

Wilms' tumour (nephroblastoma)

Wilms' tumour is generally found only in children and very rarely in adults.

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Janet Poole qualified as a medical doctor in 1978 at the University of the Witwatersrand and became a specialist paediatrician in 1983. She commenced work in the Paediatric Haematology/Oncology Unit at the Johannesburg Hospital in 1984 and has 25 years' experience in that field. She was head of the Chris Hani Baragwanath Paediatric Haematology/Oncology Unit from 1989 to 1997, after which she became head of the Unit at Johannesburg Hospital. Her special interests are childhood leukaemia, Wilms' tumour, and inherited haemoglobin defects. She has been involved with CHOC (a parent support group) since starting work in the unit.

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Epidemiology

Wilms' tumour or nephroblastoma is a cancer of the kidney that typically occurs in children and very rarely in adults. The common name is an eponym, referring to Dr Max Wilms, the German surgeon who first described this type of tumour in 1899. Wilms' tumour is the most common form of kidney cancer in children and is also known as nephroblastoma. Nephro means kidney, and a blastoma is a tumour of embryonic tissue that has not yet fully developed.

Wilms' tumour accounts for 6 - 7% of all childhood cancers, and 500 cases per annum are diagnosed in the USA. It has a female predominance and a higher incidence in black children. Seventy-eight per cent of children are diagnosed at 1 - 5 years of age, with a peak incidence at 3 - 4 years.

Wilms' tumour usually occurs sporadically, but in 1% of cases it is familial. Congenital abnormalities occur in 12 - 15% of cases. These include genito-urinary abnormalities (e.g. horseshoe kidney, hypospadias, undescended testes), congenital aniridia, WAGR syndrome (aniridia, mental retardation, genito-urinary abnormalities), congenital hemihypertrophy, Beckwith-Wiedemann syndrome, and Denys-Drash syndrome (renal disease, pseudo-hermaphroditism). Wilms' tumour is mostly unilateral, but is bilateral in 5% of cases.

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Signs and symptoms

An abdominal mass is the most common presenting sign in 60% of cases. It may be noticed by parents or it may be an incidental finding on examination. Occasionally there is abdominal pain, which usually occurs after trauma, causing haemorrhage or, rarely, rupture of the tumour. Hypertension, which is seen in 25% of patients, is caused by renin production by tumour cells. Haematuria may be macroscopic, but is generally microscopic, and occurs in 15% of patients. It may lead to iron deficiency anaemia. Rarely Wilms' tumour may present with acquired von Willebrand's disease and

a bleeding diathesis, polycythaemia, weight loss, urinary infection, diarrhoea or constipation.

The differential diagnosis of a renal mass includes hydronephrosis, polycystic kidney disease and infrequently xanthogranulomatous pyelonephritis. Non-renal peritoneal masses include neuroblastoma and teratoma (Fig. 1).

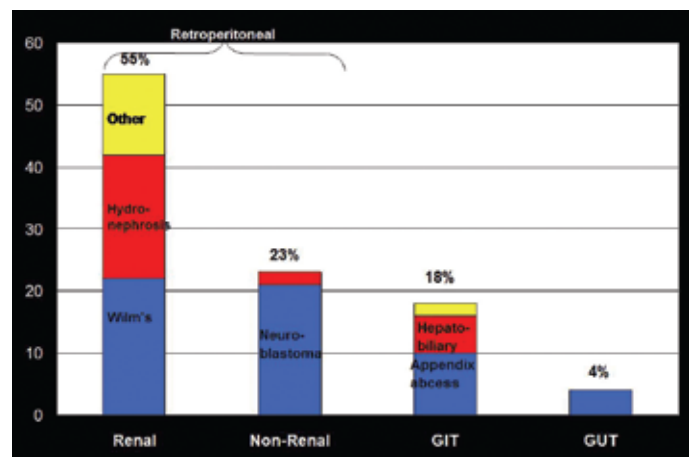


Fig. 1. Abdominal masses in infants and children.

Examination of the abdomen

An attending doctor must *always* examine a child's abdomen. Wilms' tumour is a flank mass and is usually ballotable on bi-manual palpation. It may/may not cross the midline. A flank mass on the left should always be distinguished from an enlarged spleen. There may be distended abdominal veins if there is a tumour thrombus in the inferior vena cava (IVC). If a flank mass is noted, the blood pressure should be taken and a urine dipstick test performed (Fig. 2).

Investigations

Blood tests should include a full blood count, renal chemistry (urea and electrolytes, creatinine), lactate dehydrogenase (LDH), and partial thromboplastin time (PTT) if a bleeding diathesis is suspected. A urinalysis should also be performed. A chest radiograph should be taken to exclude metastases ('coin' or 'cannonball' lesions) (Fig. 3). A plain abdominal radiograph demonstrates an opacity in either flank with displacement of bowel gas. Calcification may occur in 15% of cases. An ultrasound scan



Fig. 2. Large right-flank mass.



Fig. 3. Chest radiograph showing lung metastases.

of the abdomen is mandatory to identify a renal/non-renal mass and to distinguish between a cystic lesion and a solid tumour. It also contributes towards detecting small tumours in the opposite kidney, tumour thrombi in the IVC and liver metastases. Abdominal CT scan (Fig. 4) has largely replaced the intravenous pyelogram (IVP) examination. Special attention must be given to the presence and function of the opposite kidney, and to evidence of bilateral involvement, lymph node involvement and liver infiltration.

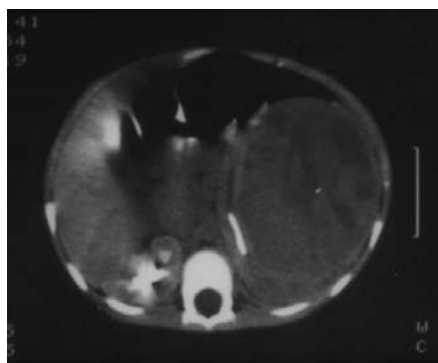


Fig. 4. CT scan showing left renal tumour.

After referral to a paediatric oncology unit a fine needle aspirate (FNA) of the flank mass may be performed. Open biopsy should be avoided at all costs, as it 'upstages' the tumour.

Hypertension is seen in 25% of cases and is caused by renin production by the tumour cells.

Survival and prognostic factors

Generally the prognosis for children with Wilms' tumour is very good. The overall survival rate is 90%, i.e. 9 out of 10 will live at least 5 years after their cancer has been diagnosed. The 5-year survival mark is the point at which a patient is considered 'cured', because these tumours almost never recur after this time. There are two main prognostic criteria, i.e. histology (pathology) and stage (Table I).

Pathology

Macroscopically, nephroblastomas are often very large and heterogeneous, with cystic, necrotic and haemorrhagic areas (Fig. 5). Microscopically, they are embryonic tumours. The classic 'triphasic' histology consists of 3 elements: very immature renal parenchymal cells (blastema), primitive tubules (epithelial cells) and supporting mesenchyme.

Prognostic histology may be divided into favourable histology (triphasic Wilms' tumour and cystic, partially differentiated nephroblastoma) and unfavourable histology (focal or diffuse anaplasia, and



Fig. 5. Cut surface of Wilms' tumour.

cells that are more abnormal and appear bizarre with large and distorted nuclei).

Staging

Staging allows the cancer team to select the best treatment approach. Staging of the abdominal mass is based on the surgical extent of the excision and the histological result.

Treatment

The treatment of Wilms' tumour is a prime illustration of success achieved with multimodality therapy in paediatric oncology (Fig. 6).

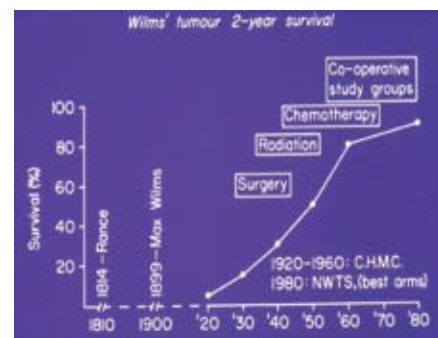


Fig. 6. Improvement in survival with multi-modality therapy.

Except in the case of a surgical emergency for rupture, a child with Wilms' tumour should *always* first be referred to a paediatric oncology unit.

Table I. Clinical pathology staging

Stage	Description
I	Tumour limited to the kidney; completely excised
II	Tumour extending outside of the kidney; completely excised
III	Residual tumour in the abdomen after surgery
	Invasion beyond capsule
	Macroscopic or microscopic residual tumour
	Involved lymph nodes (on biopsy)
	Rupture or spillage of tumour
	Tumour seedlings on peritoneal surfaces
	Pre-treatment biopsy
IV	Distant haematogenous metastases – lung, liver
V	Bilateral tumour at diagnosis

There are two approaches to treatment:

- The National Wilms' Tumour Study (NWTs), now the Children's Oncology Group (COG) (USA), where initial primary surgery is performed, with treatment according to the post-surgical stage.
- The principle of treatment of the International Society of Paediatric Oncology (SIOP) (Europe) is to give the child neo-adjuvant chemotherapy for 4 - 8 weeks to shrink and 'downstage' the tumour, with evidence from SIOP trials of fewer surgical complications. Surgery is then performed, with postoperative treatment according to the post-surgical stage.

In South Africa the European SIOP approach is used, because more than half of the tumours are extremely large and 70% of tumours in black patients are Stage III and IV. Therefore it will be beneficial to decrease the size and downstage the tumour. This does not apply to children under 11 months of age, as tumours are then often benign mesoblastic nephromas. All patients with Stage IV (metastatic) and Stage V (bilateral) tumours receive neo-adjuvant chemotherapy to assess response to treatment and to preserve renal function.

Chemotherapy is medication used to treat cancer cells throughout the body and affects fast-dividing cells. With radiation therapy high-energy X-rays reach cancer cells in a specific area of the body. In Wilms' tumour, radiation is directed at the site of the tumour in the abdomen, and sometimes also at the lungs or the liver.

Surgery

Total nephrectomy is the key step in treatment, but to be effective it has to be performed by an experienced paediatric surgeon. No laparoscopic surgery should be done, as the whole abdomen has to be explored. The approach should be through

a large abdominal (not lumbar) incision. The kidney and the tumour should be excised widely, together with the adjacent lymph nodes and peritoneal tissues.

Post-surgical treatment by stage and histology

In Stage I and II tumours with favourable histology, chemotherapy alone is sufficient. Two- or 3-drug regimens are used, which include vincristine, actinomycin D and doxorubicin. In Stage III tumours with favourable histology, 3-drug chemotherapy regimens are used plus radiation therapy to the tumour site and sometimes to the whole abdomen. Stage I tumours with unfavourable histology are treated as Stage I tumours with favourable histology. Stage II and III tumours with unfavourable histology require radiation therapy, and more intense chemotherapeutic regimens may be used.

Generally the prognosis for children with Wilms' tumour is very good. The overall survival rate is 90%.

Conclusion

Tremendous progress has been made in lowering morbidity in children with Wilms' tumour and reducing unnecessary treatment. There are ongoing clinical trials in the USA and Europe to safely further reduce chemotherapy in certain Stage I patients, precisely define histological risk groups, and improve outcome in high-risk patients with new and more effective chemotherapy. Basic research is being done to try to identify molecular and biological markers of prognosis.

Further reading

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In a nutshell

- Wilms' tumour or nephroblastoma is the most common primary renal tumour of childhood.
- Most cases are sporadic, and 12 - 15% of cases are associated with congenital abnormalities.
- The most common presentation is the presence of an abdominal swelling or mass.
- A thorough abdominal examination in children is necessary for early detection of an abdominal mass.
- The simplest investigation to diagnose Wilms' tumour is an ultrasound scan of the abdomen.
- Children with suspected Wilms' tumour should *always* be referred to a paediatric oncology unit.
- Treatment involves multimodality therapy.
- Surgery is the cornerstone of treatment, either primarily or after neo-adjuvant chemotherapy.
- Post-surgical therapy is stage and histology dependent and includes both chemotherapy and radiation therapy.
- The prognosis is good, with a 90% 5-year survival rate.