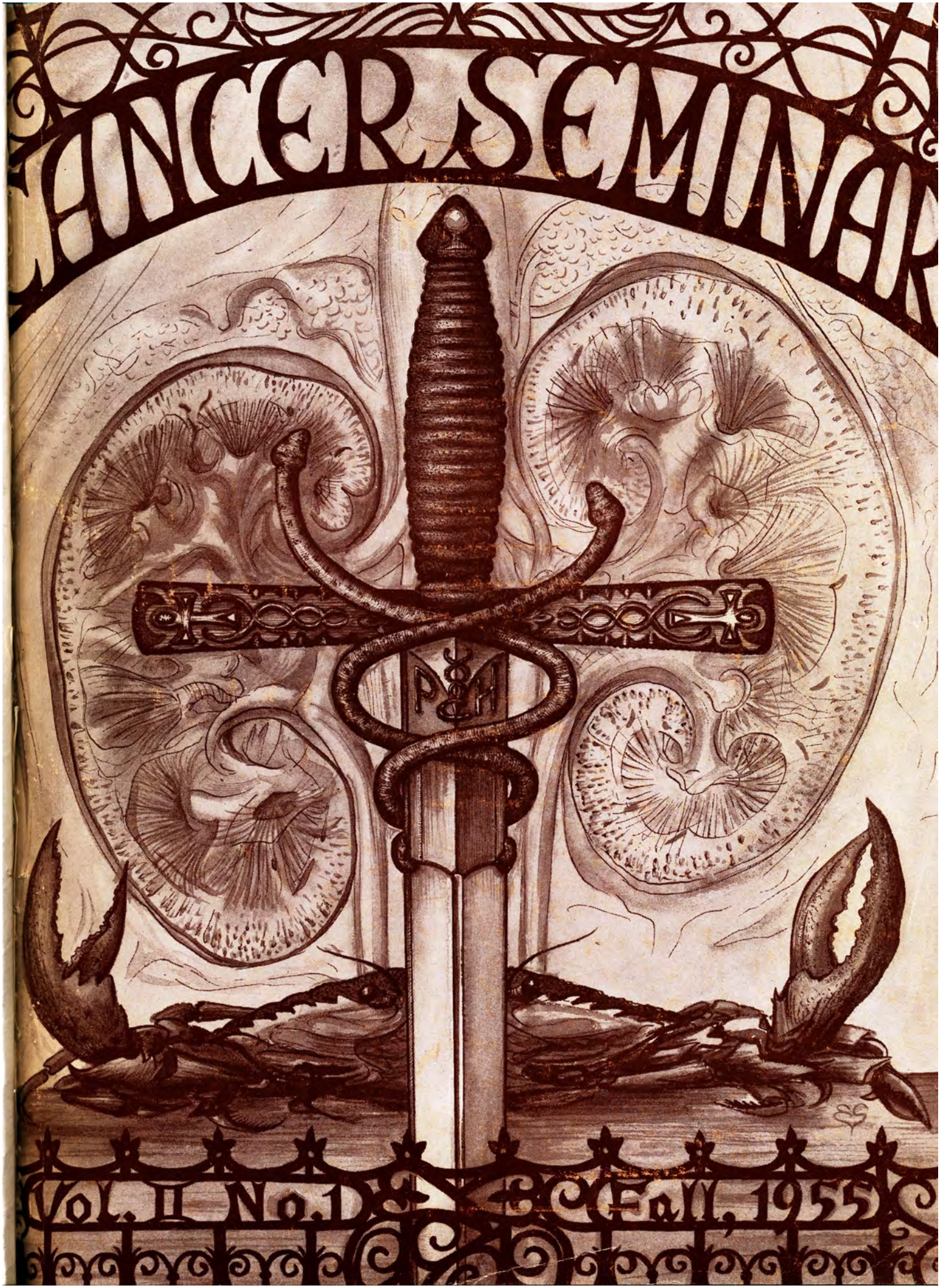
CANCER SEMINAR



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JUAN A. DEL REGATO, M. D., *Editor*

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Tumors of the Urinary Tract

TUMORS OF THE URINARY SYSTEM are among the most serious ones encountered in clinical practice and, although the system is open to radiologic and endoscopic examination, an early diagnosis is seldom made and the present day curability of this group of tumors is very low.

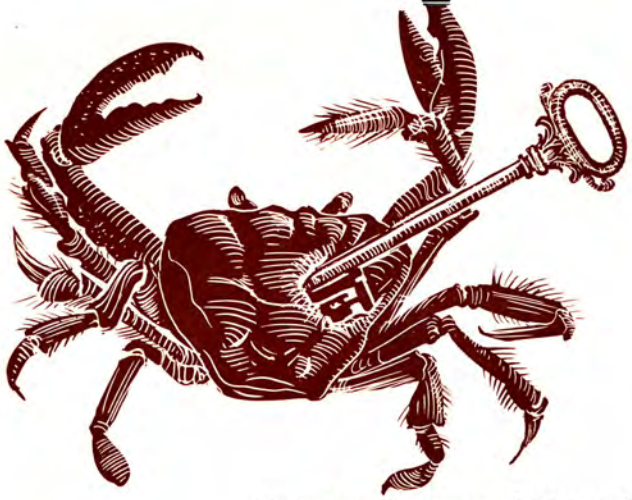
This CANCER SEMINAR was held in Colorado Springs on September 3rd, 1955 and was attended by 320 pathologists, radiologists, urologists, surgeons and internists. Our guest speakers, Dr. Fred J. Hodges, Dr. Fathollah K. Mostofi and Dr. Perry B. Hudson brought to light important facts of the differential diagnosis, surgical treatment and morphology of these tumors which constitute important clarifications in our knowledge. This exercise was repeated on March 17, 1956 at the Central University of Santa Clara, Cuba. Sydney J. Hawley, M.D., of Seattle and John J. Andujar, M.D., of Fort Worth presented their discussions in the Spanish language. Dr. John J. Modlin of Columbia, Missouri, added his interesting comments on the surgical treatment.

The selection of cases, advance preparations, choice of illustrations for reproduction and the organization of these CANCER SEMINARS require considerable work. Dr. James W. McMullen, radiologist, and Dr. Morgan Berthrong, pathologist, of the Penrose Cancer Hospital, have given generously of their time and judgment towards the success of these events. The excellency of the histologic preparations are a credit to the zeal and skill of Dr. Berthrong's chief tissue technologist, Mr. Melvin C. Barhite.

This first issue of the second volume of CANCER SEMINAR is dedicated to the participants of the 8th International Congress of Radiology, held in Mexico City under the presidency of Dr. Manuel Madrazo, July 21-28, 1956.

J. A. DEL REGATO, M. D.

Colorado Springs, August, 1956.



1. *Renal-cell Carcinoma with Capsular Calcification*

Contributed by Brodie C. Nalle, M. D., and Louis J. Kennedy, M. D., Colorado Springs, Colorado

THE PATIENT was a 30-year-old man in December 1953 when on physical examination a mass was felt in the left upper abdominal quadrant.

Dr. Hodges: This single roentgenogram shows a bilateral excretory pyelogram. The psoas muscle shadows stand out sharply. There is no apparent abnormality of the right kidney. Obviously something is profoundly wrong on the left side. From the radiological point of view this is a benign relatively innocent cystic lesion of the lower pole of the kidney. You will notice that there are lime salt deposits in this almost perfectly spherical mass, and that the lime salt is contained very extensively in the outer crust or periphery of the lesion. There are some smaller flecks which appear to be distributed in the center as seen in this single roentgenogram but actually they could be on the anterior or posterior wall. The remainder of the kidney does not appear to be abnormal though it looks tilted a little on end, and the pattern of the calyces is such that the large isolated cystic mass of the lower pole is blunting the lower pole calyces by proximity only. I am sure that there are few radiologists anywhere who would hesitate long in reporting that this is a benign cystic lesion of the kidney, and they would put the word *benign* in there not on the basis of a casual guess but because lesions of this sort often prove to be just that.

Fig. 1—Roentgenogram showing calcification around a spherical mass in the region of the lower pole of the left kidney.

At the time these cases were submitted we had a visitor among our urologists, a man from Australia. In looking at this film he immediately brightened up and said, "This is characteristic of hydatid disease." We argued that it does not occur commonly in this country, but having seen many of them, he insisted on his diagnosis. That explains why I changed from benign partially calcified cyst to hydatid cyst.

Dr. Hodges' impression: HYDATID CYST of the left kidney.

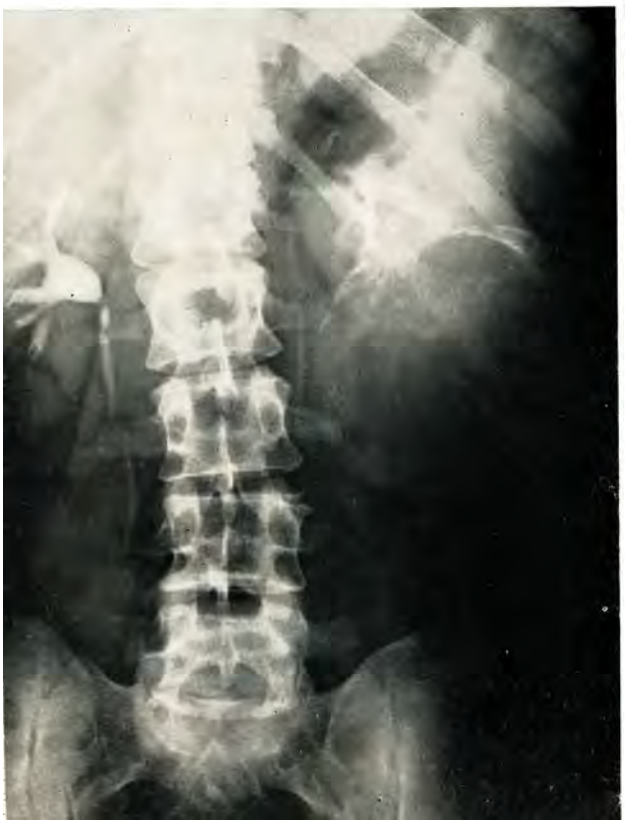
Radiologic Impressions Submitted by Mail:

Benign renal cyst	62
Pancreatic cyst	21
Echinococcus cyst	15
Mesenteric cyst	6
Malignant tumor	24
Others	3

Dr. Regato: Most experts submitted an impression of benign cystic lesion. Dr. J. T. Case, of Santa Barbara, also suggested the possibility of an echinococcus cyst. Dr. H. P. Plenk, of Salt Lake City suggested renal carcinoma. Dr. J. A. Campbell of Indianapolis and Dr. B. Felson of Cincinnati suggested hypernephroma. Dr. H. P. Doub of Detroit favored carcinoma secondary to a renal cyst. None of these gentlemen explained whether or not their light boxes are equipped with a microscopic attachment.

Philip J. Hodes, M. D., Philadelphia, Pa. (by mail): A large cystic lesion of the left kidney with evidence of calci-

Fig. 2—Gross specimen showing a large mass distorting the left kidney.



fication of the wall. The most common well circumscribed, round lesion of the lower pole with calcific density of the wall is a renal cyst.

Operative findings: On December 1954 the patient was operated upon: the left kidney was greatly distorted by a large roughly spherical mass measuring 8 x 12 cm. The wall of this tumor was thick and calcified in many areas, containing necrotic soft tumor tissue. A smaller adjacent mass 3.5 cm in diameter lay inferiorly and medially and had a similar aspect. The kidney and tumor weighed 825 grams.

Dr. Mostofi: The section shows no cysts but a primary renal neoplasm partly surrounded by a hyalinized pseudocapsule in which patchy calcification is present. In two or three areas the tumor tissue is well preserved having a definite tubular and papillary structure in which the cells are unmistakably epithelial. They vary from cuboidal to low columnar. The cytoplasm is markedly vacuolated, but occasionally it is granular and eosinophilic. The nuclei are round, they have a distinct nuclear membrane, some condensation of chromatin at the periphery and a small basophilic nucleolus. Many of the nuclei are hyperchromatic. Mitotic figures are rare, but occasionally giant or multinucleated cells are encountered. The stroma consists of a delicate well vascularized fibrous connective tissue with a scattering of lymphocytes and plasma cells. Focal iron deposition is seen both intra- and extra-cellularly. Most of the tumor, however, is poorly preserved. In these areas there is a meshwork of well vascularized delicate connective tissue stroma containing spaces some of which have only eosinophilic cellular debris, other nests of vacuoles without apparent nuclei, others a few leukocytes and still others vacuolated cell clumps. In areas the tumor is necrotic and the stroma hyalinized.

The histologic picture is quite characteristic of primary carcinoma of the renal parenchyma. We have preferred the term renal cell carcinoma but adenocarcinoma is quite acceptable. The implication of the term hypernephroma is that the tumor is derived from adrenal, for this reason, I do not use this term, however, it is well entrenched in urologic literature. Renal cell carcinoma comprises 80% of the malignant renal neoplasms, the clear cell type being the most common histologic variant.

Although those tumors in which the acini are regular and the cells of uniform size and shape are said to have a very good prognosis, our experience has so far given us no consistent histologic criteria for determination of prognosis. Each tumor must be assessed individually on the size of the lesion, the presence of vascular invasion, local extension and peripheral metastases.

The calcification observed in this tumor was limited to the capsule; however, it may be found in the tumor itself. While the presence of calcium in renal neoplasm is of aid in roentgenologic diagnosis, it is not of reliable prognostic significance.

Dr. Mostofi's diagnosis: RENAL CELL CARCINOMA.

Histopathologic Diagnoses Submitted by Mail:

Clear-cell adenocarcinoma	66
Hypernephroma	50
Adenocarcinoma	40
Renal cell adenocarcinoma	17
Tubular adenocarcinoma	8
Papillary adenocarcinoma	5
Adenoma	4

Dr. Regato: Dr. Malcolm B. Dockerty of Rochester, Minnesota, submitted a diagnosis of Grade I papillary adenocarcinoma, hypernephroma type. Dr. Rupert A. Willis, of Leeds, and Dr. Charles Oberling, of Paris, submitted clear-cell renal carcinoma.

Dr. Hudson: This is one of the most straightforward of fourteen beautifully booby-trapped cases. The mass was apparently discovered in 1953 and the radiographic diagnosis was made almost nine months later. Then twelve months after the original mass was found the patient was operated upon. There must have been some good reason why something definite was not done about this patient's condition before that time.

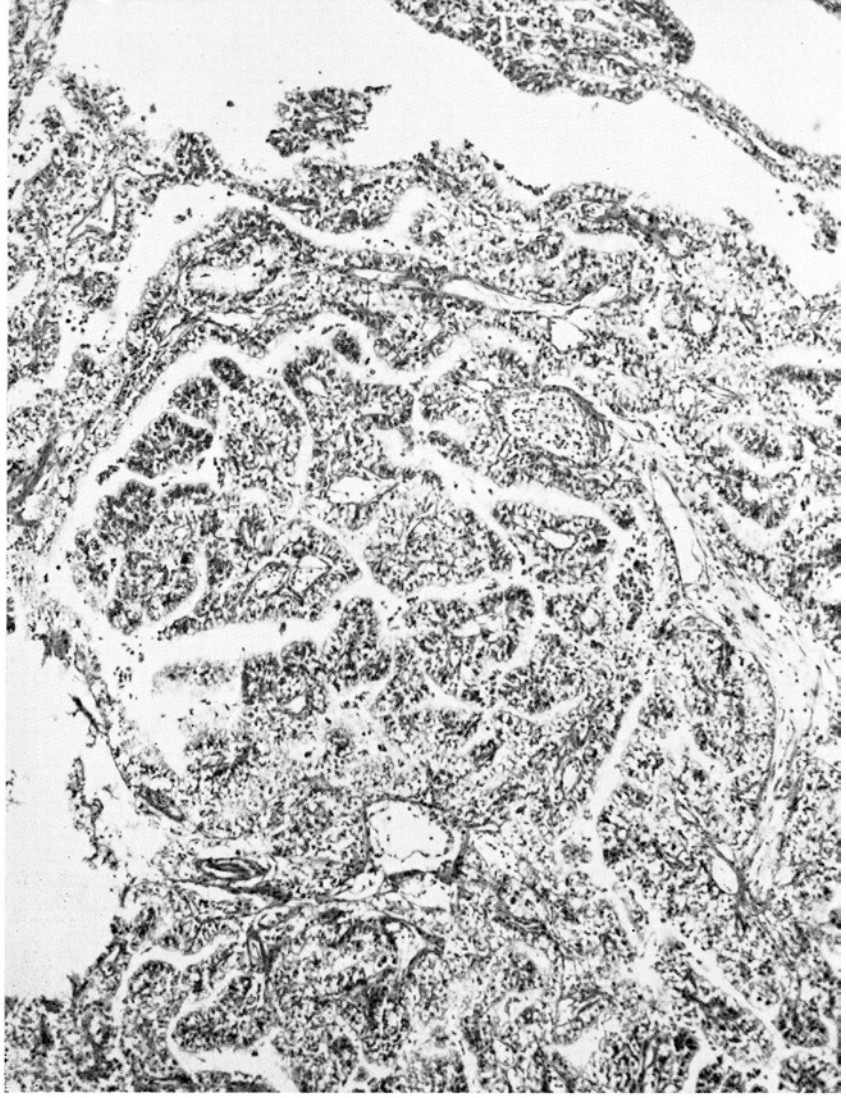


Fig. 3 — Low power photomicrograph: renal cell carcinoma showing papillary and glandular appearance of the tumor.

In seeking to elucidate the cause of a mass in the flank of a patient before operation, the surgeon often uses every procedure available to him. The most important thing of all is to determine whether the mass is in the kidney or outside the kidney. Aortography and pre-sacral insufflation of oxygen are two of the most useful diagnostic methods developed in recent years.

From a surgical point of view there are several ways of approaching a tumor of the kidney. In the past several years there have been reasons given to us by our surgical pathologist for using a slightly different kind of nephrectomy; for want of a better term, we call it "radical nephrectomy." In radical nephrectomy, the lymph nodes about the aorta and vena cava, the perinephritic fat and the entire Gerota's fascial capsule and adrenal gland are removed along with the kidney and a segment of the ureter. This kind of radical nephrectomy has come about as a result of therapeutic failures in which at autopsy tumor has been found 1) in the lymph nodes of this region, 2) in the renal veins and the vena cava on the right side, and 3) in the perinephritic fat and Gerota's fascial envelope. The fourth feature of radical nephrectomy is early ligation of the vascular pedicle from the kidney. At the Presbyterian Hospital of New York, a patient recently died as a result of a fatal embolus, during operation; the patient's kidney was being manipulated by the surgeon at the time death occurred.

At autopsy, a pulmonary embolus, which had had its origin in a cancer containing thrombus of the right renal vein, was found to be the cause of death. If early ligation can prevent this kind of thrombus from breaking away and embolizing, perhaps it can also prevent some of the post-operative pulmonary metastases which culminate in death.

There are three approaches which can be used for radical nephrectomy. The thoraco-abdominal approach is preferred when we have a diagnosis that is fairly definite and we know that a radical nephrectomy is going to be done. But unfortunately, quite often it is unwise to employ thoracotomy and to open the peritoneal cavity deliberately in order to make a diagnosis of a tumor which can't be removed. A second approach is Dr. Hugh Young's operation. It is an operation we no longer use except for Wilm's tumor. We prefer a third approach when the diagnosis of tumor is not definitely established. Our preference is for a flank incision which urologists have used for a hundred years for simple nephrectomy. The simple nephrectomy flank incision is too low, too short and too far anterior. We make a high lateral incision usually over the tenth rib, beginning one centimeter off the midline in the back and carrying the incision anteriorly roughly toward the umbilicus. The twelfth rib is removed and the upper surface of the diaphragm is exposed. The diaphragm is then divided. The exposure in this area allows direct approach to the vascular supply of the kidney and is, we believe, superior to that of the thoracico-abdominal approach. We did not think so in the beginning, but after having used this incision approximately 160 times in the last four years, we believe that it is. Retraction is obtained practically without touching the tumor so that early ligation and dissection of the vessels and dissection of the lymph nodes can be done without trauma to the kidney or squeezing out tumor cells or thrombi. Using this incision, it is possible to get at the point of extension of most retroperitoneal tumors which make those tumors unsuitable for curative surgery or attempt at curative surgery. I would like to make that point as strongly as I can, because I feel that sarcoma occurring retroperitoneally is frequently not a surgical disease in any sense of the term. In suggesting that this retroperitoneal approach be used in cases of questionable definite diagnosis, I would like to point out that it is not necessary to scatter tumor cells throughout the peritoneum nor through the pleura. It is not necessary to work for perhaps one to two hours before we find finger-like projections of sarcoma (this is especially true of liposarcoma) which extend to the back muscles and make surgical excision a futile exercise.

M. Berthrong, M. D., Colorado Springs, Colo.: This tumor was found on routine insurance examination, the patient apparently refused any treatment at that time, and did not follow advice until the Christmas vacation. I vaguely remember in one of Dr. Hugh Young's older textbooks that he discusses the frequency with which calcification appears in renal cell carcinomas, but there the calcification seen is a lumpy, or flaky calcification occurring in necrotic zones or hemorrhagic zones in the tumor. It is certainly unusual in a renal cell carcinoma to have calcification limited to the capsule.

Dr. Mostofi: We have seen calcification both in the substance of the tumor, where it is seen frequently, and also in the capsule. I believe that there are two recent articles on this subject; one maintains that calcification is a sign of good prognosis, and one that calcification is a sign of poor prognosis. I don't think you can depend on the calcification for prognosis.

G. G. Kent, Jr., M. D., Phoenix, Arizona: In your experience with a histologic lesion of this type, Dr. Mostofi, what is the differential between a benign adenoma and a renal cell carcinoma?

Dr. Mostofi: I believe in many instances it is difficult to say whether a tumor is an adenoma or a carcinoma of the kidney. Many years ago, Bell postulated that tumors more than a certain size were probably carcinoma, and tumors below a certain size (I believe it was 3 cm) were adenoma; at the same time, he said that certain tumors may be very small and still be carcinomatous. I believe the diagnosis here would have to be adenocarcinoma rather than an adenoma, because of the size of the tumor, the fact that it has invaded the capsule and because of the histological variation in the tumor.

L. Lowbeer, M. D., Tulsa, Oklahoma: I think it should be emphasized that apparent encapsulation and calcification are features very frequently seen in renal cell carcinomas and therefore could not be used to make a diagnosis of benign neoplasm. Renal-cell carcinomas are very capricious in growth and some of them grow exceedingly slowly. I remember a case of a tumor involving the entire kidney which was removed and the patient was apparently well for nine years; he died with multiple metastases and at autopsy there were large tumor cell thrombi in the renal vein and vena cava.

M. Berthrong, M. D., Colorado Springs: I was a bit disturbed to hear Dr. Mostofi agree, or at least not disagree, with the concept that if the tumor measured under two or three centimeters it was probably an adenoma and if it was bigger it was carcinoma. I am sure he does not really feel this way about it. It has always seemed to me this is an absurd way of measuring whether or not a tumor is malignant or benign; to take hundreds of patients whose small tumors, less than two centimeters, have been found incidentally at autopsy and to say that none had metastases, does not prove the point that these small tumors were benign; they could as well represent the first phase of a renal carcinoma. It has always seemed to me that the adenomas of the renal cortex which we see often in patients with severe arteriosclerosis have histologically a different pattern of appearance than the recognizable renal cell carcinomas. And it has never appeared that one has to resort to size to determine this. I would like to ask Dr. Hudson how often he has seen metastases occur from a tumor that measures less than three centimeters in diameter.

Dr. Hudson: Our orthopedic surgeons often refer cases to us in search for a primary tumor when the first thing that has been noted is bony metastases. In a considerable number of patients, when we discover the primary tumor to be in the kidney, it usually measures less than three centimeters in diameter. As the diameter of the tumor approaches three to four centimeters there is almost a geometric rise in the percentage of cases with metastases. This has also been correlated with weight at the Mayo Clinic, and as the weight of the tumor goes up, curability goes down percentagewise. There is still a teaching among urologists that there is a safe period in which you can watch a mass in the kidney. During the waiting period metastases can and do occur.

Dr. Mostofi: I am sorry if I left the impression that size of the tumor is of any significance in diagnosis. I merely made general statements based on reports in the literature and generally accepted for many years. Our experience bears out what both Dr. Hudson and Dr. Berthrong said. We have seen a small kidney tumor which was missed despite the fact that the pathologist who examined it made sections about 1 to 1½ cm. apart throughout the whole kidney. Only after the patient presented metastases and we went back and looked further, did we find a primary there.

L. E. Plank, M. D., Albuquerque, New Mexico: I wonder if the reference Dr. Mostofi had to relative size in which he quoted Bell wasn't the nephrogenic adenomas. As I

recall, Bell states that those under three centimeters that are less likely to metastasize than those which are larger; I wonder if he feels that with nephrogenic adenomas that is the case.

Dr. Mostofi: I have a lot of trouble in looking at the kidney tumors to say whether it is an adenoma or whether it is a carcinoma; as Dr. Berthrong said many of the adenomas are small and then occasionally you will find one that is quite large.

H. M. Wiley, M. D., Garden City, Kansas: I was wondering what the histological sections showed on the secondary mass which was found at the time of surgery.

M. Berthrong, M. D., Colorado Springs, Colo.: Actually by serial sections you could see that this was actually an out-thrusting of the same tumor mass.

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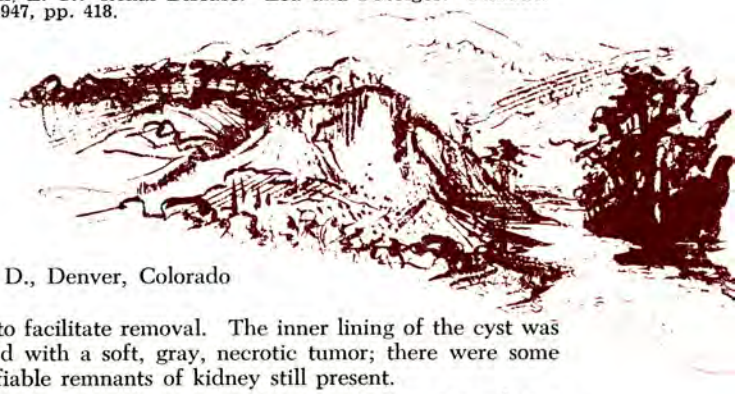

2. Retroperitoneal Leiomyosarcoma

Contributed by HARRY B. NEUSTEIN, M. D., Denver, Colorado

THE PATIENT was a 68-year-old man in August, 1954, when he noticed dark colored urine; shortly afterwards he developed pain in the right flank, bloating, chills and fever. There was a rapid loss of 22 lbs. in weight in six weeks. A nodular mass was palpated in the right upper abdominal quadrant. The urine presented albumin, red and pus cells.

Dr. Hodges: This is a spectacular roentgenogram showing a retrograde pyelogram on the right side, with some residual barium which nicely outlines a cluster of diverticula in the sigmoid, not at all uncommon at the age of sixty; it is conceivable of course that there might have been associated diverticulitis and retroperitoneal abscess, or abscess within the peritoneal cavity since the psoas muscle outline is not very well shown. But the outstanding finding is the evidence of gross downward displacement of the right kidney; it is very difficult to make out the kidney outline itself, presumably because it no longer has areolar tissue around it to set it off by differential density. It is displaced downward and it is rotated anteriorly and there is distortion of the calyces. The calyces themselves are somewhat dilated, perhaps an external pressure effect. But the striking thing is the displacement of the ureter which goes clear beyond the midline. It is almost certain nothing could have produced this other than a large retroperitoneal mass in the kidney area. It could be an abscess. On the other hand, retroperitoneal sarcomas are not too uncommon.

Dr. Hodges' impression: RETROPERITONEAL SARCOMA, right side.

Radiologic Impressions Submitted by Mail:

Retroperitoneal tumor	78
Malignant renal tumor	41
Perinephric abscess	12
Others	12

Dr. Regato: Dr. Fred A. Rose of Cleveland and Dr. Charles M. Gray of Tampa also suggesed a retroperitoneal sarcoma. Dr. Paul Swenson of Philadelphia and Dr. Peter Russo of Oklahoma City explained the distortion of the ureter by the presence of secondary metastatic masses.

P. J. Hodes, M. D., Philadelphia, Pennsylvania (by mail): An obvious retroperitoneal tumor displacing the kidney and ureter. The distortion of the renal structures is secondary to the obstruction. This is due to a retroperitoneal sarcoma.

Operative findings: In October 1954 an intervention was decided upon. A large cystic mass 15 x 25 cm was found in the retroperitoneal space, extending from the diaphragm to the pelvis; five liters of bloody fluid were aspirated to facilitate removal. The inner lining of the cyst was covered with a soft, gray, necrotic tumor; there were some identifiable remnants of kidney still present.

Dr. Mostofi: This section shows no kidney tissue but a tumor in which the cells occur in more or less interlacing bands. Many of the cells are spindle-shaped, but there is considerable variation in shape of cells, in their size and staining characteristics. The spindle-shaped cells show delicate longitudinal fibrils taking a mahogany color with Masson stain. Although spindle-shaped cells comprise the main tumor, in an adjacent nodule of fatty tissue, the tumor cells are pleomorphic. The nuclei are spindle-shaped or elongated and occasionally round or oval. Many of the nuclei have a distinct nuclear membrane and a large basophilic nucleolus usually surrounded by a clear space characteristic of the bird's eye nucleus of leiomyosarcoma. Giant cells, multinucleated cells, cells with hyperchromatic nuclei are not uncommon. Mitotic figures are fairly frequent. A large area of necrosis is seen and there is hyalinization of the tissue adjacent to the area of necrosis. Vascular invasion is apparent. In one area a group of cells is seen with clear cytoplasm, they are considered to be lipophages.

The chief problem in the differential diagnosis here is whether this is an undifferentiated carcinoma or a sarcoma. While in many instances it may be impossible to differentiate between a spindle cell carcinoma and a sarcoma, I believe that this does not apply in this instance, as the tumor is definitely a stromal tumor, it has no epithelial components, its relationship to the vessels is that of a sarcoma and not a carcinoma and cytologically it is not a carcinoma. In all such cases, however, I would like to study many sections to determine if any carcinomatous areas are present because such areas as you see in this tumor may occur in a renal cell carcinoma. A reticulum stain would also be most helpful.

If this is a sarcoma, and the evidence is in favor of this diagnosis, then we must consider a liposarcoma, leiomyosarcoma and a rhabdomyosarcoma in the differential diagnosis. A liposarcoma is suggested by the finding of some nests of mature fat cells and the existence of fat necrosis in one nodular area. Liposarcomas have a variable histologic picture ranging from a most undifferentiated tumor to fully differentiated adipose tissue. Immature and giant lipoblasts showing all stages of fat vacuolization are common. Occasionally the tumor may have a myxomatous or immature mesenchymal appearance. None of these is seen

in the present slide. I do not believe that it is a liposarcoma.

We come then to the two remaining possibilities. In the sections that I examined the spindle cells had no cross striations, the cells looked like typical leiomyosarcoma cells and I called the tumor a leiomyosarcoma. However, it is quite conceivable that other sections were predominantly rhabdomyosarcoma even with cross striations. I believe more important than the exact naming of the tumor is the realization of the potentialities of the tumor—that it may remain undifferentiated, it may differentiate to smooth muscle component, to skeletal muscle or to both.

From the single slide it is impossible to determine the site of origin. The tumor may have been primary renal or it may have secondarily involved the kidney from retroperitoneal or other areas.

Leiomyosarcomas of the kidney are rare. The five-year survival rate is said to be about 15%.

Dr. Mostofi's diagnosis: LEIOMYOSARCOMA.

Histopathologic Diagnoses Submitted by Mail:

Rhabdomyosarcoma	46
Leiomyosarcoma	34
Liposarcoma	10
Sarcoma, unclassified	31
Carcinoma	28
Others	9

Dr. Regato: Dr. E. F. Geever of Bethesda, Maryland, Dr. Charles Oberling, of Paris, and Dr. J. B. McNaught of Denver, also submitted a diagnosis of leiomyosarcoma. Dr. Rupert A. Willis of Leeds and Dr. C. A. Hellwig of Halstead favored a diagnosis of anaplastic carcinoma. Dr. A. P. Stout of New York also made a diagnosis of carcinoma with spindle and giant cells, that is to say, sarcomatous metaplasia. Dr. Raffaele Lattes of New York, Dr. M. B. Dockerty of Rochester, Minnesota, and Dr. N. Puente-Duany of Havana submitted a diagnosis of rhabdomyosarcoma. Dr. J. M. Neely of Lincoln, Nebraska, submitted hemangioendothelioma.

Subsequent history: Shortly after operation the roentgenogram of the chest showed the presence of pulmonary metastases. The patient expired in November 1954.

Fig. 1 — Retrograde pyelogram showing downward displacement and rotation of right kidney and marked medial displacement of the ureter.

Dr. Hudson: This is a unique case to me. I am interested in several features of the way the case was handled. The aspiration of a large cystic mass whose nature isn't yet known, is contraindicated in our opinion. Undoubtedly removal here was difficult but it would perhaps have been wiser to make a large incision than to aspirate this fluid. We believe that tumors of this sort and certainly renal tumors do seed in the operative wound and should not be treated by aspiration. The operation may well have hastened the death of this patient. It is our belief, after trying excisions in situations similar to this, that the operation isn't worthwhile and perhaps hastens metastases and the death of the patient. I would have preferred to expose the renal pedicle if that were possible; if it weren't I would have made a simple biopsy and no more. If the renal pedicle could be isolated the biopsy would be made, frozen section taken, and on the basis of the pathologist's report, operation performed or not performed. In the event of a finding of sarcoma (admittedly difficult on frozen section), with the size of that tumor, no excisional operation would have been done.

R. M. Mulligan, M. D., Denver, Colorado: I had the specimen in my hand and I could not identify the renal pedicle. This tumor had overgrown the entire renal pedicle and you couldn't tell whether you were afoot or on horseback. It was extensively necrotic in the center, it wasn't a cyst, it was a cystic tumor, and we had great difficulty in finding well preserved material. Actually in the well preserved material we thought it was a leiomyosarcoma and had a very characteristic reticulum pattern.

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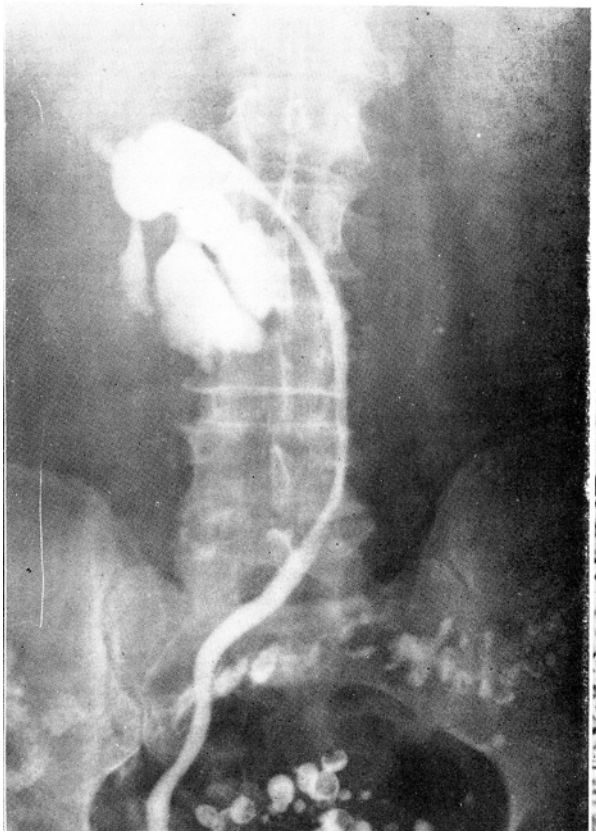
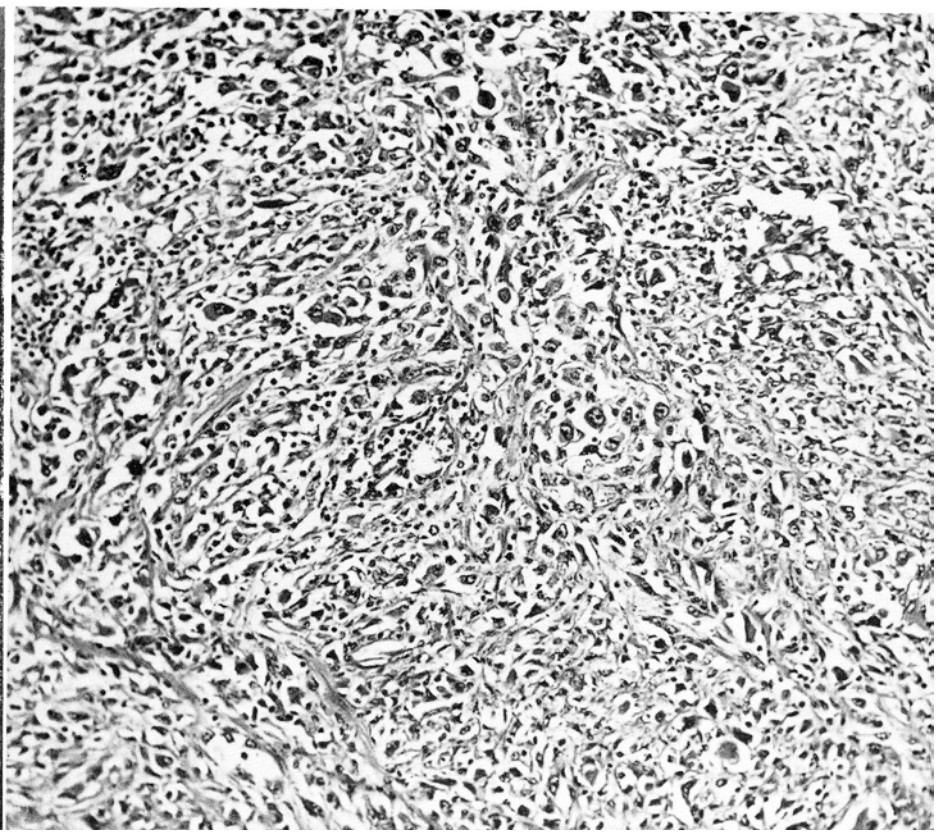
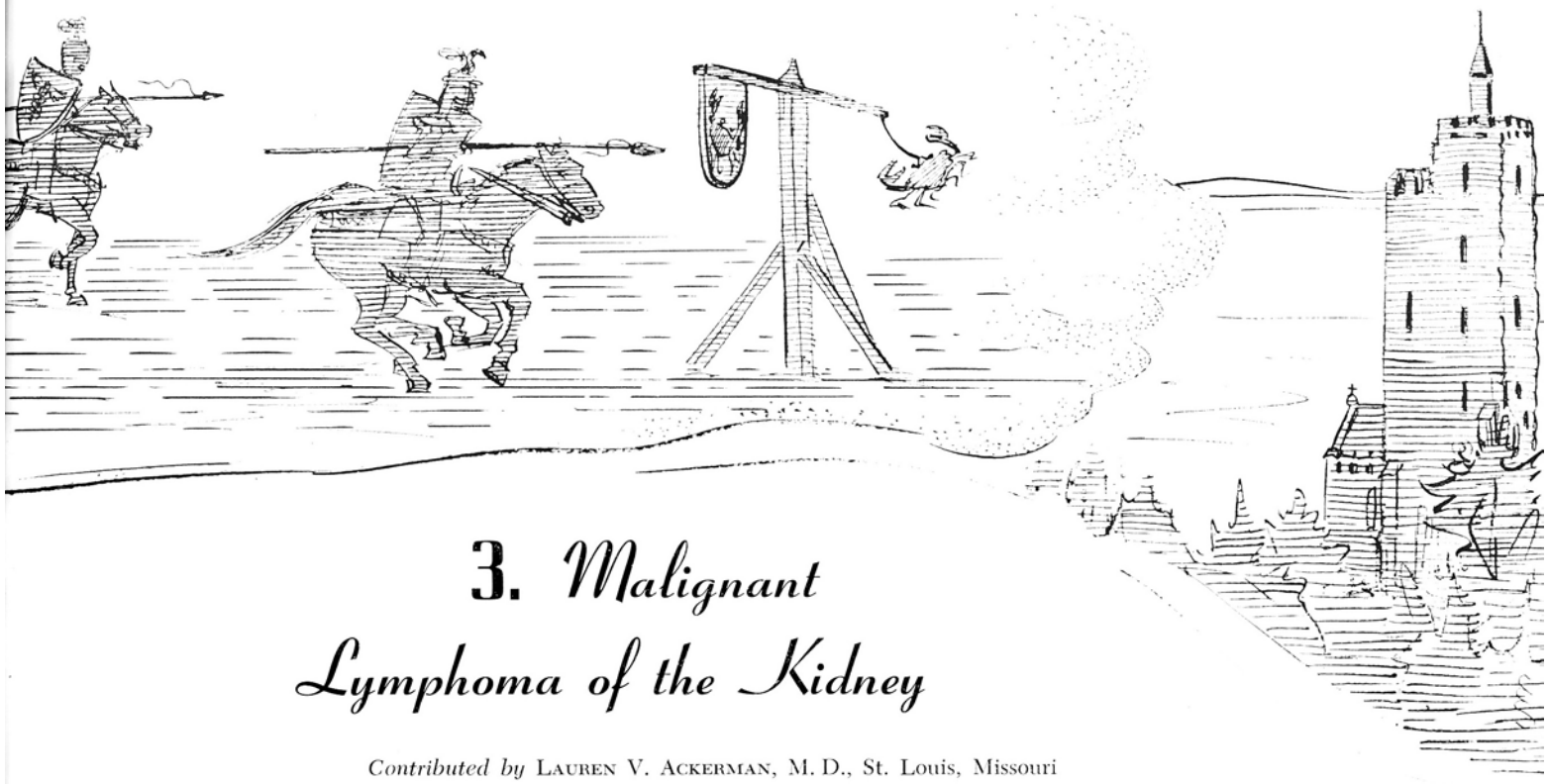
Fig. 2—Low power photomicrograph showing interlacing bands of spindle-shaped cells, the nuclei of many of which show birds' eye features.







3. *Malignant Lymphoma of the Kidney*

Contributed by LAUREN V. ACKERMAN, M. D., St. Louis, Missouri

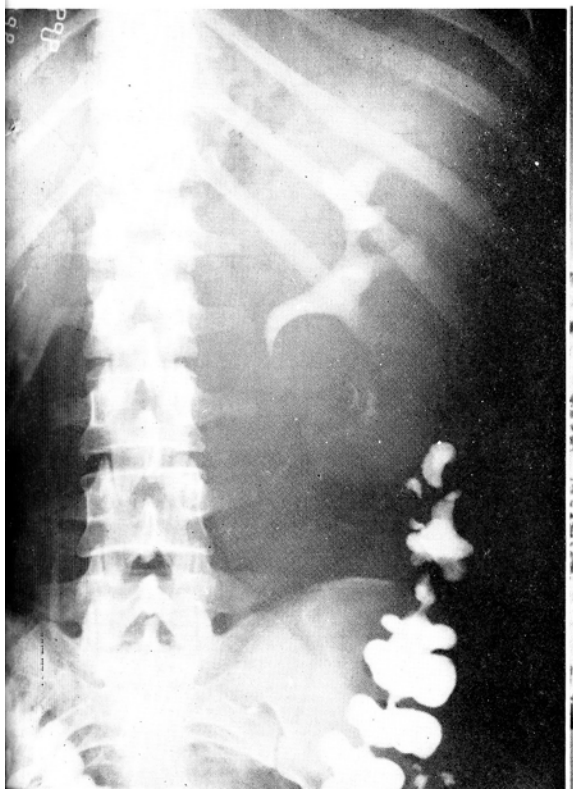
THE PATIENT was a 17-year-old girl in January 1954 when she gave a history of left flank pain of six months duration and 18 lbs. weight loss. A large mass was palpated in the left upper abdominal quadrant; the hemoglobin was 8.9 grams per cent.

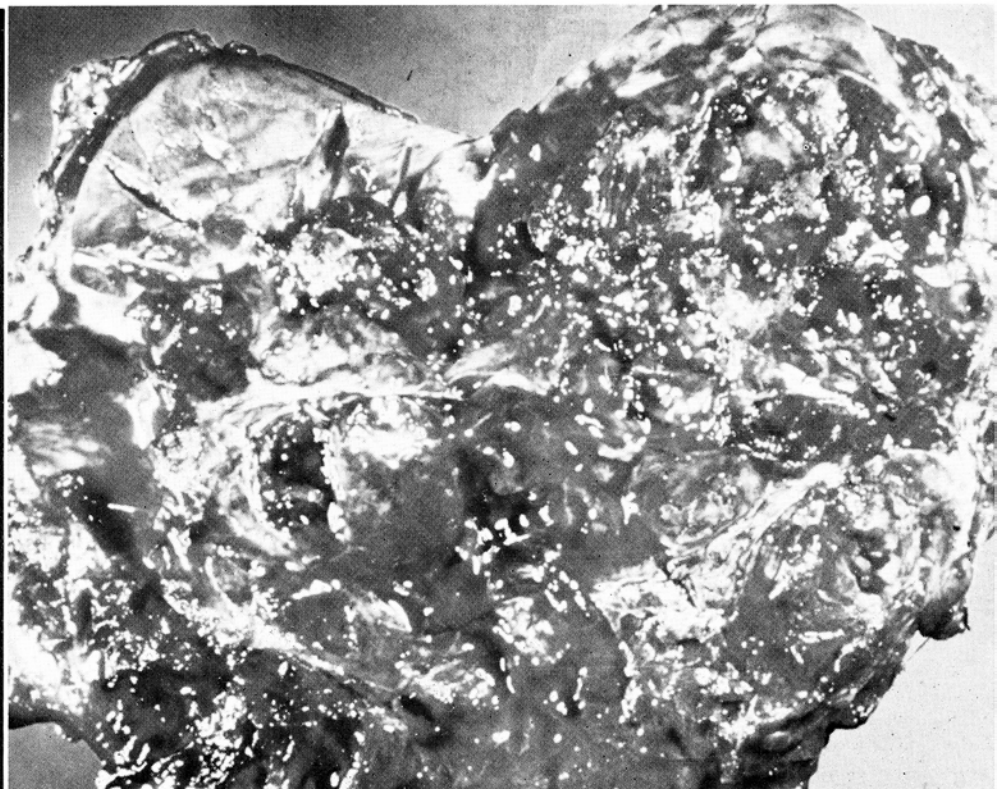
Dr. Hodges: This bilateral pyelogram shows normal ureter and calyces on the right side. The left kidney is very large, and the tapering at the pyeloureteral junction or just below it can well represent external pressure from the enlarged kidney. There are parts of the lower pole calyces that are seen to be greatly distorted. In the lower portion of the kidney, which is very much larger than it should be, there may be multiple masses crowding the calyces. A point that came up for strongest consideration with us was that the kidney on the right side appears actually smaller than normal and sometimes arteriosclerotic disease or some other form of renal atrophy on one side is associated with compensatory enlargement on the other side. The amount of enlargement in this kidney, three or four times normal, is far and away more than one would expect on that basis. I believe that this kidney contains multiple cysts with accompanying infection as suggested by the history. Renal neoplasm is a second possibility.

Dr. Hodges' impression: 1) POLYCYSTIC KIDNEY; 2) RENAL NEOPLASM.

Fig. 1 — Pyelogram showing enlargement of left kidney with great distortion of calyces.

Fig. 2 — Gross specimen of markedly enlarged kidney with large areas of necrosis.





Radiologic Impressions Submitted by Mail:

Malignant renal tumor	42
Wilm's tumor	33
Lymphosarcoma	12
Benign tumor	12
Polycystic kidney	6
Others	18

Dr. Regato: Dr. J. A. Campbell of Indianapolis and Dr. H. R. Senturia of St. Louis suggested retroperitoneal lymphosarcoma involving the kidney. Dr. Milo Harris, of Spokane, submitted an impression of primary malignant tumor; Dr. Ira Lockwood of Kansas City suggested lymphosarcoma of the kidney. Dr. Harry Hauser of Cleveland submitted sarcoma of the left kidney.

Philip J. Hodes, M. D., Philadelphia, Pennsylvania (by mail): The distortion of the lower pole of the kidney is due to a malignant tumor. I believe this is a carcinoma.

Operative findings: In February 1954 the left kidney, ureter, spleen and tail of pancreas were resected together with a retroperitoneal mass. The kidney measured 20 x 14 cm and was partially destroyed; on cut section it presented large lobular formations and areas of necrosis. The spleen weighed 260 grams and its surface was studded with white dots.

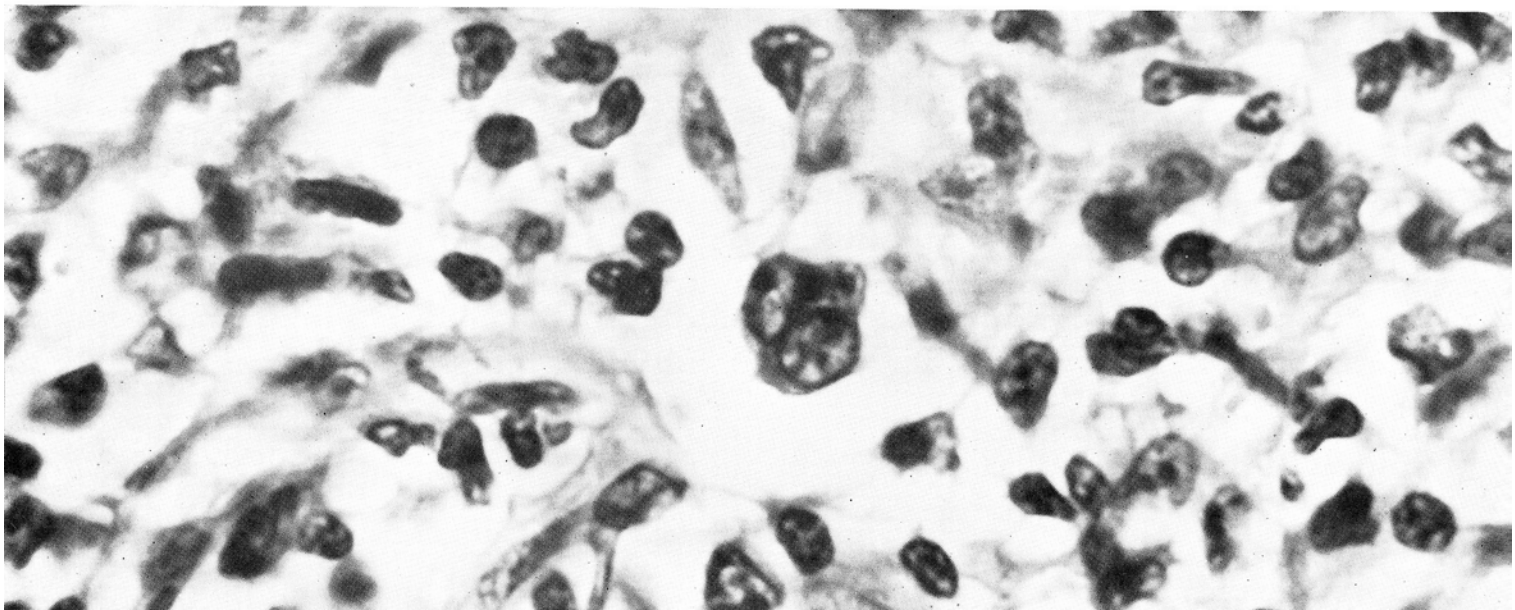
Dr. Mostofi: This section shows kidney and a tumor which is in the kidney. Although in areas the tumor suggests papillation, it is rather solid with masses of cells separated from each other by fibrous, sometimes hyalinized, connective tissue. The tumor is quite vascular with the tumor cells arranged around the vessels and suggesting rosette formation. These are obviously not rosettes because each contains a vascular channel. The tumor is quite cellular. There is little stroma except in relation to vessels. In the tumor one can identify mature lymphocytes, occurring either singly and in groups, and many definite mature reticulum cells. Most of the tumor, however, consists of cells that have little if any cytoplasm, but which when present forms a rim around the nucleus, it is barely eosinophilic and occasionally vacuolated. The nuclei which are round or oval, indented or even elongated, have a fine network of chromatin and, rarely, a basophilic nucleolus. Occasional vacuoles are present. Variation in size, shape and staining qualities of nuclei is encountered. Mitotic figures and giant cells are rare, but hyperchromatic nuclei are not infrequent. The latter, however, are mostly spindle-shaped. Except for the perivascular pallisading, the tumor has no specific pattern, most of the cells being closely packed together; in areas, however, the cells are seen separated from each other by an acellular hyaline matrix. There is evidence of old and recent hemorrhage. The tumor is separated from the kidney by a pseudocapsule and it is impossible from the available material to be certain as to the exact site of the tumor or even whether it is a primary or a secondary renal neoplasm. Thus we have an undifferentiated tumor with little or no stroma and with no specific pattern. The differential diagnosis, therefore, lies between an undifferentiated carcinoma, malignant lymphoma, adult Wilm's tumor, neuroblastoma and hemangiopericytoma.

Hemangiopericytoma may either have an organoid pattern as is seen in glomoid tumors or it may not. Where no organoid pattern is apparent the rounded or elongated pericytes are tightly packed around the capillaries without any intervening space, the blood vessels being lined by normal endothelial cells. Since anaplastic carcinomas and sarcomas may mimic such an arrangement, about the only convincing evidence in support of diagnosis of pericytoma is tissue culture growth of the tumor, impossible in this instance. The tumor cells which are lining some of the spaces which may be vascular channels, are certainly not normal endothelium and while the cells in the proximity of vascular channels are quite viable they do not resemble pericytes. I do not think that it is a hemangiopericytoma. I believe we can discard neuroblastoma since the pseudorosettes are in reality not rosettes but only pallisading of the cells at the periphery of the vascular channels, and the tumor is too anaplastic for neuroblastoma.

Adult Wilm's tumor is another condition which may be considered in the differential diagnosis. A number of Wilm's cases have been described in the adults. We have insisted that unless the tumor is histologically indistinguishable from the typical Wilm's occurring in children, that it not be designated as Wilm's. Adult Wilm's tumor is very rare and we have only four or five cases in our files, most occurring in young people and having a high mortality rate. The present tumor is certainly not typical Wilm's.

Having eliminated hemangiopericytoma, neuroblastoma and Wilm's, we are faced with the two remaining diagnoses which I am afraid are going to be difficult to differentiate. The presence of and spatial relationship of the stroma and specifically the reticulum to the tumor cells are valuable adjuncts. On this basis the tumor would be predominantly a lymphoma. Unfortunately, however, in areas there is a distinct stroma suggesting a carcinoma. The cytology of the cells suggests to me a malignant lymphoma and I would, therefore, submit the diagnosis of undifferentiated tumor probably malignant lymphoma. This diagnosis can be finalized only after we have additional clinical or pathological information, especially a lymph node biopsy.

Fig. 3 — High power photomicrograph showing a lymphosarcoma involving the kidney. Many of the cells consist of lymphocytes; occasional multinucleated tumor cells are seen.



Malignant lymphoma may rarely be initially manifested as a renal neoplasm, more frequently it occurs as secondary involvement in a generalized disease. It may form a single large tumor, several small nodules or may cause diffuse enlargement of the kidney. The prognosis has been poor.

Dr. Mostofi's diagnosis: MALIGNANT LYMPHOMA.

Histopathologic Diagnoses Submitted by Mail:

Various sarcomas	35
Lymphosarcoma	22
Wilm's	30
Carcinoma	27
Neuroblastoma	22
Hemangiopericytoma	10
Others	21

Dr. Regato: Dr. L. Lowbeer of Tulsa also favored a diagnosis of lymphosarcoma. Dr. B. Scolnik of Montevideo submitted a diagnosis of round-cell sarcoma; Dr. B. Dockerty of Rochester, Minnesota made a diagnosis of spindle-cell sarcoma, probably leiomyosarcoma. Dr. Carlo Sirtori, of Milan, favored neuroblastoma.

Subsequent history: The patient developed a subdiaphragmatic abscess and had to be re-operated. She was last seen in April 1955 when she complained of considerable abdominal pain and there was blood in the urine; a diagnosis of metastatic involvement of the opposite kidney was entertained.

Dr. Hudson: The three principal features of this disease are listed in my grandfather's book published in 1857 on malignant tumors of the kidney. The patient had lost 18 pounds, she had a mass in the flank and she had pain. She did not at that time have a fourth, hematuria, yet from the beginning, this patient should have been suspected of having a tumor in the kidney. Speaking for the patient, rather than for the surgeon, this is not a surgical disease, and if there is anyone here who has ever seen a disease with this kind of microscopic picture in the kidney cured by surgery, I would far rather hear his discussion than mine.

Dr. Regato: There is need for a definition of what is reticulum cell sarcoma. It is not important that a word was badly coined (as tracheotomy, asystole, etc.) or that it may appear incongruous (metastasizing adenomas of the bronchus) provided they convey the same meaning to all or most of those who use it. There is a great discrepancy in the meaning of reticulum cell sarcoma to different pathologists from the point of view of histogenesis and diagnosis, but also in relation to treatment and prognosis.

R. M. Mulligan, M. D., Denver, Colorado: Stout, I think, makes the correct distinction when he distinguishes between reticulum cell lymphosarcoma occurring in lymphoid tissue mainly and spreading sometimes to other tissues which do not contain lymphoid tissue, and reticulum cell sarcoma which means sarcoma of the reticulum cells as they occur throughout the soft tissues where lymphoid tissue is not normally found. If you take reticulum cell sarcoma in the latter sense it is a rare tumor.

J. B. Hartney, M. D., Chicago, Illinois: I wonder if we might have Ackerman's diagnosis on this one.

Dr. Regato: It was lymphosarcoma, apparently primary in the kidney.

M. Berthrong, M. D., Colorado Springs: I think there was a great variety of appearances because the slides came from different areas of the tumor. In mine, the cells only rarely suggest lymphoid cells. They tend to be elongated, a little spindly with very scanty cytoplasm and can be duplicated in many cases of Wilm's tumor. I agree with Dr. Mostofi that a Wilm's tumor ought to look like one, which this does not. Nevertheless it does seem to me that it belongs in the group of tumors that arise from primitive tissue, perhaps from the urogenital ridge, which may give rise to the Wilm's tumor and also, in older people, particularly women, to tumors that occur along the genital tract that have been called mesenchymal sarcomas of various kinds; perhaps they are related to the sarcomas of the endometrial stroma that have been described on the wall of the uterus and in the round ligament down into the vulva.

Dr. Hudson: May I recall what was removed from this patient: the left ureter, kidney, spleen, tail of pancreas resected together with a retroperitoneal mass. I wonder if perhaps Dr. Ackerman was on vacation when this operation was done; because if a frozen section would be useful at all, this might have been the proper place for it, avoiding the operation.

E. M. Bricker, M. D., St. Louis, Missouri: I am not acquainted with this particular case. I would like to make a comment regarding the discussions which have been offered by Dr. Perry Hudson this morning, which it has been a pleasure for me to hear, as a general surgeon interested in tumor surgery. We are critical regarding the surgery for tumor that has been performed by urologists in the past: inadequate approaches, inadequate surgery, shelling out tumors, etc. Dr. Hudson's surgical approach to malignant tumors of the kidney is a pleasure to hear.

J. J. Goforth, M. D., Dallas, Texas: I wonder if this wouldn't be a good occasion to discuss the subject needle biopsy. We have had cases here where extensive surgery was done and maybe needle biopsy with resulting diagnosis in the broad sense could have obviated such surgery. I would like to ask Dr. Mostofi his viewpoint on that.

Dr. Mostofi: I will just say I don't like needle biopsies and let it go at that.

Dr. Regato: Of course whether or not this surgery could have been obviated is to ponder whether or not the surgeon could have been obviated.

J. J. Andujar, M. D., Fort Worth, Texas: Personally, I think that needle biopsy has a definite value. I believe that frozen section would have been of value in this instance; most of us would have agreed that this is a malignant neoplastic lesion of considerable anaplasia, but I believe that would be about as much as anyone would say. As to classifying the tumor from a frozen section, my comment is: Look at the wide variety of diagnoses that have been submitted on the basis of permanent sections!

H. M. Wiley, M. D., Garden City, Kansas: Dr. Regato, since the consensus seems to rest with lymphosarcoma, I would like to know whether or not this patient received radiotherapy and whether or not you feel it would have been of value?

Dr. Regato: This patient did not receive radiotherapy; she was treated at Washington University. That surgery could have been obviated here does not necessarily mean that radiotherapy could have saved the patient's life. A preoperative diagnosis of lymphosarcoma could have substituted radiotherapy as a better means of palliation; it may have brought some relief to the patient but I rather doubt that it could have controlled the tumor permanently. Such a large mass would have probably necrotized and radiotherapy might have brought about difficulties of its own.

A Voice: Was the adrenal gland identified in this mass?

Dr. Regato: I am sorry, but I don't have that information.

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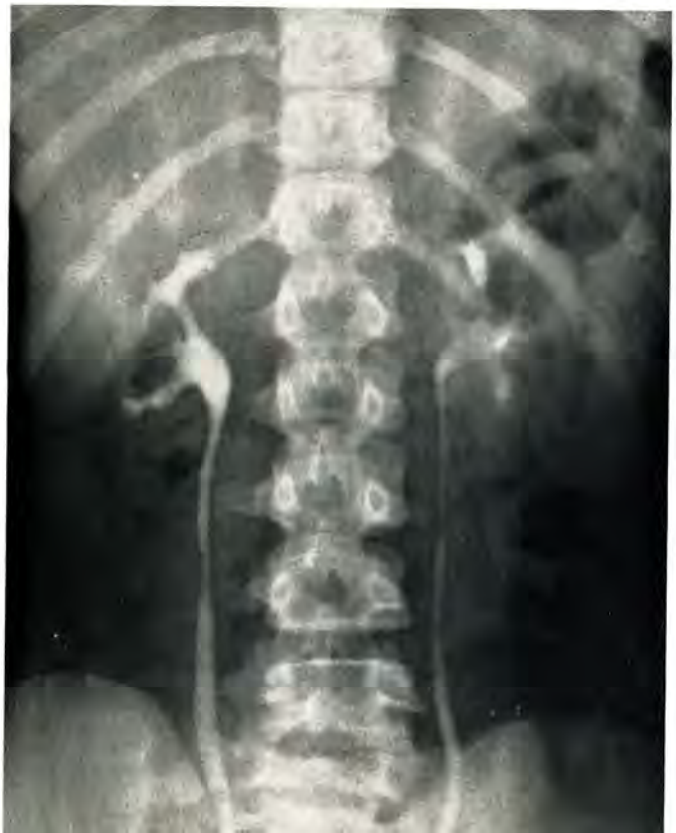
4. *Hemangioma of the Kidney*

Contributed by Donald L. Alcott, M. D., San Jose, California, and G. Robert Bartron, M. D., Watertown, South Dakota

THE PATIENT was an 11-year-old girl in May 1950 when she presented hematuria and fever. The child had received orthopedic care for a difference in length of her legs. Cystoscopic examination revealed the blood to be coming from the right ureter. The indigo dye appeared in the right ureter in low concentration after 38 minutes.

Dr. Hodges: The differential diagnosis between neoplasm and non-neoplastic disease is very difficult to make in this case. The fact that Dr. Regato threw in the juicy morsel about previous orthopedic leg-shortening procedures sounded very much like bone and joint tuberculosis which was rampant a few years ago and which was followed in many instances by urinary tuberculosis. This appearance of ragged irregularity of lower pole calyces, so called moth-eaten appearance, also seen in the middle lobe calyx, urges a radiologist to settle for inflammatory disease, probably of tuberculosis origin.

Fig. 1—Retrograde pyelogram showing an apparent pressure defect and elongation of the right middle calyx; some ragged appearance of lower calyces of both kidneys is also apparent.



Dr. Hodges' impression: Left RENAL TUBERCULOSIS.

Radiologic Impressions Submitted by Mail:

Carcinoma	42
Wilm's tumor	24
Carbuncle, abscess	23
Benign cyst or tumor	22
Hemangioma	22
Tuberculosis	18
Others	6

Dr. Regato: Dr. J. A. Campbell of Indianapolis and Dr. R. W. Ludwick of Fullerton, California, also suggested tuberculosis. Dr. Paul C. Swenson of Philadelphia proposed a hemorrhagic cyst. Dr. Don L. Vickery of Pueblo, Colorado, and Dr. Frank Gorishek of Denver suggested hemangioma.

Philip J. Hodes, M. D., Philadelphia, Pennsylvania (by mail): In spite of the history of hematuria, the kidney is not enlarged nor is its axis altered. If the kidney was enlarged, in spite of the patient's age, I would consider a Wilm's tumor.

Operative findings: On June 1950 a right nephrectomy was done. The peripelvic fat was replaced by a dark red-brown spongy tissue which enveloped the major calyces and extended into the medullary substance.

Dr. Mostofi: The section shows a kidney which is essentially normal except in the papillae. Here a number of thin-walled cavernous vascular channels are seen packed with red cells. The supporting adipose tissue shows evidence of some old and much recent hemorrhage.

The differential diagnosis here lies between a varicosity, a telangectasia and a hemangioma. The first implies a focal dilatation and tortuosity of venous channels, the second a dilatation of pre-existing vessels, the third a definite tumor albeit of probable congenital origin. I do not believe that this is a varicosity. If a telangiectasia is considered the possibility exists that the renal lesion may be a manifestation of the Rendu-Osler-Weber syndrome, the hereditary hemorrhagic telangiectasia. In these patients the chief symptoms may be renal pain, sometimes colicky in character and hematuria. The criteria for the diagnoses are as follows: establishment of hereditary tendency, visible telangiectatic areas, normal bleeding, clotting and clot retraction times, no other disease of urinary tract and no abnormalities of the pyelogram.

Our patient in this case had a distinct tumor and we have heard that the pyelogram was abnormal. Thus I would consider the diagnosis in this case as hemangioma, and not a varicosity or a telangiectasia.

Dr. Mostofi's diagnosis: HEMANGIOMA.

Histopathologic Diagnoses Submitted by Mail:

Hemangioma	142
Others	8

Dr. Regato: All experts were in unanimous agreement.

Subsequent history: In July 1955 the patient appeared in good health but was still suffering from lymphatic obstruction of the right leg; a strawberry type of hemangioma of the skin was noted on the right hip.

Dr. Hudson: Most hemangiomas of the kidney have appeared clinically as problems of unexplained bleeding; in order to make a preoperative positive diagnosis of hemangioma, it would almost be necessary to have had the multiple hemangiomatous lesions appear before the operation was performed. In this instance the first skin lesion appeared afterward. In approaching a kidney from which there has been demonstrable bleeding, we often call the operation which is done "exploration of the kidney"; often exploration of the kidney means nephrectomy. If the surgeon is willing, it is possible to divide the entire kidney. The avascular plane is very difficult to find in the operating room, and the kidney, when incised, does bleed, but with clamps available and fifteen minutes of time devoted to it, it is possible to control completely the vascular pedicle to the kidney and to divide its throughout its entire length. This procedure I learned from Dr. Herbert Brendler. As far as I know, he, Dr. Goodwin of U.C.L.A. and I, are the only surgeons who employ it. It has been worth a great deal to us. Sometimes hemangioma is not of such a size that nephrectomy need be done; moreover, similar lesions could possibly develop in the opposite kidney. This fact must always be taken into consideration when operating on one of two structures, one of which at least is essential for life. I think that removal of the lesion is probably the only way in which the bleeding could have been stopped.

A Voice: I would like Dr. del Regato to comment on the possible use of radiotherapy in hemangioma of the kidney.

Dr. Regato: The attitude we take about hemangiomas in general is that it is better not to treat them, since three-fourths of them disappear spontaneously without leaving any sequelae. On the skin of babies we treat them only, and then mildly, if we see them in their period of growth. Adult hemangiomas are not too radiosensitive and require large doses of radiations. In respect to hemangiomas of the kidney, I am afraid that I could not talk with any experience. I have never treated one and I certainly would not be in favor of irradiating them because the amount of radiation that would be necessary to make the hemangioma disappear would certainly damage the kidney. I would prefer to think of hemangiomas of the kidney as tributaries of surgery.

H. F. Elmendorf, Jr., M. D., San Antonio, Texas: Would Dr. Hudson say that aortography would have been of value for the establishing of preoperative diagnosis of hemangioma.

Dr. Hudson: I think it might have been misleading; I doubt whether it would have given us a diagnosis at all.

D. A. DeSanto, M. D., San Diego, California: One of the common causes of hemiunilateral hypertrophy is either hemangioma of the soft parts or telangiectasias or neurofibromatosis; it would be interesting to know if such lesions were present.

Dr. Regato: You have all the information we received.

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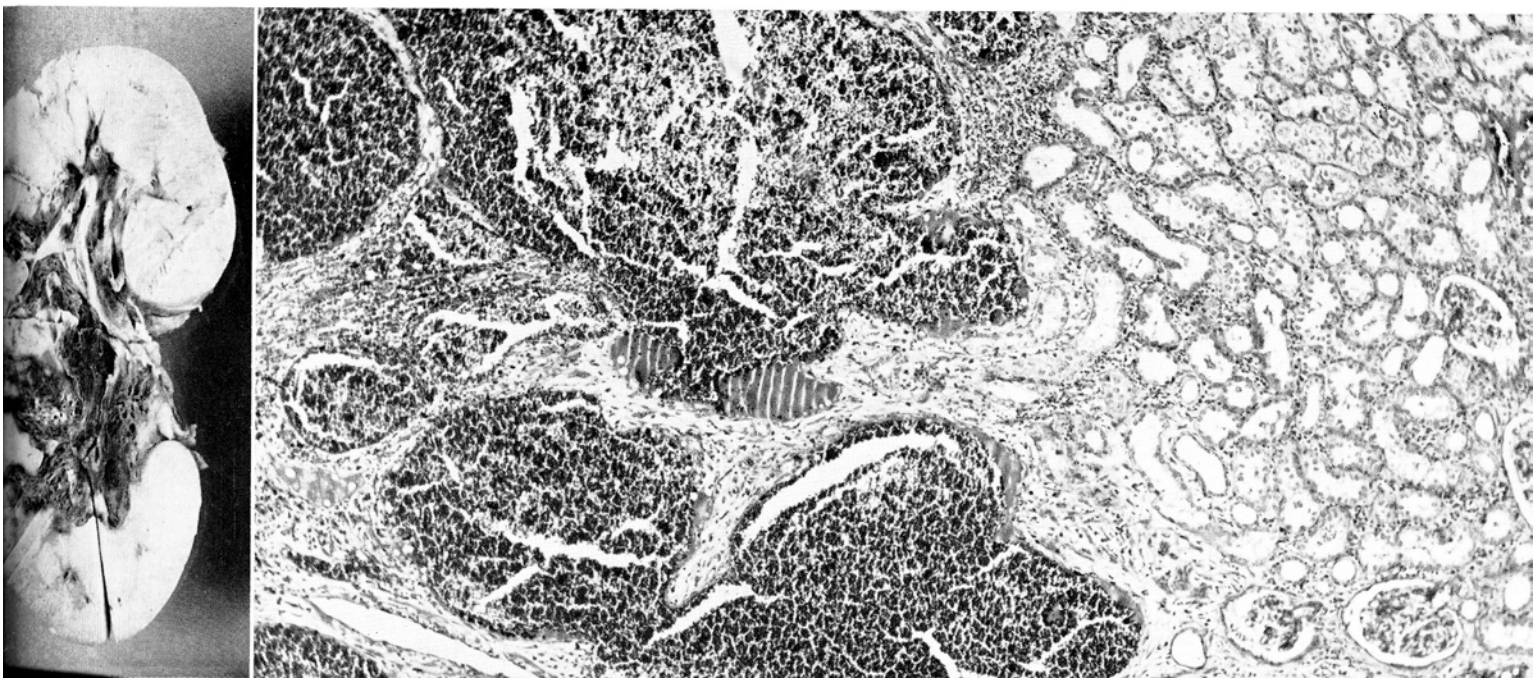
Fig. 2—Dry specimen of right kidney showing spongy tissue around major calyces.

Fig. 3—Low power photomicrograph: hemangioma of the kidney showing many cavernous channels packed with red blood cells.



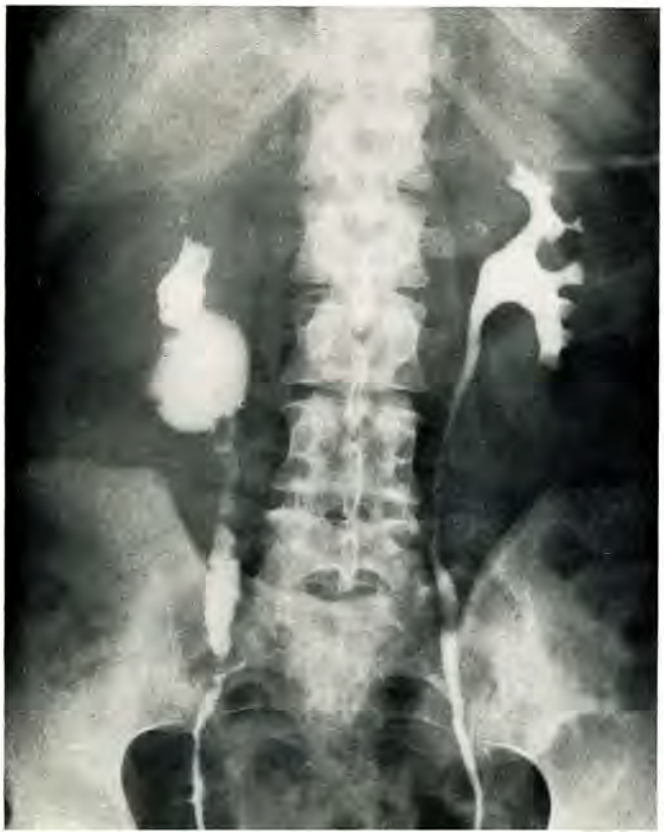
5. Pyelonephritis with Pseudo-xanthomatous Reaction (Malakoplakia)

Contributed by
JOHN B. FRERICHS, M. D., and THOMAS E. GIBSON, M. D.,
San Francisco, California, and
JOHN BARETA, M. D., Milwaukee, Wisconsin

THE PATIENT was a 51-year-old lady in June 1953 when she complained of pain in the right lower abdominal quadrant; later chills, fever, and burning on urination and a 7 lbs. weight loss took place. There was pain upon palpation of the right lower quadrant; abundant pus cells were seen in the urine; the hemoglobin was 8.6 grams per cent.

Dr. Hodges: When we looked at these roentgenograms with our urologists we observed the pelvic dilatation on the right, the narrowing of the pyeloureteral junction and the gross irregularity of the ureter, which is enlarged and yet invaded by small non-opaque masses producing defects in the lumen. The kidney is large and at the lower pole of the greatly enlarged pelvis and there is feathery irregularity of the margin. The kidney and psoas outlines are preserved. These findings suggested to us the possibility of renal neoplasm with pelvic implants, a diagnosis compatible with the patient's age. We finally veered away and pointed out that the same thing could be produced by inflammatory disease in the kidney with ureteritis cystica and voted for that without much solid reason one way or the other. The opposite kidney is normal.

Fig. 1—Pyelogram reveals dilatation of the right kidney pelvis and gross irregularity of the ureter in the form of rounded defects.



Dr. Hodges' impression: 1) TUBERCULOUS PYONEPHROSIS with URETERITIS CYSTICA; 2) NEOPLASM of the kidney with URETERAL IMPLANTS.

Radiologic Impressions Submitted by Mail:

Tuberculosis	63
Pyelo-ureteritis cystica	44
Carcinoma	39
Pyelonephritis	12
Malakoplakia?	1
Others	3

Dr. Regato: Dr. S. Thomas of Palo Alto, California, and Dr. H. P. Plenk of Salt Lake City also submitted renal tuberculosis with ureteritis cystica. An impression of ureteritis cystica was also favored by Dr. H. P. Doub of Detroit and by Dr. J. Ceballos of Galveston. Dr. B. Felson of Cincinnati also submitted this diagnosis but said that malakoplakia should be ruled out—he did not say how.

Philip J. Hodes, M. D., Philadelphia, Pennsylvania (by mail): Infection with ureteritis cystica seems a plausible diagnosis. The ureteral changes are extremely important but I wish the renal structures were better visualized; this lack of visualization makes one ponder on the possibility of carcinoma with ureteral implants.

Operative findings: On July 1953 a right nephrectomy was done: the kidney was surrounded by dense adhesions and the lower pole of the kidney was adherent to the colon. The kidney measured 15 x 7.5 x 6 cm; the pelvis was filled with 1000 cc of pus. The entire kidney appeared involved by an unusual spongy tissue of grayish-yellow color; the most characteristic lesions were in the cortex and extended to the capsule which was greatly thickened. In the pelvis there were several elevated irregular plaques 0.5 to 1.5 cm. The lumen of the ureter was completely occluded; there were two necrotic abscesses in the center area. Five enlarged lymph nodes were found; the largest 2.3 cm. The gross impression was that of a cortical carcinoma with implants in the kidney, pelvis, ureter and bladder.

Dr. Mostofi: The section shows a piece of kidney tissue. There is obvious severe pyelonephritis, but in addition to this, much of the kidney parenchyma is replaced by a tissue which consists predominantly of large cells with a distinct cellular border, finely vacuolated, eosinophilic, ground glass

cytoplasm, a small round sometimes vesicular and sometimes hyperchromatic or vacuolated nucleus. An occasional nucleoleus is encountered. The cytoplasm occasionally contains densely basophilic small round inclusions. Occasional giant cells were present, but no mitotic figures are seen. The cells occur in clumps and sheets; they may form pseudoalveoli. Often there is little if any stroma. At other times, however, there is distinct fibrous tissue component. Scattered throughout this structure are varying numbers of inflammatory cells, consisting of lymphocytes, plasma cells, monocytes and polymorphonuclear leukocytes, the latter in one or two areas forming an abscess. There is no capsule.

The first diagnosis that comes to mind is an epithelial tumor of the kidney—an adenoma or a carcinoma. The cells are vacuolated and they have either an aveolar-like or a solid pattern. However, neither the nucleus nor the cytoplasm is that of a carcinoma. The nuclei are small. They are perfectly benign looking, the cytoplasm is abundant, and finely vacuolated, the nuclear-cytoplasmic relationship is not that of a cancerous cell. The cells are obviously fat containing macrophages. In the central portions of these cellular masses, no stroma is apparent but the cells are still viable. These features rule out a renal cell carcinoma.

We have seen a number of these cases in which the lesion has been an incidental finding usually in a kidney removed for pyelonephritis and they are usually initially diagnosed on microscopy as carcinoma. The lesion has been variously described in the literature as replacement lipomatosis (which it is not because there is no lipoma), as a pseudoxanthoma of the kidney, as a specific granuloma of the kidney with lipophagic reaction and as a fibrosis and fatty replacement of the kidney, as malakoplakia, etc. The exact terminology is a matter of personal preference. As far as the term "xanthoma" is concerned, this lesion is a pseudoxanthoma. As far as the term "histiocytoma" is concerned, this term is occasionally used to designate a granuloma composed of histiocytes without eosinophiles and containing little or no fat. In contrast the cells under discussion do contain considerable fat. Moreover the term "histiocytoma" is confusing. I would, therefore, rather not designate these lesions as histiocytoma. The term malakoplakia, we have used only for the classic lesion seen in the mucosa of the bladder. Our own designation of these lesions has been pyelonephritis with pseudoxanthomatous reaction. This is my diagnosis.

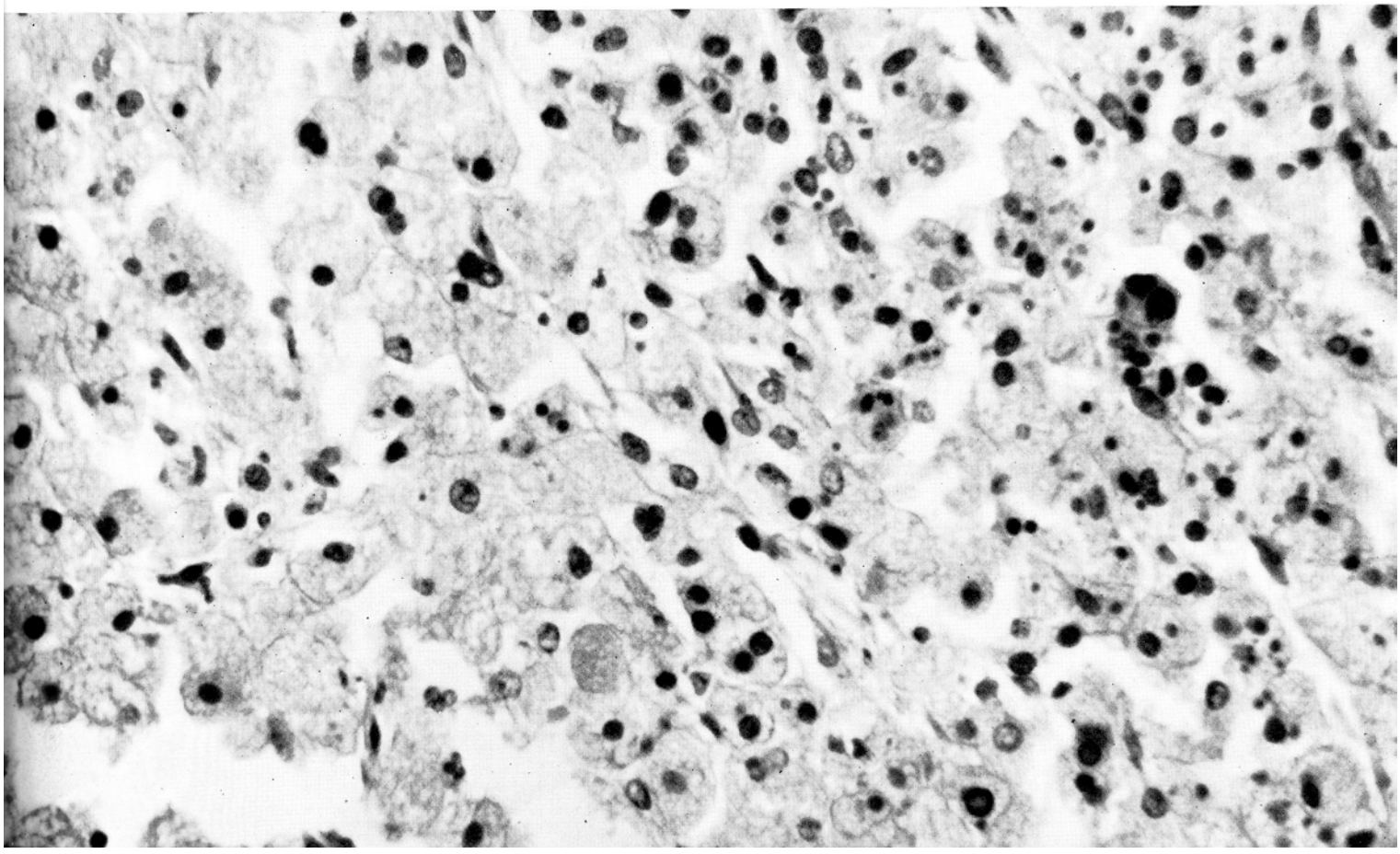
The genesis of this lesion is of interest. Many if not most of the cells are derived from histiocytes but we have seen histologically indistinguishable cells definitely lining renal tubules and I have, therefore, been led to believe that at least some of the cells may well be of tubular epithelial origin. An attempt is now being made to identify the cytoplasmic contents. The condition results from any process which destroys renal tissue. Renal calculi and chronic pyelonephritis are present in majority of cases, but these are neither specific or necessary as they are not present in about 30% of cases. The lesion is almost unilateral and terminates in fibrosis, scarring and hyalinization. I may add that grossly it has a distinct appearance in cross section, small cavities lined by a rather broad but wavy layer of bright yellow tissue.

Dr. Mostofi's diagnosis: PYELONEPHRITIS with PSEUDOXANTHOMATOUS REACTION.

Histopathologic Diagnoses Submitted by Mail:

Carcinoma	81
Myoblastoma	18
Granuloma	15
Xanthoma	6
Histiocytoma	5
Malakoplakia	5
Others	21

Fig. 2—Moderate power photomicrograph showing pseudoxanthoma of the kidney. Many vacuolated (fat) cells are seen some of which show inclusion bodies in their cytoplasm. In areas a supporting stroma is absent.



Dr. Regato: Dr. A. P. Stout of New York submitted histiocytoma. Dr. U. Gastaminza of San Sebastian, Spain, and Dr. F. Schajowicz of Buenos Aires considered this as a Grawitz tumor. Dr. R. A. Willis, of Leeds, and Dr. E. E. Aegerter of Philadelphia favored a diagnosis of granular-cell carcinoma. Dr. M. C. Wheelock of Chicago and Dr. V. R. Khanolkar of Bombay submitted myoblastoma. Dr. C. A. Hellwig of Halstead preferred sarcoid granulomas; Dr. M. B. Dockerty indicated that the lesion resembled malakoplakia. Dr. J. D. Bauer of St. Louis, Dr. A. O. Severance of San Antonio made an unequivocal diagnosis of malakoplakia.

Subsequent history: The patient was last seen in the beginning of 1955 in good health.

L. Lowbeer, M. D., Tulsa, Oklahoma: About five years ago we happend to observe a similar case which caused even greater difficulties than this. This was a 75-year-old woman who developed pyuria and a large mass which was identified as kidney and was removed. The kidney was diffusely enlarged and weighed 580 grams, surrounded by adhesions. The case of enlargement was a diffuse infiltration of the cortex and pyramids by tissue which was whitish rather than yellowish, and in addition there were several abscesses. The peculiar cell which causes this enlargement is a large cell, somewhat resembling a reticuloendothelial cell or histocyte, and replacing tubules extensively; this cell showed only a small amount of sudanophilic material, and there was a considerable amount of reticulum. This case was submitted to the Armed Forces Institute of Pathology for consultation; we received a report that the majority of consultants thought it was in inflammatory lesions with a peculiar reaction of the reticuloendothelial system but two very prominent consultants felt it was a diffuse carcinoma of tubular origin and another thought it was a plasmocytoma. The lesion was classified as (a) inflammatory lesions with reticuloendothelial cell response and (b) carcinoma, with a question mark. This patient is still alive and in perfect health. Dr. Arthur Purdy Stout had the case in a tumor seminar which he conducted in Tulsa in May of this year. He made a diagnosis of histiocytoma which is a peculiar variety of what Dr. Mostofi has described as a lipogranulomatous lesion since lipid did not play any considerable part in it.

J. B. McNaught, M. D., Denver, Colorado: I believe that this is the most instructive case that we have had for the day. You notice that the pathologists favored four-to-one a malignant tumor. I was among those. I thought it was a solid type of adenocarcinoma. Had I seen a gross picture I think I would have had a different impression of it, but I have never seen this condition before and obviously most of the pathologists who saw the sections had never seen it before. We have had now an opportunity of seeing such a lesion and knowing it existed.

A. O. Severance, M.D., San Antonio, Texas: I first met this lesion in New York City at the Arthur Purdy Stout Club, when Dr. Stout presented it, and I missed it. Dr. Stout had considered it as a possible granular cell myoblastoma until their urology department put him straight. But having met this condition in the urinary bladder it seemed to me that it might occur in the pelvis of the kidney and ureter even though I had never seen it there before. And I thought I saw some of those little hematoxylin staining bodies that go with this condition, so I thought I was on pretty good grounds when I made that diagnosis.

J. B. Frerichs, M. D., San Francisco, California: This patient was alive and well when seen by Dr. Gibson two weeks ago. I think that most of us have not seen this condition before, but once seen, it is perfectly characteristic. Dr. Gibson said it was also characteristic clinically, he regrets that he will probably never have an opportunity to put this knowledge to any use since the condition is very rare.

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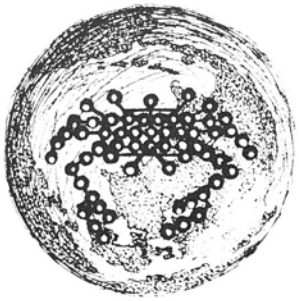
6. Aneurysm of the Renal Artery



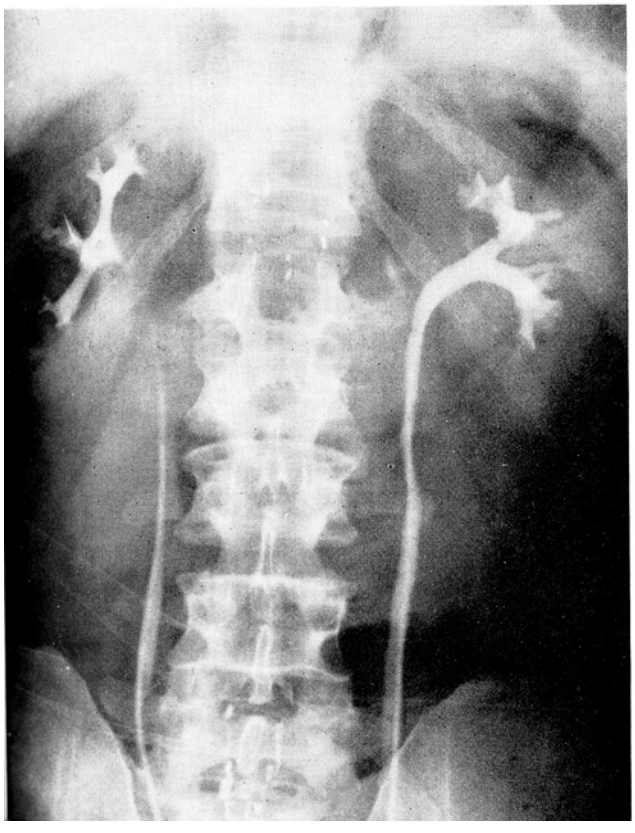
Contributed by ROBERT O. BEADLES, M. D., Colorado Springs, Colorado

THE PATIENT was a 48-year-old man in July 1954 when he noticed hematuria and pain in the left flank; he had recently gained 10 lbs. in weight. Twenty-one years previously a 4 cm neurofibroma had been removed from the 12th dorsal root. Upon palpation there was tenderness of the left flank but no mass could be felt. Cystoscopy revealed only the presence of clots; the indigo dye appeared in five minutes on the right and in ten minutes on the left.

Dr. Hodges: I believe that the configuration of the pyelogram on the left side is entirely compatible with normal status. There is however a striking difference from normal in position of the kidneys. The right kidney which should be lower and ordinarily is in a high percentage of normal individuals, is actually higher than the kidney on the left. In a recent review of 1500 patients in our hospital the left kidney was low in seven per cent. One-third of these patients had explainable renal abnormalities of one sort or another. (McClellan). One cause of downward renal displacement is a suprarenal mass. Tucked away in the clinical note in this protocol is the story that the patient had recently gained 10 lbs. in weight. This makes one wonder whether or not we are dealing with Cushing syndrome and suprarenal tumor.

Dr. Hodges' impression: SUPRARENAL TUMOR with CUSHING'S SYNDROME?

Fig. 1—Pyelogram showing some distortion of upper calyces of left kidney with apparent enlargement and downward displacement.



Radiologic Impressions Submitted by Mail:

Renal tumor	72
Suprarenal tumor	27
Extrarenal tumor	15
Quien sabe?	1
Others	21

Dr. Regato: Dr. H. P. Plenk of Salt Lake City also submitted a radiologic impression of suprarenal tumor. Dr. S. Thomas of Palo Alto, California, also felt that the left kidney was subject to extrinsic pressure. Dr. B. Felson of Cincinnati suggested hamartoma as a pure guess.

Philip J. Hodes, M. D., Philadelphia, Pennsylvania (by mail): There is a distortion of the lower pole of the left kidney which suggests the possibility of a tumor, but there is no clear evidence.

Operative findings: On July 1954, a left nephrectomy was done. The kidney measured 10 x 7 x 3.5 cm; the lining of the pelvis appeared hemorrhagic presenting enlarged vessels; there were several dark zones on the cortex.

Dr. Mostofi: The section shows a kidney in the hilum of which are seen several large arteries which show moderate to marked, but rather uneven subintimal thickening of their walls. There is no calcification. The peripelvic fat is somewhat increased. It shows some inflammatory reaction with fat necrosis and reparative process.

In discussing the differential diagnosis here, it would be valuable to know the operative technique and findings at the operation which was performed 20 years ago with specific reference to the nature of the lesion that was removed. Results of angiography would also be definitely valuable. The differential diagnosis lies between a vascular anomaly of renal pelvis and an aneurysm. The fact that in addition to the arteries several dilated venous channels are also present would suggest a vascular anomaly. However, this kidney is so well developed that it is difficult to conceive that there was a congenital anomaly of the vessels. Similarly such an anomaly would undoubtedly have been observed at the earlier operation. There is presumptive evidence, therefore, that the vascular lesion may well be acquired, the most likely being an aneurysm, either of renal artery or arterio-venous. The diagnosis of renal artery aneurysm, I believe, can be made on roentgenologic examination.

Aneurysm of renal artery is quite rare—about 100 cases have been described in literature. They may be congenital, arteriosclerotic, inflammatory and traumatic. About 30—50% of renal artery aneurysms have been attributed to trauma. With the history of spinal operation, there is a definite possibility of trauma to the renal artery leading to the formation of an arteriovenous shunt. In addition to this there is evidence of arteriosclerotic involvement of renal artery which may result in an aneurysm. The kidney shows some evidence of arteriosclerosis as well as blood derivative casts in the tubules.

The histologic picture is not that of an angiomyolipoma. This is a tumor most frequently encountered in tuberous sclerosis complex and is usually grossly small, multiple and asymptomatic but may be large, single and symptomatic. Histologically, these tumors have a complex structure con-

Fig. 2—Gross specimen showing enlarged vessels.

sisting of thick-walled vessels, mature fat cells, distinct fibrous and smooth muscle components. The tumors usually do not metastasize but may recur. The histologic picture, therefore, is quite different from that seen in this case.

The slide that I examined showed no hemorrhage. Rupture of an aneurysm is the most frequent complication of this contdition and I would not be suprised to find that there was hemorrhage either spontaneous or due to operative manipulation. I do not believe that this is an arteriovenous aneurysm because the walls of the veins are not as thick as I would have expected in an arteriovenous aneurysm. My diagnosis, therefore, is an aneurysm of the renal artery.

Dr. Mostofi's diagnosis: ANEURYSM of the renal artery.

Histopathologic Diagnoses Submitted by Mail:

Vascular anomaly	50
Arterio-venous shunt	30
Angiomyolipoma	19
Hemangioma	8
Hemorrhage	13
Others	26

Dr. Regato: Dr. E. F. Geever, of Bethesda, Maryland, submitted a diagnosis of anomalous blood vessels of the kidney pelvis. Dr. Carlo Sirtori of Milan and Dr. J. B. McNaught of Denver, submitted congenital vascular malformation. Dr. Engelbreth-Holm of Copenhagen and Dr. Charles Oberling of Paris questioned the possibility of an arterio-venous aneurysm. Dr. J. D. Bauer of St. Louis submitted a diagnosis of hamartoma.

Dr. Hudson: It is probably a good thing that this kidney has been removed. If this is a true aneurysm of the renal

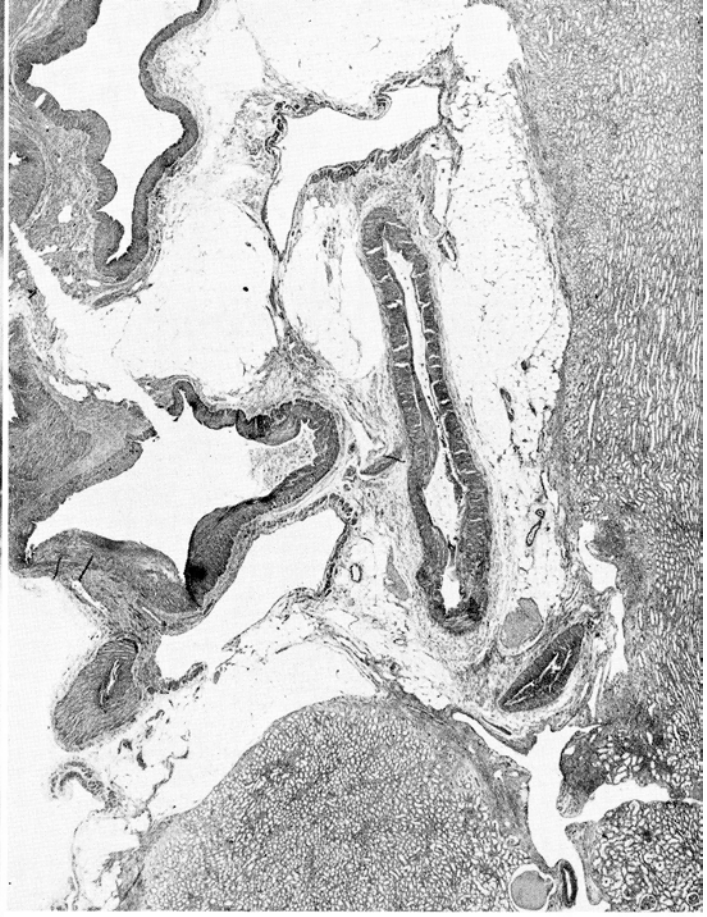


Fig. 3—Low power photomicrograph: aneurysm of renal artery showing dilated arteries with focal thickening of their walls.

artery, an artery which at normal calibre discharges 600 to 700, even 750 cc of blood a minute, the chances of saving a patient following rupture of this artery are not too good.

Dr. Hodges: Before the days of renal angiography, one depended for diagnosis of aneurysm renal artery on the deposition of calcium and the recognition of any calcific rings as seen in various projections. I gather, Dr. Mostofi, that you did not find any great calcium deposition in here. But on the other hand if one had injected opaque material into the renal artery by whatever means, certainly this very bizarre situation would not have come to light in a hurry.

A. F. Lincoln, M. D., Denver, Colorado: In my section, one of the larger arteries was completely surrounded by what appeared to be a dissecting hemorrhage, and I wondered if this vessel in a short time might not have terminated in a fatal hemorrhage.

Dr. Hudson : When one considers the man's age that possibility is a very distinct one. This man is only 48 years of age and to expect him to go through life with this rupturing vessel I think would be very optimistic. I am sure that this vessel would have ruptured and probably killed the patient.

Dr. Regato: So that it would appear proper to treat these lesions when diagnosed and that there would be no other solution but nephrectomy.

Dr. Hudson: It is possible now to interpose plastic cloths or homografts, but I don't believe this can be done in the kidney with this disorder.

Dr. Mostofi: In some cases of aneurysm of the renal artery I believe an attempt has been made to replace the original portion by graft, but I do not believe it could have been done in this case.

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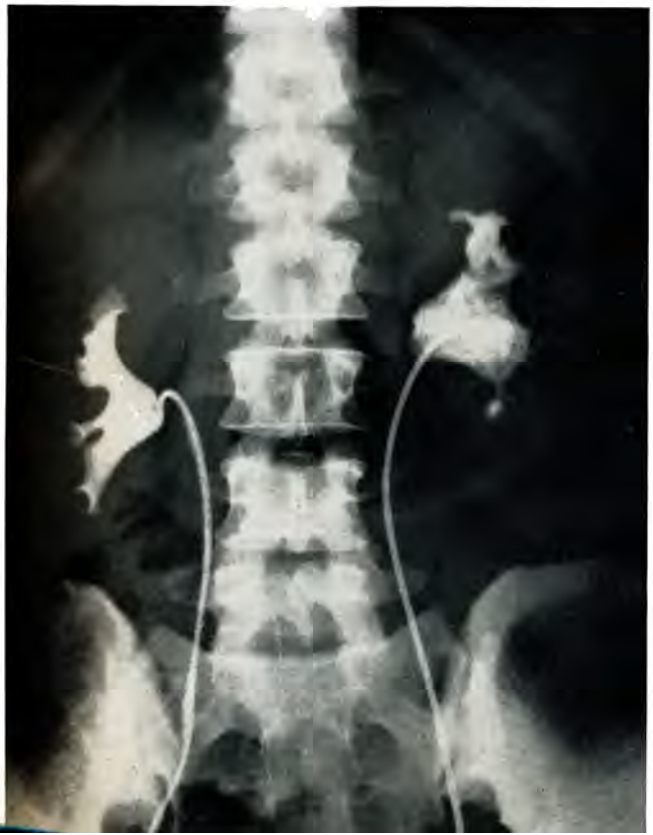
7. Pyelonephritis, Granular Pyelitis and Squamous Metaplasia (Leukoplakia)

Contributed by ROBERT F. THOMPSON, M. D. and FREDERICK P. BORNSTEIN, M. D., El Paso, Texas

THE PATIENT was a 40-year-old lady in October 1952 when she complained of left dorsolumbar pain and general malaise; she had suffered "kidney infections" with each of her two recent pregnancies. Cystoscopy revealed evidence of inflammation of the bladder; the urine from left kidney was markedly purulent and presented a flaky appearance. The hemoglobin was 10 grams per cent. In August 1953 the symptoms recurred with fever of 103° F.

Dr. Hodges: This roentgenogram caused a great stir of interest when reviewed at our hospital, largely for the reason that on the left side there are peculiar linear defects in the pyelographic opaque material. In addition the lower pole calyces are extensively deformed and distorted. We do not know whether or not this lesion was opaque in its own right before the ureteral catheters were inserted. The fact that this looks like a perfectly normal pyelogram on the right side could still be misleading because the urologist could have injected this side and not the left; this appearance could be due to a large and irregular pre-existing calcification producing a cast of the entire hollow portion of the kidney. I gather that is not the case and we are viewing a retrograde pyelogram and that what we are seeing are defects in the opaque material. Defects in the opaque material when they are transparent as they are here, could be renal stones, of course, but they are seldom found in flakes and plaques of this sort. Other lesions in which we have encountered anything like this are inflammatory disease of the kidney with desquamation of detritus into the pelvis. The story of passing flakes in the urine which we now get, seem to fit with that pretty well. Our urologist pointed out, however, that it was perfectly possible from the clinical viewpoint to see this sort of thing in papillary tumors of the renal pelvis with desquamation of tumor cells.

Fig. 1—Retrograde pyelogram showing bizarre irregularity of the left kidney pelvis.



Dr. Hodges' impression: CHRONIC PYELITIS with DESQUAMATION of renal pelvis.

Radiologic Impressions Submitted by Mail:

Pyelonephritis	75
Tuberculosis	39
Staghorn calculus	15
Never seen one like it!	1
Others	21

Dr. Regato: Dr. L. C. Collins and Dr. V. P. Collins of Houston also suggested chronic pyelonephritis. Dr. H. P. Doub of Detroit felt that this case has signs of pyelonephritis with some superimposed pathology. Dr. M. T. Harris of Spokane and Dr. P. C. Swenson of Philadelphia considered tuberculosis.

Philip J. Hodes, M. D., Philadelphia, Pennsylvania (by mail): I believe we may be dealing with a large dendritic calculus of the left kidney, possibly secondary to tuberculosis.

Operative findings: On September 1954 a left nephrectomy was done. The kidney capsule stripped off with ease revealing tiny nodules containing pus. On section several small abscesses were seen throughout the parenchyma; the pelvis was dilated and its lining was thickened and whitish in color.

Dr. Mostofi: The section shows kidney and the renal pelvis. Of interest is the lesion seen in the pelvis. Most prominently there is squamous metaplasia and keratinization of part of renal pelvis. This is commonly referred to in the urologic literature as leukoplakia. About 100 cases of such lesions have been described, but I believe that the lesion is more frequent than this would imply. Vitamin A deficiency, individual susceptibility, inherent deficiency, and chronic irritation are the chief factors of importance in the development of this change. It would be of interest to know if the patient had any calculi, these patients usually do. The chief complication of leukoplakia of renal pelvis is, of course, carcinoma, the incidence of which is said to be 8.4% of these patients. The squamous metaplasia in this instance does not involve the entire pelvis since a substantial portion of the pelvis is still lined by transitional epithelium. In this area there is severe inflammatory reaction of the pelvis which is apparently forming polypoid projections suggestive of an early phase in the development of follicular pyelitis. The kidney itself shows several large abscesses, pyelonephritis and arteriosclerosis.

My diagnosis in this case is therefore renal abscess, pyelonephritis, granular pyelitis and "leukoplakia" of renal pelvis. The infiltrating cells are inflammatory and not neoplastic and there is no evidence for the diagnosis of leukemia or myeloma.

Dr. Mostofi's diagnosis: RENAL ABSCESS, PYELONEPHRITIS, GRANULAR PYELITIS AND "LEUKOPLAKIA" OF THE RENAL PELVIS.

Histopathologic Diagnoses Submitted by Mail:

Pyelonephritis	83
Squamous metaplasia	38
Leukoplakia	12
Leukemia	19
Myeloma	12
Others	27

Dr. Regato: Dr. M. B. Dockerty of Rochester, Dr. Terrance H. Cochran of Salt Lake City, Dr. J. D. Bauer of St. Louis and Dr. A. O. Severance of San Antonio also submitted pyelonephritis and leukoplakia of the kidney pelvis. Dr. D. Brachetto-Brian of Buenos Aires submitted a diagnosis of plasma-cell leukemia. Dr. Engelbreth-Holm of Copenhagen and Dr. Raffaele Lattes of New York made a diagnosis of suppurative pyelonephritis and noted squamous metaplasia.

Subsequent history: This patient was last seen, in excellent health, in July 1955. The case has been published in the June 1955 issue of the Journal of Urology.

Dr. Regato: Published cases of leukoplakia of the renal pelvis seldom have been diagnosed pre-operatively. In the kidney pelvis as elsewhere "leukoplakia" is a gross diagnostic impression, not a histopathologic diagnosis; here, however, there is not the same cancerous or pre-cancerous significance which the lesion evokes elsewhere. Most cases present a concommitant chronic inflammation or infection and consequently have a history of repeated pollakiuria, pyuria, etc. The passing of "flaky debris" or "gritty flakes" through the urine becomes diagnostic. Pyelograms have been said not to be characteristic due to the fact that there may be associated chronic inflammation. Close observation

Fig. 2 (below) — Gross specimen of left kidney showing thickening and whitish appearance of pelvic lining.

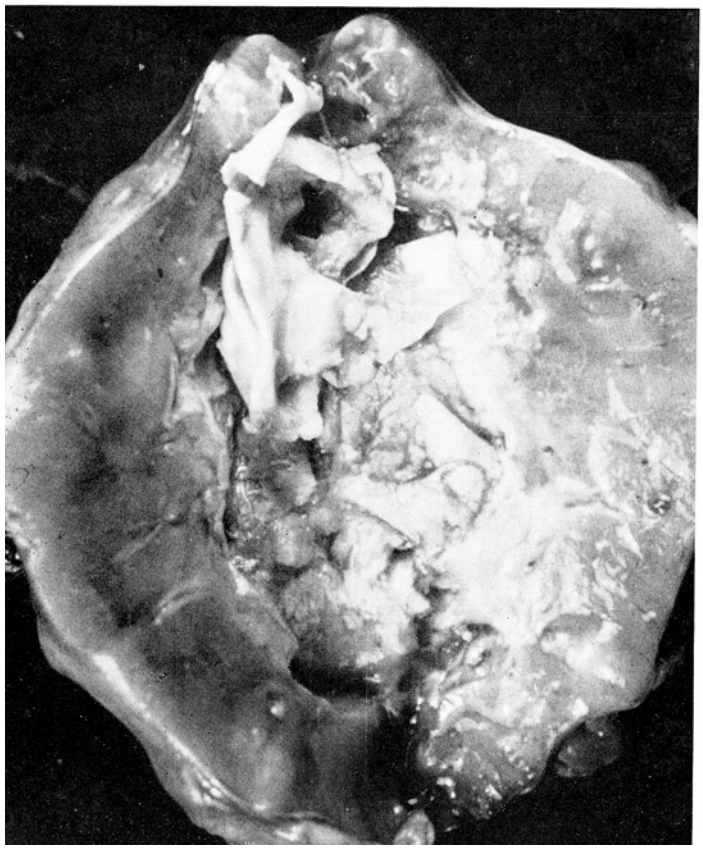
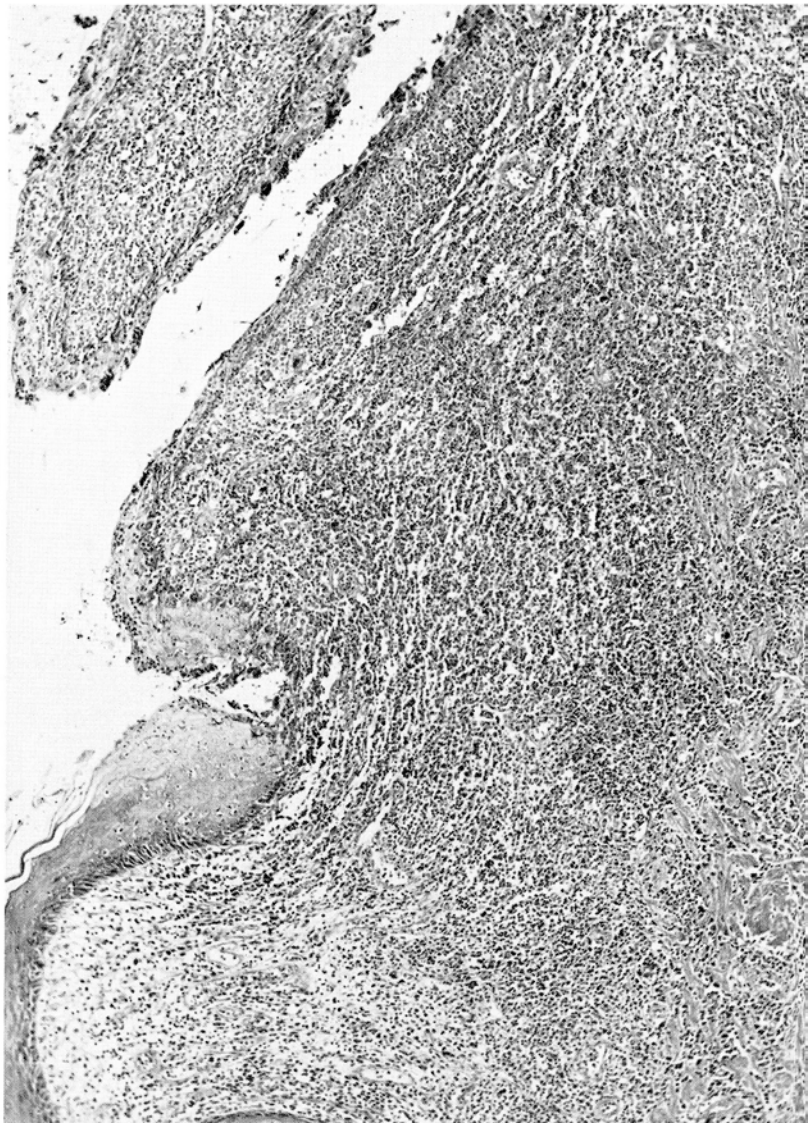


Fig. 3 (at right) — Low power photomicrograph: leukoplakia of renal pelvis. The transitional epithelium is replaced by keratinizing stratified squamous epithelium. There is severe pyelitis.



of pyelograms of most cases will reveal the presence of "lacy striations" and an overall "moth-eaten" appearance of the kidney pelvis which should suggest the diagnosis preoperatively.

Dr. Hudson: This woman developed what is usually called pyelonephritis of pregnancy, and finally her disease terminated in what in other times would have been called multiple cortical abscesses of the kidney; before the days of sulfa drugs and antibiotics this disease was almost universally fatal. In some way the urologist who managed this case came to precisely the right solution, that is, to remove the kidney. We have had in our medical center five cases in the last five years in which this disease developed, the antibiotics were not effective, eventually the patient's temperature returned to normal while the patient was dying of septicemia from organisms that we previously thought of as rather innocuous, B. coli and aerogenes, in practically every one of these five instances. The matter of leukoplakia is perhaps open to further discussion and I would like very much to hear another pathologist comment on Dr. Mostofi's impression that this is leukoplakia, in quotation marks. It certainly does not seem to be the kind of leukoplakia that appears elsewhere in the genito-urinary tract; both this matter and that of the radiodiagnosis are still rather unclear in my own mind.

Dr. Hodges: I would say that in this particular instance there is enough here that is definite that I very much hope that I won't miss the next one. I think there are pretty definite radiologic signs.

F. P. Bornstein, M. D., El Paso, Texas: I am very unhappy to see these cases called leukoplakia. When I reported on this case I called it squamous metaplasia with epidermization which gives a clear, anatomical description of what is happening in the renal pelvis; this is a specific condition except that it looks white and bears a similarity to leukoplakia in other areas. I think we should abandon the term leukoplakia with its connotation of premalignancy; we should instead describe the microscopic findings.

H. T. Low, M. D., Pueblo, Colorado: The etiology of leukoplakia of the pelvis of the kidney or any other portion of the urinary tract is chronic infection usually a chronic pyelonephritis. When you get flecks of tissue passed down through the urine, a diagnosis can be made before a pyelogram has been done. We believe that there is a strong possibility that this is a precancerous condition. Leukoplakia is rarely confined to the renal pelvis alone, usually starts there and will reach the ureter and involve the bladder. The case that we reported was confined entirely to the renal pelvis. I believe nephrectomy is necessary. If the radiologist or pathologists would get an accurate history, they would make the right diagnosis more often.

Dr. Hudson: I think that nephrectomy was definitely right, but not for the diagnosis of leukoplakia. One might be faced with the ridiculous situation in which the disease is bilateral, and under such circumstances no one could contemplate nephrectomy, unilateral. I think it is fortunate that the nephrectomy was done because of the cortical abscess. If this diagnosis is preoperatively made or made at the time of operation, I think the nephrectomy is the treatment of choice.

M. Berthrong, M. D., Colorado Springs, Colo.: I would like to suggest that perhaps the squamous metaplasia that is present in this sort of a case of intense pyelonephritis is obviously a good deal different than that peculiar and unusual metaplasia that is associated with so much hyperplasia of the whole urinary tract, and so often does give rise to carcinoma. I would like to ask Dr. Mostofi to comment on perhaps different types of squamous metaplasia, one reactive to inflammation and one apparently a primary and mysterious condition.

Dr. Mostofi: I think in the urinary tract we cannot deny the presence of the whole range. In other words we start with this case where the epithelium is thin, and you have a layer of keratinization on the top, and go to the other extreme, where the epithelium is not only squamous but markedly thickened and obviously hyperplastic. I think that the second category makes you worry a lot more than the first one because there is not only squamous change of the epithelium but there is distinct hyperplasia; this type is definitely associated many times with stones.

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8. Renal-cell Carcinoma in a Twelve-year-old Child

Contributed by PETER E. RUSSO, M. D., Oklahoma City, Oklahoma

THE PATIENT was a 12-year-old Negro girl in February 1955 when she gave a history of single episode of hematuria three months previously and complained of chills and fever, and 15 lbs. weight loss in four months. Examination revealed a mass in the left upper abdominal quadrant extending 10 cm below the costal margin; the hemoglobin was 7.8 grams per cent.

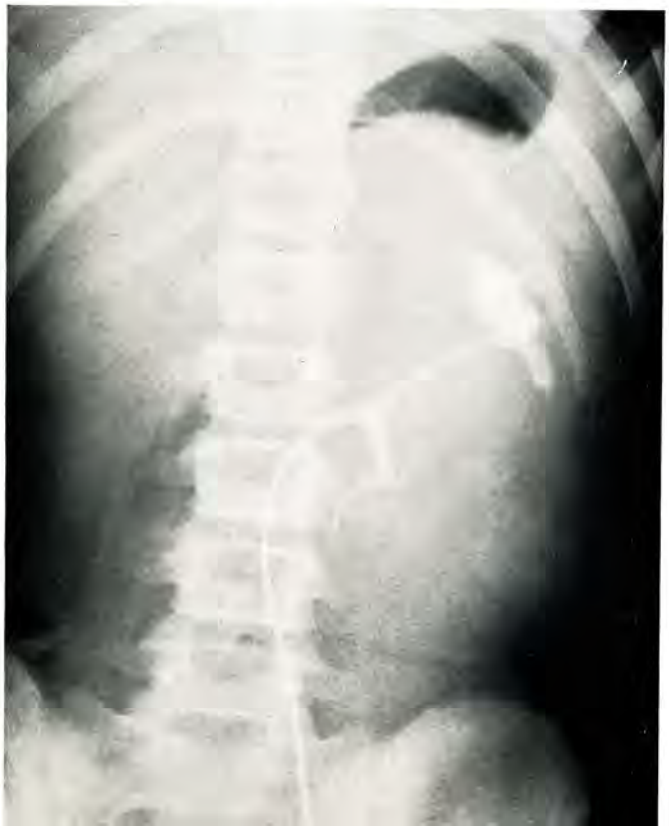
Dr. Hodges: This is the sort of pyelographic evidence that certainly bespeaks a mass inside the kidney proper because it is elongated. The distorted lower pole calyces and the enormous enlargement of the kidney are sufficient to boost the ureter across the spine. The mass is shown even to a little better advantage by the fact that in the gas bubble of the stomach the upper pole of the kidney is making an indentation. Whether or not this is all contained within the capsule of the kidney one can't be sure, but certainly the appearance suggests a tumor growing in the kidney. Because of the child's age I believe it will turn out to be Wilm's tumor.

Dr. Hodges' impression: MALIGNANT TUMOR of the left kidney, probably WILM'S TUMOR.

Radiologic Impressions Submitted by Mail:

Wilm's	84
Carcinoma	24
Malignant renal tumor	16
Renal cyst	15
Sarcoma	12
Others	3

Fig. 1 — Retrograde pyelogram revealing enlargement of left kidney and medial displacement of the ureter.



Dr. Regato: Dr. H. Lacharite of Montreal and Dr. F. A. Rose of Cleveland also considered Wilm's tumor as the best possibility. Dr. M. L. Sussman of Phoenix, Arizona submitted hypernephroma. Dr. Paul Swenson of Philadelphia felt that this was probably a large size sarcoma.

Philip J. Hodes, M. D., Philadelphia, Pennsylvania (by mail): This is a huge renal tumor with ureteral displacement and encroachment upon the stomach. In spite of the child's age I believe this is a Wilm's tumor, the most common renal tumor in the young. If there were any calcifications I would suggest a neuroblastoma.

Operative findings: On February 1955 a left nephrectomy was performed. The kidney measured 15 x 14 x 10 cm and was almost completely involved by a tumor, only a remnant of normal structures remained in the upper pole.

Dr. Mostofi: The section shows a kidney most of which is replaced by a tumor. The tumor cells are large, they have a granular eosinophilic cytoplasm showing varying degrees of vacuolization. The nuclei are rather large, round or oval, hyperchromatic. One, two or three large basophilic nucleoli are seen. Mitotic figures, multinucleated cells and giant cells are frequent. Considerable variation in size, shape and staining characteristics of the nuclei and the cells is apparent. Cytoplasmic vacuolization is quite prominent in areas and the nuclei are definitely smaller and more vascular. Although a distinct alveolar pattern is seen, not infrequently the tumor cells occur in solid sheets separated from each other by delicate richly vascular fibrous septae. Areas of necrosis are frequent. An interesting feature of the tumor is its intimate relationship to the vascular channels. At times all that exists between the tumor cells and the vascular channels is a thin layer of endothelial cells suggesting an organoid or endocrine pattern, and in several areas invasion of large venous sinuses is present.

The differential diagnosis here lies between (a) a nonchromaffin paraganglioma or granular cell myoblastoma, (b) an adrenal cortical carcinoma arising either in abberant adrenal or in the normal adrenal and extending to the kidney and (c) a renal cell carcinoma.

Paragangliomas consist of large round, oval, polyhedral or even cylindrical cells with granular, acidophilic or clear cytoplasm and well defined round or oval vesicular, finely reticulated nuclei having a single prominent nucleoli. The cells occur in groups of 8 - 25 cells and have a typical organoid pattern in which the cells nests are separated from each other by capillaries accompanied by delicate reticular fibers which do not penetrate or separate individual tumor cells, but surround a group as a whole. Vascular invasion is quite a prominent feature. Although in its most viable areas the tumor does resemble paraganglioma, the distinct alveolar pattern and the presence of areas of definite clear cell carcinoma tend to rule out a paraganglioma.

An adrenal cortical carcinoma is also suggested by the appearance of cells and by the organoid pattern. I hesitate to mention this diagnosis lest we become involved in a fruitless discussion of adrenal origin of renal carcinomas. Perhaps this can be forestalled if we agree that most renal

carcinomas arise from renal tubules, but that it is not inconceivable to have a few primary renal carcinomas originate in adrenal rests. As far as the present tumor is concerned I believe it can be said without any hesitation that on the basis of available information this tumor is not a functioning adrenal cortical carcinoma. As far as a nonfunctioning carcinoma of adrenal origin is concerned, histologically, the present tumor is not an adrenal tumor because (a) while acinus or tubular formation is seen in adrenal carcinoma this it not very common and when it is seen it is not as extensive as is found in the present case; and (b) areas of clear cell carcinoma seen in this section are not usually found in carcinoma of adrenal. Thus while we cannot be dogmatic about the fact that this is not carcinoma of adrenal origin, the evidence is against it.

The diagnosis is therefore a renal cell carcinoma with early vascular invasion. Vascular invasion, of course, materially affects the prognosis. The occurrence of a renal cell carcinoma in a twelve-year-old child is quite unusual, most of the tumors occurring in the 40 - 70 year age group. In the group currently under study at the Armed Forces Institute of Pathology we have seen four or five less than fourteen years of age, the youngest being six years old. Renal cell carcinomas, therefore, do occur in the younger age group. We have not as yet observed any difference in their clinical behavior in contrast to the tumors seen in adults.

Dr. Mostofi's diagnosis: RENAL-CELL CARCINOMA.

Histopathologic Diagnoses Submitted by Mail:

Carcinoma (dark cell, granular cell, tubular mixed type)	120
Hypernephroma	11
Wilm's	9
Others	15

Dr. Regato: Dr. Fridtjof Bang of Copenhagen, Dr. Ruben Farias of Merida, Yucatan, and Dr. Raffaele Lattes of New York all submitted a diagnosis of tubular adenocarcinoma.

Subsequent history: In May 1955 pulmonary metastases were observed in the roentgenogram. In July 1955 she was hospitalized with bone metastases.

Peter Russo, M. D., Oklahoma City, Oklahoma: This patient expired in the latter part of August, 1955.

Dr. Regato: How about the age of patients with Wilm's tumor?

Dr. Mostofi: The majority of them occur in patients less than six years of age, but cases have been reported up to twelve years of age.

V. Vermooten, M. D., Dallas, Texas: I am interested in kidney tumors and particularly in dark cell carcinoma as compared to the clear cell hypernephroid type of tumor. I would like to have Dr. Mostofi tell us what is the difference between them; clinically I think there is a great deal of difference between them. I feel that as a rule, the dark cell carcinoma is more or less a growth of embryonal type, of remnants of tubules, whereas the clear cell carcinoma is almost always in the cortex rather than in the medulla. In a couple of occasions I found a tumor which was almost pedunculated off the kidney, I have removed just the tumor itself and left the kindney behind and these patients have never shown any local recurrence, altho subsequently some of them have developed metastases. For that reason I feel that the clear cell carcinoma is a tumor which always has a false capsule and there is very seldom any actual tumor more than one centimeter beyond it. Consequently, I feel that the prognosis and management is completely different with the dark cell carcinoma where radical surgery is very urgent and important; there is of course frequent mixture of the two.

Dr. Regato: Dr. Vermooten, what is the oldest patient you have seen with a Wilm's tumor?

V. Vermooten, M. D., Dallas, Texas: I have seen a Wilm's tumor in one patient 26 years old and in another 41 years old. The 41-year-old I questioned and consequently the sections were sent to various pathologists. They all agreed that it was a Wilm's tumor.

Dr. Mostofi: Some years ago N. Chandler Foote wrote a very nice article about kidney tumors and correlation of microscopic appearance with prognosis; he found that in those tumors in which the acini were regular, the cells were clear, there were no mitotic figures, no anaplastic areas, etc., the prognosis was definitely better. But it can be said from our own experience, that some of the tumors with clear cells and regular acini, behave in a less malignant

Fig. 2—Low power photomicrograph showing renal cell carcinoma. The acini are small; they are lined by a single layer of epithelial cells. Note the intimate relationship of the cell nests to vascular channels.

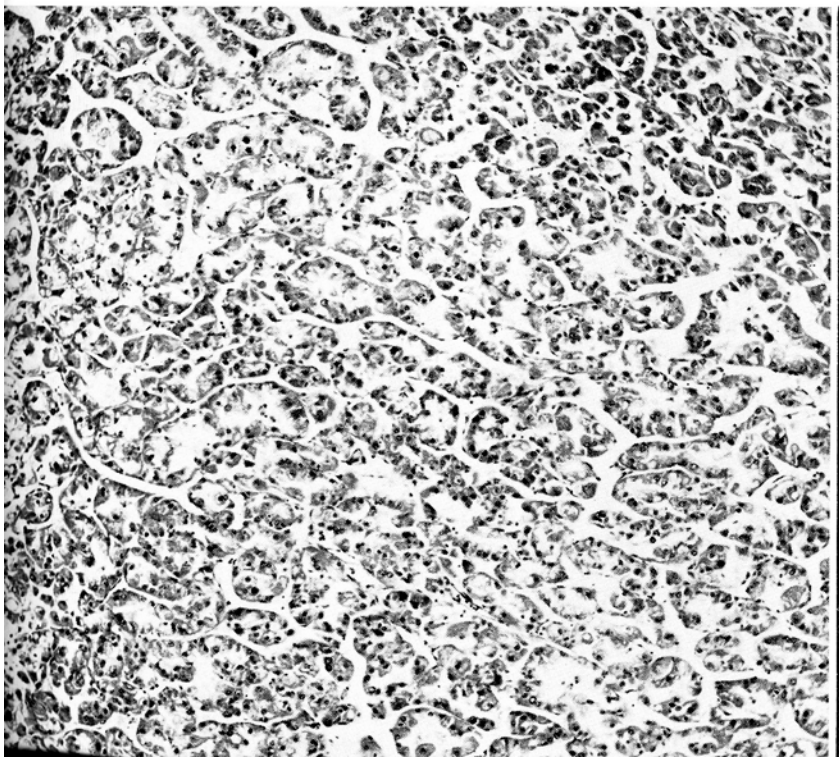
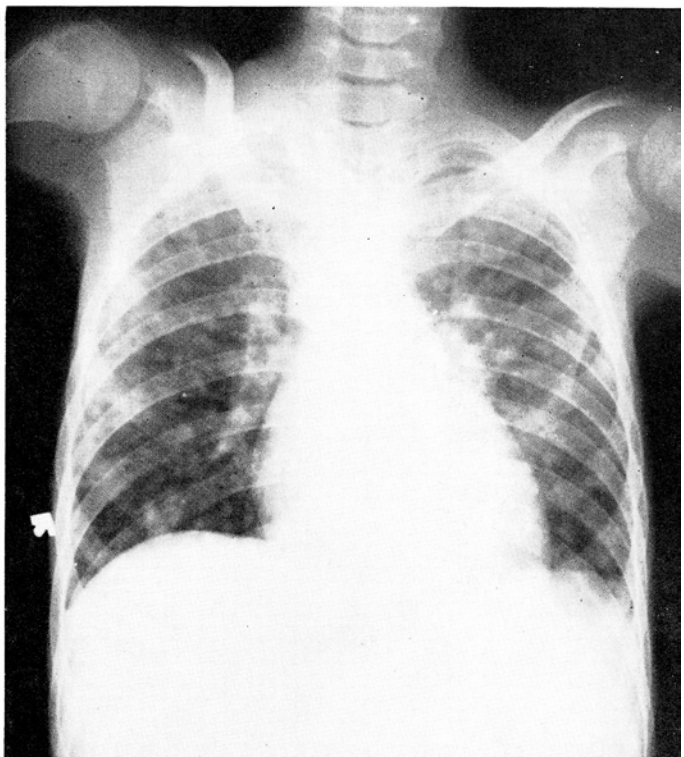


Fig. 3—Roentgenogram of the chest showing bilateral pulmonary metastases.



fashion. Beyond that it is difficult to say much of anything, because actually we have found that if you cut multiple sections of a kidney tumor, you almost invariably find areas of granular carcinoma, clear cell carcinoma, spindle cell carcinoma, and so on. For this reason we don't use the term clear cell or dark cell or granular cell. I think the important thing is what the tumor is doing. Is the tumor invading blood vessels like this one was? Then the prognosis is bad. I think that the so-called dark cell carcinoma that Dockerty described from the Mayo Clinic some years ago were small numbered, and they all occurred in females.

Dr. Hudson: I would like to comment on Dr. Vermooten's remarks regarding his own work with the conservative types of operations for certain kinds of kidney tumor; if Dr. Vermooten is convinced that he can determine when he has a less malignant kind of tumor, perhaps he is justified in doing a conservative operation and preserving the kidney. What I would like you to keep in mind is the fact that kidney cancer in general has only about an 11% cure rate in the United States and that cure rate of resectable kidney cancer, that which is thought by the surgeon at the time of operation to be resectable, approaches 40%; it does not seem to me that we ought seriously to think about conserving renal tissues in a disease which is still killing approximately 90% of our patients.

J. D. Barger, M. D., Phoenix, Arizona: I would just like to make the observation that although Wilm's tumor is unusual in the human, it is the most common tumor that is encountered in pigs; if you want to study the tumor, the most beauitful specimens you can get are from the tumors which occur in pigs.

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9. *Rhabdomyosarcoma Primary (?) in the Kidney*

Contributed by LUCIEN M. PASCUCCI, M. D., Tulsa, Oklahoma

THIS PATIENT was a 70-year-old lady in April 1954 when she gave a history of single episodes of hematuria six and one months previously and complained of aching pain over the right flank. Examination revealed no important findings; the hemoglobin was 4.4 grams per cent.

Dr. Hodges: I would like to point out that this roentgenogram shows nothing frankly wrong on the left side. The argument centers about the peculiar accumulation of opaque material on the right. There appears to have been considerable rotation of this kidney around its long axis and around its short axis as well. Occasionally one finds normal pyelograms which do not differ materially from this one. I asked the opinion of the urologist in our group and others in our hospital. No one was willing to call this an abnormal pyelogram.

This morning Dr. del Regato showed me another film which came to his possession only recently. (This roentgenogram was not submitted to other participants.) This other pyelogram, made with opaque material followed by the injection of gas, shows the outline of the ureter very nicely indeed and certainly there is information which now comes to light which cannot be seen with any degree of certainty in the first film. There is considerable increase in the capacity of the pelvis and of the lower pole calyces on this side. Obviously this is hydronephrosis; I am not sure I would be able to determine the cause.

Dr. Hodges' impression: HYDRONEPHROSIS, right, cause undetermined.

Radiologic Impressions Submitted by Mail:

Ureteral obstruction (pelvic tumor, abnormal vessel, etc.)	60
Carcinoma renal pelvis	39
Carcinoma of the ureter	20
Hypernephroma	16
Others	25

Dr. Regato: Most of the experts conjectured as to the cause of the obstruction and suggested congenital vascular anomaly, ureteral stricture, carcinoma of the ureter, etc.

Paul C. Swenson, M. D., Philadelphia, Pennsylvania (by mail): Ureteropelvic obstruction, probably due to something unusual, otherwise it would not be in the CANCER SEMINAR, but it is not apparent in this film.

Philip J. Hodes, M. D., Philadelphia, Pennsylvania (by mail): I suspect we may be dealing with a tandem type kidney. I believe this may be a carcinoma of the upper pole of the right kidney.

Charles M. Gray, M. D., Tampa, Florida (by mail): While the illustrations submitted are as fine as any I have ever seen, there is still room for finer detail; this combines with meager and probably misleading histories and mitigates against even logical guessing. In submitting my impressions I have played the game for you, rather than with you! I don't like guessing games, there is too much guessing in life as it is.

Dr. Regato: Dr. Gray's views are shared by many others. The limitations of our educational exercise seem to irk them. Actually the interpretation of the shadows seen in a roentgenographic study is often a guess which has to be improved by frequent correlation with pathologic findings. I wonder if what Dr. Gray does not like is the probability of finding out that his guess was wrong. Such probability is greater in a CANCER SEMINAR case, and thereby all the more fruitful, for it is learned without possible harm to a patient. May we here thank Dr. Gray as well as our guest roentgenologist and all the others who have contributed to our CANCER SEMINAR in spite of its admitted limitations, so that others may find some consolation in the error which may be common to many and in the information which is thereby gathered.

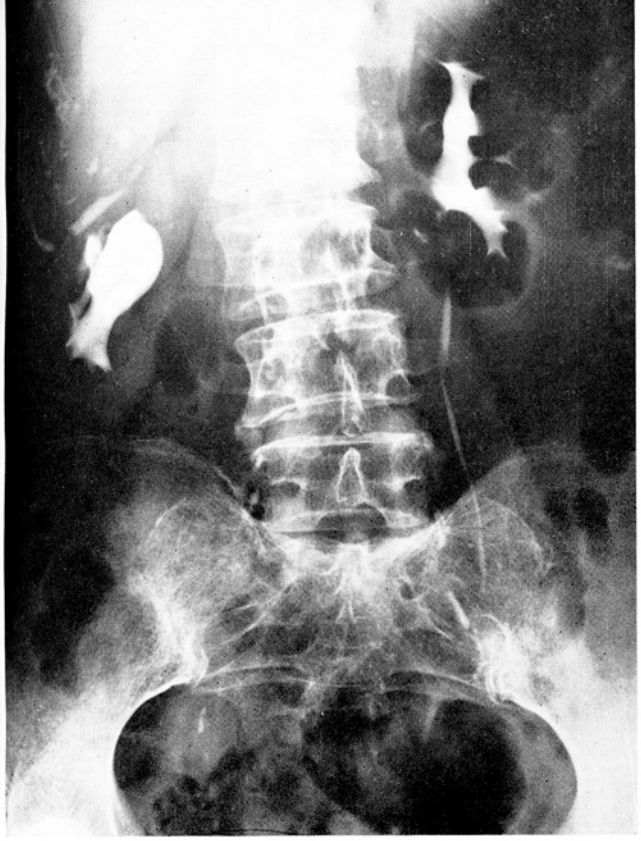


Fig. 1—Intravenous pyelogram showing some apparent dilatation of the right kidney pelvis.

Operative findings: On November 1954 a right nephrectomy was done without difficulty. The kidney measured 11 x 6 x 5 cm and the parenchyma was very friable. The middle calyx was distended by a grayish tumor which extended into the renal pelvis, and which was continuous with a friable mass that replaced the middle pyramid.

Dr. Mostofi: The tumor consists of more or less interlacing bands of spindle-shaped cells. The cells display marked variation ranging from round cells resembling large lymphocytes to cells that are uni- or bi-polar to those that are distinctly spindle-shaped. The cytoplasm is eosinophilic, and in the spindle cells it is fibrillar. A Masson stain shows a mahogany stain of the cytoplasm of these cells. A definite nuclear membrane is seen sometimes augmented by the condensation of chromatin at the periphery. The nuclei contain a considerable amount of coarsely granular chromatin material and an occasional basophilic or eosinophilic nucleolus. Many hyperchromatic cells are found. Many giant nucleated cells are present containing hyperchromatic nuclei with intra-nuclear vacuoles and eosinophilic staining inclusion bodies. Multinucleated giant cells are also present. Both giant cell types have ample eosinophilic cytoplasm. In areas there is a suggestion of cross striations. The tumor is well vascularized and shows vascular invasion. There are no areas of necrosis. The tumor is non-encapsulated and appears to compress the renal parenchyma.

The tumor is obviously a malignant tumor of mesenchymal origin. Among the possibilities are liposarcoma and myosarcoma. We have already discussed liposarcoma which has a very different histologic picture than that which is seen in this slide. I believe that the tumor is a myosarcoma differentiating into rhabdomyosarcoma. I have hesitated to make a definite and unequivocal diagnosis of rhabdomyosarcoma without finding cross striations, however, histologically the tumor is quite characteristic of immature type of rhabdomyosarcoma.

Altho foci of skeletal muscle are not infrequent in many Wilm's tumors, pure rhabdomyosarcoma of kidney are extremely rare, especially in adults.

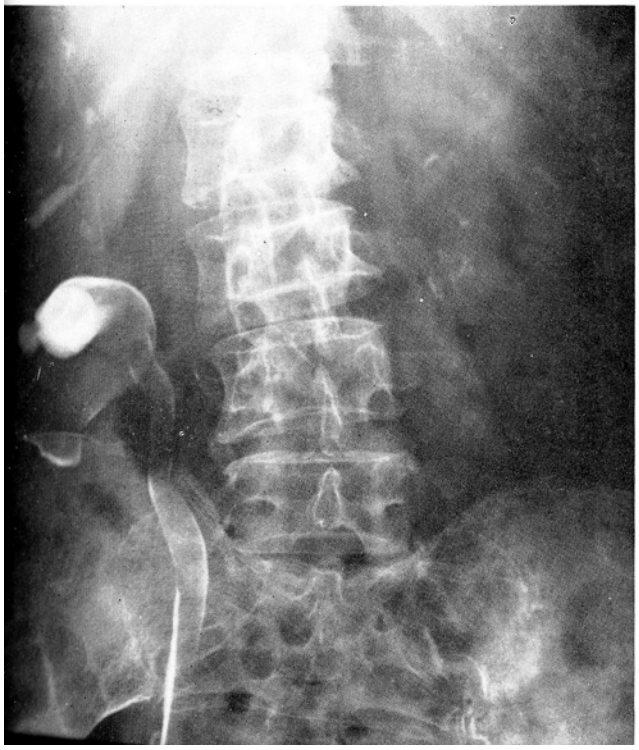
Dr. Mostofi's diagnosis: RHABDOMYOSARCOMA.

Histopathologic Diagnoses Submitted by Mail:

Leiomyosarcoma	38
Rhabdomyosarcoma	37
Liposarcoma	13
Sarcoma, unclassified	20
Nephro-sclerosis	10
Hydronephrosis	15
Others	20

Dr. Regato: Most of our foreign participants received a slide from the wrong block of tissue and saw only fibrosis or chronic pyelonephritis. Dr. M. B. Dockerty of Rochester, Dr. T. W. Richey of Denver, Dr. J. D. Bauer of St. Louis and Dr. Raffaele Lattes of New York also submitted a diagnosis of rhabdomyosarcoma. Dr. A. O. Severance of San Antonio and Dr. Charles Oberling of Paris preferred leiomyocarcoma.

Fig. 2—Double contrast pyelogram showing increased capacity of the kidney pelvis and lower pole calyces.



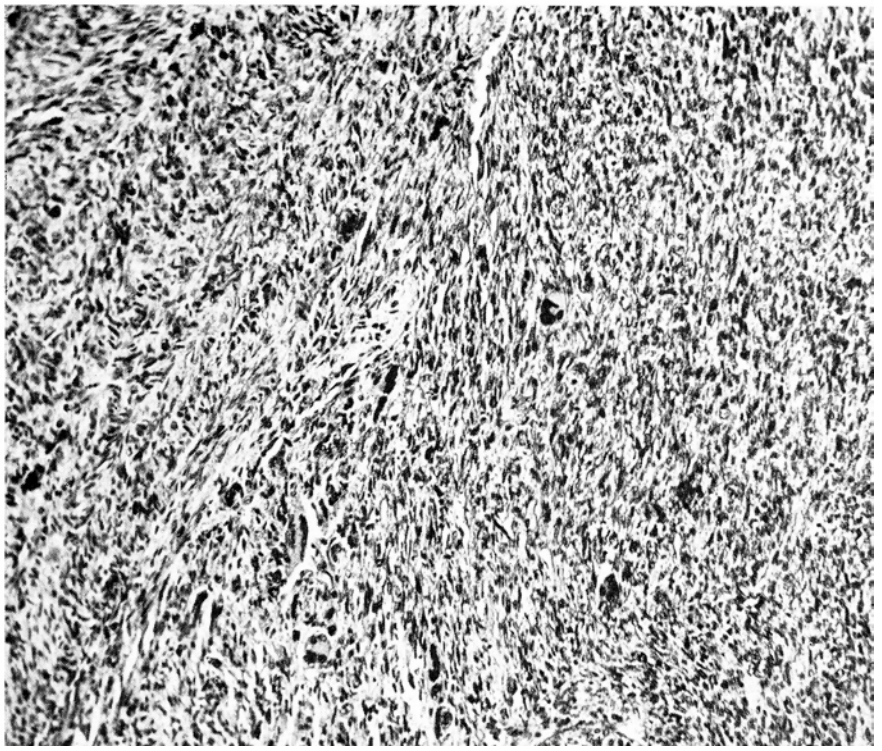


Fig. 3 — Low power photomicrograph: rhabdomyosarcoma of the kidney showing large multinucleated cells scattered among spindle-shaped cells.

Subsequent history: On July, 1956, the patient was reported doing well.

Dr. Hudson: It is our impression that if the tumor of this sort begins within the kidney there is the advantage gained from the natural boundary given by the renal capsule and consequently the whole outlook is much brighter than a similar or identical kind of tumor which begins in the retroperitoneum. Our cure rate with retroperitoneal tumors of this sort is, we believe, much lower than it is with the ones which begin within the kidney. One is still at a loss to explain the extremely low hemoglobin in this patient. The size of the mass doesn't seem to be enough to account for 4.4 grams per cent of hemoglobin. I don't believe as yet there is adequate explanation for it.

Dr. Mostofi: I am sorry that I have not had too much experience with retroperitoneal rhabdomyosarcomas. In the kidney they are so rare that it is very difficult to say what they are going to do or what they are not going to do. The literature points to a very bad prognosis. But then are these the tumors that arose in the kidney and extended out, or are they the ones that are coming in from outside? I don't believe I can answer that.

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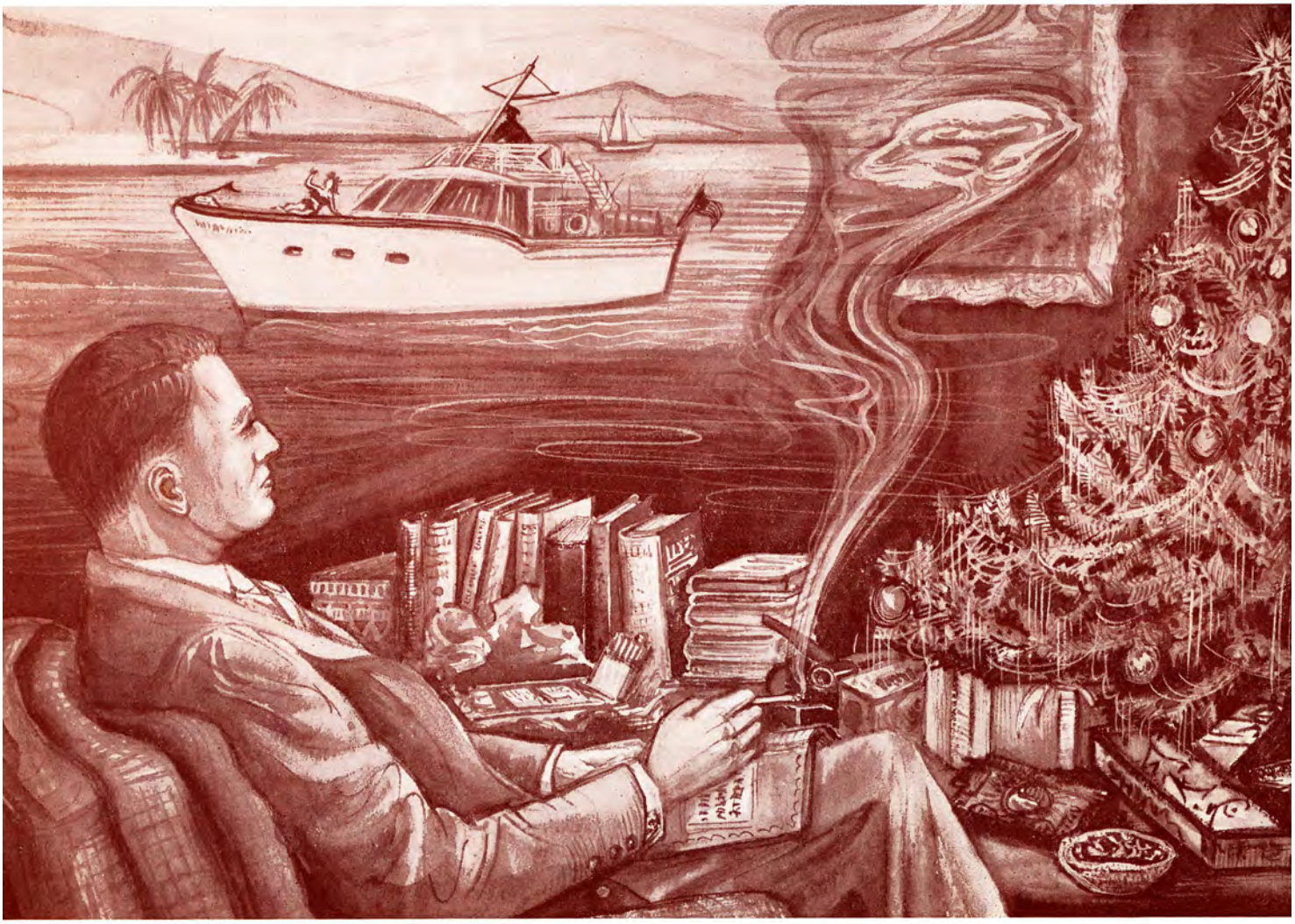


Editor's Note: *SUCCESS may be getting what you want, but HAPPINESS depends on your wanting what you get.*

10. Necrotizing Renal Papillitis and Diabetic Intercapillary Glomerulosclerosis

Contributed by AARON MARGULIS, M. D.
and MURRAY W. FRIEDMAN, M. D., Santa Fe, New Mexico

THE PATIENT was a 51-year-old lady in February 1950 when she gave a history of hematuria ten years previously and complained of right dorso-lumbar pain spreading around the flank to the groin and slight fever; she was a known diabetic. On examination an ill defined mass, very tender to palpation, was felt in the upper right abdominal quadrant. On cystoscopy bloody urine was seen coming from the right ureter; the urine contained traces of sugar, albumin and red cells.

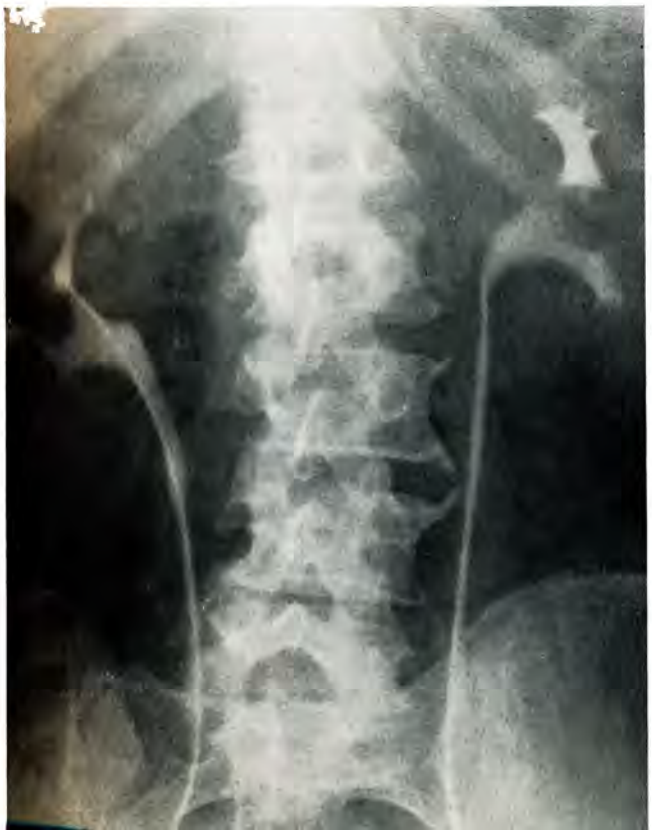
Dr. Hodges: The radiologic abnormality in this case is not difficult to find. It is seen in the lower pole of the right kidney where a major calyx ends abruptly. On close examination of the film it is easy to see an irregularity of the margins of the calyx indicative of invasion. The outline of the lower pole of the kidney indicates that there is considerable tissue below the last point of patency in the calyx. The patient's age is 51. This is certainly compatible with primary neoplasm, but we were given the information that the patient has diabetes and certainly cortical abscesses are sufficiently commonly encountered in such people to tip the scales in that direction.

Dr. Hodges' impression: CORTICAL RENAL ABSCESSES, right.

Radiologic Impressions Submitted by Mail:

Renal cysts	37
Necrotizing papillitis	30
Malignant tumor	27
Cortical abscesses	23
I give up!	1
Others	32

Fig. 1 — Retrograde pyelogram showing filling defect of the lower pole of the right kidney.



Dr. Regato: A considerable number of the experts overlooked the history of diabetes and submitted an impression of polycystic kidneys. Dr. J. T. Case of Santa Barbara, Dr. Ben Felson of Cincinnati, Dr. J. Ceballos of Galveston, and Dr. D. L. Vickery of Pueblo all submitted an impression of acute necrotizing papillitis.

Operative findings: On March 1950, a right nephrectomy was carried out. The kidney measured 16 x 16 x4 cm and weighed 480 grams; it was surrounded by a thick pad of hemorrhagic fat. On section the upper pole pyramids showed diffuse necrosis which involved the papilla; there was also an area of central necrosis in the lower pyramids. The calcyes were narrow and elongated with bulbous enlargement around the papillae. The ureter was narrowed but not obstructed. Postoperatively the patient was found to have E. coli bacilluria.

Dr. Mostofi: The kidney is the seat of typical advanced diabetic change with necrotizing papillitis, pyelonephritis, arteriosclerosis and intercapillary glomerulosclerosis. Extensive ischemic necrosis of the renal papillae is seen with rather marked acute inflammatory cell infiltration at the periphery and extending for some distance into the renal parenchyma. Marked tubular atrophy and necrosis is present with acute inflammatory cell infiltration of the tubules and the interstices. The glomeruli show extensive changes: periglomerular fibrosis, thickening of glomerular basement membrane, thickening and hyalinization of the glomerular capillary walls, circumferentially laminated acidophilic hya-

line thickening of the glomerular capillaries with peripheral distribution of nuclei around these hyaline masses.

Glomerulosclerosis is considered by some as diagnostic of diabetes, by others as not. In my experience most if not all cases of glomerulosclerosis are diabetic. Papillary necrosis per se is not diagnostic of diabetes, only about 60% of patients with papillary necrosis are diabetic. The lesion may also be seen in severe pyelonephritis, in certain blood dyscrasias, in some of the infections and in hypertensive renal disease.

The gross appearance of this lesion is quite pathognomonic, the extent and degree of involvement depending on the severity of the disease. The tips may be affected or the process may extend to involve most of the papillae and even the pyramids. In the early stages and less severe cases, the papillae may be covered with a grayish-white, hemorrhagic or shaggy membrane. In the more severe cases the papillae are yellowish-gray, necrotic and friable and demarcated from the rest of the kidney by a zone of hyperemia. The necrotic portion may be desquamated leaving a volcano-crater-like deformity of the papilla. The lesion is usually bilateral especially in the diabetic patient but it may be unilateral. In the severe cases it is usually fatal, death being due to uremia or severe sepsis.

Dr. Mostofi's diagnosis: NECROTIZING PAPILLITIS, PYELONEPHRITIS, ARTERIOSCLEROSIS and INTERCAPILLARY GLOMERULOSCLEROSIS.

Histopathologic Diagnoses Submitted by Mail:

Necrotizing papillitis	90
Diabetic kidney	11
Kimmelstiel-Wilson	41
Leukemia	8
Others	9

Dr. Regato: With minor variations, most experts found acute necrotizing papillitis and glomerulosclerosis.

Fig. 2 — Low power photomicrograph showing papillary necrosis and pyelonephritis. The insert shows intercapillary glomerulosclerosis.

M. M. Friedman, M. D., Santa Fe, New Mexico: We lost track of this patient following her discharge from the hospital. However, a week ago a letter of inquiry addressed to her residence was returned by the post office department marked "Deceased, No Forwarding Address!"

Dr. Hudson: I don't think this is a surgical disease generally speaking, but I would not take exception to the operation which was performed. There are two considerations which may have a bearing on the diagnosis: One is the possibility of blood clot in the collecting system of the kidney, that is in the minor or major calyces, the pelvis or even in the ureter; these can appear as filling defects in the roentgengrams and unless they are repeated (the clots will usually be lysed by urine within 24 or 48 hours) they may be considered something they are not. The other consideration is that of studies of the urinary sediment. So far there has been no comment by the pathologist concerning the value or lack of value of Papanicolaou stains, or solid blocks as we make, of urinary sediment in a search for cancer cells. Our experience has been that in papillary transitional-cell carcinoma it is a most worthwhile maneuver and will yield 80 to 90% positive tests. With solid tumors of the kidney we found it virtually worthless.

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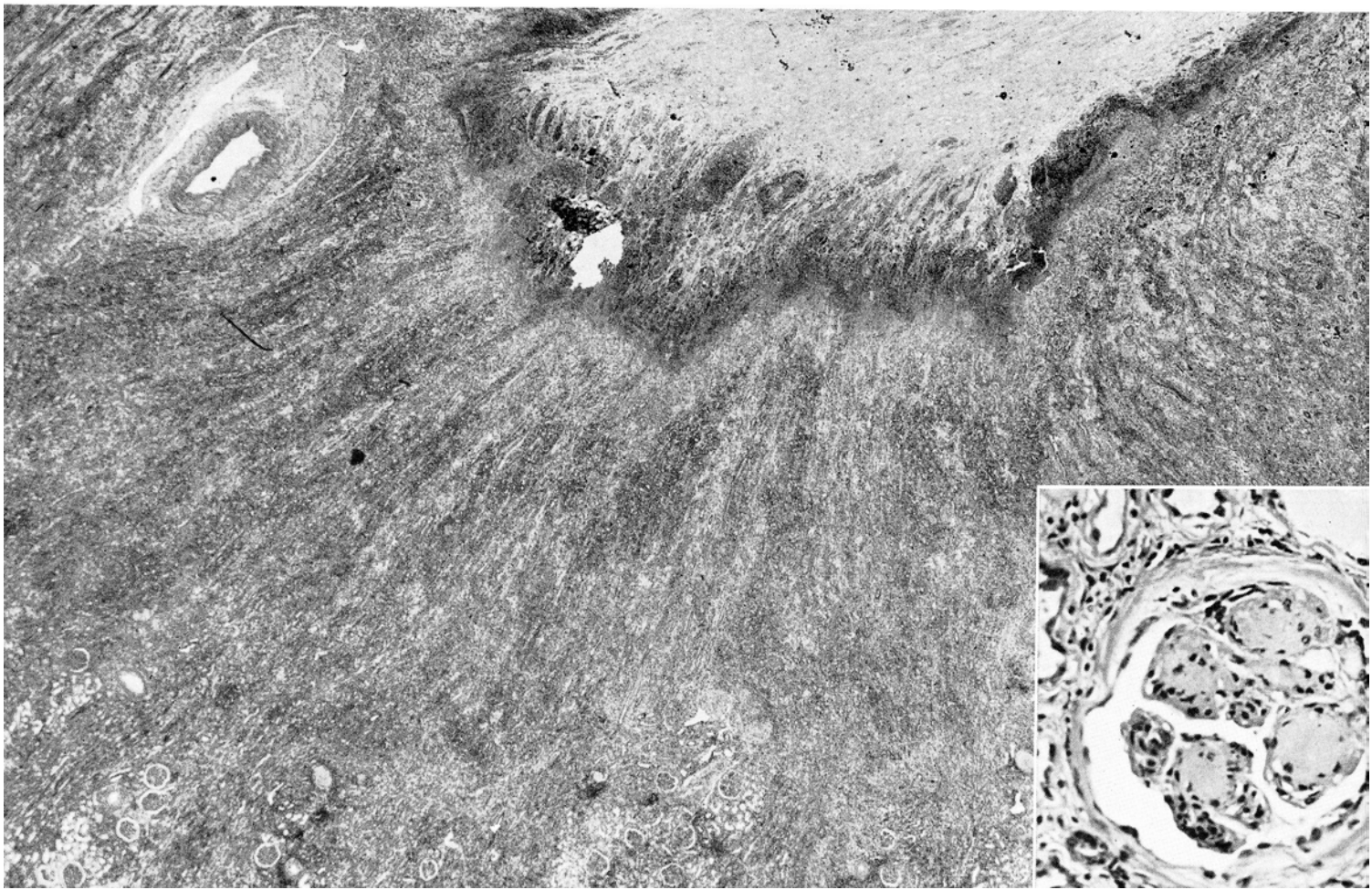


11. *Renal Infarct with Cyst Formation*

Contributed by JORGE CEBALLOS, M. D., ROBERT N. COOLEY, M. D. and JOHN H. CHILDERS, M. D., Galveston, Texas

THE PATIENT was a 74-year-old man in September 1954, when he gave a history of repeated attacks of chills, fever and dysuria in the previous twelve months; complained of severe lumbar pains and hematuria. On physical examination the prostate was found enlarged; the urine presented abundant leukocytes and albumin.

Dr. Hodges: In this particular instance it would have been very nice to have had a preliminary film, in order to determine whether the opaque material which has accumulated in this abnormal pocket in the superior pole is hiding a pre-existing calculus or calcium bearing structure. The remainder of the pyelogram was within normal limits. The outline of the kidney is very faintly shown. This pocket goes out into the solid portion of the kidney and certainly appears to communicate with the major calyces. In my opinion this represents hydrocalycosis with abscess formation. We have no way of guessing the nature of the exciting agent.

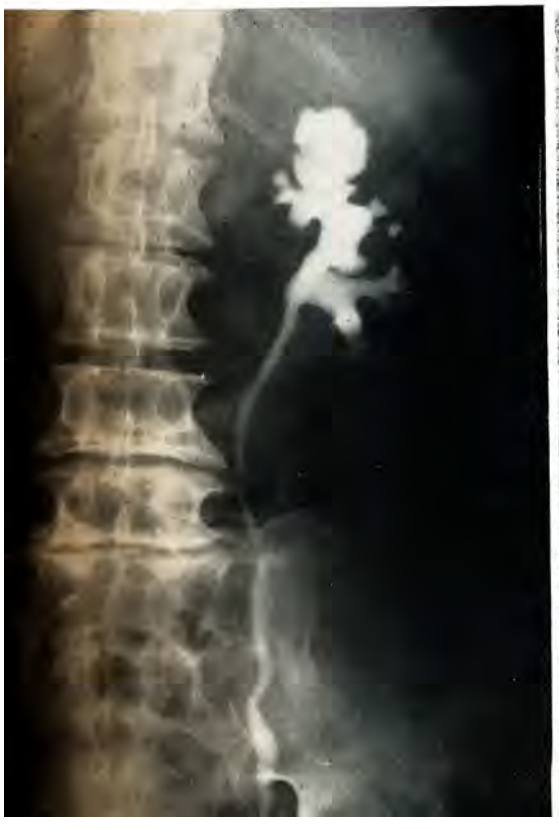
Dr. Hodges' impression: HYDROCALYCOSIS with ABSCESS FORMATION, left kidney.

Radiologic Impressions Submitted by Mail:

Cortical abscesses	54
Tuberculosis	36
Cyst	23
Diverticulum	12
Malignant tumor	9
I pass!	1
Others	15

Fig. 1 (below) — Retrograde pyelogram showing opaque material accumulated in pocket in upper pole of the left kidney.

Fig. 2 (at right)—Low power photomicrograph showing a healing infarct of the kidney. The margin of hemorrhagic area is seen in the lower portion, surrounded by an area of granulation tissue, which in turn is bordered by scar tissue containing remnants of atrophic tubules.



Dr. Regato: Dr. H. R. Senturia of St. Louis also favored a hydrocalycosis. Dr. F. A. Rose of Cleveland, Dr. Ben Felson of Cincinnati and Dr. M. J. Geyman of Santa Barbara all thought of a cortical abscess which had ruptured into an upper pole calyx. Dr. S. Thomas of Palo Alto, California suggested calyceal cyst.

Philip J. Hodes, M. D., Philadelphia, Pennsylvania (by mail): This looks like an abscess of the upper pole that has drained spontaneously.

Operative findings: On September 1954 a left nephrectomy was done. The kidney measured 12 x 6.5 x 4.5 cm. The upper pole contained an encapsulated area 3 cm in diameter containing pus and presenting evidence of hemorrhagic fibrosis and calcification.

Dr. Mostofi: The section shows a severely damaged kidney. There is a large cyst lined mostly by a single layer of epithelium. The cyst appears to extend from the capsule deep into the renal parenchyma. Whether it is a true cyst or pseudocyst cannot be determined but it may explain the deformity of the renal outline. The kidney itself shows a picture which I have interpreted as a healing infarct. At the peripheral cortical areas there is extensive fibrous scarring and hyalinization of the renal parenchyma. Next is a zone of organizing reparative tissue with newly formed fibrous connective tissue which shows edema and moderate amounts of inflammatory cell infiltration and hemosiderin deposition. Next there is granulation tissue and finally a small area of recent hemorrhage and necrosis. Few if any functioning glomeruli are seen. The arteries and veins both show moderate to marked thickening and hyalinization of their walls. It is possible that the cyst represents a secondary cystic formation in an infarct.

Arterial infarction of the kidney is most frequently the result of arterial occlusion, it is usually bilateral and usually multiple. Early in infarction, because of the swelling of the region, the area is raised above the rest of the contour of the kidney and it is red; later, however, because of scarring it is depressed and gray.

In some of the sections I understand there was severe pyelonephritis.

Dr. Mostofi's diagnosis: 1) Healing INFARCT of the kidney, 2) CYST of the kidney, possibly secondary to infarct.

Histopathologic Diagnoses Submitted by Mail:

Pyelonephritis	37
Infarction	36
Nephrosclerosis	26
Hydronephrosis	24
Thrombosis	19
Others	17

Dr. Regato: Dr. U. Gastaminza of San Sebastian, Spain, and Dr. E. Contreras of Mexico City submitted a diagnosis of recent hemorrhagic infarct in focus of arteriosclerosis. Dr. D. F. Babb, of Ponce, Puerto Rico, and Dr. Mark Wheelock of Chicago submitted a diagnosis of chronic hydronephrosis. Dr. J. Engelbreth-Holm of Copenhagen submitted endarteritis obliterans.

J. H. Childers, M. D., Galveston, Texas: There is one bit of information which might be added to your protocol: The patient had undergone a herniorrhaphy in July, 1954. Following the nephrectomy in September 1954, the patient did very well. About two weeks later he had a transurethral resection of his prostate to relieve a partial obstruction. Three days following this procedure he developed a sudden severe epigastric pain followed by acute pulmonary edema, tachycardia, and death. At autopsy there was occlusion of the anterior descending branch of the left coronary vessel. There was no neoplastic involvement of any of the examined tissues in his body.

Dr. Hudson: While this isn't a case of malignant disease it is an interesting entity which occasionally can be diagnosed preoperatively. I would like to remind you of three cases which were published by Captain Malcolm in the Navy and J. A. C. Colston at Johns Hopkins. We observed all three of these patients in whom there were two or three common denominators. First each of the patients had had some history of pain which could be described as an embolic phenomenon. Secondly there had been a preciptous rise in the blood pressure in each patient, in some instances to more than 200 systolic in patients who had had previously normal blood pressure levels. The third factor was the one which I believe most of us would be inclined to overlook; serial roentgenograms had shown a progressive shrinkage in the size of the kidney in each of these patients. In all of them the kidney was removed with the resultant return to normal blood pressure. These are the only three patients in whom I have ever seen the removal of a single kidney produce the return to normal blood pressure. I think this disease or disorder can be detected preoperatively if one has the diagnosis in mind.

F. P. Bornstein, M. D., El Paso, Texas: I just wonder how many pathologists got a slide like mine that showed a rather large artery containing an organizing thrombus; this made the diagnosis quite obvious. (Eight, by a show of hands.)

D. de Santo, M. D., San Diego, California: I have seen two acute infarctions that have involved the entire kidney. One of them was in a 30-year-old man who had symptoms of acute hypertension, like the onset of a malignant nephrosclerosis which was never diagnosed preoperatively, and who died with a picture more or less of extrarenal azotemia; at autopsy he had the aneurysm and the entire kidney was infarcted. The other was an old man who was operated on for acute appendicitis and then died; he had the infarct in the arteriosclerotic kidney.

M. Berthrong, M. D., Colorado Springs, Colorado: Cases of vascular accident of the kidney with development of hypertension have also been extensively studied in the department of internal medicine of Columbia University, and it has been the universal experience that such vascular accidents in a kidney in many may produce a hypertension which usually follows the course of a malignant variety, a very rapidly progressive variety of hypertension. It is in those patients that the unilateral removal of the kidney may result in a very excellent treatment. It was our thought in studying the cases at Hopkins that it probably was not the dead tissue that caused the difficulty; in those patients in whom we were able to demonstrate literally total necrosis of the cortex, there was no clinical correlation with hypertension. But the patients in whom the infarct was surrounded by relatively large zones of ischemic tissue, at least illustrated by the progressive tubular atrophy in these areas, did develop persistent hypertension. There have been a number of reports concerning the sporadic occurrence of hypertension, which cleared up after a few days or a week, particularly in patients with mitral stenosis and who had what appeared to be embolus to the kidney, infarction presumably and transient ischemia with subsequent fall of the hypertension.

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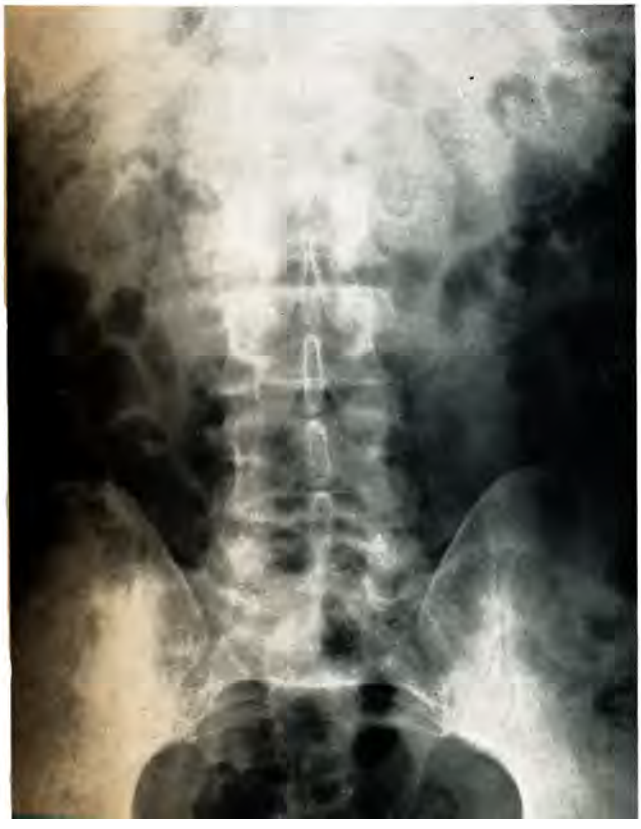
12. Reticulum-cell Sarcoma of the Testis

Contributed by Sam W. Downing, M. D.,
Alexis E. Lubchenco, M. D.
and Kenneth D. A. Allen, M. D., Denver, Colorado

THE PATIENT was a 45-year-old man in January 1955 when he noticed the painless enlargement of his left testis. On examination the left testis was found uniformly enlarged but not hardened. The Friedman's test was negative.

Dr. Hodges: This single roentgenogram was taken under circumstances which were somewhat short of ideal. The amount of gas which is scattered throughout the intestinal tract, plus other materials that are mixed with the gas, make it difficult to identify the kidney outline or other urologic structures that might be of help. We can see psoas muscle shadows on either side and we can find the outline of a shadow which cannot be fitted into the contents of colon. One may suppose that this represents a soft tissue mass, perhaps a lymph node invaded by neoplasm. In view of the patient's story of testicular enlargement, we can presume there was a primary testicular tumor capable of metastasis and by a flight of fancy call it seminoma metastasizing to retroperitoneal lymph nodes. Obviously, with so little radiologic evidence, I am on very thin ice.

Fig. 1 — Roentgenogram of the abdomen showing no definite abnormalities.



Dr. Hodges' impression: METASTATIC SEMINOMA?

Radiologic Impressions Submitted by Mail:

Testicular tumor	42
Para-aortic metastases	21
Tuberculosis	18
Bone metastases	15
Can't get it!	1
Others	33

Dr. Regato: Dr. Lois C. Collins of Houston, and Dr. A. Greenberg of Colorado Springs also had the impression that this film showed evidence of retroperitoneal metastases.

Operative findings: On February 1955 the spermatic cord was transected at the internal ring and a left orchectomy was done. One week later a retroperitoneal node dissection was carried out. Iliac, para-aortic and renal nodes were found involved.

Dr. Mostofi: The section shows an epididymis with an adjacent cellular mass which may represent the testis but no seminiferous tubules can be identified. The cellular mass consists mainly of two types of cells: Those that can be definitely identified as lymphocytes — both mature and young. The second cell is more difficult to identify. The cells occur individually or in aggregates. They are large, their shape varies from round to polygonal and angulated. The nuclei are round or oval, vesicular. They have a delicate irregularly distributed chromatin network and a fine nuclear membrane. There is usually a single basophilic or eosinophilic nucleolus. Some of the nuclei show fine or coarse vacuolation. Hyperchromatic nuclei are not infrequent. The nuclei are surrounded by variable amounts of eosinophilic cytoplasm. These cells I have interpreted as reticulum cells. A few giant cells are seen and there is occasional mitosis. A rich meshwork of reticulum is found in close relationship to the cells. The lesion is quite vascular with vascular slits frequently lined by cells. The stroma is scant but there is edema and fibrosis.

In the differential diagnosis here, first, we must decide whether this is a tumor or not and if a tumor the type of tumor. The gross appearance of the specimen leaves little doubt that this is a tumor. Microscopically, although there are many mature lymphocytes, definite neoplastic cells are also present. The second point to consider is the type of neoplasm, the differential being between a primary testicular seminoma and a malignant lymphoma. In both there may be, and usually is, a lymphocytic component consisting mostly of mature lymphocytes.

Cytologically, the tumor cells in this case are different from those seen in seminoma. In seminoma the cells are usually uniform, they are polyhedral or round, the cell

borders are definitely visible, the cytoplasm is clear, the nuclei are round and usually have one nucleolus. The cells occur packed in groups and separated into lobules by a delicate reticulum containing varying numbers of mature lymphocytes and a few if any reticulum cells. Thus, both cytologically and histologically the tumor that we see in this slide is not seminoma but a tumor in which the malignant component consists of reticulum cells.

Where any doubt exists as to the diagnosis, examination of a lymph node is advised. This is usually positive and leaves no doubt as to the diagnosis of lymphoma.

My diagnosis in this case is a malignant lymphoma, reticulum cell type. We have had the opportunity to study some 25 of these tumors which I have designated as malignant lymphoma initially manifested as testicular tumor. The five-year follow-up is not as yet complete in the Armed Forces Institute of Pathology series but several of the patients have already returned with the picture of unmistakable malignant lymphoma.

Dr. Mostofi's diagnosis: RETICULUM-CELL SARCOMA of the testis.

Histopathologic Diagnoses Submitted by Mail:

Lymphosarcoma	86
Hodgkin's	14
Carcinoma	10
Seminoma	10
Dysgerminoma	2
Others	26

Dr. Regato: Dr. A. P. Stout of New York also submitted a diagnosis of reticulum cell sarcoma. Dr. R. A. Willis of Leeds offered a diagnosis of inflammatory granuloma; Dr. Fridtjof Bang of Copenhagen suggested fibroxanthoma; Dr. H. K. Giffen of Omaha submitted androblastoma; Dr. Marshall Neely of Lincoln preferred dysgerminoma. Dr. Raffaele Lattes of New York questioned the possibility of an undifferentiated carcinoma; Dr. Boris Scolnik of Montevideo made a diagnosis of seminoma; Dr. C. Oberling of Paris considered atypical seminoma; Dr. Mark Wheelock of Chicago and Dr. F. J. Dixon of Pittsburgh submitted Hodgkin's.

Subsequent history: Following operation in March-April 1955, roentgentherapy was applied to the scrotum, lumbar and thoracic spine areas. A "tumor dose" of 1300 roentgens was said to have been administered in 43 days. On August 1955 the patient remained well and working as a salesman.

S. W. Downing, M. D., Denver, Colorado: This young man is apparently well at the present time; he is a traveling salesman. His last physical examination and roentgenogram of the chest revealed no abnormality. Because this tumor is a lymphosarcoma we are led to believe that it isn't apt to be primary in the testicle. If it is metastatic of course there is nothing to be done about it, from the standpoint of surgery. At operation it was most interesting because unlike other tumors I have seen arising in the testicle, the nodes were innumerable and very small, about the size of half a grain of wheat, spread up to the renal pedicle along spermatic veins. Obviously, retroperitoneal gland dissection would be of no real value to the patient. The node which Dr. Hodges saw on the flat roentgenogram, which was taken under less than ideal circumstances, was not there.

H. T. Low, M. D., Pueblo, Colorado: I would like to know how frequent is this particular type of tumor found in the testicle?

Dr. Mostofi: In some 1800 to 2000 testicular tumors in the files of the AFIP we have about thirty of these cases. These are patients in whom the tumors manifested initially in the testes. Involvement of the testes in any of these malignant lymphomas is not as infrequent as that.

J. B. Frerichs, M. D., San Francisco, California: There were just enough diagnoses of teratoid tumor of one kind or another, seminoma, etc., to make me wonder how much these slides varied. My own showed a histiocytic sarcoma and I wondered particularly what the nodes showed microscopically.

S. W. Downing, M. D., Denver, Colorado: The nodes were all positive and they showed the same type of tumor you saw on the slide that was projected.

Dr. Hudson: I don't think that a radical operation is indicated for this kind of tumor. The adequate excision in this instance consisted of removing the testis, which was done. I was trying to learn from Dr. Mostofi's comment on these bilateral lesions whether or not he is going to urge us to do bilateral orchiectomy in these cases; if we regard it as a generalized disease we should pass the case to the radiotherapeutist.

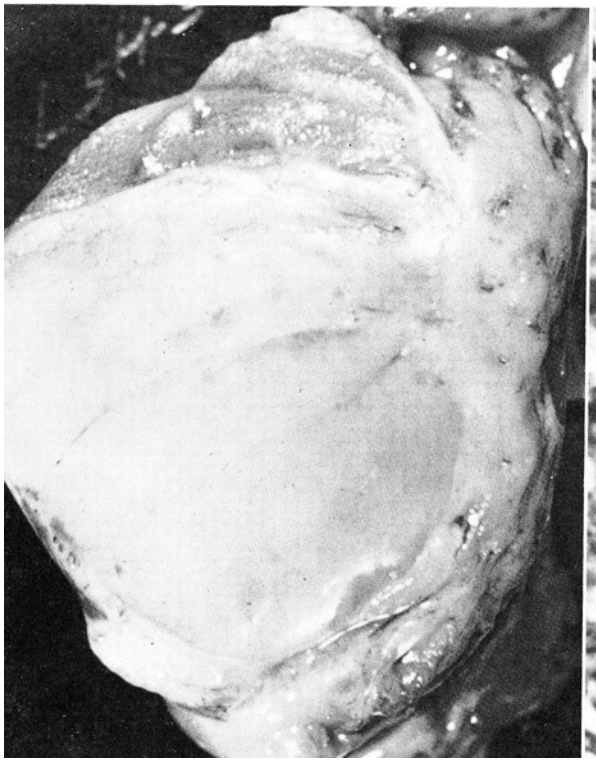


Fig. 2—Gross specimen of testicular tumor.

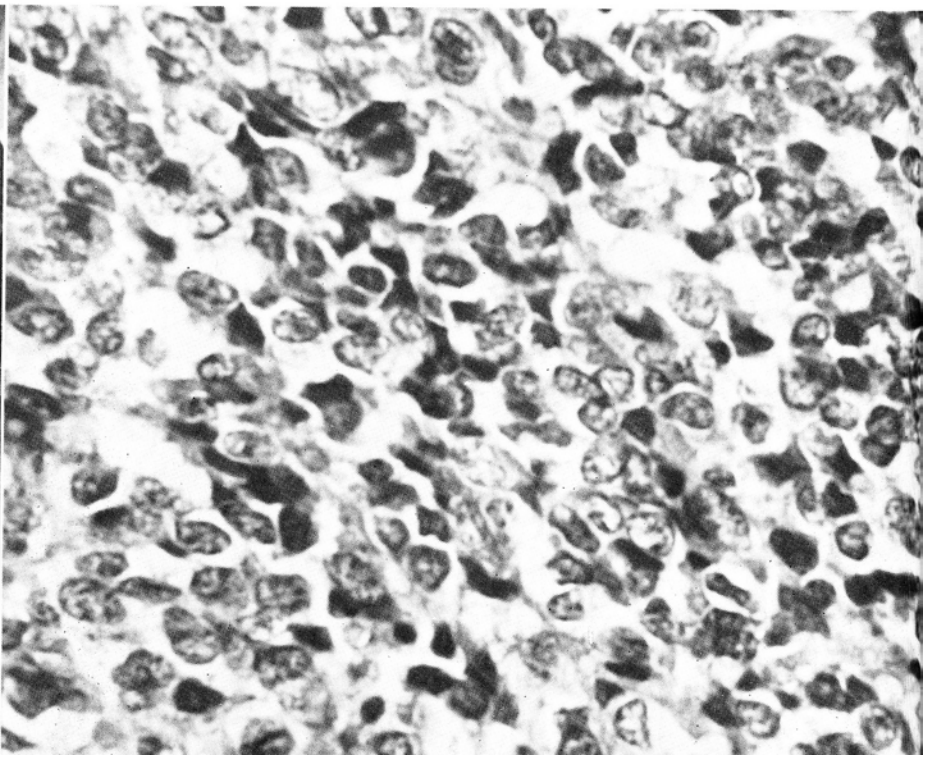


Fig. 3 — High power photomicrograph: malignant lymphoma (reticulum cell sarcoma) initially manifested as testicular tumor; many large reticulum cells are seen.

Dr. Mostofi: I have designated these tumors as malignant lymphoma initially manifested as testicular tumor. While it is quite possible that some of these tumors may be limited to the testes and orchiectomy may cure the patient, I think in the majority of the cases it is a systemic disease. Our experience has shown that many times they become bilateral and generalized.

Dr. Regato: I could not disagree any more strongly with our distinguished colleague, Dr. Mostofi. We cannot assume that this is of necessity a systemic disease, but we cannot blame the pathologist, for either he would not see the patients at all or by the time the patients get to him they have indeed a systemic disease. There is all the necessary evidence to prove that lymphosarcoma is a curable disease if treated before distant spread takes place; it is paramount to the interest of the patient that we should not forget this. Lymphosarcomas arising in the testis are rare and we cannot talk with authority as to the manner of their treatment except by generalization of what we know about other primary tumors of the testis and of lymphosarcomas arising in other organs. Dr. Hudson, would you tell us what is your experience with Hodgkin's disease of the testis?

Dr. Hudson: None, excepting in cases in which the diagnoses was not generally agreed by pathologists. I have never treated the disease.

Dr. Regato: In what pertains to the treatment of testicular tumors our feeling is that an orchectomy is an excellent means of establishing diagnosis and to treat the primary lesions. We are in disagreement with those who would do a needle biopsy or an incisional biopsy and proceed to irradiate what is left of the testicle; we feel that nothing is gained by these procedures. On the other hand, we feel certain that the evidence at hand does not justify the application of the so-called radical retroperitoneal dissection of nodes. In this case, in view of the histopathology this was still less justified. Dr. Kenneth Allen received the patient after surgery and gave him a thorough irradiation; this could have been done with equal effectiveness without benefit of surgery. Dr. Hudson, would you care to comment on the usefulness of retroperitoneal node dissections in testicular tumors?

Dr. Hudson: We gave up a program which has turned out to be a trial of tragedies, a program of doing radical dissections, of the retroperitoneum for reticulum cell sarcoma, preliminary to irradiation by a very affable radiotherapeutist; we abandoned it together.

The greatest body of material available to anyone is that group of cases managed mainly at the United States Army Walter Reed Hospital during the second world war and which has been very diligently followed. It has been interesting to me to learn in the last year from the published material that two different groups studying the same material have come to diametrically opposed views about pure seminoma, as far as retroperitoneal dissection of lymph nodes is concerned. One group concluded that radiotherapy alone is sufficient, the other has concluded that radical lymph node dissection ought to be done in all cases. Knowing some of the personalities involved in the two publications, I will not refer to their names but the papers are available for everyone to read. How these two completely opposite opinions can be given on the same material is a mystery to me. The argument in favor of routine retroperitoneal node dissection (which I do not believe indicated for pure seminoma) is that the metastasis from that seminoma can be carcinomatous. Dr. Mostofi can clear this matter up for us too and perhaps we can come to some rational decision, because the entire concept of doing a radical lymph node dissection without producing any higher cure rate, which I believe is the actual fact, does not appeal to me. The lymph node dissection for carcinoma is quite another matter, in that the lesion is frequently not radiosensitive in the same sense that seminoma is.

Dr. Mostofi: If one could be certain that the tumor that one sees in three or four sections of the testes, is entirely a seminoma, that it is radiosensitive, that it has no other components, that if it metastasizes, it will continue to remain a seminoma and nothing else; then I think we could say that all seminomas should be treated by radiations. Unfortunately, seminomas do not know that they should be radiosensitive all the time, they don't know that they should metastasize as seminomas. Unfortunately also, when massive doses of radiation have been given to the patients, some of them have been much worse off than if they had been left alone.

Dr. Hudson: In the past, before I began to work in a cancer hospital, I used to take this kind of pot shot at the radiotherapeutist, too. But I don't believe that the Walter Reed series of cases, which is what we are actually discussing, is in any wise a fair example of what may or may not happen to a patient who is given modern supervoltage radiotherapy by a sane person. Others who have used this modality have not had the same incidence of perforation of bowel and of other major complications that has come out of that group of cases. There is certainly a sensible upper level of tumor dosage of radiotherapy, by whatever technique it is given, which has to be respected. And although retroperitoneal lymph node dissection hasn't resulted in a high mortality rate, it has not produced a series of cases in which nodes are positive and the cure rate is high.

Dr. Regato: As a therapeutic radiologist, I am very thankful to Dr. Hudson for the fairness of his statements.

An analysis of the series of cases treated at Walter Reed Hospital by Drs. Lewis and Friedman would reveal that nothing was gained by the retroperitoneal dissection when the nodes were found invaded. On the other hand radiotherapy, as administered to these patients, resulted in the unnecessary death of patients who actually had no metastases, through untoward effects of radiations. We feel that the dose administered was unduly high and that the daily rate of administration was also high; in consequence there were necrosis of the bowel, and soft tissue as well as bone sarcomata resulted in a few instances. A high daily dose and a high total dose are not necessary for the sterilization of seminomas which are second only to lymphosarcomas in radiosensitivity. A rapid and an excessive delivery of radiations to any given group of patients may cancel the sought after benefit. We are convinced that post-operative radiotherapy to the potential area of metastatic involvement is justified and useful as a routine procedure, but it should be applied with caution.

Subsequent history: In June, 1956 this patient was reported in good health, weighing 200 pounds.

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13. Andenocarcinoma of the Bladder

Contributed by Eleanor H. Valentine, M. D., Ben Eiseman, M. D. and Oliver G. Stonington, M. D., Denver, Colorado

THE PATIENT was a 60-year-old man in May 1954, when he complained of hematuria and nycturia. The cystoscopic examination revealed a mass on the anterior wall of the bladder surrounding the vesical neck and the left ureteral orifice.

Dr. Hodges: The roentgenogram suggests to me that there is some calcification in the lower urinary tract associated with what appears to be irregular enlargement of the prostate. There appears to be invasion of the lower edge of the bladder on the left side. This might well have been a primary carcinoma of the bladder with extension to the prostate or a primary neoplasm of the prostate with extension to the bladder. There is a remote chance that this may be a case of tuberculosis of the prostate with calcification in the lower urinary tract.

Fig. 1—Cystogram showing irregular filling defect of the floor of the bladder.

Dr. Hodges' impression: 1) NEOPLASM OF THE PROSTATE; 2) Neoplasm of the bladder: 3) Prostatic tuberculosis.

Radiologic Impressions Submitted by Mail:

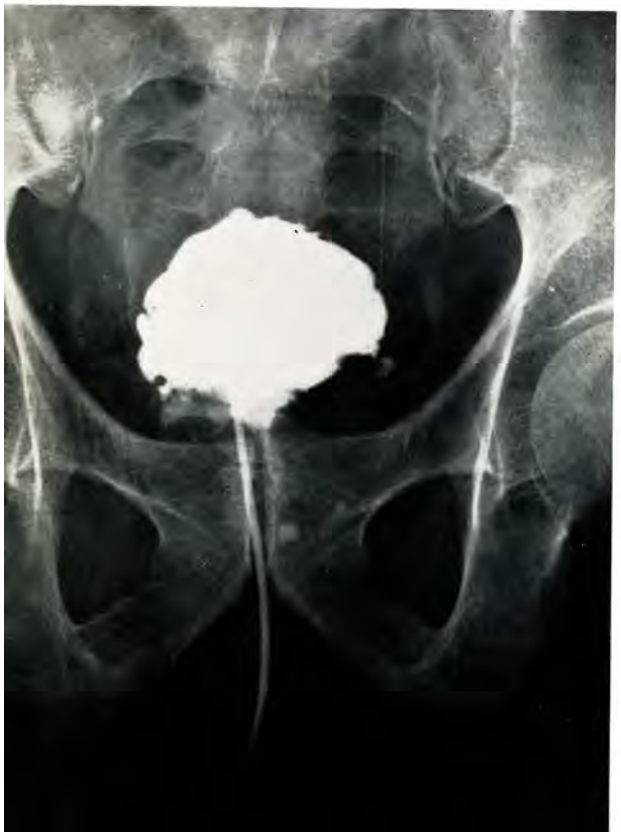
Carcinoma, bladder	85
Carcinoma, prostate	35
Others	9

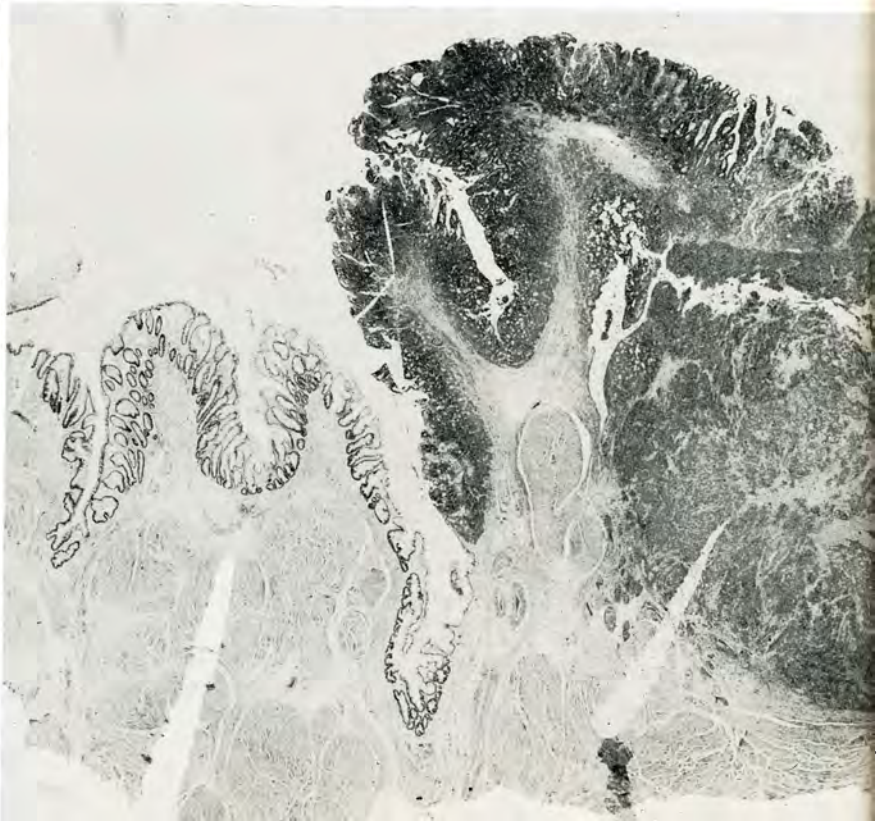
Dr. Regato: Dr. D. C. Gastineau of Indianapolis, Dr. Ira Lockwood of Kansas City and Dr. S. F. Thomas of Palo Alto, all submitted an impression of sarcoma of the prostate and vesical neck. Most other experts were satisfied with a diagnosis of carcinoma of the bladder.

Philip J. Hodes, M. D., Philadelphia, Pennsylvania (by mail): Probable carcinoma with considerable encroachment upon the base of the urinary bladder. It is possible, of course, that this represents a primary carcinoma of the bladder.

Operative findings: On September 1954 the patient decided to submit to surgery. A total cystectomy and retroperitoneal node resection were carried out, with rectoureterostomy and perineal colostomy.

Fig. 2—Low power photomicrograph showing papillary and infiltrating carcinoma of bladder. The transitional epithelium visible at one margin is replaced by glandular epithelium.





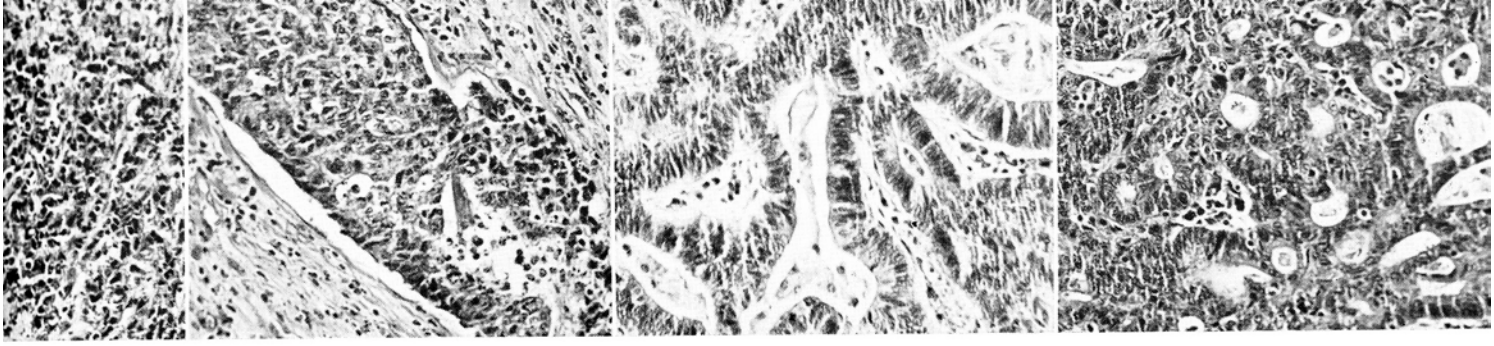


Fig. 3—Photomicrographs of different areas of the same tumor show varied character.

Dr. Mostofi: This is a very interesting papillary and infiltrating epithelial tumor of the urinary bladder. In areas the tumor is glandular with tall columnar pseudostratified or multi-layered epithelium forming small and large sometimes branching glands and acini frequently filled with mucin. The nuclei are large, elongated, rather vesicular. The cytoplasm is scant and shows little if any mucin. The bulk of the tumor, however, shows no glandular pattern but consists of transitional or undifferentiated epithelium. This cell type is cuboidal and polygonal. The nucleus is large, round or oval, and vesicular with a distinct nucleolus and a fine network of chromatin. The cytoplasm is amphoretic. Hyperchromatic nuclei and mitotic figures are frequent. In a few areas especially in the deeper portions, the tumor cells have a pavement-like appearance. Infiltration deep into the muscularis and vascular invasion are quite apparent.

It is of interest to note that along one margin the surface epithelium of the bladder displays change from unmistakable transitional cells to transitional cells containing mucin and to mucous containing columnar epithelium forming tubular glands which are devoid of any anaplasia. Thus you have an epithelial tumor which manifests areas of glandular mucus containing carcinoma, areas of transitional carcinoma, areas of anaplastic carcinoma and areas suggestive of squamous carcinoma. There is also mucous metaplasia of vesicle epithelium with glandular cystitis.

The differential diagnosis here lies, first, between a primary and a secondary adenocarcinoma of the bladder and, second, between a primary vesical and a primary urachal tumor.

If the tumor was a pure mucous adenocarcinoma without these other components (transitional and squamous), a secondary adenocarcinoma of bladder (primary in gastrointestinal tract) could not be ruled out on the basis of the available information and material. But since the tumor has areas of definite transitional and even more or less squamous carcinomas, it is most likely a primary vesical or urachal carcinoma.

To make a definite diagnosis of urachal tumor, we believe that the primary tumor should be in the dome or the anterior wall, it should be intramural and should have deep ramifications in the bladder wall. Also of help in such a diagnosis are the findings of (a) an intact or ulcerated mucosa without any glandular or cystic change or mucous metaplasia; and (b) ramifications and extensions to the space of Retzius, anterior abdominal wall and even the umbilicus. On the basis of available information while such a diagnosis may be strongly suspected, it cannot be definitely made. All we can say with certainty is that it is an infiltrating tumor of the bladder, showing definite mucous adenocarcinoma.

I have had an opportunity to study some 60 to 70 of these adenocarcinomas of the urinary bladder, they comprise about one to two percent of bladder tumors. They fall into two general categories: those that primarily originate in the bladder and those that originate in the urachal remnants and extend to the bladder. The primary mucous adenocarcinoma of bladder have a better prognosis than the urachal adenocarcinomas—the five-year survival rate of primary vesical adenocarcinoma was 33%, the five-year success rate 25% as compared to the five-year survival rate of urachal adenocarcinoma which was 16% and the five-year success rate (freedom from tumor) of 6% respectively. The poor prognosis of urachal tumors was believed to be due to two factors: (a) being located in the silent area of the bladder these tumors tended to remain undetected for a long time. (b) These tumors tended to spread along pre-existing urachal tract remnants and therefore were apt to be incompletely removed.

A word may be said about the histogenesis of these tumors. There are two main theories: (a) that these tumors arise from remnants of enteric mucosa and (b) that they arise from transitional epithelium of the urinary bladder through certain changes in the appearance and cytoplasm contents of these cells. While the possibility of an enteric remnant cannot be ruled out, I believe that there is overwhelming evidence to support the second theory.

Dr. Mostofi's diagnosis: ADENOCARCINOMA.

Histopathologic Diagnoses Submitted by Mail:

Adenocarcinoma	110
Urachal-mucinous carcinoma	21
Transitional-cell carcinoma	12
Carcinoma in ectopic colon	6
Carcinoma of rectum	7
Others	12

Dr. Regato: Dr. Mark Wheelock of Chicago submitted a diagnosis of adenocarcinoma of the rectum invading the bladder. Dr. F. Schajowicz of Buenos Aires and Dr. E. E. Aegerter of Philadelphia and Dr. C. Sirtori of Milan offered adenocarcinoma probably arising on cystitis glandularis. Dr. M. B. Dockerty of Rochester, Minnesota and Dr. A. O. Severance, of San Antonio suggested the possible origin of the adenocarcinoma in the urachus. Dr. R. A. Willis of Leeds offered metaplastic mucoid adenocarcinoma and Dr. Raffaele Lattes of New York and Dr. V. R. Khanolkar of Bombay concluded to adenocarcinoma arising from ectopic rectal mucosa.

Subsequent history: On May 1955 the patient had gained weight, his hydronephrosis had improved; he had good control of urine in his rectum which is now his bladder.

B. Eiseman, M. D., Denver, Colorado: Dr. Stonington and I operated in this case. We started with a retroperitoneal node dissection just below the renal arteries, we stripped the aorta and went out to the left lateral pelvic wall where we found a mass. The frozen sections of the pelvic and retroperitoneal nodes were negative. At one point we thought that the mass was adherent to the iliac artery, but we were able to free it without leaving tumor behind. The total cystectomy together with the node dissection was carried out according to the procedure of Dr. Lowsley: The ureters were implanted in a cuff of the rectosigmoid to be used as an artificial bladder and taking the severed end of the sigmoid and bringing it down, anteriorly to the rectum under the anal sphincter.

O. G. Stonington, M. D., Denver, Colorado: The purpose of this type of procedure is to assure a radical excision of the tumor and possible metastatic nodes and at the same time attempt to obtain separate control of the urinary and fecal streams.

Last week the patient had already gained 20 pounds in weight, was feeling fine and his perineal colostomy was

operating well; his control over it is not yet perfect, but it is improving.

I would like to hear from Dr. Mostofi as to the manner of spread of cancer of the bladder, from Dr. Vermooten and from Dr. Regato in respect to radiotherapy in its different modalities as opposed to total cystectomy and from Dr. Bricker in respect to his method of bladder substitution.

Dr. Mostofi: Carcinoma of bladder might spread locally, it might spread through the lymphatics, or it might spread through the vascular system. I think the lymphatic spread is supposed to be the most common one of the three.

V. Vermooten, M. D., Dallas, Texas: For some time I have devoted my interest to radiation therapy of cancer of the bladder rather than to total cystectomy and diversion of the urinary stream. With the use of radioactive Cobalt we have been able to get very excellent results with the local growth. I have felt that the extensive surgery which is necessary to do a cystectomy and to remove all lymphatic nodes is not worthwhile from the morbidity point of view, and if the patient has already extensive lymphatic spread, I don't think that I can cure by dissecting some of the lymph nodes, consequently, I have let those go and have treated them locally only. I feel that the use of radioactive Cobalt in nylon sutures gives you about the most ideal type of radiation therapy to bladder tumors because you can place your sutures exactly where you want to, you can get an excellent implant. We always remove the excess amount of carcinoma so that there is only a centimeter or half a centimeter of carcinoma left; the radioactive Cobalt is sown into the tumor in very adequate patterns. Up to the present we have had amazingly excellent results from this type of therapy.

E. M. Bricker, M. D., St. Louis, Missouri: I have had no personal experience with the method of substituting for the urinary bladder that has been described this afternoon. I am most interested in the functional as well as the physiological results that can be obtained. Our experience has been chiefly in patients who have required exenteration of all the pelvic viscera. In such cases, of course, there is no rectum to be used and we have solved the problem by using short segments of ileum which acts simply as a conduit for the transference of the urine from both ureters to a convenient place on the abdominal wall for the wearing of a Ruxton bag. In some 100 patients, we have found the incidence of hyperchloremic acidosis to be zero. The incidence of infection and hydronephrosis is rather low.

Dr. Hudson: Almost any method can be used to control bladder tumors which don't infiltrate more than half way through the bladder wall, and almost all methods, even combination of methods, have failed to cure more than 15% roughly of all tumors which infiltrate beyond that point. Our problem is to determine what is the extent of the tumor and then consider what kind of surgery is reasonable to use for the particular case. Our own experience with adenocarcinoma of the bladder has been universally bad. This is a tumor which quite often forms mucin and that can seed in the wound; we have implanted this tumor subcutaneously in incurable volunteers in the most avascular region we could find, and have found that the tumor, even in the few days remaining before death, grew and formed mucin. It is a tumor, therefore, which should never be cut across by the surgeon if it is possible to avoid this. It is one which probably doesn't differ from other kinds of bladder cancer when it involves lymph nodes. As far as I know, from my own work and from that of others in the field of cancer, no one has yet cured a carcinoma of any type of the bladder which involves lymph nodes at or above the iliac level. It is our policy on the finding of carcinoma in any of the lymph nodes well outside the bladder and certainly if they are upon the true pelvic wall near the vessels, to abandon the procedure and to do only palliative operations that might be indicated. We have several patients in whom we have done radical pelvic surgery for cancer of the bladder and in whom the patient has been followed religiously and there has been distant metastases and death from the metastases with negative local findings at autopsy.

I would expect that the slim margin of safety given by leaving the patient's rectum intact, would probably doom this operation to failure, due to the fact that in the male it isn't possible to do the same sort of anterior exenteration that can be done in the female, because the two layers of Denonvilliers' fascia are fused above the seminal vesicles, so that there is a single layer of fascia which is protecting the surgeon or giving him a margin between the line of resection and the tumor. I think that the usefulness of an operation of this sort is highly questionable and the usefulness of the urinary diversion operations will depend upon how good or bad the surgery is for the primary cancer. I think that radical pelvic surgery for cancer of the bladder, adenocarcinoma, transitional cell carcinoma or any other sort is at the moment in the stage of a clinical experiment. We regard it that way in our hospital. It is never performed except after a period of radiotherapy which constitutes our total program for infiltrating bladder cancer.

Dr. Regato: There are those who remove or destroy carcinomas of the bladder through the cystoscope, those who do partial or total cystectomy and those who do a radical cystectomy. On the other hand, there are those who irradiate by means of insterstitial implantation of radon or Cobalt during surgical exposure, those who do intracavitary irradiation by means of radium capsules within an inflatable balloon and finally there are those who have attacked the problem of external pelvic irradiation using high voltage roentgen therapy or Cobalt units. I have been impressed, in analyzing many series of reported results, that regardless of the approach, good results are always obtained in the non-infiltrating tumors, whereas the results with the infiltrating lesions are consistently bad. Thus, an analysis of results is often hampered by the fact that much depends from the composition of the small series usually reported.

Having allowed a fair opportunity to the radical surgical approach and being disappointed in its results, we are now concentrating our efforts on the external irradiation by means of Cobalt 60. We aim at an extensive irradiation of the pelvis exploiting both the highly penetrating radiations of Cobalt 60 and the advantages of fractionation which we carry to twelve weeks of total treatment. We do not have as yet long follow-up results to report, but, as everyone who hopefully considers the early results of his endeavors, we are "pleased" and "gratified."

J. R. Maxfield, M. D., Dallas, Texas: Dr. Vermooten and my brother, Dr. Jack Maxfield, have been working with interstitial in-nylon-Cobalt in carcinomas of the bladder. Three are the important advantages of this type of treatment: The first one is, these patients are out of the hospital and back at work in a reasonable period of time following operation and irradiation. Secondly, the cost to the patient is reduced by the fact that the hospitalization is short and that the rehabilitation is fast; this is an important factor. And thirdly, the cure rate appears high with interstitial Cobalt.

Subsequent history: In May, 1956, the patient expired; he had extensive pelvic recurrence.

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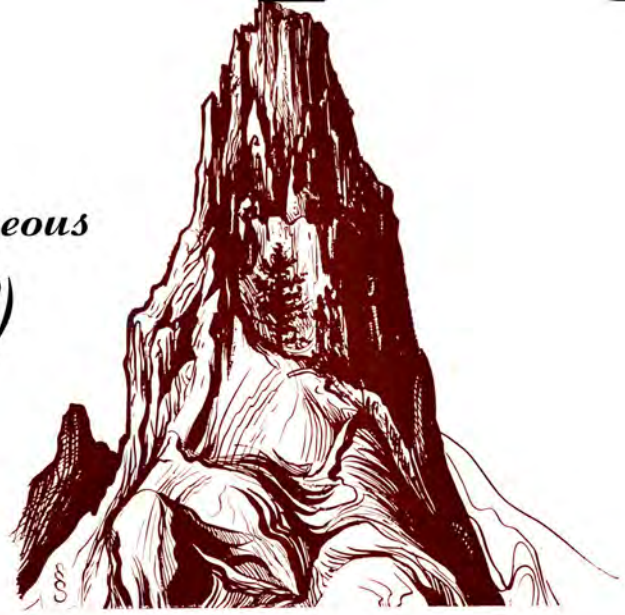
14. *Chronic Ureteritis with Osseous Metaplasia (Amyloidosis?)*



Contributed by WENDELL P. STAMPFLI, M. D.
and WILLIAM D. MILLETT, M. D., Denver, Colorado

THE PATIENT was a 76-year-old lady in September 1954 when she gave a history of sudden fever and pain in the right lumbar region; a similar attack had taken place three months previously.

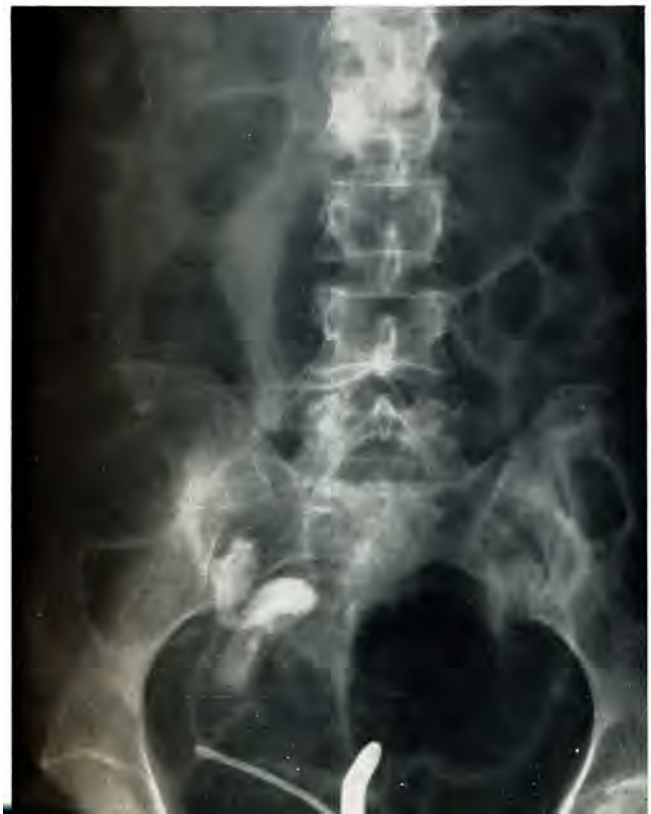
Dr. Hodges: This roentgenogram stimulates in one a great desire to use stereoscopy and oblique filming in order to learn a good deal more about what is going on in the extreme lower end of the ureter. The catheter is perhaps some little distance into the ureter, and then we see what appears like a very indistinct shadow running almost at right angles to the end of the catheter tip. The opaque material shows a dilated and tortuous ureter which can be followed some distance. One wonders whether or not it would be possible to get the air into this ureter, or perhaps use some of the other methods that are available to learn a little more about it. In any event, there certainly is segmental narrowing and one must guess what could produce this sort of appearance. There is a good deal of gas in the intestinal tract which makes visibility low and I think the use of multiple films and other techniques would have been very helpful.

Dr. Hodges' impression: CONSTRICTING TUMOR, lower extremity of right ureter, with consequent hydronephrosis.

Radiologic Impressions Submitted by Mail:

Carcinoma, ureter	60
Pelvic tumor	21
Ureteral obstruction	12
Non-opaque calculus	15
Ectopic kidney	18
Others	29

Fig. 1 — Roentgenogram showing tortuous deformity of the lower part of the right ureter.



Dr. Regato: Dr. F. A. Rose of Cleveland and Dr. V. P. Collins of Houston and Dr. Frank Gorishek of Denver also favored a carcinoma of the ureter.

Philip J. Hodes, M. D., Philadelphia, Pennsylvania (by mail): This filling defect of the distal ureter with a proximal dilatation makes one think of a non-opaque calculus.

Operative findings: On September 1954 the right kidney and ureter were resected. The kidney measured 13 x 9 x 4 cm; the ureter was 1.5 cm thick and presented a mass 2 cm in diameter near its lower end which obstructed the lumen.

Dr. Mostofi: The section shows the ureter involved in a pseudotumorous process. The mucosa is present in only one area and ulcerated elsewhere. The lamina propria is partly thickened by an amorphous hyaline acellular mass which varies from pale basophilic to pale eosinophilic. The mass is sometimes fragmented, the fragments being separated by acute and chronic inflammatory cells in which many lipophages are seen. In one area it has the appearance of necrotic tissue with ghost-like remnants of tissue superimposed with the amorphorus material. These amorphous masses are found not only in the lamina propria but also focally throughout the ureteral wall. Here the masses are surrounded by a laminated capsule suggesting plugged vascular spaces. At times foreign body giant cell reaction is seen in association with these masses. In one or two areas the mass forms a collar around vascular channels. Nests of amorphous material are also formed in the periureteral fatty and fibrous tissue. Associated with the amorphous material there is focal calcification, osteoid formation and ossification. Under polarized light two types of refractive material are seen in the amphorous substance: (a) string-like shreds scattered throughout and (b) focal thick masses distributed peripherally. The fibromuscular tissue of the ureteral wall shows regenerative reaction with giant cell formation, young muscle cells and young fibrous connective tissue cells. In one or two areas hemosiderin deposition is seen.

A crystal violet stain was done on a section and although the substance was metachromatic, it did not give the true amyloid reaction. The same slide was restained with Congo Red and again it did not give a typical response.

In discussing the differential diagnosis here we have two problems: (a) the nature of the ureteral lesion and (b) the nature of the amorphorous material seen in the wall of the ureter.

As far as the nature of the ureteral lesion is concerned I believe that it is safe to say that we are dealing with chronic ureteritis with necrosis, foreign body reaction, repair and osseous metaplasia. The basis of the lesion could be a rupture of the ureter secondary to a stone; or traumatic, secondary to instrumentation; or an inflammatory reaction accompanying pyelitis and pyelonephritis.

As far as the nature of the hyaline-like mass is concerned, there are two possibilities (a) that this is amyloid

or (b) that this is a foreign matter, either extruded urinary sediment, or material that has been introduced into the urinary tract from outside, such opaque dye, with associated necrosis of tissue. The exact nature of amyloid is unknown. Evidence seems to point to the fact that it is a mucopolysaccharide, bound to a globulin, and related to the cartilage and other polysaccharides. The reaction to Congo Red and metachromatic dyes depends on the nature of the side chains. Although four varieties of amyloidosis are ordinarily recognized, for our purpose we may consider the typical amyloid in contrast to the atypical variety. Typical amyloid is characteristic by lack of tissue reaction and by the striking staining reaction with Congo Red and metachromatic dyes. This certainly is not typical amyloid, and would have to be considered atypical amyloid if it is amyloid at all. The second alternative is that this substance consists mostly of urinary sediment or opaque dye with the associated necrosis and inflammation of the ureteral wall.

My diagnosis in this case is chronic ureteritis with necrosis, foreign body reaction, repair and osseous metaplasia (amyloidosis?).

Necrotic tissue itself may "pick up" one of the polysaccharides and given an atypical metachromatic response without being amyloid. Whether the material is atypical amyloid or necrotic matter, debris, etc., associated with or resulting from extrusion of urinary sediment or opaque dye, I cannot determine with the available material and information. A Wilder's stain, elastic van Giesson stain, Masson, PAS, APS, a good Congo Red and fluorescent microscopy, microincineration and microchemical analysis, etc., are necessary for the determination of its nature and even these may not settle the question as some will undoubtedly insist that this is all atypical amyloid.

Dr. Mostofi's diagnosis: CHRONIC URETERITIS with necrosis, FOREIGN BODY REACTION, repair and OSSEOUS METAPLASIA (amyloidosis?)

Histopathologic Diagnoses Submitted by Mail:

Osseous metaplasia	58
Necrotizing ureteritis	52
Amyloidosis	45
Chronic inflammation	15
Others	6

Dr. Regato: Dr. C. A. Hellwig of Halstead, Kansas, Dr. T. H. Cochran of Salt Lake City and Dr. E. F. Geever of Bethesda, Maryland, submitted a diagnosis of amyloidosis with secondary infection and bone deposition. Dr. R. A. Willis of Leeds and Dr. Boris Scolnik of Montevideo suggested chronic inflammatory reaction and metaplastic ossification around retained calculi.

Subsequent history: On July 1955 the patient was reported well.

Dr. Hudson: The placement of transitional cell epithelial lining next to the fascia, outside the urinary tract, results clinically in the formation of bone. I think this is a very interesting scientific curiosity. I know absolutely nothing about the disease this patient had.

W. D. Millett, M. D., Denver, Colorado: It was our opinion that this was atypical amyloid. We had some Congo Red stains and got a reddish-orange coloration in the nodular areas but quite faint orange in other areas. I think our crystal violet was a little more red, too. On this basis we diagnosed this as a localized amyloidosis or para-amyloid which is an atypical staining amyloid.

D. de Santo, M. D., San Diego, California: I don't know whether the uric acid deposits are urates, but I know it looks very much like the uric acid deposits that you see in soft tissues of gout and I would like to pass that word on if there is some histochemical stain that would show this is a gouty type of deposit in an unusual location. At least I would hate to have the possibility overlooked.

Dr. Mostofi: We didn't think it was uric acid.

Subsequent history: In March 1956 this patient was hospitalized with persistent bladder infection; hypertrophy of the mucosa at the bladder neck was surgically corrected and she remains well.

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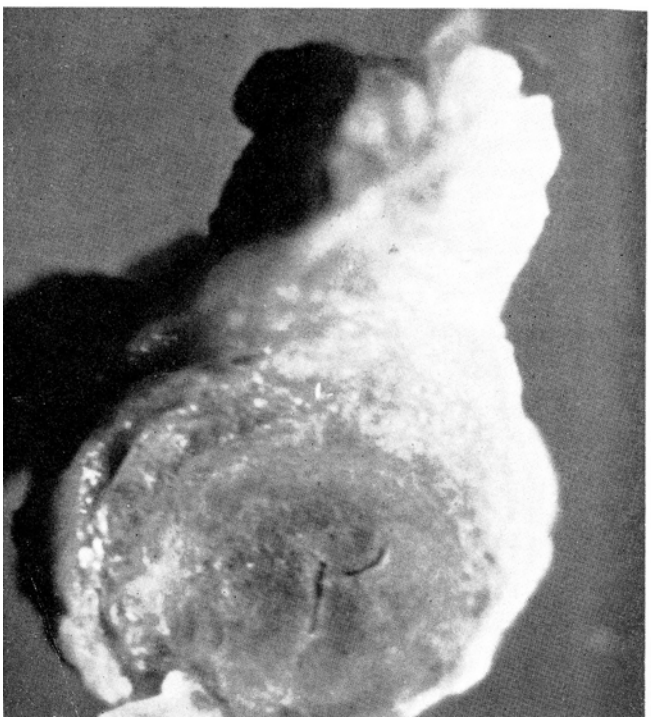

Fig. 2—Gross specimen showing thickened ureter.

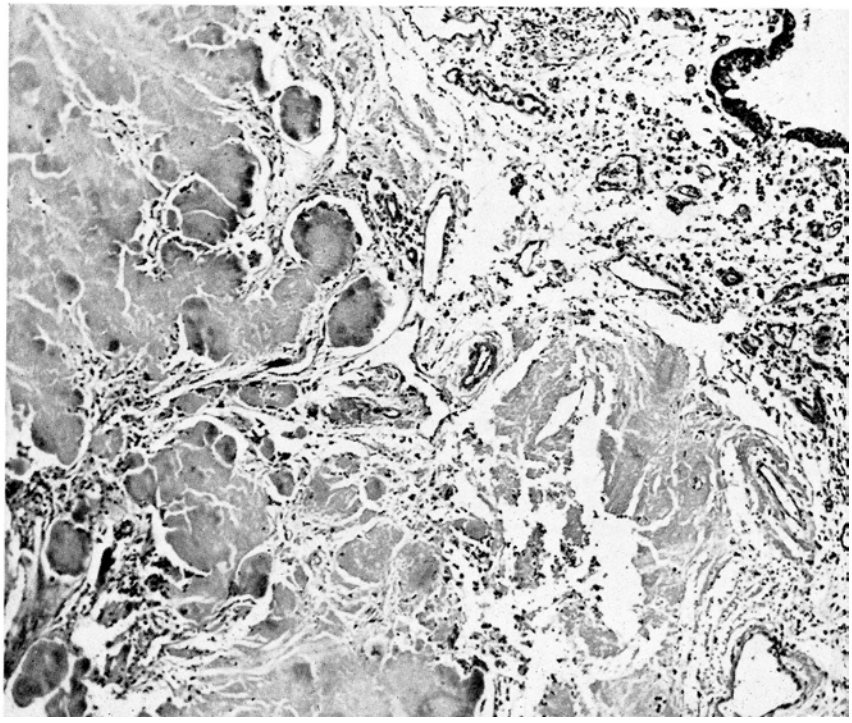

Fig. 3 — Low power photomicrograph: chronic proliferative ureteritis with necrosis, foreign body giant cell reaction and repair. The hyaline acellular material may represent atypical amyloid. Elsewhere in the section osseous metaplasia was seen.

Our Guest Speakers

Fred J. Hodges, M. D., Professor of Radiology, University of Michigan, at Ann Arbor. Dr. Hodges graduated from Washington University Medical School in 1919. He is one of the outstanding teachers of Radiology in the United States and the author of numerous didactic publications on this branch of Medicine. Dr. Hodges was the guest of the Penrose Cancer Hospital.

Fathollah K. Mostofi, M. D., Chief of the Genito-Urinary Pathology Section, Central Laboratory for Anatomical Pathology Research, Veteran's Administration, Armed Forces Institute of Pathology, Washington, D. C. Dr. Mostofi graduated from Harvard Medical School in 1939. Dr. Mostofi was the guest of the College of American Pathologists.

Perry B. Hudson, M. D., Assistant Professor of Urology, Columbia University and Chief Urologist to the Frances Delafield Hospital of New York. Dr. Hudson graduated from the University of Georgia School of Medicine and received training in Urology at the Johns Hopkins University Hospital. Dr. Hudson was the guest of the Penrose Cancer Hospital.