GLASGOW MEDICAL JOURNAL

VOL. 35 (Vol. 153 Old Series). FEBRUARY 1954 No. 2

THE JOURNAL OF THE ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW.

RENAL TUMOURS IN CHILDHOOD.

L. STUART SCOTT, M.B., F.R.C.S.(Ed.), F.R.F.P.S.G.
from the Royal Hospital for Sick Children, Glasgow.*

In 1828, Ebenezer Gairdner, an Edinburgh physician, published the first account of a renal tumour in a child, diagnosing the condition as fungus haematodes of the kidney. Since then many papers have been written on the subject and practically every form of tumour found in the adult kidney has, at one time or another, been reported in a child. Ever since Wilms (1899) published his classical monograph on the subject, it has been recognised that the vast majority of these neoplasms are embryomata. The complex histological appearance of these tumours, coupled with their prodigious capacity to kill, have intrigued alike the pathologist and the surgeon.

This contribution to the subject presents a series of 70 cases of renal tumour admitted to the Royal Hospital for Sick Children, Glasgow, between 1916 and 1952. The patients' ages ranged from two months to twelve years. The 70 tumours consisted of 61 embryomata, 1 haemangioma of renal pelvis, 1 carcinoma, 1 sarcoma, 1 teratoma and 5 malignant reticuloses. Some of the earlier cases were included in a previous series reported from this Hospital (McCurdy, 1934).

I. Embryoma (Wilms' Tumour).

In this group, the diagnosis was established histologically in 51 cases and, in the remaining 10 cases, was made on the macroscopic appearance of the tumour at laparotomy or autopsy.

Incidence. Embryoma is the commonest tumour of the urinary tract in childhood. It represented 21 per cent of 100 consecutive malignant tumours in children examined by Blacklock in the Pathology Department of this Hospital and accounted for 1 in 3,000 admissions to the Hospital over a period of 17 years (McCurdy, 1934).

Sex ratio. Both sexes were affected in more or less equal proportions in this series, there being 35 males and 26 females. This is consistent with the findings of Walker (1897) who reported 55 males and 51 females and Riches *et al.* (1951) who reported 93 males and 96 females.

* Present address: Urological Department, Western Infirmary, Glasgow.

Side involved. The tumour has no apparent predilection for one side or the other. The left kidney was involved in 36 cases, the right in 24 and in one case the condition was bilateral. Bilateral cases are not common and many large series have reported none. The only example in this series is typical of many previously reported cases, in that one side was obviously involved while the presence of a smaller, and hitherto unsuspected, tumour on the other side was only discovered at autopsy. Many authors still believe that the contralateral kidney is involved by metastatic spread from the original growth but cases of bilateral primary tumours, both detectable on clinical examination, have been reported (Sheach, 1953).

Age incidence. Cases have been reported in the foetus (Nicholson, 1931) and in adults up to the age of 75 years (Twinem, 1946) but the overwhelming majority of these tumours arise in the first five years of life. In the present series, 59 cases (96%) occurred in children of five years or under (Table 1).

TABLE 1.
Age groups.

Age group	Number of cases	%
Under 1 year	17	28
1 - 5 years	42	68.5
6 - 12 years	2	3.5

Symptomatology. The presenting symptom is generally a palpable swelling discovered accidentally by the child's mother. It is very unusual to get the classical ' triad ' of swelling, pain and haematuria, so commonly found in renal tumours in adults. Of the 61 cases in the present series, a palpable swelling was present in 60 (98%) and it was the first symptom in 28 (45%). Abdominal pain, not renal in type, was present in 18 (29%) and was the first symptom in 12 (20%). Haematuria was present in 13 (21%) and was the presenting symptom in 12 of these (20%). The classical ' triad ' was present in only 6 (9%) and in 9 cases the onset was ' silent,' *i.e.*, symptoms referable to the renal tract were absent, the tumour being discovered during investigation for general debility, loss of weight, etc. Haematuria is often stated to have a bad prognostic significance as it signifies extension into the pelvis and it is notable that all the patients with haematuria, in this series, died within nine months of operation.

Clinical findings. As a rule, the only clinical finding is a large mass occupying one of the flanks. It is rarely tender and, when large, the

overlying skin is stretched tightly across it and traversed by dilated veins (Fig. 1). Urinalysis is seldom of any help in the diagnosis and there is no significant change in the blood urea or non-protein nitrogen. Hypertension has been reported (Koons & Ruch, 1940 ; Bradley & Drake, 1949), both papers giving examples of relief of the hypertension following nephrectomy.

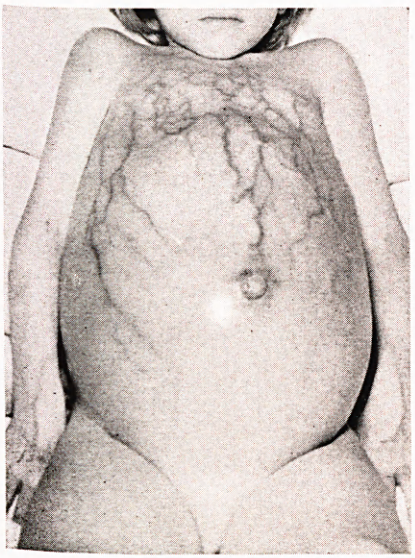

Fig. 1. Girl aged 5 years, with large left-sided Wilms' tumour showing the typical massive abdomen traversed by distended veins. (Infra-red photograph.)

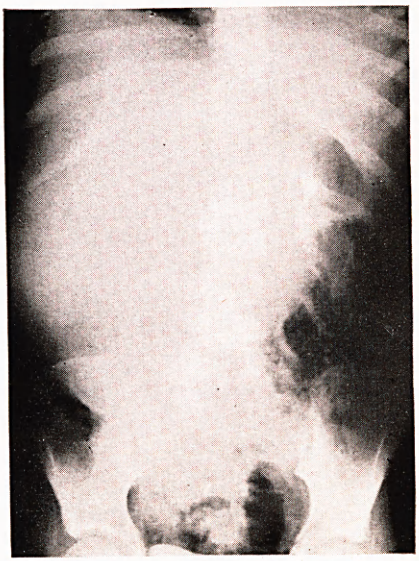

Fig. 2. Intravenous pyelogram showing the typical appearance in a large Wilms' tumour of the right kidney. The left kidney is normal but the right one is almost functionless. A massive soft-tissue shadow has obliterated the whole of the right side and part of the left side of the abdomen.

Radiological findings. Intravenous pyelography is carried out as a routine in this Clinic and, on the occasions when it has been found impossible to locate a vein, the opaque medium has been injected subcutaneously, using hyalase to hasten his absorption. Pyelography fulfils the double purpose of demonstrating the presence of the contralateral kidney and, at the same time, helping to differentiate the lesion from sympathicoblastoma, hydronephrosis and polycystic kidney, the three conditions with which embryoma is most likely to be confused. It has been stated (Harvey, 1950) that the pyelographic findings include mechanical distortion of the renal pelvis, obstruction of the ureter, elongation of the calyces and non-visualisation of the opaque medium on the affected side, the last-named being the commonest finding in the cases under review (Fig. 2).

Pathology. Adequate descriptions of the gross and microscopic appearances have been published elsewhere and need not be stressed in

Fig. 3. Wilms' tumour. The solid appearance of the tumour mass with irregular areas of necrosis is shown and, in particular, some kidney substance is almost invariably present, thinned out and contorted as in the example shown.

Fig. 4. Photomicrograph of a typical Wilms' tumour. In the centre, are primitive tubules surrounded by mesenchyme with undifferentiated hyperchromatic cellular tissue completing the picture. In this field there is no striated muscle. (H. & E. × 110)

this paper. The tumour arises within the kidney substance and, as it grows, it expands the renal capsule which surrounds the neoplasm for a considerable period of time before rupturing. It is usually solid although cystic spaces and areas of degeneration and haemorrhage are common. The surface vessels are generally distended and the neoplasm tends to be sharply demarcated from the compressed renal substance by a band of dense fibrous tissue (Fig. 3). The renal pelvis becomes narrowed, elongated or otherwise distorted but is seldom actually invaded until late in the course of the disease. The histological appearances are so varied that its terminology has included embryoma, nephroblastoma, embryonal sarcoma, rhabdomyosarcoma, chondromyxosarcoma, lipomyosarcoma, etc. Culp and Hartman (1948) actually found 53 different designations in the literature. Nevertheless, in a detailed study of an embryoma, where multiple sections have been taken at different levels, a composite picture can be built up which will give a clear-cut histological diagnosis (Fig. 4).

TABLE 2.

Sites of metastatic spread.

Site	Number
Lungs	12
Liver	6
Peritoneum ..	5
Mesenteric glands	3
Spine	2
Skull	1
Humerus ..	1
Scrotum	1

Metastases occurred in 20 (32%) of the cases and 15 cases (24.5%) developed a recurrence under the scar. The commonest site of secondary growth is undoubtedly the lungs (Fig. 5) but many other structures were involved (Table 2). Uncommon sites for a secondary tumour were (1) the scrotum, in which both tunicae were involved and (2) spinal cord involvement in one of the cases with vertebral metastases. There was renal vein involvement in two cases—in one of them the tumour was traced, at autopsy, along the renal vein and up the inferior vena cava to the right auricle (Fig. 6).

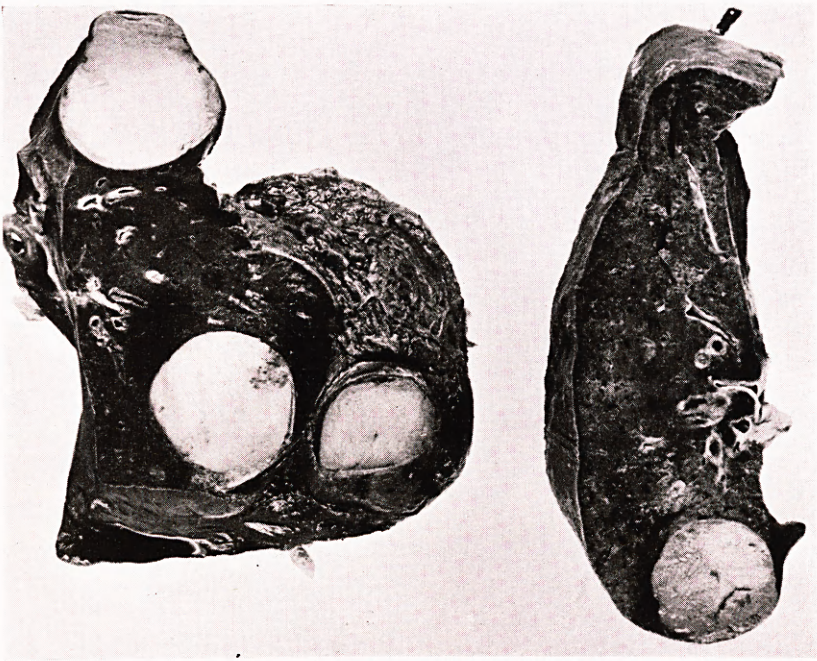

Fig. 5. Large spherical metastatic tumour masses in the lungs which have the typical histological pattern of Wilms' tumour.

Treatment. There is, as yet, no standard method of treatment for the condition but, in most centres, a combination of surgery and radiotherapy has been found to give the best results. The different forms of treatment that were employed in the present series are summarized in Table 3. Of the 61 cases reported, 8 had a laparotomy performed but were found to be hopelessly inoperable and 12 were admitted in a moribund condition and died before operative treatment could be carried out ; all these cases occurred in the years before the value of palliative radiotherapy was appreciated.

In view of the fact that the vast majority of recurrences occur within nine months of operation, the standard of probable ' cure ' is generally taken as a freedom from recurrence or metastases for two years after operation. While accepting survival for this statutory period as a probable cure, one must bear in mind that recurrences have been reported as late as five years post-operatively (Gross & Neuhauser, 1950), and an embryoma of the contralateral kidney has been reported ten years after apparently successful treatment (Ritter & Scott, 1949).

Although 61 cases have been included under the heading of 'embryoma' 10 of these are excluded from the statistical analysis as there is no histological proof of the diagnosis. The fate of 8 of the 51 proved cases is unknown. Of the 43 cases which have been followed up, 35 are known

Fig. 6. Wilms' tumour growing in the lower half of the right kidney with neoplastic invasion of the renal vein and inferior vena cava—the latter has been outlined in the photograph. There is obstructive hydronephrosis in the right kidney but the left kidney is normal.

TABLE 3.

Method of treatment employed.

Treatment employed	Number of cases
Nephrectomy alone	24
Nephrectomy and post-operative radiotherapy ..	12
Pre-operative radiotherapy and nephrectomy ..	2
Nephrectomy with pre- and post-operative therapy	2
Radiotherapy alone	1
No treatment	20
Total	61

to have died and only 6 cases can be regarded as probable cures, based on the above standard (Table 4). Two other cases are alive and free from recurrence but have not yet reached the 2 year 'standard' of probable cure.

TABLE 4.

Details of probable cures.

Age	Sex	Treatment	Period of survival
1 yr. 3 mths.	Male	Nephrectomy alone	24 years
5 yrs. 3 mths.	Male	Nephrectomy and post-operative therapy ..	15 years
10 months	Male	Nephrectomy and post-operative therapy ..	8 years
10 months	Male	Nephrectomy and post-operative therapy ..	6 years
2 months	Male	Nephrectomy alone	3 years
2 years	Female	Nephrectomy and post-operative therapy ..	2 years

Of the 39 patients in whom the affected kidney was removed, 31 are known to have died; 15 of these developed a recurrence under the scar at periods ranging from two to ten months after operation. This represents a survival rate of 15.4% in treated cases with an over all mortality of 88.3%. The immediate operative mortality of the series was 4.5%.

II. Haemangioma of renal pelvis.

In spite of the fact that Virchow (1867) stated that, with the exception of the liver, the kidney is the organ most frequently the seat of angioma, a perusal of the literature on the subject tends to show that, far from being a common site, it is actually a great rarity. Kidd (1924) stated that, in a series of 2,500 autopsies in which he had personally searched for its presence, he had never found one and Mackey (1930) stated that Muir found no specimen of renal angioma in any of his autopsies in Glasgow.

Case 1. A girl, aged 6 years, was admitted in 1931 for investigation of recurrent attacks of painless haematuria of four months' duration. No swelling was palpable in either loin. The urine was blood-stained and acid. Numerous red blood cells, together with a few casts, were seen on microscopic examination. The non-protein nitrogen was 37.7 mg. per cent and the urea clearance and concentration tests were normal. The urine was repeatedly examined for evidence of tuberculosis with negative results. Cystoscopy revealed a normal healthy bladder but blood was seen coming from the right ureteric orifice. Nephrectomy was performed and the child made an uninterrupted recovery.

On bisecting the kidney, a small vascular tumour was found in the pelvis and histological examination, by Professor Blacklock, showed it to be a small haemangioma in the sub-epithelial tissues.

III. Sarcoma.

The diagnosis of sarcoma of the kidney in a child has nowadays tended to fall into disrepute. A careful examination of the tumour generally shows the presence of primitive renal tubules and glomeruli, revealing the fact that the correct histological diagnosis is embryoma. With the exception of the one case, quoted below, whose histological sections are not available for review, all the ' sarcomata ' which have been re-examined have been found to contain the above structures and have, therefore, been re-labelled ' embryomata.'

Case 2. A boy, aged 4 years, was admitted in September, 1933, with a left sided renal tumour. Nephrectomy was performed and the child made an excellent recovery. The histological diagnosis was a mixed cell sarcoma with extensive myxosarcomatous change. He was readmitted in January, 1935, with a large mass under the scar which was proved, by biopsy, to be a recurrence of the previous growth.

IV. Carcinoma.

Only one case had been diagnosed as carcinoma, but the histological evidence is no longer available. As it is an accepted fact that embryomata show bizarre and widely differing patterns in different parts of the same tumour, it is felt that this tumour might well have fallen into the embryoma group, had these sections been available for review. Willis (1953) states that he has never seen a renal carcinoma in a child but quotes one case of clear-cell carcinoma reported by Nicholls (1936).

Case 3. A girl, aged 3 years, was admitted in 1941 with a painful swelling in her right loin and a diagnosis of renal tumour was made on the clinical and radiological findings. Laparotomy was performed but the tumour, which was involving the right kidney, was hopelessly inoperable and a small portion was taken for biopsy. Her condition deteriorated rapidly and she was eventually sent home to die. No autopsy was performed. The histological report stated that there were numerous round cells present with large pale nuclei. The cells were formed into an alveolar arrangement, small groups being separated by strands of connective tissue. Many mitotic figures were present. As no attempt to form renal elements was seen in this small biopsy specimen, the appearances were considered to be very suggestive of a highly malignant anaplastic carcinoma.

V. Teratoma.

Teratomata of the kidney are also extremely rare but are recognised as a definite clincal entity, differing from embryomata in that structures derived from all three germ layers are represented (Willis, 1953). There was one classical example of a true teratoma in the present series.

Case 4. A boy, aged 3 weeks, was admitted in 1925 because his leg had become swollen. He was six weeks premature and exhibited multiple congenital deformities including spina bifida, meningocele and hypospadias. A large mass was found to be present in the left hypochondrium. There was no history of haematuria or pyuria. His abdomen became increasingly distended and he died within a few weeks of admission. At autopsy, a large retro-peritoneal tumour containing cystic spaces and areas of haemorrhage and necrosis was found on the left side. The remains of the left kidney were compressed into a narrow rind and stretched across its upper pole (Fig. 7). Histologically, the cystic spaces were seen to be lined by

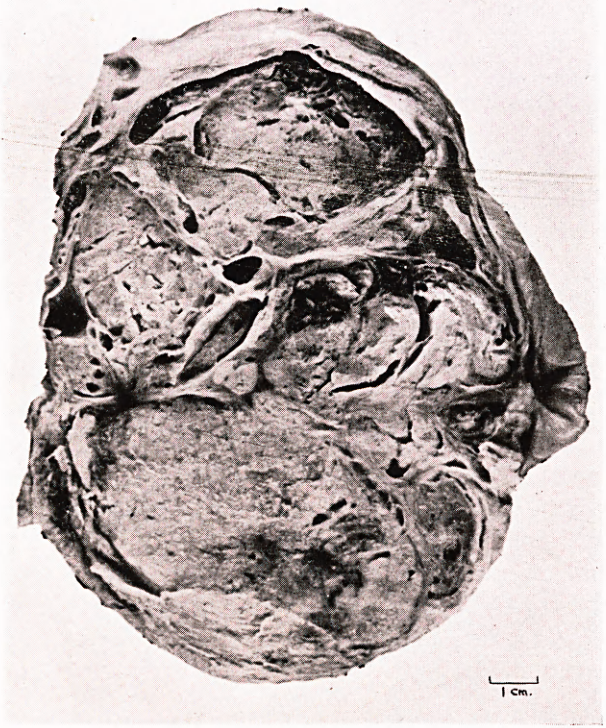

Fig. 7. Case 4. Renal teratoma. A thin band of tissue at the upper pole of the tumour was all the recognisable normal kidney substance. The tumour is ovoid and varies in consistency. Cysts containing gelatinous fluid, cartilage and sebaceous material can be seen together with areas of necrosis.

squamous epithelium. Tactile corpuscles, poorly developed hair-follicles, bone, cartilage, sweat glands, bronchial epithelium, keratinised squamous epithelium and myelinated nerve fibres were all identified, giving the complex picture of a true renal teratoma (Fig. 8).

VI. Malignant reticulosis.

Four cases of lymphosarcoma and one of lymphadenoma have been grouped together under one heading, as suggested by Gall and Mallory (1942) and others. Coley (1907) was one of the first to propose that the name ' Hodgkin's disease ' should be replaced by lymphosarcomatosis and, since then, many authors have written in support of this view. Harput *et al.* (1945) reported six cases in which the diagnosis had been changed from lymphadenoma to lymphosarcoma and then back again to the original diagnosis. At autopsy, each case showed areas of lymphadenoma, lymphosarcoma and reticulum-cell sarcoma. In the writer's opinion the general term of malignant reticulosis covers all these histological variants.

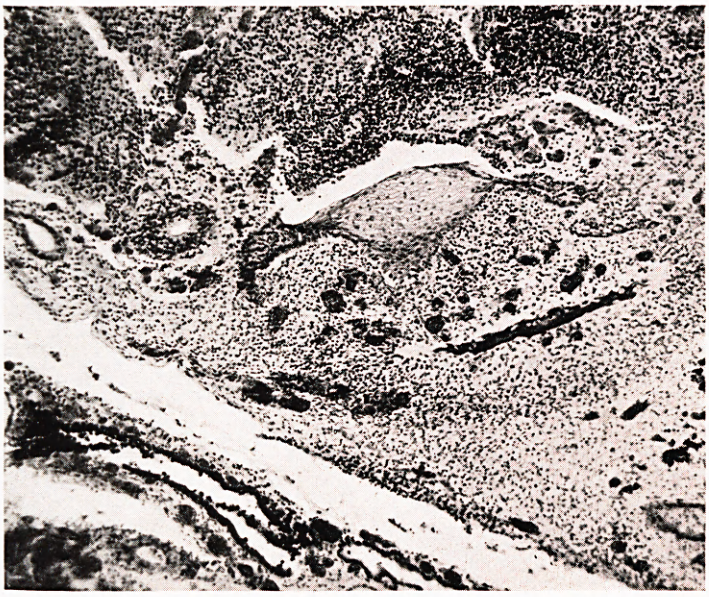

Fig. 8. Case 4. Renal teratoma. Photomicrograph to indicate the main features on which the diagnosis was made. In the centre squamous epithelium is shown. There is a rosette to the left centre, typical of neuroblastic growth. Bone has formed below and to the right of the squamous epithelium, surrounded by undifferentiated mesenchyme. In the left lower corner, pigmented cubical epithelium may be seen lining a cleft; the pigment is melanin and the tissue is related to the choroid, a feature common to ovarian and other teratoma. (H. & E. × 110)

Case 5. A boy, aged 8 years, was admitted in 1924 with vomiting, ascites and pleural effusion. Palpable masses were detected in the epigastrium and right iliac fossa. The ascites was tapped repeatedly but he died within a few weeks of admission. At post-mortem, he was found to have lymphosarcoma of the small bowel with secondaries in liver, peritoneum and pleura. Both kidneys were extensively involved, as were the abdominal and mediastinal glands.

Case 6. A boy, aged 3 years, was admitted in 1926 with diarrhoea and a palpable mass in the right iliac fossa. There was no history of urinary upset. He died three days later following a severe haematemesis together with rectal haemorrhage and epistaxis. At post-mortem, he was found to have a lymphosarcoma of the caecum with involvement of the abdominal and mediastinal glands and both kidneys.

Case 7. A boy, aged 1 year, was admitted in 1940 with bilateral renal swellings. There was no bowel or urinary upset. He died within a few days of admission. At autopsy, both kidneys were found to be almost entirely replaced by lymphosarcoma and there was extensive involvement of the abdominal, mediastinal and cervical glands.

Case 8. A boy, aged 10 years, was admitted in 1944 with swellings in the scalp and lower jaw together with slight proptosis of the left eye. There was no history of urinary upset. Palpable masses were detected in the left hypochrondrium and the right iliac fossa. His condition steadily deteriorated and he died within a few weeks. At autopsy, both kidneys showed massive invasion with lymphosarcoma (Fig. 9). The caecum was also involved and the small bowel was infiltrated throughout its length. There was generalized glandular involvement.

Case 9. A boy, aged 5 years, was admitted in 1927 with diarrhoea, a right-sided abdominal swelling, lassitude, anorexia and night sweats together with swelling of face and legs. A palpable mass was detected in the right loin and the liver was enlarged. There was no urinary upset. He died shortly after admission. Autopsy revealed a large white tumour at the lower pole of the right kidney. The glands were all entensively involved and the spleen was infiltrated. Histological examination of the renal tumour showed typical lymphadenomatous changes in an advanced stage of fibrosis.

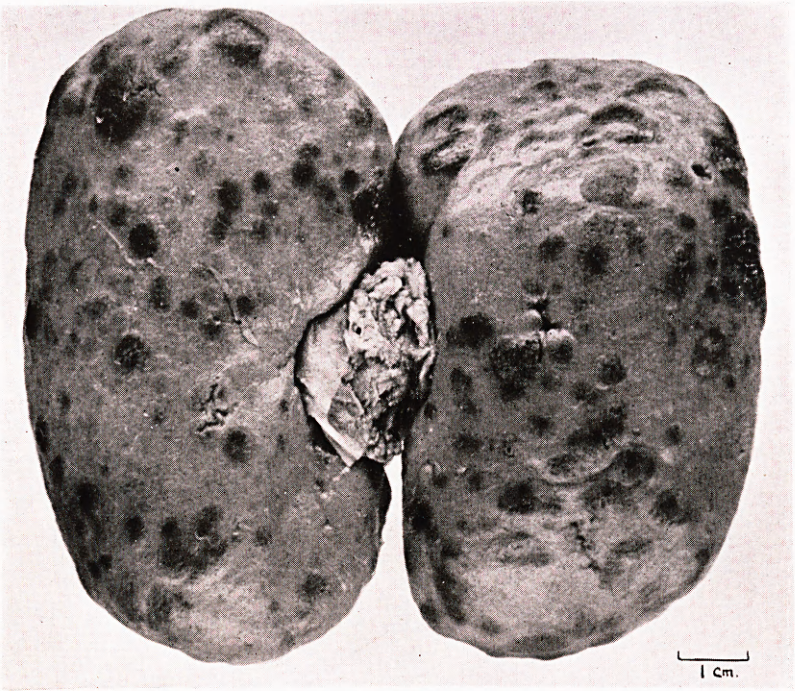

Fig. 9. Case 8. Subcapsular surface of a bisected kidney with numerous secondary neoplastic growths which have the histological pattern of lymphosarcoma.

These five cases are presented in some detail because, although the kidneys were extensively destroyed in all the cases, in only two cases were the renal tumours palpable and none of them exhibited symptoms pointing to renal damage.

SUMMARY AND CONCLUSIONS.

A variety of tumours of the kidney in childhood is reported. It is noted that the overwhelming majority belong to the embryoma group. Details of age, sex and side involved in 61 cases of embryoma are given and the exceptionally high mortality rate from this tumour is noted. The different forms of treatment employed have been mentioned and, although Ladd and White (1941) believe that surgery alone is the answer and Dean (1945) puts forward the view that they should be treated by radiotherapy alone, Riches (1952) states the view of most surgeons when he says, ' surgery and irradiation must work in collaboration and not in competition.'

Re-examination of many cases, previously diagnosed as sarcoma, has shown that careful study of multiple sections of the kidney, cut at different levels, will always show the presence of primitive glomeruli and tubules and a plea is put forward for abandoning the histological diagnosis of renal sarcoma in this age group. It is also stressed that the diagnosis of carcinoma of the kidney in childhood is very improbable (Willis, 1953).

It is noted that haemangioma of the kidney, of which one example is reported, is an extremely rare condition, although occasional cases are to be found in the literature, some of which have had tumours large enough to be detectable on urography (Jenkins & Drennan, 1928 ; Jacobs & Rosenberg, 1927), the latter naming the condition ' telangiectasis of the kidney.'

One case of teratoma of the kidney is also reported, together with five cases in which the kidneys were involved in a generalised malignant reticulosis. Before the diagnosis of teratoma of the kidney can be made, all three germ layers must be identified histologically and it is pointed out that the use of the word teratoma as a synonym for Wilms' tumour, so commonly seen in the literature, is quite inaccurate.

ACKNOWLEDGEMENTS.

I am indebted to the members of the staff of the Royal Hospital for Sick Children, Glasgow, for permitting access to their records and, in particular, I wish to thank Mr. Matthew White for providing the stimulus for the investigation and for invaluable advice and criticism in the preparation of the manuscript. I also wish to thank Dr. A. M. Macdonald for much time and energy spent in re-examining the histological sections of the tumours reported, and finally the technicians of the Pathology Department for preparing the specimens and Mr. J. L. A. Evatt for the photographs.

REFERENCES.

Bradley, J. E. & Drake, M. E. (1949). *J. Pediat.* **35** : 710
Coley, W. B. (1907). *N.Y. med. J.* **85** : 577
Culp, O. S. & Hartman, F. W. (1948). *J. Urol.* **60** : 552
Dean, A. L. (1945). *N.Y. State. J. Med.* **45** : 1213
Gairdner, E. (1828). *Edinb. med. surg. J.* **29** : 312
Gall, E. A. & Mallory, T. B. (1942). *Amer. J. Path.* **18** : 381
Gross, R. E. & Neuhauser, E. B. D. (1950). *Pediatrics.* **6** : 843
Harput, P. A., Miller, F. R. & Erf, A. L. (1945). *Amer. J. Path.* **21** : 233
Harvey, R. M. (1950). *Radiology.* **54** : 689
Jenkins, J. A. & Drennan, A. M. (1928). *J. Urol.* **20** : 97
Jacobs, P. A. & Rosenberg, W. (1927). *J. Urol.* **17** : 337
Kidd, F. (1924). *Proc. Roy. Soc. Med.* **17** : 56
Koons, K. M. & Ruch, M. K. (1940). *J. Amer. med. Ass.* **115** : 1097
Ladd, W. E. & White, R. R. (1941). *J. Amer. med. Ass.* **117** : 1858
McCurdy, G. A. (1934). *J. Path. Bact.* **39** : 623
Mackey, W. A. (1930). *Brit. J. Surg.* **18** : 308
Nicholls, M. F. (1936). *Proc. Roy. Soc. Med.* **29** : 372
Nicholson, G. W. (1931). *J. Path. Bact.* **34** : 711
Riches, E. W. (1952). *Proc. Roy. Soc. Med.* **45** : 191
Riches, E. W., Griffiths, I. H. & Thackray, A. C. (1951). *Brit. J. Urol.* **23** : 297
Ritter, J. A. & Scott, E. S. (1949). *J. Pediat.* **34** : 753
Sheach, J. M. (1953). *Brit. J. Urol.* **25** : 109
Twinem, F. P. (1946). *J. Urol.* **55** : 246
Virchow, R. (1867). *Die Krankhaften Geschwulste*, **1** : 306, Berlin
Walker, G. (1897). *Ann. Surg.* **26** : 529
Willis, R. A. (1953). *Pathology of Tumours*, 2nd edn. London : Butterworth
Wilms, M. (1899). *Die Mischgeschwulste der Niere*, Leipzig