadias and bilateral undescended testes. The blood group of each twin was A Rhesus positive.

Twin 1. At the age of 15 months the mother felt a lump in the abdomen while bathing him. An intravenous pyelogram (IVP) showed that the calyces of the left kidney were distorted by a large intrarenal mass. At laparotomy a large inoperable, multifocal tumour of the left kidney was found. Biopsy confirmed the diagnosis of Wilms's tumour. He was then referred to St. Bartholomew's Hospital where he was given a course of radiotherapy, and nephrectomy was carried out one month later. The tumour had invaded the renal vein. The patient rapidly developed local recurrence and pulmonary metastases from which he died.

Twin 2. One month after the diagnosis of Wilms's tumour had been made in the first twin, the mother noticed that the other twin had started to lie on his face, something he had never done before. She took him to St. Bartholomew's Hospital where he was found to have a small left-sided abdominal mass. IVP showed appearances consistent with a Wilms's tumour of the left kidney. Nephrectomy was carried out on the same day, as for the first twin, but the tumour was found to involve only the upper pole of the kidney and to be completely encapsulated with no involvement of the renal vein. He was given a

Table *Previous reports of Wilms's tumour in twins and their families (with age at diagnosis)*

Report	Twin 1	Twin 2	Family
Ottawa 1951 (Gaulin, 1951)	Boy 15 m; Left Wilms's tumour; died	Boy 15 m; Right Wilms's tumour; died	—
New York 1968 (Murphy, 1968)	Girl 8 m; right Wilms's tumour; survived	Girl 18 m; right Wilms's tumour; survived	—
Louisiana 1975 (Juberg <i>et al.</i> , 1975)	Boy 24 m; right Wilms's tumour survived	Unaffected at age 5 yr	Brother 12 m; right Wilms's tumour; survived

4-day course of actinomycin D after surgery and a course of radiotherapy to the left hemiabdomen. He remains disease-free 12 years later.

Pathology. The histological appearance of the tumour was similar in each twin. Both tumours were composed mainly of rhabdomyosarcomatous tissue with areas of primitive mesenchyme and attempts at early tubule formation.

There was no history on either side of the family of Wilms's tumour and a sister who was born one year after the twins had no congenital abnormalities and remains disease-free.

Discussion

Wilms's tumour occurring in twins is rare. 3 cases have been reported in detail (Table). When Gaulin (1951) reported the first pair of twins who presented with Wilms's tumour at the age of 15 months, he noted that the tumour was left-sided in one twin and right-sided in the other. It was thought that embryonal tumours in identical twins would always be similar, simultaneous, and symmetrical. Subsequent reports have not supported the 'mirror-image' theory; in the present case both tumours were in the left kidney. In addition, though the histological appearance was identical, the tumours did not become clinically obvious at the same time. The tumour in the second twin was only diagnosed when a completely nonspecific symptom worried a mother who already had an ill child; the disease was found to be less advanced than in the first twin and therefore more amenable to treatment. In the twins described by Murphy (1968), there was a 10-month gap between the diagnosis of the tumour in the first twin and that of the second twin, but both survived after treatment.

The case which has been of most interest is that reported by Juberg *et al.* (1975) in which one of a pair of proven monozygous twin boys developed a right-sided tumour at the age of 24 months. This is

the only reported pair of twins in which there has been completely adequate evidence of monozygosity, but the second twin remains free of disease at the age of 5 years. However, the younger brother also developed a right-sided Wilms's tumour at the age of 12 months. There is no history on either side of the family of Wilms's tumour. Whatever the genetic explanation for the occurrence of familial Wilms's tumour, this case suggests that there is a variable degree of penetrance in the inheritance of Wilms's tumour.

The present cases and the 3 reported ones all support the previously noted fact that familial Wilms's tumour tends to occur at a younger age than average for Wilms's tumour patients (Cochran and Froggatt, 1967). In the series of 87 patients with Wilms's tumour treated at The Hospital for Sick Children from 1960 to 1973, the average age at diagnosis of unilateral Wilms's tumour was 3½ years and of bilateral Wilms's tumour 15 months (Bond, 1975a).

It has been suggested that the nonhereditary form of Wilms's tumour is unilateral, occurs sporadically with a later age of onset, and produces a unifocal tumour. In contrast, the hereditary form occurs at a younger than average age and produces multiple tumours (Knudson and Strong, 1972). The incidence of bilateral tumours is higher than expected in hereditary Wilms's tumour. In addition, patients with simultaneous bilateral multifocal tumours have been found to have a high incidence of associated urogenital anomalies (Bond, 1975b). However, few if any patients with simultaneous bilateral tumours have as yet survived after treatment to produce children of their own. This is in direct contrast to patients with retinoblastoma in whom local treatment to the tumour is extremely effective and does not impair fertility. It is thus possible to show a definite pattern of inheritance in patients with retinoblastoma in a way which has not so far been possible in other embryonal tumours of childhood. Although both the patients in this report had

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.