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A Clinico-Pathological Study on the Prognosis of Wilms' Tumor*

A Report of 29 Cases with Special Emphasis on Histopathological Findings.

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Nephroblastoma or Wilms' tumor is one of the commonest neoplasms in childhood.[1-3] Its prognosis was regarded as very poor before the last two decades.[4] Only a few cases have been cured and the reported rate of survival was 9% until 1933. Recently, the survival rates reached 47.3%. Lattimer reported a 90% survival rate for patients under the age of one year.[6,7] The factors which have helped to reduce the mortality rate are early diagnosis, prompt nephrectomy and immediate post-operative radiation therapy combined with chemotherapy. The prognosis is better for patients less than two years of age.

In some cases, the prediction of prognosis of the treated patients was found to be difficult, solely on the basis of clinical findings. The purpose of this study is to evaluate the role of the pathological findings in the prognosis of Wilms' tumor.

Materials and Methods

In this review, 29 cases of pathologically proven Wilms' tumor cases from St. Christopher's Hospital for Children in Philadelphia from 1950 through March 1964 are studied. In Table I some of the important findings related to the type of treatment and the length of the follow-ups after surgery are summarized. The emphasis is given to the following aspects in the examination of surgically removed tumors:

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* This study was done at St. Christopher's Hospital for Children, Temple University School of Medicine, Philadelphia, USA., between the years 1961-1964 by the author as a special fellow in Pediatric Pathology.

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TABLE I

Cases as Numbered	Name, Date of Admission	Pathology Number	Age and Sex	Nephrectomy	Side	Radio-therapy	Chemo-therapy	Follow-up
1	R. A. 5–5–50	S–69–50	81/2 yrs. F	Yes	L	Post-op	None	Died (7 mos)
2	F. F. 4–12–51	S–100–51	8 yrs. F	Yes	L	Post-op	None	Died (3 mos.)
3	C. S. 8–21–51	S–171–51	5 Y M	Yes	L	Post-op	None	Survived (9 yrs. follow-up)
4	E. M. G. 10–16–52	S–443–53	13 mos. M	Yes	R	Post-op	None	Survived (7 yrs. follow-up)
5	P. P. 2–12–54	S–2–54	7 mos. F	Yes	R	Post-op	None	Survived (7 yrs. follow-up)
6	C. B. 12–11–54	S–338–54	13 mos. M	Yes	L	Post-op	None	Died (4 wks.)
7	R. S. 4–5–56	S–100–56	20 mos. M	Yes	R	Post-op	None	Survived (5 yrs. follow-up)

The list of the 29 Wilms' tumor cases seen at St. Christopher's Hospital for Children from 1950 to March 1964

TABLE I (Continued)

Cases as Numbered	Name, Date of Admission	Pathology Number	Age and Sex	Nephrectomy	Side	Radio-therapy	Chemo-therapy	Follow-up
8	J. D. 14–14–56	S–105–56	7 1/2 yrs. M	Yes	L	Post-op	Act. D.	Died (22 mos.)
9	T. S. 2–12–57	S–57–57	18 mos. M	Yes	R	Post-op	Nitrogen mustard	Survived (7 yrs. follow-up)
10	R. S. 8–8–57	S–275–57	6 yrs. M	Yes	R	Post-op	None	Died (7 mos.)
11	M. T. 6–19–58	S–198–58	3 1/2 yrs. M	Yes	L	Post-op	None	Died (9 mos.)
12	E. C. 9–19–59	S–345–59	11 mos. M	Yes	L	Post-op	None	Survived (3 yrs. follow-up)
13	E. M. 11–24–59	S–410–59	17 mos. F	Yes	L	Post-op	None	Survived (4 1/2 yrs. follow-up)
14	S. M. 12–11–59	S–433–59	21/4 yrs. M	Yes	L	Post-op	Act. D	Died (2 1/2 yrs.)
15	P. Y. 1–27–60	S–25–60	16 mos. M	Yes	L	Post-op	Act. D	Died (10 mos.)

TABLE I (Continued)

Cases as Numbered	Name, Date of Admission	Pathology Number	Age and Sex	Nephrectomy	Side	Radio-therapy	Chemo-therapy	Follow-up
16	J. T. 2-24-60	S-59-60	5 yrs. M	Yes	R	Post-op	Act. D	Died (8 mos.)
17	C. A. K. 1957	S-427-60	3 1/2 yrs. F	Biopsy Left Nephrectomy	L R	Post-op	None	Died (3, 2/12 yrs.)
18	C. L. 1-18-61	S-22-61	3 11/12 yrs. F	Yes	R	Post-op	None	Survived (3 10/12 yrs.)
19	R. C. 6-24-61	S-271-61	16 mos. M	Yes	R	Post-op	Act. D	Survived (4 yrs.)
20	J. D. 11-27-61	S-463-61	18 mos. M	Yes	L	Post-op	Act. D	Died (3 mos.)
21	T. S. 4-17-62	S-152-62	3 4/12 yrs. F	Yes	R	Post-op	Act. D	Survived (2 5/12 mos)
22	N. D. C. 4-11-62	S-152-62	1 yrs. F	Yes	R	Post-op	Act. D	Survived (2 yrs.)

TABLE I (Continued)

Cases as Numbered	Name, Date of admission	Pathology Nnumber	Age and Sex	Nephrectomy	Side	Radio-therapy	Chemo-therapy	Follow-up
23	B. J. N. 8–16–62	S–402–62	17 mos. F	Yes	L	Post-op	Act. D	Died (6 mos.)
24	W. H. 6–12–63	S–306–63	15 mos. M	Yes	R	Post-op	None	Died (15 days)
25	D. W. 11–16–63	S–367–63	2 1/2 yrs. M	Yes	R	Post-op	Act. D	Died (2 yrs.)
26	M. M. D. 8–16–63	S–443–63	11 mos. M	Yes	R	Post-op	Act. D	Survived (16/12 mos.)
27	345–64	S–182–64	17 mos. M	Yes	R	Post-op	Act. D	Survived (9 mos.)
28	K. T. 6–3–64	S–370–64	2 mos. M	Yes	R	Post-op	Act. D	Survived (9 mos.)
29	C. I. 3–5–58	A–104–58	8 mos. F	No	L	Pre-op	None	Died (9 mos.)

Macroscopic pathological findings: 1. The size of the tumor. 2. The presence of tears in the capsule. 3. Tumor invasion in the calyceal system and the renal pelvis. 4. Tumor invasion in the vessels.

Microscopic pathological findings: For the evaluation of the microscopic findings ten to twenty random sections were examined in each tumor. The type and the differences of the tissues, and the degree of differentiation were noted. The emphasis was given to the following aspects: 1. Areas resembling sarcoma: (Undifferentiated mesenchyma, rhabdomyolastic tissues), 2. Areas resembling carcinoma: (areas resembling embryonic carcinoma, partial tubular and glomerular differentiation), 3. Mature tissues: Striated muscle, bone cartilage, adipose tissue, nerve cells, squamous epithelium. 4. Microscopic invasion of capsule, vessels, renal pelvis and calyceal system by the tumor.

In the microscopic sections, hematoxylin-eosin stains from each paraffin block and Masson's trichrome and PTAH stains from some were used.

Clinical findings:

Sex: As seen in Table I, 20 cases including two male pseudohermaphrodites (68.9%) were males, 9 cases (31.1%) were females.

Age: In Table II and III the percentage of survival according to age is shown. In these tables, two cases (No: 27,28) are not included, since, the duration of their follow-ups was not long enough to consider them cured. However case No: 28, which was only followed 9 months without metastasis is included in the percentage.

TABLE II

Age yrs.	Numbers/Cases	Survived	Died	% of Survival
0–1	4	4	–	% 100
1–2	10	5	5	% 50
2–9	13	3	10	% 23.6
0–9	27	12	15	% 44.3

Percentage of survival according to the age of the 27 treated Wilms' Tumor cases.

The survival rate varied significantly with the patients' age (Table IV). It was 100% in cases up to one year of age, 50% in patients of one to two years of age and 23% in patients of two to nine years of age. In conclusion, the survival rate in Wilms' tumor cases was very good in children under two years of age.

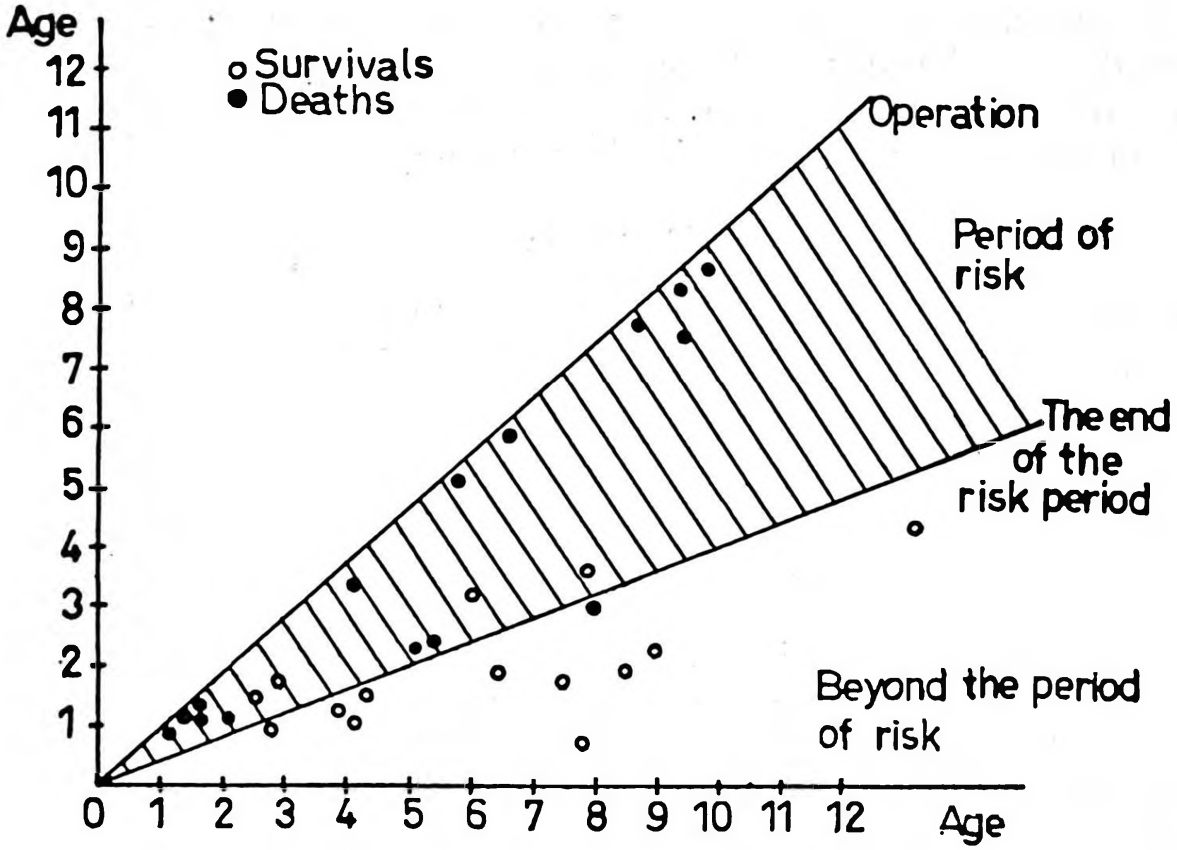
TABLE III

Age yrs.	Female	Died	Survived	Male	Died	Survived
0–1	1	–	1	3	–	3
1–2	2	1	1	8	4	4
2–3	–	–	–	2	2	–
3–4	3	1	2	1	1	–
4–5	–	–	–	2	1	1
5–6	–	–	–	1	1	–
6–7	–	–	–	–	–	–
7–8	2	2	–	1	1	–
8–9	1	1	–	–	–	–
Sum	9	5	4	18	10	9

The number of deaths and survivals according to the age and sex of the 27 treated Wilms' tumor cases.

TABLE IV

THE DISTRIBUTION OF THE SURVIVALS AND THE DEATHS ACCORDING TO THE RISK PERIOD OF THE 29 WILMS' TUMOR CASES



The site of the tumor: In fourteen cases the tumor was located in the right kidney, and again in fourteen, in the left kidney. In one case, there was bilateral involvement (Case No: 17). In 8 cases out of 14, where the tumor was located on the right side and 4 cases out of 14 where the tumor was located on the left side, the patient survived.

Associated congenital anomalies: In five cases of this series some of the developmental anomalies were associated. As shown in Table V, undescended testes in 4, congenital aniridia in 2, male pseudohermaphroditism in two, and mental retardation in two cases were present. The percentage of the associated congenital anomalies in this series was found to be 17.2.

TABLE V

WILMS' TUMOR CASES WITH CONGENITAL ANOMALIES

Cases as Numbered	Age	Congenital Anomalies	Last State
18	47 mos.	Interatrial septal defect	Survived
19	17 mos.	Undescended testis	Survived
24	15 mos.	Undescended testis	Died
25	30 mos.	Syndactylia, high-arched palate, congenital cataract, congenital glaucoma, male pseudohermaphrodite, undescended testis, mental retardation	Died
28	25 mos.	Male pseudohermaphrodite, undescended testis aniridia microcephaly, mental retardation	Survived

Symptoms, signs and laboratory findings: Abdominal pain in 2, abdominal swelling in 9, vomiting in 5, fever in 5, no complaint in 3, constipation in 1, and pallor in 1 were the most common complaints accordingly.

Case Nos. 2, 3, 9 had abdominal pain imitating acute abdomen. The initial diagnosis was that of acute appendicitis. Case No. 2 was operated upon and the appendix was found to be normal. After 4 months, reoperation was done because of the impression of an abdominal mass and an intrarenal tumor was found. But there was also tumor thrombus in the inferior vena cava. This case died in three

months following a second operation. Although in Case Nos. 3 and 9 the initial diagnosis was that of acute appendicitis, the nephrectomy was done in 24-48 hours following admission. These two cases are alive and they are now beyond the period of risk.

The Case Nos. 4,5 and 13 (which were under two years of age) came to the Well Baby Clinic without complaints, but were found to have abdominal masses. These patients are also alive.

The duration of the complaints varied from between 2-3 days to 3 months. Most of the cases came to the hospital with the presenting complaints which occurred one week prior to admission. Case No. 14 complained of poor appetite and pallor. Diagnosis could not be established. After 8 months, the patient was brought to the hospital and the diagnosis was made after finding pulmonary metastases on the chest film.

Physical examination: A palpable abdominal mass was the most common finding. It was found in all cases, except for two (Nos. 2,14) at the time of the first admission. All patients went to surgery in 24-48 hours.

Elevated blood pressure: This condition was noted in almost half of the cases. In patients between the ages of 2-8 years, the systolic pressures varied between 110-190 mmHg, and the diastolic pressure varied between 80-130 mmHg. Four out of them survived; one of which had a blood pesure of 195/110 mmHg.

Hemoglobin level: The lowest hemoglobin value was 8.3 gm/100 ml. Hb values below 10 gm/100 ml were present in 10 cases 6 out of these did not survive.

Urinary findings: Microscopic hematuria was found in three cases (Nos. 6,15,27). In Case Nos. 15 and 27, the tumor grossly infiltrated the renal pelvis. The neoplastic infiltration of the calyceal system could not be demonstrated in Case Nos. 6 and 15 and they did not survive. In this series, no hematuria was present in 9 cases, but the macroscopic and/or the microscopic examination revealed tumor infiltration in the pelvis. One case showed albuminuria and pyuria.

Radiologic examination: Direct chest X-Ray and intraveneous urography (IVP) were done in almost all cases prior to surgery. The X-Ray survey of the long-bones was also done in 1/3 of the patients. In case No. 2, no IVP was done and in case No. 10 no X-Ray information could be found in the patient's chart. In summary, in 23 cases

out of 27 in which IVP was done, deformity of the renal pelvis and calyceal system on the affected side was demonstrated. In two cases, calcification was seen in plane abdominal film. On preoperative chest X-Ray, metastases were found in three patients.

Treatment: Transperitoneal nephrectomy was done in 28 cases. All the patients operated on received radiotherapy of the renal fossa starting the same day of surgery. The total X-Ray dose was 2100-2700 r. Only one case (No. 3) received 4000r irradiation.

In 13 cases Actinomycin D was given with radiotherapy, a total dose of 75/kg. divided into five doses was given intravenously. Seven out of these 13 patients did not survive. In the cases where metastases developed, radiation was given to the area of metastases. Actinomycin D was combined in the treatment in some of those cases.

Complications of the treatment: Two cases (Nos. 6,25) died in the first month following surgery with the rate of death in this period being 3.4%. Complications were those of agranulocytosis associated fulminant pseudomonas septicemia, and infarction of the opposite and only kidney due to renal vein thrombosis. In Case Nos. 15 and 16 however, septicemia also developed, following appearance of metastases for which a high dose of Actinomycin D was given.

In Case No. 11, splenectomy was done with nephrectomy. This case also died 9 months after the operation; but no metastasis was present. Case No. 20 had nephrotic syndrome and the patient died without metastasis. The cause of death was neither the tumor, nor complication of the treatment, but was due to renal failure.

In our series, only minor complications of radiation therapy were seen.

Pathological findings: These results are discussed in two groups. A-Macroscopic findings: The weight of the tumor, the tears in the capsule, tumor invasion in the renal pelves, in the ureter and in the vessels, and the location of the tumor in the kidney are evaluated. The distant or close organ as well as lymph node metastasis, tumor invasion in the renal capsule and in the perirenal fat tissue indicated the presence of metastasis, up to the time of nephrectomy.

In Case No. 17 there was biopsy material only from one side; in case No. 25 there were no adequate gross studies of the tumor and in case 29 no nephrectomy was done. These 3 cases could not be included in this part of the study.

In Case No. 23, since demonstration of a lung metastasis five weeks after surgery was shown, it was suggested that the metastasis was present at the time of the operation but could not have been visualized.

As seen in Table VI and VII, the weight of the tumor varied from 420 gm to 1420 gm. in fatal cases, and 87-965 gm in those cases that survived. The mean weight appeared to be smaller in the latter group. No relation between change of survival and the weight of the tumor could be established.

Rupture of the capsule at the time of surgery: The percentage of the tears in the capsule of the tumor in the fatal 12 cases was 58% (7 out of 12). While, in cases that survived, the percentage of the tears in the capsule of the tumor was 30.7% (4 out of 13) (Case No. 28 is not included)

Tumor invasion in the renal pelves and the ureter: There was tumor infiltration in the renal pelves and or in the ureter in 5 of 13 fatal cases (38.5%) and 4 of the 14 survival cases (28.5%).

Metastasis up to the time of nephrectomy: In this group, distant organ metastasis, lymph node metastasis and tumor invasion in the pericapsular tissue were evaluated. As seen in Table VII no metastasis was detecteed in survivors (0 %). In the other group, it was present in 8 out of 13 (66.6%). In this group, Case No. 20 died not because of the tumor but from another disease.

Tumor in blood vessels: It is both macroscopic and microscopic in finding. In deaths, the percentage was 66.6 (8 cases). In Case No. 20, no invasion in the blood vessels was present. In two cases of survivors, the blood vessel invasion was found to be 14.2%. One of these, (Case 28) is still alive with metastasis, but the patient has not passed the period of risk. If we exclude this case, the percentage will be 7.6 %.

B-Microscopic findings: Section of the tissuses were studied in two respects (Figures 1-8): Part I- Epithelial elements: a. undifferentiated cell groups, b. tubular structures in different stages of differentiation, c. well-differentiated glomerular structures, d. solid or cystic areas of squamous epithelium.

Part II- Mesenchymal Elements: a. undifferentiated mesenchyma (the tissue of the blastema), b. rhabdomyoblastic areas, c. well-differentiated striated muscle.

Undifferentiated Elements in Part I appear as Cancer; in Part II they appear as sarcoma. Correlation of mortality and

TABLE VI

MACROSCOPIC FINDINGS OF THE WILMS' TUMOR CASES THAT DIED

Cases as Numbered	Weight of Tumor	Tear of the Capsule	Tumor in the Pelvis and Ureter	Metastases up to the Time of Nephrectomy	Tumor in Vessels	Pole
1	630 gm	Yes	Yes	No	Yes	Upper
2	1420	Yes	Yes	Yes	Yes	Lower
6	850	Yes	Yes	Yes	No	Lower
8	900	Yes	No	Yes	Yes	Lower
10	465	No	No	No	No	Lower
11	305	Yes	No	Yes	Yes	Upper
14	890	No	No	Yes	Yes	Lower
15	4300	No.	Yes	No	No	Upper
16	750	Yes	No	Yes	Yes	?
20	500	No	No	No	No	Lower
24	1000	No	No	Yes	Yes	Lower

TABLE VII

MACROSCOPIC FINDINGS OF THE WILMS' TUMOR CASES THAT SURVIVED

Cases as Numbered	Weight of Tumor (gm)	Tear of Capsule	Tumor in the Pelvis and the Ureter	Metastases up to the Time of Nephrectomy	Tumor in Vessels	Pole
3	327 gm	No.	No	No	No	Upper
4	165 gm	No	No	No	No	Lower
5	87 gm	Yes	No	No	No	Upper
7	412 gm	Yes	Yes	No	Yes	Upper
9	920 gm	No	Yes	No	No	Lower
12	335 gm	No	No	No	No	Center
13	250 gm	No	No	No	No	Upper
18	965 gm	No	No	No	No	Diffuse
19	422 gm	Yes	No	No	No	Upper
21	750 gm	Yes	No	No	No	Upper
22	500 gm	No	No	No	No	Upper
26	445 gm	No	Yes	No	No	Lower
27	595 gm	No	Yes	No	No	Lower
28	695 gm	Yes	No	No	Yes	Lower

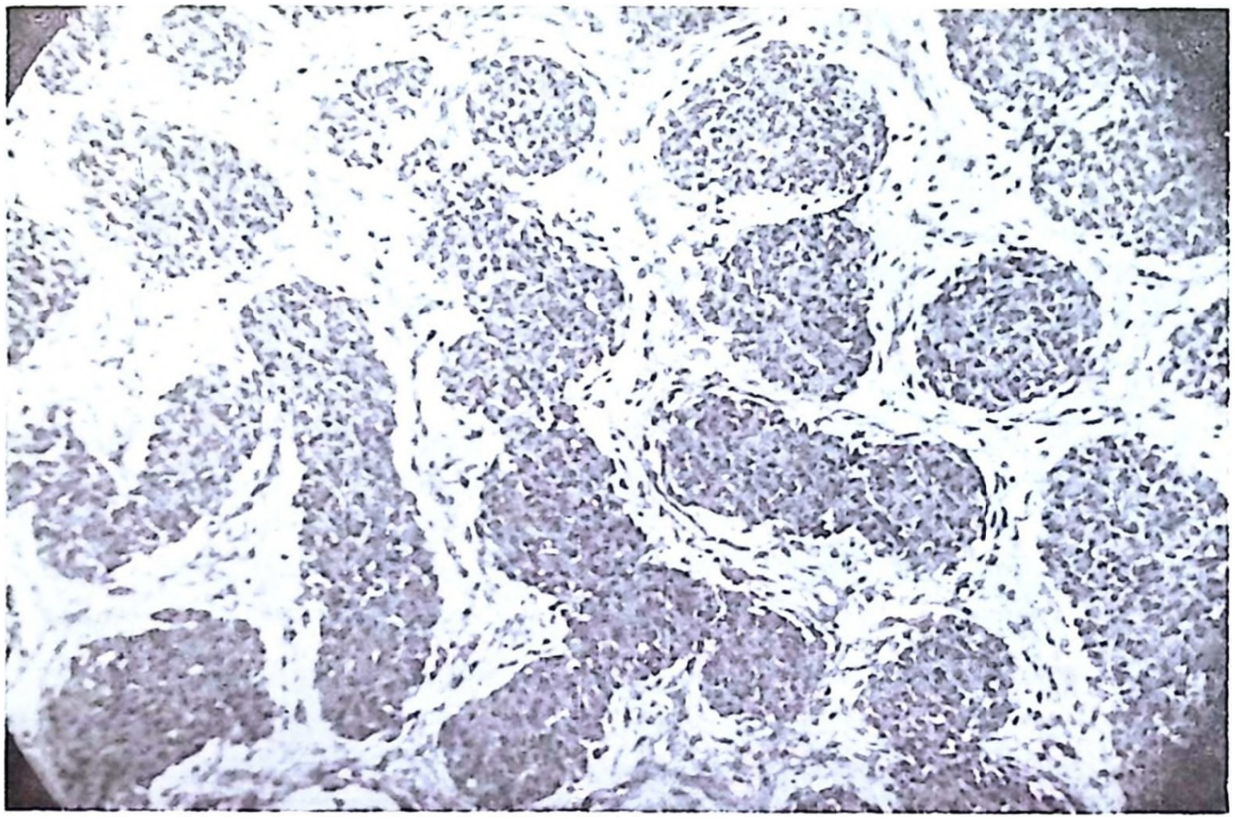


Figure 1

Masses of undifferentiated mesenchyme. H and E stain, 75 x

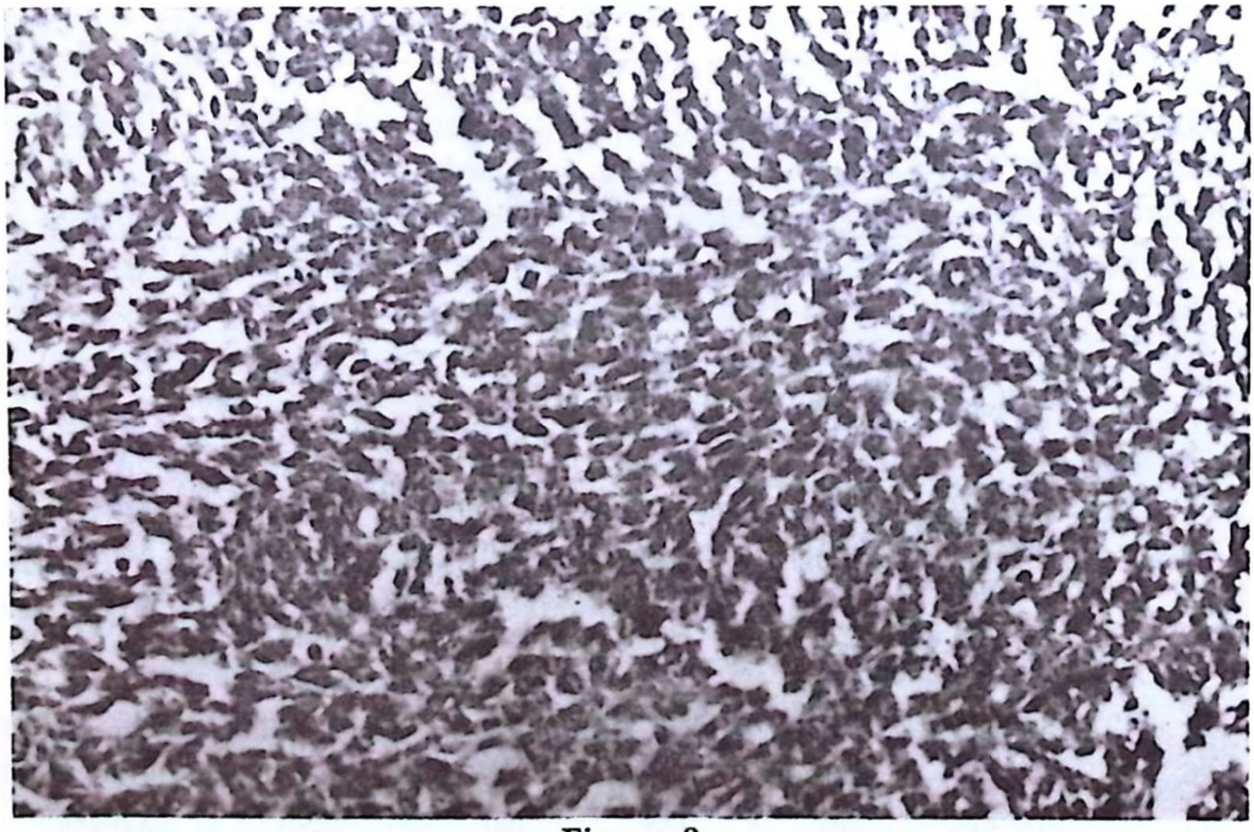


Figure 2

Sacomatous appearance under higher magnification. H and E stain 640 x

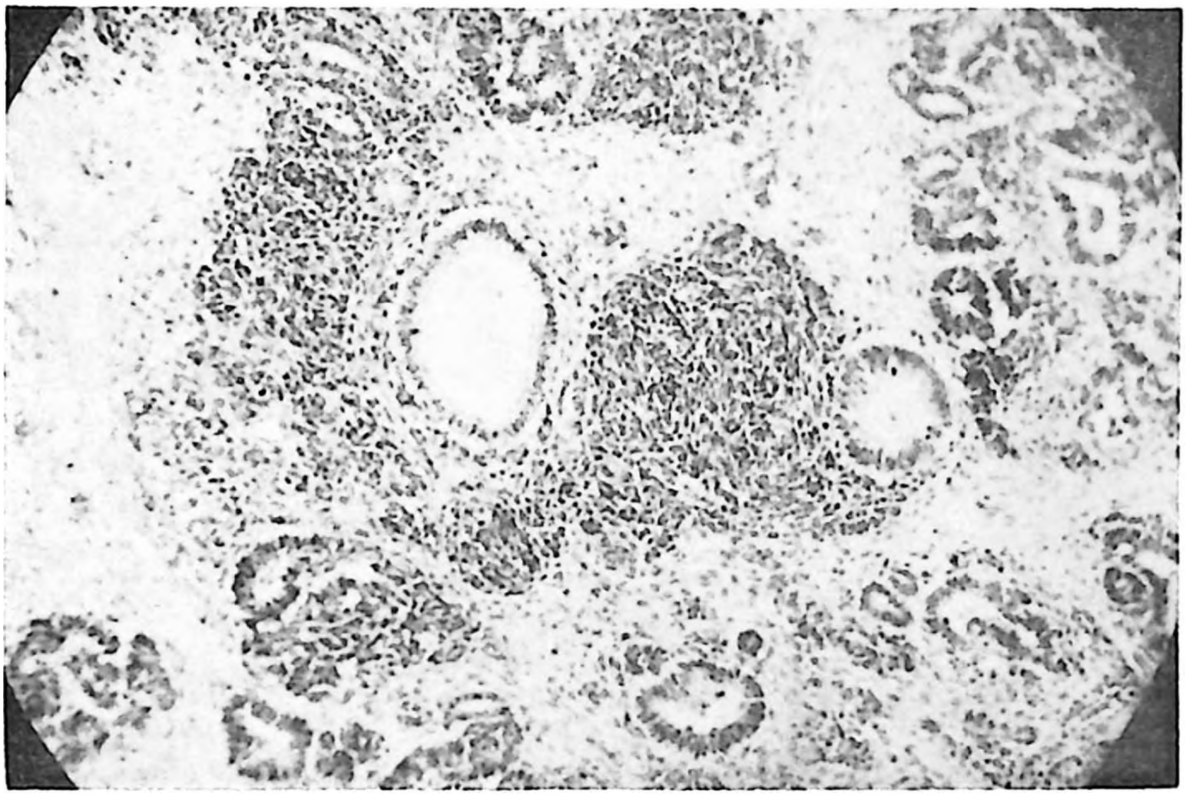


Figure 3

Poorly and well-differentiated tubular structures between the islands of embryonic mesenchyma. H and E stain 100 x

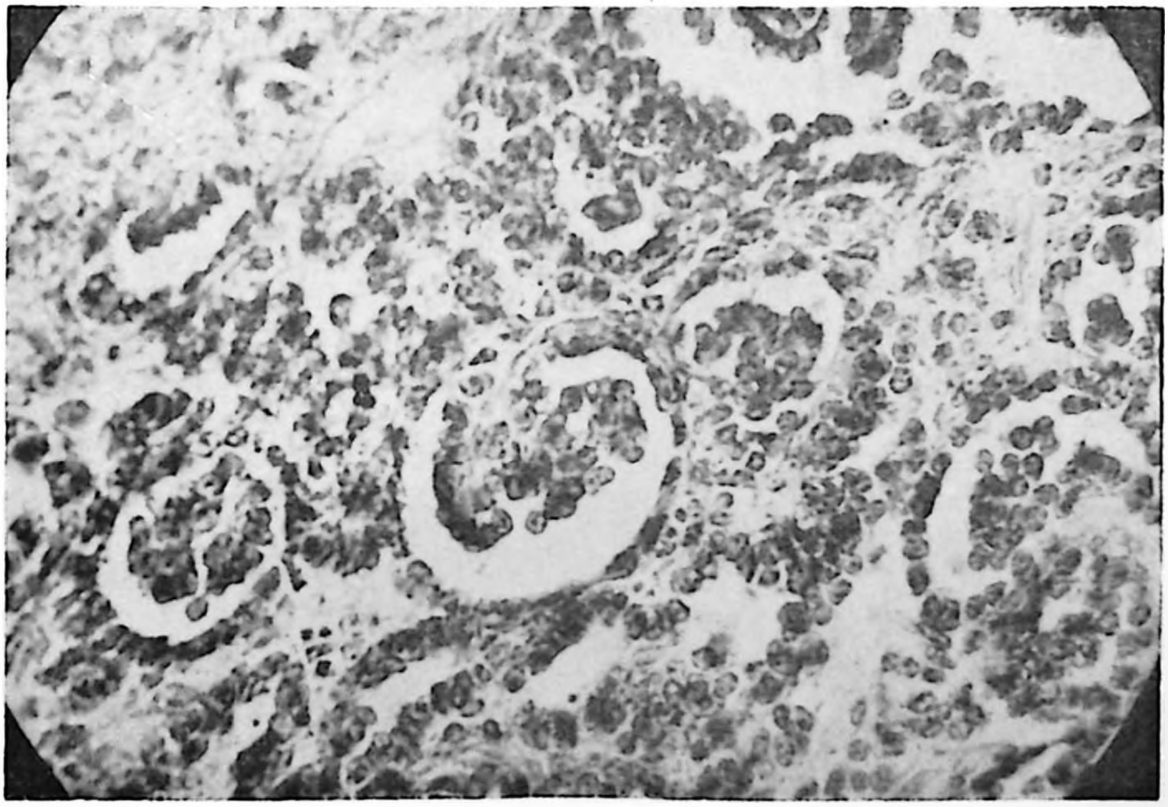


Figure 4

Glomerul-like differentiation. H and E stain 340 x

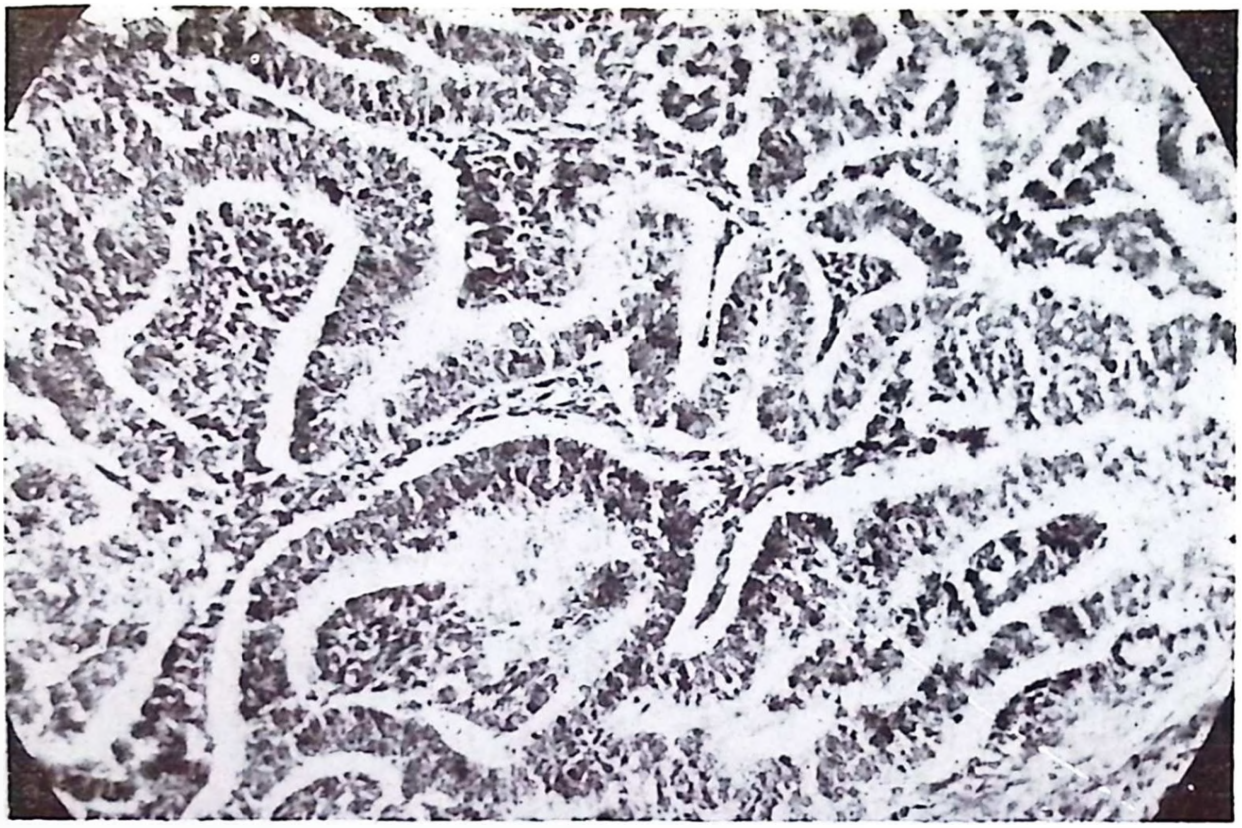


Figure 5

Carcinomatous areas, H and E stain 150 x

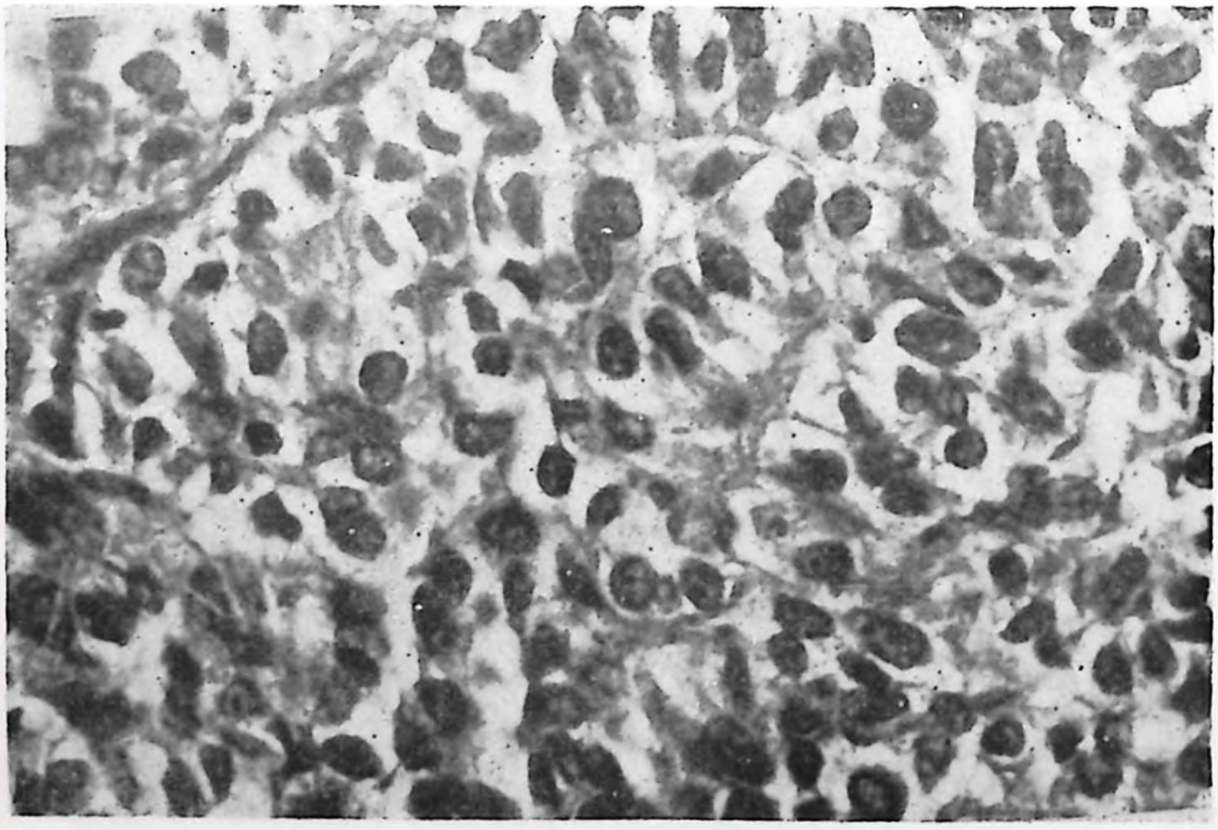


Figure 6

Areas of carcinoma under higher magnification. H and E stain 640 x

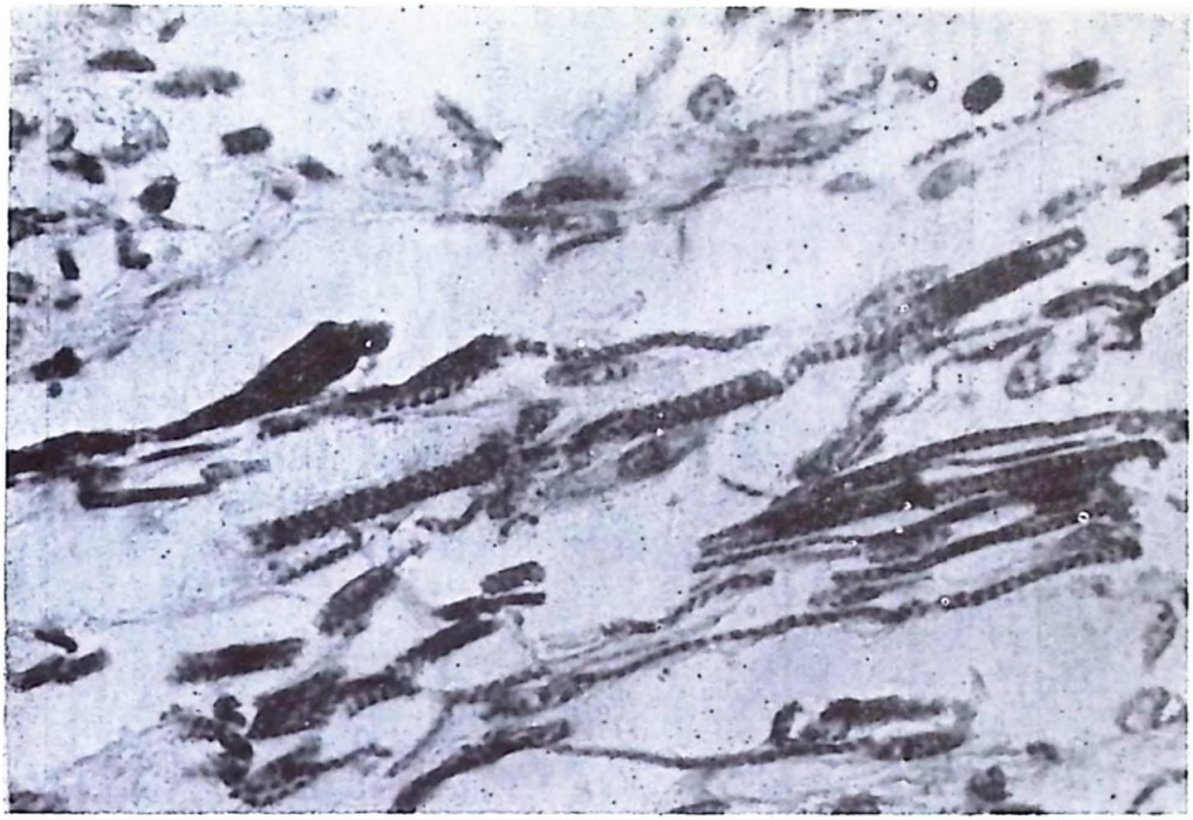


Figure 7

Well-differentiated striated muscle: Cross-striation. PTAH stain 640 x

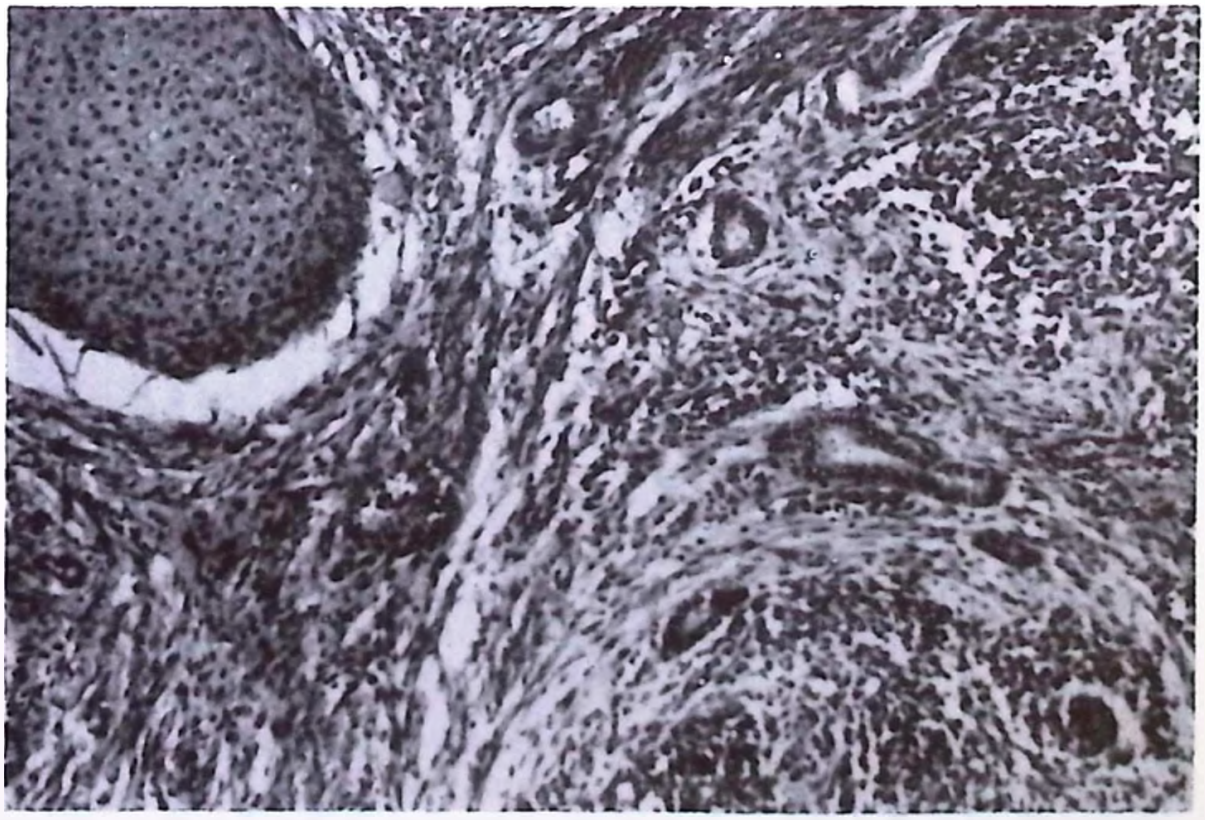


Figure 8

Island of cartilage with tubular structures. H and E stain 100 x

TABLE VIII

MICROSCOPIC FINDINGS OF THE WILMS' TUMOR CASES THAT SURVIVED

	Epithelial Elements				Mesenchymal elements			
Cases as Numbered	Groups of Undifferentiated cells	Tubular Structures	Glomerular Structures	Cystic Structures and Squamous Epithelium	Undifferentiated Mezenchyma	Rhabdomyoblastic Elements	Mature Straited Muscle	Bone, Cartilage, Fat.
4	−	+	−	−	++	+	−	+ Fat
3	+	+	+	−	+++	+	+	−
		Differentiated						
5	−	+++	+	−	+++	−	−	+ Fat
7	−	+	−	−	+++	+	−	−
		Differentiated						
9	−	+	−	−	+++	+	++	+ cartilage
12	−	+	+	−	++	−	−	−
13	−	+	+	−	++	+	−	−
18	−	+	++	−	++	+	−	+ Fat
19	−	+	+	−	++	+	++	−
21	−	+	+	−	++	+	−	−
22	−	+	+	−	++	+	++	+ Bone
26	−	+	−	−	++	+	++	−
27	−	+	+	+	++	++	+	−
28	+	++	+	−	++	−	−	−

X This case had metastases and had been followed for nine months.

TABLE IX

MICROSCOPIC FINDINGS OF THE WILMS' TUMOR CASES THAT DIED

	Epithelial Elements				Mesenchymal Elements			
Cases as Numbered	Groups of Undifferentiated Cells	Tubular Structures	Glomerular Structures	Cystic Structures and Squamous Epithelium	Undifferentiated Mesenchyma	Rhabdomyoblastic Elements	Mature Striated Muscle	Bone, Cartilage, Fat
1	−	+	−	−	++	+	−	−
2	−	+	−	−	++	+	−	−
6	++++	+	−	−	−	−	−	−
8	+++	+	−	−	+	−	−	−
10	+++	+	−	−	+	+	−	−
11	++	++	−	−	+	+	−	−
14	++	++	−	−	+	+	−	−
15	++	++	+	−	+	−	+	−
15	++	++	+	−	+	−	+	−
16	+++	+	+	−	+	−	−	−
17	+++	+	−	−	+	−	−	−
20*	−	−	−	+	+++	+	++	+ Bone
23	+	+	−	−	+	++	+	−
24	+++	+	−	−	+	+	−	−
25**	−	+	−	−	−	−	++	−

* This case had the nephrotic syndrome after nephrectomy and died because of acute renal failure.

** The microsocopic examination is done on the metastatic lesion of the lung and not in the primary tumor.

survival is investigated with respect to the predominance of one of the above-mentioned groups.

Maturation can be partial or complete. In partial maturation tubular and glomerular structures are not developed well and or rhabdomyoblastic structures resemble embryonic tumor cells. In complete maturation, tubular structures are well developed, although ,sometimes they are cystically dilated and mature striated muscle cells can also be seen.

In certain cases, solid masses of undifferentiated cells appear as embryonic carcinoma. In both groups (deaths and survivals), both mesenchymal and epithelial elements were present. Because of the preponderance of one of these elements the following conclusions were made (Tables VIII, IX).

1. In fatal cases there was a preponderance of epithelial elements, while the preponderance of mezenchymal elements were found in those that survived.

2. There were more glomerular structures in these that survived, but few were seen in patients who did not survive.

3. Mature mezenchymal structures were seen more often in the survivors then in the fatal cases.

Discussion

Wilms' Tumor comprises 1/5 of the malignant neoplasms in childhood.[8] Three-quarters of the affected children are below five years of age.[1, 9] Although, it is a childhood neoplasm, at least 100 cases are reported in adults,[10] and the oldest patient is 80 years old.[11] The tumor has also been described in stillborns. Hartenstein collected 13 cases of patients with Wilms' tumor which were apparent during the newborn period.[12]

Wilms' Tumor is not a rare neoplasm. If it is not treated, the mortality rate is very high. Without appropriate treatment, the patients usually die in one year following diagnosis.[2] At present, it is not considered a hopeless disease as was regarded twenty years ago.

According to the Collin's period of risk,[13] generally metastases and/or resideves are not seen in a case of Wilms' Tumor beyond the risk period. Collins demonstrated this in two series.[13, 14] Knox has also confirmed it in 92 cases.[15] Two years after the surgery for patients without metastasis and reoccurrences corresponds to the period of

risk[8] as shown in Gross and Neuhauser,[5] and Kerr's[16] series. That is, cases that had no metastasis during a 2-year period following surgery were considered as cured (Table IV). Accordingly, we considered as cured 2 of our cases, (Nos. 21, 28). In the same table, Case No. 17 appears to be against the Collin's rule. The explanation for this is as follows: This child had the operation at the age of 3.5 years. Right nephrectomy was done after a 3.5 year period without metastasis following surgery; at the age of 7 years the patient came to the hospital because of abdominal pain. A tumor, 8x8 cm in size was found in the left kidney; biopsy proved it to be a Wilms' tumor. Was it a metastasis or a second primary tumor in the other kidney? In general, the site of the metastasis for almost all Wilms' tumors is the lung and usually it appears at least in 1 year following surgery. The patient died 3 months after admission for the second tumor. This patient actually died during the period of risk for the second tumor. We consider this to be a case of bilateral Wilms' tumor.

Age is a very important factor in the prognosis. The younger the child with the Wilms' tumor the better is the prognosis. In this series no deaths are seen in cases below the age of 1 year. At 1-2 years of age the survival rate is 50% while at 2 to 9 years, it is 23%. Gross and Neuhauser[14] showed in their series (38 cases) the survival rate to be 80%, in patients of 0-1 years of age, and 43.3% in children older then 1 year of age. This study revealed a percentage similar to that of Lattimer's series. In Harvey's 472 cases the rate of survival is 43.5 % in patients less than 1 year of age. All these indicate that the prognosis is better if the patient is less than 1 year of age. Since the cases are collected from different hospitals, the percentage of survivals is found to be low in the Harvey[17] and Knutrud[18] series.

In our series, the rate of survival in a 1-2 year old children is 50%. One would expect to have it higher. Five out of 10 cases between 1-2 years of age did not survive. Two out of this group died not because of Wilms' tumor. Their deaths were due to acute renal failure and to post-operative renal infarct and infection, respectively. In Case No. 23 there probably was metastasis at the time of surgery, as mentioned above. If we exclude these patients, a higher survival rate in this period of 1-2 years could be expected.

Sex: In this series 68.9% were males and 31% were females. It seems that here the preponderance of males may be coincidental; since there are series reported in the literature where males and females are equally effected or even with females more frequently affected.[5, 19, 20]

Site: The tumor was located in 14 chlidren on the left side and in 14 children on the right side. One case showed bilateral involvement. Stated incidences of bilateral Wilms' tumor vary in the literature.[21, 23] As mentioned before, there is a preponderance of the involvement of the right kidney in the survivors in this series. This finding does not correspond to Lattimer's results.[6]

Association of congenial anomalies: According to Willis, most of the children with Wilms' tumor were developmentally normal.[20] By 1962, in the literature as an associated anomaly with Wilms' tumor, only one male pseudohermaphrodite and a case of horse-shoe kidney were present. In 1964 Miller collected 440 Wilms' tumor cases and investigated them for congenital anomalies.[24, 25] In 6 cases aniridia was recorded (1/73), while the incidence of aniridia at birth in the normal population is 1/50000. It was 1/14.5 in our series. Miller also recorded 11 cases of undescended testes in his study. There are 4 cases of undescended testes in our series and the percentage is 1/7.2. We found 1 case of interatrial septal defect. Miller recorded one patient with patent foramen ovale and one with tetralogy of Fallot. It seems that the presence of congenital anomalies can give us a clue as to the early detection and treatment of the tumor. Case No. 28 came to the hospital at the age 2 months. At that time, aniridia was diagnosed and were the patient to have been followed at certain intervals for detection of the tumor, it could have 1 been expected that the diagnosis would have been made before the age of 25 months when the palpable mass was present and the removed tumor weighed 695 gm.

Physical and laboratory findings: Thirty-six percent of the cases came to the hospital complaining of abdominal pain. In 1 case error of the initial diagnosis was the cause of 4 months of delay for the nephrectomy (Case No. 2). In case No. 16, an 8 month delay caused lung metastasis to develop. Rarely different interpretations of the signs cause error in diagnosis and delay of prompt treatment.

Hematuria: Microscopic hematuria was recorded in three cases. Some authors mentioned that the presence of hematuria is a poor sign of the prognosis.[2] Two of these cases in our series did not survive. No conclusion can be made from this rather small series.

Anemia: There is no significant finding as far as the prognosis is concerned.

Hypertension: The blood pressure was recorded in 15 cases and found to be high in 10 cases; that is in 2/3 of the cases in this study.

In Lattimer's series it was 60%. Daniel says hypertension can often be found in Wilms' tumor cases.[26] It is thought that the space occupying tumors causes ischemia of the kidney, resulting in hypertension. Six individuals out of 10 with hypertension in this series did not survive. On the other hand, the case which showed the highest blood pressure (195/110) mm Hg was cured. It is clear, that no couclusion could be made in this respect due to the small size of our series.

Diagnosis: Early diagnosis and adequate treatment is very important in the prognosis of Wilms' tumor. As mentioned above, in the youngest patient the prognosis was better. In 28 cases of our series nephrectomy was done in 24-48 hours following the finding of a palpable abdominal mass. Radiation therapy was started right after surgery in all cases. In 13 patients chemotherapy was associated with post-operative radiotherapy. With this type of treatment, the survival rate in this series (27 cases) was found to be 44.3%. Gross and Neuhauser reported the survival rate to be 47% in the series of 38 cases.[5] They recorded no operative deaths. In our series the operative mortality rate was 3.4%.

The role of radiotherapy in the prognosis: Wilms' tumor is in the group of radiosensitive childhood tumors. In these studies, the time of the administration of radiotherapy was right after surgery. There is only 1 case in which radiothrapy was given without surgery (Case No. 29). In the literature, survival has been reported only after radiotherapy.[7, 27, 28] However, none of these were proven pathologically as cases of Wilms' tumors. On the other hand, in some centers, the combination of preoperative radiotherapy, nephrectomy and post-operative radiotherapy was used.[4, 29-31] When the results are compared with those from the series in which nephrectomy and post-operative radiotherapy were used, it was unsatisfactory since the rate of survival was low. Ladd and White mentioned no matter low large the tumor was, it could be removed without surgical death.[4] They recorded a case in which a large tumor (the tumor was 1/4 of the body-weight of that infant) was successfully removed without complication. At the time of preoperative radiotherapy, because of the destruction of the neoplastic tissue the tumor cells could easily get into the blood stream. We administered post-operative radiotherapy and obtained a survival rate very close to the best results reported in the literature. We believe that radiotherapy following surgery is the best type of treatment. Scott mentioned examination of the Wilms' tumor following irradiation and revealed that there was destruction of the embryonic mesenchymal tissue where as very little or no change was noted in the epithelial ele-

ments.[21] One can conclude from our study, that in the tumors where there is a preponderance of epithelial structures, radiotherapy could be ineffective. In this study prognosis was found to be poor in the case having similar histologic appearance.

Chemotherapy: Actinomycin D was used in 14 cases in this series with 6 survivors. Because of the small number of cases the value of this treatment is not evaluated and is not compared with those in the literature.[32-33]

The value of the pathological findings in the prognosis: In the long run, the weight of the tumor did not seem to be significant in the prognosis. As seen in Table VI and VII, in Case No. 18, the weight of the tumor was 965 gr. and the patient is living without metastasis. In Case No. 11, however, the weight of the tumor was 305 gr. but the patient did not survive. There was no direct correlation between the weight of the tumor and the prognosis in this series, as Lattimer found. The lower pole appeared to be more frequently involved in fatal cases (8 out of 12). This finding didn't correspond to Lattimer's result.[7] We did not consider that there was any relationship between the location of the tumor and the prognosis.

In 69.3% of the survivors no capsular tears were detected. Lattimer reported a 74% survival rate in the capsulated tumors without tears. The rate for tumor invasion in the renal pelves and the ureter was 38.5% in fatal cases and 28.5% in those still alive, indicating that this also had no significant part with regard to the prognosis of the tumor.

The percentage of tumor invasion in the vessels was 66.6% in the fatal cases and 7.6.% in those who survived. Absence of tumor invasion in the vessel appears to be a good sign concerning prognosis.

Metastasis: 66% of the deaths showed metastasis. No metastasis was present in the group of survivors. It is clear that the presence of metastasis is a very significant sign in so far as the prognosis is concerned.

Evaluation of the histologic findings (Table VIII, IX):

Wilms' tumor may contain a variety of relatively differentiated tissues derived from embryonic mesenchyma.[20] The histopathologic appearance of Wilms' tumor is different from tumor to tumor and also different in the same tumor from one area to another.[34] Differentiation of the embryonic mesenchyma varies as follows: There may be a presence of a well-differentiated tubulus abortive glomerulus and a broad sheet

of undifferentiated mesenchymal cells. The presence of the muscle cartilage bone represents more advanced maturation. We had seen ganglion cells in Case No. 25, although Masson described neurofibrils in nephroblastoma. Willis considered their description unconvincing.[20] How can we explain the presence of these ganglion cells? We think that these cells which were found in the metastasic lesion probably do not belong to the neoplasm.

Microscopic examinations were done of various blocks from the specimen representing different areas of the same tumor and the following conclusions were obtained:

1. Sheets of undifferentiated mesenchymal cells were present both in the cases that died and in the survivors. No correlation with the prognosis could be established.

2. Undifferentiated epithelial cells were rarely present in the survivors, while they were often found in the fatal cases. They seem to represent a poor prognostic sign.

3. Glomerular structures were rarely present in cases that died, while they were oftan present in the survivors. It is considered as a good prognositc sign.

4. Tubular structures and well-differentiated skeletal mucsle do-not seem to play an important part in the prognosis.

5. It is not practical to evaluate the presence of fat, cartilage, and bone despite the fact that they are often seen in survivors since so many sections need to be examined.

Summary

A clinico-pathological study was done in 29 cases of Wilms' tumor with children whose ages ranged between 7 months to 9 years in order to evaluate the factors related in the prognosis. From the clinical standpoint the following results were obtained:

1. Prompt nephrectomy followed by post-operative radiation therapy and/or Actinomycin D administration was the type of treatment and the rate of survival was 44%.

2. The rate of survival below the age of 1 year was 100%, 1-2 yrs 50% and 2-9 yrs 23%.

A) Pathological findings seen as a poor prognostic sign included:

1. The presence of metastasis 2. Tumor invasion in the vessels, 3. Tears in the capsule 4. The presence of undifferentiated epithelial cells.

B) Pathological findings seen as a good prognostic sign: Presence of glomerular structures.

C) No relation could be found as far as prognosis was concerned regarding the following factors:

1. The weight of the tumor 2. Tumor invasion in the renal pelves and the ureter 3. The area of the kidney involved by the tumor 4. The presence of undifferentiated mesenchymal cell sheets 5. Tubular structures and differentiated skeletal muscle.

D) Doubtful findings with regard to any prognostic significance: Presence of fat, cartilage and bone in the tumor.

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REFERENCES

1. Arey, J. B.: Cancer in infancy and childhood, Pennsylvania M. J. 55: 553, 1952.
2. Ariel, M. I., and Pack G. T., eds.: Cancer and Allied Diseases of Infancy and Childhood, Boston, Little, Brown and Company, 1960.
3. Dargeon, H. W.: Tumors of Childhood. A Clinical Treatise, New York,Paul B. Hoeber, Inc., 1960.
4. Silver, H. K.: Wilms' tumor (embryoma of kidney), J. Pediatr. 31: 643, 1947.
5. Gross, R. E., and Neuhauser, E. B. D.: Treatment of mixed tumors of kidney in childhood, Pediatrics 6: 843, 1950.
6. Lattimer, J. K.: Nephroblastoma (Wilms' tumor). Prognosis more favorable in infants under one year of age, J.A.M.A. 171: 2163, 1959.
7. Lattimer, J. K., Melicow, M. M., and Uson, A. C.: Wilms' tumor: a report of 71 cases, J. Urol. 80: 401, 1958.
8. Platt, B. B., and Linden, G.: Wilms' tumor--a comparison of 2 criteria for survival, Cancer 17: 1573, 1964.
9. Arey, J. B.: Abdominal masses in infants and children, Pediatr. Clin. North Am. 10: 665, 1963.
10. Moore, T. (Manchester): Mixed tumor of kidney in adult, Br. J. Surg. 30: 381, 1943.
11. Cresson, S. L., and Palling, IV. G. L.: Renal tumors, Pediatr. Clin. North Am. 6: 473, 1959.
12. Hartenstein, H.: Wilms' tumor in newborn infant; report of case with autopsy studies, J. Pediatr. 35: 381, 1949.
13. Collins, V. P., Loeffler, R. K., and Tivey, H.: Observations on growth rates of human tumors, Am. J. Roentgenol. 76: 898, 1956.

14. Collins, V. P.: The treatment of Wilms' tumor, Cancer 11: 89, 1958.
15. Knox, W. E., and Pillers, E.: Time of recurrence or cure of tumors in childhood, Lancet 1: 180, 1958.
16. Kerr, H. D., and Flynn, R. E.: Role of irradiation in treatment of Wilms' tumor in children, Am. J. Roentgenol. 75: 971, 1956.
17. Harvey, R. M.: Wilms's tumor: evolution of treatment methods, Radiology 54: 689, 1950.
18. Knutrud, O.: [Treatment of Wilms' tumor (nephroblastoma)], Acta Paediatr. 51: 102, 1962.
19. Dickey, L. B., and Chandler, L. R.: Embryoma of kidney (Wilms' tumor) in children, Pediatrics 4: 197, 1949.
20. Willis, R. A.: The Pathology of the Tumors of Children, Springfield, Illinois, Charles C. Thomas Publishers, 1962.
21. Scott, L. S.: Wilms' tumor: its treatment and prognosis, Br. Med. J. 1: 200, 1956.
22. Doyle, G. B.: Bilateral Wilms' nephroblastoma, Arch. Dis Child. 31: 51, 1956.
23. Harper, J. M., and Anderson, L. E.: Bilateral diffuse Wilms' tumor: a case report, J. Pediatr. 35: 381, 1949.
24. Miller, R. W., Fraumeni, J. F., Jr., and Manning, M. D.: Association of Wilms' tumor with aniridia, hemihypertrophy and other congenital malformations, N. Engl. J. Med. 270: 922, 1964.
25. Miller, R. W., et al.: Excessive concurrence of Wilms' tumor with aniridia hemihypertrophy and other congenital defects, J. Pediatr. 65: 1088, 1064.
26. Daniel, W. E.: Hypertensive factor in Wilms' tumor, South, M. J. 32: 1014, 1939.
27. Dean, A. L.: Wilms' tumors, New York State J. Med. 45: 1213, 1945.
28. Nesbit, R. M., and Adams, F. M.: Wilms' tumor; review of 16 cases, J. Pediatr. 29: 295, 1946.
29. Kinzel, R. C., Mills, S. D., Childs, D. S., Jr., and Deweerd, J. H.: Wilms' tumor: a review of 47 cases. A discussion of the findings and results of treatment of histologically proved cases in a 15-year period, J.A.M.A. 174: 1925, 1960.
30. Rusche, C.: Treatment of Wilms' tumor, J. Urol. 65: 950, 1951.
31. Weisel, W. Dockerty, M. B., and Priestley, J. T.: Wilms' tumor of kidney; clinopathologic study of 44 proved cases, J. Urol. 50: 399, 1943.
32. Pinkel, D : Cyclophosphamide in children with cancer, Cancer 15: 42, 1962.
33. Tan, C. T., Dargeon, H W , and Burchenal, J. H.: The effect of actinomycin D on cancer in childhood, Pediatrics 24: 544, 1969.
34. Willis, R. A.: The Borderland of Embryology and Pathology, ed. 2, London, Butterworths, 1962.