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Wilms' Tumor

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I. WILMS' TUMOR

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Twenty per cent of all neoplasms in infancy and childhood are renal in origin while only five-tenths of one per cent of those in adults occur in the kidney. The only neoplasms which are more common in the first decade of life[37,33] are those of the eye and orbit.

It is characteristic of Wilms' tumors that: (1) nearly all of them occur in infancy and childhood, usually before the age of five years; (2) they are congenital in origin; (3) the clinical course is usually silent and rapid; (4) the usual outcome is death; (5) the degree of malignancy is high; (6) the histological picture varies widely; (7) dissemination of the tumor via the blood stream and lymphatics and by direct extension occurs late. There are many theories in regard to pathogenesis.

Historical Facts

Gairdner[71], in 1828, reported the first neoplasm of the kidney in infants. He used the term "fungus hematodes". Van der Byl[213], in 1857, reported a renal tumor with a circumference of eighty-two and one half centimeters and weight of thirty-one pounds in a boy of eight years. In 1870 Catanni[42] was the first to recognize sarcomatous elements in these renal tumors. Kocher[115], in 1876, performed the first transperitoneal nephrectomy for this lesion. In England one year later, Jessop[110] successfully removed a Wilms' tumor in a two and one half year old boy. The patient died nine months later of metastases. Jacobi[106], in 1884, was the first to demonstrate that these malignancies exist at birth and have a typical structure. He proposed that some relationship existed between the rapid growth of the tumor and the rapid development of the kidney. He also reviewed the literature and showed conclusively that the majority of these growths were sarcomatous. Eberth[60] was the first to observe the mixed histologic picture. Israel[105], in 1894, reported a survival in a ten year old operated upon six years before. The most comprehensive study was written by Wilms in 1899.

The first use of postoperative irradiation was made by Hermann[91] in 1915; the patient died three and one half months after the X-ray treatment was begun. One year later, Friedlander[67] used irradiation as the primary treatment. Geraghty[75], in 1923, used preoperative irradiation for the first time. His patient died five and one half years later.

Incidence

Porter and Carter[167] and Walker[216] have reported Wilms' tumor in the fetus. In Porter and Carter's case the neoplasm had to be removed before delivery could be accomplished. Hartenstein[85], Brogan[31], and Ahari and Michael[6] described these tumors in the newborn.

At least fifty per cent of these neoplasms occur before the age of three years and about ninety per cent are to be found under the age of ten years[22, 216,221]. In Walker's review of the literature one hundred and twenty six cases were under the age of five years and twenty-two occurred between the fifth and fourteenth years. Albarran and Imbert[7] confirm Walker's statistics.

The incidence of Wilms' tumors in adults is very low. Esersky et al[62] reviewed the literature up to 1947 and added three cases of their own to bring the total reported to fifty-nine cases in adults. In almost all these fifty-nine the diagnosis was not made preoperatively. The prognosis and treatment does not differ from that in infancy and childhood.

Origin

There is no unanimity as to how these tumors originate. Eberth[60] in 1872 said they arose from inclusions of the Wolffian body. Cohnheim[46] in 1875 and Ribbert[181] in 1886 thought that aberrant germ plasm was the source. Birch-Hirschfeld[21] in 1894 agreed with Eberth. Busse[34] and Muus[156] in 1899 believed

that remnants of the Wolffian body do not occur in the kidney, and suggested that the tumor arose from a segregated portion of the renal blastema which failed to develop normally.

In his monograph Wilms[229] stated in 1899 that undifferentiated mesodermal tissue could produce the various types of tissue found in mixed renal tumors.

Fraser[66] in 1920 thought that the adenomatous tissue present, by a process of metaplasia, became sarcomatous. This change first occurred in the central part of the kidney and extended to the periphery. The muscular tissue of the renal pelvis produced the non-striated muscle. The blood vessels were of primitive structure. Most important was the error in the development of renal blood vessels which produced the erratic growth of the nephrogenic cells.

Geschickter and Widenkorn[76] proposed the term "embryonal nephroma". They thought the tumor was a neoplastic exaggeration of the normal growth processes in the growth zones of the renal cortex in late fetal life and in the first few months of infancy.

Hinman and Kutzman[94] in 1924 said that the simple types of Wilms' tumor might be explained by Birch-Hirschfeld's theory and the more complex ones by Wilms' theory of origin. In 1931 Nicholson[16] believed the origin "was a physiologic evolution of a somatic tissue after abnormal stimulation at a time when growth is active and differentiation begins. The tumor does not arise in a malformed organ but represents and is a malformed organ." Since the degree of differentiation and number of tissues represented varied markedly, Dean and Pack[52] in 1932 thought it was evident that these neoplasms originated at different developmental periods in the embryo. If the microscopic appearance is like that of the kidney with primitive glomeruli and tubules, the predominating contributing structure is the renal blastema. However, if the tumor anlage separates before the urogenital ridge has formed the nephrotome, the multipotency of the cells may account for the multiple types of tissue found. By metaplasia the smooth muscle can be converted into striated muscle. Ewing[63] proposes the renal blastema as the source of these tumors; and believes that metaplasia plays an important role.

Pathology

The Wilms' tumor usually grows expansively until it attains a tremendous size. In most instances it is covered by a cap of normal renal tissue which may exhibit pressure atrophy. Eventually the capsule is infiltrated and neoplasm extends into the perirenal tissue. Lymphatics and blood stream are usually invaded late.

The usual sites of metastases are the lung, liver, and regional lymph nodes. Metastases have been reported in the brain, adrenals, vertebral column, bladder, subcutaneous tissues, bone marrow and bone[11,64,140,148]. McDonald and Priestley[176] reported that forty-five per cent of their cases had tumor thrombus in the renal vein, or involvement of perineural lymphatics or both. Bland-Sutton[23] described a tumor thrombus filling the entire inferior vena cava. Osler[163] observed a tumor thrombus in the renal vein which became detached and blocked the atrio-ventricular orifice. Tanner[209], Yu[236] and Wilson[230] have reported spontaneous intraperitoneal rupture of these neoplasms. Helwig[89] described a fecal fistula and resultant fibrinopurulent peritonitis.

On section, the neoplasm may be subdivided into lobules. It is gray and opaque and not unlike brain tissue. Hemorrhage and necrosis are commonly seen, and in the larger tumors cysts are not infrequent.

The microscopic appearance varies in different sections from the same tumor. This variegated histology has accounted for the numerous names applied to it: embryonal nephroma, adenosarcoma, rhabdomyosarcoma, malignant embryonal adenocarcinosarcoma, myosarcoma striocellulare, renal sarcoma of infancy, adenomyosarcoma, embryonic sarcoma and, most

commonly, Wilms' tumor.

Epithelial or connective tissue elements may predominate. The former are high cylindrical or cuboidal cells which may be solid or exhibit stages in the differentiation of the tubules. Occasionally structures resembling glomeruli are present. The connective tissue consists of small spindle shaped undifferentiated mesenchymal cells. One third of these tumors have, in addition, a more complex structure in the form of masses of striated and smooth muscle, cartilage, bone and multinucleated giant cells. Metastases may consist of epithelial or connective tissue or both.

Most of the twenty-eight bilateral Wilms' tumors in the literature were discovered at autopsy[39,71,100,114,118,122,123,126,130,140,216]. This probably represents a secondary invasion of the other kidney. Walker's[216] series of one hundred and forty-one embryonal nephromas contained ten bilateral cases. Weisel, Dockerty and Priestley[221] found none in forty-four embryonal nephromas. Ritter and Scott[182] reported a Wilms' tumor in the remaining kidney ten years after a nephrectomy had been done for a similar neoplasm. Gross and Neuhauser[82] reported a patient with bilateral Wilms' tumor who was living and well nine years later. The right kidney was irradiated and then removed; the left kidney was irradiated. Bilateral tumors occurred in about two per cent of the 1130 cases reviewed.

Wilms' tumor in a horseshoe kidney has been reported[61,142,185]. Of the three patients operated upon two are living, five and nine months postoperatively.

Chapian[44] described such tumors in two brothers, both of whom died within seven months after surgery. Bobbio (quoted by Maslow[137]) reported three embryonal nephromas in the same family. Only one of the three had histologic proof of diagnosis. Walker[216] mentioned that Strumpell discovered Wilms' tumors in two brothers - but no pathologic study was mentioned.

Symptoms and Signs

Unfortunately, these tumors are characterized by a lack of symptoms. The classical triad of tumor, pain and hematuria, usually associated with renal neoplasms in adults, occurs in fewer than twenty per cent of embryonal nephromas.

In eighty to ninety per cent of Wilms' tumors, an abdominal mass noted by mother or physician is the first sign.

Pain in the lumbar or abdominal area occurs in about one-third of the cases. This symptom may be attributed to hemorrhage into the tumor, infiltration of the adjacent structures, invasion of the nerves of the renal pedicle, pressure or traction upon the renal pedicle, ureteral occlusion by tumor, or spontaneous rupture of the neoplasm[209,230,235].

Hematuria is present in seven to fifteen per cent. This may be caused by the neoplastic growth into the renal pelvis, the capillaries of the glomeruli, or the renal vessels.

Urgency, frequency, and dysuria are due to a superimposed infection of the urinary tract.

In some instances the presenting complaint may be refererable to the gastrointestinal system. Anorexia, nausea, vomiting, diarrhea, or obstipation are not infrequent.

A low-grade fever occurs in about twenty per cent of these patients. Israel[105] has attributed it to an anaphylactic phenomenon due to albumin emitted by the tumor. Abeshouse and Weinberg[4] believe it is secondary to the hemorrhage and necrosis so commonly found in the embryonal nephroma.

Anemia is not infrequent. It may be produced by neoplastic infiltration or toxic depression of the bone marrow, by malnutrition, or by chronic bleeding into the renal pelvis or into the tumor itself.

The occurrence of hypertension in Wilms' tumor is not uncommon[29,30,49,96,116,195]. Bradley and Pincoff[29] noted a decrease of the elevated blood pressure following nephrectomy in two of five consecutive cases of hypertension and embryonal nephroma. When metastases appeared, hypertension recurred. They concluded that a pressor substance, which was never isolated, existed in the neoplasm. Since hypertension does not accompany all or even most Wilms' tumors, this theory does not seem to have much basis. The consensus is that the tumor produces ischemia by compressing the renal vessels, thus causing severe arteriolar spasm and hypertension[30,49,96,116]. The entire mechanism may not be unlike Page's cellophane bag experiments. If the blood pressure remains elevated after removal of the tumor, it is probably due to prolonged hypertension producing sclerotic changes in the arteries of the remaining kidney.

Varicocle, distended abdominal veins, weight loss, ascites, edema of the lower extremities, dyspnea and cough, cachexia, convulsions, malaise and asthenia are late manifestations.

The average duration of symptoms from onset until diagnosis is made is about two and one half months.

Diagnosis

The presence of an abdominal mass in the first decade of life does not establish the diagnosis of embryonal nephroma.

Excretory urography and if necessary retrograde pyelograms are in most instances successful in making the differential diagnosis. Age is usually no contraindication to the use of cystoscopy and ureteral catheterization, providing the subject's general condition does not contraindicate the use of anesthesia. Some renal tumors may occur in non-functioning kidneys, so that retrograde pyelograms must be done. Excretory urograms are very important in determining the status of the other kidney. The enlarged and often irregular renal outline, elongation and distortion of the calices, and the medial displacement of the ureter are characteristic. Areas of calcification in the tumor are not common.

Transillumination of the mass is of value in determining the presence or absence of a large renal cyst or thin walled hydronephrosis in an infant. Obviously, if the sedimentation rate of the blood is determined it should precede instrumentation. It is usually accelerated. Infrequently, a barium enema is of value in arriving at the correct diagnosis.

Needle biopsy is the most controversial method of diagnosis. It is usually resorted to when all other diagnostic procedures have failed. "The interpretation of the tissue aspirated requires clinical assistance and is a new field to the pathologist who must revive and re-learn many criteria[205]." Stewart[205] at Memorial Hospital has reported 2500 cases of aspiration biopsy including several of the kidney without untoward reactions. If preoperative irradiation is to be utilized, Neely[157] and Mandeville[137] strongly advocate needle biopsy. Adams and Hunt[5] and Mandeville and Nelson[136] report cases in which this diagnostic method confirmed or changed the pre-existing clinical impressions.

Many others feel that the advantages of aspiration biopsy are by far outweighed by the disadvantages[52,123,159,191]. They say it is an unsafe surgical procedure likely to break down the natural barriers to the tumor and to implant malignant cells outside the tumor. The possibility of producing infection is slight. The trauma to vascular structures, though usually not serious, cannot be ignored. Walker[216] reported three cases of peritonitis and death following needle biopsy. Nesbit and Adams[159], Ladd and White[125], and others[52,190] believe the tissue obtained is too frequently not diagnostic.

McLean and Sugura[145] have shown experimentally that the aspiration biopsy produced no implantation or dissemination of tumor which, however, were not naturally occurring lesions.

Differential Diagnosis:

Retroperitoneal neuroblastoma is the most difficult growth to differentiate from Wilms' tumor. However, unilateral hydronephrosis, lymphosarcoma of the retroperitoneal lymph nodes, leukemic infiltration of the kidney and adjacent structures, splenomegaly, cystic kidneys, hepatic tumors, pancreatic tumors, renal tuberculosis, psoas abscess and ovarian tumors must be considered in the differential diagnosis.

Unfortunately, it is not always a simple task to arrive at the correct diagnosis. Bandler and Roen[13] removed a kidney with a huge solitary cyst which they thought was a Wilms' tumor. Kerr[114] cites a similar error in a patient with a unilateral polycystic kidney. Vuori[214] removed a Wilms' tumor in a patient who had been treated elsewhere for splenomegaly.

Treatment

The treatment of Wilms' tumors is a controversial subject. There are five therapeutic methods: nephrectomy; preoperative irradiation and nephrectomy; nephrectomy and postoperative irradiation; preoperative irradiation, nephrectomy and postoperative irradiation; and X-ray therapy alone.

Nephrectomy

Theoretically at least, transperitoneal nephrectomy, with the immediate ligation of the renal pedicle before much manipulation of the tumor has occurred, is the surgical technique of choice. However, despite many statements to the contrary by surgeons who really know better, it is often impossible for technical reasons to ligate the renal vessels before the kidney is mobilized even when the transperitoneal route is used. McNeill and Chilko[146] in 1938 reported a twenty-eight per cent operative mortality in lumbar nephrectomy as compared with twenty-six per cent in transperitoneal nephrectomy. However, there are so many other variables, especially irradiation, that a statistically significant comparison cannot be made.

With the advancement in preoperative and postoperative management, our increasing knowledge of electrolytes, blood transfusions, antibiotics, and development of surgical techniques, the operative mortality has been materially reduced from the thirty-six per cent reported by Walker[216] in 1897. Ladd[125] at Children's Hospital in Boston is the most ardent advocate of primary nephrectomy. He has reported thirty-seven consecutive nephrectomies during thirteen years with two deaths (5.4 per cent).

It appears that the age of the patient is no longer as serious a hazard as it used to be. Deming[57] and Campbell[38] removed a renal neoplasm from a twenty-nine day and a forty-two day old infant, respectively. Both infants survived.

Preoperative Irradiation and Nephrectomy:

Appel[9], Baird[10] and many others[13,30,68,132,149,177,191,192] advocate preoperative irradiation and nephrectomy. Claimed advantages are: large and previously considered inoperable tumors may shrink so much that their removal becomes feasible; the fibrosis which follows irradiation reduces the operative blood loss; there is less likelihood of rupturing the tumor at operation; the patient can be transfused and the general health improved during the period of irradiation; and finally, all these factors tend to reduce operative mortality.

Ladd and White[125], Nesbit and Adams[159] and Bothe[26] believe that waiting two to six weeks after irradiation is dangerous. Ladd[125] theorizes that during the early period of softening of the tumor which results from X-ray therapy, the possibility of metastasis is increased. He cites a case that developed pulmonary metastases at the end of the preoperative irradiation and postulated that if operation had been done immediately the metastases might not have occurred, a highly speculative conclusion. Available methods of determining the presence or absence of metastases are very crude, so that the pulmonary metastases might well have been present but unrecognizable

before irradiation. This is suggested by Kretschmer's experience with a patient who had a normal chest at X-ray immediately before death, but at autopsy had many pulmonary metastases[120,121].

Almost everyone agrees that the preoperatively irradiated Wilms' tumor, when removed, still contains some viable tumor cells. Randall[177] described a case which was deemed inoperable at operation. After the tumor was irradiated, a nephrectomy was done. At autopsy two years later no metastases were found. Death was due to post-irradiation pneumonitis.

Nephrectomy and Postoperative Irradiation

Postoperative irradiation is used in the hope of destroying residual tumor cells. Nesbit and Adams'[159] two cases with retroperitoneal extension at operation were living and well four and eleven years after nephractomy and postoperative irradiation. Hazzard[88], Helwig[89], and Clayton, Jr.[45] also advocate this plan of therapy. At Children's Hospital in Boston with an increase in the intensity and amount of the postoperative irradiation, the survival rate rose from 32.2 per cent to 47.3 per cent[82]. These figures appear to be based on a postoperative survival of one and one half to two years, and are therefore inconclusive.

Preoperative Irradiation, Nephrectomy, and Postoperative Irradiation

This is the most widely used treatment of Wilms' tumors[5,9,13,38,95,97,114,121,167,168,190,199], and is the one which appears to yield the highest rate of survival[86].

Irradiation

The foremost advocate of irradiation is Dean at Memorial Hospital. In 1939, he reported five five-year survivals in twenty cases so treated; but there was no histologic proof of diagnosis[53]. Barringer[15], from the same hospital, and Portmann[168] feel that a number of Wilms' tumors can be controlled by prolonged high voltage X-ray therapy. However, Priestley and Broders[172] failed to obtain favorable results with irradiation alone.

Nesbit and Adams[159] and Sauer[188] each reported a patient, the presence of whose tumor had been proved histologically, living and well ten years following irradiation. Poblie and Ritchie[166] reported a tumor of the kidney deemed inoperable at exploration, but the patient living and well almost six years after X-ray therapy. No tissue from the neoplasm was examined by the pathologist. Chandler and Dickey[59] have one patient living and well eight years following irradiation. A biopsy was done prior to irradiation.

The following cases found in the literature unfortunately had no histologic proof of diagnosis. Bixler, Stenstrom and Creevy[22] described a patient who had pulmonary metastases before treatment who was living and well three years following irradiation. Kerr's two cases lived more than four years after being treated with X-ray. In one patient pulmonary metastases developed almost five years later. A patient living and well two years and ten months after irradiation was mentioned by McNeill and Chilko[146].

Though the results may not seem encouraging with this method of treatment, it should be kept in mind that most patients treated with only irradiation were considered inoperable.

With repeated courses of X-ray therapy the tumors seem to become radioresistant.

Other Types of Therapy

Coley[47] treated a patient after nephrectomy for two years with his serum. He was living and well twenty-nine years later.

Foster and Medilaharzen[65] implanted radium twice into a renal tumor. The patient was well eight months later.

Complications of Irradiation

Whereas the skin of infants and children tolerates irradiation better than that of adults, anorexia, nausea, vomiting, diarrhea, fever, anemia, and leukopenia are not uncommon. No report of impaired would healing was found in the literature, but it is a possibility.

Some more serious end results have been described following irradiation. Randall[177] mentioned irradiation pneumonitis as a cause of death. Wishard[231] and Campbell[41] reported four cases of irradiation nephritis in the tumor free kidney. Only one patient was living.

Epiphyseal arrest in the vertebrae and pelvis is not fatal but is ultimately disfiguring. Orthopedic procedures are frequently successful in correcting the deformities.

Barringer[15] reported one case of fatal bleeding following irradiation.

Prognosis

As in the case with all neoplasms, the sooner it is discovered and removed, the better the prognosis. Unfortunately, since symptoms appear late, the disease is frequently far advanced with metastases when the patient is taken to the physician.

Millin[149] reports that forty to sixty per cent of Wilms' tumors are inoperable when first seen. Priestley and Broders[172] found this to be true in thirty-seven of sixty-five embryonal nephromas.

Ladd and White[125] believe there is no correlation between the size of the tumor, or the predominance of one cell type, and the prognosis. However, they feel that the prognosis is better if the neoplasm is found in patients under the age of one year. This was confirmed by Harvey[86].

When dealing with malignancies, the term "survival" should be used instead of the word "cure". Since most recurrences of tumor take place during the first year after treatment, Campbell[38] and Ladd[125] believe a one and one half year survival following surgery is a "cure". This may be true in some cases but there are so many exceptions as to make this an unwarranted conclusion. Deaths from metastases have been reported two and one half years, three, four and one half and almost five years post-operatively[2,13,70,114,146,159]. Prather and Crabtree[169] reported a seventy per cent mortality within fifteen months of onset of symptoms; twelve and three tenths per cent survived surgery for two years.

University of Minnesota Hospital Series

From 1930 to 1950 twenty-eight patients have been treated for Wilms' tumors at the University of Minnesota Hospitals. However, in five of the twenty-eight patients there was no histologic proof. I shall review first the twenty-three proven embryonal nephromas.

The ages of the patients ranged from two months to twenty-three years. The average age was four years and nine months. Eighteen were under the age of five years and twenty were less than ten years old. There were twelve females and eleven males; one negro was in the series.

Symptoms

The duration of symptoms varied from one day to one year; the average was two and three-tenths months.

The initial symptoms were as follows:*

Mass	10	
Hematuria	5	(two had a history of trauma)
Weight loss	3	
Fever	2	
Anorexia	2	
Abdominal pain	2	
Irritability	1	

*In two instances the patient had two initial symptoms.

The tumor involved the right kidney in eleven and the left in thirteen patients. One patient had bilateral lesions.

One of the twenty-three patients had pulmonary metastases on admission and, although no nephrectomy was performed, autopsy confirmed the diagnosis of Wilms' tumor.

The blood pressure was elevated in six of the thirteen patients in which it was recorded preoperatively. Following nephrectomy the blood pressure returned to normal in three cases.

Diagnosis

All patients had excretory or retrograde pyelograms. In five cases the affected kidney was functionless. Linear calcification was present in two of the neoplasms.

The sedimentation rate of the blood was measured in five patients and was elevated in all.

Needle biopsy was done six times. The pathologist reported necrotic tissue three times, Wilms' tumor twice, and lymphoblastoma once. In only one individual was there any untoward reaction to aspiration biopsy. The hemoglobin dropped five grams within a week and evidence of peritoneal irritation was noted for several days. There was no local recurrence of tumor in any of these cases but three are dead: one had diffuse tumor spread before biopsy was done, one had bilateral Wilms' tumor, and the third died eight months postoperatively.

There were three incorrect diagnoses. One patient had retrograde pyelograms but no needle biopsy. The diagnosis was Wilms' tumor and ascites. Numerous paracenteses were done. At autopsy, six weeks after first being seen here, a large pseudocyst of the pancreas adhering to the left kidney was discovered.

Another patient had preoperative irradiation with questionable response of the tumor. At operation and on gross examination by the pathologist the diagnosis was malignant nephroma. However, the specimen was a large multilocular cyst of the lower pole of the kidney. The third patient was referred to the University Hospitals with a diagnosis of ruptured appendix. Eight months after nephrectomy the patient died.

Of the twenty-three patients two were not candidates for surgery; one had pulmonary metastases on admission and the other patient had bilateral Wilms' tumor.

Preoperative irradiation was used in thirteen cases and postoperative irradiation was used in twenty-one patients. The response to preoperative irradiation was good in eleven and poor in two patients.

Nine Patients Treated Prior to 1945

Preoperative & postoperative irradiation & nephrectomy
4 patients
2 five year survivals 50%

Nephrectomy & postoperative irradiation
3 patients
2 five year survivals 66%

Six lumbar and one transperitoneal nephrectomy
All four five-year survivals had lumbar nephrectomy.

Eight Patients Treated Between 1946 & 1948 inclusive

Preoperative & postoperative irradiation & nephrectomy
3 patients
2 two-year survivals 66%

Nephrectomy & postoperative irradiation
5 patients
2 two-year survivals 40%

Six Patients Treated
Between 1949 & 1950 Inclusive

Preoperative & postoperative irradiation & nephrectomy
6 patients
2 patients alive 8 months postoperatively
1 patient terminal

In Summary

44% 5 year survivals (4 of 9)
47% 2 year survivals (8 of 17)
Irradiated: 2 year survivals, 7 cases with 4 survivals.
Nonirradiated: 8 cases with 4 survivals.

WILMS' TUMOR WITH HISTOLOGICAL PROOF OF DIAGNOSIS

	Age	Sex	Preoperative X-ray	Nephrectomy	Postoperative X-ray	Comment
1.	3 mos.	M	-	L	+	A 9 yrs. & 9 mos. postoperative
2.	2 mos.	F	-	L (elsewhere)	+	A 5 yrs. & 3 mos. postoperative
3.	18 yrs.	M	+	L	+	A 8 yrs. & 9 mos. postop. - no tumor tissue found in specimen - aspiration biopsy.
4.	18 mos.	M	+	L	+	A 11 yrs. & 8 mos. postoperative
5.	4 yrs.	F	-	exploration & biopsy	-	Bilateral Wilms' tumor - no follow-up
6.	27 mos.	F	-	L (elsewhere)	+	D 9 mos. postop.
7.	18 mos.	F	+	T (elsewhere)	+	D 10 mos. postop.
8.	37 mos.	M	+	L	+	D 3 yrs. & 9 mos. postop. - tumor in renal pelvis & ureter
9.	50 mos.	M	+	-	-	D 3 mos. - lung metastases on admission
10.	18 mos.	F	-	T	+	A 2 yrs. & 2 mos. postop.
11.	8 mos.	M	-	T	+	A 1 yr. & 7 mos. - metastases to spinal column & lungs
12.	6 yrs.	F	-	L (elsewhere)	+	A 1 yr. & 6 mos. later - metastasis to spinal column
13.	4 yrs.	F	+	L	+	A 3 yrs. & 6 mos. postop.
14.	18 mos.	F	-	T	+	A 2 yrs. & 2 mos. postop.
15.	8 mos.	M	-	T	+	A 1 yr. & 8 mos. - metastases to spinal column 1 yr. postop.
16.	51 mos.	F	+	L	+	A 2 yrs. & 5 mos. postop. - peritoneum & adrenal adherent, 2 positive noes at renal pedicle
17.	28 mos.	F	+	L	+	D 8 mos. postop. - tumor in ureter and psoas muscle
18.	5½ yrs.	F	+	L	+	D 8 mos. postop. - tumor in renal vein
19.	30 mos.	M	+	L	+	D 8 mos. postop. - involved lymph noes around I.V.C., tumor ruptured at operation
20.	43 mos.	M	+	L	+	A 8 mos. postoperatively
21.	31 mos.	M	+	L	+	D 8 mos.postop. - tumor left behind at operation.

WIIMS' TUMOR WITH HISTOLOGICAL PROOF OF DIAGNOSIS (Cont.)

	Age	Sex	Preoperative X-ray	Nephrectomy	Postoperative X-ray	Comment
22.	23 yrs. & 7 mos.	M	+	T	+	Terminal in 6 mos. postop. - spleen, ureter, transverse & descending colon adhered to & removed with tumor.
23.	8 yrs. & 8 mos.	F	+	T	+	At 8 mos. postop. - spleen, kidney, descending colon, adrenal removed together.

There were twenty-one nephrectomies, seven transperitoneal and fourteen lumbar; three of the former and five of the latter are still alive. There were no operative deaths.

Metastases were found from two months to one and one half years after treatment was begun. The average time before onset of metastases was seven and one half months. In addition to the more common sites of metastases, there were two with involvement of the dura necessitating decompression and/or X-ray treatment. In addition, one patient had involvement of the skull and one had a rectal shelf.

Besides the usual constitutional reactions to irradiation, scoliosis as a result of epiphyseal arrest and hypoplasia of one half of the pelvis occurred in three patients. Orthopedic correction was used in two of these.

There were five additional cases with the presumptive diagnosis of Wilms' tumor.

	Age	Sex	Irradiation		Comment
1.	2 yrs.	F	+	A	9 yrs. & 1 month after irradiation was begun
2.	10 yrs.	M	+ (slight response)	D	one year after first being seen at University Hospitals. Surgery was refused because tumor was frozen to surrounding tissues
3.	3½ yrs.	M	+	D	one month after admission; lung metastases on admission
4.	5 yrs. & 8 mos.	M	+	D	10 months after first being seen at University Hospitals. No surgery because of ? peritoneal implants & ascites
5.	9 mos.	M	+	D	10 months. Autopsy showed fibrosis & calcification in lower ½ of right kidney.

Case Number 1: The diagnosis of right Wilms' tumor was made and irradiation was begun elsewhere. Because of a cold the patient failed to return to the University Hospitals until two months later at which time a left apical metastasis was present. After a short interval, metastases appeared in the other lung. Following irradiation the lung metastases and right mass disappeared. There has been no evidence of metastases and the patient has been well for the past nine years.

Case Number 5: Six weeks after irradiation of the tumor, the mass had disappeared. The patient died ten months later, at which time hypertension, uremia and pyelonephritis were present. At autopsy there was fibrosis and calcification of the lower pole of the right

kidney; no tumor was found (Chart I)

Chart I

University of Minnesota Hospitals Series
(23 Cases)

	No. Cases Prior to 1946	No. Cases 1946 thru 1948	No Cases 1949 to 1950
Pre- & Postoperative Irradiation, Surgery	4(2 alive)	3(2 alive)	6(2 alive)
Postoperative Irradiation, Surgery	3(2 alive)	5(2 alive)	-
Exploration	1(bilateral Wilms' tumor)	-	-
No Operation	1	-	-
Total No. Cases	9	8	6

Review of the Literature on Results of Treatment

One thousand one hundred and seventy cases of Wilms' tumors were collected from the literature. Unfortunately the treatment was not specified in more than half the cases. Therefore, it is impossible to obtain a satistically significant evaluation of the best method of treatment. Harvery[86], in 1950, reviewed 444 of these neoplasms. He felt that pre- and postoperative irradiation and nephrectomy yielded the best results (Chart II).

Chart II

Survivals According to Method of Treatment
(Harvey)

Treatment	No. Cases	Survival For Two Years or More
Preoperative Irradiation, & Nephrectomy	27	5 (18.5%)
Nephrectomy and postoperative irradiation	109	33 (30.0%)
Pre- and postoperative irradiation & nephrectomy	69	21 (32.3%)
Nephrectomy	180	28 (15.5%)
Irradiation	63	10 (15.7%)

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The survivals of the 1170 Wilms' tumors are charted below according to the method of treatment. There were 153 two year, 82 five year, and 38 ten year survivals (Chart III).

Chart III

Survivals of Wilms' Tumors According to Method of Treatment*
(1170 Cases)

Treatment	Number of Survivals 2 Years	5 Years	10 Years
Preoperative irradiation & nephrectomy	16	12	3
Nephrectomy & postoperative irradiation	37	13	5
Pre- & postoperative irradiation & nephrectomy	23	6	1
Nephrectomy	52	34	22
Nephrectomy, irradiation not stated	12	9	5
Irradiation	13	8	2

*The percentage of survival with the various methods of treatment is not stated because therapy was not specified in most of the deaths due to Wilms' tumor.

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Gross and Newhauser[82] and Harvey[86] believe the prognosis is better if the neoplasm occurs in patients under the age of one year. This might be attributed to early diagnosis and removal of the neoplasm. (Charts IV and V)

Chart IV

Survival Rate of Patients with Wilms' Tumor According to Age
(Harvey)

	No. of Cases	Survival
Under 12 months	65	27 (41.5%)
Over 12 months	407	75 (18.4%)

Chart V

Boston Children's Hospital Series
Mixed Tumor of Kidney

Period of Study	Probable Cures		
	Patients below 12 mos. (per cent)	Patients above 12 mos. (per cent)	All Patients all ages (per cent)
1914-1930 Inclusive 27 Cases (4 Cures)	42.8	5.0	14.9
1931-1939 Inclusive 31 Cases (10 Cures)	71.4	20.8	32.2
1940-1947 Inclusive 38 Cases (18 Cures)	80.0	43.3	47.3

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Gross and Newhauser[82] reported a nine year survival of a patient with bilateral Wilms' tumors. The right kidney was irradiated and then removed. The left kidney was treated with irradiation. There was no tissue examination of the left kidney.

Conclusions

1. A review of the literature reveals 153 two year survivals, 82 five year survivals and 38 ten year survivals among 1170 Wilms' tumors.

2. Twenty-three Wilms' tumors were treated at the University of Minnesota Hospitals prior to 1950; 8 two year survivals among 17 patients treated prior to 1949 (47% survival). Four of 9 cases treated five or more years ago were living $5\frac{1}{4}$ to 11 2/3 years (44.5% survival).

3. The prognosis of Wilms' tumors has improved the past two decades but is still not very good.

4. There is no agreement as to the best method of treatment.

5. Needle biopsy does not appear to be a dangerous procedure.

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International Clinics, 3:231, '46.

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Embryonal mixed tumor (Wilms' tumor) of the kidney.
Chinese Med.J., 59:223, '41.

II. MEDICAL SCHOOL NEWS

Coming Events

March 1	Clarence M. Jackson Lecture: "Fractures About the Hip -- Early and Late Therapy," Carl E. Badgley; Museum of Natural History Auditorium; 8:00 p.m.
March 1 - 3	Continuation Course in Fractures and the Surgery of Trauma for General Physicians
March 26 - 28	Continuation Course in Pediatrics for General Physicians
April 2 - 6	Continuation Course in Urology for General Physicians and Surgeons
April 5 - 7	Symposium on Lupus Erythematosus

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III. UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
WEEKLY CALENDAR OF EVENTS

Visitors Welcome

February 18 - 24, 1951

Sunday, February 18

University Hospitals

9:00 - 10:00	Surgery Grand Rounds; Station 22.
10:30 -	Surgical Conference; Todd Amphitheater.

Monday, February 19

Medical School and University Hospitals

9:00 - 9:50	Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and Staff; Todd Amphitheater, U. H.
9:00 - 10:50	Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; M-109, U. H.
10:00 - 12:00	Neurology Rounds; A. B. Baker and Staff; Station 50, U. H.
11:00 - 11:50	Physical Medicine Seminar; Scoliosis -- Spinal Fusion; John Moe; E-101, U. H.
11:00 - 12:00	Cancer Clinic; K. Stenstrom and A. Kremen; Eustis Amphitheater, U. H.
12:00 - 12:50	Physiology Seminar; Studies of Aging in Mice; Maurice B. Visscher; 214 Millard Hall.
12:15 - 1:20	Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H.

Monday, February 19 (Cont.)

Medical School and University Hospitals (Cont.)

1:30 - 2:30 Pediatric-Neurological Rounds; R. Jensen, A. B. Baker and Staff; U. H.

4:00 - Public Health Seminar; 113 Medical Sciences.

4:00 - Pediatric Seminar; Iron Metabolism; Dr. Lund; Sixth Floor West, U. H.

4:30 - 5:30 Dermatological Seminar; M-436, U. H.

5:00 - 5:50 Clinical Medical Pathologic Conference; Todd Amphitheater, U. H.

5:00 - 6:00 Urology-Roentgenology Conference; C. D. Creevy, O. J. Baggenstoss, and Staffs; Powell Hall Amphitheater.

Minneapolis General Hospital

9:00 - 10:00 Pediatric Rounds; Dr. Tobin; 5th Floor Annex.

10:00 - 11:00 Pediatric Rounds; Franklin Top; 7th Floor Annex.

1:00 - 2:00 Staff Meeting; Classroom; 4th Floor.

2:00 - 3:00 Journal Club; Classroom, Station I.

Veterans Administration Hospital

9:00 - G. I. Rounds; R. V. Ebert, J. A. Wilson, Norman Shrifter; Bldg. I.

11:30 - X-ray Conference; Conference Room; Bldg. I.

1:00 - Metabolic Disease Rounds; N. E. Jacobson and G. V. Loomis; Bldg. I.

4:00 - Medical-Surgical Conference; Conference Room, Bldg. I.

Tuesday, February 20

Medical School and University Hospitals

9:00 - 9:50 Roentgenology Pediatric Conference; L. G. Rigler, I. McQuarrie and Staffs; Eustis Amphitheater, U. H.

9:00 - 12:00 Cardiovascular Rounds; Station 30, U. H.

12:30 - 1:20 Pathology Conference; Autopsies; J. R. Dawson and Staff; 102 I. A.

1:00 - 2:00 Physiology Seminar on Cardiac Metabolism; 129 Millard Hall.

3:15 - 4:20 Gynecology Chart Conference; J. L. McKelvey and Staff; Station 54, U. H.

4:00 - 5:00 Physiology-Surgery Conference; Todd Amphitheater, U. H.

4:00 - 5:00 Pediatric Rounds on Wards; I. McQuarrie and Staff; U. H.

Tuesday, February 20 (Cont.)

Medical School and University Hospitals (Cont.)

5:00 - 6:00 X-ray Conference; Eustis Amphitheater, U. H.

*8:00 p.m. Minnesota Pathological Society Meeting; The Effects of Cortisone and ACTH on Tissue Damage by Bacteria and Bacterial Toxins; Lewis Thomas; Medical Science Amphitheater.

Ancker Hospital

8:00 - 9:00 Fracture Conference; Auditorium.

1:00 - 2:30 X-ray Surgery Conference; Auditorium.

Minneapolis General Hospital

8:00 - 9:00 Pediatric Rounds; Forrest Adams; 4th Floor Annex.

8:30 - Pediatric Allergy Rounds; Dr. Nelson; 4th Floor Annex.

Veterans Administration Hospital

8:45 - Surgery Journal Club; Conference Room; Bldg. I.

8:30 - 10:20 Surgery Conference; Seminar Conference Room, Bldg. I.

9:30 - Surgery-Pathology Conference; Conference Room, Bldg. I.

10:30 - 11:50 Surgical Pathological Conference; Lyle Hay and E. T. Bell.

10:30 - Surgery Tumor Conference; Conference Room, Bldg. I.

1:00 - Chest Surgery Conference; J. Kinsella and Wm. Tucker; Conference Room, Bldg. I.

1:30 - Liver Rounds; Samuel Nesbitt.

2:00 - 2:50 Dermatology and Syphilology Conference; H. E. Michelson and Staff; Bldg. III.

3:30 - 4:20 Autopsy Conference; E. T. Bell and Donald Gleason; Conference Room, Bldg. I.

Wednesday, February 21

Medical School and University Hospitals

8:00 - 8:50 Surgery Journal Club; O. H. Wangensteen and Staff; M-109, U. H.

8:00 - 9:00 Roentgenology-Surgical-Pathological Conference; Allen Judd and L. G. Rigler; Todd Amphitheater, U. H.

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* Indicates special meeting. All other meetings occur regularly each week at the same time on the same day. Meeting place may vary from week to week for some conferences.

Wednesday, February 21 (Cont.)

Medical School and University Hospitals (Cont.)

11:00 - 12:00 Pathology-Medicine-Surgery Conference; Surgery Case; O. H. Wangensteen, C. J. Watson and Staffs; Todd Amphitheater, U. H.

12:00 - 1:00 Radio-Isotope Seminar; Measurement and Beta Radiation with Scintillation Dosimeter; James C. Carlson; 113 Medical Sciences.

5:00 - 5:50 Urology-Pathological Conference; C. D. Creevy and Staff; Eustis Amphitheater.

5:00 - 7:00 Dermatology Clinical Seminar; Dining Room, U. H.

8:00 p.m. Dermatological Pathology Conference; Todd Amphitheater, U. H.

Ancker Hospital

8:30 - 9:30 Clinico-Pathological Conference; Auditorium.

3:30 - 4:30 Journal Club; Surgery Office.

Minneapolis General Hospital

9:00 - 10:00 Pediatric Rounds; J. D. Tobin; 5th Floor Annex.

11:00 - 12:00 Pediatric Rounds; Franklin Top; 7th Floor Annex.

12:15 - Staff Meeting; Follow-up Study of Congenital Heart Disease; M. J. Shapiro; 4th Floor Annex.

1:30 - Pediatric Rounds; E. J. Huenekens; 4th Floor Annex.

Veterans Administration Hospital

8:30 - 10:00 Orthopedic-Roentgenologic Conference; Edward T. Evans and Bernard O'Loughlin; Conference Room, Bldg. I.

8:30 - 12:00 Neurology Rehabilitation and Case Conference; A. B. Baker.

2:00 - 4:00 Infectious Disease Rounds; Main Conference Room, Bldg. I.

4:00 - 5:00 Infectious Disease Conference, W. Spink; Conference Room, Bldg. I.

7:00 p.m. Lectures in Basic Science of Orthopedics; Conference Room, Bldg. I.

Thursday, February 22 -- HOLIDAY

Friday, February 23

Medical School and University Hospitals

8:30 - 10:00 Neurology Grand Rounds; A. B. Baker and Staff; Station 50, U. H.

9:00 - 9:50 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U. H.

Friday, February 23 (Cont.)

Medical School and University Hospitals (Cont.)

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:50 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Department, U. H.

11:45 - 12:50 University of Minnesota Hospitals Staff Meeting; Hydrocephalus; Carrel M. Caudill, Gerald L. Haines, William T. Peyton; Powell Hall Amphitheater.

1:00 - 2:50 Neurosurgery-Roentgenology Conference; W. T. Peyton, Harold O. Peterson and Staff; Todd Amphitheater, U. H.

2:00 - 3:00 Dermatology and Syphilology Conference; Presentation of Selected Cases of the Week; H. E. Michelson and Staff; W-312, U. H.

3:00 - 4:00 Neuropathology Conference; F. Tichy; Todd Amphitheater, U. H.

4:00 - 5:00 Clinical Pathological Conference; A. B. Baker; Todd Amphitheater, U. H.

4:15 - 5:15 Electrocardiographic Conference; 106 Temporary Bldg., Hospital Court, U. H.

5:00 - Urology Seminar; Trauma of the Urinary Tract; Theodore Sweetser; Eustis Amphitheater, U. H.

Ancker Hospital

1:00 - 3:00 Pathology-Surgery Conference; Auditorium.

Minneapolis General Hospital

9:00 - 10:00 Pediatric Rounds; J. D. Tobin; 5th Floor Annex.

9:30 - Surgery-Pediatric Conference; O. S. Wyatt and T. C. Chisholm; 4th Floor Annex.

11:00 - 12:00 Pediatric Rounds; Franklin Top; 7th Floor Annex.

Veterans Administration Hospital

10:30 - 11:20 Medicine Grand Rounds; Conference Room, Bldg. I.

1:00 - Microscopic-Pathology Conference; E. T. Bell; Conference Room, Bldg. I.

1:30 - Chest Conference; Wm. Tucker and J. A. Myers; Ward 62, Day Room.

3:00 - Renal Pathology; E. T. Bell; Conference Room, Bldg. I.

Saturday, February 24

Medical School and University Hospitals

7:45 - 8:50 Orthopedic X-ray Conference; Wallace H. Cole and Staff; M-109, U. H.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; E-221, U. H.

9:00 - 10:30 Pediatric Grand Rounds; I. McQuarrie and Staff; Eustis Amphitheater, U. H.

9:15 - 10:00 Surgery-Roentgenology Conference; J. Friedman, O. H. Wangensteen and Staff; Todd Amphitheater, U. H.

10:00 - 11:30 Surgery Conference; O. H. Wangensteen and Staff; Todd Amphitheater, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:00 - 12:50 Obstetrics and Gynecology Grand Rounds; J. L. McKelvey and Staff; Station 44, U. H.

11:00 - Anatomy Seminar; Blood and Bone Marrow Studies in Normal Laboratory Monkeys, Virginia Winkle; Hematopoietic Response to Radiation, Joseph Wagner; 226 Institute of Anatomy.

Ancker Hospital

8:30 - 9:30 Surgery Conference; Auditorium.

Minneapolis General Hospital

8:00 - 9:00 Pediatric Rounds; Forrest Adams; 4th Floor Annex.

11:00 - 12:00 Pediatric Clinic; Charles May; Classroom, 4th Floor Annex.

Veterans Administration Hospital

8:00 - Proctology Rounds; W. C. Bernstein and Staff; Bldg. III.

8:30 - Hematology Rounds; P. Hagen and E. F. Englund.