SPONTANEOUS TUMORS IN THE ROCHESTER STRAIN OF THE WISTAR RAT*

RICHARD C. CRAIN, M.D.

From the Division of Pharmacology, Department of Radiation Biology and the Department of Pathology, University of Rochester School of Medicine and Dentistry, Rochester, N.Y.

The increasing demand for long term toxicity studies of rats has stimulated the interest of the pathologist and toxicologist in the spontaneous disease processes and neoplasms that arise in old rats. To evaluate the possible carcinogenic effect of compounds under study, the spontaneous tumor incidence must be known for the strain of rat being used. It is the purpose of this paper to describe 200 spontaneous tumors found in 786 albino rats† 18 to 24 months old (Table I).

From what has been written of spontaneous tumors in rats, it is evident that considerable variation exists in type and frequency of tumors in different strains and species. In one of the earlier papers on the subject, written in 1909, McCoy[1] described 103 tumors in a group of 100,000 wild rats of the species *Mus norvegicus*. Bullock and Curtis,[2] in the course of the experimental production of sarcoma of the liver in rats by feeding cat tapeworm larvae, examined 31,868 rats and found 521 primary spontaneous tumors in 489 rats. Ratcliffe,[3] in 1940, described 302 spontaneous tumors found in 273 rats of the Wistar Experimental and Stock Colonies. Saxton, Sperling, Barnes and McCay[11] reported 234 spontaneous tumors in 498 albino rats of the Osborne-Mendel (Yale) strain. Other reports have described a small series of tumors limited to one organ system or an unusually high incidence of one particular type of tumor.

MATERIAL AND METHODS

The rats used represented 11 different 2-year toxicity studies conducted over a span of 6 years. Of the 786 rats examined for tumors, 139 were fed control diets while the remainder received an experimental diet judged not to be carcinogenic as determined by comparison with simultaneous control groups. A description follows of the usual organization of a 2-year feeding study.

Groups of 30 to 50 male and 30 to 50 female rats of the Rochester strain were assembled by random sampling at the time of weaning.

* This paper is based in part on work performed under contract with the United States Atomic Energy Commission at the University of Rochester Atomic Energy Project, Rochester, New York.

Received for publication, July 11, 1957.

† The Rochester albino rat was obtained from the Wistar Institute in 1923.

TABLE I

Summary of Spontaneous Tumors

Tumors	Control male	Control female	18 to 24-month male	18 to 24-month female	Total
Breast					
Fibroadenoma		11		42	53
Adenoma				5	5
Cystadenoma		1		3	4
Fibroma		1		1	2
Carcinoma		1			1
Skin and subcutaneous tissue			2	2	4
Mesenteric lymph nodes	4	1	14	4	23
Lung					
Lymphoma, malignant	1		10	7	18
Fibrosarcoma				2	2
Kidney					
Papillary cystadenoma			1		1
Lipomatous hamartoma				1	1
Adrenal					
Medullary adenoma			5	5	10
Uterus					
Leiomyoma				2	2
Mesodermal tumor		1		6	7
Adenocarcinoma		1		2	3
Liver					
Undifferentiated spindle cell tumor				1	1
Ovary					
Fibroma		1		2	3
Adenocarcinoma				1	1
Testis					
Interstitial adenoma					
Unilateral	4		26		30
Bilateral	1		4		5
Pituitary adenoma	1	2	1	7	11
Alimentary tract					
Mucoid carcinoma			1		1
Adenocarcinoma		1		1	2
Squamous cell carcinoma			1		1
Thyroid adenoma			1	1	2
Lipoma			1	1	2
Miscellaneous			1	4	5
Number of rats	55	84	279	368	786
Tumor bearers	11	20	64	94	189
Number of tumors	11	21	68	100	200

Groups were matched initially for body weight and maintained thereafter on the control and experimental diets for 2 years. In most instances there were 4 equal groups of each sex, one control group and 3 dietary levels of the compound being tested. The control diet consisted of Purina Fox Chow meal. For the experimental diet the test product was mixed with control food by machine. Rats were generally housed 5 to a cage in metal cages with wire doors; the bottom pan was filled with wood shavings. Food and drinking water (Rochester tap water) were supplied *ad libitum*. A program of serial sacrifice was instituted whereby a small number (10 per cent) were sacrificed and necropsied at 6 month intervals. Microscopic examination was carried out upon tissue from all major organ systems. The animals were weighed weekly throughout the experiment; at necropsy, individual organ weights were recorded. Animals which died naturally during the first 18 months of the study were necropsied to determine the cause of death, but sections were seldom taken. During the last 6 months (18 to 24 months), however, whenever an unusually high mortality had been noted, moribund animals were sacrificed and complete gross and microscopic examinations were performed on each to insure that a sufficient number of tissues would be available at the termination of the study for meaningful comparison. The animals were sacrificed by decapitation and tissue samples were taken of heart, lung, spleen, stomach, small intestine, large intestine, pancreas, liver, adrenal, both kidneys, bladder, gonad, bone marrow, brain and thyroid. In addition, any tumor or unusual appearing tissue was sectioned for histologic study. Tissues were fixed in Zenker's solution with acetic acid, and sections were stained with hematoxylin and eosin.

Results

Tumors of Mammary Gland

Spontaneous mammary tumors constituted the largest single group of neoplasms in this series, accounting for 65 of the 200 tumors. It was difficult to draw comparisons with previous studies recorded in the literature because of variation in the criteria for selection. However, it was evident that mammary tumors were prevalent in many strains. Bullock and Curtis[2] reported an incidence of mammary tumors of 18 per cent among 521 tumors. Ratcliffe[3] reported an incidence of 75 per cent among 302 tumors found in rats at the Wistar Institute. The selection of rats in the latter study depended upon visual external recognition of body tumors; consequently mam-

mary tumors would be expected to constitute a greater proportion. Bryan, Klinck, and Wolfe[4] reported an unusually high incidence of 51 per cent among 51 female rats of their colony. This study was followed by further work on the same colony by Wright, Klinck, and Wolfe[5] showing a reduced incidence of breast neoplasms, with approximately 11 per cent among 1,827 rats over 5 months of age.

By the nature of the normal concentration of mammary glands at the cephalad and caudad ends of the mammary line, mammary neoplasms were most commonly encountered in these regions. Wright and co-workers[5] noted that roughly two thirds of the mammary tumors they encountered were in the axillary regions of the foreleg while the remainder were near the groin. There was about equal distribution between the right and left sides.

In the study reported here, no record of tumor site was kept. Most of the neoplasms were single; a small number of animals had two separate neoplasms and one rat had 3 fibroadenomas. The lesions varied greatly in size, some measuring less than a centimeter while the largest tumor weighed 256 gm. It appeared that these tumors were well tolerated by the animal until they approached half the total weight of the rat; thereafter the rat began to lose weight and became moribund.

Mammary tumors usually appeared as ovoid, spherical or occasionally discoid masses; they were covered by the skin but usually not attached to it. The tumors were nodular, firm, and elastic to compression. Some of the larger lesions showed loss of hair at points of friction, or ulceration with secondary infection. The bearers of large tumors frequently showed marked emaciation and body deformity and had locomotor difficulties. When exposed, the lesions were lobulated and surrounded by a capsule. The cut surfaces pouted above the capsule and gave the classical whorled silk appearance observed in leiomyomas of the uterus. Some of the larger tumors exhibited focal hemorrhage, necrosis, and cystic degeneration probably resulting from insufficient blood supply.

Histologically, the tumors ranged from fibromas consisting entirely of connective tissue to adenomas of solid glandular content (Fig. 2). The fibroma of mammary origin differed from dermal fibromas in the presence of rare isolated ducts and glands in the stroma. The intermediate range was represented by various combinations of glandular and stromal elements designated as fibroadenomas (Fig. 2). Depending on the arrangement of the glandular elements, the lesions were designated as cystic or papillary. Of the 65 breast tumors, 4 were classified as cystadenomas (Fig. 3), and one of these showed a

papillary arrangement of the glandular elements (Fig. 4). In some cases cystic, papillary, fibrous and adenomatous variations were all seen in different portions of the same tumor. Wright and co-workers[5] described intracanalicular and pericanalicular fibroadenomas; these were not seen in our animals.

The criterion for malignant neoplasm was the demonstration of metastasis. The sole example of malignant tumor in this group was a lesion histologically indistinguishable from the benign cystadenoma, but a metastasis was found in the lung.

Tumors of Lymph Nodes

A group of lymph nodes draining the ascending colon and situated in the ileo-colic mesentery was the site of one of the most common tumors encountered in this series, a malignant lymphoma (Figs. 5 and 6). The tumor has been variously known as polymorphous cell sarcoma, lymphoblastic lymphosarcoma, and reticulum cell sarcoma, all of which fall under the same family heading of malignant lymphoma. Although lymphomas were most commonly seen in cecal lymph nodes and occasionally as metastatic lesions disseminated over peritoneal surfaces, the peribronchial lymphoid tissue also was a frequent site for this tumor. Some lymph nodes contained a small nidus of malignant neoplasm in one portion of the node. In other instances there were varying degrees of alteration of architecture ranging to complete replacement of the node by neoplasm. Total replacement occurred in most cases. Cecal lymph nodes and peribronchial lymphoid tissue have been found to be frequent sites of lymphoid hyperplasia, accompanying ulcerative cecitis[6] in the former and bronchiectasis, bronchitis and bronchopneumonia in the latter.[7] The high correlation between the incidence of lymphoid hyperplasia and occurrence of tumor has led to speculation concerning the character of the neoplasm and the role played by inflammation in its production.

Saxton and co-workers[11] reported 91 cases of lymphosarcoma of the lung among 234 tumors. Bullock and Curtis[2] found that malignant lymphoma accounted for 78 of the 521 tumors in their group of animals. Of the 200 tumors examined in this study, 41 were of lymphomatous nature. In 23 rats cecal nodes were the seat of the lesion; some of these rats had lymphoma in the pulmonary lymphoid tissue as well. Lymphoma of peribronchial origin alone was seen in 18 rats. The cecal lymphomas sometimes occurred as nodular masses in the mesentery, attaining a size of several centimeters in diameter. They were contiguous with the cecum or appeared as several separate

nodules. In some cases, the tumor invaded the wall of the cecum, or by peritoneal metastasis, reached the serous surfaces of stomach, pancreas, adrenals, kidneys, liver and spleen. In one case, lymphoma was found to be widely distributed throughout the liver with compression and necrosis of hepatic tissue. Lymphomatous lesions in the lung were not easily recognized grossly and were frequently mistaken for inflammatory lesions.

To gross examination, the lymphoma appeared gray-white and soft, and the masses were prone to develop necrosis, cystic degeneration and hemorrhage. The histologic appearance was similar in all and was characterized by large loosely arranged cells containing scant cytoplasm and large, irregular nuclei of varied size. The chromatin was heavy and irregularly clumped. Bizarre mitotic figures were numerous and nucleoli were large and frequently multiple. The nuclear membrane was heavy and the nuclei were round, oval, lobulated, or polyhedral in configuration. The cells formed no consistent pattern but were separated by a vascularized loose connective tissue (Figs. 5 and 6).

Tumors of the Testis

Reports of testicular neoplasm in rats are uncommon. Bullock and Curtis[2] reported one testicular tumor which proved to be similar to those encountered in our colony. Gilman, Gilbert and Spence[8] referred to a high incidence of interstitial cell adenomas of the testis in rats of the Wistar strain. Saxton and co-workers[11] reported one interstitial cell tumor and one embryonal carcinoma of the testis.

Testicular adenomas comprised a substantial portion of the present series. There were 35 of these among the 200 tumors. The lesions were generally small and did not extend beyond the confines of the *tunica albuginea*. When the existence of neoplasm was recognized grossly, the involved testis was brown and soft. The contralateral testis was occasionally atrophic, but in 5 of the 35 cases the opposite testis also contained an adenoma.

The tumors appeared to originate from small nests of hyperplastic interstitial cells which presumably multiplied gradually, causing compression and atrophy of adjacent tubules. The adenomas were formed of solid sheets of cells with distinct outlines and abundant acidophilic cytoplasm filled with numerous small vacuoles (Figs. 7 and 8). In some areas, the vacuoles were prominent, giving the cell the foamy appearance of a lipid-filled macrophage (Figs. 9 and 10). In other regions, the vacuoles were very small and indistinct. Nuclei were uniform in size and had dark nuclear membranes. Chromatin was not prominent; occasional mitotic figures were noted. Scattered de-

posits of yellowish-brown pigment were evident in many of the smaller tumors.

In the larger tumors, two different cell types were evident. The characteristic cell with foamy cytoplasm formed nodules of varied sizes, surrounded by smaller compact cells with scanty, ill-defined cytoplasm and uniform small dark nuclei. Collections of golden-brown pigment were numerous in these peripheral areas. Large vascular sinusoids appeared within the tumors and red cell extravasation was a common finding. No extension beyond the testis was encountered (Figs. 9 and 10).

Tumors of the Adrenal Glands

Bullock and Curtis[2] described only 4 adrenal tumors resembling those encountered in this study. Staemmler[9] observed focal hyperplasia of the adrenal medulla in rats but considered this to be a result of nicotine poisoning. Yeakel[10] examined the adrenal glands of 16 female and 15 male rats of the Wistar strain and 3 male and 3 female gray Norway rats, all over 700 days old. Thirty-six glands from females of both species were available for study. Hyperplastic changes of the medulla were noted in 11 per cent. Fifty-one per cent of the 35 glands from males of both species showed similar hyperplasia. Saxton, Sperling, Barnes and McCoy[11] reported the occurrence of 5 tumors of the adrenal glands in 498 rats. Recently, Gilman and coworkers[8] reported a study of 167 male and 189 female rats from the Wistar Institute with an age range from one month to more than 2½ years. The adrenal glands of these rats were carefully examined microscopically. The incidence of medullary hyperplasia or adenoma varied between 50 and 76 per cent in female rats 13 to 30 months old, and 82 to 86 per cent in male rats in the same age range. These investigators used the term "phaeochromocytoma" to designate the tumors of the medulla and suggested a possible relationship to the high incidence of chronic myocarditis, hepatic necrosis, and endocrine tumors (interstitial adenoma of testis, fibroadenoma of breast, thyroid adenoma, and pituitary adenoma) found in their series.

Ten medullary adenomas were encountered among our own animals. In most cases, the tumor was not recognized on gross examination. The frequency with which the adrenals of old rats were enlarged, cystic, and sometimes hemorrhagic as the result of acute infections made size a dubious criterion in detecting small adenomas.

The smallest adenomas appeared as small clusters of intensely basophilic cells in the medulla. The sparse cytoplasm and marked basophilic staining of the nuclei were in distinct contrast to adjacent

medullary elements (Fig. 11). The larger tumors formed nodular clusters about sinusoids; occasionally there were multiple clusters in separate portions of the medulla. The largest medullary tumors caused compression and narrowing of the cortex. Indeed, the largest in this series, measuring 1 cm. in diameter, had penetrated the cortex and capsule into the adjacent perirenal fat. In this, the nuclei were larger, vesicular and less basophilic, and the cytoplasm more abundant and more clearly demarcated. The difference in cell type was not a regular feature and considerable variation was encountered. The cells of the small adenomas were arranged in solid cords separated by a delicate capillary network, whereas in the larger tumors the vascular network consisted of large sinusoids and venous lakes. Frank invasion was not observed in this study, although Gilman and co-workers[8] reported direct extension of the tumor into the inferior vena cava and embolization to the lung.

The necropsy sections and the organ:body weight ratios of the rats in this series were analyzed in an effort to establish a correlation between possible pressor substance secretion by the adrenal tumors and cardiovascular alterations. All but two of the heart weight:body weight ratios were within or below the normal range. In the two rats in which this range was exceeded, only microscopic adenomas were present, and there were no other necropsy findings to indicate either an endocrinopathy or cardiovascular disease.

Another tumor of the adrenal, seen in a rat under 6 months of age, has been included in this report because of its unusual nature. This lesion most nearly resembled a neuroblastoma. It originated in the left adrenal medulla and invaded the spleen and adjacent peritoneum. The splenic metastases consisted of several nodules of friable gray-white tissue which varied from 0.6 to 1.8 cm. in diameter. The largest nodule was hemorrhagic and necrotic and accounted for the presence of free blood in the peritoneal cavity. The tumor was cellular and its nuclei were variable in size and shape. In a few areas, tumor cells were arranged in rosettelike fashion.

Tumors of the Uterus

Bullock and Curtis[2] found the uterus of the rat to be a common site of neoplasm. They reported 48 tumors of this organ with the following structure: "leiomyoma, 4; myosarcoma, 2; fibrosarcoma, 2; polymorphous cell sarcoma, 2; spindle cell sarcoma, 1; mixed cell sarcoma, 16; papilloma, 1; squamous cell epithelioma, 10; adenocarcinoma, 4; adenoacanthoma, 1; carcinoma, 1; carcinosarcoma, 4." Ratcliffe[3] reported 10 tumors of the uterus.

In the present series, 12 of the 200 tumors were of uterine origin and were characterized as: leiomyoma, 2; mesodermal tumor, 7; adenocarcinoma of the endometrium, 3. Most of these lesions were not described grossly. The leiomyoma was a well circumscribed nodule composed of interlacing bundles of smooth muscle and fibrous tissue with considerable uniformity of cell type.

The group of mesodermal tumors showed variation in cell type and numerous cystic areas (Figs. 12 to 15). The predominant cells were primitive mesenchymal elements with oval, stellate, and spindle-shaped nuclei. Portions of some mesodermal tumors were composed of bizarre giant multinucleated cell forms. There was considerable variability of cell type and no correlation with the occurrence of metastasis.

The cases of adenocarcinoma of the endometrium showed widespread metastases to the peritoneum, lung, and liver. The tumors exhibited considerable necrosis and marked acute inflammatory reaction (Fig. 16).

Tumors of the Kidney

The series reported by Bullock and Curtis[2] included 6 embryonal carcinomas, 1 carcinoma, and 1 sarcoma of the kidney. Eker[12] reported a group of renal adenomas in Wistar rats 6 to 16 months of age. These appeared as simple cysts, papillary cystadenomas, solid eosinophilic adenomas, and solid basophilic tubular adenomas and varied in size from barely visible nodules to 0.8 cm. In Eker's series, the adenomas appeared to arise from tubules, and none contained glomeruli.

In the present series there were only 3 renal tumors. One was a papillary adenoma of the cortex which was not recognized grossly and appeared microscopically as a small cystic space lined by papillary invaginations of plump epithelial cells. A second lesion designated as a lipomatous hamartoma showed numerous reduplicated folds of pelvic epithelium. The cortex and medulla of one portion of the kidney were replaced by fat that blended with normal appearing renal parenchyma on either side (Fig. 17). Isolated tubules and glomeruli were present within the fatty portion. A third tumor was included in this report because of its infrequent occurrence even though the rat was only slightly over one year of age. This was an embryonal carcinoma of the upper pole of the left kidney. It measured 0.3 by 1.8 by 1.5 cm., was grayish-brown and did not appear to have invaded adjacent structures. Microscopically, the tumor showed structures resembling tubules and glomeruli (Fig. 18).

Tumors of the Pituitary

Chromophobe adenomas of the pituitary accounted for 92 of the 234 spontaneous tumors reported by Saxton and co-workers.[11]

Eleven adenomas of the pituitary were identified in this series. No gross description of these tumors was recorded. All the lesions were similar histologically although there was variation in vascularity (Fig. 19). The tumors were composed of cords of plump basophilic cells separated by a delicate reticulum and congested vascular spaces. The cytoplasm was scant and poorly defined. Nuclei were large, oval or round and had prominent nuclear membranes with a light sprinkling of chromatin. Many nuclei contained a prominent central nucleolus. Deposits of brown pigment resembling hemosiderin were present in the cytoplasm of some of the cells and within vascular sinusoids. There was no invasion of adjacent structures. Mann's stain showed no chromophilic element in these adenomas.

Tumors of the Thyroid Gland

The 2 thyroid adenomas encountered may not accurately reflect the incidence of thyroid neoplasm since sections of thyroid were made in only 24 per cent of the necropsies. The tumors of the thyroid gland reported by Bullock and Curtis[2] included 1 adenoma and 1 carcinoma.

One of the adenomas consisted of solid cords and tubes of uniform large cells separated by delicate strands of connective tissue. The cytoplasm was abundant, granular, and pink staining, and the nuclei were large and vesicular. Small amounts of colloid were present in portions of the adenoma (Fig. 20). A second well-circumscribed adenoma revealed marked compression of the acini in a narrow rim of remaining thyroid about the periphery of the nodule. The tumor was very similar to the first example.

Tumors of the Alimentary Tract

Gastrointestinal neoplasms were not common. Bullock and Curtis[2] reported 1 adenocarcinoma of the stomach, 10 cecal tumors, 1 fibroma of the jejunum, and 9 sarcomas of the stomach. Willis[13] reported 2 examples of adenocarcinoma of the colon in albino rats. Saxton and co-workers[11] reported one squamous cell carcinoma of the stomach.

Four neoplasms of the alimentary tract were identified in this series. A squamous cell carcinoma of the esophagus was composed of nests of large irregular squamous cells which invaded peri-esophageal tissues. Pearl formation and desmoplasia were prominent features

of this tumor (Fig. 21). A second tumor was an adenocarcinoma of the colon which almost completely filled the lumen and invaded the wall and mesenteric fat. Focal areas of necrosis were accompanied by large numbers of acute inflammatory cells. Neoplastic acini were irregular and lined by pseudostratified columnar epithelium with large, hyperchromatic nuclei and numerous mitotic figures (Fig. 22). A third tumor was an adenocarcinoma of the stomach which invaded the adjacent mesentery. There were large areas of necrosis, and neoplastic acini were composed of pleomorphic cells with hyperchromatic nuclei. Bizarre mitotic figures were numerous. A mucoid carcinoma of the stomach was the fourth neoplasm. The tumor invaded the stomach wall and was characterized by large amounts of mucin, scattered signet ring cells and occasional acini (Fig. 23).

Tumors of the Ovary

Bullock and Curtis[2] reported 5 tumors of the ovary: a fibroma, a bilateral sarcoma, and 3 cystadenocarcinomas. Ratcliffe[3] found 3 carcinomas of the ovary. Saxton and co-workers[11] reported 5 adenomas and 2 fibromas of the ovary.

In the present series there were 3 neoplasms. One was a fibroma, not recognized grossly. This tumor was composed of large cells with little or no cytoplasm and moderately uniform oval or round nuclei. Occasional mitotic figures were seen. A second fibroma, similar to the first, measured over 2 cm. in diameter and showed large areas of necrosis in its center. The third tumor was a papillary serous cystadenocarcinoma, 2 cm. in diameter. The neoplasm was composed of branching papillary septae covered by cuboidal and columnar epithelium (Fig. 24). Peritoneal implants had occurred.

Tumors of Skin and Subcutaneous Tissue

Both benign and malignant neoplasms of skin and subcutaneous tissue comprise a substantial number of spontaneous rat tumors reported by other investigators. Bullock and Curtis[2] reported 121 tumors of skin and subcutaneous tissue among 521 spontaneous neoplasms.

Of the 200 tumors in this series, only 4 originated in the integument. One, a fibroma of the chest wall, was composed of wavy collagen bundles and sparse spindle cells with long tapering cytoplasmic processes. Occasional leukocytes were scattered through the tumor. A dermatofibrosarcoma was removed from the snout of a 24-month-old rat. The tumor was dome shaped, measured 0.8 cm., and was

covered by skin except for one small area of ulceration. It was composed of interlacing bundles of spindle cells with cigar-shaped nuclei. Invasion and destruction of skeletal muscle were seen at its base. The third subcutaneous tumor was large and consisted of a thin border of viable neoplasm, the central portion of which was composed of organizing blood clot and large vascular spaces. The cell type was thought to be of mesenchymal origin. The last tumor in this group was histologically similar to the mesodermal tumors of the uterus. It contained numerous cystic areas. Cytoplasm was indistinct, nuclei were small and relatively uniform, and mitotic figures were uncommon.

Tumors of Miscellaneous Origin

A small number of tumors could not be fitted into any category. One lipoma of the spermatic cord was found to the left of the bladder and measured 1 cm. in diameter. A second lipoma was found in the wall of the large intestine between the mucosa and the muscularis. A malignant spindle-cell tumor was present both in the lung and beneath the skin of the same rat. It was impossible to determine whether these were independent or one had metastasized from the other. The cutaneous lesion contained a large area of central infarction. In another instance a highly undifferentiated malignant neoplasm of undetermined origin had invaded liver, pancreas and mesenteric fat and was present on the serosal surfaces of spleen, bladder, and gastrointestinal tract. Tumor cells were variable in size; giant nuclear forms and multinucleated forms were numerous. Chromatin was coarse and irregularly distributed. Bizarre mitotic figures were numerous. Primary carcinoma of the liver, metastatic sarcoma, or an undifferentiated carcinoma of unknown source were possibilities considered here. In one rat with a lymphoma of the mesenteric nodes, there was metastatic squamous cell carcinoma in the frontal portion of the cerebrum. The source was undetermined.

Summary

Two hundred spontaneous tumors of the Wistar Rat have been reported and described. These occurred in 189 of 786 albino rats ranging in age from 18 to 24 months; a tumor incidence of approximately 25 per cent (Table I). Primary tumors were identified in all organs except those of the cardiovascular and locomotor systems. Approximately one third were considered malignant. The most common tumors in the order of incidence were fibroadenoma of breast, malignant lymphoma of the lung and mesenteric lymph nodes, and

interstitial cell adenoma of testis. It was of interest that many of the tumors of the rat resembled those arising in similar sites in the human host.

Comparison with previous reports of spontaneous tumors in rats showed two striking variations. In the present series there was a paucity of tumors of skin and subcutaneous tissue and an absence of thymic tumors.

REFERENCES

1. McCoy, G. W. A preliminary report of tumors found in wild rats. *J. Med. Res.*, 1909, **21**, 285–296.
2. Bullock, F. D., and Curtis, M. R. Spontaneous tumors of the rat. *J. Cancer Res.*, 1930, **14**, 1–115.
3. Ratcliffe, H. L. Spontaneous tumors in two colonies of rats of the Wistar Institute of Anatomy and Biology. *Am. J. Path.*, 1940, **16**, 237–254.
4. Bryan, W. R.; Klinck, G. H., Jr., and Wolfe, J. M. The unusual occurrence of a high incidence of spontaneous mammary tumors in the Albany strain of rats. *Am. J. Cancer*, 1938, **33**, 370–388.
5. Wright, A. W.; Klinck, G. H., Jr., and Wolfe, J. M. The pathology and pathogenesis of mammary tumors occurring spontaneously in the Albany strain of rats. *Am. J. Path.*, 1940, **16**, 817–834.
6. Stewart, H. L., and Jones, B. F. Pathologic anatomy of chronic ulcerative cecitis: a spontaneous disease of the rat. *Arch. Path.*, 1941, **31**, 37–54.
7. Innes, J. R. M.; McAdams, A. J., and Yevich, P. Pulmonary disease in rats. A survey with comments on "chronic murine pneumonia." *Am. J. Path.*, 1956, **32**, 141–159.
8. Gilman, J.; Gilbert, C., and Spence, I. Phaeochromocytoma in the rat; pathogenesis and collateral reactions and its relation to comparable tumours in man. *Cancer*, 1953, **6**, 494–511.
9. Staemmler, M. Die chronische Vergiftung mit Nicotin. Ergebnisse experimenteller Untersuchungen an Ratten. *Virchows Arch. path. Anat.*, 1935, **295**, 366–393.
10. Yeakel, E. H. Medullary hyperplasia of the adrenal gland in aged Wistar albino and gray Norway rats. *Arch. Path.*, 1947, **44**, 71–77.
11. Saxton, J. A., Jr.; Sperling, G. A.; Barnes, L. L., and McCay, C. M. The influence of nutrition upon the incidence of spontaneous tumors of the albino rat. *Acta, Unio Internat. Contra Cancrum*, 1948, **6**, 423–431.
12. Eker, R. Familial renal adenoma in Wistar rats. A preliminary report. *Acta path. et microbiol. scandinav.*, 1954, **34**, 554–562.
13. Willis, R. A. Carcinoma of the intestine in rats. *J. Path. & Bact.*, 1935, **40**, 187–188.

The assistance of Professor J. Lowell Orbison is acknowledged.

[*Illustrations follow*]

LEGENDS FOR FIGURES

All sections shown in these photographs were stained with hematoxylin and eosin stain.

FIG. 1. Fibroadenoma of mammary gland, the most common type of spontaneous tumor in the Rochester Wistar rat. × 60.

FIG. 2. Adenoma of mammary gland. × 60.

FIG. 3. Cystadenoma of mammary gland. × 100.

FIG. 4. Papillary cystadenoma of mammary gland. × 100.

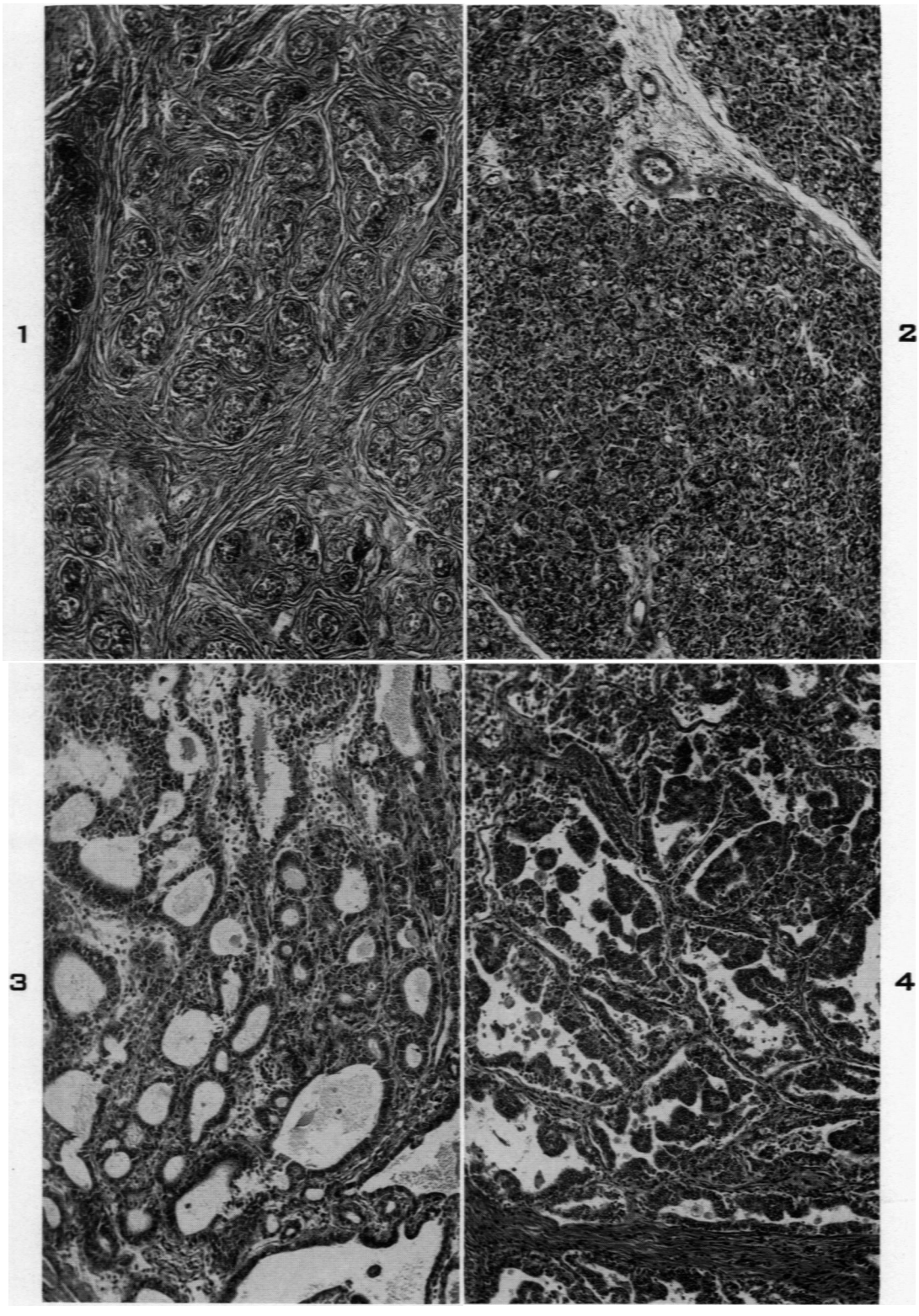
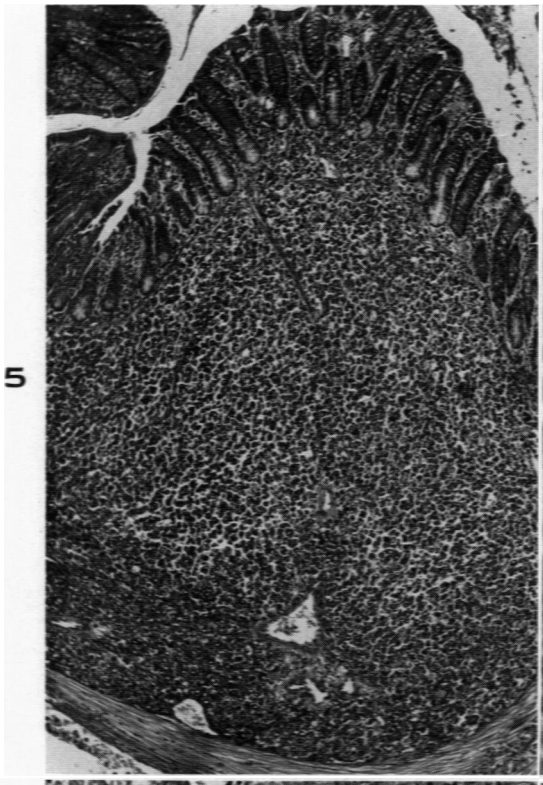

1
2
3
4

FIG. 5. Malignant lymphoma in wall of cecum. × 60.

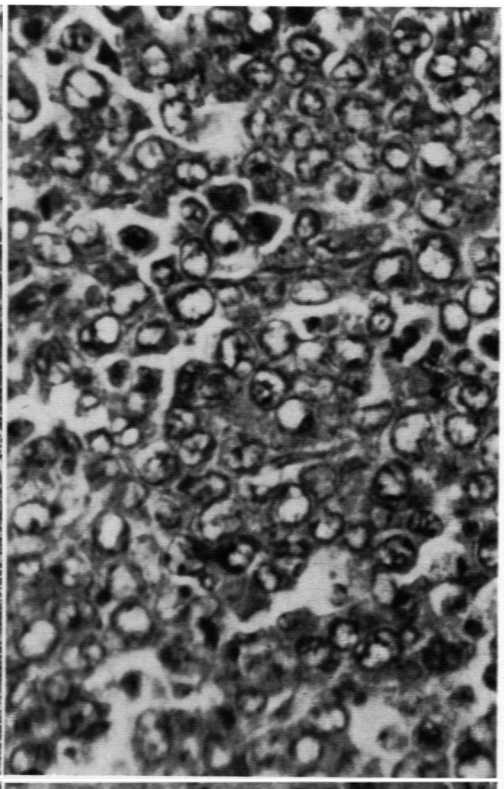
FIG. 6. Higher magnification of Figure 5. × 430.

FIG. 7. Small interstitial cell adenoma of testis, composed of uniform cells with acidophilic cytoplasm. × 100.

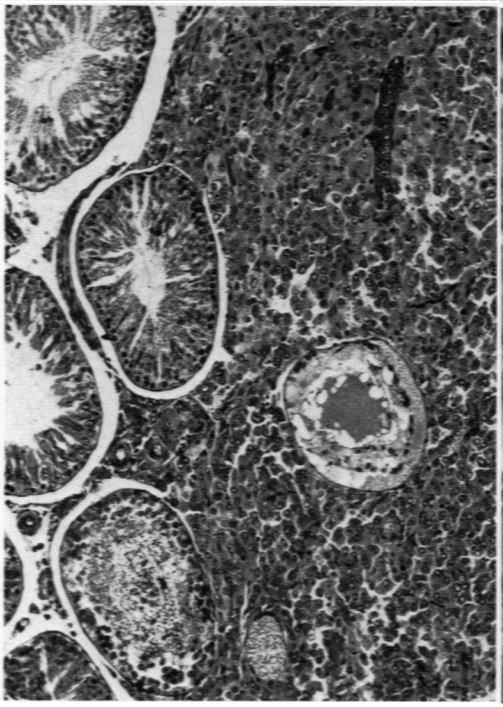
FIG. 8. Interstitial cell adenoma of testis. Higher magnification of Figure 7 × 430.



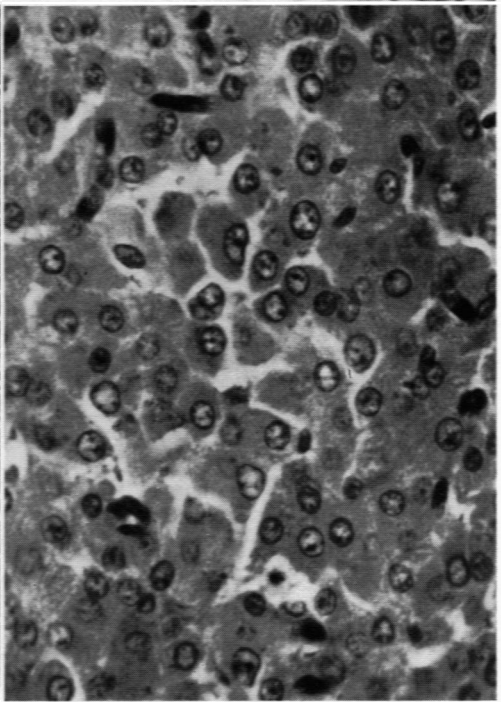
5



6



7



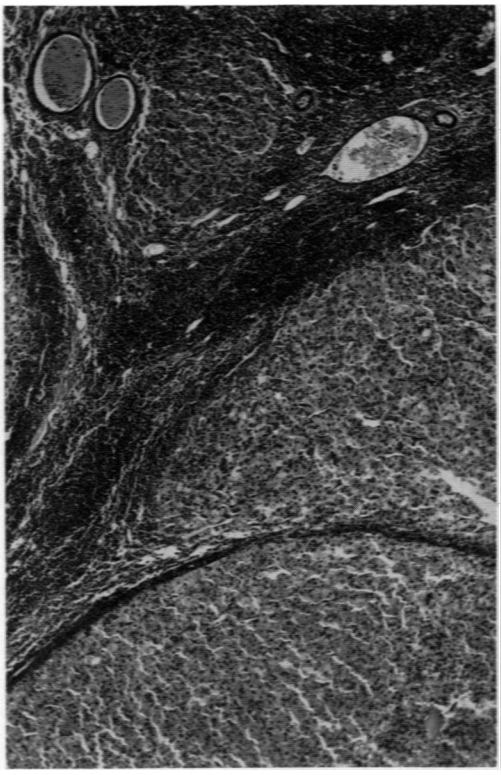
8

FIG. 9. Large interstitial cell adenoma of testis illustrating two characteristic cell types. Large nodules composed of pale cells with abundant foamy cytoplasm were separated and surrounded by small, closely packed cells with deeply basophilic nuclei. × 60.

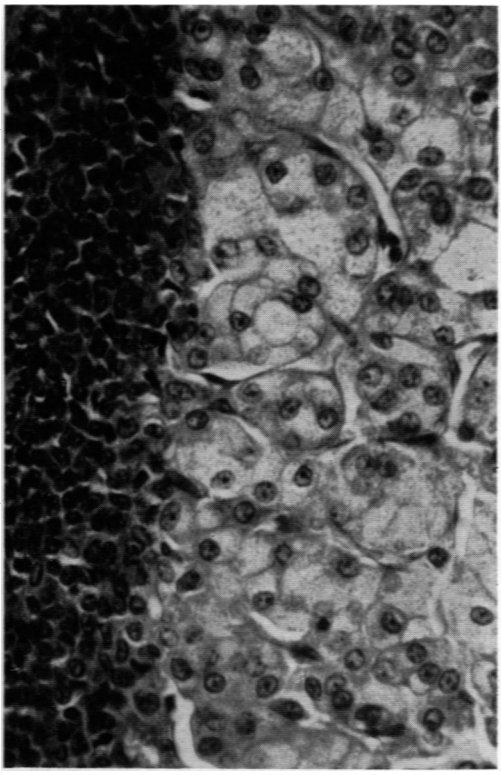
FIG. 10. Higher magnification of Figure 9. × 430.

FIG. 11. Adenoma of adrenal medulla characterized by cords and nests of cells. × 60.

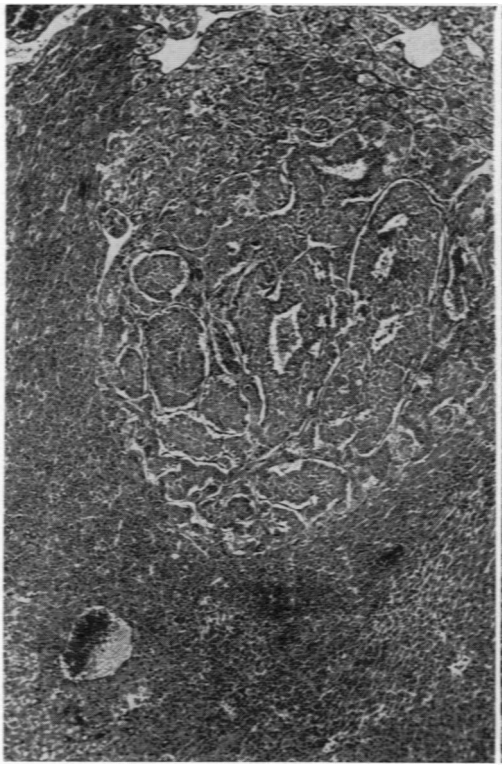
FIG. 12. Mesodermal tumor of uterus showing cellular area. × 100.



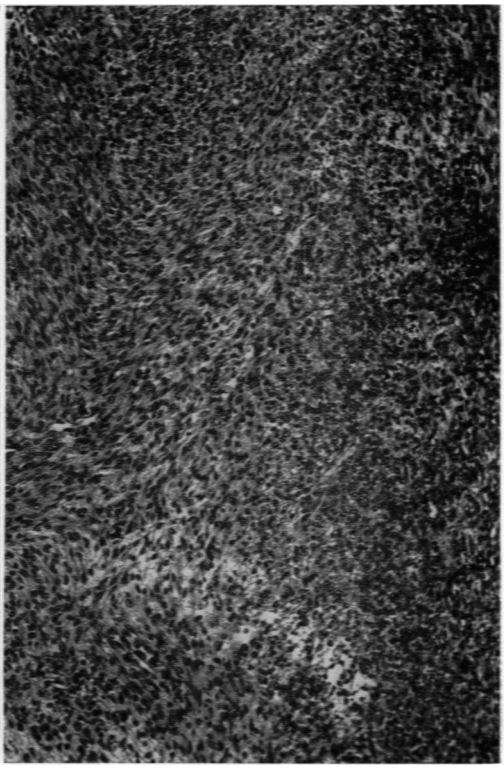
9



10



11



12

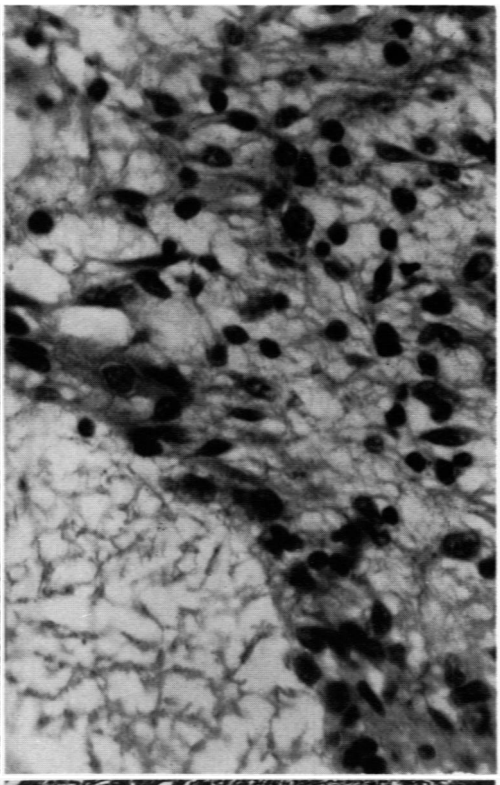
FIG. 13. Mesodermal tumor of uterus showing cystic areas. × 60.

FIG. 14. Higher magnification of Figure 13. × 430.

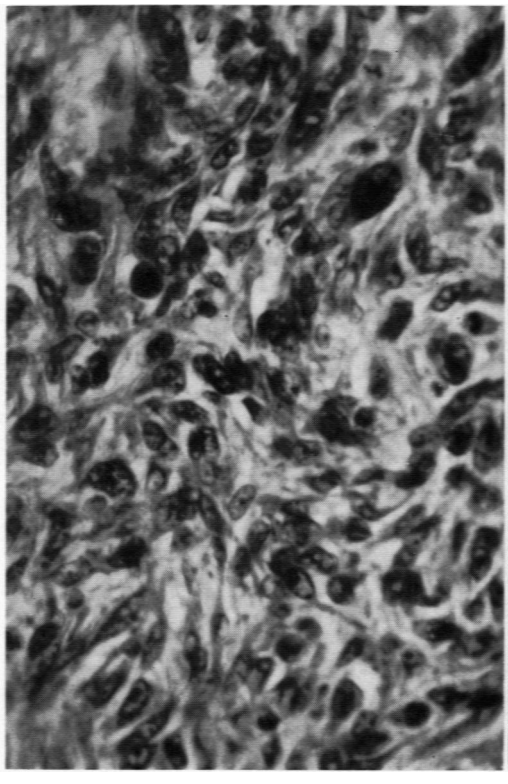
FIG. 15. Mesodermal tumor of uterus showing cellular pleomorphism and occasional giant nuclear forms. × 430.

FIG. 16. Adenocarcinoma of the endometrium with marked acute inflammatory cell reaction. × 100.

13



14



15

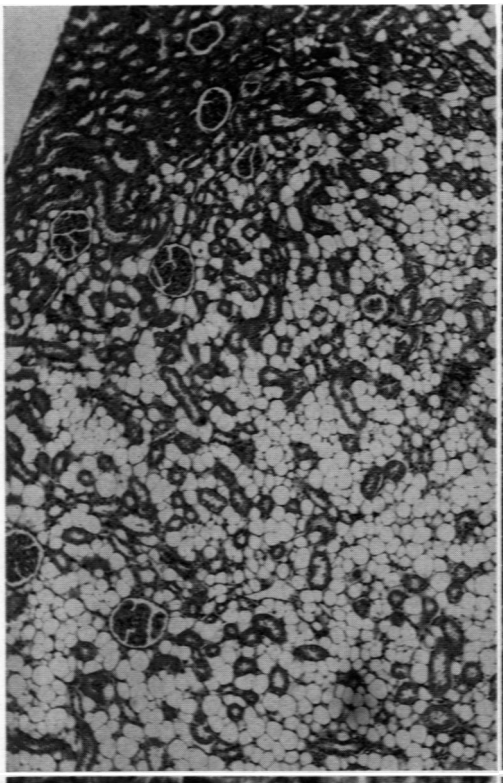
16

FIG. 17. Lipomatous hamartoma of kidney. × 60.

FIG. 18. Embryonal carcinoma of kidney. × 60.

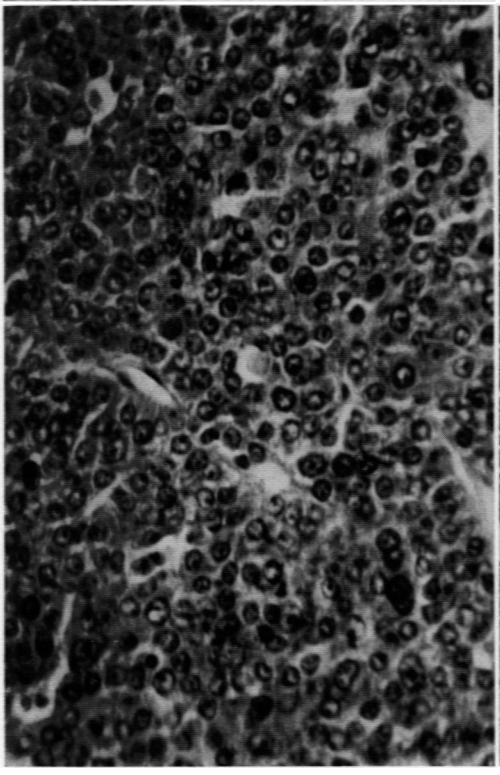
FIG. 19. Pituitary adenoma. × 430.

FIG. 20. Thyroid adenoma. × 60.

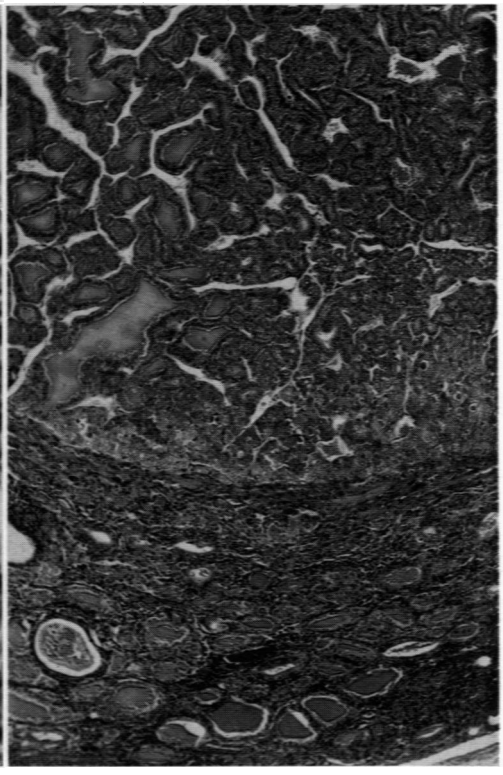


17

18



19



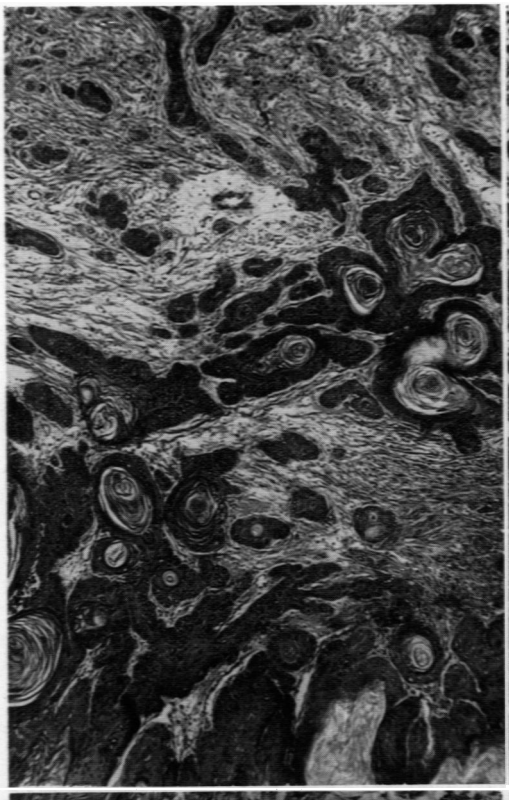
20

FIG. 21. Squamous cell carcinoma of esophagus. × 60.

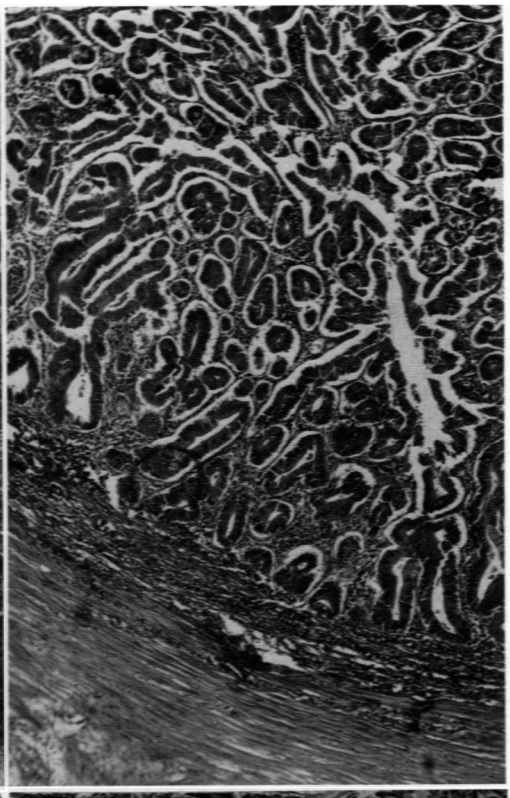
FIG. 22. Adenocarcinoma of colon. × 100.

FIG. 23. Mucoid carcinoma of stomach. × 60.

FIG. 24. Papillary cystadenocarcinoma of ovary. × 60.

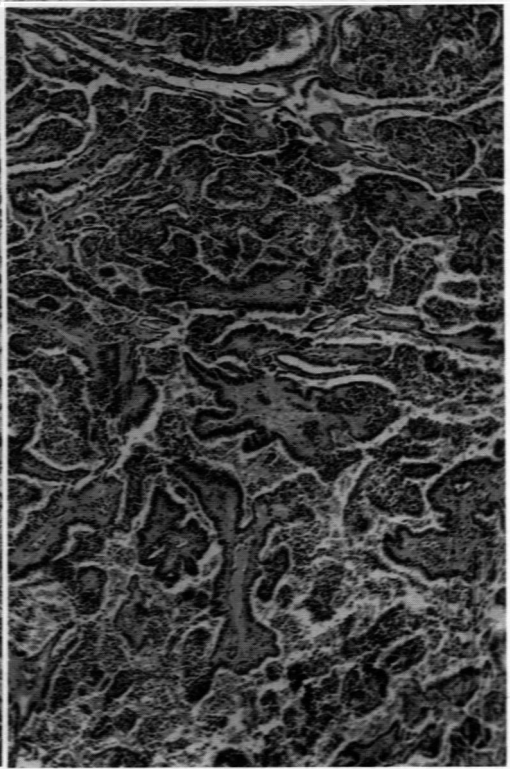


21



22

23



24