Primary tumors of the kidney occur not infrequently throughout the animal kingdom, and, in general, seem to exhibit the variations and peculiarities seen in human renal tumors. As an indication of the comparative pathology of renal tumors the following review of the literature is presented:

Mouse: Few cases of primary renal tumors have been described among the great numbers of other tumors found in this species. Tyzzer (1) found 4 renal growths, which he interprets as hypernephromas, among 83 primary tumors in mice. One of these mice, an old female, had also an adenoma of the lung, a carcinoma of the ovary, and a lymphoma infiltrating both kidneys; another had an adenoma in the lung. At the time this paper was written the interpretation of hypernephroma was more liberal than at present, and the illustrations might now be interpreted by many pathologists as papillary adenoma of the kidney, which was Tyzzer's original diagnosis in two of his cases.

Among the 300 mice with spontaneous tumors described by Haaland (2), there were but two renal tumors. One was a large growth in the kidney of a twenty-two months old male mouse, and had invaded a vein but produced no metastases; microscopically the structure was that of an adenocarcinoma. The second tumor, in a mouse of the same sex and age, resembled
perfectly in structure a human hypernephroma; there were no metastases, although the lung contained an adenoma. Inoculation of the hypernephroma into 40 mice was without result.

Murray (3) also described a spindle-cell growth surrounding the kidney without infiltrating it, apparently a primary retroperitoneal sarcoma and related to the kidney by position only.

Further than the above we can find no reports of primary renal tumors in mice, although Stumpf (4) has contributed a discussion of the behavior of carcinomas inoculated into the kidney.

Rats: Of 103 tumors found in 100,000 rats autopsied in plague work by McCoy (5), 11 were in the kidney, and were classified as 4 adenomas, 6 carcinomas, and 1 papilloma. Woolley and Wherry (6) in 23,000 rats found 22 tumors, of which 3 were in the kidney; all were of renal-cell type. Bullock and Rohdenburg (7), in a compilation of the literature on rat tumors, found 123 (including those cited above) of which 7 were fibroadenomas, 1 a papilloma, and 8 carcinomas of the kidney. Among 32 cases of their own in laboratory white rats, there were 10 adenomas of the kidney. Therefore, of 155 rat tumors 26 were of renal origin. A further case of carcinoma of the kidney in a wild rat was reported by Beatti (8). Loewenstein (9) described tumor-like papillary outgrowths arising in the pelvis of the kidney, as well as in the ureter and bladder, of rats infected with Trichodes crassicauda specifica.

Since sarcomas are much more common than carcinomas in rats, the fact that all the renal tumors in rats are of epithelial structure is of interest.

Squirrels: In 250,000 ground squirrels (Citellus beecheyi) autopsied in plague work, McCoy (10) found 8 tumors, of which one was described as an angiosarcoma of the kidney. A case of hypernephroma in the kidney of a grey squirrel (Sciurus carolinensis pennsylvanicus) was reported by Fox (11).

Birds: Fowls are rarely subject to renal tumors. Of 880 examined by Curtis (12), 79 had tumors, 5 of which were in the kidneys; but these were not microscopically corroborated and there is reason to doubt their true neoplastic nature. In 34 cases of tumor in fowls compiled by Wernicke (13), not one was
primary in the kidney although in 3 cases renal metastases were found. In 852 autopsied fowls Bürger (14) found 12 tumors of which none was in the kidney, although a sarcoma of the ovary had produced metastases in the kidney in one case.

The review of the literature on tumors in fowls and birds by Joest and Ernesti (15) who collected 112 cases and added about 50 more, reports no further renal tumors.

Other birds seem to have renal tumors perhaps more frequently, as is indicated by the following reports: White (16) described a fibrosarcoma in the kidney of a goose. Fox (17) reported in the kidney of a male chestnut eared finch (Amadina castanotis) a medullary carcinoma, becoming scirrhous in places, with metastases to the lungs and three cases of benign adenoma of the kidneys in undulated grass parrakeets (Melopsittacus undulatus). He had previously reported (18) two cases of papillary cystadenoma and also a "cyst adeno-carcinoma papilliferum" (19) in the same species; besides an adenocarcinoma of the kidney in a saffron finch (Sycalis flameola), (20) and a spindle-cell sarcoma of the left kidney with metastasis into the left tibia in a scaly ground dove (Scardapella squamosa) (21). Seligmann (22) reported as a diffuse carcinoma a growth which involved both kidneys, with metastases in the liver and mesentery, in a Chilian pintail (Dafila spinicauda) which was twenty-six years old. Baird (23) reported a case of keratinizing epithelioma in the kidney of a fowl, and Borrel and Masson (24) also described a renal tumor in a fowl which showed both cylindrical and squamous elements.

Domesticated mammals. Rabbits, which are less subject to tumor than most mammals, seem to have a relatively large proportion in the kidney, for Scott (25) stated that of 39 new growths reported, 5 were benign renal adenomas, resembling Wilms' tumors in structure.

Swine also seem to be particularly subject to renal tumors, for of the 12 cases of tumors in swine collected by Sticker, 7 arose in the kidney, and other cases reported since then indicate the same tendency. Many of these tumors were of the mixed embryonal tumor type.
In horses renal tumors are far from rare. In Sticker's (26) compilation, of 509 cases of malignant tumors in horses 37 were in the kidneys. McFadyean (27), in 63 cases of tumor in animals included 5 in the horse kidney, none with metastases. Of 142 equine neoplasms among 77,224 horses slaughtered in Japan, there were 9 in the kidney, as compared with 49 in the testicle (Kimura) (28).

According to Trotter's (29) figures, renal tumors are much less frequent in cattle, for of 305 cases but 1, a colloid cancer, arose in the kidney; but Sticker's figures show 10 of 78 bovine tumors in the kidneys. Steinke (30) described as hypernephroma a tumor of the kidney in a cow. Roussy and Wolf (31) in their review on cancer in animals, gave a picture of a tumor from a bovine kidney resembling a hypernephroma, and stated that cancer of the kidney in horses resembles that in man, while in swine the adenosarcoma of the kidney is among the most common tumors. Cadiot (32) quoted a case of an enormous cancer of the kidney in a mare.

No reports of cases of renal tumors in sheep can be found.

Of 766 primary cancers in dogs in Sticker's tables 19 were in the kidney. McFadyean also described two renal tumors in dogs, each case exhibiting metastasis. No renal tumors appeared in the 21 cats with tumors in Sticker's lists, nor in Roffo's 7 cases (33) nor in Murray's 11 cases (34) but Teutschlaender mentioned the cat (Kater) on his list of animals in which carcinoma of the kidney has been reported. Murray also described 48 cases of tumors in dogs, 12 in horses, and 18 in cows, with none arising in the kidneys.

We are indebted to Dr. L. E. Day for his summary of 316 tumors found among 2000 animal specimens sent to the Chicago Laboratory of the Bureau of Animal Industry. These do not represent all the tumors that are observed in the slaughter house, but merely specimens sent to the laboratory by the inspectors when in doubt concerning the diagnosis. Among 175 tumors of cattle there were no renal tumors although there were four adrenal tumors, two diagnosed as sarcomas and two as hypernephromas. Among 93 tumors in pigs no less than 52 were in the kidney,
47 being diagnosed as embryonal adenosarcomas and 5 as sarcomas; there were no adrenal tumors. In considering the tumors in swine it is to remembered that nearly all swine are slaughtered before they are two years old, so that not many of the slaughtered animals have reached an age for developing carcinomas. Among 48 tumors from sheep none whatever were found in the kidney or adrenal. These figures emphasize the infrequency of renal tumors in cattle and sheep and the frequency of mixed tumors of the kidney in swine, which resemble the typical mixed tumors of the human kidney.

Other incidental cases are: Sarcoma of the kidney in a swine (Hamburger) (35), the report of which leaves some uncertainty whether the growth may not have been leukemic.

Papillary adenoma in the left kidney in a mongoose lemur (White) (36). A tumor involving the kidneys, liver, lungs, and ovaries of a python, the primary site not being determined (Bland-Sutton) (37). A leiomyoma in the kidney of a horse, described by Wells (38). Pick (39) described a soft adenoma involving both kidneys of an eel. Williams (40) stated "A malignant renal tumor (derived from an adrenal 'rest') has been described by Bland-Sutton in a marmot." In Tutschlaender's compilation (44) were listed the following cases from the literature: Hemangioma of the kidney in a horse; carcinoma of the kidney in fowl, frog, pike, and buzzard.

While the above compilation is certainly not entirely complete, it serves to bring together much of the literature on the comparative pathology of renal tumors, and to indicate their general distribution and frequency.

Adrenal tumors. We can find no reports of primary adrenal tumors in mice, despite the great numbers of mice that have been examined at autopsy and the not infrequent occurrence of adrenal tumors in other species. Thus, Kimura (42) found in the literature records of adrenal tumors in 24 horses and 46 cattle, and he himself found 5 adrenal tumors among 46 tumors from horses. The extensive discussion of the comparative pathology of adrenal tumors by Steinke (43) mentioned tumors only in horses and cows, commenting on the absence of such tumors in
other species except for an adrenal tumor of parasympathetic-cell character in a two-year-old swine, reported by Klawitter.

There is, however, the interesting case reported by Smallwood (44) as a carcinoma of the kidney of a frog and believed to be derived from the adrenal tissues. Murray, who re-examined this specimen, corroborated its carcinomatous nature, but his statement suggests that he was not convinced that it developed from adrenal rather than renal cells. The illustrations in Smallwood’s article suggest a papillary renal tumor.

Fox (45) described as a hypernephroma a tumor that arose in the adrenal of a California hair seal (Zalophus californianus), and also described a hypernephroma in the adrenal of a brown cebus (Cebus fatuellus) (46).

As stated previously, in the 316 animal tumors examined by Day in the Chicago Stock Yards, but 4 arose in the adrenal, all in cattle, 2 being diagnosed as sarcoma and 2 as adenoma.

RENAI TUMORS IN MICE IN THE SLYE STOCK

In 33,000 autopsies performed on mice of the Slye stock, but 16 cases of unquestionable primary tumor arising in the kidney have been observed, supporting the impression that the kidney of the mouse is not among the common sites of primary neoplasm. These renal tumors are, according to the histological evidence, to be classified as follows: 1 carcinoma, 3 adenomas, 1 hypernephroma, 7 sarcomas, 3 mesotheliomas, and 1 sarcoma in the renal pelvis. It will be noted that we have observed no instances of the mixed tumors of the kidney that are so common in man and some other species, nor have we had any papillary tumors of the renal pelvis. The features presented by these several types of renal tumor are best described by giving briefly the findings in each of the several cases that we have observed.

EPITHELIAL TUMORS OF THE KIDNEY

1. Primary carcinoma of the kidney (fig. 1). Female mouse (1934). This mouse showed a white solid mass in the right kidney about the size of a normal kidney. Beyond this there were no
abnormalities found, except that the spleen was about three times the normal size. The left kidney was normal, and no metastases were found. Microscopically the tumor is composed of cells of epithelial type, but without the characteristics of either adrenal cells or of tubular epithelium of the kidney. They are arranged in large, pseudo-alveoli with much central necrosis, so that the persistence of the tumor cells near the bands of stroma gives in places the impression of a papilloma. Although the growth does not infiltrate the kidney very much, it has no capsule of its own, infiltrates the renal capsule in places, and is undoubtedly

Fig. 1. Primary Carcinoma of the Kidney

The junction of the compressed renal tissue and the tumor is shown. Apparently this tumor is derived from renal epithelium. Mouse 1934. × 110.
malignant. Evidently it is a tumor derived from the renal epithelium and may be properly designated as a carcinoma, although the term mesothelioma might also be appropriately used. Presumably it is in an early stage of malignancy in view of the relatively small amount of extension of the growth.

2. Solid adenoma arising in bilateral cystic kidneys. Male mouse (9907), age two years, thirteen days. Both kidneys were converted into masses of small cysts of various sizes, resembling the congenital cystic kidneys, although no cysts were found in the liver. Some of the cysts contain colloid masses, and between them are occasional foci of small round cells. There remains more kidney tissue in a functional condition than is usually seen in fatal human cases of congenital cystic kidney, but this tissue is far from normal, the tubules containing many hyaline casts, the interstitial tissue being infiltrated with round cells, and many of the glomeruli being more or less hyalinized. In the lower pole of each kidney was a fleshy nodule about 3 to 4 mm. in diameter. Microscopically these nodules are composed of a solid tissue, made up of groups of large epithelial cells somewhat resembling renal epithelium. About these is a delicate stroma containing some collections of small round cells. The nodule is distinctly encapsulated and seems to be in the renal substance rather than within one of the cysts. In many respects the structure resembles that of the benign ovarian adenomas of mice (47). No abnormalities of importance were noted in the other organs.

3. Adenoma of the kidney (fig. 2). Male mouse (10220), which died with advanced sarcosporidiosis; had marked chronic nephritis, both kidneys being large and nodular, with atrophic areas alternating with areas of swollen and dilated tubules, some of the latter being distinctly cystic. Beneath the capsule of one kidney was a nodule 4 mm. in diameter, with a well defined capsule. It consists of a mass of large epithelial cells with solid cytoplasm, arranged in large cords with a very delicate stroma between them. The arrangement of the cells resembles that of the adrenal adenomas, and a diagnosis of benign hypernephroma might readily be made. The cells are less vacuolated than those
of the typical adrenal cortex, having a denser cytoplasm, and are not dissimilar to the epithelial cells found lining the distended renal tubules; it seems probable, therefore, that this adenoma is derived from renal epithelium. There are some clefts containing colloidal material, and numerous calcific granules in the form of calcospherites.

4. Adenoma of the kidney. Male mouse (24073), with a large liver cyst containing a tapeworm, exhibiting in one kidney a solid subcapsular nodule 5 mm. in diameter, with a delicate but definite capsule. This is composed of a solid mass of large

![Fig. 2. Adenoma of Kidney](image)
epithelial cells with abundant foamy cytoplasm and small dark nuclei. The cells are in large cords or alveoli with a very delicate stroma between them. There are numerous small foci of calcification of the tumor tissue. The foamy character of the tumor cells, together with their arrangement, suggests an adrenal origin for this growth, but the post-mortem changes have so altered the nuclear and cytoplasmic details that this cannot be determined positively. In places there is a tendency to tubular arrangement of the tumor cells, suggesting a renal origin. Outside the tumor the kidney shows an advanced chronic nephritis with many hyaline and fibroid glomeruli.
5. Hypernephroma in the kidney (fig. 3). Male mouse (3639) with no other lesions of significance. The left kidney was replaced by an encapsulated, hemorrhagic mass, measuring 22 x 22 x 18 mm. The right kidney was slightly enlarged and soft, and showed a moderate degree of chronic nephritis. No remains of renal tissue are found in the tumor mass, which presents the typical appearance of a hypernephroma. More than half the mass contains no cells, being composed of the residue of old hemorrhages and necrosis. The living portions consist of large foamy cells arranged in cords and alveoli with a delicate stroma. It is completely surrounded by a capsule which shows no invasion by tumor cells. In all respects this growth corresponds perfectly to the human renal hypernephromas. No metastases can be found.

In the hilum of the right kidney, attached to a large artery, is a nodule about 2 mm. in diameter which, in the center, resembles a small leiomyoma, but about it is a mass of granulation tissue. It bears no resemblance to the hypernephroma and its nature is unknown.

In view of the fact that chronic nephritis is one of the commonest diseases in mice, and appears in forms often quite similar to nephritis in man, it is strange that we have found so few instances of epithelial neoplasms in mice, especially the benign adenomas which are so often found in human kidneys showing chronic nephritis.

SARCOTMA OF THE KIDNEY

The diagnosis of sarcoma, always difficult and often unsafe, is particularly dubious in the case of the kidney which presents so many non-sarcomatous growths that resemble sarcoma, and especially in the face of the statement made by Ewing (48): "Birch-Hirschfeld’s group of adeno-angiosarcoma, derived from Wolffian remnants, and the lipomyosarcomas remain, however, the only well-defined varieties of renal sarcoma which have been fully divorced from a probable epithelial origin." Nevertheless, since the kidney contains connective tissue it is perfectly possible for sarcomas to arise therein, and in this mouse material we have
several specimens for which only the diagnosis of sarcoma can be made, after excluding all other possibilities. In doing this we have carefully eliminated numerous growths of doubtful character, some of which also may really be sarcomas. These cases are briefly described as follows:

6. Bilateral sarcoma of kidneys. Male mouse (7667), with both kidneys symmetrically enlarged to equal size, about 17 x 10 x 9 mm. They contained little recognizable kidney tissue, and were for the most part infiltrated by a fleshy, pinkish white tissue which involved equally the cortical and medullary portions. No lesions were found elsewhere. Microscopically both kidneys show infiltration replacing about 80 to 90 per cent of the renal elements. The neoplasm is composed everywhere of slightly oval cells, a little larger than lymphocytes, with deeply staining nuclei and very little cytoplasm. No evidence of neoplastic epithelial or mixed tumor elements can be found. This tissue infiltrates between the tubules much as do the cells in leukemic infiltrations, and the capsule is also invaded. The diffuseness of this infiltrative growth and its equal involvement of both kidneys makes it resemble a leukemia or pseudoleukemia, but this diagnosis is untenable in view of the lack of involvement of other organs or lymph-nodes. The diagnosis of sarcoma is made largely by exclusion.

1 We wish to quote here a statement of the criteria used in our consideration of sarcoma throughout this work as expressed in our paper on Primary Spontaneous Sarcoma in Mice (Jour. Cancer Res., 1917, ii, 1). "We recognize fully the difficulties that attend the differentiation of sarcoma, and for the purpose of this study have excluded every form of new growth concerning the nature of which there seemed any possible room for question. Therefore, we have not included numerous cases in which we think that the growths are probably sarcomatous, and many more in which we cannot be sure that the neoplasm is not sarcoma. On the other hand, the statistical value of our figures is lessened by the fact that we have undoubtedly omitted some growths that are true sarcomas. Our figures represent minimal values only. From the standpoint of investigations in heredity, with which our work is particularly concerned, it is just as undesirable to call a sarcoma something else as to include a granuloma among the sarcomas, and hence the rigid classification adopted in this study of sarcomas is no more satisfactory for our heredity statistics than would be a lax classification that included some growths of doubtful nature. Therefore, in charting the heredity statistics it is necessary to recognize the absence of positive criteria for the differentiation of sarcoma, and to admit the borderline cases with a mark of interrogation to indicate this fallibility."
7. Sarcoma of kidney. Old male mouse (24979), with the right kidney entirely replaced by a tumor, 16 x 12 x 10 mm., which infiltrated the adjacent tissues, including the ureter and the pelvis of the opposite kidney. The regional lymph-nodes were also invaded, and there was a mass in the root of the mesentery about 20 mm. in diameter, which seemed also to infiltrate the pancreas.

Microscopically, the right kidney is found to be almost completely replaced by a growth of large round cells, uniform in size, with very little cytoplasm, but with nuclei much larger than those of lymphocytes. There is no tendency to structural arrangement, the tumor cells infiltrating freely the tissues about the kidney, including the adjacent muscles and the pelvis of the opposite kidney, the ureter of which is surrounded by a mass of tumor. The regional lymph-nodes are replaced by tissue of the same character, but the mesenteric mass is completely necrotic, with few cells resembling those of the tumor. By virtue of its highly infiltrative character and the large size of the cells, this seems to be an undoubted sarcoma. The other tissues showed no evidence of either leukemia or pseudoleukemia.

8. Sarcoma of the kidney. Female mouse (26867) with much sarcoспорidiosis, showed a marked enlargement of the left kidney, which was between two and three times the normal size, and infiltrated diffusely with a pink, fleshy tissue. Elsewhere in the body there were no important changes. Microscopically it is found that the enlarged kidney is infiltrated extensively, nearly all the renal elements being replaced by a tissue composed of round and elongated cells, considerably larger than lymphocytes and with more cytoplasm. They tend to be arranged in wide bands, growing out from the blood-vessels, but this arrangement is not constant or well developed. The neoplastic tissue grows out from the pelvis and tends to invade the adjacent tissues and the hilum of the opposite kidney. No similar tissue is to be found elsewhere in the mouse. The probable diagnosis is primary sarcoma of the kidney.

9. Sarcoma of the kidney. Female mouse (27148), with the right kidney much enlarged (18 x 15 x 32 mm.) and consisting of
a firm tissue overlaid with softer portions. Microscopically we found that the kidney is diffusely infiltrated with a growth consisting of polyhedral cells, smaller than epithelial cells usually are, but with more cytoplasm than lymphoid cells. These cells exhibit no structural organization and have replaced all but a few of the original renal elements. About one-third of the tissue is necrotic. A small amount of the neoplastic tissue infiltrates the hilum of the left kidney, which also shows amyloidosis. No similar tissue is found elsewhere in the body, and there are no evidences of diffuse lymphoid hyperplasia or similar conditions. The lung contains a small benign adenoma.

The tumor shows much variation in the size of the nuclei, hyperchromatism being common, and occasional very large cells are seen. Unfortunately there is too much post-mortem change for exact details to be seen. The general character of the growth and the absence of similar changes in other tissues make a diagnosis of sarcoma seem inevitable.

10. Bilateral sarcoma of kidneys, with metastasis in spleen. Female mouse (306), with the uterus enormously distended with fluid because of vaginal obstruction by a seminal mass, and with great enlargement of both kidneys by a uniform white tissue. The right kidney measured 18 x 13 mm., the left 15 x 13 mm. On the anterior surface of the left kidney is a depressed scar. In the spleen there is a tumor nodule, 4 x 3 mm. No other tumor growths were found. The adrenals were normal.

Microscopically, both kidneys are found to be infiltrated diffusely, with replacement of 80 to 90 per cent of the renal tissue by a growth uniformly composed of small oval cells in solid masses, without any particular organization. No similar tissue can be found in any other organ except the spleen, which has a tumor nodule of the same structure as the renal tumor. The adrenals are in contact with, but not invaded by tumor. The tumor forms large masses in the hilum of one of the kidneys, or within the kidney itself. The left kidney is more involved than the right, and probably was the starting point of the sarcoma.

11. Lymphosarcoma of kidney. Female mouse (13124), with two separate mammary carcinomas, and in the left kidney a
TUMORS IN KIDNEY AND ADRENAL OF MICE

1. A spherical mass about 14 mm. in diameter, which was partly necrotic. Microscopically this growth is composed of a dense mass of small round cells without visible cytoplasm, packed closely together without attempt at formation of any structure. It infiltrates the adjacent renal tissue freely, and there is a small amount of infiltration of the hilum of the opposite kidney. The structure is of distinctly neoplastic character, and there is no similar infiltration of other organs, or lymph-node enlargement, such as characterizes pseudoleukemia. The diagnosis of sarcoma, in structure corresponding to lymphosarcoma, is the only one that can be made on the features presented.

12. Lymphosarcoma of kidney. This seems to be similar to case 11, but unfortunately post-mortem decomposition has advanced so far that accurate microscopic study is not possible. Such tissue as remains stainable resembles a lymphosarcoma. The mouse was a female (12533) with no other tumors, and the right kidney was replaced by a soft pink mass measuring 14 x 12 x 12 mm. A small amount of the same tissue invaded the hilum of the left kidney.

MESOTHELIOMA OF THE KIDNEY

In our previous papers on tumors in the ovary (49) and testicle (50) of mice we have called attention to the not infrequent occurrence of tumors composed of polyhedral cells, presenting some characteristics resembling carcinoma and some resembling sarcoma, (figs. 4, 6, 7 and 8) and hence suitably designated mesothelioma, in accordance with Adami. These tumors are characteristic of the urogenital anlage, and hence it is not surprising that growths of the same structure are found in the adrenal and kidney. We have observed the following cases of renal tumors that seem to belong to this group.

13. This is a remarkable case in that a female mouse (21663), when but one month old exhibited two independent carcinomas of the mammary gland, and osteosarcomatous growths in the spinal column near the pelvis and in the left fifth rib. It lived but eighteen days more and at autopsy showed its left kidney also almost completely replaced by a tumor measuring 18 x 12 x
10 mm.; the right kidney, similarly involved, measured 10 x 6 x 6 mm. (fig. 4). These renal growths are entirely different in structure from the other four tumors. They are alike and vary in appearance in different parts, some portions resembling spindle-cell sarcoma while others are composed of larger, more polyhedral cells, arranged in a somewhat alveolar fashion, often separated by highly vascular septa. This structure corresponds to the type of growth often seen in tumors of the ovaries, testicles,

Fig. 4. Mesothelioma of Kidney

This portion of the growth presents a sarcomatous character; other portions exhibit more resemblance to epithelial growth. The tumor was found in a mouse but one month old, with four other tumors, which if not congenital must have developed very soon after birth. Mouse 21663. × 110.
and adrenals in mice, and agrees with the tumors called mesothelioma by Adami and Woolley. Since, except for this case, there have been very few other cases of malignant tumors arising in mice less than six months of age, the occurrence in so young an animal of at least four independent primary growths representing three distinct types of malignant neoplasm, is a most remarkable condition, without, as far as we know, a parallel in either mouse cancers or in those of any other animal.

14. Male mouse (10011), with no other lesions of importance, had its right kidney largely replaced by a whitish tumor, forming a mass measuring 14 x 12 x 10 mm. Microscopically the tumor has largely replaced the kidney and has infiltrated the capsule in places. It is composed of small cells with a dark, round nucleus and a small amount of cytoplasm. These cells tend to form bands or pseudo-alveoli in some places, but for the most part the growth is composed of cells in a structureless mass. The left kidney was not involved by the tumor.

15. This seems to be similar to case 14. Male mouse (9779) had an enlarged left kidney without other lesions of note. Microscopically the kidney is largely replaced by a mass composed of small cells slightly larger than lymphocytes and with more cytoplasm, showing no structural arrangement. The main neoplastic mass lies at one side of the kidney, which it infiltrates slightly. The kidney itself shows some foci of round-cell infiltration. Some of these areas slightly resemble the tumor, but probably are not a part of it. There are some small areas of calcification, some scars, and numerous hyaline casts. Post-mortem changes are too advanced for more accurate study. The opposite kidney contains no tumor, but there is the same amount of amyloid and calcification.

SARCOMA OF RENAL PELVIS

We have excluded numerous cases in which a retroperitoneal tumor of sarcomatous character has invaded the kidney hilum, but there is one case in which both the gross and microscopical findings distinctly indicate that the tumor had its origin in the tissues of the pelvis itself.
Female mouse (348) had a pale swelling extending downward and inward from the pelvis, composed of tissue of about the same consistency as the kidney and of uniform yellow color. On cross section the pelvis of the kidney was in the center of the mass formed by the tumor and the kidney, which measures 12 x 9 mm. The left kidney was of normal size with a pale area of swelling on the anterior surface. No other changes of importance were found except severe edema of the lungs.

Microscopically the growth is found to lie symmetrically about the pelvis of the kidney and the upper end of the ureter, invading the wall of these structures extensively. From here it passes along the vessels deeply into the kidney, but does not extend far into the cortex. The kidney is about one half as large as the tumor, the tubules being much dilated and the glomeruli more or less hyalinized. The tumor also extends some distance along the renal capsule as a thin layer. As no growths are found elsewhere it is evident that this growth arose in the tissues about the hilum of the right kidney. There is only a small amount of invasion of the left kidney hilum. The growth is composed of large round cells with a delicate reticulum. There are several delicate vessels packed with lymphoid cells, but no other evidences of lymphatic origin in this tumor. The cells of the tumor are polymorphous with considerable cytoplasm, and deeply staining nuclei much larger than those of the ordinary lymph-cell, and usually larger than the nuclei of the renal epithelium. No mitoses are seen. No changes of importance are found in the other organs.

This tumor is much less complex in structure than the cases of sarcoma of the renal pelvis in children described by de Vecchi and Salomon (51).

ADRENAL TUMORS

As mentioned above, no cases of adrenal tumors have hitherto been described in mice. We are able to report a few unquestionable instances of such tumors. Despite the frequency of benign cortical adenomas of the adrenal in man, we have found but one such tumor in mice. It may be recalled that adrenal tumors have not been found frequently in other species of animals.
Cortical adenoma of misplaced inter-renal adrenal rest (fig. 5). Between the kidneys of a female mouse (1921), with marked amyloidosis and chronic nephritis, was found a spherical mass about 5 mm. in diameter, attached neither to the kidneys nor to the intestines. Both adrenals were present at their normal site and were of normal structure and size, except for some peripheral round-cell infiltration.

The tumor nodule is composed of a solid mass of cells resembling those of the adrenal cortex except in lack of orderly arrangement, closely packed together, and flattening out a thin shell of

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**Fig. 5. Cortical Adrenal Adenoma**

The tumor developed in an inter-renal rest of adrenal cortex tissue. A small zone of compressed adrenal tissue is seen at one side. Mouse 1921. ×225.
adrenal cortex, evidently all that remains of an adrenal rest, since no medullary elements are to be found. In all respects this tumor corresponds to the simple adenoma of the adrenal cortex seen in man.

MESOTHELIOMA OF THE ADRENAL

This seems to be the commonest tumor of the adrenal, as also of the testicle, of mice, and it is quite impossible to distinguish on the basis of microscopic appearance between the mesotheliomas arising in the different organs derived from the urogenital anlage. The cases in which the diagnosis seems certain are the following:

1. Male mouse (10390) had in place of the right adrenal a spherical mass 5 mm. in diameter, which is completely encapsulated and does not involve the kidney. No other nodules or findings of importance elsewhere. Microscopically the nodule contains no remains of adrenal tissue, but consists of a solid tumor made up of masses of large cells with considerable cytoplasm and large oval or spherical nuclei, arranged in atypical alveoli or broad bands with a very small amount of stroma containing thin-walled blood-vessels. In numerous places the capsule is infiltrated with tumor cells and there is some invasion of the areolar tissues about the adrenal, but no invasion of the adjacent kidney. This seems to be a typical mesothelioma of the adrenal in an early stage of malignancy.

2. Mesothelioma of adrenal with peritoneal metastasis. Female mouse (12744), with abdomen greatly distended by a bloody exudate, presented at the site of the left adrenal a whitish mass about the size of the kidney. All through the abdominal cavity are masses of partially necrotic whitish tissue, especially attached to the liver and uterus, which do not seem to be involved by this growth. There are enlarged retroperitoneal lymph-nodes, but elsewhere no lymphatic involvement. There are no tumors in the lungs.

Microscopically the tumor shows the usual features of the typical mesotheliomas, as described in the other cases, with slight tendency to alveolar arrangement. It does not seem to have
infiltrated or produced metastases in the viscera. The right adrenal is surrounded, but not invaded, by the tumor and seems normal. The retroperitoneal nodes are replaced entirely by tumor tissue.

This growth surrounded the lymph nodes and was widely disseminated through the perirenal tissues. Mouse 7699. × 110.

3. Bilateral malignant mesothelioma of adrenals (fig. 6). Female mouse (7699) with much subcutaneous edema, showed numerous enlarged subcutaneous lymph-nodes, some red and some pale, the largest measuring as much as 8 x 10 mm. There was a milky fluid in the peritoneal cavity, presumably because of pressure of enlarged lymph-nodes on the thoracic duct, for
the retroperitoneal nodes were greatly enlarged, up to 6 x 12 mm. The mesenteric nodes were also enormously enlarged, one mass at the root of the mesentery measuring 40 x 20 x 20 mm. Both adrenals were greatly enlarged, each being about the size of the kidney, which was adherent to the adrenal but not enlarged or infiltrated by neoplastic tissue. The uterus seemed to be infiltrated by tumor. The liver was not affected, and the lungs showed only a single small nodule, although there was some tissue increase in the upper mediastinum; both lungs showed a bloody edema, and there was a bilateral hydrothorax.

Although the gross appearance suggested a general lymphosarcomatosis or pseudoleukemia, yet the microscopic structure is of an entirely different character. Everywhere the neoplastic tissue presents the same appearance, being composed of a solid growth of cells with considerable cytoplasm, so that they look much like epithelium. The nuclei, which vary greatly in size, are much more solid than those of epithelial cells usually are. Mitotic figures are abundant. The invaded lymph-nodes are largely replaced by tumor cells, which are also found in the lymph-vessels of the lungs, but not in the liver. Both adrenals seem to be entirely replaced by the tumor, which lies upon the capsule of the adjacent kidney without any invasion of this organ. There are some areas of hemorrhage, but not much necrosis. The cells show no attempt at definite arrangement, but simply form a solid mass with numerous, poorly defined blood spaces.

This tumor resembles in structure other growths found arising in the urogenital anlage, and in view of this and of the complete replacement of both adrenals it is most probable that it did arise in these tissues, although the extensive lymph-node involvement is unusual in adrenal tumors. The structure is not essentially dissimilar to that of the adrenal tumor 10390, except for the amount of extension.

**UROGENITAL MESOTHELIOMAS OF UNCERTAIN ORIGIN**

Because of the identity in appearance of mesotheliomas from all organs originating in the urogenital anlage, it is not always
possible to decide the place of origin of some tumors which involve two or more of these organs, as shown by the following cases.

12307. Mesothelioma of either adrenal or ovary. It is not possible to determine the origin of this tumor, which we have described in our paper on tumors of the ovary in the following words:

The abdominal cavity shows several nodules whose exact origin is difficult to determine as the mate has partly devoured the body. The right ovary is, however, easily distinguished. It measures 18 x 12 x 12 mm. What seems to be the left ovary is 10 x 8 x 6 mm. There are 8 other similar nodules in the abdominal cavity, one being in the position of the left adrenal, measuring 10 x 8 x 8 mm. The other nodules are apparently in the mesentery. One lobe of the liver is converted into a tumor nodule 14 x 10 x 18 mm., irregular and lumpy in outline, pink in color.

The tumor shows everywhere the same structure, consisting of irregular alveoli composed of large cells with abundant cytoplasm with well defined borders and deeply staining nuclei. Mitotic figures are numerous. The character is that usual to mesothelial growths. The ovary cannot be positively identified, but one mass exhibited in the capsule structure suggests compressed ovarian tissue with degenerated ova. In all respects this tumor is identical with the malignant ovarian tumors just described.

It seems probable that this tumor arose in the ovary which exhibited the largest growth, but it is not possible to exclude the adrenal as the primary site.

The malignant tumors of the adrenal, ovary, and testicle commonly exhibit identically the same histological picture as that seen in this case.

We have also observed two other cases, described in the paper on ovarian tumors in which we cannot state whether the renal growth was primary or secondary.

12876. The left kidney contained a mass of pink, fleshy tissue, 18 x 14 x 14 mm. The right kidney, which was slightly enlarged, contained no tumor. The right ovary consisted of a pinkish tissue resembling that in the kidney, and measured
12 x 8 x 8 mm. In the mesentery was a similar, slightly paler mass, 16 x 8 x 8 mm. The retroperitoneal and subcutaneous nodes were not enlarged and no nodules were found in the lungs.

Microscopically the tumor is alike in all three places, consisting of a diffuse infiltrating growth of large round cells, which also invade the connective tissues about the kidney and ovary. It does not at all resemble the typical ovarian tumors, being apparently a round-cell sarcoma. We have no way of telling which of the three tumors was primary. The next case presents similar difficulties.

26. This mouse had a tumor mass about 8 x 10 mm. in the upper portion of the liver, with other smaller nodules near it. A similar small nodule was found in the right kidney. The right ovary was enlarged to two-thirds the size of a kidney, and was solid. Microscopically all these growths are composed of round cells, apparently a round-cell sarcoma. It is impossible to say which growth was primary.

Among several tumors arising in the retroperitoneal tissues, mostly of sarcomatous type, are a few of a structure identical with the characteristic mesothelioma type of growth that arises in the urogenital anlage. In the two cases described below this character of growth was so marked that it seems probable that the tumors have arisen in some misplaced embryonic rest, since the organs of this series were distinctly not the starting point of the growths. Numerous tumors of this sort have been described in man.

(22380) Malignant retroperitoneal mesothelioma with extension through the body wall. Male mouse presenting externally a subcutaneous tumor, involving the left hip and extending to the anus, the external measurements being 30 x 25 x 25 mm. When the body was opened it was found that this mass was an extension of a huge mass (40 x 20 x 18 mm.) which had surrounded the left kidney and pushed it to the ventral midline, invaded the spleen and pushed it mostly to the right of the midline by formation of a mass that measured 20 x 15 x 13 mm., and extended downward through the pelvic cavity where it surrounded the rectum and seminal vesicles and broke out through the
body wall. There was slight infiltration of the lower pole of the right kidney. The liver was slightly enlarged and mottled with areas of infiltration. There was some tumor in the lower part of the mediastinum, and the lungs show many small spots of neoplastic tissue. There seemed to be no involvement of the lymph-nodes, either subcutaneous or abdominal. The testicles were not involved.

Microscopically the tumor everywhere consists of masses of large cells with much deeply staining cytoplasm, somewhat resembling liver cells, with a slight tendency to arrangement in

**Fig. 7. Secondary Mesothelioma in Liver**

The primary growth was either in the adrenal or in a retroperitoneal embryonic rest; it infiltrated the body wall and retroperitoneal tissues, and produced innumerable metastases in the lungs and liver. This section shows the masses of tumor cells compressing and replacing the larger liver cells. Mouse 22380. ×110.
cords or bands. Where the tumor invades the liver it can be seen that the cells are a little smaller and paler than the liver cells (fig. 7).

The growth infiltrates the liver widely, invades the muscle of the body wall, invades the renal capsule but not the kidney, infiltrates the abdominal sympathetic ganglia, surrounds densely the rectum and spreads into the seminal vesicle, invades the spleen, and in the lung appears as multiple tumor cell emboli within the vessels and as large tumor nodules largely replacing portions of the lung (fig. 8). The left adrenal was found entirely embedded in but not infiltrated by the tumor.
The microscopic appearances are identical with those usual in malignant adrenal tumors, but the adrenal was not involved; and in view of the retroperitoneal origin, the growth may be presumed to have arisen in an embryonal rest of the urogenital anlage.

(9979) Malignant retroperitoneal mesothelioma infiltrating kidneys. Small female mouse with extensive infiltration of the right thigh by a typical spindle-cell sarcoma, and with a mass above the left kidney, about as large as the kidney itself, which was infiltrated by the growth. The entire mass measured 20 x 14 x 10 mm. The right kidney was not so much enlarged. The growth seemed to have arisen at the site of the left adrenal, and to have pushed the kidney forward. The liver was invaded by tumor and enlarged. No metastases were found elsewhere. Microscopically the tumor about the kidney bears no resemblance to the spindle-cell sarcoma of the thigh, being composed of a mass of polyhedral cells arranged in solid masses, with a slight tendency to form bands or cords. The nuclei are not much larger than those of lymphocytes, but the cells have much more cytoplasm. The chief mass lies above and behind the left kidney, which shows considerable invasion through the capsule and about the blood vessels. There is a similar invasion of the right kidney but much less tumor about it. The right adrenal cannot be located; the left is free from tumor although there is a necrotic area between it and the kidney. The liver shows a large nodule of the same sort of tumor.

SECONDARY TUMORS OF THE KIDNEYS AND ADRENALS

The mouse kidneys seem to be extremely insusceptible to metastatic invasion by tumors. In our entire series of primary tumors of mice, now in the neighborhood of 5000 cases, of which the predominating form is carcinoma of the mammary gland, we have never met with a metastatic growth from one of these tumors into the kidneys, with one possible exception, despite the frequency of pulmonary metastases, which often replace most of the lung. The only metastatic carcinomas of the kidney that we have seen have been found
in four cases of primary carcinoma in the lung (3098, 11777, 12373, 14242). A photograph of the first of these four cases appears in our paper on lung tumor (52). These carcinomas of the lung are especially likely to produce extensive metastases, and the suggestion of some authors that these pulmonary growths in mice should not be included among the true tumors is evidently based on ignorance of their character. The fact that they have furnished our only instances of metastatic carcinoma in the kidney is sufficient evidence of their true neoplastic character and the high malignancy of some types.

Although we have seen many instances of widespread metastasis in sarcoma, the kidneys are almost immune from vascular sarcoma embolism. In our series of 87 cases of sarcoma in mice, although 23 showed metastasis but one hematogenous secondary nodule was found in the kidney, this coming from a mediastinal sarcoma (11791). Since then we have seen one other case of vascular metastasis of sarcoma into the kidney, from a sarcoma of the uterus (12058), with a large nodule of the same structure almost replacing the lower pole of the right kidney, and metastasis in the right ovary. Even the widespread growths of small round cells, which resemble the condition called lymphosarcomatosis in man, seem to affect the kidney but little, for among a considerable number of such cases we have but one with a distinct metastatic nodule in the kidney (7572), although several cases show extension from retroperitoneal metastases into the capsule, and then into the kidney. On the other hand, the kidneys exhibit extensive diffuse infiltration in leukemia and massive perivascular growths in pseudoleukemia in mice as in man.

The malignant retroperitoneal growths, most of which resemble lymphosarcoma, and the malignant tumors derived from the adrenals, commonly invade the kidney by direct extension into the hilum, often very extensively. The sarcomas primary in one kidney also tend to spread into the hilum of the opposite kidney. This ready invasion of the hilum of the kidney is a point of similarity of human and mouse neoplasms.
No instance of tumor metastasis into the adrenal has ever been observed, except possibly in the few cases of widespread mesotheliomatous growths invading both the ovaries and adrenals, the origin of which is uncertain.

**SUMMARY**

In a series of 33,000 autopsies on mice of the Slye stock, dying natural deaths at all ages, but as far as possible living out their natural span of life, there have been observed the following cases of true primary neoplasm arising from renal or adrenal tissues: First, from the kidney, 16 tumors, classified as follows: 1 carcinoma, 3 adenomas, 1 hypernephroma, 7 sarcomas, 3 mesotheliomas, and 1 sarcoma of the renal pelvis. Second, from the adrenal, 4 tumors, as follows: 1 cortical adenoma from a misplaced inter-renal adrenal rest, 3 mesothelial tumors. Third, five cases of tumors of the mesothelial structure characteristic of urogenital anlage neoplasms, but of which the exact origin could not be determined because of their widespread growth at the time of death. As these 25 tumors occurred in 33,000 mice presenting not far from 5000 other tumors, they are evidently uncommon tumors of mice, at least in this particular stock.

It will be noted that in this series there has been no instance of a mixed renal tumor of the Wilms type, which is so common a type of renal tumor in man and apparently also in swine. Although inflammatory conditions are very prevalent in the kidneys of mice, epithelial tumors are rare, and especially to be noted is the absence of even a single case of typical malignant hypernephroma, although one benign growth of this type was found. No epithelial tumors of the renal pelvis were found, although there was one case of sarcoma that seemed to take its origin in the pelvis.

Several instances of malignant retroperitoneal tumors have been observed, mostly of sarcomatous structure, which usually invade the kidney. These have not been included in this series, except two cases in which the structure resembled that of the
mesotheliomas, suggesting that the tumor had its origin in mis-
placed rests of the urogenital anlage.

Secondary tumors have never been found in the adrenals,
and but rarely in the kidneys. Although this series includes at
least 3000 cases of mammary carcinoma, often with widespread
metastases in the lungs, we have never seen a secondary carcino-
matous growth in the kidney. The only secondary carcinomas
of the kidney as yet observed are four cases in which the
primary carcinoma was in the lung, thus establishing the true
neoplastic nature of these lung growths. In but two cases have
metastatic sarcomas been seen in the kidney, if we exclude the
numerous cases of invasion of the kidney by direct extension
from para-renal growths.

As to sex: In the entire group of renal and adrenal tumors, we
have equal numbers in males and females, agreeing with the
observation made on other tumors in mice that, in tumors not
peculiar to the sex glands, there is usually little difference in the
incidence in the two sexes.

Differing from the tumors previously studied, coincidence of
other tumors with the renal and adrenal tumors is uncommon.
One mouse in this series had a spindle-cell sarcoma of the thigh.
One mouse had a small, benign papillary adenoma of the lung.
Only two mice had a mammary carcinoma, and one of these
(21663) was a remarkable case, for this animal, when but one
month old, was found with two independent mammary carcinomas,
and with osteosarcomas in the spinal column and in a rib.
It lived eighteen days more, and at autopsy there was also found
a mesotheliomatous type of growth involving both kidneys.
Except for this unique case there have been practically no in-
stances of malignant tumors in mice less than four months of
age, and few under six months. Most of the renal sarcomas
occurred between the ages of seven months and one year, which is
somewhat earlier than the usual time of appearance of epithelial
growths; this, of course, corresponds to experience with human
neoplasms.

The epithelial renal and adrenal tumors furnished no illustra-
tion of metastasis, but in three cases of sarcomatous or meso-
theliomatous growths there was noted involvement of the adjacent lymph-nodes; in two there were pulmonary, in two hepatic, and in one splenic metastasis, and in one case there were numerous peritoneal growths. The mesothelial type of growths produced the most extensive metastasis and the most widespread infiltration of the body wall.

A review of the literature on renal tumors throughout the animal kingdom, which constitutes the introductory part of this article, discloses but six other cases of renal tumors in mice, all epithelial, and no other adrenal tumors.

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