We have obtained some alleviation of the disfigurement of port wine stains by excising the skin down to the lower layers of dermis and then applying free grafts.

Factors that may cause one to deviate from surgical excision or cautery destruction occasionally arise, such as position, size or wide spotty distribution of the growth, and preconceived ideas of treatment by the patient, parent or physician. For many of these, instead of surface radiation we prefer interstitial radiation in the form of gold radon seed and have had some very favorable results about the ears, eyelids and face. However, radiation therapy is slow in action, there may be much more discomfort than with excision, and the resulting scar may require as much surgery as the excision of the original lesion. The possible bad effect of radiation on neighboring tissues, mentioned by Dr. Davis, is also worthy of consideration in view of Dr. Brooks' findings of a definite diminution of bone growth from exposure to x-rays. Further, actual radiation burns are not so infrequent as might be thought; in a series of 97 radiation burns on Dr. Blair's service 11 resulted from treatment for hemangiomas. In one patient there was loss of vision of one eye and in another there was so much damage about the orbit that vision was markedly impaired.

Dr. John E. Cannaday, Charleston, W. Va.—In this class of work the results obtained by the use of radium are rather poor. The skin is disfigured too much, especially if the location is on the face. In some cases I have attained reasonably successful restults by the injection of boiling water. This method has been used successfully in a number of cases by such well known members of our profession as Dr. Francis Reder, of St. Louis, and Dr. Irvin Abell, of Louisville.

I quite agree with Dr. Davis that the excision method has a number of advantages, particularly with reference to the conservation of tissue and the elimination and prevention of deformity.

RADIATION THERAPY OF RENAL CORTICAL NEOPLASMS*

WITH SPECIAL REFERENCE TO PREOPERATIVE IRRADIATION

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Our attention was first directed to the radiosensitivity of cortical renal tumors by the response to irradiation in the following case: the patient, a man, aged 52, was admitted to the Brady Urological Institute April 10, 1923, complaining of pain of eight weeks' duration in the left kidney region. There was a visible, palpable mass to the left of the midline, projecting beneath the costal margin, which moved with respiration. It was firm, nodular, irregular and extended 11 cm. below the border of the ribs. The late Dr. J. T. Geraghty's note stated: "The pyelogram shows a typical picture of hypernephroma. The patient is referred for deep x-ray therapy. If the size of the mass is decreased by x-ray, nephrectomy may be advised at a later date. The mass at the present time is inoperable."

Within ten days the mass had decreased in size so that it was barely palpable beneath the costal margin. The patient returned to his home for a six weeks' rest, but did not return for operation. We have recently learned that the patient died in 1929, five and one-half years after irradiation. Operation was never carried out. Our results in preoperative treatment of cortical renal tumors are based on the study of eleven cases.

It is evident that in this case we were dealing with an extremely radiosensitive tumor. Its prompt response to radiation and its striking and phenomenal conversion from an inoperable to an operable tumor at once suggested the advisability of radiating preoperatively all tumors of this type, not alone with the idea of simplifying nephrectomy, but of devitalizing the tumor and thus minimizing the risk of metastasis.

Marked reduction in the size of the primary tumor has followed intensive irradiation in other cases in which nephrectomy was not indicated because of the size of the tumor or the presence of demonstrable metastasis. In these cases, however, death has always occurred within five and one-half years.

Further experience in the irradiation of cortical tumors has shown considerable variation in the rapidity and degree of regressive changes in different cases. It would seem that the desired result is dependent upon the selective action of the x-ray for certain cells, and particularly those cells which are undergoing rapid division or mitosis. Ewing has pointed out that tumors which revert to the embryonic type of growth and present a considerable degree of anaplasia are most radiosensitive. On the other hand, squamous cell tumors exhibit marked resistance to irradiation as do those derived from transitional epithelium. The refractory response to irradiation of the papillary tumors of the renal pelvis and bladder are thus accounted for.

*Read in General Clinical Session, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

*From the Brady Urological Institute, The Johns Hopkins Hospital, Baltimore, Maryland.

An analysis of these cases makes very evident the fact that the percentage of cures will probably not be materially increased until earlier diagnosis makes possible the institution of treatment before metastasis has occurred. The importance of hematuria as the first symptom in the majority of cases cannot be too strongly emphasized and when present, either grossly or microscopically, should call for a thorough and exhaustive investigation of the urinary tract.

When the diagnosis of renal tumor is definitely established it is desirable, because of the selective action of the x-ray for certain types, to attempt a differentiation between the radiosensitive and radioresistant tumors. The great majority of the cortical tumors respond to irradiation and these cases should receive treatment preoperatively. For papillary tumors of the pelvis, because of their peculiar characteristics, a different therapy is indicated.

The immediate result of irradiation in radiosensitive cortical renal tumors is the remarkable reduction in the size of the tumors. In all cases the tumor has been reduced to less than half its original size. A certain amount of nausea and general malaise has accompanied this therapy, but with well regulated doses this may be kept at a minimum. The reduction in the size of the tumors begins very promptly, within two or three days, and continues for probably two to three weeks following the cessation of treatments. There will be, however, some cases requiring more radiation, depending upon the degree of radiosensitivity of the tumor, and in these cases a second series of irradiation should be given before operation.

However, it is our belief, at this writing, that the great majority of the radiosensitive tumors will be sufficiently shrunken and destroyed with the first series. In these cases the optimum time for operation is approximately three weeks following the irradiation. It has been shown in two cases, *5* and *6*, that the tumor may begin to grow after a prolonged rest period.

In six cases, the tumor was so large that operation would have been practically impossible at the time the patient first reported. The operators in these cases have not found operation any more difficult than in non-radiated cases.

It is, of course, essential that the tumor be removed with as little manipulation as possible to prevent pressing tumor cells into the blood stream. Preoperative irradiation has diminished the size of the tumor and allowed more freedom at operation. The operation should be planned so that the pedicle of the kidney may be ligated before freeing of the tumor, thereby preventing metastasis by way of the renal veins. Adequate exposure may be obtained in certain instances through a lateral rectus incision. In certain large tumors, as in the sixth case, where the tumor has recurred and was very large, a T-shaped incision allowed adequate exposure. A long S-shaped oblique abdominal incision similar to that used in the lumbar approach might be used in the transperitoneal approach.

In addition to remarkable reduction in the size of radiosensitive tumors, irradiation has produced decided changes in the tumor pathology. First, we have noted extensive fibrosis around the tumor with thickening of the capsule which would inhibit the expansion of the tumor. Second, we have noted sclerosis of the small blood vessels and capillaries which supply the tumor. This change is observed principally within and beneath the tumor capsule.

Necrosis is a common finding in large cortical tumors following irradiation. In one case (*6*) we observed a remarkable reduction in the size of the tumor mass after the first and second series of x-ray therapy. Later, after a period of rest, the tumor again grew. The gross pathological specimen shows a large central area of necrosis surrounded by a thick fibrous membrane, which in turn is surrounded by a zone of tumor showing none of the effects commonly produced by x-ray. It may be that the first radiation produced the central necrosis and a greatly thickened fibrous membrane, leaving a few living tumor cells to recommence the growth which so symmetrically surrounded the necrotic area.

Tumor tissue in adults has shown certain cellular alterations which may be due to irradiation. These findings are constant and consist of loss of cell outline, diminution in size of the nuclei, and loss of staining quality with hematoxylin. The latter quality varies, but has been noted before in tumors subjected to irradiation. A further microscopic change is in the more or less extensive deposition of hyaline material and marked fibrosis. Deposition of iron pigment is a fairly constant finding and occurs with the death of tissue.

One tumor, in a child of 3 years, showed a most remarkable reaction to irradiation. It decreased to one-twentieth its size after one series of x-ray. The pathological specimen showed very remarkable thickening of the tumor capsule. The tumor in gross resembled a hyperne-

phroma. The tissue appeared compressed and the tumor was very much firmer than the usual hypernephroma. Microscopically, there was most extensive fibrosis with hyalinization, necrosis and deposition of iron pigment. There was no tumor tissue that pathologists could recognize as viable. A few very tiny microscopic areas showed masses of clear, small cells, compressed between connective tissue fibers. These cells had clearly defined outlines and small dark nuclei without mitotic figures. There was no papillary or adenoid formation, but the type of cell described with the gross appearance of the tissue made the diagnosis of hypernephroma quite certain. None of the characteristics of Wilms' tumor was noted.

The last patient to receive preoperative irradiation was treated very intensively without reduction in gross size of his renal tumor. On gross examination the mid-pole cortical tumor presented a picture very similar to the other specimen. However, there were no areas of necrosis, no large cysts and no blood-filled spaces. On microscopic examination, the diagnosis of papillary carcinoma or malignant papillary cystadenoma was made. We are at a loss to explain the radioresistance of this tumor, but the case offers a remarkable contrast to the effect produced by irradiation of the so-called hypernephroma. It is well known that these carcinomata do not invade the blood vessels as early as hypernephroma, and metastases are late. The characteristic of the tumor is implantation and it is of great importance to remove these tumors without opening their capsules. It may be that we have in deep therapy a test whereby papillary carcinoma or cystadenoma may be differentiated from other cortical renal tumors of the hypernephroma type before operation.

It has further been noted that the renal tissue outside the tumor which received irradiation appears normal. The glomeruli and Bowman's capsules are intact. The tubular epithelium shows no hyalinization and no fatty degeneration. There is no interstitial fibrosis or thickening. The capillaries show a very slight degree of sclerosis, but with regulated x-ray dosage this has been kept at a minimum and pathologically we are unable to observe any gross or microscopic change in the secreting substance of the kidney indicative of nephritis.

The international "r" as adopted by the second International Congress of Radiology in Stockholm, Sweden, has been employed uniformly in the measurement of our dosage and 800 "r" has been used as our erythema skin dose. Daily doses averaging between 195 "r" to 345 "r," depending upon the degree of reaction, have been given. We have employed the saturation curves recommended by Weatherwax in the estimation of the loss of radiation effect in the tissues. Voltages of 200 kv. with 0.5 mm. copper and 2 mm. aluminum filters, 4 ma., at 50 cm. focal skin distance have been uniformly employed in our cases. Cross sectional charts of each case are made to estimate the location and depth of the tumor in order to arrive at an approximately correct tumor dose. Weatherwax has shown that with the above technic a 32 per cent loss in tissue effect is acquired in seven days. For the purposes of accuracy and simplicity, and because we believe it is possible to give a greater tumor dose with safety with this method, we have adopted it. The approximate length of time required to give a single series of treatment is three weeks. The question of nausea, the destructive effect on the blood cells and the infrequent occurrence of diarrhea all tend to influence the time factor. Each case necessarily will manifest individual characteristics and must be treated accordingly. *Fig. 1* illustrates the irradiation chart for *Case 5*. Eleven patients have received preoperative irradiation, seven of whom have come to operation. Careful clinical notes are available regarding the regression of these tumors following irradiation and the specimens removed at operation have been studied pathologically to determine the gross and microscopic changes produced.

We report in detail four cases which illustrate what may be accomplished by irradiation therapy.

Case 2.—R. M., aged 26, came to the Brady Urological Institute May 21, 1929, complaining of pain in the lower left quadrant of the abdomen, of about three weeks' duration, associated with intermittent hematuria, frequency and urgency of urination. A large soft mass was palpable in the left flank extending almost to the crest of the ilium, extending anteriorly and medially to the lateral border of the rectus muscle.

The phenolsulphonephthalein test showed appearance time 5 minutes and an output in one-half hour of 55 per cent. The left pyelo-ureterogram showed great deformity of the pelvis and calices, with marked elongation of the kidney. There was marked cupping of the calices suggestive of polycystic kidney. The ureter was dilated and displaced medially over the lateral portion of the lumbar vertebrae.

Between July 21 and September 18 the patient received a total tumor dose of 4243 "r."

He was readmitted to the hospital October 1, 1929, with slight nausea and a feeling of dullness in the

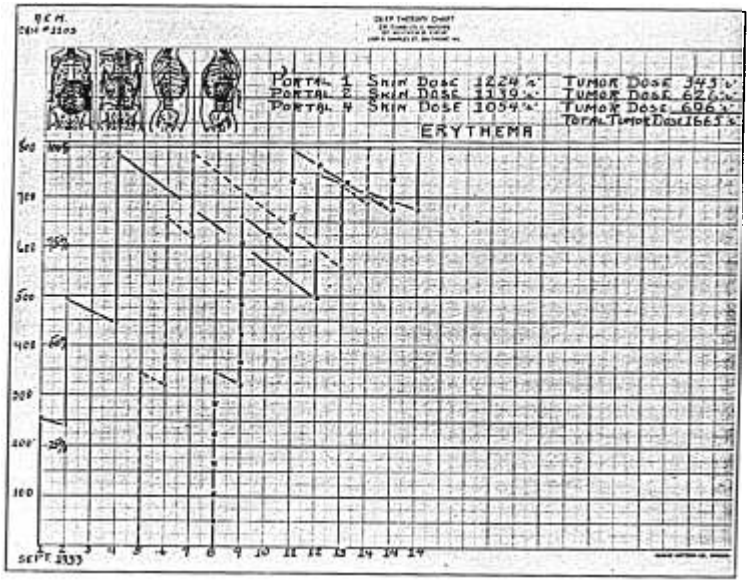

Fig. 1

Case 5. Roentgen chart showing the amount of irradiation given this case with complete regression of the tumor as far as palpation is concerned.

right flank. He had had no more hematuria. The tumor mass had decreased in size so that the tumor was barely palpable beneath the costal margin. The series of pyelo-ureterograms, *Figs. 2* and *3*, very beautifully demonstrates the diminution in the size of the tumor. The differential phenolsulphonephthalein test showed appearance time on the right of 3 minutes, the half hour collection being 51 per cent; appearance time on the left side was 15 minutes, with a half hour output of 7 per cent.

Nephrectomy, left, was carried out October 14, 1929. Lumbar extraperitoneal nephrectomy was accomplished without difficulty. The tumor was very adherent at the kidney pedicle and at the diaphragm. Pedicle clamps were left in place and removed 9 days after operation.

Pathology (*7336*).—The specimen is a left kidney, presenting a large upper pole tumor 9x8x11 cm. The tumor is covered by renal capsule which is adherent and infiltrated with tumor. The tumor is yellow with red hemorrhagic areas and large areas of necrosis. The kidney pelvis has been compressed downward, but there is no direct involvement of it. The upper and middle calices are distorted and compressed by the tumor. There is some dilatation of the lower pole calices.

Microscopic sections do not stain well with hematoxylin. The tumor is made up of large opaque cells with indefinite cell outline and with very tiny pyknotic darkly staining nuclei. There is much hemorrhage between the cells and in the large tissue spaces. There is much hyalinization and fibrous change. Mitotic figures are very prominent and in a section from the mid portion of the kidney we see invasion of the renal tubules with large clear foam cells in papillary formation. The x-ray has produced definite fibrosis within the tumor, shrinkage of the cells and possibly caused necrosis, although necrosis is frequently seen in large cortical renal tumors without radiation. There is apparently new growth involving the mid portion of the kidney. The diagnosis is hypernephroma with changes due to irradiation.

The patient was discharged one month after operation in good condition. He received 1017 "r" over the site of the tumor between January 8 and February 4, 1930. In February, 1930, x-ray of the chest showed definite areas of metastasis, which were treated by x-ray. In June, 1930, 1068 "r" were given over the site of the tumor and reexamination of the chest showed no evidence of recurrent metastasis. The patient died one year after operation of generalized metastasis.

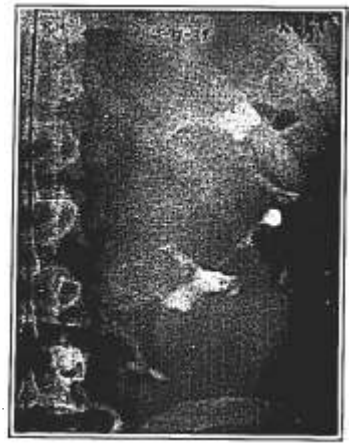

Fig. 2

Case 2. Left retrograde pyelogram showing tremendous involvement of the entire kidney before irradiation.

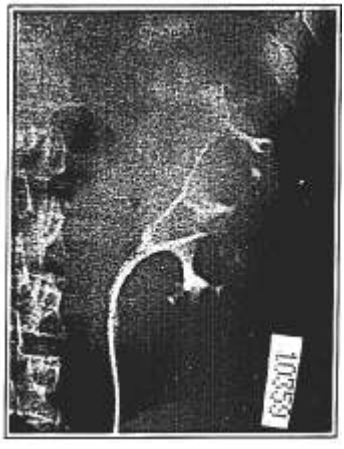

Fig. 3

Case 2. Pyelogram after tumor received 2512 "r" units. Note the definite reduction in the size of the tumor and the marked improvement in the filling of the pelvis and calices.

Case 4.—C. S., a colored child, aged 4 years, was referred by Dr. Lawson Wilkins October 20, 1933, and admitted to the Provident Hospital with an enormous mass in the right side which filled three-fourths of the abdomen. The tumor extended across the midline to the left half of the abdomen as far as the lateral border of the left rectus muscle and downward behind the crest of the ilium. The intravenous urograph showed a kidney displaced towards the midline, with marked compression of the calices and pelvis, indicating a large cortical tumor. The patient was emaciated, anemic, the red blood cells numbered 3,650,000, and hemoglobin 60 per cent. A transfusion of blood was given and the patient was referred for deep x-ray therapy, a tumor dose of 1397 "r" being given between July 5 and July 20, 1933. During this period the abdominal tumor disappeared and could be palpated as a mass only the size of a hen's egg at the lower pole of the right kidney. Hemoglobin on August 10 had dropped to 48 per cent and the red cell count was 3,800,000. Further transfusions were given and a second series of irradiation was undertaken in September, during which time a tumor dose of 1336 "r" was given.

Transperitoneal nephrectomy, right, was carried out by Dr. Lawrence Wharton October 12, 1933, through a right rectus incision. The intestines were packed off and the pedicle ligated before any operative procedure upon the kidney or tumor was undertaken. The kidney was removed separately from the tumor, after excision of the renal capsule. The tumor with renal capsule was then removed in one piece.

Pathology.—The specimen consists of a right kidney with the large tumor covering its posterior surface. The kidney measures 9.5x4.5x2.5 cm. and the tumor 9.5x5.5x2 cm. The kidney had been completely decapsulated and was removed separately from the tumor. Apparently the tumor lies within the true renal capsule. The kidney tissue on the surface appears to be normal. There is posterior compression of the renal substance and the cortex of the kidney is very thin. The tumor itself is well encapsulated and there is no involvement of the renal pelvis or calices. The tumor is firm, slightly less dense than normal kidney tissue. The capsule varies from 1 to 2 mm. in thickness, is white and glistening. The tumor is composed of large islands of yellow tissue with small areas of hemorrhage. One of these islands lies beneath the capsule at the upper pole and is separately encapsulated. The center of this area is necrotic and immediately beneath the capsule there is an extensive deposit of iron pigment. There is a great deal of fibrosis throughout the tumor and the tissue appears to be contracted.

Microscopic sections show a very thick fibrous capsule around the tumor. There is much necrosis, extensive hyalinization and extensive deposit of iron pigment between the fibrous tissue cells. The tumor cells are rather small and appear to be dehydrated. Many nuclei are seen at the periphery of the cells, which are indefinitely outlined. (There are a few islands of cells in this specimen that show definitely the structure of the original tumor. They are made up of large clear cells with very small darkly staining nuclei, fairly typical of hypernephroma.) There is no papillary or adenoid formation. Study of the kidney tissue outside the tumor shows normal glomeruli. The tubules are

Fig. 4

Case 4, Path. 8847. Photomicrograph showing a nest of large opaque tumor cells with their tiny nuclei surrounded by a fibrous zone in which there is an accumulation of leucocytes and extensive deposition of iron pigment. Most of tumor destroyed by irradiation.

Fig. 5

Case 4, Path. 8847. Photomicrograph showing contracted tumor cells with increased amount of fibrous tissue, deposition of iron pigment and shrinkage due to irradiation.

normal. There are no casts. Near the pelvis there is some interstitial round cell infiltration (*Figs. 4* and *5*).

The diagnosis is hypernephroma. The tumor is practically totally destroyed by irradiation.

The patient's convalescence was uneventful.

Case 5.—A. E. M., a young woman, aged 15, was admitted to the Church Home and Infirmary August 25, 1933, because of hematuria, which had been intermittent for one year. There was marked loss of weight and the patient had felt some fullness in the left side of the abdomen for six months. Her family physician stated that the left-sided abdominal tumor was barely palpable two months before admission to the hospital. A hard, irregular nodular mass was palpable in the left kidney region, extending to the midline of the abdomen at the umbilicus and downward as far as the crest of the ilium (*Fig. 6*).

On cystoscopy, bloody urine was obtained from the left kidney. The pyeloureterogram shows deformity of the median portion of the kidney pelvis with displacement of the middle calices. The patient received 1665 "r" (see *Fig. 1*) and in 11 days the tumor had decreased in size so that it was barely palpable beneath the costal margin (*Fig. 6*). A differential phenolsulphonephthalein showed, on the right side, appearance in 5 minutes, and half hour collection 25 per cent; on the left side, the appearance time was 14 minutes, and half hour collection 8 per cent.

Pyelograms before and after preoperative irradiation (*Figs. 7* and *8*) show the very marked shrinkage of the tumor by irradiation.

Following irradiation the patient's red blood cells were 4,050,000, white blood cells 12,300, and hemoglobin 74 per cent.

Operation was advised following the decrease in the size of the tumor by x-ray treatment, but the parents refused. The tumor began to increase in size early in November, two months after irradiation, so that the family finally consented to operation, which was carried out November 27, 1933.

Operation was performed by Dr. Lawrence Wharton.

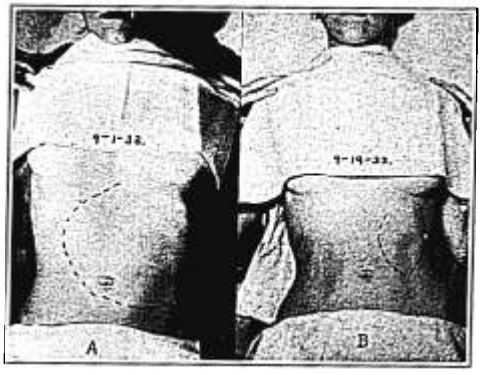

Fig. 6

Case 5. Dotted lines indicate size of tumor. A. Before irradiation. B. Nineteen days later. Note marked reduction in size of tumor. Tumor dose, 1665 "r" units. Forty-eight days after institution of irradiation no mass could be felt, but intravenous urogram still shows evidence of a mass in the upper pole of the kidney as shown in Fig. 8.

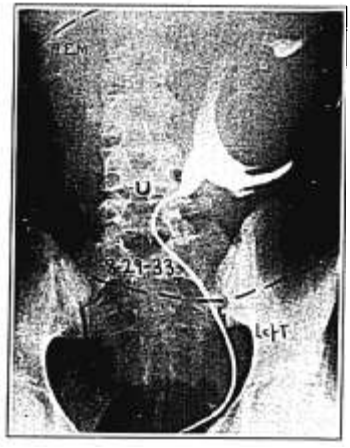

Fig. 7

Case 5. Retrograde pyelogram of the left kidney showing a typical mid-pole cortical tumor before irradiation. The dotted line shows the relative position of the kidney as noted on palpation.

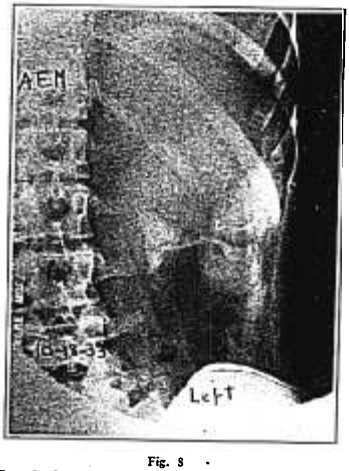

Fig. 8

Case 5. Intravenous urogram showing marked regression of the lower part of the tumor. The pelvis has returned to its relative normal position, although there is still evidence of a mass involving the upper pole.

The abdomen was opened through a long left rectus incision. The lateral peritoneal attachment of the descending colon and splenic flexure was divided and the intestines were retracted medially. The pedicle was exposed and ligated before the tumor was approached. There were several aberrant vessels to the tumor which were clamped and ligated. The suprarenal gland was adherent at the upper pole and was removed with the tumor. Eight cm. of ureter were also removed. The posterior peritoneum was closed and the usual closure of the abdominal wall was carried out.

The specimen measures 11x14x10 cm. At the upper and lower poles a small amount of compressed renal parenchyma is seen. The lower pole of the kidney is replaced by a large soft round mass 13 cm. in diameter. It is entirely encapsulated. The tumor has extended into the upper pole of the kidney by a wide pedicle between the pelvis and posterior capsule. The pelvis is dilated to 7 cm. in diameter and the ureter shows slight dilatation in its upper 9 cms. On section we find the large lower pole mass filled with necrotic material and old blood. Among the cystic border papillary projections of friable tumor are seen. The upper pole extension is solid with much coagulated blood. The tumor capsule varies from 4 to 7 mm. in thickness.

Microscopic sections from the lower pole mass show papillary projections of tumor extending from the wall into the cyst. The cytoplasm of the cells is practically all destroyed, leaving darkly staining irregular pyknotic nuclei with tags of shrunken cytoplasm attached. The cells along the blood vessels are better preserved, but no true picture of the original tumor is available.

The tumor tissue at the upper pole is likewise destroyed and there is much fibrosis. Certain areas show iron pigment and hyalinization. The renal substance presents dilated tubules as in hydronephrosis. There is some hyalinization and slight interstitial fibrosis. The glomeruli are intact, but small, suggesting interference with their blood supply. A small section of the suprarenal gland is normal and we can find no change in that organ due to irradiation.

The impression is embryonal carcinoma.

Case 6.—S. W., aged 12, was admitted to the Johns Hopkins Hospital December 20, 1932, because of a hard mass in the left side. Three months before admission the patient developed an unexplained fever, with left upper abdominal pain and a temperature of 102°. He was kept in bed for 2 or 3 days and his temperature returned to normal. His physician found a mass in the left upper quadrant of the abdomen which he considered an enlarged spleen. The patient had had no hematuria. His temperature usually rose in the afternoon to 101°. He had had very little pain, but had noticed the firm mass in the left upper quadrant of the abdomen.

The patient was a thin, pale boy of 12 years, very alert and cooperative. Examination of the head was negative. There was no general enlargement of the lymph nodes. The lungs were clear. The abdomen presented, on inspection, a fullness in the left upper quadrant, and on palpation a firm, quite irregular, nodular mass, extending to within 2 cm. of the crest of the ilium and almost to the midline of the abdomen. The right kidney was not palpable. The liver was not enlarged. The external genitalia were negative. Temperature, pulse and respirations on admission were nor-

Fig. 9
Case 6. Intravenous urogram showing a typical mid-pole cortical tumor before irradiation.

mal. The red blood count was 1,870,000, white count 10,000, and hemoglobin 85 per cent. Plain x-ray film showed a large mass in the left upper abdomen. Pyeloureterogram showed a mid-renal filling defect probably caused by cortical tumor (*Fig. 9*).

The patient was referred for deep x-ray therapy, receiving a tumor dose of 1775 "r."

January 16, 1933, the tumor was considerably shrunken in size so that it was palpable on inspiration about half way between the costal margin and the crest of the ilium. It had receded laterally so that the border of the tumor reached the lateral border of the left rectus muscle. On expiration the tumor moved upward for a distance of 2 cm. Phenolsulphonephthalein test showed an appearance time of 3 minutes, half hour collections 65, 20, 10 and 5, total 100 per cent. The blood urea was 32 mg. per 100 c. c., hemoglobin 61 per cent. The patient had been having nose bleeds and it was considered that some of his loss of hemoglobin was due to this cause. Three hundred c. c. of citrated blood were given on January 17, 1933. Between February 6 and February 22, 1933, he received an additional tumor dose of 1146 "r." A tumor dose of 2210 "r" was given between May 4 and May 31. Seven transfusions were given during this interval. During the summer and fall the patient lost weight and had several nose bleeds. On October 23, 1933, the blood count showed a polycythemia with hemoglobin 110 per cent, red cells 6,400,000, and white cells 9,200.

October 27, 1933, operation was done under spinal anesthesia, with 150 mg. novocaine and nitrous oxide oxygen. Nephrectomy by Dr. H. H. Young was accomplished through the transperitoneal route, incision being made along the border of the left rectus muscle and then opened laterally in the form of a T. The large vessels over the surface of the tumor were ligated. Because of the large size of the tumor, the pedicle could not be tied immediately. The tumor was freed from the peritoneum medially, after releasing adhesions to the descending colon. The mesenteric vessels were not injured. Due to the extraordinary size of the vessels and close approximation of the splenic vein, ligation of the pedicle was very difficult. The kidney was quite adherent posteriorly, but it was not attached to the diaphragm. There was considerable bleeding, possibly from one of the renal veins which was controlled by pressure until the mass could be removed. When this was accomplished and all vessels tied, the pack was removed and no further bleeding occurred. The patient was considerably shocked and was given 2,000 c. c. of 5 per cent glucose and 500 c. c. of citrated blood during the operation. The tumor apparently was completely removed and also a glandular structure that lay above the renal vessels posterior to the upper pole of the kidney.

Pathology (8865).—The specimen is a large rounded mass 15x12x9 cm. It consists of the left kidney, with a large mid-renal tumor, completely covered by the

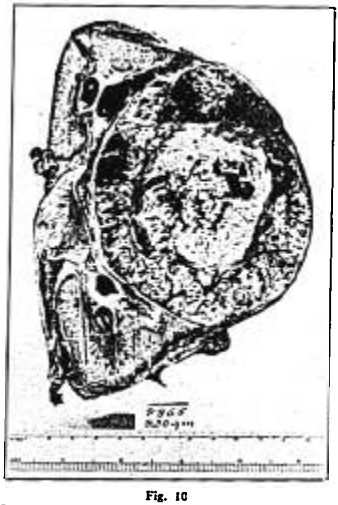

Fig. 10
Case 6, Path. 8865. Saggital section of left kidney with large mid-pole tumor. The tumor is well encapsulated and there is no direct invasion of the pelvis or calices. Note the central area of necrosis separated from the actively growing tumor by fibrous tissue. The necrotic center is undoubtedly the result of irradiation. The peripheral tumor evidently has grown in the four months' interval between the last irradiation and nephrectomy.

true renal capsule. Portions of the extrarenal capsule have been removed with the tumor. Over the surface are large veins and arteries, the largest of which is seen on the anterior surface, coming from the lower pole with many small branches over the anterior surface of the tumor. Posteriorly, there are several branches from the main renal vein. The tumor measures 10x11x9 cm. It is slightly irregular on the surface and presents nodularities over which the capsule is adherent. There are several areas of subcapsular hemorrhage. The tumor involves the anterior and posterior surfaces of the kidney in the mid-pole, but there is no invasion of tumor in the upper or lower pole. The pelvis is mostly extrarenal and communicates with the ureter just below the mid-portion of the tumor. There is some hydronephrosis with considerable dilatation of the ureter. The tumor is slightly more dense than normal kidney tissue, but at the most lateral point of the tumor there is some softening suggesting necrosis. On cross section we have an extraordinary picture of a mid-cortical tumor, which has invaded the kidney anteriorly and posteriorly, leaving the upper and lower portions of the kidney free of tumor. The tumor is fairly well encapsulated. The center of this tumor is entirely necrotic. This area measures 5 cm. in diameter and is surrounded by a zone of fibrosis varying from 4 to 7 mm. in thickness. There seems to be no active tumor within this fibrous zone, but outside of this zone there is an area 2 cm. thick, which presents a typical picture of hypernephroma, with islands of cells, yellowish red with a zone of iron pigment about them. There are cystic areas and many areas are filled with blood clot. There are also areas of hyaline degeneration. Examination of the renal vessels shows no inclusions of the tumor within the vessels and there is no involvement of the superficial vessels that cover the tumor (*Fig. 10*).

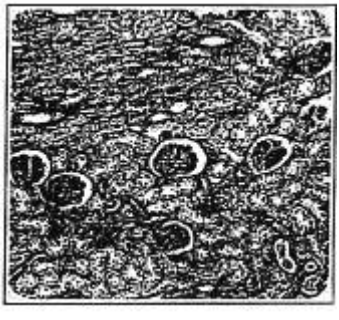

Fig. 11

Case 6. Normal renal tissue of removed kidney. No damage by preoperative irradiation.

Sections from the kidney tissue outside the tumor show small hemorrhages immediately beneath the capsule. These are probably caused by trauma at operation. The glomeruli are intact and Bowman's capsules are normal. There is no interstitial fibrosis. There are a few polymorphonuclear cells near the pelvis between the tubules, but there is no abscess formation. There is slight, cloudy swelling of the tubules near the periphery, but there is nothing to indicate interstitial nephritis as it can be developed by irradition (*Fig. 11*). Sections from the tumor show a thickened fibrous capsule which is here and there infiltrated with tumor cells. The tumor is composed of extraordinarily large, clear cells in more or less papillary formation, with large spaces, some of which are blood filled. The nuclei are rather small and present numerous mitotic figures. It is quite typical of hypernephroma (*Fig. 12*). In some areas we see adenoid formation. The outstanding fea-

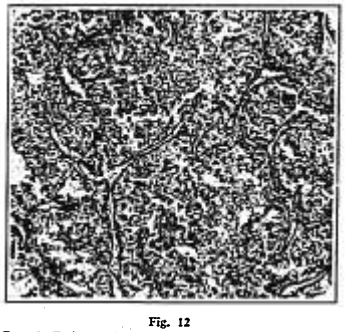

Fig. 12

Case 6, Path. 8865. Photomicrograph from the actively growing tumor on the periphery. Note the extraordinary size of the cells with small, darkly staining nuclei, the papillary formation and blood-filled spaces.

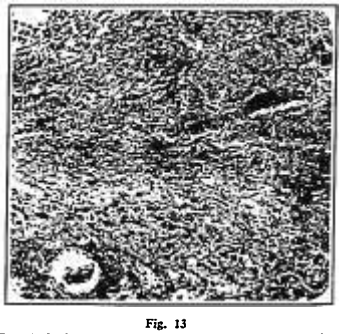

Fig. 13

Case 6, Path. 8865. Photomicrograph showing fibrous tissue dividing the area of active tumor and area of necrosis. On one side we see large clear cells in papillary formation with small, dark nuclei and blood-filled spaces, typical of hypernephroma. On the other side of the septum, necrotic tissue with fibrous change and apparently dead epithelial cells.

ture is the extraordinary size of the individual cells. Separating the living tumor from the necrotic area in the center, we have a thick band of fibrous tissue which is infiltrated by tumor cells. The central portion of the tumor is a large mass of necrotic tissue without definite morphology (*Fig. 13*).

CONCLUSIONS

(1) Tumors of the hypernephroma type and embryonal carcinomata are radiosensitive.

(2) Papillary carcinomata of the renal pelvis and the malignant papillary cyst adenomata are radioresistant.

(3) Irradiation has caused a striking reduction in the size of radiosensitive renal tumors.

(4) Irradiation has produced extensive morphological changes in sensitive tumors with extensive fibrosis, hyalinization and necrosis. The cells become shrunken. The cytoplasm may contract around the nucleus. In certain cases the tumor has been almost completely destroyed and replaced by fibrous tissue.

(5) Normal renal tissue has not been injured by irradiation in the dosages employed in our cases.

(6) Palpation of the tumor should be avoided as much as possible to prevent expressing tumor cells into the blood stream.

(7) Tumors which were inoperable because of their great size have been rendered operable by shrinkage following irradiation.

(8) Reduction in the size of sensitive tumors begins almost immediately after the institution of irradiation. Remarkable reduction in the size of the tumor takes place within three weeks.

(9) We recommend operative removal of the tumor after completion of the first series of radiation (approximately 3 weeks), allowing a few days for rest and transfusion if the degree of anemia justifies it.

(10) A regrowth of the tumor may occur if operation is long delayed after completion of irradiation.

(11) Preoperative irradiation has not made operation more difficult in our experience and in certain cases has simplified nephrectomy.

(12) The renal pedicle should be ligated before freeing the tumor, thus diminishing the risk of metastasis.

PRIMARY LYMPHOSARCOMA OF THE SMALL INTESTINE WITH METASTASES TO THE GALLBLADDER AND BOTH SUPRARENALS*

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In 1932, Ullman and Aheshouse[1] reviewed an article by Graves who, in 1919, had collected 249 cases of lymphosarcoma of the intestines. They collected 125 additional cases and reported one of their own, bringing the number to 375, which, with the one here reported, makes 376. Their thorough review of the literature will be referred to frequently.

This tumor occurs more frequently in the small intestine than in the large, the ratio being about 2 to 1, the most common site being the ileum.

It occurs most frequently in the first, third and fourth decades of life. Males show a greater predisposition than females in the ratio of 5 to 2, mostly in the white race. The etiology is obscure, although trauma has been strongly considered as a factor.

There is no characteristic clinical syndrome. In most cases the predominant symptoms are those of an acute or a chronic intestinal obstruction. The type of the symptoms varies, and seems to be chiefly dependent upon the duration of the growth and the degree of obstruction produced by it; whether by intussusception, adhesions or invasion of the wall by the growth. Abdominal pain occurred in every case studied. Usually it is constant and confined to the location of the tumor, is of an indefinite nature, sometimes colicky, but not affected by eating. Nausea and vomiting are commonly present. A tumor mass may be felt in various parts of the abdomen, most frequently in the lower quadrants. The stools contain blood in only one out of six cases. When the clinical picture suggests intestinal obstruction, the administration of contrast substances by mouth is often dangerous, as an incomplete obstruction may be converted into a complete one. However, if the obstruction be suspected

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