THE DIAGNOSIS AND TREATMENT

OF

EMBRYONIC RENAL TUMOURS

IN

INFANCY AND CHILDHOOD

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By

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INTRODUCTION

Renal tumours may appear at any age but they are commonest at the extremes of life. In the first decade, the tumour generally takes the form of an embryoma or, on rare occasions, a teratoma; whereas in adult life, the predominant tumour of the kidney is the hypernephroma or adenocarcinoma.

The embryonic type of renal tumour, with which this paper is concerned, is generally considered to be the prerogative of infants and young children but many cases have been reported in adults and they are not uncommon in domestic animals - cases having been reported in oxen (Feldman, 1932), sheep (Feldman, 1933) rabbits (Bell and Henrici, 1916) and rats (Bullock and Curtis, 1930); and they are the commonest malignant tumour in the pig (Willis 1953).

Owing to the fact that these tumours seldom produce symptoms referable to the renal tract, the diagnosis was, for many years, generally made in the autopsy room. Earlier diagnosis has become possible as a result of the introduction of pyelography but even this, coupled with improved surgical technique and the advent of radiotherapy, has failed to reduce the overall mortality below 80 per cent.

This paper is based on the writer's personal experience of five of these rare tumours, together with a detailed analysis of the clinical, histological and post-mortem findings of a further fifty-eight cases of embryonic renal tumour admitted to the Royal Hospital for Sick Children, Glasgow, between 1916 and 1953. The fortunate few, who have survived, have either been personally examined or have replied to a letter requesting details of their present health.

Although this is a comparatively large series of cases of a relatively rare condition, it is appreciated that no single hospital can amass a sufficient number of cases to allow satisfactory evaluation of the different methods of diagnosis and treatment and, for this reason, full use has been made of previously published cases, which have been abstracted from an extensive review of over two hundred papers on the subject.

INCIDENCE

Embryomata are the commonest tumours of the urinary tract in childhood. They represented 21 per cent of 100 consecutive malignant tumours examined in the Pathology Department of the Royal Hospital for Sick Children, Glasgow, (Scott, 1954) and accounted for 1 in 3000 admissions to this hospital.

In an effort to establish the frequency of these tumours as causes of death in childhood, the Registrar General's Annual Reports (Scotland) have been carefully analysed for the years 1941 to 1949 inclusive. During this period, there were 82,007 deaths in children under the age of 12 years, of which 61 (0.07 per cent) were due to renal tumours.

The incidence of tumours of the kidney in relation to other malignant tumours and to diseases of the urinary tract have also been abstracted from these statistical Reports and are shown in Tables I and II.

These Tables show that renal tumours were responsible for 17 per cent of all tumour-deaths in this age group and they were second only to nephritis as a fatal disease of the urinary tract in childhood.

TABLE I

Deaths due to Malignant Tumours in Childhood

Scotland (1941-1949)

Site of Tumour	No. of Deaths.
Nervous System	80.
Kidney	61.
Digestive System	46.
Buccal Cavity and Pharynx	15.
Respiratory System	11.
Male Genital Organs	5.
Female Genital Organs	5.
Skin	4.
Other Sites - Unspecified	109.

TABLE II

Deaths from Diseases of the Urinary Tract in Childhood.

Scotland (1941-1949)

Disease	No. of Deaths.
Acute Nephritis	183.
Chronic Nephritis	92.
Renal Tumours	61.
Diseases of Male Genitalia	15.
Diseases of Bladder	7.
Diseases of Urethra	4.
Urinary Calculi	4.

CHAPTER I HISTORICAL

The value of the historical approach to medical subjects has already been amply demonstrated by many famous medical men. To determine the exact date of a new procedure or idea may not be vitally important but to follow the evolution of these related facts, in chronological order, may show the subject in a truer perspective. The purpose of this chapter is to illustrate the highlights in the development of ideas and procedures relative to the study of malignant tumours of the kidney in children.

In the Edinburgh Medical and Surgical Journal of 1828, Ebenezer Gairdner described a case of bilateral renal tumours in a three-year old child and this paper has now become universally accepted as the first published account of a renal tumour in this age group. It was recently pointed out, however, that credit for the original description should be given to Rance who, in 1814, reported bilateral renal tumours in a seventeen-month old girl (Scott, 1955).

It is, of course, quite obvious from Gairdner's paper that he was aware of similar cases having been met with before 1828, as he concludes his paper by saying, "... not that there are wanting in our records a number of similar cases in which the nature of the disease was not discovered till after death."

Further proof that earlier physicians had encountered these tumours is given by Eve who, in a paper read before the Pathological Society of London in 1882, stated that there was a specimen (No.1908) in the Hunterian Museum of the Royal College of Surgeons which had been "Bottled" in the late eighteenth centry and which was described on the label as "The kidneys of a child with medullary tumours."

Prior to 1870, malignant tumours of the kidney in children, as well as in adults, were all considered to be carcinomatous in nature and the terms "medullary cancer", "encephaloid cancer" or "encaphaloid degeneration" were used to designate these malignant growths. Credit is generally given to Catanni as being the first to recognise the occurrence of sarcomatous elements in these tumours, but in actual fact, reference was made to the connective tissue changes by Smith (1865), who, describing a tumour of the kidney found at post-mortem examination in a

boy aged nineteen-months, noted that "... the microscopic structure was seen to be of a fibro-cellular nature."

It was very soon realised that renal tumours in children were of a most unusual type and, for that reason, they received particular attention from pathologists; notably Eberth (1872), Cohnheim (1875), Birch-Hirschfeld (1894) and Wilms (1899), each of these men, in turn, propounding a new theory for the pathogenesis of the tumour in an effort to explain the presence of such apparently exotic structures as striated muscle fibres.

Eberth gave the first satisfactory histological description of the tumour and named it an adeno-myo-sarcoma. It was he who first identified the presence of striated muscle, at the same time observing the peculiar embryonic character of the tumour. He attempted to explain the muscular elements by assuming that, in some way or other, portions of the Wolffian body became included in the kidney and subsequently developed in it.

In 1875, Cohnheim propounded the theory that these muscle fibres originated from the primitive vertebrae because, as he pointed out, these vertebrae lie in almost direct contact with the original anlage of the urogenital tract.

Kocher and Langhans (1878) reported the first example of an embryonic renal tumour in an adult and, in 1884, Paul demonstrated their presence at the opposite extreme of life when he described the first case of "congenital renal sarcoma" to be found in a still-born child.

In 1886, Ribbert put forward the theory that these tumours resulted from changes in the aberrant totipotent sex cells at the blastomere stage, the changes actually taking place prior to the development of the germ layers.

In 1894, there appeared the epochal paper of Birch-Hirschfeld. He collected a series of cases from the literature and brought forth the hypothesis that these "embryonic adenosarcomata", as he named them, had their histogenic origin from the Wolffian body, thereby tending, in a way, to corroborate Eberth and Cohnheim.

In 1899, Wilms published his classical monograph on the subject and, in this, he not only agreed with Birch-Hirschfeld but went further, deriving these tumours from embryonic tissue in its very earliest development. By this hypothesis, the striated muscle was derived from the myotome; bone and cartilage from the sclerotome or vertebral anlage and glandular elements from the Wolffian body; while the fibrous tissue, fat and smooth muscle originated from the mesenchyme.

This theory only differs from Ribbert's in the time of displacement of the tumour anlage - being later than Ribbert's idea but before the mesodermal derivatives have been differentiated. Ever since this monograph was published, his name has been associated with the common eponym "Wilms' Tumour." This is generally considered as a renal tumour of childhood although, in actual fact, he studied the entire field of mixed tumours and a close examination of his book has revealed the incredible fact that his deductions on renal tumours were based on the detailed histological study of only five cases plus a brief review of forty-six cases which he had collected from the literature.

Busse (1899) later attacked Birch-Hirschfäd's theory, bringing forth the fact that remnants of the Wolffian body had never been found in the kidney. He, as well as Muus (1899) considered these mixed tumours as originating from the renal blastema and thought that the presence of epithelial cells and muscle fibres could be explained by metaplasia. In 1940, in his book "Neoplastic Diseases," Ewing expressed the belief that the theory of Muus and Busse was probably the most acceptable and noted that, by it, can be explained why some tumours have the appearance of embryonal adenocarcinoma.

In 1931, Nicholson, on the basis of a study of an embryoma in the kidney of a full-term foetus, stated that, in his view, the tumour itself is essentially a malformation of the embryonic kidney. He believes that the change takes place at the matanephros stage and supports this view by the fact that both constituents of the kidney -- the metanephrogenic blastema and the ureteric diverticulum of the Wolffian duct -- are present in the tumour. He points out that, in the foetal kidney, a considerable number of plain muscle fibres surround the collecting tubules and connective tissue is present in excess, differing thus from the adult kidney which is very sparsely supplied with connective tissue and, in which, muscle is restricted to a few plain fibres lying beneath the mucous membrane of the pelvis and in the capsule.

Finally in 1953, in the second edition of his book "Pathology of Tumours, Willis states that "... the epithelial and non-epithelial components are composed of indigenous renal tissues. The seemingly exotic components, such as skeletal tissues and striated muscle, are the products of aberrant differentiation in the same primitive embryonic blastema."

He continues, " ... it should be noted that, in the normal kidney, the formation of new nephrons from the embryonic nephrogenic cap continues throughout foetal life and is still in progress for a brief time after birth. It is therefore possible that embryonic tumours may take origin at any time during the foetal or early post-natal period."

The evolution of urography

Since Morgagni (1761), declared that the diagnosis of disease of the kidney and urinary organs was "... uncertain and fallacious," great strides have been made in this field of study. Diagnosis, prior to the use of x-rays, was based entirely on the acute clinical sense of the surgeon and this, coupled with the fact that embryomata seldom reveal any symptoms referable to the renal tract, generally led to the diagnosis being made in the post-mortem room.

In 1879, Nitze introduced the first practical cystoscope, using an incandescent lamp to obtain the necessary illumination but it was not until 1906 that Voelker and von Lichtenberg, while experimenting with different media for cystography, accidentally discovered that, in some cases, overdistension of the bladder caused a reflux of dye up the ureter and into the renal pelvis. This chance finding led them to consider the possibility of outlining the renal tract from below and employing x-rays in the diagnosis of renal conditions. They used a 2 per cent solution of collargol, introduced through ureteric catheters, but the objections to the use of silver compound were numerous, the chief one being their toxicity.

These toxic properties soon led to them being supplanted by thorium nitrate but this, in turn, had to be abandoned because of its irritant action on the bladder mucosa.

After the introduction of the halogen compounds in 1918 and the encouraging results obtained by Rountree and his associates using sodium iodide, it soon became obvious that pyelography was not only possible but that full clinical success only awaited the discovery of a satisfactory contrast medium.

Roseno (1928), using a combination of urea and sodium iodide called "Pyelognost", was the first to report a series of cases with clear-cut clinical interpretation; that this was not entirely successful was due only to its very slow elimination from the body.

Lenarduzzi and Pecco (1927) conducted a series of experiments in animals, in which they attempted to increase the intensity of the contrast medium by first tying off the ureters. Although this method appeared, at first sight, to have no practical application in the human, it led, indirectly, to Ziegler and Kohler (1929) employing the same theoretical principle when they initiated the use of external compression of the ureter.

The quest for a non-toxic, easily visualised medium was continued at the Altona Clinic in Germany, where Lichtwitz and von Lichtenberg began to experiment with a compound called Uroselectan, which had previously been synthesised by Professor Binz. Swick, from the same Clinic, reported the results of these experiments to the Urological Congress at Munich in 1929 and stated that, as far as could be ascertained, Uroselectan appeared, at last, to be the ideal medium. Although Uroselectan has now been supplanted by newer and safer media, the work of these pioneers in urography has now converted the diagnosis of renal conditions from the "guess" and the "clinical impression" to an orderly scientific procedure.

The changing face of surgical opinion

Although advances in the treatment of these tumours cannot claim to have kept abreast with the improvement in diagnosis, a better understanding of pre- and post-operative management and improved surgical technique have, together, considerably lowered the immediate post-operative mortality.

In 1876 Heuter, a German surgeon, attempted the first abdominal nephrectomy for a malignant renal tumour in a girl aged four years. He was unsuccessful but two years later Jessop, writing in the Lancet, reported the first successful operation through a lumbar incision, in a boy of two and a half years. He noted that there was free haemorrhage but, in spite of this, he managed to remove a sixteen pound tumour, closing the wound round a whipcord drain. The child survived the operation but died nine months later from a recurrence under the scar and it was not until sixteen years later that Israel, employing a T-shaped lumbar incision in a six year old girl, reported the first five-year "cure".

In 1894, in a paper on renal tumours in childhood, Keith stated that, "... in young children it is doubtful whether it is ever right to operate; indeed such operations must be looked upon as a surgical

possibility rather than as an operation of advantage to the patient." This somewhat sweeping statement is not without some justification as a perusal of the literature shows that the results of nephrectomy in children, at the end of the nineteenth century, were indeed quite frightening. In 1884, Weir had an immediate operative mortality of 50 per cent and in 1885, Gross quoted a figure of 44 per cent. In 1887, Taylor analysed his own operative mortality in children and found that, out of twenty deaths following nephrectomy, seven had died from "... accidents occurring during the operation" and a further eight died within a few days from shock or peritonitis. This latter condition was also invoked as a major bugbear by Czerny, who found that out of twelve nephrectomies in his own Clinic prior to 1890, there had been no fewer than nine operative deaths whereas, after 1890, he had successfully removed nine renal tumours from children with no deaths at all. It is significant that, in the year 1890, he changed from a transperitoneal approach to an extraperitoneal one and he attributes this vast improvement in his immediate results to avoidance of the peritoneal cavity and to the cessation of use of the carbolic spray in his wounds.

In 1896, deep x-rays were used to treat a patient with carcinoma of the breast but it was not until 1916 that Friedlander reported the use of radiotherapy as a primary treatment of renal tumours in children.

Foster and Mendilharzu (1925) treated a fourteen-month old boy by implanting radium needles directly into the tumour; noting that, by the end of the second week, the tumour had completely disappeared. The child was alive and well two years later. Radium needles were also recommended by Young & Davis (1926) but are no longer considered to be of any value in the treatment of these tumours.

Although radiotherapy, used in conjunction with surgery, is the treatment of choice in most clinics at the present day, its exact role is still a topic of much controversy as will be seen in a later chapter.

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CHAPTER II — BILATERAL EMBRYOMATA

Although bilateral tumours are not uncommon in paired organs, most of the published cases of bilateral embryomata have been discovered accidentally at autopsy and there is no doubt that many cases, which have been reported as bilateral, actually represent a unilateral primary tumour with secondary involvement of the opposite kidney.

While many cases have probably been overlooked and others may not have been reported, bilateral embryomata are still a great rarity and, for that reason, a separate complete chapter has been devoted to the condition.

Incidence of bilateral cases

In 1897, Walker collected 141 cases of renal tumour in childhood, of which no less than 10 were bilateral but he failed to give any information about them and Eve, in a paper read before the Pathological Society of London in 1882, described 6 collected cases, of which 4 were bilateral.

In 44 cases of embryoma reported by Weisal, Dockerty & Priestley (1943), from the Mayo Clinic, there were no examples of bilateral involvement and according to Campbell (1948), none were found by Dean in 100 cases seen at the Memorial Hospital, New York. In the British Association of Urological Surgeons' statistical review of renal tumours, 189 cases of embryoma were collected and only one was bilateral (Riches et al, 1951). In a recent paper on the subject, Scott (1955) reported 906 cases of embryoma, collected from the literature, of which 33 were bilateral - an incidence of 3.6 per cent. There is only one example of primary bilateral involvement in the series of cases under review and a brief resume of the case history is recorded below.

Case 7.

Female, aged 11 months. Three months before admission, her mother noticed a swelling on the left side of her abdomen and, since then, she had lost her appetite and become obstinately constipated. Latterly, she had vomited up every feed. On examination, a large non-tender swelling was found to extend from the left costal margin down to the umbilicus, completely filling the left hypochondrium and left loin. A straight x-ray of her abdomen revealed a large soft tissue shadow obliterating the whole of the left side of the abdomen and displacing the bowel to the right.

Case 7 (Continued)

A left nephrectomy was performed but the tumour was very adherent to the splenic flexure of the colon. Her condition deteriorated very rapidly during the course of the operation and she died ten hours later. At autopsy, the right kidney was found to be enlarged and numerous pale areas of tumour were scattered throughout its substance. There was no evidence of any tumour in the renal vessels and none of the local lymphatics were involved. Histological examination of the left kidney revealed the typical picture of an embryoma and this picture was identically reproduced in each of the pale areas that had been noted on naked-eye examination of the opposite kidney.

This case is very interesting in that the opposite kidney appeared to be the seat of multiple metastatic embryomata although there was no evidence of tumour growth in the lymphatics or blood vessels and there were no other metastases elsewhere in the body.

Review of the literature

In order to facilitate discussion and, at the same time prevent repetition, the cases that have previously been reported have been classified into groups - based on the methods by which they were diagnosed.

TABLE III

Classification of Bilateral Embryomata

GROUP I:	Cases in which bilateral embryomata, previously undiagnosed, were found at autopsy.
GROUP II:	Cases in which bilateral renal swellings were palpable on admission.
GROUP III:	Cases in which a unilateral tumour was palpable on admission but, in which, the contra-lateral kidney was found to be involved, on clinical examination, at a later date.
GROUP IV:	Cases in which a unilateral tumour was palpable on admission but the contra-lateral kidney was found to be involved at autopsy.
GROUP V:	This represents a miscellaneous group of cases that have been reported in the literature, in which neither the history nor the clinical findings were recorded.

TABLE IV

Summary of 32 Published Cases

Group	Author	Sex	Age
I	Gairdner (1828)	F	3 years.
	Eberth (1872)	F	17 months.
	Cohnheim (1875)	?	10 months.
	Landsberger (1877)	?	7 months.
	Abercrombie (1880)	M	18 months.
	Stern & Newns (1938)	M	2 years.
	Kerr (1939)	M	3½ years.
	Campbell (1948)	M	24 days.
II	Loughnane (1914)	F	18 months.
	Ladd (1938)	F	6½ years.
	Campbell (1948)	M	18 months.
	Harrison (1948)	M	1 year.
	Barr & Schulte (1950)	M	4½ years.
	Rusche (1951)	?	?
	Sheach (1953)	F	1 year.
III	Rance (1814)	F	17 months.
	Strong (1903)	M	4 years.
	Kretschmer & Hibbs (1931)	M	1 year.
IV	Abercrombie (1879)	M	3 years.
	Abercrombie (1879)	F	2 years.
	Abercrombie (1879)	F	4 years.
	Kretschmer & Hibbs (1931)	M	5 months.
	Ueda (1935)	?	8 months.
V	A group of 9 cases reported by Hansen (1873); Weigert (1876); Eve (1882); Merkel (1898); Huguenin et al (1953) and Gross (1953) - 4 cases.		

Discussion

The most controversial and, indeed, the most interesting point about these bilateral cases revolves around the question as to whether both tumours are separate, primary growths or whether one kidney is primarily involved with metastatic spread to its opposite number.

It is most noticeable, on reviewing the literature, that since nephrectomy, either alone or used in conjunction with radiotherapy, has become the accepted form of treatment, the proportion of bilateral cases has dropped markedly and the writer has been impressed by the large number of cases occuring in patients who died of advanced malignant cachexia, where no attempt had been made to deal with the primary growth and, in whom, the bilateral involvement was only discovered at autopsy. Indeed, out of a total of 234 cases of embryoma that were reported in the literature between 1814 and 1903, no less than fourteen (6 per cent) were found to have bilateral involvement whereas, in 672 cases reported between 1903 and 1953 - in which details of the side involved were recorded - only nineteen (2.8 per cent) were bilateral. These figures suggest that, if the tumour is left alone and allowed to progress to a fatal termination, it may, in time, metastasise to the opposite side.

This secondary spread, when present, is almost certainly not due to direct invasion of the opposite kidney as it is an accepted fact (Gross, 1953) that embryomata, in contra-distinction to sympathicoblastomata, rarely spread across the midline and Rusche (1951) reported a case (not the case included in Table IV) in which there was an embryoma of one kidney with secondary invasion of the peri-renal tissues on the opposite side but with no involvement of the actual kidney substance.

Spread to the opposite kidney may take place via lymphatic channels or blood vessels, the latter route being the pathway of spread in Case 63 of the present series, in which tumour tissue was traced, at autopsy, from the right kidney along the right renal vein to the inferior vena cava and also along the lumen of the left renal vein to the left kidney.

The eight cases in Groups III and IV all tend to suggest secondary involvement of the other kidney, particularly those cases in which a tumour appeared on the opposite side some time after the first tumour had been detected (Group III). In Rance's case, a swelling was first noted in the left loin and, six months later, a second swelling appeared in

the right loin. In Strong's patient, the second tumour made its appearance three weeks after a nephrectomy had been performed on the opposite side. Kretschmer and Hibbs' patient had a right nephrectomy performed for renal embryoma. The child developed post-operative anuria and a decapsulation of the left kidney was performed, during which it was noted that "... the kidney was enlarged and pale, but free from tumour." Five weeks later, a mass appeared in the left loin and laparotomy revealed a typical embryoma in the opposite kidney. The child died shortly afterwards and, in addition to bilateral renal involvement, metastases were found in the liver and lung. This case, at least, appears to be a genuine example of metastatic involvement of the remaining kidney.

As the interval of time elapsing between the discovery of the separate tumours was very much greater in the case described by Ritter and Scott (1949), it has not been included in the present series but it does seem worthy of mention. In this case, the second kidney became involved ten years after an apparently successful nephrectomy and, as there were no other metastases elsewhere in the body, this second tumour was considered, by the authors, to be a second primary growth.

On the evidence of some of the reported cases, it would seem that, at least, a few of them were examples of bilateral primary involvement, particularly those cases falling into Group II. Of interest, in this Group, is the case described by Barr and Schulte, where the child had been in hospital six months previously (for another complaint) and no mass was palpated in his abdomen. On the second admission, masses were palpable in both flanks and the diagnosis was confirmed at autopsy.

In case 7 of the present series, although the second kidney was involved in several discrete areas suggesting metastatic spread, there was no macroscopic or histological evidence of tumour cells in the surrounding lymphatics or blood vessels and, after all, as embryomata can arise spontaneously in the opposite kidneys of identical monovular twin boys (Gaulin 1951), there is surely no reason why they should not arise as separate primary tumours in both kidneys of a normal monovular child.

PART ONE

DIAGNOSIS

CHAPTER III — CLINICAL DIAGNOSIS

(i) AGE INCIDENCE

Cases have been reported in the foetus (Weigert, 1876; Nicholson, 1931 and others) and in adults up to the age of seventy-five years (Twinem, 1946) but, as this paper is only concerned with embryomata in childhood, no reference will be made to its incidence in adult life.

TABLE V

Age Incidence of 63 cases

(Royal Hospital for Sick Children, Glasgow)

Age in years	0-1	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11
No. of cases	18	8	14	10	6	5	-	-	1	-	1

From this Table it can be seen that, in this series, 61 cases (96 per cent) occurred in children of five years or under. Statisticians might argue that no conclusions could be accurately drawn from such a relatively small number of cases so, in order to corroborate this impression, 1000 cases were abstracted from the literature and the age groups are shown in Fig. 1, which demonstrates the fact that 88.3 per cent of the children were aged five years or under.

The age incidence is perhaps of more importance in this condition than in most because, as will be shown in a later chapter, the chances of survival appear to be better if the tumour makes its appearance in the first twelve months of life.

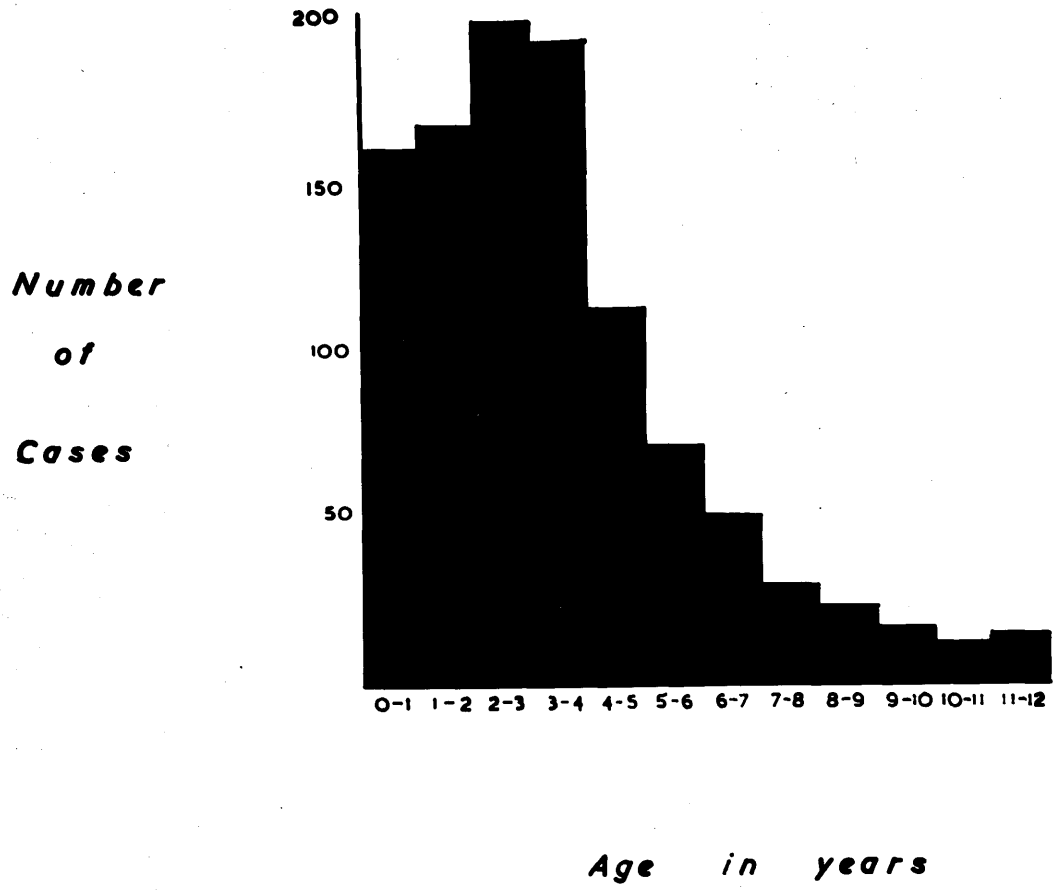


Fig. I: Age incidence of 1000 published cases.

(ii) SEX RATIO

Contrary to the reported findings in many earlier papers on this subject, the sexes were affected in more or less equal proportions in the cases under review; there being 35 males and 28 females. These figures correspond closely with those in Table VI, which has been compiled from papers in the literature (in which the number of cases reported was 10 or more and, in which, details of the sexes were stated.)

TABLE VI

Incidence of involvement of the sexes

Author(s)	Male	Female
Bandler & Roen (1944	16	15
Brown (1951)	5	8
Dean & Pack (1932)	8	8
Dickey & Chandler (1949)	6	6
Geschickter & Widenhorn (1934)	18	15
Goddard (1950)	17	22
Kerr (1939)	9	5
Kretschmer & Hibbs (1931)	14	3
Loughnane (1914)	18	15
Mixter (1932)	16	14
Riches et al (1951)	93	96
Rusche (1951)	21	19
Stern & Newns (1938)	10	16
Walker (1897)	55	51
Weisal et al (1943)	29	15
Present series	35	28
TOTAL	370	336

(iii) SIDE INVOLVED

It has frequently been stated that these tumours are much commoner in the left kidney than in the right, but although it is true that, in this series, the left kidney was involved in 34 cases and the right in 28, analysis of a large number of cases shows that the tumour does not really appear to have any predilection for one side or the other (Table VII).

In addition to these cases - in which only one kidney was involved - several instances of bilateral involvement have been reported. (See Chapter II).

TABLE VII

Incidence of involvement of each kidney

Author(s)	Side Involved	
	Left	Right
Brown (1951)	9	4
De Vries (1954)	5	4
Goddard (1950)	19	20
Higgins & Shively (1941)	10	16
Kerr (1939)	5	8
Kretschmer & Hibbs (1931)	10	5
Ladd (1938)	22	22
Loughnane (1914)	13	17
Mixter (1932)	14	16
Riches et al (1951)	104	82
Rusche (1951)	24	15
Stern & Newns (1938)	15	10
Walker (1897)	73	58
Weisal et al (1943)	21	23
Present series	34	28
TOTAL	378	328

(iv) SYMPTOMATOLOGY

The histories of these unfortunate children have varied quite remarkably. Frequency of micturition was noted in five cases, dysuria in two and one child was admitted with severe renal colic; but no less than forty-one (65 per cent) had no symptoms referable to the urinary tract. It is also interesting to note that in many of the cases the discovery of the abdominal swelling was preceded, for weeks or even months, by such vague symptoms as anorexia, lassitude, irritability and loss of weight.

The classical "triad" of swelling, pain and haematuria, so commonly found in adults with hypernephroma, is rarely found in this age group and was only present in five cases (8 per cent) of which two were the result of trauma. Haematuria will be dealt with separately in a later chapter, as this symptom appears to have a grave prognostic significance. It was present in sixteen cases (25.4 per cent) and was the initial symptom in ten of them. A further sixteen cases were admitted to hospital because of the accidental discovery of a symptomless swelling in an otherwise healthy child.

A resume of the salient points in the symptomatology of the remaining cases is given below, as it is felt that only by reviewing the individual histories, can the reader obtain a clear mental picture of the wide variety of symptoms which these tumours may present.

Case 3: Male, aged 5 years. He had been vomiting more or less continually for 10 days before admission and had completely lost his appetite. The swelling was only discovered on the day before admission.

Case 5: Male, aged 6 months. He had been off colour for 3 weeks before admission and had vomited every feed for the last 3 days. The mass was discovered on the day before admission.

Case 7: Female, aged 11 months. Three months before admission, her mother noticed a swelling on the left side of her abdomen. Since then she has lost her appetite and become obstinately constipated. Latterly she had vomited every feed.

Case 8: Female, aged 11 months. The finding of an abdominal swelling was preceded for 6 weeks by complete anorexia and marked loss of weight.

Case 12: Female, aged 2 years. Vague abdominal pain had been present for two weeks and she was losing weight steadily. The abdominal mass was only found on admission.

Case 14: Male, aged 2 years. He was admitted because of abdominal pain, constipation and vomiting of 3 days duration. The swelling was not discovered until admission.

Case 17: Male, aged 3 years. Frequency of micturition had been present for one month and severe dysuria for 4 days. For about a week he had been having recurrent bouts of abdominal pain.

Case 18: Female, aged 3 years. This little girl was admitted as a case of suspected splenomegaly. The swelling had been present for 3 weeks but she had been losing weight steadily for 2 months.

Case 20: Male, aged 4 years. Anorexia and marked pallor began one month before admission and a few days later his mother noticed a swelling in the left side of the abdomen.

Case 22: Male, aged 8 years. His mother had noticed a swelling in the right side of his abdomen three months before admission, but nothing was done about it until he became extremely irritable and began to lose weight.

Case 27: Male, aged 4 years. He developed severe right sided abdominal pain a few hours before admission. A tender mass was found on the right side and a laparotomy was performed on a pre-operative diagnosis of appendix abseess.

Case 28: Female, aged 4 years. For three weeks before admission she had been listless and had completely lost her appetite. One week later she developed severe abdominal pain and vomiting.

Case 29: Female, aged 4 years. Abdominal swelling and pain had been present for one month together with frequency of micturition. Anorexia and lassitude were marked and, for two days prior to admission, she had been vomiting almost continuously.

Case 30: Male, aged 10 months. A swelling was accidentally discovered in his left loin three months before admission. Shortly after this, he lost his appetite and had recurrent bouts of vomiting.

Case 32: Female, aged 2 years. This girl was admitted as an emergency with severe abdominal pain and a smallish palpable mass. A laparotomy was performed on the pre-operative diagnosis of intussusception.

Case 33: Male, aged 6 months. He was admitted for investigation of abdominal pain and vomiting of four weeks duration and the swelling was discovered after admission.

Case 35: Female, aged 2 years. For two weeks she had been having vague abdominal pain. A swelling was discovered in the left loin a week before admission and shortly after that she began to have frequency of micturition.

Case 37: Male, aged 2 years. This boy was admitted for investigation of loss of weight, loss of appetite, pallor and listlessness of six weeks duration. The swelling was discovered in hospital.

Case 38: Female, aged 2 years. She was admitted to another hospital with a short history of severe renal colic and vomiting. Examination revealed a large mass in the right loin and she was transferred to this hospital as a suspected renal tumour.

Case 39: Female, aged 3 years. For six months she had been having vague abdominal pain but it was not until a few days before admission that a mass was discovered in her abdomen.

Case 41: Female, aged 5 years. She had been having recurrent attacks of abdominal pain for nearly a year and had recently started to vomit after every meal. The abdominal swelling was only noticed on the day of admission.

Case 42: Female, aged 5 years. Frequency of micturition had been present for some weeks but it was only with the onset of diarrhoea and vomiting, on the day of admission, that a mass was detected in the right upper abdomen.

Case 47: Female, aged 7 months. This girl was admitted to the medical wards because of the chance finding of an abdominal swelling by the general practitioner who had been treating her for three weeks for "gastro-enteritis."

Cast 49: Male, aged 11 months. This boy had been "off colour" for two or three months but was not admitted to hospital because he had no pain and no urinary symptoms. On the day of admission, the family doctor found a small mass in his abdomen.

Case 52: Female, aged 15 months. She was admitted as a case of suspected splenomegaly. She had been vomiting on and off for over a week and had lost a considerable amount of weight. She eventually became obstinately constipated.

Case 54: Female, aged 2 years. She had been having recurrent attacks of abdominal pain for three weeks but was only admitted to hospital because of the discovery of an abdominal mass on the day of admission.

Case 55: Male, aged 2 years. He was admitted as a case of suspected splenomegaly. The left sided swelling was found on the previous day by the family doctor who had been called in because the child had been having vague abdominal pain for several days.

Case 56: Male, aged 2 years. About a week before admission he became listless and apathetic and he completely lost his appetite but the abdominal mass was only discovered on the day before admission.

Case 58: Male, aged 3 years. For several months his abdomen had been noticeably distended and, about eight months before admission, he lost his appetite and began to lose weight. A left sided mass was eventually discovered and he was admitted for investigation of a suspected enlarged spleen.

Case 59: Female, aged 3 years. For three months she had been listless and irritable and had complained of vague abdominal pain. Her abdomen had become increasingly distended but it was not until one week before admission that the family doctor, who had been called in to see her because of an accident to her back, found that the abdomen was hard and tender.

Case 62: Female, aged 4 years. This girl was admitted in a moribund condition with a history of dysuria of five weeks duration plus an abdominal swelling which had been present for nearly a month.

Case 63: Male, aged 5 years. Six weeks before admission he started vomiting and lost his appetite. One week later, a swelling was noticed on the right side of his abdomen and he was eventually admitted to hospital when it was noticed that the swelling was increasing in size.

(v) HAEMATURIA

Unlike hypernephromata and other adult tumours of the kidney, embryomata seldom give rise to haematuria; this being largely due to the fact that these tumours remain encapsulated for a considerable length of time. Haematuria in renal tumours indicates ulceration into, or invasion of, the renal pelvis and, in embryomata, the pelvis tends to become distorted and compressed by the situation and bulk of the tumour rather than actually invaded by it. It is an interesting point that although haematuria, in this condition, is generally accepted as an indication of very advanced disease, it is seldom encountered in the terminal phase of an untreated tumour, although its presence has been noted by Gairdner (1828) and others. In this respect, Cases 12 and 62 are of considerable interest because although, in both cases, there was never any haematuria, the pelvis and upper ureter were found, at autopsy, to be blocked with tumour tissue and blood-clot.

In this series, haematuria was present in sixteen cases (25.4 per cent) and was the initial symptom in ten. In one of these cases, haematuria was due to rupture of the tumour following a trivial accident. In an additional two cases, red blood cells were found on microscopic examination of the urine, although there had been no

naked-eye evidence of blood.

The reported incidence of haematuria has varied considerably in different papers. Dean (1939) found it in only 3 per cent of his cases whereas Walker (1897) found haematuria in thirty-five (38 per cent) out of ninety collected cases and noted that it was the first symptom in thirteen.

The relative frequency of haematuria in different tumours of the kidney is extremely well shown in Table VIII, which has been compiled by the writer from a statistical report of the British Association of Urological Surgeons on "Tumours of the Kidney and Ureter."

As would be expected, this Table shows that tumours of the renal pelvis give rise to the highest incidence of haematuria, but it is the marked difference between tumours of the renal parenchyma in adults and in children that is of chief interest in this study.

TABLE VIII

Relative Frequency of haematuria in different renal tumours

Tumour	Total Cases	Haematuria Cases
Simple papilloma of pelvis	74	87%
Carcinoma of renal pelvis	241	80%
Hypernephroma	1705	61%
Embryoma	189	18%

Summary of Case Reports of the Patients with Haematuria

Case 9: Male, aged 17 months. He was admitted for investigation of a swelling in the left loin of five days duration, but had had occasional bouts of painless haematuria for several weeks. The tumour was found to have perforated its capsule at one point and, although nephrectomy was performed, he died within four months.

Case 10: Male, aged 22 months. He was admitted for investigation of a swelling in the right loin which had been preceded, for three months, by painless spasmodic haematuria, headaches, listlessness and anorexia. The tumour appeared to be completely encapsulated but, although nephrectomy was performed, he died within three months.

Case 11: Female, aged 2 years. She had a history of painless haematuria on two occasions, two months and two days respectively, before admission. She had bouts of vague abdominal pain and a large swelling was found in the right side of her abdomen. The tumour appeared to be encapsulated but, in spite of a successful nephrectomy, she died within two months.

Case 15: Female, aged 2 years. Two days before admission, her mother noticed a swelling in the left side of her abdomen and it later transpired that shehad passed blood in her urine six months previously. The tumour had perforated its capsule at several points and, although nephrectomy was performed, she died a few months later.

Case 16: Male, aged 3 years. Three months before admission, he had been kicked in the right loin but, although this did not produce any local bruising, he passed bright red blood about a week later. He had been having haematuria, on and off, ever since. On examination of the kidney, there was no evidence of trauma or invasion of the capsule but, although a nephrectomy was performed, he was dead within three months.

Case 19: Male, aged 3 years. He had been unwell for about two months and had passed blood in his urine about one month later. The abdominal swelling had only been detected two days before admission. The tumour was extremely vascular and did not appear to have broken through its capsule but, although a nephrectomy was performed he died a few weeks later.

Case 23: Female, aged 10 years. This girl was admitted as a suspected ruptured kidney. She tripped and fell while playing and later complained of severe abdominal pain, accompanied by the passage of bright red urine. At operation, it was found that a huge tumour mass had been ruptured in two places. Nephrectomy was performed, but she developed a recurrence under the scar and died nine months after the original accident.

Case 25: Female, aged 3 years. This girl had been having abdominal pain for about six weeks, accompanied by increasing distension of the abdomen, but it was only after she developed haematuria that her admission to hospital was expedited. At laparotomy, the tumour

Case 25: (Continued)
was seen to have burst through its capsule in several places and was so adherent to the posterior abdominal wall that it was deemed to be inoperable. In spite of a course of radiotherapy, she died within four months.

Case 36: Male, aged 2 years. This boy had passed bright red blood on two occasions in the previous month but the abdominal swelling was only detected a few days before admission. The tumour was large and extremely vascular and, although he had a nephrectomy followed by a course of radiotherapy, he died within seven months.

Case 40: Male, aged 4 years. Painless haematuria had been present for three weeks before a swelling was noticed in the left side of his abdomen. His admission to hospital was expedited because of severe abdominal pain. The tumour was very adherent locally and removal was not complete. He received a course of post-operative radiotherapy but died three months later.

Case 43: Male, aged 2 weeks. This baby was admitted as an emergency because of incessant vomiting and the passage of "pencil clots" in his urine during the previous twenty-four hours. He had a hopelessly inoperable tumour and died five days after admission. At post mortem, an extremely vascular tumour was found to have almost completely replaced the left kidney.

Case 51: Male, aged 11 months. Three months before admission, he had passed bright red blood in his urine. Two months later, his abdomen became distended and he developed a left-sided varicocoele. The tumour was considered to be hopelessly inoperable and he died a few months later.

Case 53: Male, aged 19 months. This boy was admitted for investigation of a swelling in the left loin. On the day after admission he had frank haematuria. The tumour was considered to be hopelessly inoperable and he died shortly afterwards.

Case 57: Female, aged 2 years. She was admitted to the Medical Wards for investigation of an abdominal swelling which had been increasing in size over the past four months. She had passed blood in her urine on three occasions in the two months prior to admission. The swelling was diagnosed, on clinical and radiological examination, as an inoperable renal tumour and her parents took her back to Arisaig to die at home.

Case 61: Female, aged 3 years. She had been complaining of frequency of micturition during the previous two months she was listless and apathetic and, ten days before admission, she passed bright red blood in her urine. An abdominal swelling was later discovered by her mother. Laparotomy was performed but a huge vascular tumour of the left kidney was found and was considered to be inoperable. She died, at home, a few months later.

The Significance of haematuria in childhood.

From a study of the above cases, the writer has been impressed by the grave prognosis attached to the symptom of haematuria. All the cases with haematuria, in this series, died within nine months and a perusal of the literature shows that, with very few exceptions, the presence of haematuria has nearly always been followed by death within a year. On the other hand, Stern and Newn (1938), Daw (1948) and others have reported survivals in cases with haematuria; the most interesting being that reported by Weisal, Dockerty and Priestley, (1943), of a six-year "cure" in a girl who had been having intermittent haematuria for three years before admission.

Haematuria is rare in infancy and the presence of blood on a diaper cannot be accepted as haematuria until vaginal and intestinal bleeding have been eliminated. In older children, on the other hand, it is most likely to mean nephritis, tumour or genito-urinary tuberculosis, although it can be produced by trauma or by the passage of urinary calculi. Gross haematuria is comparatively rare in non-tuberculous urinary infections but is very common in acute glomerular nephritis.

Examples of "essential haematuria" have been investigated from time to time in this hospital but, in most cases, the cause of the bleeding remains undetected. In one such case, however, the bleeding from one kidney was so profuse that a nephrectomy was eventually performed and a small haemangioma was found in the sub-epithelial tissues of the renal pelvis (Scott, 1954).

(vi) THE ABDOMINAL SWELLING

A palpable mass was found in every case in this series and, as has been previously stated, it was the only abnormality present in 15 of the cases. The mass is, as a rule, firm, smooth and easily outlined. It is rarely tender and, when large, produces a change in the abdominal contour which can readily be detected on inpsection (Fig. 2).

Although a firm mass in the loin of a child is most likely to be a renal tumour, in my experience tumours of the adrenal glands have caused the greatest difficulty in differential diagnosis and, indeed, the final diagnosis has generally been made at operation or autopsy.

There are, however, a variety of abdominal swellings with which

renal tumours may be confused and their various diagnostic features are discussed below. In particular, reference will be made to diagnostic problems encountered by the writer during the period of this investigation.

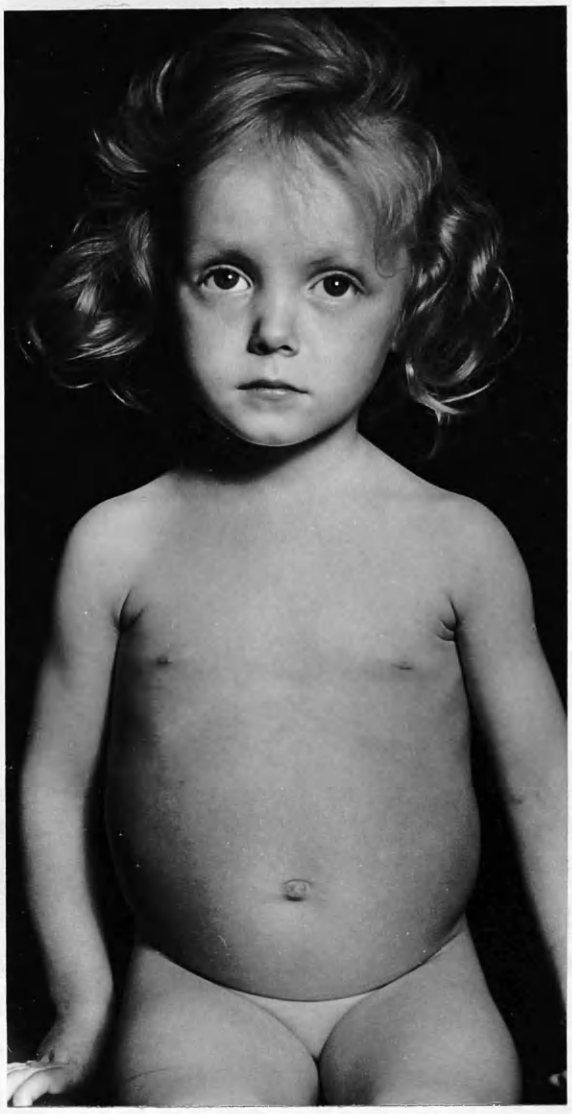


Fig. 2.
Girl, aged $2\frac{1}{2}$ years.
Right-sided embryoma producing bulging of the flanks and eversion of the umbilicus.

(1) Tumours of the sympathetic nervous system

Sympathicoblastomata are the commonest sympathetic tumours found: Thus Scott (1933) and his colleagues noted that, of 162 sympathetic tumours, mostly from the literature, only 8 were ganglioneuromata and Blacklock (1934), reporting 18 sympathetic tumours from the Royal Hospital for Sick Children, Glasgow, found that 17 were sympathicoblastomata; of these, 15 had originated in the adrenal medulla. These tumours generally occur in the same age group as embryomata but are not usually so large. They tend to metastasise early, mainly to liver and bone, especially in the region of the orbit .

Fig. 3.

Exophthalmos produced by orbital metastases from a left-sided sympathicoblastoma.

It is extremely difficult, if indeed possible, to differentiate embryomata from sympathicoblastomata on the size and consistency of the swelling as both may produce identical clinical findings. A sympathicoblastoma generally has a less clearly defined border and, when large, it extends across the midline, whereas an embryoma has a better delineated border and rarely reaches beyond the vertebral column. Embryomata tend to produce a large abdominal swelling before metastases are recognisable, whereas children with sympathicoblastoma frequently die with a primary tumour which is insignificant in comparison with the hepatic or orbital metastases.

(2) Hydronephrosis.

This is not uncommon in infancy and childhood and is second only to sympathicoblastoma as an impersonator of renal tumours. The swelling is generally more tense and cystic, on palpation, as compared with the first solid mass of an embryoma. The final diagnosis will generally be made on x-ray examination but it must be remembered that, although a hydronephrosis is easily recognisable on intravenous pyelography, the dilatation may, itself, be due to pelvi-ureteric compression by a renal tumour and exploration is, therefore, indicated in all doubtful cases.

(3) Enlarged spleen.

No less than six of the cases under review were admitted to hospital with this provisional diagnosis. Although it is generally stated that an enlarged spleen can be readily identified by the palpation of the splenic notch and the fact that the swelling is dull to percussion, differentiation from a left renal tumour is extremely difficult, even to experienced pediatricians. Splenomegaly, in infancy and childhood, may be due to disorders of lipoid metabolism such as Gaucher's disease and Niemann-Pick disease, to various diseases of the blood and to amyloid degeneration resulting from chronic sepsis. In practically all of these conditions the liver is also enlarged and the characteristic blood pictures should leave the clinician in no doubt as to the final diagnosis.

(4) Retroperitoneal tumours.

Retroperitoneal tumours such as sarcoma, fibrosarcoma and liposarcoma have all been described in this age group (Hansmann and Budd 1932); and Campbell (1933) described two cases of pararenal teratoma. Only one such case has been traced in the records of this hospital.

Case: A boy, aged 5 years, was admitted as a case of suspected splenomegaly and died 2 days after admission. At autopsy, he was found to have a retroperitoneal tumour, enclosed in a thick white capsule but, although it was flattening the left kidney by direct pressure, there was no evidence of continuity between the kidney and the tumour. Metastases were present in the liver and one of these had undergone necrosis and ruptured - producing intraperitoneal dissemination.

(5) Congenital polycystic kidney.

Polycystic disease of the kidneys may be divided into two types - the infantile type and the adult type. In the infantile form, the child is either stillborn or dies in infancy and rarely lives longer than a year. It generally affects both kidneys and shows hereditary and familial tendencies. The final diagnosis will generally rest on the radiological findings but, in view of the above statement it is rarely the cause of an abdominal swelling in children between the ages of 1 and 12 years.

(6) Renal hygroma (Syn: Peri-renal hydronephrosis):

Renal hygroma, which was originally described by Munkowski (1906), is a cystic envelopment of the kidney in which the renal capsule forms the parietal cyst wall. It is very rare; only 12 previous cases having been reported (Campbell 1941). It is extremely difficult to differentiate from a renal tumour on clinical examination as there is a firm palpable swelling in the loin, associated with a displaced renal pelvis and diminished renal function on pyelography. The following case, which the writer encountered in 1952, serves to illustrate the diagnostic difficulties.

Case: A girl, aged 5 years, fell from the piano and struck her right side. On admission, she was found to have a palpable swelling in her right loin, associated with haematuria. A diagnosis of ruptured kidney was made and conservative treatment was instigated but, although the haematuria ceased within 48 hours the swelling became definitely larger. Intravenous pyelography was performed and revealed a large soft tissue mass displacing the kidney upwards. The diagnosis was then changed to renal tumour and a laparotomy was performed. A large "tumour mass" was found to be filling the upper right quadrant of the abdomen but, when the parietal peritoneum was incised, the renal "tumour" was found to be a renal hygroma. The fluid was evacuated, leaving the kidney substance alone, and the child made an uninterrupted recovery.

(7) Congenital lesions of the gall-bladder:

These generally present in the form of enormous cystic swellings which occupy most of the abdominal cavity and the following case, which was encountered by the writer in 1953, illustrates the salient features of the condition.

Case: A boy, aged 5 years, was admitted with a painless right-sided abdominal swelling which had been present for five months but had been progressively increasing in size. The swelling extended downwards from the costal margin to below the umbilicus and was smooth, tense and cystic. Intravenous pyelography revealed a large soft-tissue shadow extending across the midline and the right renal pelvis, together with its ureter, was displaced. A laparotomy was performed and an enormous cystic swelling was found to be filling almost the entire peritoneal cavity. A needle was inserted into the cyst and seven pints of dark bile were aspirated. The liver was thinned out and perched like a mushroom-cap on top of the cyst but there was no evidence of any gallbladder. The cyst was removed and pathological examination revealed a choledochal cyst, arising from the right hepatic duct, with a tiny gallbladder embedded in the cyst wall.

(8) Malignant reticulosis:

The kidney may become secondarily invaded by either lympho-sarcoma or lymphadenoma (Scott, 1954), both of which give rise to palpable swellings in the loin. Differentiation from embryomata should seldom present any difficulty as examination of a blood film, together with the probable involvement of other lymph nodes, should help to clinch the diagnosis.

(9) Leukaemic kidney:

The kidneys may become involved in either acute lymphatic or myeloid leukaemia but both of these, in the majority of cases, give rise to bilateral renal swellings. The symptoms are predominantly those of acute nephritis and, although haematuria will frequently be present, the blood picture is diagnostic.

(10) Cystic Swellings in the abdomen:

Mesenteric, pancreatic and ovarian cysts are all rare in this age group. The swellings are generally midline; have a different consistency from renal tumours and are usually much more evident and circumscribed on inspection. (Fig. 4).

(11) Acute abdominal emergencies.

Two of the present cases were admitted as acute abdominal emergencies - one as an appendix abscess and the other as an irreducible intussusception.

Fig. 4. Obvious discrete abdominal swelling produced by a dermoid cyst of the right ovary in a girl aged 12 years.

It has been stated by some American authors that when there is any doubt about the diagnosis of a renal tumour in a child, a course of deep x-ray therapy should be given and if the tumour decreases in size, a diagnosis of embryoma can confidently be made. This oft-repeated statement is quite fallacious as these tumours may be relatively or totally radio-resistant. Magoun (1946) reported a six-year old boy who had received a course of pre-operative radio-therapy to a so-called "embryoma" and, following shrinkage of the mass, the kidney was removed. No trace of tumour could be found in any part of the kidney, the diagnosis eventually turning out to be a closed pyonephrosis. I have been unable to trace any other similar accounts in the literature and, on discussing the case with a radiotherapist of some repute, was informed that there must have been some mistake. By a strange chance of fate, a few weeks later, a five-week old boy was admitted to the Royal Hospital for Sick Children with a large firm left sided abdominal swelling which was considered to be an inoperable renal tumour (Fig. 5). The child was given a course of palliative deep x-rays and the swelling slowly but steadily decreased to about one-fifth of its original size. A nephrectomy was performed and, to everyones amazement - not least the radiotherapist - a large hydronephrosis was found to be present, with absolutely no evidence of any tumour tissue whatsoever.

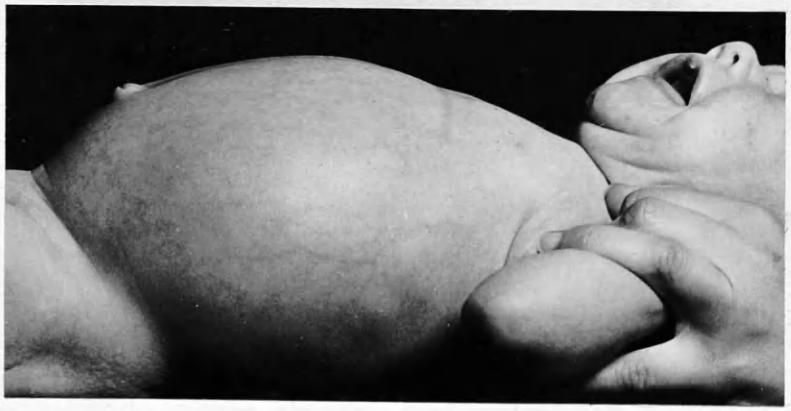


Fig. 5. Infant with gross abdominal swelling produced by a large left-sided hydronephrosis.

As if to further demonstrate the difficulties involved in making a pre-operative diagnosis of renal tumour, on the same operating list as the above nephrectomy a five year old girl had a laparotomy performed with a view to exploring a mass in her right loin. This had produced the classical appearances of sympathicoblastoma on pyelography; indeed the picture was so typical that photographs of the x-ray plates were taken for teaching purposes (Fig. 6.) The tumour proved to be an embryoma arising from the upper pole of the right kidney, the adrenal gland on that side being perfectly normal.

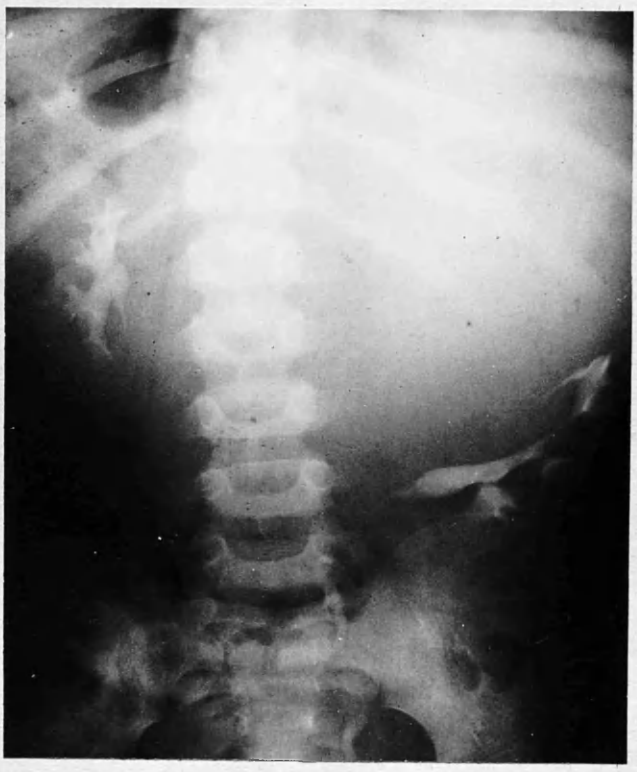


Fig. 6. I.V.P. Embryoma of upper pole causing distortion and displacement of renal pelvis - similar to that which is produced by sympathicoblastoma.

CHAPTER IV — RADIOLOGICAL DIAGNOSIS

Pyelography fulfills the useful double purpose of demonstrating the presence and degree of function of the contra-lateral kidney and, at the same time, helping to differentiate the various conditions with which embryomata are most likely to be confused. In addition, the straight x-ray which is taken routinely before injection will frequently show the outline of the larger tumours and generally reveals displacement of bowel shadow by the bulk of the growth (Fig. 7).

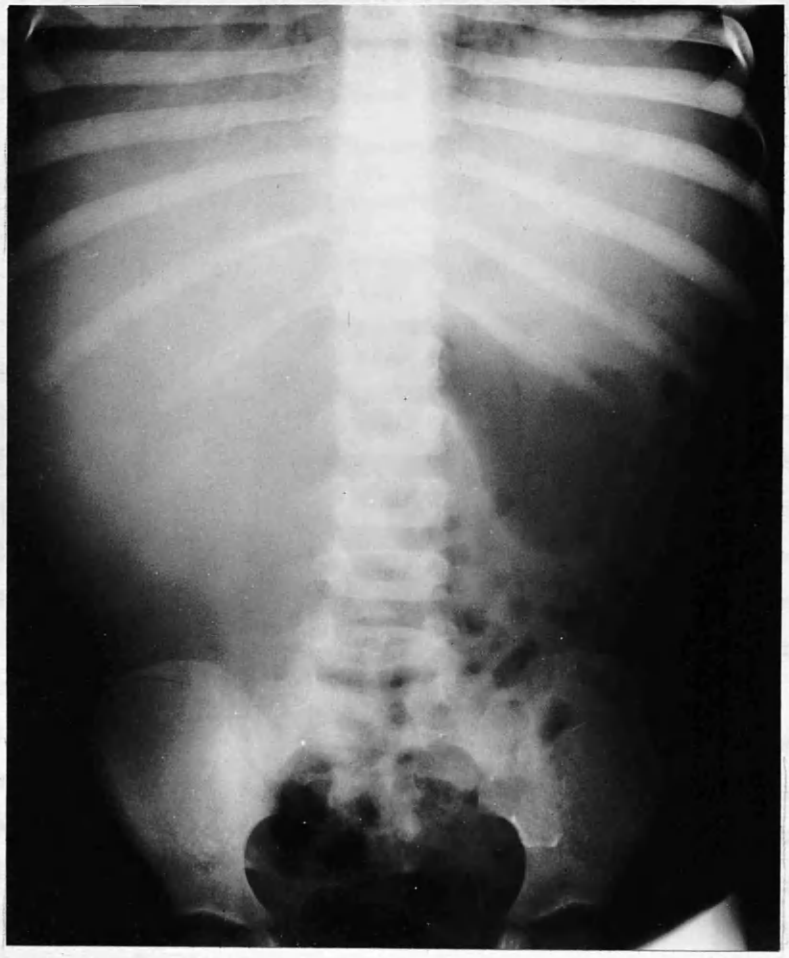


Fig. 7. Straight x-ray of abdomen showing a large right-sided opacity due to a renal tumour, with displacement of bowel shadows to the left.

(a) Preparation of the patient.

The preparation of infants and young children is not as easily achieved as it often is in adults and attempts to withhold food and empty the bowel by the use of laxatives generally result, not in a clearer field, but in an increase in amount of intestinal gas. Excessive gas, in adults, can generally be cleared by an injection of pitressin but Campbell (1941) carried out a series of experiments with this drug in children and found that it reduced the calibre of the renal pelvis and ureter by one half. As a result of these experiments, he now strongly deprecates the employment of any of the peristalsis-stimulating drugs in this age group.

Mattei recently discovered, quite by chance, that excretory pyelograms in infants were greatly clarified by giving the infant 8 to 10 ounces of milk immediately before the x-ray was taken. This produces considerable gastric distension which, in turn, pushes the gas-filled intestines downwards, leaving a clear field through which the pelves and adjacent ureters are visualised. The lower two thirds of the ureters are, of course, almost completely obliterated but Matthei claims that amazing clarity of the upper urinary tract can be obtained by this method. Although most radiologists find that pyelograms, in children, give a clearer picture if the child is x-rayed without any preparation whatsoever, Nesbit and Douglas (1939) state that limitation of fluids from 10 p.m. on the previous evening, together with the administration of a small dose of Magnesium Citrate, gives, in their opinion, the best results.

In the Royal Hospital for Sick Children, Glasgow, no special preparation is used but, if the child is an in-patient, fluids are withheld for a few hours beforehand. This technique was investigated by Furnival (1950) who quoted a series of 100 pyelograms in which the patients had undergone varying periods of fluid restriction, ranging from 0 to 17 hours. One patient was given fluid a quarter-of-an-hour before injection and showed no medium in the kidneys at any time up to thirty minutes; but when repeated after three hours restriction of fluids, the renal pelves and calices were well outlined. This worker concluded from his studies that (i) a short period of fluid restriction is a necessary preliminary to successful intravenous pyelography; and

(ii) there is no advantage in prolonging the restrictive period beyond three hours.

(b) Intravenous pyelography.

In cases where renal pathology is suspected, intravenous pyelography is now carried out as a routine in this hospital and it has proved, in our hands, to be the most universally successful route of administration. The definition obtained has nearly always been satisfactory and there have been few occasions on which it has proved to be technically impossible on the grounds of failure to locate a vein. Diodone is preferable to Iodoxyl in children as the latter gives rise to more local venospasm. It can be used in strengths of 35 and 50 per cent; the dosage being 8 ml. from one to three years and 10 ml. from three to twelve years. Children aged twelve to fifteen years may be given 15 ml. and, after sixteen years, the adult dosage may safely be given.

(c) Subcutaneous Pyelography.

Nesbit and Douglas (1939) reported 31 patients in whom they had employed the technique of injecting 20 ml. of 35 per cent Diodrast dilated with 80 ml. of normal saline, given subcutaneously in amounts of 50 ml. into the subcutaneous tissues over each scapula. No discomfort or sloughing was reported and the wheals had completely disappeared within 45 minutes. Absorption is very rapid and they claim that films taken at 10, 20 and 30 minutes after injection gave satisfactory visualisation in 30 out of the 31 cases.

Many radiologists prefer to use sterile water as the diluent and it is now the common practice, when employing the subcutaneous route, to dissolve one milligramme of hyaluronidase in the water before the dilution is carried out. Astley (1952) recommends a standard dose of 10 ml. of 35 per cent Diodone, diluted with an equal volume of water, for all ages between a few weeks and five years. He found that the medium was seen in the renal pelvis in about 5 minutes and noted that the best films were obtained between 15 and 45 minutes. These times compare favourably with those following intravenous injections and are considerably shorter than after intramuscular injection. Subcutaneous pyelography was only employed in two of the present cases and the definition was found to be very much poorer than with intravenous injections.

(d) Intramuscular Pyelography.

Adams and Hunt (1939) described 55 cases in which they had administered the dye intramuscularly. They used a 35 per cent solution of diodrast and injected 10 to 15 ml. intramuscularly into the glutei. There were apparently no untoward results in these children but they only recommend its use in cases where the intravenous route is impracticable and, in most clinics, subcutaneous pyelography is considered to be the better alternative.

(3) Retrograde Pyelography.

Although it is a well recognised fact that retrograde pyelography will give clearer definition of the outline of the renal pelvis and, indeed, will allow earlier detection of small lesions in the minor calices, in cases where renal embryoma is suspected it is looked on with disfavour in this hospital owing to the unnecessary additional handling which this investigation entails. Opinions are divided with regard to the advisability or otherwise, of using retrograde instrumentation for these cases; this being amply demonstrated by the fact that two of the leading authorities on renal tumours in childhood hold entirely opposite views. Campbell (1941) uses retrograde pyelography as a routine and claims that the typical pyelographic appearances can only be demonstrated by this method whereas Gross (1953) states that it is both unnecessary and dangerous.

The writer has had experience of all but the intramuscular route and is firmly of the opinion that, in children with suspected embryomata - where additional handling of the abdomen may be the last straw in the dissemination of tumour cells - the intravenous route, where practicable, is the most satisfactory.

RADIOLOGICAL APPEARANCES IN RENAL EMBRYOMA

The changes which can be seen in the outline of the renal pelvis result from mechanical distortion of the pelvis by the growth, obstruction of the pelvi-ureteric junction or upper ureter and, on rare occasions, ulceration due to necrosis of the tumour or invasion of the renal pelvis. These various pathological changes result, in turn, in distortion and elongation of the calices, the production of a hydronephrosis or a filling defect in the pelvis.

The 30 most recent cases in this series were investigated by pyelography and the findings are depicted in Table IX.

TABLE IX

Pyelographic Findings in 30 cases of Renal Embryoma

Royal Hospital for Sick Children, Glasgow.

Pyelographic Appearance of the affected kidney.	No. of Cases.
No evidence of function	19
Hydronephrosis	6
Distortion of Calices with flattening of pelvis.	2
Caudal displacement with flattening of pelvis.	1
Distortion of Calices with filling defect in pelvis.	1
Hydronephrosis and hydroureter.	1
TOTAL	30

This Table shows that in the overwhelming majority of the cases the radiological picture was that of a huge "soft tissue shadow" completely obliterating a large part of the abdomen, with no evidence of function in the affected kidney (Fig. 8).

Only one case (Case 39) demonstrated a filling defect in the renal pelvis but hydronephrosis was relatively common. Elongation of the calices, said to be one of the commonest findings by Harvey (1950) and others, was not seen in this group of cases but, in Case 42, a caudal displacement, together with distortion of the renal pelvis, was produced by a large tumour in the upper pole of the right kidney (Fig. 6).

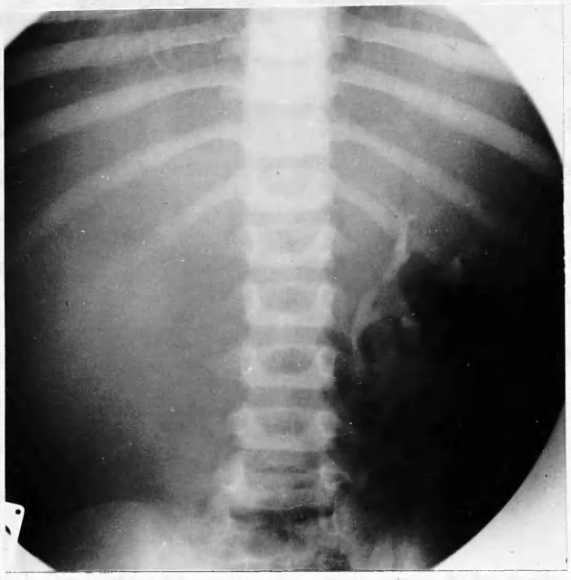


Fig. 8. I.V.P. showing the typical appearance in a large Wilms' tumour of the right kidney. The left kidney is normal but the right one is almost functionless. A massive soft-tissue shadow has obliterated the whole of the right side and part of the left side of the abdomen.

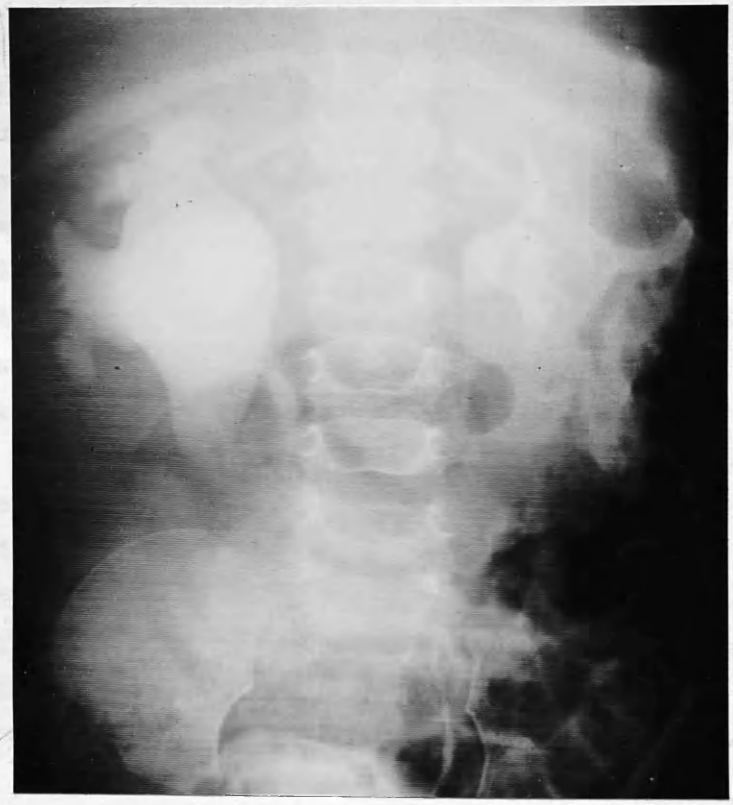


Fig. 9. I.V.P. showing hydronephrosis produced by a right-sided embryoma.

CHAPTER VI — PATHOLOGICAL DIAGNOSIS

As the whole value of a thesis lies in the fact that it is a presentation of original observations made by the author and, as this thesis is intended to be essentially clinical in nature, no attempt has been made to present a detailed description of the complicated histological appearances which may be encountered. On the other hand, it is essential that the surgeon should be able to recognise the distinct features in the naked-eye appearance of these tumours and it is advantageous if he can appreciate the main characteristics on which the histological diagnosis is made. For this reason, and in order to present a complete picture in the diagnosis of these tumours, a variety of histological sections have been studied and a brief description of the macroscopic and microscopic findings are presented below, together with the salient histological features of the various tumours with which embryomata may be confused.

A. MORBID ANATOMY

These tumours may originate in any portion of the renal parenchyma but the exact site of their inception is generally indeterminable due to the bulkiness of the growth. The tumours that were examined were found to be ovoid, globular or nodular; the size varied from that of an orange up to tumours weighing as much as thirty-six pounds and the consistency was generally comparable to that of brain tissue. Most of them were "surrounded" by a pseudo-capsule, composed of loose connective or dense fibrous tissue . Areas of degeneration, necrosis, liquefaction and haemorrhage were found to be common (Fig. 10); thus presenting a play of colours ranging from grey to orange, yellow, red and brown. The surface vessels were generally dilated and the neoplasm had frequently compressed the remaining renal substance so that, on hemi-section, the kidney appeared as a narrow "rind" stretched out over the upper or lower pole of the tumour (Fig. 11). The renal pelves were narrowed, elongated or otherwise distorted but there was seldom any evidence of actual invasion.

Fig. 10. Cut-section of an embryoma which has undergone extensive liquefaction, necrosis and haemorrhage.

Fig.11. Large solid embryoma of lower pole. Normal renal tissue is represented by a "rind" stretched out over the upper pole of the tumour.

Fig.12. Embryoma of lower pole which has produced gross hydronephrosis.

Fig. 13. Renal Teratoma.

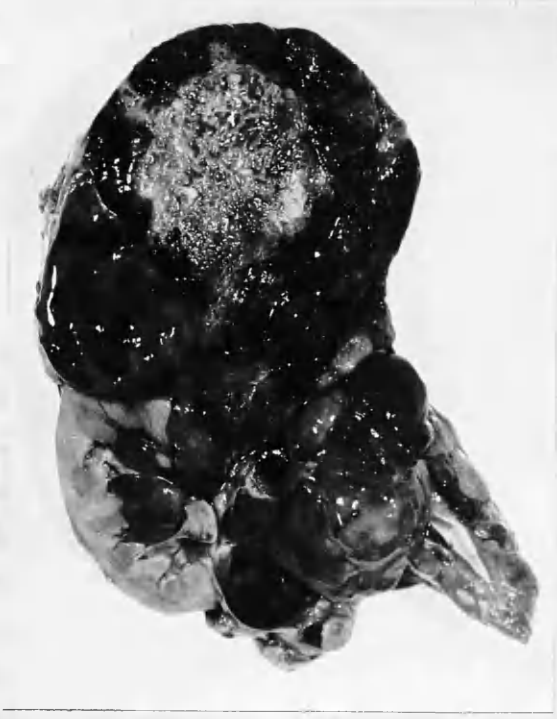


Fig. 14. Sympathicoblastoma indenting - but not invading - the kidney.

B. HISTOLOGY.

These embryonic tumours of the kidney are now universally known as embryomata or Wilms' tumours but, prior to the use of these names, the nomenclature was very complex. The histological appearances are so varied that its terminology has included such names as adeno-rhabdo-myo-sarcoma, blastocytoma, chondro-myxo-sarcoma, embryoma, embryonal sarcoma, lipo-myo-sarcoma, nephroblastoma and even fibro-adeno-rhabdo-myomatous mesothelioma; indeed, Culp and Hartman (1948) found 53 different designations in the literature.

In a typical histological section, it was found that most of the tumour was composed of embryonal mesoblastic tissue. The cells generally constituted the bulk of the tumour and presented in the form of diffuse sheets or masses (Fig. 15). In addition, there were usually varying degrees of organisation, revealing transition from the diffusely arranged cells to attempts at formation of primitive tubular and glomerular structures. Striated muscle fibres were frequently observed. This appears to have given rise to much needless debate in the literature as smooth muscle is a normal component of the kidney and, according to Willis (1953), its presence in embryonic renal tumours merely represents an example of aberrant differentiation of embryonic muscle cells under abnormal conditions.

Contrary to their gross appearance, histological examination revealed that the tumours were practically never completely confined by the connective tissue capsule; instead, the neoplastic tissue was seen to be irregularly infiltrating the adjacent renal parenchyma.

The presence of other tissues have frequently been reported, but it has been pointed out, (Scott, 1954), that the use of the word "teratoma" as a synonym for embryoma, so commonly seen in the literature, is quite inaccurate as these very rare renal teratomata constitute a separate pathological entity, in which all three germ layers are clearly represented (Fig.16). In addition, teratomata, on hemisection, reveal areas of bone and cartilage and these tissues have even been known to show up on x-ray. Fig. 13 is an example of a genuine renal teratoma with areas of bone and cartilage scattered throughout its substance.

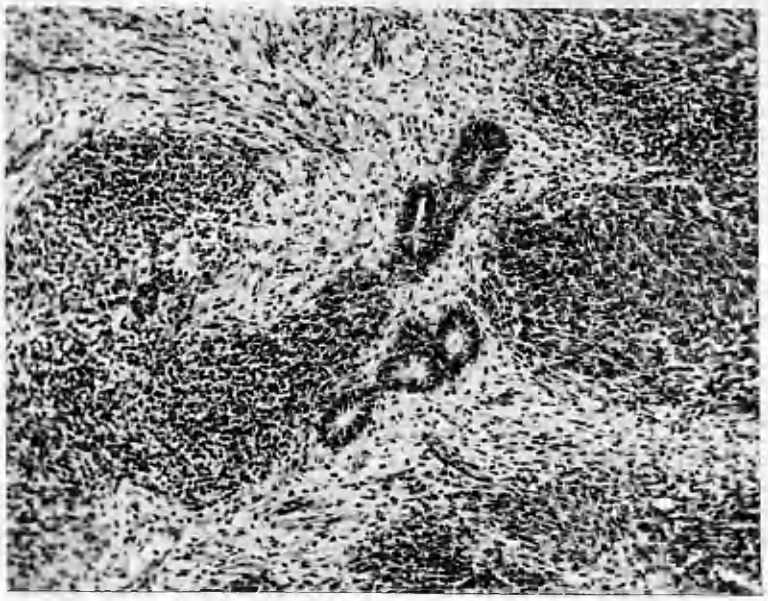


Fig. 15. Photomicrograph of a typical Wilms' tumour. In the centre, are primitive tubules surrounded by mesenchyme with undifferentiated hyperchromatic cellular tissue completing the picture. In this field there is no striated muscle.

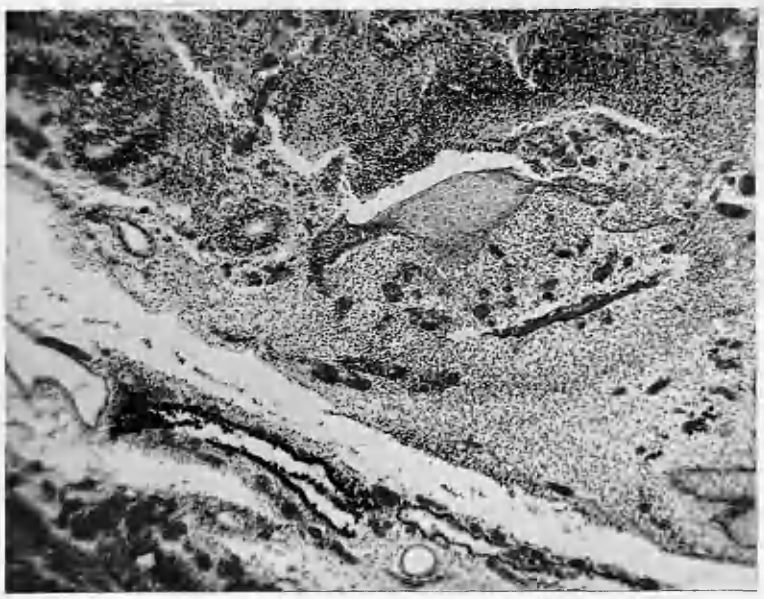


Fig. 16. Renal teratoma. Photomicrograph to indicate the main features on which the diagnosis was made. In the centre squamous epithelium is shown. There is a rosette to the left centre, typical of neuroblastic growth. Bone has formed below and to the right of the squamous epithelium, surrounded by undifferentiated 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.

DIFFERENTIAL PATHOLOGICAL DIAGNOSIS

Present-day pathologists have little difficulty in making a histological diagnosis as careful examination of multiple sections of the tumour, cut at different levels, should leave no doubt whatsoever as to the correct interpretation (Scott, 1954). The majority of the earlier cases in this series were labelled "sarcomata" but re-examination of the available sections has revealed the fact that, in every case, the typical features of an embryoma were present.

Apart from teratomata, the only other tumours which seem likely to give rise to some confusion, in histological interpretation, are carcinoma and sympathicoblastoma. Several cases of clear-cell carcinoma of the kidney have been reported in childhood and, although Willis (1953) believes that few of them can withstand critcal examination, there has been one such case at the Royal Hospital for Sick Children since the material for this paper was collected.

One would imagine that sympathicoblastomata, although commonly mistaken for embryomata on clinical examination and, indeed, at operation, would rarely give rise to confusion in the histological appearance, but a critical review of the histology in some of the published cases of embryomata shows quite clearly that many of them were really sympathicoblastomata as revealed by the presence of rosettes and neuro-epithelium (Fig. 17). The kidney substance may occasionally become invaded by a sympathicoblastoma but the adrenals are always intact in cases of embryoma. Fig. 18 demonstrates an example of misinterpretation of the characteristics of embryomata, as this specimen, taken from the Museum of the Royal Hospital for Sick Children, Glasgow, (which was "bottled" many years ago) was diagnosed as a renal sarcoma although naked-eye examination, alone, revealed the fact that the renal substances was still intact and the tumour, on re-examination, proved to be a sympathicoblastoma.

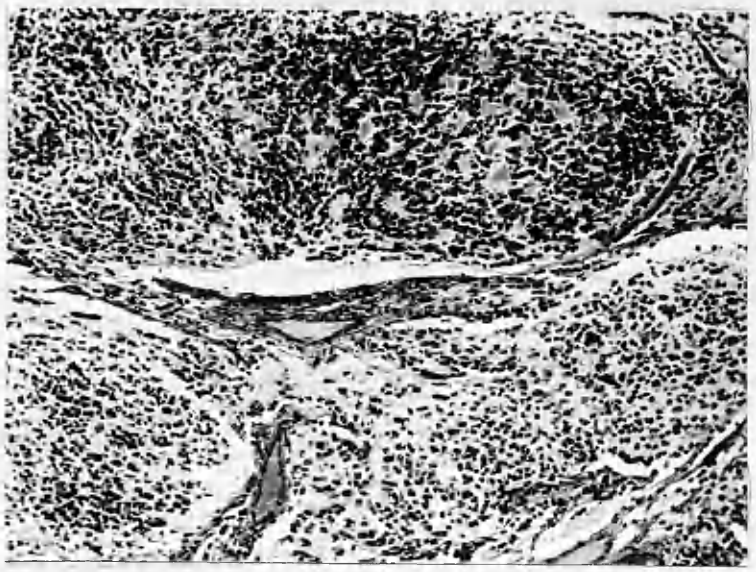


Fig. 17. Photomicrograph of a Sympathicoblastoma showing typical rosettes of neuro-epithelium.

Fig. 18. Post-mortem specimen of a kidney with a large tumour attached. Histologically, the tumour proved to be a sympathicoblastoma.

METASTASES

A study of the post-mortem findings in these cases has proved conclusively that embryomata spread both by the lymphatics and by the blood-stream and that local invasion of adjacent structures is almost unknown. This latter characteristic is well illustrated by Case 49 where the liver was deeply indented by the tumour although there was no evidence of infiltration. The same factor, in reverse, led to a change in the diagnosis in one case from embryoma to sympathicoblastoma. This case was entered in the hospital records as "a nephroblastoma with local invasion of liver substance" but, because of this "invasion", the histological sections have been re-examined and the presence of rosettes and neuro-epithelium showed that the original diagnosis was an error.

In none of the cases, examined at post-mortem, was there any evidence of actual bowel invasion although, in many cases, the bulk of the tumour had displaced the bowel across to the opposite side of the abdomen.

Of the 20 cases on which an autopsy was peformed, distant metastases were found in 17 and the distribution of these metastases is shown in Table X. Six of these cases are of particular interest:

Case 16: The renal vein and inferior vena cava were completely blocked by tumour tissue.

Case 26: Metastases were present in both lungs and further metastases had destroyed three thoracic vertebrae (T.8. to T.10). The growth had spread into the spinal canal from the level of T.6. to T.10. so that the cord lay embedded in tumour tissue.

Case 29: Metastases were present in both lungs and in the orbit. This latter site is extremely rare and generally justified a clinical diagnosis of sympathicoblastoma.

Case 35: Multiple metastases were present and a large secondary growth was found in the scrotum, invading both tunicae and pushing the testicles down to the bottom of the scrotal sac.

Case 62: Tumour tissue was traced from the kidney along the renal vein to the inferior vena cave right up to, and into, the right auricle.

Case 63: Tumour tissue was found in the right renal vein, the inferior vena cava and along the left renal vein into the medulla of the opposite kidney.

TABLE X

Distribution of Metastases in 17 Post-mortems

Situation of Metastases	No. of Cases.
Lungs	11
Lymphatic Glands Mesenteric 6 Para-aortic 3 Mediastinal 1 Cervical 1	11
Liver	6
Renal Vein	4
Inferior Vena Cava	3
Bone Vertebrae 1 Orbit 1 Humerus 1	3
Omentum	2
Peritoneum	1
Spinal Cord	1
Scrotum	1
Opposite kidney	1
Operation scar	1

From this Table, it can be seen that the commonest sites for secondary tumours are the lungs (Fig. 19), lymphatic glands and liver (Figs. 20 and 21).

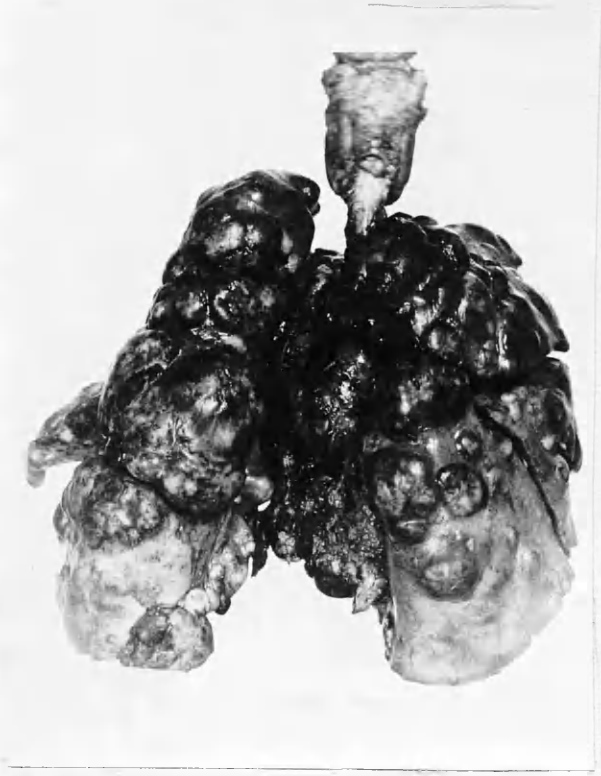
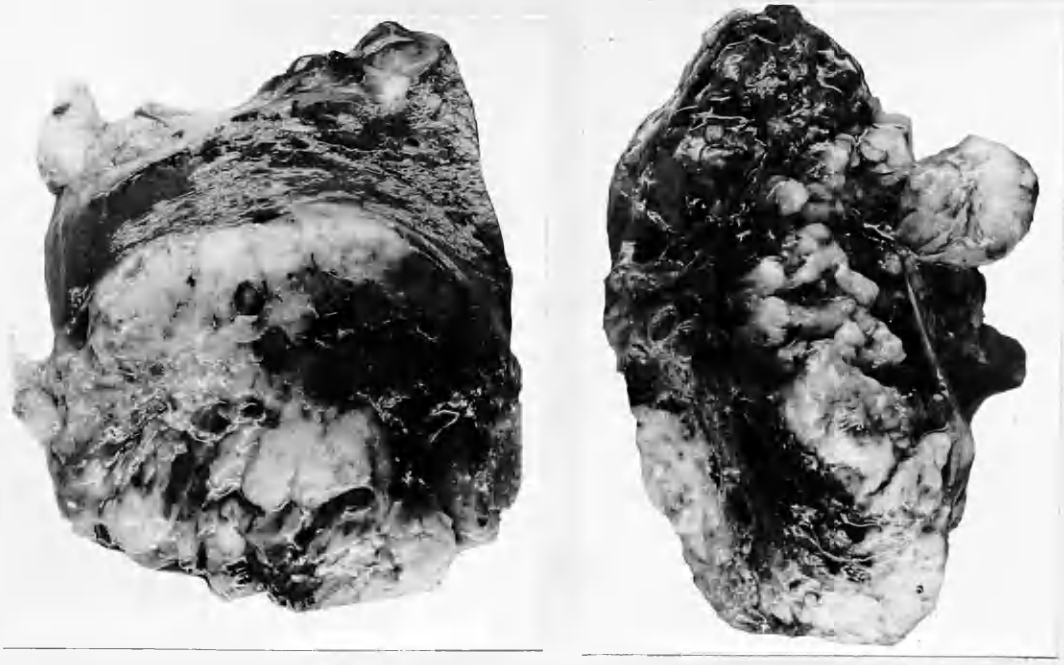


Fig. 19. Metastases in lung.
(Post-mortem specimen from Case 33).



Figs. 20 & 21. Metastases in liver. (Antero-posterior and lateral views of Post-mortem specimen from Case 42).

PART TWO

TREATMENT AND PROGNOSIS

CHAPTER VI - GENERAL PRINCIPLES OF TREATMENT

There are five basic methods by which these tumours may be treated, each of which will be discussed later in the light of the results obtained therefrom but, at the present day, most clinics follow the principles of one of the three main schools of thought:

1. The first group, basing its principles on the teaching of the Boston Childrens' Hospital, favour immediate nephrectomy followed by a course of post-operative radiotherapy.

2. The second group favour pre-operative therapy followed, after shrinkage of the tumour, by nephrectomy and post-operative therapy.

3. The third, and minority group, employ pre-operative radiotherapy followed by nephrectomy but consider that, if the pre-operative therapy has been adequate, further irradiation is both valueless and unnecessary.

Few surgeons, to-day, favour treatment solely by radiation -- although, for a time, this appeared to hold great promise -- and fewer still employ surgery alone. Radiotherapy by itself may, however, still have a limited place in the treatment of advanced cases as occasional dramatic "cures" have been reported even in the presence of lung metastases (Kerr, 1939, Silver, 1947).

THE ROLE OF SURGERY

It is now universally agreed that, in the absence of demonstrable metastases, the tumour mass must be excised at some point in the treatment if there is to be any hope of permanent cure.

It has already been noted that, towards the end of the nineteenth century, the operative mortality in these cases was often as high as 50 per cent but improvements in anaesthetic and surgical techniques, combined with a better understanding of pre- and post-operative care, have reduced this figure to less than 4 per cent (Scott, 1954); and in the Childrens' Hospital, Boston, where the large size of a tumour has never been considered a contra-indication to operation, there have been no operative deaths in the past twenty years (Gross, 1953).

It is also interesting to note that, whereas Czerny experienced a marked reduction in his operative mortality when he changed from a transperitoneal to an extraperitoneal approach, the pendulum has now swung to the opposite extreme and it is generally accepted that the kidney should be exposed transperitoneally in order to allow early ligation of the renal pedicle, thereby preventing the escape of malignant cells into the blood stream while the tumour is being handled.

The usual loin incision,while providing adequate exposure for most operations on the kidney, is totally inadequate for the radical excision of an embryoma and early ligation of the pedicle is almost impossible. As the majority of these tumours are very large by the time the patient reaches hospital, the employment of a transabdominal exposure through a T-shaped or wide transverse incision is recommended.

Of the 63 cases admitted to the Royal Hospital for Sick Children, an attempt was made to remove the tumour in 47, but, in 7 cases, the local invasion was found to be too extensive (at laparotomy) and they were deemed to be inoperable. Out of 40 nephrectomies that were sucessfully carried out, 31 were performed transperitoneally and 9 through a loin incision; the latter route being used only in the earlier cases.

Tender age is no bar to operation and small infants are better treated by early nephrectomy without pre-operative therapy. Deming (1923) successfully removed an embryoma, under local anaesthesia,

from a boy aged twenty-nine days; Campbell (1951) reported a 17-year survival following excision of an embryoma in a child aged six weeks and Case I of the present series is alive and well four and a half years after a successful nephrectomy which was performed at the age of eight weeks.

Operative Technique for Excising Embryomata.

The incision may run transverse or vertically and, when utilising the latter, it may have to be carried the entire length of the abdomen from the costal margin to the pubis. The ascending or descending colon, according to whether the tumour is right or left sided, is then freed from its lateral peritoneal reflection and is turned downwards and medially to expose the renal mass. At this point, the renal pedicle should be dissected out and the vessels clamped off. If convenient, they may now be ligated and divided but it will frequently be found that ligation is more easily performed after the main mass has been liberated. When this has been completed, dissection is then directed at freeing the tumour mass from its bed. No attempt should be made to clear the perinephric fat from the renal capsule as all this tissue should be removed in bulk along with the tumour and involved kidney, taking care to ligate the numerous dilated branches of the lumbar veins which are frequently seen traversing the tumour. When the mass has been completely freed, the ureter is clamped and divided and the whole structure is removed from the wound. Thereafter, all bleeding points are secured and an attempt should be made to dissect the lymphatics off the main vessels right up to the diaphragm. The colon is then replaced in its original bed in order to cover the denuded area and the abdominal wall is carefully closed in layers.

If any obvious tumour tissue is found - which cannot be completely removed - metal skin clips may be inserted into it as this allows much more accurate and intensive direction of subsequent radiotherapy.

Alternative exposures for these tumours which are, at present, in vogue in the United States are:

(1) The Dorso-Lumbar Flap Exposure (Nagamatsu, 1950)

The incision runs along the upper border of the 12th rib as far as the angle and then sweeps upwards in a vertical direction just medial to the angle of the ribs and just lateral to the border of the sacrospinalis muscle, ending in the 9th interspace. After dividing

the latissimus dorsi and freeing the lumbar muscles from the lower three ribs, a segmental resection of the 11th and 12th ribs is carried out, followed by division of the costo-vertebral ligament and the lateral arcuate ligament of the diaphragm; thus providing a wide exposure of the kidney by retraction of the osteoplastic flap.

(2) The Trans-thoracic Exposure (Chute, Soutter and Kerr, 1949)

The incision is made in the line of the 11th rib and runs from the costo-vertebral angle downwards and forwards to within two inches of the umbilicus. The kidney is exposed by resecting the 11th rib and dividing the pleura and diaphragm in the line of the incision.

THE ROLE OF RADIOTHERAPY

Radiotherapy was at one time thought to be preferable to surgery in the treatment of these tumours and Dean (1937) went so far as to state that "...probably if all operations upon these patients were abandoned and full doses of radiation substituted, the survival rate would greatly improve."

In 1934, Portmann called attention to the marked vascularity of these tumours and put forward the theory that post-radiation fibrosis obliterated the terminal blood-vessels and lymphatics, thereby inhibiting growth by devascularisation. In the same year, Randall pointed out that irradiation does not completely destroy all the neoplastic cells and that recurrences following irradiation exhibit a markedly increased resistance to this form of therapy so that, eventually, new growth of the tumour exceeds irradiation destruction.

Bothe (1935) corroborated the "devascularisation theory" of Portmann and, in addition, showed that although the embryonic connective tissue cells were completely destroyed, the epithelial elements showed very little evidence of change. From these observations, he deduced that tumours with an excessive preponderance of epithelial cells would be largely unaffected by radiotherapy, thereby explaining the occasional cases that show no clinical evidence of regression following treatment.

Occasional dramatic results following the use of radiotherapy alone have however been published from time to time; 10-year survivals being reported by Sauer (1948) and by Nesbit and Adams (1946). At the present day, radiotherapy, although still employed, is used almost exclusively in conjunction with surgery because, in spite of the "shrinking" effect which is produced in the vast majority of these tumours, in every case which has been studied histologically after this form of treatment, viable cancer cells have been found and it is not uncommon to get metastases appearing four or more years after an apparent "cure" by means of radiotherapy alone (Kerr, 1939; Bixler et al.; 1944, Nesbit & Adams, 1946).

In a personal communication, Dean (1954) quotes a case, treated by radiotherapy alone, in which the tumour completely disappeared and, 14 years later, when the same kidney was removed because of infection, histological examination showed "... a considerable amount of microscopic viable Wilms' tumour .... although the patient had long been considered cured."

As has already been stated, the vast majority of these tumours are highly radiosensitive with the result that a large, bulky and apparently inoperable tumour can be made to regress to an operable size. In many clinics, a course of pre-operative therapy is now given routinely, and Rusche (1951) looks upon it "... not as a cure, but as a procedure, much as iodine is used preparatory to thyroid surgery."

In most cases, shrinkage will be noticeable within a few days and, although Dean (1945) stated that "...by the end of two weeks the mass will not infrequently have disappeared," this has not been our experience. It is now generally agreed that as soon as maximum regression has taken place -- as determined by clinical and radiological examination -- the tumour should be removed. Occasionally there is no apparent change in the size of the tumour mass after radiotherapy and, if no visible or palpable improvement is noted after six or eight treatments, it is unlikely that it will commence at a later date. Under these circumstances, pre-operative therapy should be abandoned and nephrectomy performed at the earliest opportunity.

While there is still disagreement as to the therapeutic value of pre-operative therapy, most surgeons would agree that radiotherapy is an essential and integral part of the post-operative regime.

At the Royal Hospital for Sick Children, radiotherapy is withheld for two to three weeks in order to allow the wound to heal and, although there is ample evidence in the literature that, in children, early post-operative exposure to x-rays has little or no effect on wound healing (Gross, 1953), this view is still widely held. At the Boston Childrens' Hospital, radiotherapy is started immediately after operation - before the child has recovered from the anaesthetic - and one cannot but be impressed by the fact that, since this regime was instituted, the survival rate in that hospital has increased to 47.3 per cent.

Details of the Cases that received radiotherapy.

Case 24: Aged 18 months. The tumour was considered to be hopelessly inoperable on clinical examination and she was given a palliative course of 2000r in 10 treatments over a period of two weeks. Her condition deteriorated steadily and, although the tumour decreased in size, it remained palpable to the end and she died a few months later.

Case 25: Aged 3 years. The tumour was found to be inoperable at laparotomy and she was given a palliative course of 2000r in 14 treatments over a period of three weeks. She was re-admitted three months later with paralysis of the lower limbs and incontinence due to spinal metastases.

Case 26: Aged 18 months. He was given a course of 1900r in 17 treatments over a period of six weeks and, three weeks later, a transperitoneal nephrectomy was performed. The tumour had burst through its capsule and was densely adherent to the diaphragm. He developed a recurrence within two months and died shortly afterwards.

Case 27: Aged 4 years. He was given a course of 1650r in 14 treatments over a period of three weeks and, eighteen days later, a transperitoneal nephrectomy was performed. Two months later he developed a recurrence which was given 800r in 5 treatments over a period of one week but the recurrence increased in size and he died eight months after the original operation.

Case 28: Aged 4 years. She was given 2000r in 15 treatments over a period of three weeks. The tumour decreased markedly in size and, 14 days later, a nephrectomy was performed. She died one month after operation with metastases in both lungs, liver and lymphatic glands.

Case 29: Aged 4 years. She was given a course of 4000r in 20 treatments over a period of four weeks. The abdominal mass was steadily decreased in size and three weeks later, a nephrectmmy was performed. The tumour was extremely adherent and was almost considered inoperable. Six months later she developed metastases in the chest and orbit.

Case 29: (Contd.) A palliative course of 1500r in 6 treatments was given over a period of one week but she went downhill rapidly and died, at home, a few months later.

Case 30: Aged 10 months. A transperitoneal nephrectomy was performed and, three weeks later, she had a course of 1200r in 14 treatments given over a period of three weeks. He is alive and well eight and a half years later.

Case 31: Aged 10 months. A lumbar nephrectomy was performed and, four weeks later, he was given 1000r in 14 treatments over a period of four weeks. He is alive and well eight and a half years later.

Case 32: Aged 2 years. She was admitted as an emergency and was "opened" as an irreducible intussusception. The renal tumour was discovered and a nephrectomy was performed followed, three weeks later, by a course of 1800r in 15 treatments given over a period of three weeks. She is alive and well three and a half years later.

Case 33: Aged 6 months. A transperitoneal nephrectomy was followed, two weeks later, by a course of 1900r in 15 treatments given over a period of three weeks. At operation, glandular metastases were found near the renal pedicle and the tumour burst in three places during removal. He died six weeks later.

Case 34: Aged 15 months. A transperitoneal nephrectomy was followed, three weeks later, by a short course of 400r in 2 treatments over a period of six days. Four months later, he developed a recurrence under his scar. A palliative course of therapy was given without improvement. He went downhill very rapidly and died.

Case 35: Aged 2 years. An incomplete right nephrectomy was performed; removal being incomplete because of adherence of the tumour to a mass of paravertebral glands. Five weeks later, she was given 3750r in 19 treatments over a period of four weeks. Four months later she developed a recurrence under her scar. She was found to have metastases in her lungs and liver and died shortly afterwards.

Case 36: Aged 2 years. A transperitoneal nephrectomy was followed, three weeks later, by a course of 3000r in 15 treatments over a period of three weeks. He died seven months later with metastases in lung and left humerus.

Case 37: Aged 2 years. A transperitoneal nephrectomy was followed, three weeks later, by a course of 3000r in 20 treatments over a period of four weeks. He died, at home, eight months later.

Case 38: Aged 2 years. A transperitoneal nephrectomy was performed and, three weeks later, she had a course of 1800r in 15 treatments over a period of three weeks. She developed a recurrence under her scar eight months later and died soon after.

Case 39: Aged 3 years. A transperitoneal nephrectomy was performed and, two and a half weeks after, she had a course of 1800r in 14 treatments over a period of three weeks. Nine months later, she developed a recurrence under the scar and died.

Case 40: Aged 4 years. A transperitoneal nephrectomy was performed and, seven weeks later, he had a course of 1700r in 9 treatments over a period of two weeks. He developed a recurrence under the scar three months later and died shortly afterwards.

Case 41: Aged 5 years. A transperitoneal nephrectomy was performed and was followed, three weeks later, by a course of 1700r in 15 treatments over a period of three weeks. Ten months later she developed a recurrence under the scar and a second course of 1000r in eight days was given without effect. She was sent home but returned three months later with a massive recurrence (Fig. 24) and died, in spite of a third course of 1000r.

Case 42: Aged 5 years. A transperitoneal nephrectomy was performed and, two weeks later, she had a course of 1676r in 22 treatments over a period of five weeks. Four months later, she developed a recurrence under the scar and metastases in her liver and died shortly afterwards.

Summary

(1) The total dosage of therapy has varied from 400r to 4000r but there seems to be no correlation between the dosage administered and the survival rate.

(2) The interval between nephrectomy and the start of post-operative therapy was three or more weeks in 78 per cent of the cases. This would appear to be much too long and does not seem to be justified by the argument that radiotherapy delays wound healing in the child.

(3) All but one of the cases that received therapy as a primary treatment showed a marked reduction in the size of the tumour.

(4) Of the 16 cases that were treated by a combination of surgery and radiotherapy, nine (56 per cent) developed a recurrence under the scar and, in each case, the recurrence proved to have developed a high degree of radio-resistancy.

THE EFFECTS OF RADIOTHERAPY

(1) On the Skin:

The skin reaction to deep x-rays appears to be much less severe in children than it is in adults and there seems to be no evidence that wound-healing is delayed by the early institution of irradiation.

(2) On the Leucocyte Count:

In contra-distinction to the mild reaction of the skin, the leucocytes in children appear to be extremely vulnerable to high dosage of x-rays and the constitutional upset is frequently more severe and more rapid in onset than is found in adults. Daily white cell counts must be made during the course of treatment and a study of these counts in our own patients shows that it occasionally drops alarmingly low -- in some cases necessitating temporary cessation of the therapy (Cases 26 and 39). This rapid drop in the leucocyte count is clearly demonstrated in Table XI.

TABLE XI

The Effect of Radiotherapy on the Leucocyte Count.

Case No.	White Cell Count					
	Before Therapy	2nd Day	4th Day	6th Day	8th Day	10th Day
26	10,000	6,000	4,200	3,400	-	1,800
33	14,000	12,000	10,000	9,200	7,000	6,500
34	10,000	6,000	5,400	-	-	-
39	10,600	8,400	8,000	7,000	5,200	3,200
40	10,600	8,500	7,600	6,200	-	4,600

(3) On the Epiphyses and Bone Growth:

Experimental work concerning the effect of radiotherapy on the growth of bones in animals (Gates and Warren, 1943; Barr et al, 1943) has shown that when an epiphysis was exposed to 600r or more, some retardation of growth usually occurred. The degree of stunting with higher doses seems to depend on the age of the animals as well as on the dosage; complete inhibition of epiphyseal growth being produced by 1200r or more.

Neuhauser, Wittenborg, Berman and Cohen (1952) reported 34 children who had received radiotherapy to fields which included the spine -- these cases being studied at intervals ranging from two to thirteen years after treatment. They found that dosages under 1000r (tissue dose) seldom produced a gross permanent deformity of the vertebrae in a growing child, irrespective of the age at which the treatment was given. Children over two years of age were found to tolerate between 1000 and 2000r with only minor growth disturbances but a dosage in excess of 2000r (tissue dose) produced retardation of growth, irrespective of the age of the child. Scoliosis was rarely seen in these cases, the usual finding being non-specific growth retardation and irregularity of ossification of the epiphyseal cartilage. These authors believe, however, that when renal tumours are being irradiated, the x-ray beam can be so directed as to produce minimal disturbance of spinal development.

No significant evidence of growth stimulation has been observed (Frantz, 1950) and the picture of cartilage regeneration is inconsequential.

(4) On the Tumour:

It has been possible to study this effect -- both clinically and histologically -- in five cases, in each of which radiotherapy was employed as a primary treatment.

Of the two cases that were treated by radiotherapy alone, one developed measles and was transferred to a fever hospital before the effect could be ascertained; the other -- who died shortly afterwards -- showed a steady decrease in the size of the tumour, although it remained palpable to the end.

Four cases had a course of pre-operative radiotherapy and, in each of these, the tumour diminished considerably in size; the shrinking effect starting within a week of the first dose. On naked-eye inspection of the affected kidney (at autopsy in one case, and after nephrectomy in four) the tumour was, in all cases, still quite evident (Fig. 22) but the degree of liquefaction and necrosis was very much greater than is normally seen in an untreated embryoma.

On histological section, the most noticeable changes were a marked increase in the amount of necrotic and fibrous tissue (Fig. 23) and, although islands of active tumour cells could almost always be found, the degree of destruction was sometimes so great that it was extremely difficult to detect the presence of any renal elements at all.

The histological reports on these five cases are given below in precis form:-

Case 25: The tumour was composed chiefly of spindle cells in which abundant muscle strands ramified. There was very little attempt to form renal tubules or glomeruli although here and there, some isolated primitive tubules were seen. Some sections showed extensive necrosis with complete loss of structural detail.

Case 26: The majority of the tumour was composed of dense fibrous tissue and mature skeletal muscle fibres but there were scattered areas of highly cellular tumour tissue. (Fig. 23).

Case 27: (This specimen is seen in Fig. 22) There was no living tissue at the centre of the tumour. Well-differentiated tubules were seen together with scattered, and partly fibrosed, glomeruli. No active tumour cells could be found.

Case 28: The necrosis and fibrosis was so widespread that practically no normal stainable tissue could be seen. There was, however, enough pattern left to classify it as an embryoma.

Case 29: Widespread areas of necrosis were present, but there were extensive areas of tumour cells invading and separating normal renal tubules.

Barringer (1937) noticed that regression of the tumour, following radiotherapy, was only temporary and that the tumour grew again within a few months. In addition, he found that a second course of radiotherapy to the re-forming tumour never seemed to give rise to the dramatic regression in size that generally follows primary irradiation and it should be remembered that some embryomata are partially or totally radio-resistant.

(5) On Metastases:

Although radiotherapy was directed at localised metastases in a few of the cases under review, it was always given in palliative doses -- more as a placebo to the child's parents than a serious attempt at obliterating the growth -- and, as a result, it has not been possible to assess its true value in this field.

On the other hand, Nesbit and Adams (1946) reported a 10-year "cure" following irradiation of pulmonary metastases and 4-year "cures" have been reported by Kerr (1939) and Bixler (1944). Randall (1934) even went so far as to recommend pre-operative irradiation of the chest in an effort to create "...an infertile field for metastatic transplants which might be dislodged at operation."

Fig. 22: (Case 27). Bisected kidney with embryoma of upper pole which had been treated by pre-operative radiotherapy.

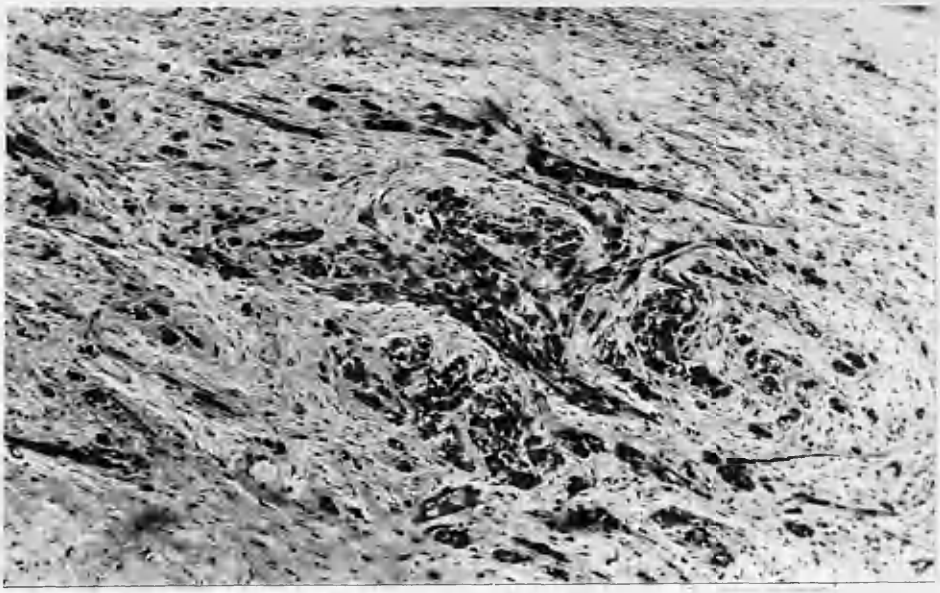


Fig. 23: (Case 26). Photomicrograph of embryoma after a course of pre-operative radiotherapy. Note extensive fibrosis surrounding islets of active malignant cells.

CHAPTER VII - RESULTS OBTAINED BY DIFFERENT METHODS OF TREATMENT

Owing to the fact that the overwhelming majority of recurrences and metastases appear within a year of treatment, a two-year survival is now more or less universally accepted as the standard of probable "cure". While accepting survival for this statutory period as a probable cure, one must bear in mind that metastases have appeared as late as five years post-operatively (Gross and Neuhauser, 1950) and an embryoma of the contra- lateral kidney has been reported ten years after apparently successful treatment (Ritter and Scott, 1949).

For the sake of comparison with the published results in the literature, it has been necessary to review the results in the present series on the basis of this "standard of cure" and henceforth, reference to the words "cure" or "survival" should be taken to mean a freedom from recurrence or metastases for a period of two years after the institution of treatment.

Of the 63 cases under review, efforts to trace 8 of them have proved unsuccessful although, in each case, the last record in their respective case sheets suggests that a fatal outcome was almost inevitable. Of the remaining cases, 49 are known to have died and only 6 can be regarded as probable cures, based on the above standard. This represents an overall mortality for the whole series of 90.5 per cent compared with 85.7 per cent in the 42 treated cases.

In this series, six had a laparotomy performed but were found to be hopelessly inoperable and a further fifteen died within a few days of admission and before any form of treatment had been started.

As it was felt that these findings, based on a relatively small number of cases, might be subject to statistical error, the literature has been extensively reviewed and an analysis of 1141 published cases -- together with the 42 treated cases from this series -- is shown in Table XII.

In an effort to make this analysis as accurate as possible, only those published cases in with the method of treatment was clearly stated have been included and, for those who are interested in statistics, the individual series from which these figures have been abstracted are

TABLE XII

Results obtained by different methods of treatment.

(A) = 42 treated cases from the Royal Hospital for Sick Children.
(B) = 1141 treated cases from the literature.

TREATMENT EMPLOYED	No. OF CASES		2-YEAR SURVIVALS		SURVIVAL RATE	
	A	B	A	B	A	B
Radiotherapy alone	2	118	-	13	-	11%
Nephrectomy alone	23	463	3	87	13%	18.7%
Nephrectomy + pre-operative therapy	4	81	-	21	-	25.9%
Nephrectomy + post-operative therapy	13	347	3	83	23%	23.9%
Nephrectomy + pre & post-operative therapy	-	132	-	42	-	31.8%
T O T A L S	42	1141	6	246	14.3%	21.5%

tabulated in Appendix A to E, the appropriate references being given at the end of the paper.

While it is true that most cases that survive for two years remain permanently free from recurrence -- provided that the tumour has been excised at some point in the treatment -- the 11.0 per cent survival rate for radiotherapy alone would be very much smaller indeed if the standard of "cure" was judged as a 10-year survival.

In the present series of cases, the most satisfactory method of treatment proved, without doubt, to be nephrectomy combined with post-operative radiotherapy and in Boston, where this form of treatment is employed routinely, Gross and Neuhauser claim the most favourable results ever reported in the literature for a large series of cases. It is their contention that, while pre-operative therapy admittedly reduces the size of the mass, tumour cells may be liberated into the blood-stream during the time required for this treatment to take effect and this, in turn, may result in the formation of metastases before nephrectomy can be carried out. It is significant also that, at the Memorial Hospital, New York, -- so long the champion of pre-operative therapy and, in the earlier days, of radiotherapy alone -- where over 100 cases of embryoma have been treated, Dean (1954), in a personal communication, states that it is now their practise to employ early nephrectomy followed by immediate post-operative therapy.

In spite of this powerful evidence in favour of nephrectomy and post-operative therapy, the results depicted in Table XII suggest that, in the hands of the surgeon who is not accustomed to dealing with these tumours, the combination of nephrectomy with pre- and post-operative irradiation probably gives the best chance of survival as the nephrectomy is undoubtedly facilitated by the pre-operative "shrinkage".

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CHAPTER VIII - PROGNOSIS

The figures referred to in Table XII represent only those cases in which the actual form of treatment was stated and in order to appreciate the gradual but steady decrease in the overall mortality, a total of 1581 cases have been abstracted from the literature, of which many received no treatment whatsoever as they were considered to be inoperable; in others, the form of treatment was not stated and the cases could not therefore be included in Table XII.

The overall results are depicted in Table XIII -- the results having been divided into three arbitrary periods for the sake of comparison.

(1) Before 1935: A period when practically all the operable cases were treated by nephrectomy alone and in which, as a result of delayed diagnosis, a relatively high number were admitted in a moribund condition and received no specific treatment.

(2) 1935 - 1944: A period during which radiotherapy was added to the surgeons' armamentarium and earlier diagnosis was facilitated by the advent of pyelography.

(3) 1945 - 1954: A period during which there has been an improvement in anaesthetic techniques which, in turn, has led to more varied and wider exposures of the tumour and, in addition, there has been a marked improvement in the pre- and post-operative care as a result of the introduction of anti-biotics and the more frequent use of blood transfusions.

From Table XIII, it can be seen that, out of these 1581 cases, only 271 survived for two or more years, giving an overall mortality of 82.9 per cent. At the same time, it is heartening to note that, although the prognosis is still extremely poor, there has been a marked improvement in the past half-century as seen from the fact that, whereas in 1897 Walker reported an

overall survival rate of 5.4 per cent in 106 collected cases, Gross (1953) claims a 40.5 per cent survival in 69 personal cases treated by a combination of surgery and radiotherapy between 1931 and 1947.

At the Royal Hospital for Sick Children, Glasgow, radiotherapy was not used in the treatment of these tumours until 1945, but since its introduction the survival rate has increased from 2.6 per cent to 20 per cent (Table XV).

TABLE XIII

Comparison of Survival Rates in different eras.

(1581 Published Cases)

PERIOD OF STUDY	No. OF CASES	No. OF SURVIVORS	SURVIVAL RATE
Before 1935	458	39	8.5%
1935 - 1944	411	74	17.1%
1945 - 1954	712	158	22.1%
TOTALS	1581	271	17.1%

TABLE XIV

Comparison of the Survival Rates before and after 1945

(Royal Hospital for Sick Children)

PERIOD OF STUDY	No. OF RENAL TUMOURS	No. of CASES TREATED	UNTREATED	SURVIVORS	SURVIVAL RATE
Before 1945	38	19	19	1	2.6%
1945 onwards	25	23	2	5	20%

It is significant also that, whereas 50 per cent of the cases admitted before 1945 were considered to be inoperable, only two cases fell into this category after the introduction of radiotherapy; both of whom died within a few days of admission.

Recurrence of tumour growth after operation

These tumours are notoriously liable to recur even after an apparently successful nephrectomy. Out of the 40 cases in which a nephrectomy was performed, no less than 20 (50 per cent) developed a recurrence under the scar within ten months of operation.

TABLE XV

Interval between operation and development of recurrence

	MONTHS AFTER OPERATION										Total	%
	1	2	3	4	5	6	7	8	9	10		
After Surgery alone	-	3	6	1	-	-	1	-	-	-	11	48%
After Surgery plus Radiotherapy.	-	1	1	3	-	-	-	3	-	1	9	52%
T O T A L S	-	4	7	4	-	-	1	3	-	1	20	50%

These figures suggest that the interval between operation and the development of a recurrence tends to be longer if radiotherapy has been employed at some point in the treatment; 82 per cent of the recurrences following surgery alone being present within three months of operation compared with only 22 per cent of those following a combination of surgery and radiotherapy.

Post mortem findings suggest that these recurrences, which can reach massive proportions, are generally centred in omental tissue. (Fig.25). They continue to grow unchecked by any form of treatment until shear bulk, together with a degree of concomitant ascites, causes the skin of the abdominal wall to become stretched like a fine parchment traversed by grossly distended veins (Fig. 24). In the terminal stages, the size of the tumour causes respiratory embarrassment and the cachexia leads to gross emaciation of the face, arms and legs.

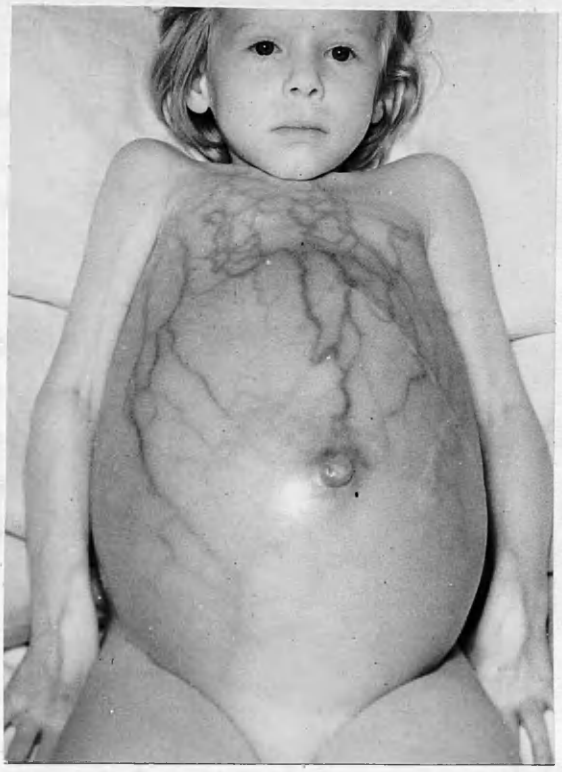

Fig. 24: Photograph of distended abdomen traversed by dilated veins due to massive recurrence.

Fig. 25: Post-mortem specimen of the omental recurrence which produced the clinical findings seen above.
The mass weighed 5260 gms. (11 ½ lbs.)

FACTORS AFFECTING THE PROGNOSIS

In an effort to determine whether or not there are any recognisable features which might affect the survival rate either adversely or otherwise, various factors have been studied in relation to the present series of cases.

(1) Sex of the Child:

As these tumours involve the sexes with equal frequency (Table VI), one is impressed by the fact that of the six cures in this series of cases, five of them were males. However, in an effort to substantiate this apparent predominance of male survivors, the published cures in the literature have been reviewed and it has been found that, over a large series of cases, the mortality is just as high in males as it is in females.

(2) Side involved:

Both kidneys are affected with an approximately equal frequency (Table VII) and there appears to be no correlation between the side involved and the survival rate.

(3) Age at onset:

The chances of survival appear to be considerably increased if the tumour makes its appearance either in adult life or before the child has reached 18 months of age. Statistics with regard to survival from adult embryomata have been adequately dealt with by Culp and Hartman (1948) and will not be referred to in this paper but it is considered significant that four out of the six survivors in this series were under 18 months of age on admission and, on reviewing the published cures, it has been found that 40 per cent of them were in children in this age group.

From a study of Table XVI, it is seen that, in the present series of 63 cases, of those cases in which the tumour appeared in the first year of life, 17.6 per cent survived for two or more years compared with only 6.5 per cent of the older children and, in the larger series of published cases, the survival rate in infants under one was 18 per cent compared with 9 per cent in children over one. Even allowing for a margin

of statistical error, it seems justifiable to state that if a child develops a renal tumour within the first year of life, it has a much better chance of surviving than it would have if the tumour appeared at a later age; this statement being consistent with the findings of Harvey (1950).

TABLE XVI

The Effect of Age on the Survival Rate

AGE IN YEARS	NUMBER OF CASES.		NUMBER OF SURVIVORS		SURVIVAL RATE	
	A	B	A	B	A	B
Under 1	17	161	3	28	17.6%	17.4%
Over 1	46	844	3	77	6.5%	8.7%

A = Cases in the present series.

B = Published cases whose ages were stated, compared with published "survivors" whose ages were stated.

(4) Duration of Symptoms before Admission:

As previously stated, embryomata are notoriously liable to remain symptomless until a late stage in the disease and, frequently, by the time the child's mother discovers the "lump" in the abdomen, the tumour is already too far advanced to hold out any prospect of permanent cure.

Table XVII shows the duration of symptoms of the 63 cases under review and it is notable that three out of the six survivors were admitted for treatment within forty-eight hours of the appearance of the first symptom. The other fact which emerges from this Table is that, of the 15 cases whose symptoms had lasted over three months, none survived and it would appear that brevity of symptoms has some bearing on the chance of ultimate cure.

TABLE XVII

The Effect of Duration of Symptoms on the Survival Rate

DURATION OF SYMPTOMS	CASES	SURVIVORS	SURVIVAL RATE
Under 48 hours	8	3	37.5%
Less than 1 week	14	3	21.4%
Less than 1 month	39	5	12.9%
Less than 3 months	48	6	12.5%
Over 3 months	15	-	-

(5) The effect of delay in instituting treatment:

This factor also appears to have some effect on the chances of survival. Gross stresses the danger that "... these abdominal masses are apt to creat considerable interest on the part of physicians, nurses and students" with the result that they are handled unnecessarily often. In Boston, these cases are regarded as semi-emergencies and it is the practice of that hospital to operate on the day of admission, following minimal pre-operative handling of the tumour: in the present series of cases, on the other hand, delays in instituting treatment of up to three weeks were not uncommon, particularly those cases that were admitted primarily to a Medical Unit.

(6) The presence of Haematuria:

This has already been fully dealt with (Page 23) and it was noted that haematuria was an ill-omen; the overwhelming majority of the cases being dead within a year.

(7) The size of the Tumour:

The size of the tumour bore no relationship to the prognosis in the present series of cases and this finding has also been noted by many other workers.

(8) Operation Findings:

While it is always difficult, if not impossible, to give an accurate long-term prognosis in any case of malignancy, the immediate prognosis can generally be judged by an experienced surgeon based on the operability of the tumour and the presence or absence of metastases. This is not the case, however, when one is dealing with renal embryomata as even the most experienced paediatric surgeons are unable to distinguish the "hopeful" from the "hopeless" at operation.

At first sight, this statement might be considered as heresy but it is made, with some justification, after an intensive study of these tumours - both firsthand and from the records of different surgeons and pathologists -- which has been carried out continuously over a period of two and a half years; and the writer feels fully justified in stating that, in the absence of demonstrable metastases, neither the surgeon who operates on the case nor the pathologist who examines the specimen can give any indication whatsoever as to either the immediate or the remote prognosis.

Time and time again, there appears in the literature the statement that "... at operation, the tumour was found to have burst through its capsule and the prognosis was therefore quite hopeless." In order to refute this statement, while at the same time admitting that in the majority of the cases it is probably an accurate summation, it is interesting to note that Case 32 -- which was admitted as an emergency and "opened" as an irreducable intussusception -- proved to be a right renal tumour which had burst through its capsule and tumour tissue was spilled into the wound during removal. She was given a course of post-operative radiotherapy and is alive and well three and a half years later, although thought to be hopeless at operation.

The operation findings in Case 1 were equally at variance with the ultimate prognosis because, although discrete nodules were found in the omentum at operation (and were later proved histologically to be metastases from an embryoma) the child is alive and free from recurrence four years later, without even having had the benefit of post-operative therapy.

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CONCLUSIONS

1. Embryonic renal tumours are the commonest tumours of the renal tract in infancy and childhood.
2. They may appear at any age but the overwhelming majority arise in the first five years of life.
3. They have no apparent predilection for one side or the other and about 3 per cent are bilateral when first seen.
4. The presenting sign is generally a palpable swelling discovered accidentally by the child's mother but, in many cases, the swelling is preceded for weeks or even months by such vague symptoms as lassitude, anorexia, fretfulness and loss of weight.
5. A palpable swelling is almost always present.
6. The classical "triad" of swelling, pain and haematuria is only found in about 8 per cent of the cases.
7. Few of these cases have symptoms referable to the renal tract although approximately 20 per cent have blood in their urine at some point in their history.
8. Sympathicoblastoma and enlarged spleen are the abdominal swellings most likely to be confused with renal tumours, although several other diseases may, on occasion, give rise to difficulty in the differential diagnosis.
9. A study of the naked-eye and microscopic features has shown that these tumours spread by way of the lymphatics and the blood-stream and that metastases occur most often in the lungs, liver and lymphatic system.
10. It is suggested that these cases should be investigated by intravenous pyelography and it is noted that the commonest radiological finding is a non-functioning or distorted kidney with a large overlying soft tissue shadow.
11. There are five basic methods of treatment for these tumours, each of which has been discussed. Most of the tumours are highly radio-sensitive but it is noted that a combination of surgery and radiotherapy produces vastly superior results to those obtained by employing either method by itself.

12. A wide transperitoneal or transthoracic exposure of the kidney is recommended in order to obtain early ligation of the renal pedicle and to permit a wide dissection of the adjacent fatty tissue and lymphatics.

13. It is suggested that the ideal form of treatment for these tumours -- irrespective of their size -- is prompt nephrectomy (following minimal pre-operative handling) together with intensive radiotherapy to the loin (beginning immediately after operation). For surgeons who have had little or no previous experience in dealing with these tumours, a course of radiotherapy followed by nephrectomy (not more than three weeks later) is perhaps the treatment of choice, as the therapy will reduce the size of the tumour sufficiently to allow a much simpler nephrectomy.

14. It is unjustifiable to postpone nephrectomy because of a dramatic improvement following radiotherapy, as viable tumour cells will still be present in the growth and delay only increases the chances of their dissemination.

15. Whether or not radiotherapy has been employed before operation, a further course should be given post-operatively in order to kill off any remaining cancer cells.

16. The destructive effect of x-rays on the leucocytes of a child has been noted, but it is suggested that the effects in wound-healing are less marked in childhood and should not prevent early institution of post-operative therapy.

17. Experimental work on the effect of x-rays on the growth of bones is quoted and it is seen that whereas a tissue dose of less than 1000r seldom results in permanent changes, 2000r or more will generally produce retardation of growth irrespective of the age of the child.

18. The effects of radiotherapy on the tumour itself has been studied in five cases and it has been shown that regression in size -- as determined by clinical and radiological examination -- is the rule. Microscopic changes, following radiotherapy, include fibrosis and degeneration but it is noted that, in practically every case, focal islets of actively malignant cells can still be detected.

19. Freak "cures" have been produced by irradiation of localised metastases although it is felt that such results must be considered to be the exception rather than the rule. Prophylactic irradiation of the chest is not recommended.

20. The overall mortality is in the region of 80 per cent although recent publications suggest that, as a result of earlier diagnosis and, consequently, earlier treatment, this figure is now being steadily reduced. At the Royal Hospital for Sick Children, the introduction of radiotherapy has increased the survival rate from 2.6% to 20%.

21. Neither the size of the tumour nor the side that is involved appears to have any bearing on the eventual outcome.

22. The mortality in boys is just as high as it is in girls.

23. It is noted that if the tumour makes its appearance before the child is 18 months old, the chances of survival are considerably improved.

24. The prognosis appears to vary indirectly with the duration of the symptoms. The best results are obtained in those cases whose symptoms have been present for less than 48 hours but a hopeful outcome may still be anticipated if they have not lasted more than a week; thereafter the mortality increases considerably and the prognosis is very poor if treatment is not instituted within 3 months of the onset.

25. Haematuria -- which is a late sign and denotes ulceration or invasion of the renal pelvis -- is a symptom which has a grave prognostic significance; the great majority of these cases die within a year of its appearance.

26. These tumours are very prone to recur within 9 months of nephrectomy and recurrences following radiotherapy tend to be highly radio-resistant. It is also noted that when radiotherapy had been employed, although the percentage of recurrences was essentially similar, the interval between operation and the development of a recurrence is substantially prolonged.

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ACKNOWLEDGEMENTS

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APPENDIX "A"

Published cases which were treated by Radiotherapy alone

Author(s)	No. of cases treated by this method	No. of 2 - year survivors
Barringer (1937)	7	3
Bradley & Drake (1949)	5	-
Bixler et al. (1944)	9	1
Daw (1948)	2	-
Dean (1945)	20	5
Gahagan & Yearwood (1949)	2	-
Garrett & Mertz (1953)	9	-
Goddard (1950)	5	-
Huguenin et al. (1953)	9	-
McGee (1944)	1	-
McNeill & Chilko (1946)	2	1
Mertz et al. (1941)	3	1
Nesbit & Adams (1946)	3	1
Pohle & Ritchie (1935)	3	1
Priestley & Broders (1935)	12	-
Riches et al. (1951)	18	-
Rusche (1941)	3	-
Schenck (1948)	5	-
Totals	118	13

APPENDIX "B"

Published cases which were treated by a course of pre-operative therapy followed by nephrectomy.

Author(s)	No. of cases treated by this method	No. of 2 - year survivors
Adams & Hunt (1939)	4	-
Apfel & Goldfader (1943)	1	1
Barringer (1937)	1	-
Bradley & Drake (1949)	6	2
De Vries (1954)	3	-
Dickey & Chandler (1949)	3	2
Gahagan & Yearwood (1949)	2	-
Garrett & Mertz (1953)	2	-
Goddard (1950)	12	3
Hazzard et al. (1949)	2	1
Higgins & Shively (1941)	4	1
Huguenin et al. (1953)	3	-
Kretschmer & Hibbs (1931)	1	-
Long (1939)	4	1
McNeill (1941)	2	2
Maslow (1940)	1	-
Mertz et al. (1941)	1	1
Nesbit & Adams (1946)	3	2
Priestley & Schulte (1942)	3	-
Randall (1934)	3	-
Riches et al. (1951)	13	2
Rusche (1951)	5	2
Senger et al.(1950)	2	1
Totals	81	21

APPENDIX "C"

Published cases which were treated by nephreetomy alone

Author(s)	No. of cases treated by this method	No. of 2 - year Survivors
Abbe (1912)	1	1
Baker et al. (1949)	1	-
Brown (1951)	1	-
Deming (1946)	8	4
Dickey & chandler (1949)	2	-
Gage & Adams (1923)	3	-
Gahagan & Yearwood (1949)	1	-
Gaulin (1951)	2	-
Goddard (1950)	4	-
Gross (1953)	60	14
Hazzard et al. (1949)	5	3
Higgins & Shively (1941)	8	2
Huguenin et al. (1953)	6	-
Hyman (1925)	10	1
Kretschmer & Hibbs (1931)	7	-
Ladd & White (1941)	59	13
Long (1939)	5	-
Loughnane (1914)	12	4
McNeill & Chilko (1946)	2	-
McGinn & Wickham (1946)	1	-
Mixter (1932)	22	5
Monsarrat (1907)	93	16
Nesbit & Adams (1946)	6	3
Priestley & Broders (1935)	4	1
Priestley & Schulte (1942)	13	1
Riches et al. (1951)	21	7
Ritter & Scott (1949)	1	1
Rusche (1951)	2	-
Senger et al. (1950)	1	-
Silver (1947)	4	3
Stern & Newns (1938)	16	3
Walker (1897)	74	4
Weisal et al. (1943)	8	1
Totals	463	87

APPENDIX "D"

Published cases which were treated by nephrectomy followed by a course of post-operative therapy.

Author(s)	No. of cases treated by this method	No. of 2 - year survivors
Adams & Hunt (1939)	1	-
Barringer (1937)	4	-
Bixler et al. (1944)	1	1
Bradley & Drake (1949)	1	-
Burgess (1947)	1	1
Cox (1933)	1	1
Daw (1948)	4	3
Dean & Pack (1932)	16	2
De Vries (1954)	5	3
Dickey & Chandler (1949)	4	1
Gahagan & Yearwood (1949)	5	1
Garrett & Mertz (1953)	5	1
Goddard (1950)	6	1
Gross (1953)	36	18
Hazzard et al. (1949)	7	-
Higgins & Shively(1941)	6	-
Huguenin et al. (1953)	27	2
Kretschmer (1946)	2	-
Kretschmer & Hibbs (1931)	4	1
Kruse et al. (1954)	47	12
Long (1939)	3	1
Maslow (1940)	1	-
Nesbit & Adams (1946)	3	2
Ockerblad & Carlson (1943)	1	1
Pohle & Ritchie (1935)	1	-
Priestley & Broders (1935)	8	-
Priestley & Schulte (1942)	11	2
Rowe & Frazer (1944)	1	-
Riches et al. (1951)	53	8
Rusche (1951)	19	7
Saranina et al. (1954)	35	8
Schenck (1948)	8	-
Senger et al. (1950)	1	-
Silver (1947)	5	3
Taylor (1950)	1	1
Weisal et al. (1943)	13	2
Totals	347	83

APPENDIX "E"

Published cases which were treated by a course of pre-operative therapy plus nephrectomy and a course of post-operative therapy.

Author(s)	No. of cases treated by this method	No. of 2 - year survivors
Banham & Jollies (1946)	1	-
Barringer (1937)	1	-
Bixler et al. (1944)	3	1
Daw (1947)	1	-
De Vries (1954)	1	-
Dickey & Chandler (1949)	1	-
Gahagan & Yearwood (1949)	5	1
Garrett & Mertz (1953)	6	5
Goddard (1950)	9	2
Hazzard et al. (1949)	4	-
Higgins & Shively (1941)	3	1
Huguenin et al. (1953)	15	9
Kretschmer (1946)	5	2
Long (1939)	2	-
McNeill & Chilko (1946)	2	1
Nesbit & Adams (1946)	1	-
Pohle & Ritchie (1935)	2	-
Prather & Friedman (1936)	1	1
Priestley & Broders (1935)	11	1
Priestley & Schulte (1942)	12	3
Riches et al. (1951)	4	1
Rowe & Frazer (1944)	3	2
Rusche (1951)	8	4
Senger et al. (1950)	2	-
Schenck (1948)	4	-
Silver (1947)	4	4
Weisal et al. (1943)	21	4
Totals	132	42

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