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ABSTRACT

THE INCIDENCE AND CHARACTERISTICS
OF NEOPLASMS IN CATS
by Robert E. Schmidt

This thesis is a study of 256 neoplasms of cats in the Michigan State University, Department of Pathology, collection. Emphasis was placed on sex and age incidence of the cats. A complete histologic description was given for each tumor type.

The average age of cats in this study was 7.9 years. Ninety-one males and 110 females were affected. Classifying the tumors on the basis of cell of origin, 33 different tumor types were studied. The majority of the tumors (72%) was malignant, with mesenchymal tumors being more prevalent than epithelial tumors.

Malignant lymphoma was the most common type, and was considered to be the most significant tumor of cats. Tumors of fibrous tissue comprised the 2nd largest group, and this was the only group in which there were more of the benign than the malignant type. Mammary gland tumors were 3rd in occurrence, and included 1 mixed mammary tumor. This tumor is apparently very rare in cats, as no reports of its occurrence could be found. The 4th largest group was the squamous cell carcinoma. These tumors occurred primarily in the oral cavity and the skin of the head.

In contrast to some reports, the mastocytoma was a frequently occurring neoplasm, making up 5% of the total number. The basal cell carcinoma had a histologic pattern of cells arranged in small islands which resembled

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INTRODUCTION

Neoplasia in cats has been recognized for some time, but has not been considered an important field of study. Compared to reports dealing with neoplasia in animals such as the dog, the literature concerning tumors in cats is scanty, and only in recent years has there been much effort to study feline neoplasms.

As late as 1957, Cotchin stated that little information was available about the incidence of tumors in cats. Most reports fall into 2 categories: single case reports and reports of a series of tumors. The latter usually concentrated on figures indicating age and sex incidence and classification of the tumors according to tissue of occurrence. Unfortunately, most of these reports have little or no histologic description of the neoplasms.

The objectives of this study of the tumors in the Michigan State University collection were as follows: (1) To tabulate the incidence of tumors in cats with respect to age, sex, and cell of origin, and to compare these figures with those reported in the literature. (2) To give a complete description of the histologic features of each tumor type. (3) To discuss the more important tumors occurring in cats, emphasizing the similarities and differences as compared with neoplasms in other species.

REVIEW OF LITERATURE

A. General Articles

Crocker (1919) listed a series of 401 necropsies of cats, with only 4 tumors reported. Included were an osteosarcoma, a cavernous hemangioma of the liver, and a fibroma of the cerebellum. No histologic description was given, and the exact classification according to cell type cannot be critically reviewed. Feldman (1932) referred to the scarcity of reports pertaining to the frequency of tumors in cats. He stated that in 1929 and 1930, 582 cats were treated at the New York State Veterinary College, only 1 having a tumor. Conclusions drawn by Feldman concerning feline neoplasms were that they were not common in young cats, and that the most common type was carcinoma. Morrill (1937) stated, "accurate data on the incidence of tumors in cats are not available". He concluded that because of the low economic and sentimental value of cats, many were not seen by veterinarians. In Morrill's series of 108 tumors, only 1 was from a cat, and it was an adenocarcinoma of the mammary gland.

Lasserre, Lombard and Labatut (1943) reported on a series of 4496 cats they had examined. Of these, 46 (1%) had tumors. Twenty-three of the tumors were adenocarcinomas of the mammary gland. Lombard (1943) cited much of the earlier French literature to the effect that cancer in cats was rare. Douglas (1951) said, "neoplasms were so rare in the cat as compared with the dog, that it was not easy to describe any common types". He further stated that epithelioma of the esophagus was the most frequent neoplasm of cats.

Mulligan (1951), in a series of 66 tumors in cats, found that more occurred in females than in males, and that the squamous cell carcinoma was the most common type. Plummer (1951) reported 2 feline tumors in a series of 60 from domestic animals. These were an hemangioma, and an embryonal nephroma. In 1956, Plummer reported a series of 636 tumors in domestic animals with only 7 from cats. Two of the 7 were described as papillary carcinomas of the mammary gland.

Cotchin (1951, 1952, 1956a, 1957, 1958b) reported on the incidence of tumors in cats as indicated by his series. The majority of the tumors were either from the skin or the alimentary tract, with the next most common sites being the mammary gland and the lymphoid tissue. Alimentary tract tumors were primarily squamous cell carcinomas of the upper tract, and lymphosarcomas involving the intestine. Of interest in connection with the high incidence of upper alimentary neoplasms was the observation that the cat is the only species other than man in which spontaneous cancer of the esophagus occurs commonly. Cotchin postulated that the cats might be ingesting a carcinogenic agent. Cotchin did not report any tumors of the central nervous system, but he stated that in most necropsies of cats an examination of the nervous system was not done.

Cotchin's studies indicated that the majority of the tumors were from male cats, and most were from older animals, with a peak incidence at 9 years of age. He postulated that the occurrence of tumors in older cats might reflect the long latent period of carcinogenic action in some cases. A tumor reported to be more peculiar to the cat than to other species was the ceruminous gland tumor (Cotchin, 1961). No reasons for this occurrence were given. In many of Cotchin's reports, little or no histologic description of tumor types was given.

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Smith and Jones (1961) listed a series of 8159 neoplasms of domestic animals compiled from several sources. Only 174 of these were from cats, with squamous and basal cell carcinoma of the skin, malignant lymphoma, mammary adenocarcinoma, and squamous cell carcinoma of the esophagus being reported most frequently.

B. Tumors of the Skin and Subcutis

Most of the reports which deal with tumors of the integument are cited in section A. Squamous and basal cell carcinomas were listed most frequently. Of special interest is the squamous cell carcinoma of the ear of white cats. Moulton (1961) stated that there was a significantly high incidence of this condition in California. Solar radiation was considered an etiologic factor.

Seawright and Grono (1964) and Meier (1957a) have reported cases of cutaneous mastocytoma in the cat. The histologic description given in the above cases was similar to that described in dogs, with cords of neoplastic cells arranged in clusters and separated by delicate connective tissue. In the case described by Seawright and Grono the tumor recurred after surgery, and there were metastases to the regional lymph nodes, liver, and spleen. The authors stated that the spleen is always involved in mastocytoma.

C. Tumors of Bone and Cartilage

Reported tumors involving bone in cats have included a giant cell tumor of the tibia (McClelland, 1941) and an osteogenic sarcoma (Purdy, 1961). In addition, Cotchin (1951, 1952, 1956a) listed tumors of the skeletal system in several of his series. Barron and Saunders (1959) reported the unusual case of a primary chondrosarcoma of the uveal tract.

D. Tumors of the Vascular, Hemopoietic, and Lymphoid Tissues

Lillie (1931) stated that reported cases of leukemia in the cat were rare. He reported 1 case, with leukemia and splenic and hepatic involvement. The neoplastic cells were described as having basophilic granules, and the diagnosis was mast myelocyte leukemia.

Visceral lymphosarcoma appears to be peculiarly frequent in the cat (Nielsen and Holzworth, 1953; Holzworth and Nielsen, 1955). The average age of affected cats was 8 years, and the condition occurred more commonly in males. The organs primarily affected were the small intestine, mesenteric lymph nodes, liver, and kidney. The intestinal lesion was usually an annular enlargement with occlusion of the intestinal lumen. Multicentric origin of the neoplasm was suggested in 5 cats with bilaterally affected kidneys, although in most cases it was considered difficult to differentiate between multicentric origin and true metastasis. The tumors were classified histologically as either lymphoblastic or lymphocytic lymphosarcoma.

Another common site of occurrence of visceral lymphosarcoma was the pericardiac mediastinum. Holzworth (1958) considered the most frequent cause of thoracic transudate in the cat to be lymphosarcoma arising in the thymus or mediastinal lymph nodes. This neoplasm can occur in the thymus of cats under 1 year of age as reported by Morgan (1959).

Two cases of intestinal lymphosarcoma in which surgical treatment was attempted were reported by Patterson and Meier (1955). Multicentric origin in Peyer's patches was suggested by the segmental distribution of the lesions. Holzworth (1960) reported 155 cases of leukemic disorders of cats. She stated that malignancies of the blood forming tissues were a prominent cause of fatal illness in the cat. Holzworth's data indicated

In the report of Labie and Fontaine (1960), as in the reports of Lillie (1931) and Holzworth (1960), there appears to be a difference of terminology regarding cases of basophilic granulocytic leukemia. Michels (1963) said that in mammals the mast leukocyte is one of the granulocytes and has no morphogenetic relationship to tissue mast cells. Boyd (1961) stated that mast cells have no relation to the basophils of the blood. Moulton (1961) described mastocytoma as occurring mostly in the dermis. However, Selye (1965) stated, "it seems reasonable to assume that the blood basophil represents the circulating form of the mast cell system." It is apparent that the question of relationship is far from settled.

Reports of tumors arising from cells of the blood vessels of cats are rare. Moulton (1961) said that hemangiomas and hemangiosarcomas have been noted in cats, but apparently are not common. The occurrence of an hemangio-endothelioma at the base of the tongue was reported by Lombard (1964). Hemangiopericytoma in a cat was reported by Donnert (1961). The tumor mass occurred at the medial canthus of the left eye, and the neoplastic cells formed whorls around the small vascular spaces within the tumor.

E. Tumors of the Respiratory System

Bronchogenic carcinoma in the cat has been reported by Troy (1955). Primary alveolar carcinoma in a 13-year-old cat was reported by Sedlmeier and Dahme (1958). Stllnzi (1958) discussed 4 cases of papilliform columnar cell adenocarcinoma. The growths were described as being derived from surface epithelium of the bronchi.

F. Tumors of the Alimentary Tract and Liver

Squamous cell carcinoma and lymphosarcoma have accounted for the majority of reported tumors of the alimentary tract of the cat. Reports

that the majority of the malignancies were of the lymphoid type, twice as many males as females were affected, and 50% of the cats were 1 to 5 years of age. Although nothing definite could be said about the possible etiologic agent or agents, it was observed that many cases followed anemia, and the possibility of overstimulation of the bone marrow was raised. Of the 155 cases, 9 were myeloid leukemia. One of these was a basophilic leukemia with an enlarged spleen. The author interchanged the term basophilic leukemia with mast cell leukemia in this report. Also mentioned were 1 case each of eosinophilic leukemia, monocytic leukemia, and multiple myeloma.

Squire (1964) reported that lymphosarcoma was responsible for 10% of all feline deaths at Angell Memorial Hospital. He indicated that the condition was usually visceral lymphosarcoma. Granulocytic leukemia was rare, and its most common pathologic feature was splenomegaly according to Squire. Intraocular lymphosarcoma has been reported by Saunders and Barron (1964). In their 2 cases, the choroid, iris, and ciliary body were involved in both, and the retina in 1. They mentioned that neoplastic infiltration of the cornea was often mistaken for infectious keratitis.

More rare in occurrence are reticulum cell myeloma (Holzworth and Meier, 1957) and erythemic myelosis (Zawidzka, Janzen and Grice, 1964). The latter group reported a case in which the bone marrow was hypercellular with a maturation arrest affecting all cell lines. Very few well differentiated cells were present in the marrow.

Labie and Fontaine (1960) described splenic mastocytoma in 3 cats. In each case the splenomegaly was due to infiltration by round cells with basophilic cytoplasm. The authors commented on the difficulty in differentiating between mast cells and myelocytes of the basophilic series, and their description closely resembled reports of granulocytic leukemia (Squire, 1964).

dealing with these neoplasms are discussed in sections A and D. An adamantinoma was reported by Olafson (1939), and 2 cases of salivary gland tumors in cats were among those listed by Koestner and Buerger (1965). Two cases of adenocarcinoma of the intestine were described by Taylor and Kater (1954). In both cats the tumor took the form of a ring-like thickening in the wall of the intestine. According to Moulton (1961) this is the usual form of intestinal adenocarcinoma, with stenosis of the intestine and eventual obliteration of the lumen as a frequent result.

Chang (1964) reported primary carcinoma of the bile ducts of 3 cats whose livers were infected by flukes. The author stated that the carcinoma was caused by the flukes, a condition that has occurred in man. This opinion was contrary to that of Moulton (1961), who said that no etiologic relationship was indicated in cases of bile duct carcinoma.

G. Tumors of the Urogenital System and Mammary Gland

Fitts (1960) described a bilateral embryonal sarcoma of the kidneys of a cat. He stated that this tumor had not been previously reported in the cat. Carcinoma of the urinary bladder was reported by Thoonen and Hoorens (1960).

Carcinoma of the uterus is rare in cats (Meier, 1956). Meier considered that early spaying of female cats was a factor in the low reported incidence. Another rare tumor is the granulosa cell tumor of the ovary (Baker, 1956). Two instances of vaginal leiomyomas that caused constipation by compressing the rectum were reported by Wolke (1963). Meier (1957b) reported 2 cases of Sertoli-cell tumors in cats. One cat was a bilateral cryptorchid, and it had metastatic tumors in the liver and spleen. No feminizing signs were noted in either case. Meier commented on the

scarcity of reported testicular tumors in the cat and considered that early castration might be a factor in the low reported incidence.

A large number of tumors arise in the female mammary gland. Several of the reports discussed in section A have indicated a high incidence of mammary tumors in the cat (Cotchin, 1952, 1956a; Lasserre et al., 1938). It is interesting that in contrast to the dog, which has a high percentage of mixed mammary tumors, all reports concerning the cat have been of mammary carcinoma or adenoma (Moulton, 1961). The mammary adenocarcinomas apparently are not influenced by spaying (Nielsen, 1952b).

H. Tumors of the Nervous System

A glioma arising from the left half of the floor of the 4th ventricle was described by Knowlton (1905). However, there have been few reports of tumors of the nervous system since that time. An astroblastoma was reported by Milks and Olafson (1936). More recently, meningiomas have been reported by several authors (Dahme, 1957; Gonzalez-Monteagudo and Purpura, 1959; Cooper and Howarth, 1956). Smit (1961) said that the incidence of meningiomas in cats is high, but gave no specific figures.

In a series of 155 necropsies of cats, Luginbuhl (1961) noted 8 meningiomas. They were characterized histologically by cells arranged in whorls and curving columns, and degenerative changes were a feature of several of the tumors. None of the tumors in Luginbuhl's report caused any clinical signs. Luginbuhl concluded that thorough examination of the nervous system of cats was seldom done at necropsy, and therefore the reported incidence of intracranial neoplasia was low.

Schiefer and Dahme (1962) discussed a tumor located in the right olfactory bulb of a cat which was diagnosed as an ependymoma. Astrocy-

tomas have been reported by Cooper and Howarth (1956), and Stunzi and Perlstein (1958). Cooper and Howarth (1956) also reported the occurrence of 1 oligodendrocytoma in a series of 60 cat brains examined histologically.

I. Miscellaneous Tumors

An extraskeletal giant cell tumor was described by Nielsen (1952a). Carcinoma of the thyroid was reported by Holzworth, Husted and Wind (1955). The cat was an obese, 15-year-old castrated male. What apparently was a true thymoma was described by Loveday (1959). The mass was located in the mediastinum, and on histologic examination had spindle-shaped epithelial cells arranged in whorls. These cells surrounded small eosinophilic masses which had the appearance of Hassall's corpuscles.

MATERIALS AND METHODS

The material used in this study was taken from the registry of the Department of Pathology, Michigan State University. All recorded instances in which neoplastic disease had been diagnosed in cats were selected for study. For each tumor type selected, data were recorded in tabular form under the following headings: tumor type, sex, age range, average age, and no data available (age and sex).

The histologic slides for each case were grouped according to the type initially diagnosed. All slides had been stained with hematoxylin and eosin (H & E) (Armed Forces Institute of Pathology, 1960). In certain instances the following special stains were used to accentuate a specific cytologic feature or to confirm the microscopic diagnoses: Heidenhain's aniline blue (A.F.I.P., 1960), lithium silver (Gurr, 1960), Mallory's phosphotungstic acid hematoxylin (A.F.I.P., 1960), May-Grunwald-Giemsa (A.F.I.P., 1960), and a modified reticulum technique as outlined by Lillie (1954).

All slides in the series were examined by the author and a senior pathologist at the Department of Pathology in order to confirm the diagnoses. The available gross descriptions for each type of tumor were recorded, and a composite gross description was made for each type. Histologic descriptions of each tumor were also recorded, and again a composite description for each group made, emphasizing points of similarity and difference within the group. Photomicrographs were taken of representative sections of the majority of the tumor types, and selected gross photographs were included for illustrative purposes.

RESULTS

I. General

Age Incidence. The age distribution is shown (Figure 1). The ages of the subjects ranged from under 1 to 21 years, with an average of 7.9 years. The largest number of tumors recorded for a given group was 17, which occurred at 6 and 11 years of age. Over 50% of the cats were under 10 years old. The ages of 47 cats were unknown.

Sex Incidence. There were 91 males and 110 females in this series. For 55 of the cases, no data were available concerning the sex of the cat. Because records were often incomplete, no attempt was made to separate castrated from entire animals.

Tumor Types. The basis for classifying the various neoplasms was the cell of origin. In all instances standard nomenclature was used, with Moulton (1961) as a guide. Using this classification, there were 33 different types of tumors studied (TABLE 1). These included both benign and malignant varieties (e.g., fibroma and fibrosarcoma), as arising from 1 cell type.

Degree of Malignancy. Malignant and benign tumors are listed by basic tissue type (TABLE 2). The column heading of "mesenchymal" includes tumors of muscular and endothelial tissue. The column headed "questionable" refers to tumors such as the basal cell carcinoma and adnexal carcinoma, the behavior of which is not synchronous with the malignancy suggested by

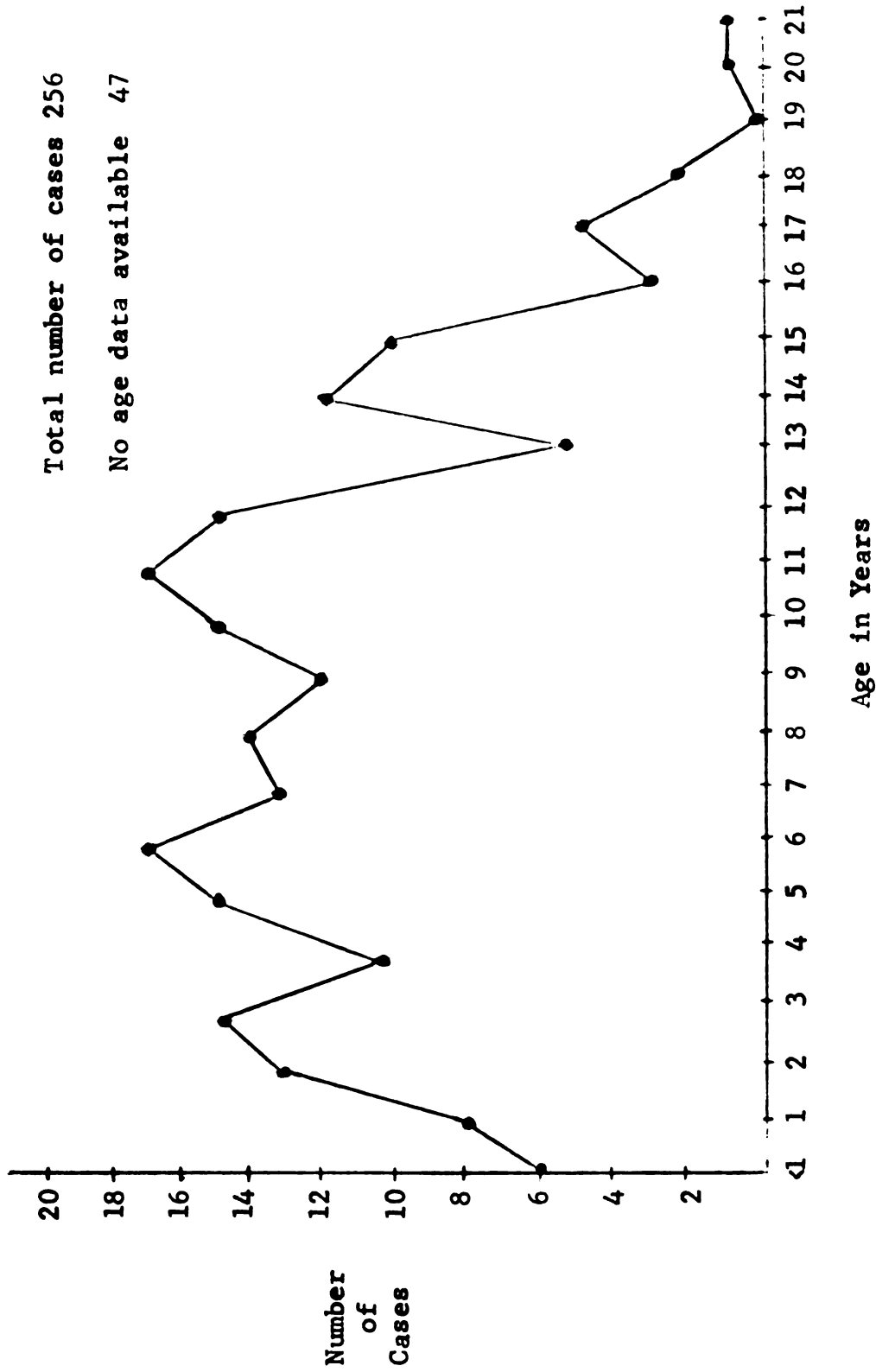


Figure 1. Age distribution of cats with neoplasms.

TABLE 1. Age and sex incidence of each tumor type.

| Tumor type | Total Number | Sex | | Age Range in Years | Average Age in Years | No Data Available | |
|----------------------------|-----------------|-----|----|-----------------------|-------------------------|----------------------|-----|
| | | M | F | | | Age | Sex |
| Basal cell carcinoma | 9 | 4 | 5 | 1.0-17.0 | 9.8 | - | - |
| Melanoma | 4 | 2 | 2 | 9.0-17.0 | 12.7 | - | - |
| Adnexal carcinoma | 2 | - | 1 | 10.0-12.0 | 11.0 | - | 1 |
| Papilloma | 2 | 1 | 1 | 1.0- 6.0 | 3.5 | - | - |
| Squamous cell carcinoma | 22 | 7 | 9 | 3.0-16.0 | 11.2 | 2 | 6 |
| Adenocarcinoma: | | | | | | | |
| All types | 59 | 12 | 32 | 2.0-17.0 | 8.2 | 18 | 15 |
| Uterus | 1 | - | 1 | 4.0 | 4.0 | - | - |
| Liver | 2 | 2 | - | 6.0- 8.5 | 7.2 | - | - |
| Pancreas | 3 | 1 | 1 | 5.0-17.0 | 11.0 | - | 1 |
| Ceruminous gland | 2 | - | 1 | 13.0- 5.0 | 14.0 | - | 1 |
| Salivary gland | 1 | 1 | - | 6.5 | 6.5 | - | - |
| Bile duct | 4 | 1 | 2 | 3.0- 6.0 | 4.5 | 2 | 1 |
| Sweat gland | 4 | - | 1 | 12.0 | 12.0 | 3 | 3 |
| Mammary gland | 21 | - | 21 | 4.0-15.0 | 10.7 | 4 | - |
| Intestine | 1 | - | 1 | 4.0 | 4.0 | - | - |
| Origin unknown | 20 | 7 | 4 | 2.0-17.0 | 8.5 | 8 | 9 |
| Adenoma: | | | | | | | |
| All types | 12 | 2 | 9 | 3.0-13.0 | 10.1 | - | 1 |
| Mammary gland | 6 | - | 6 | 5.0-15.0 | 9.7 | - | - |
| Pancreas | 2 | 1 | - | 7.0-15.0 | 11.0 | - | 1 |
| Sweat gland | 1 | - | 1 | 8.0 | 8.0 | - | - |
| Sebaceous gland | 1 | 1 | - | 9.0 | 9.0 | - | - |

TABLE 1--continued.

| Tumor type | Total Number | Sex | | Age Range in Years | Average Age in Years | No Data Available | |
|---------------------------|-----------------|-----|----|-----------------------|-------------------------|----------------------|-----|
| | | M | F | | | Age | Sex |
| Ceruminous gland | 1 | - | 1 | 12.0 | 12.0 | - | - |
| Uterus | 1 | - | 1 | 3.0 | 3.0 | - | - |
| Fibroma | 18 | 7 | 3 | 5.0-10.0 | 4.4 | 9 | 8 |
| Fibrosarcoma | 11 | 3 | 6 | 2.0-21.0 | 8.0 | 2 | 2 |
| Malignant Mesenchymoma | 1 | - | 1 | 20.0 | 20.0 | - | - |
| Rhabdomyosarcoma | 3 | 2 | 1 | 4.0- 8.0 | 5.3 | - | - |
| Leiomyosarcoma | 6 | 2 | 3 | 5.0-10.0 | 8.6 | - | 1 |
| Leiomyoma | 3 | - | 2 | 3.0-11.0 | 7.0 | 1 | 1 |
| Mastocytoma | 13 | 3 | 6 | 0.5-15.0 | 7.9 | 2 | 4 |
| Chondrosarcoma | 2 | - | - | - | - | 2 | 2 |
| Osteogenic sarcoma | 5 | 3 | 2 | 8.0-15.0 | 11.6 | - | - |
| Osteoma | 3 | 1 | 1 | 6.0-12.0 | 9.6 | - | 1 |
| Osteochondroma | 1 | - | 1 | 4.0 | 4.0 | - | - |
| Lipoma | 6 | 2 | 2 | 2.0-11.0 | 7.2 | 2 | 2 |
| Neurofibroma | 2 | 1 | 1 | 2.0-16.0 | 9.0 | - | - |
| Neurofibrosarcoma | 2 | - | 1 | 5.0 | 5.0 | - | 1 |
| Meningioma | 1 | 1 | - | 7.0 | 7.0 | - | - |
| Myxoma | 1 | 1 | - | 13.0 | 13.0 | - | - |
| Myxosarcoma | 1 | - | - | - | - | 1 | 1 |
| Hemangiosarcoma | 3 | 2 | - | 6.0-10.0 | 8.0 | 1 | 1 |
| Malignant lymphoma: | | | | | | | |
| Reticulum cell type | 14 | 8 | 3 | 0.7-17.0 | 6.7 | 1 | 3 |
| Lymphosarcoma type | 43 | 24 | 14 | 0.7-18.0 | 4.9 | 6 | 5 |

TABLE 1--continued.

| Tumor type | Total Number | <u>Sex</u> | | Age Range in Years | Average Age in Years | <u>No Data Available</u> | |
|-----------------------------|-----------------|------------|---|-----------------------|-------------------------|------------------------------|-----|
| | | M | F | | | Age | Sex |
| Mixed mammary tumor | 1 | - | 1 | 12.0 | 12.0 | - | - |
| Teratoblastoma | 1 | - | 1 | 5.0 | 5.0 | - | - |
| Undifferentiated Sarcoma | 4 | 2 | 2 | 5.0-18.0 | 12.3 | - | - |
| Carcinoma | 3 | 1 | 1 | 10.0-11.0 | 10.3 | - | 1 |

TABLE 2. Tumors listed by type of tissue.

| | Epithelial | Mesenchymal | Mixed | Total |
|--------------|------------|-------------|-------|-------|
| Benign | 11 | 37 | 1 | 49 |
| Malignant | 88 | 95 | 1 | 184 |
| Questionable | 10 | 13 | - | 23 |
| | <hr/> | <hr/> | <hr/> | <hr/> |
| Total | 109 | 145 | 2 | 256 |

their names, and the cutaneous mastocytoma, which is difficult to classify either by clinical behavior or histologic evaluation.

II. Specific Tumor Types

All tumors are listed by type, total number, sex, age range, and average age (TABLE 1). Also included are figures indicating no data available regarding age and/or sex of the animal for certain tumors.

A. Epithelial Tumors

Basal Cell Carcinoma. Gross: No particular site of predilection was noted for this tumor. It was usually a slowly developing lesion in the skin and subcutis, and often was ulcerated. In several cases the clinical diagnoses of chronic inflammation had been made.

Microscopic: Inflammatory changes were noted in the majority of the basal cell carcinomas. The tumor cells were usually small and uniform, or slightly pleomorphic. Nuclei were round or oval and nuclear chromatin often was hyperchromatic. Nucleoli were usually not significantly enlarged. The number of mitotic figures in different specimens was variable.

The tumor cells formed 2 microscopic patterns. The most common consisted of small solid islands of cells surrounded by connective tissue stroma (Figures 2 and 3). Isolated islands often resembled tubules. The cells at the periphery of the island were usually arranged at right angles to the encircling connective tissue. The other pattern was that of infiltrating cords and loops of tumor cells. In many tumors there was a variable amount of pigment, often in the center of the solid islands of cells. In some tumors, the neoplastic cells made an abrupt transition from the more normal epithelium (Figure 4).

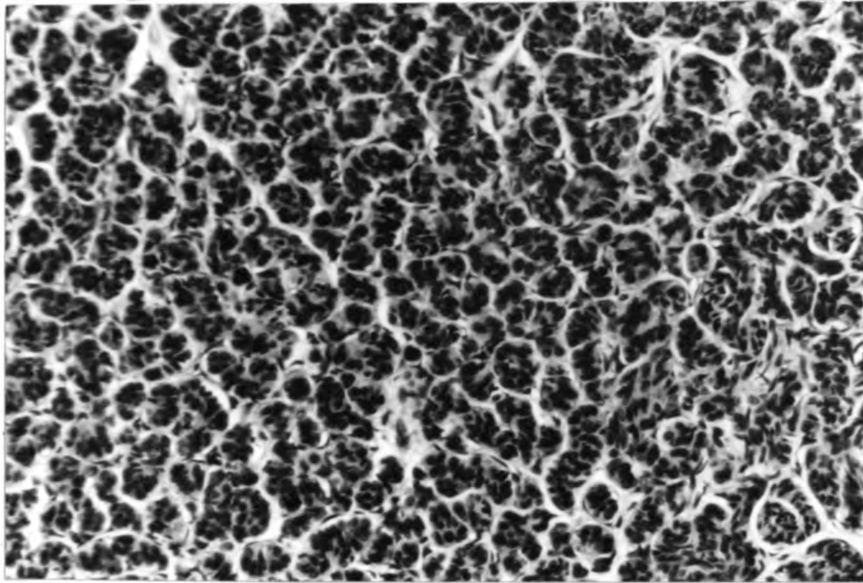


Figure 2. Basal cell carcinoma. Small nests of cells separated by delicate stroma. Hematoxylin and eosin. x 188.

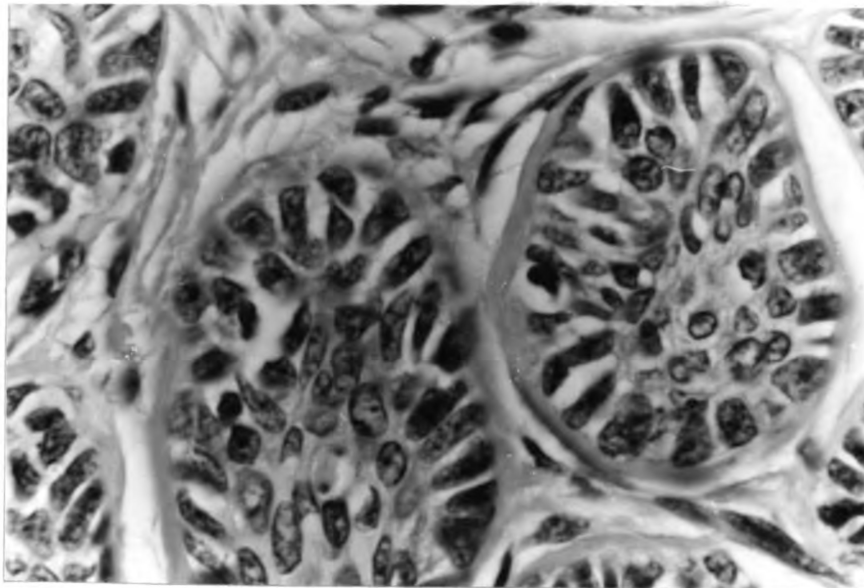


Figure 3. Basal cell carcinoma. Note nests of cells that resemble tubules, with peripheral cells arranged perpendicularly to the basement membrane. Hematoxylin and eosin. x 750.

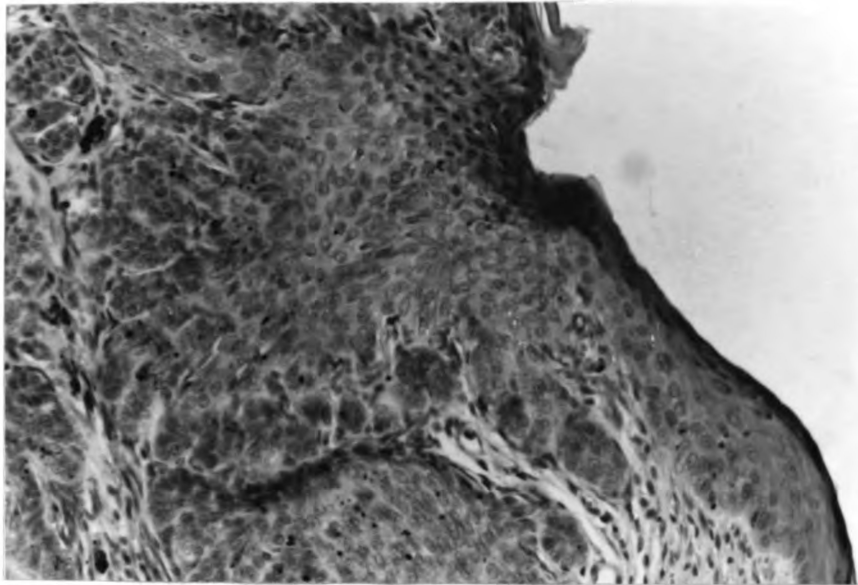


Figure 4. Basal cell carcinoma. Abrupt transition from normal to neoplastic epithelium. Some small cellular nests can be seen. Hematoxylin and eosin, x 188.

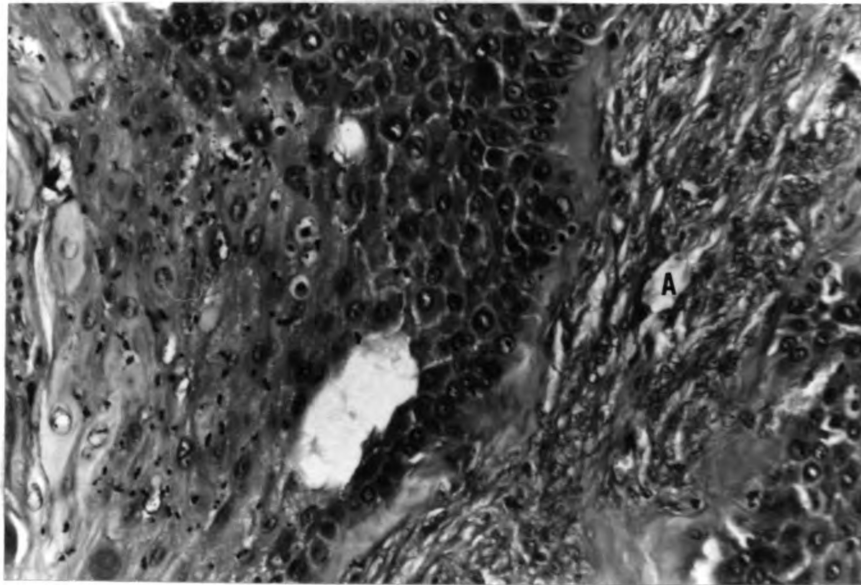


Figure 5. Squamous cell carcinoma. Note nucleoli, tonofibrils, and dense collagenous stroma (A). Hematoxylin and eosin, x 188.

Papilloma and Squamous Cell Carcinoma. Gross: The 2 papillomas were small pedunculated growths projecting from the skin. Eighteen of the 22 squamous cell carcinomas were located in the oral cavity or the skin of the head and neck. They were usually rapidly developing tumors, and many had recurred at least once. The majority of them was ulcerated.

Microscopic: The papillomas were composed of a fibrous core, with overlying epithelium that was hyperplastic and which had elongated rete pegs.

Surface ulceration was a common feature of the squamous cell carcinoma. The tumor cells were cuboidal or polyhedral and often pleomorphic, usually with abundant cytoplasm. Cell boundaries were usually distinct and tonofibrils were a constant feature (Figure 5). Nuclei were large, vesicular, and hyperchromatic with enlarged nucleoli. Mitotic figures were usually common.

The cells were arranged in cords or solid islands which infiltrated into the dermis and subcutis, or into the lamina propria and submucosa of the oral cavity. Dense fibrous stroma was present in all tumors. Some of the tumors had beginning "pearl" formation, but only 2 had well formed keratin pearls.

In 1 tumor there was extreme pleomorphism and many of the cellular elements had taken on the characteristics of mesenchymal cells. In several cases, the center of the solid islands of tumor cells was necrotic, and under low power magnification these areas resembled glandular acini.

Melanoma. Gross: The melanomas studied were all from the skin in the form of small nodules less than 2 cm. in diameter. No particular site of occurrence was noted. Pigmentation was not marked grossly.

Microscopic: The neoplastic cells were ovoid and, in many areas, resembled young fibroblasts. Nuclei were vesicular, with moderately prominent nucleoli. There were few mitotic figures. The majority of cells carrying pigment was within or close to the overlying epithelium (Figure 6), although some pigmented cells were scattered throughout the tumors. The general arrangement of neoplastic cells was in curving bundles with some whorls. Junctional changes in the epidermis were noted, but were not prominent.

Adnexal Carcinoma. **Gross:** This tumor occurred in the skin as a slowly growing nodule.

Microscopic: The tumor was made up of pleomorphic epithelial cells. The cells had moderate amounts of cytoplasm and round to oval hyperchromatic nuclei. Mitotic figures were not numerous. The neoplastic cells were arranged in a solid sheet in the dermis and appeared to arise from the epithelium of hair follicles (Figure 7).

Sebaceous Adenoma. **Gross:** The only example of this type of tumor was a small, slightly pigmented, hairless growth on the back.

Microscopic: The tumor was composed of enlarged sebaceous cells forming enlarged but otherwise normal appearing glands (Figure 8). There were inflammatory changes in the overlying epidermis and around some of the glandular elements.

Sweat Gland Adenoma and Adenocarcinoma. **Gross:** Little information on the gross appearance of these tumors was available, except that they all occurred in the skin of the head region.

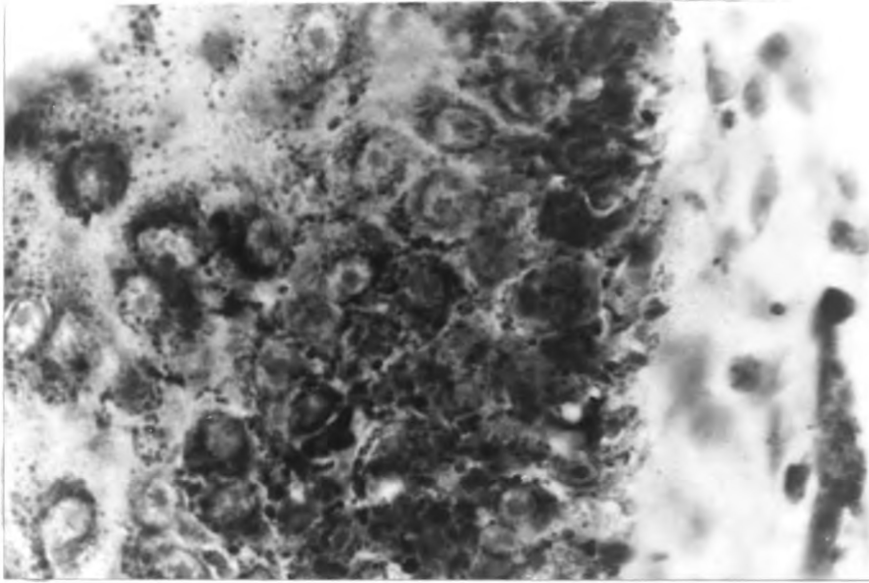


Figure 6. Melanoma. Concentration of pigment carrying cells in the basal epithelium. Note enlarged nucleoli of the neoplastic cells. Hematoxylin and eosin. x 750.

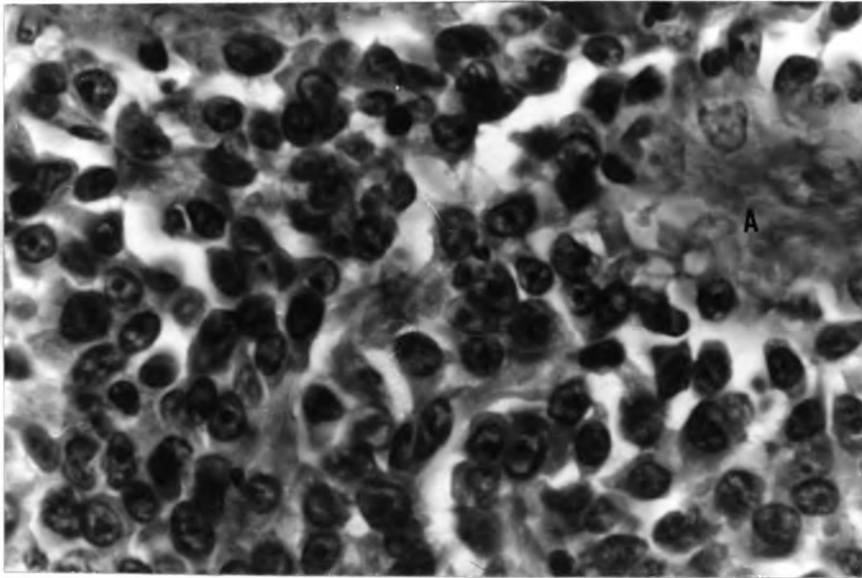


Figure 7. Adnexal carcinoma. Small epithelial cells clustered around the base of a hair follicle (A). Hematoxylin and eosin. x 750.

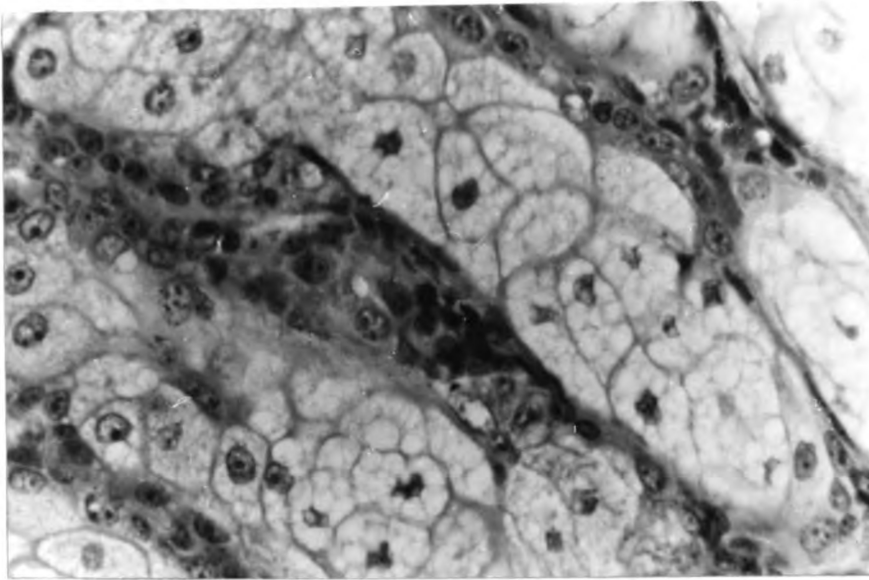


Figure 8. Sebaceous adenoma. Enlarged sebaceous cells with hyperchromatic nuclei. Hematoxylin and eosin. x 469.

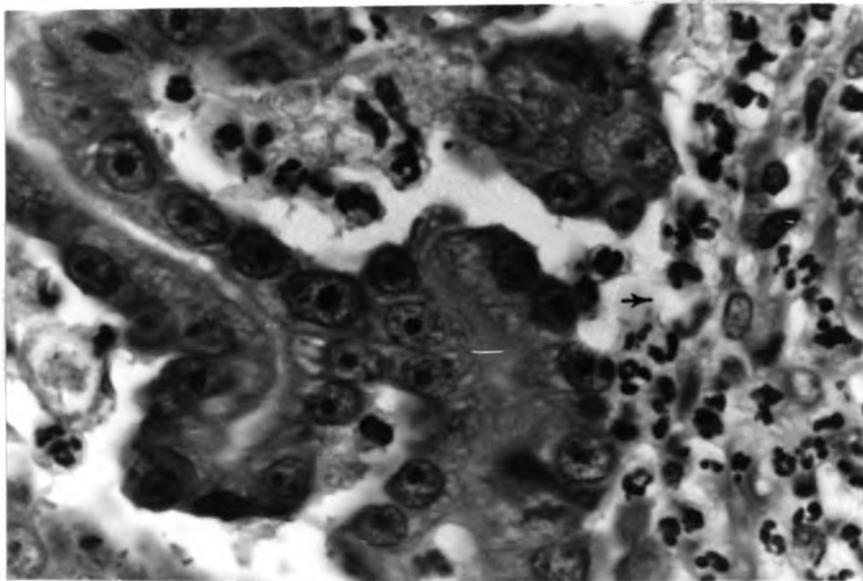


Figure 9. Ceruminous gland adenocarcinoma. Note large nucleoli and prominent inflammatory reaction (arrow). Hematoxylin and eosin. x 750.

Microscopic: The cells were roughly cuboidal, being more pleomorphic in the malignant tumors. The nuclei were round or ovoid with prominent nucleoli. Mitoses were variable in number. The cells were supported by a fibrous stroma and formed acini and ducts which were elongated, cystic, and had papilliferous projections in the more malignant carcinomas. There was some secretory activity in the benign tumors. Necrosis and inflammation were constant features of these tumors.

Salivary Gland Adenocarcinoma. Gross: The 1 example of this type of tumor was a friable growth in the right parotid region.

Microscopic: The neoplastic cells were columnar with elongated hyperchromatic nuclei. There were many mitotic figures. The cells were arranged in acini which varied from round to elongate. Piling up of the tumor cells in an asymmetrical pattern was common, and in some areas the glandular lumen was almost obliterated by the cellular proliferation. The glandular acini were separated by thin fibrous septa.

Ceruminous Gland Adenoma and Adenocarcinoma. Gross: These tumors were located within the external ear canal. They were soft in consistency, and all had some degree of secondary inflammation. They varied from dark red-brown to yellow-cream.

Microscopic: Typical tumor cells were large and cuboidal, and had vesicular nuclei and prominent nucleoli. The malignant tumors had many mitotic figures. In addition, the adenocarcinomas were characterized by a moderate degree of cellular anaplasia and pleomorphism. The cells had formed irregular acini and ducts, some with papillary infoldings. There was a secretion present in many acini, and extensive areas of inflammation were common in all tumors of this group (Figure 9).

Mammary Gland Adenoma and Adenocarcinoma. Gross: The only consistent gross features were inflammation and ulceration of the tumors. Their sizes were variable, and lymph node involvement was inconsistently noted. From 1 to several glands were involved, and recurrences after surgery were common. Many had metastasized to distant organs.

Microscopic: Mammary adenomas and adenocarcinomas assumed several microscopic patterns. Of infrequent occurrence was the solid type (Figure 10), where the majority of the cells was arranged in a sheet, with fibrous stroma intermixed. More common were the cystadenoma and cystadenocarcinoma. The most common type of pattern was that of neoplastic cells arranged in acini or glandular lobules, divided by variable amounts of fibrous connective tissue (Figure 11).

The cells in the adenocarcinomas were similar in all patterns of arrangement, and were somewhat pleomorphic with large hyperchromatic nuclei and prominent nucleoli. Mitotic figures were numerous. The acini were irregularly shaped, and of various sizes. Many had papillary projections into the lumen (Figure 12). In some areas the proliferation and piling up of neoplastic cells almost obliterated the acinar lumens.

Cells in metastatic lesions were more anaplastic, and acinar formation was not as distinctive as in the primary lesion (Figure 13). Necrosis and inflammatory exudate were commonly observed in the primary sites of mammary tumors.

The few adenomas were only slightly altered from the normal glandular appearance. Mitotic figures were rare, and the acini appeared slightly enlarged and irregular, with well differentiated glandular epithelium.

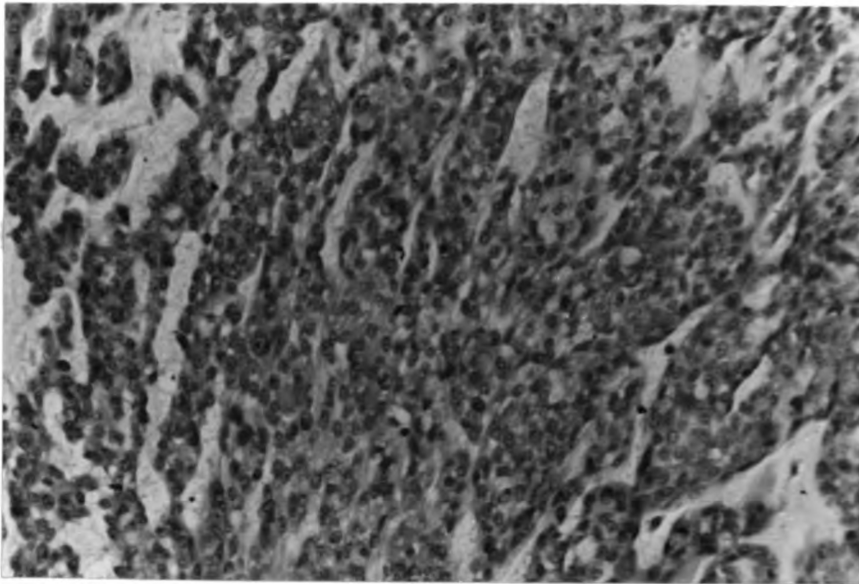


Figure 10. "Solid" type mammary adenocarcinoma. Hematoxylin and eosin. x 188.

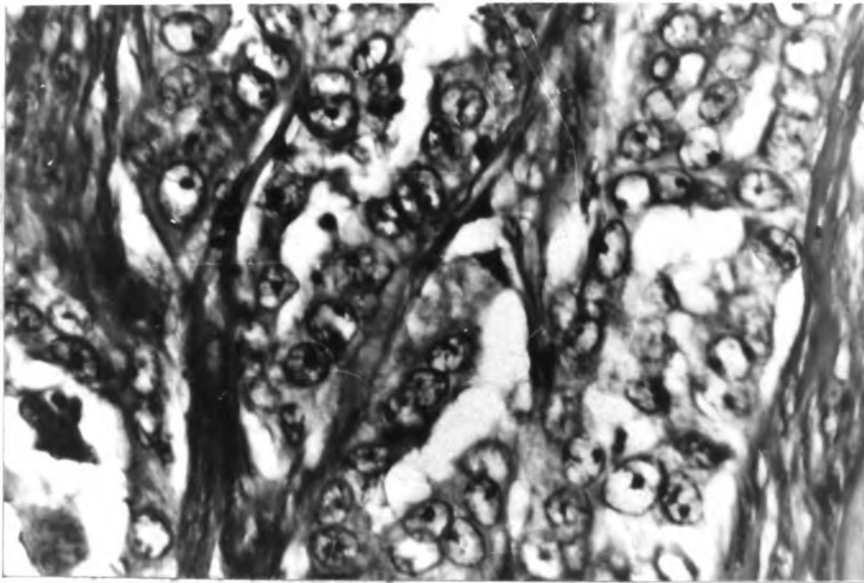


Figure 11. Mammary adenocarcinoma. Vesicular nuclei with prominent nucleoli. Cells have formed fairly well differentiated acini. Hematoxylin and eosin. x 469.

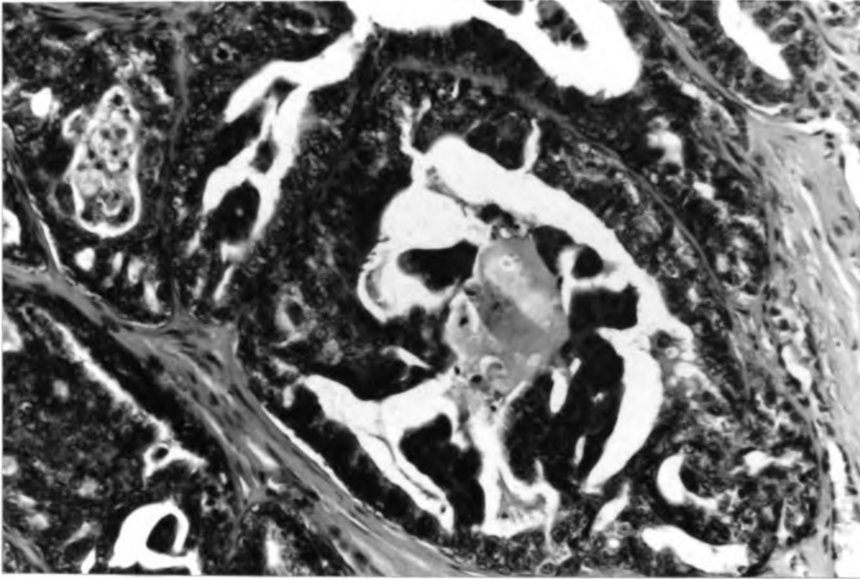


Figure 12. Mammary adenocarcinoma. Cystic acinus with papillary projections into the lumen. Hematoxylin and eosin, x 188.

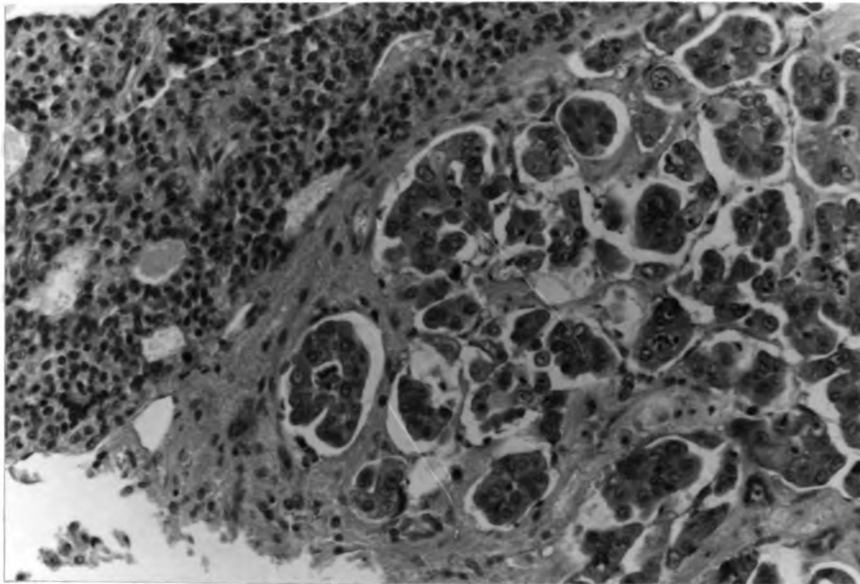


Figure 13. Mammary adenocarcinoma. Metastatic lesion in pituitary. Pleomorphic cells which have formed acinar structures. Hematoxylin and eosin, x 188.

Uterine Adenoma and Adenocarcinoma. Gross: The 1 adenoma was reported to be present in the "uterine tube" and was 2.5 x 2.0 cm. in size. On cut section it appeared cystic. The adenocarcinoma was 10.0 cm. in diameter and projected forward from the uterus toward the stomach.

Microscopic: The adenoma had dense collagenous stroma which contained cystic glands of varying size. Several glands had some piling up of glandular epithelium on 1 side of the acinus.

The adenocarcinoma had neoplastic areas that varied from cystic papilliferous glands to more solid lobules of cells divided by thin fibrous stroma. The cells were pleomorphic, with vesicular nuclei, prominent nucleoli and moderate numbers of mitotic figures. There was extensive invasion of the myometrium by neoplastic cells.

Hepatocarcinoma. Gross: These tumors gave a diffuse nodularity to the liver. Metastatic nodules were present in the spleen in both cases and in mesenteric lymph nodes in 1 case.

Microscopic: The neoplastic cells had nuclei that resembled the nuclei of normal liver cells, except for some variation in size. The cells were also hyperchromatic. The cytoplasm was scanty and more basophilic than normal. Mitotic figures were common.

The transitional zone from normal to neoplastic cells was abrupt, with the adjacent normal cells compressed and displaced by the tumor masses. The cellular pattern varied from fairly solid groups of cells to areas divided into nests or lobules by delicate collagenous stroma. The areas between the lobules appeared to serve as vascular channels.

The metastatic lesions were composed of cells similar in appearance to those of the primary site (Figure 14). In the metastatic lesions there was considerable stroma and vascularity, but the lobular pattern was not as well developed as in the primary.

Bile Duct Carcinoma. Gross: Primary lesions consisted of variably-sized nodules in the liver. The lungs consistently had metastatic lesions, and there were often omental and peritoneal implantations.

Microscopic: Within the primary focus, a change from more normal to neoplastic bile ducts could be seen in the portal triads. The cells were cuboidal or columnar, with some degree of nuclear polarity evident. Nuclei were hyperchromatic and nucleoli enlarged. Mitotic figures were variable in number.

The primary tumors were composed of ducts which varied in appearance from small and fairly well differentiated to some that were cystic with papillary infoldings. The liver parenchyma was destroyed and compressed at the advancing edge of the tumor.

Cells in the metastatic lesions were usually more pleomorphic than those in the primary, although a slight degree of nuclear polarity was evident. In many metastatic foci, the cells formed small nests rather than ducts or acinar structures.

Pancreatic Adenoma and Adenocarcinoma. Gross: These tumors were in the form of nodules or large masses in the pancreas. Size varied from 1.0 x 2.0 to 3.0 x 7.0 cm. The small intestine and spleen were encroached upon and invaded by the tumor in some cases. In 1 case, there were metastases to the lung and myocardium.

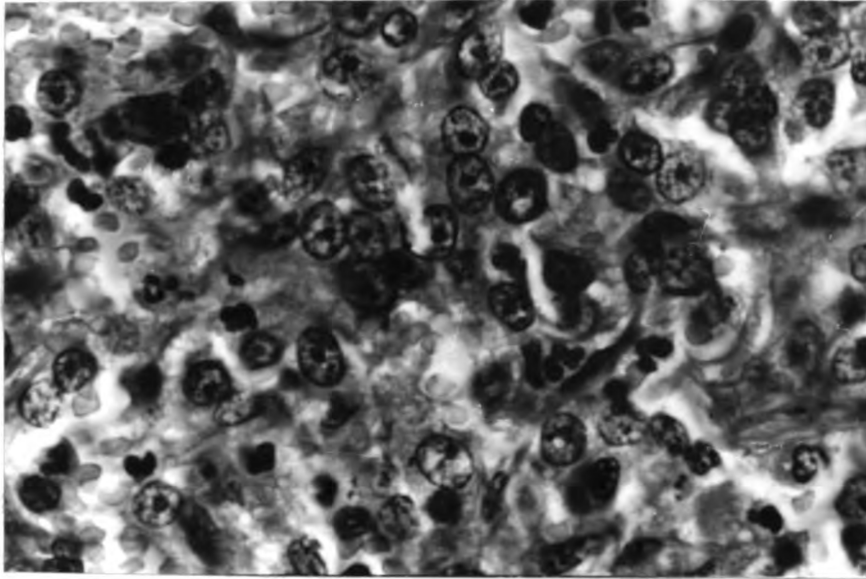


Figure 14. Hepatocarcinoma. Metastatic lesion in the spleen. The neoplastic cells have large vesicular nuclei with prominent nucleoli. Hematoxylin and eosin. x 750.

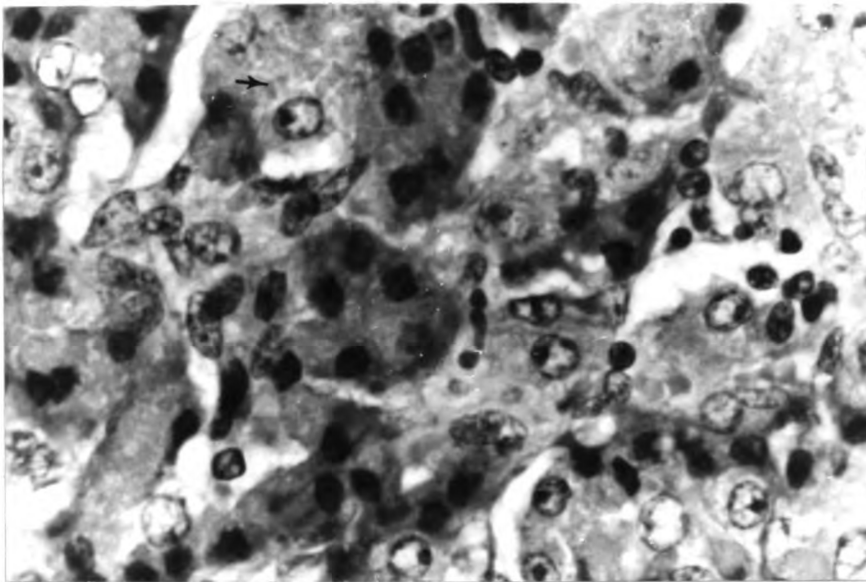


Figure 15. Pancreatic adenocarcinoma. Implanted lesion in wall of the intestine. Note the occurrence of zymogen granules in several of the neoplastic cells (arrow). Hematoxylin and eosin. x 750.

Microscopic: In the pancreatic adenomas, the cells were slightly enlarged, paler than normal, and had enlarged vesicular nuclei with prominent nucleoli. Zymogen granules were present within the cells, and the normal glandular pattern was only slightly altered.

The adenocarcinoma cells were pleomorphic with hyperchromatic nuclei. The normal glandular pattern was often lost, and there was a disarray of cells leading to the formation of dilated irregular glandular structures.

In the metastatic lesions, some areas were fairly well differentiated, and many of the cells contained eosinophilic material resembling zymogen granules (Figure 15). In other areas, however, the cells were extremely anaplastic and bore little resemblance to pancreatic glandular epithelium.

Intestinal Adenocarcinoma. Gross: One case of intestinal adenocarcinoma was included in this study. The terminal 8 inches of the ileum had an annular thickening, and the lumen was almost completely obstructed. The regional lymph nodes were enlarged.

Microscopic: The cells were pleomorphic with vesicular nuclei and enlarged nucleoli. Many mitotic figures were present. The neoplastic process appeared to be originating at the base of an ulcerated area of mucosa.

The cells were forming irregular and slightly cystic acini, and considerable amounts of bluish-staining mucin were present and filled many of the acini. There were neoplastic cells in acinar formation within the submucosa and the inner layer of the muscularis (Figure 16).

Adenocarcinoma of Undetermined Origin. Gross: The majority of these tumors (9) occurred in various abdominal organs, lymph nodes, and mesentery. Eight of the tumors were in the skin or mucous membranes, while 3 tumors

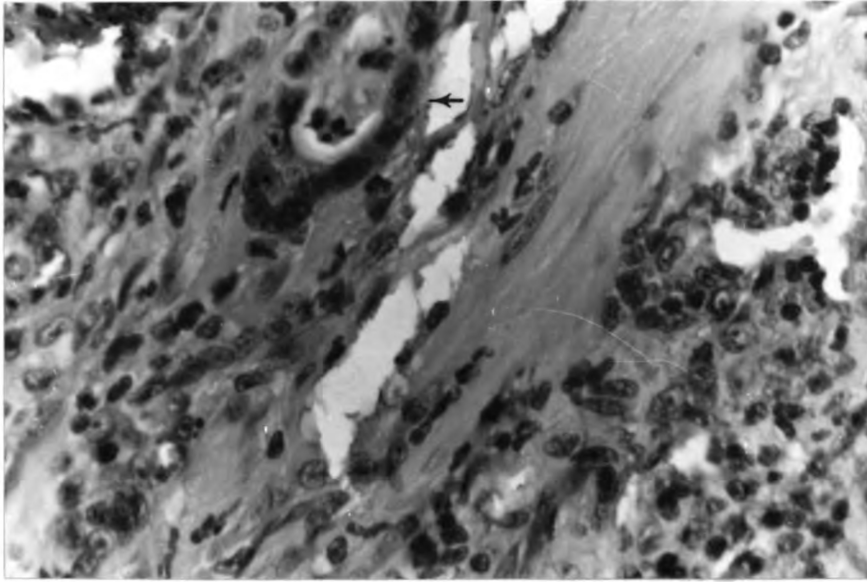


Figure 16. Intestinal adenocarcinoma. Neoplastic cells in the smooth muscle. Some acini being formed (arrow). Hematoxylin and eosin, x 469.

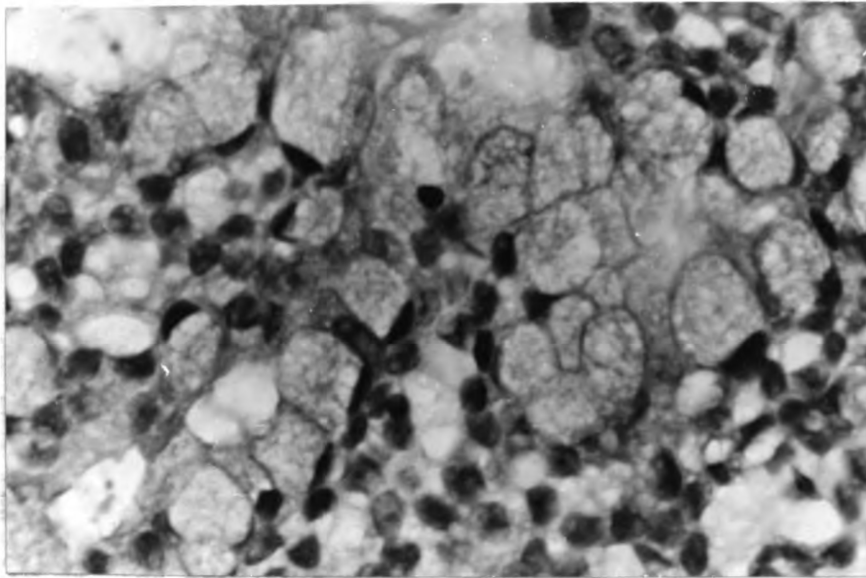


Figure 17. Mucous adenocarcinoma. Note large neoplastic cells with foamy cytoplasm. Hematoxylin and eosin, x 750.

were located in both the abdominal and thoracic cavities. Most of the tumors were described as nodular masses in the various organs involved, and the range in size was from less than 1.0 cm. to greater than 10.0 cm. in diameter. Most of the tumors from the skin and mucous membranes had been traumatized and were inflamed.

Microscopic: The adenocarcinomas in the skin and mucous membranes were composed of cuboidal or columnar cells with rounded or oval nuclei and enlarged nucleoli. Some had very anaplastic cells with many mitotic figures.

The cells were arranged in irregular acini or solid lobules divided by thin fibrous septa. Some had papillary projections within the acini. The acinar walls varied from 1 to several cells in thickness. Some of the tumors from mucous membranes had cells that were filled with a pale bluish-staining foamy material which was probably mucin (Figure 17).

The general characteristics of the adenocarcinomas of the abdominal and thoracic cavities were similar to those from the skin, but appeared more malignant. The cells were pleomorphic with vesicular nuclei and enlarged nucleoli (Figure 18) and were very anaplastic in some cases. Mitotic figures were frequently seen. The acinar patterns were irregular in size and shape. In none of the tumors in this group could the cell of origin be determined from the material available.

Undifferentiated Carcinoma. Gross: The few tumors in this group came from the jaw and the forelegs.

Microscopic: The cells were large and epithelial in appearance, with vesicular nuclei and large nucleoli. In some areas they were in sheets, while in others the arrangement was of small nests of neoplastic cells surrounded by fibrous stroma. No definite cell type could be determined.

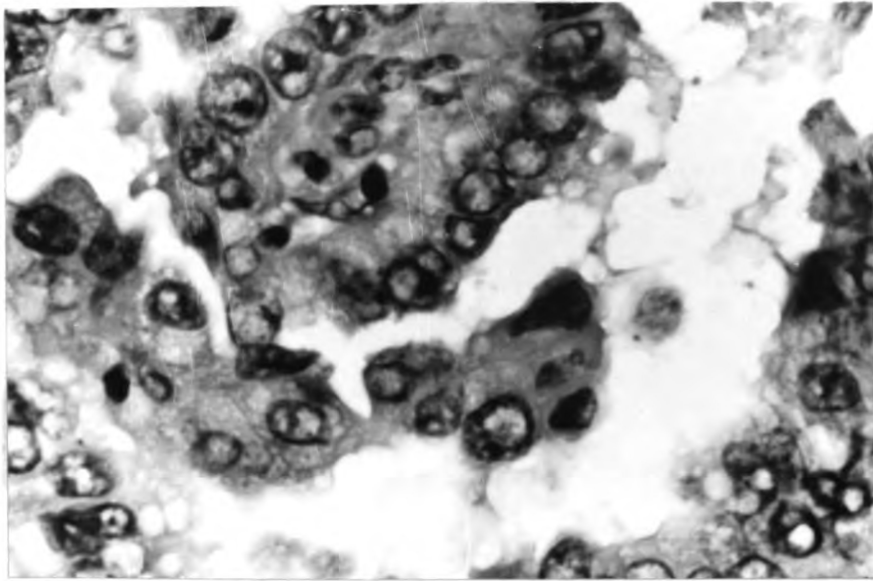


Figure 18. Adenocarcinoma in mesentery. Very anaplastic cells with only slight tendency toward glandular formation. Hematoxylin and eosin. x 750.

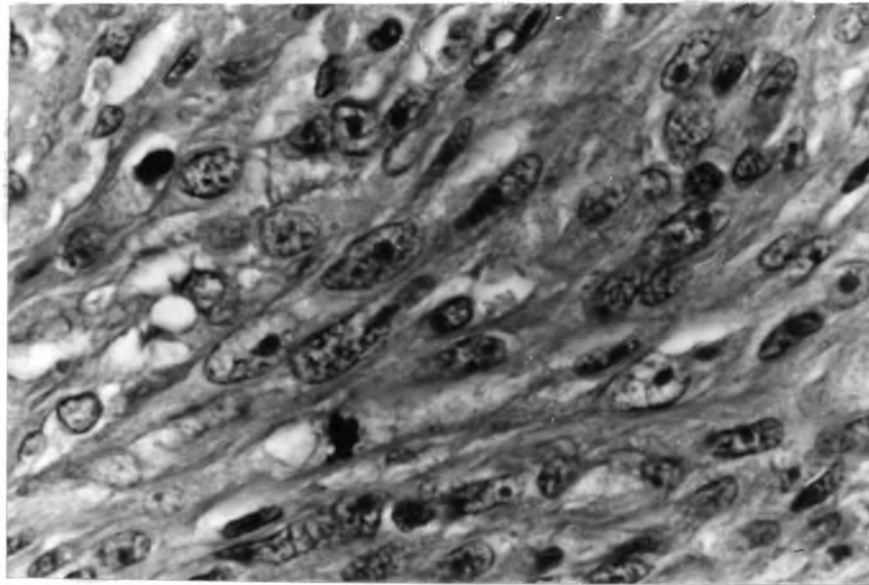


Figure 19. Fibrosarcoma. Pleomorphic hyperchromatic nuclei, prominent nucleoli and mitoses. Hematoxylin and eosin. x 750.

B. Mesenchymal Tumors

Fibroma. Gross: Fibromas occurred randomly in the subcutaneous tissue, the oral cavity, and the reproductive tract. They were of variable size, and all were encapsulated. Most of them were firm and light in color.

Microscopic: The cells were generally spindle shaped, with indistinct cellular outlines. Nuclei were variable in shape, from small and rounded to thin spindle forms. Nuclei were slightly hyperchromatic and nuclear chromatin was scattered like fine dust within. Mitotic figures were rare.

The cells were arranged in wavy bundles, and little whorling was seen. Usually the fibers were long, but occasionally they were short and gave the appearance of a random scattering of fibers with no particular organization. Occasionally the tumors were predominantly fibrous and acellular.

Fibrosarcoma. Gross: Fibrosarcomas were less noticeably encapsulated and more invasive than fibromas. They tended to recur after excision and infrequently metastasized. Many were subject to necrosis and inflammation within the tumor.

Microscopic: The cells of the fibrosarcoma were pleomorphic, and the cell nuclei were vesicular with enlarged nucleoli. Mitotic figures were common (Figure 19). The cellular pattern was similar to the fibromas, but there was more interlacing of bundles and more tendency toward the formation of whorls.

Malignant Mesenchymoma. Gross: The 1 example of this type of neoplasm was a slowly growing tumor of the gingiva..

Microscopic: This tumor was made up of fibrous tissue, smooth muscle, myxomatous tissue, and bone (Figures 20 and 21). There were many large

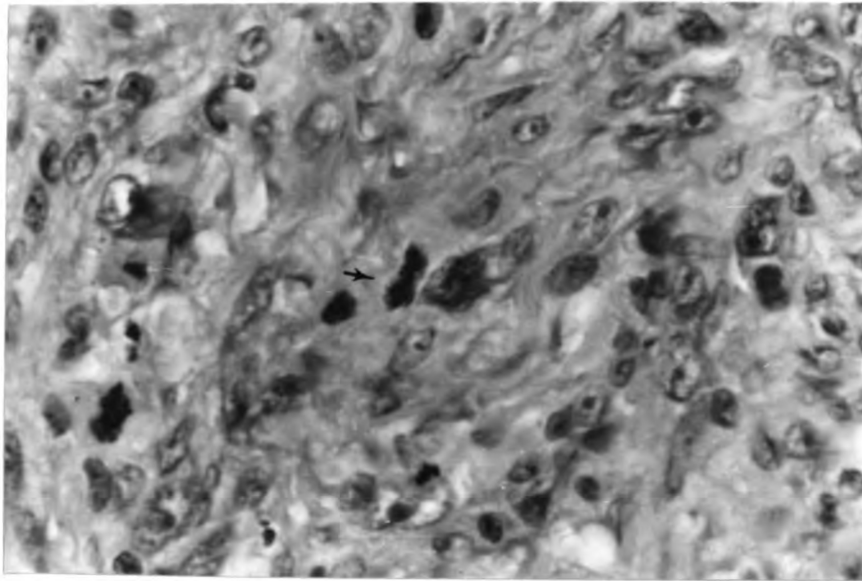


Figure 20. Malignant mesenchymoma. Section of anaplastic fibrous elements with mitotic figures (arrow). Hematoxylin and eosin, x 750.

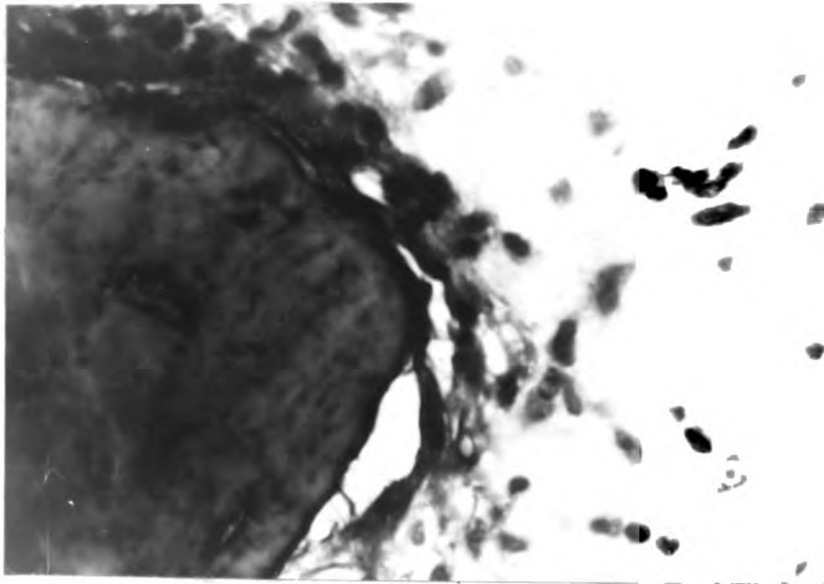


Figure 21. Malignant mesenchymoma. Myxomatous tissue and bone. Hematoxylin and eosin, x 750.

multinucleated giant cells. Several of the cellular elements had malignant characteristics.

Neurofibroma and Neurofibrosarcoma. Gross: These tumors were not remarkable grossly, except that 2 of them arose in the vicinity of cranial nerves, 1 filling the retrobulbar area and the other in the cranial cavity.

Microscopic: The cells varied from spindle and stellate to slightly cuboidal. The cytoplasm was moderate in amount, and the nuclei of the malignant tumors were hyperchromatic with enlarged nucleoli. The major points of difference between the benign and malignant varieties were the greater degree of anaplasia and more frequent mitoses.

The cellular pattern was that of undulating columns and whorls, with areas of palisading of cells. In some cases the neoplastic cells seemed to arise from the periphery of nerve bundles (Figure 22).

Myxoma and Myxosarcoma. Gross: The myxoma was located in the subcutaneous tissue of the right front leg. The neoplasm was rounded, yellow, and soft in consistency. The sarcoma was located in the liver and myocardium of the right atrium.

Microscopic: The cells of the myxoma had a small amount of cytoplasm, and the nuclei were rounded or ovoid to rod shaped and somewhat hyperchromatic. They were arranged in regular sheets in some areas and in others were in an interlocking cord pattern of 1 or 2 cells thick. The spaces between the cords contained an amorphous pink-blue staining material (Figure 23). The microscopic appearance of the myxosarcoma was similar, except for an increase in the number of mitotic figures.

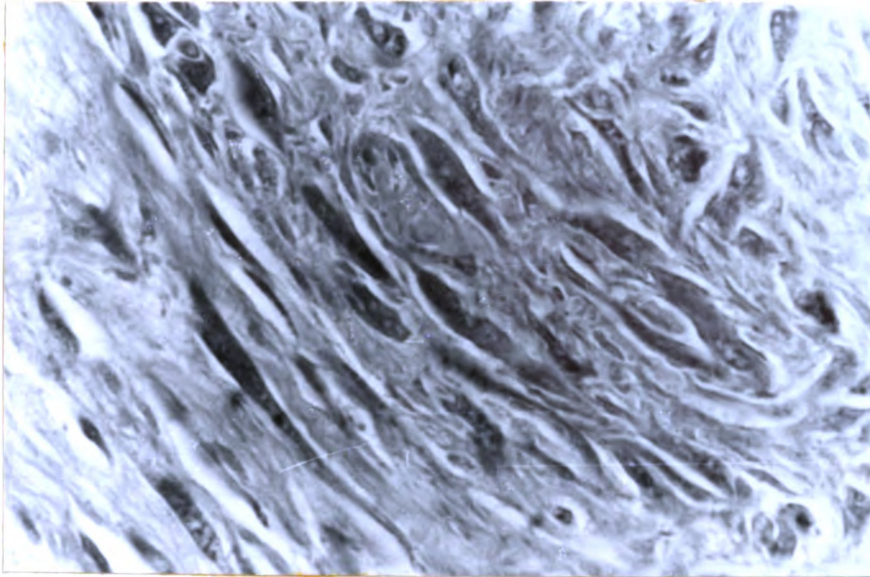


Figure 22. Neurofibrosarcoma. Neoplastic cells which have apparently originated from a nerve bundle. Hematoxylin and eosin. x 750.

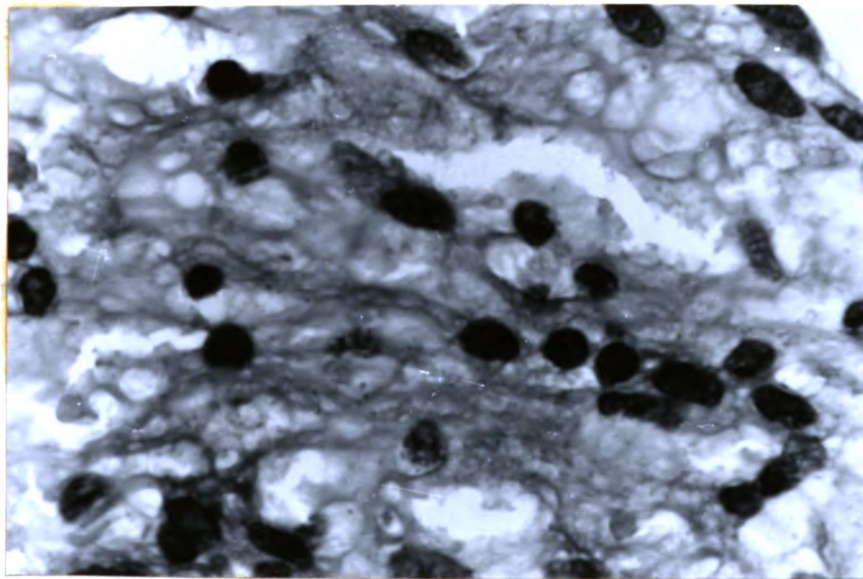


Figure 23. Myxoma. Scattered nuclei and abundant myxomatous ground substance present. Hematoxylin and eosin. x 750.

Meningioma. Gross: The 1 example of this tumor was a small mass located lateral to the cerebrum.

Microscopic: The cells were spindle shaped with sparce cytoplasm. Cell nuclei were pale and finely granular. The cells were arranged in tight whorls and larger curving columns. Extensive degeneration and mineralization were present within the tumor (Figure 24).

Leiomyoma and Leiomyosarcoma. Gross: The leiomyomas in this study were from the female genital tract and appeared as nodular growths. The largest of these was 7.0 cm. in diameter. The sarcomas arose from smooth muscle in various areas of the body.

Microscopic: The cells of the leiomyosarcoma had slightly vesicular, cigar-shaped nuclei, many of which appeared twisted (Figure 25). Mitoses were not found in the leiomyomas and were infrequent in the sarcomas. The cells were arranged in bundles that had a wavy pattern in most areas. There was a variable amount of fibrous stroma, and in some cases it was as plentiful as the muscle elements. One of the leiomyomas seemed to arise from the muscular layer of small arteries and arterioles (Figure 26).

Rhabdomyosarcoma. Gross: Gross description of these tumors was not available. In 1 case the tumor had metastasized to the lungs.

Microscopic: The cells were large and bizarre in shape. Many were multinucleated, and strap cells could be seen. The tumors had considerable amounts of fibrous stroma. Under high magnification fine striations could be seen in some cells in sections stained with phosphotungstic acid hematoxylin (Figure 27).

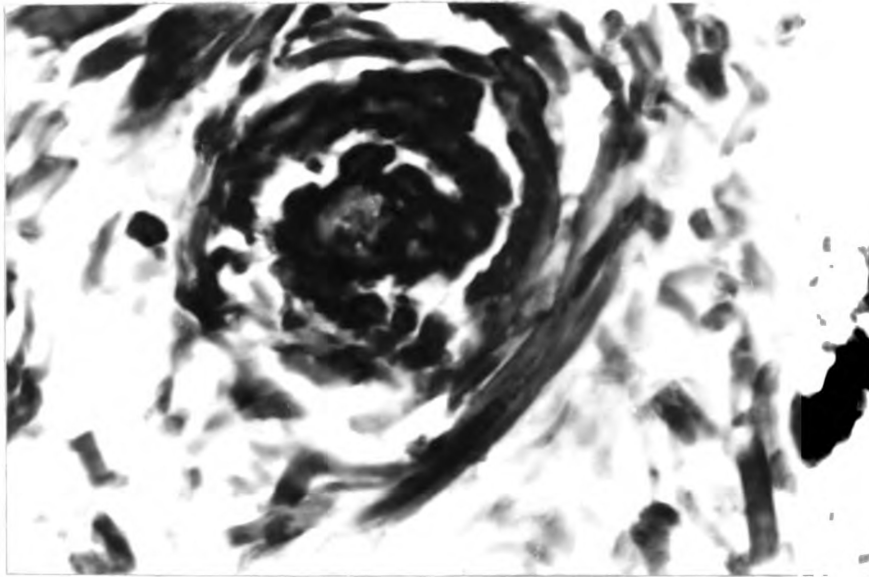


Figure 24. Meningioma. Whorling arrangement of degenerative neoplastic cells which have undergone mineralization. Hematoxylin and eosin. x 750.

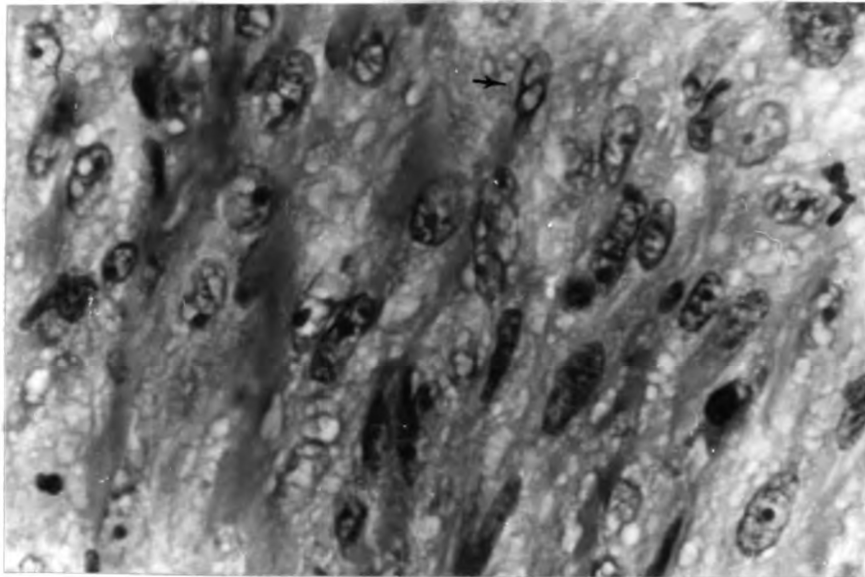


Figure 25. Leiomyosarcoma. Although the nuclei are pleomorphic, the "twisted" appearance of several can be noted (arrow). Hematoxylin and eosin. x 750.

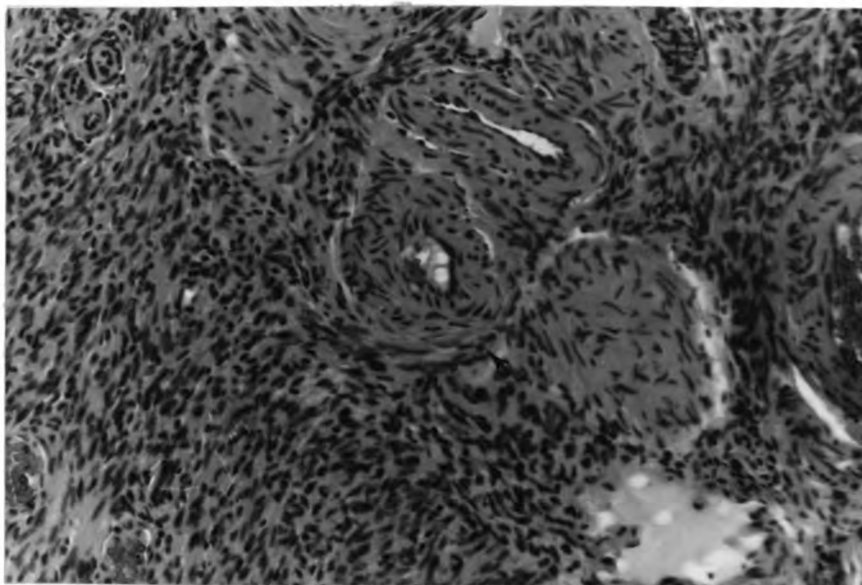


Figure 26. Leiomyoma. The tumor cells can be seen adjacent to the walls of the vessels (arrow). Hematoxylin and eosin, x 188.

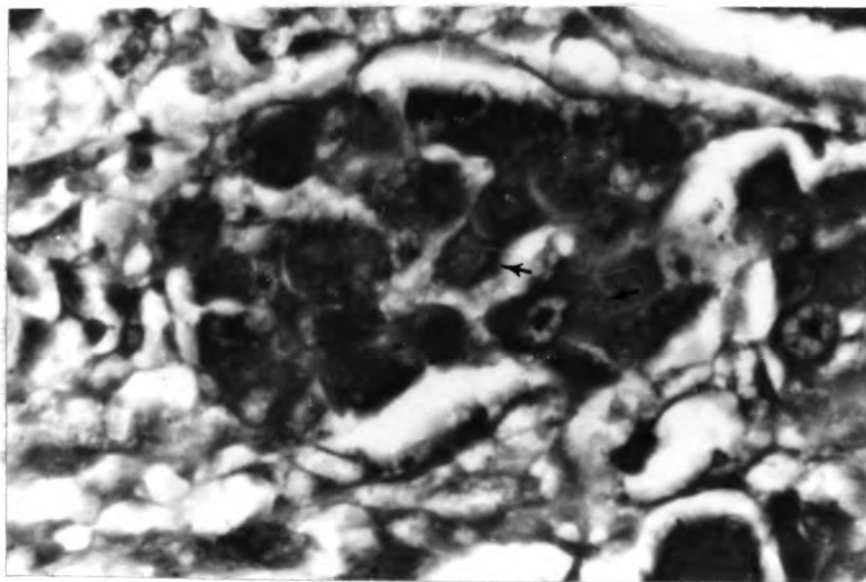


Figure 27. Rhabdomyosarcoma. Bizarre-shaped cells with faint cross striations in the cytoplasm (arrows). Phosphotungstic acid hematoxylin, x 750.

Lipoma. Gross: These were variably-sized tumors which represented circumscribed accumulations of fat.

Microscopic: The lipomas in this series were all benign in appearance, usually resembling normal fat. The salient feature of the microscopic appearance was the variation in the amount of stroma between the fat cells, being nonexistent in some and moderate to dense in others (Figure 28).

Chondrosarcoma. Gross: No gross description was available for the 2 cases in this series.

Microscopic: These tumors were variable in appearance within themselves. Some areas resembled relatively normal cartilage, while others were more like a fibrosarcoma. The more anaplastic chondroblasts were stellate shaped with vesicular nuclei and enlarged nucleoli. Often the transitional zone between undifferentiated and differentiated elements was abrupt (Figure 29).

Osteoma and Osteosarcoma. Gross: One of the osteomas was a small tumor attached to the mandible, and the other was a nodule in the subcutaneous tissue. Osteosarcomas in this study were variably-sized tumors always associated with bone.

Microscopic: The osteomas were composed of mature bone, with some evidence of a collagenous tissue capsule. Cells of the osteosarcomas were anaplastic and pleomorphic, usually being stellate or fusiform. The cell nuclei were hyperchromatic, and mitotic figures were common. Large multinucleated giant cells were scattered throughout, often closely associated with osteoid material or bony spicules (Figure 30). The osteoid material and the bone were not uniform in occurrence. Some of the more anaplastic

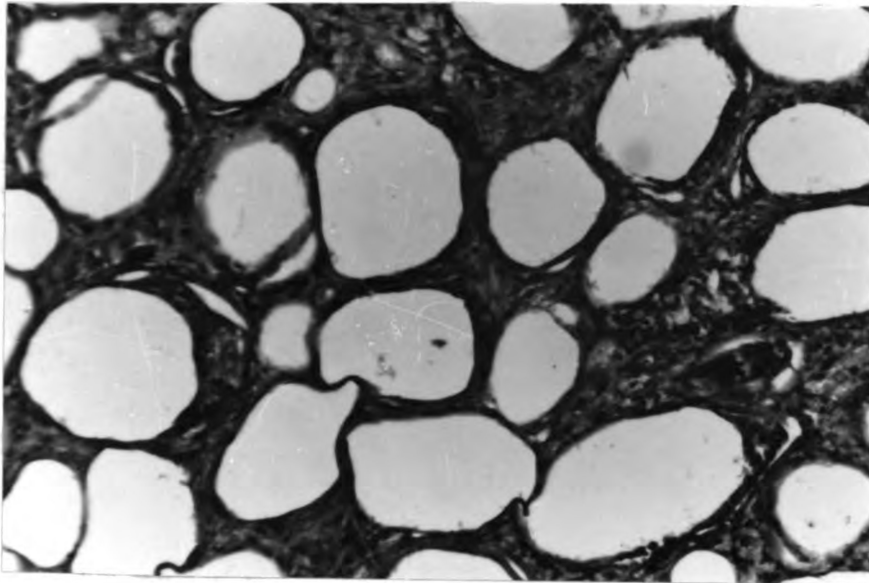


Figure 28. Lipoma. Fat cells separated by abundant collagenous stroma. Hematoxylin and eosin. x 188.

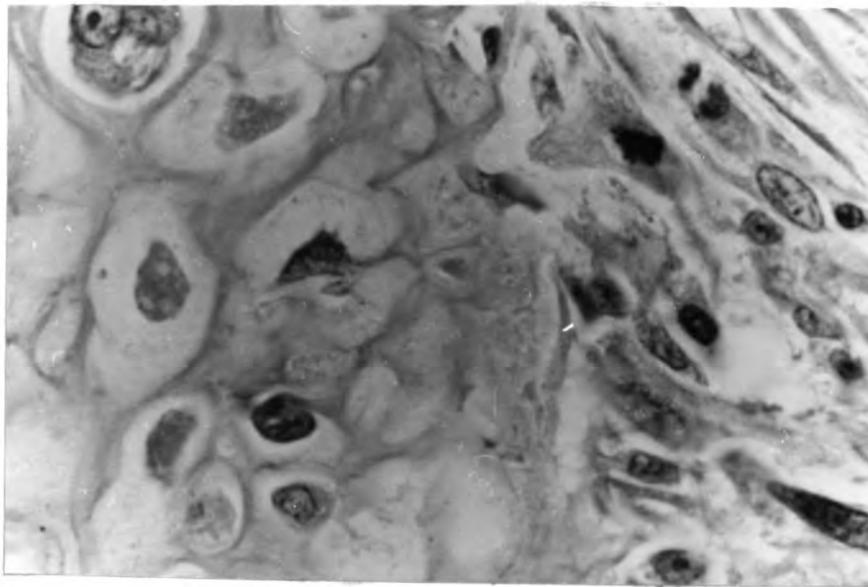


Figure 29. Chondrosarcoma. Abrupt change from anaplastic chondroblasts to more mature cartilage. Hematoxylin and eosin. x 750.

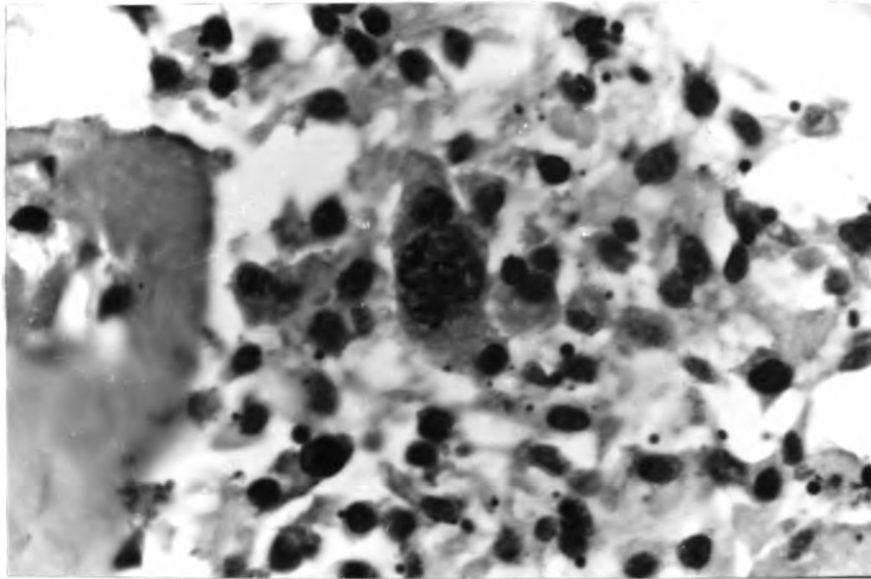


Figure 30. Osteogenic sarcoma. Stellate osteoblasts, osteoid, and giant cell. Hematoxylin and eosin. x 750.

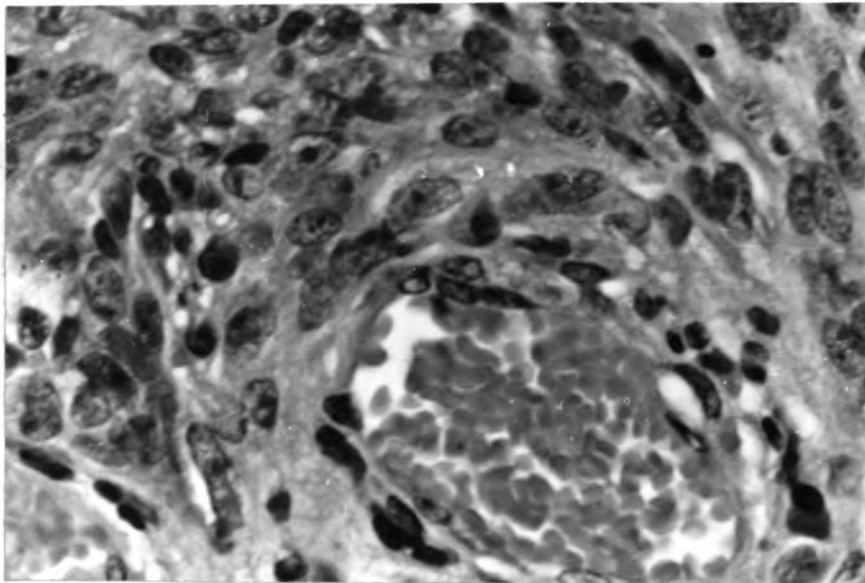


Figure 31. Hemangiosarcoma. Anaplastic endothelial cells around a vascular space. Hematoxylin and eosin. x 750.

areas in these tumors closely resembled fibrosarcomas. Hemorrhage and inflammation were common findings.

Osteochondroma. Gross: This tumor was located on the proximal portion of the right humerus. It was cauliflower-like in shape and encapsulated.

Microscopic: The major portion of this tumor was composed of mature cartilage which was being replaced at 1 side by osteoid material. Some mineralization had taken place.

Hemangiosarcoma. Gross: The only gross description available was that there was intestinal involvement in 1 animal.

Microscopic: The cells were pleomorphic, ovoid or elongated. Cell nuclei tended to be vesicular with enlarged nucleoli. The anaplastic cells lined the vesicular channels and, in some instances, had proliferated in a circular pattern around them (Figure 31). In less vascular areas they were arranged in curving columns or solid sheets.

Mastocytoma. Gross: Mastocytomas occurred in the skin as raised circular plaques, often with ulceration and serous or purulent exudation. They occurred in all parts of the body and were often diagnosed grossly as inflammatory lesions. There were no reports of recurrences or metastases of any of these tumors.

Microscopic: The cells were variable in size and shape, being rounded, ovoid, or sometimes stellate. The nuclei were often hyperchromatic and eccentrically located. The cytoplasm of the cells was usually abundant, and granules could occasionally be seen in H & E-stained sections. With Giemsa-stained sections, the nuclei were often obscured by metachromatic

granules (Figure 32). In the more anaplastic tumors the cells were often difficult to distinguish from cells of the lymphoid series without special stains.

The cells were usually arranged in sheets. The tumor cells were often densely packed, but occasionally had a loose arrangement, with much stroma between cells (Figure 33). Occasionally they were in cords 1 cell in thickness, which formed anastomosing patterns within the stroma. There were eosinophils present to some degree in all the tumors. The eosinophils were scattered at random throughout the tumor. Inflammatory changes were consistently noted in the surface areas.

Malignant Lymphoma. Gross: Malignant lymphoma occurred in several sites (TABLE 3). The gross lesions were usually nodular, of variable size, and gray-white or yellow (Figure 34). Occasionally there was virtual replacement of an organ, such as the kidney, by neoplastic tissue (Figure 35). In some cases both kidneys were uniformly involved. At times the masses in the mediastinum were large enough to fill most of the thoracic cavity. When the intestinal tract was involved, it was thickened in an annular pattern, and the intestine was often stenotic with the lumen almost completely obliterated (Figure 36).

Microscopic: Reticulum Cell Sarcoma type: Cells making up this tumor were noticeably pleomorphic and had abundant cytoplasm. Some appeared mature, and others undifferentiated and anaplastic. The nuclei were vesicular and the nucleoli were enlarged. Many of the nuclei were irregular in shape, and often looked like myeloblastic nuclei. They were often eccentrically located within the cells. Mitotic figures were common (Figure 37).

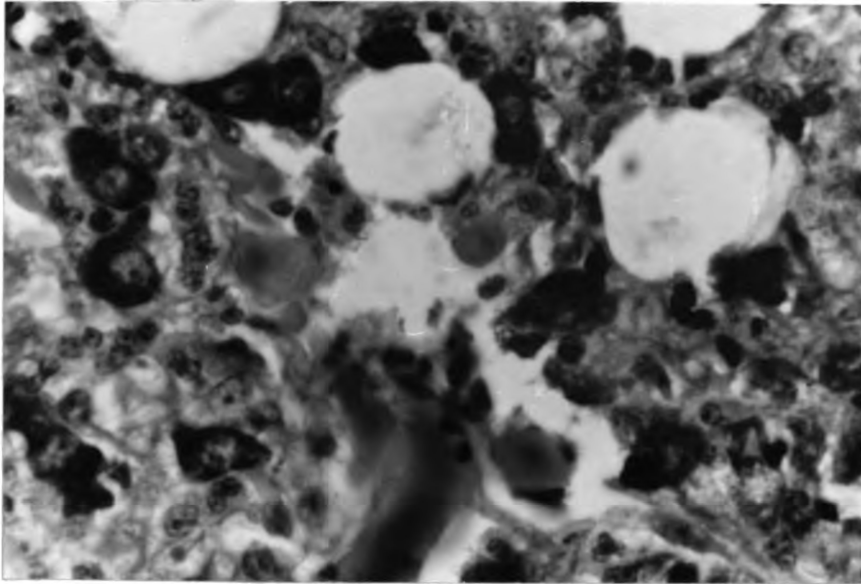


Figure 32. Mastocytoma. Metachromatic granules which have obscured the nucleus in many of the neoplastic mast cells. May-Grunwald-Giemsa. x 750.

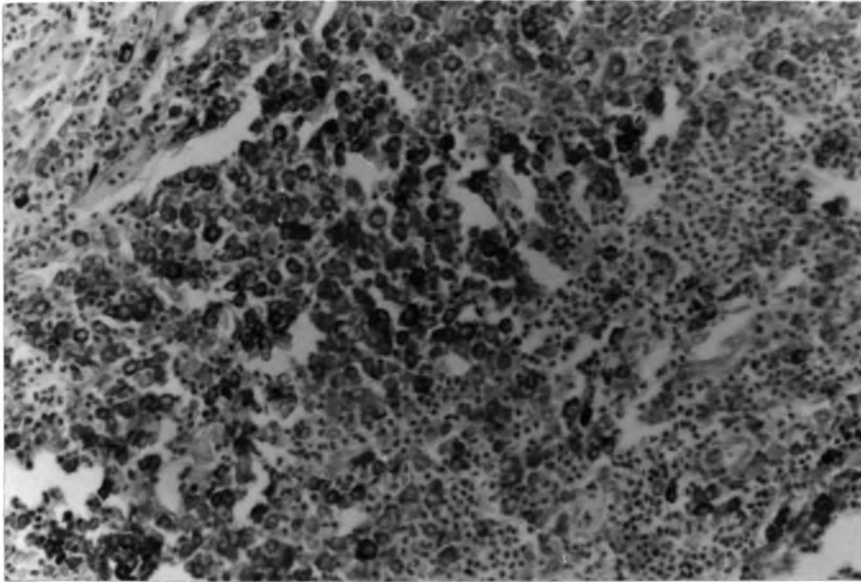


Figure 33. Mastocytoma. Note loose, scattered arrangement of the mast cells. May-Grunwald-Giemsa. x 188.

TABLE 3. Site of involvement in malignant lymphoma.

| Site | Number of Cases |
|------------------------|-----------------|
| Kidney | 14 |
| Mediastinum | 14 |
| Liver | 12 |
| Spleen | 9 |
| Internal lymph nodes | 9 |
| Lung | 6 |
| Peripheral lymph nodes | 5 |
| Gastrointestinal tract | 5 |
| Mesentery | 4 |
| Other | 9 |



Figure 34. Malignant lymphoma, reticulum cell type, in the myocardium.

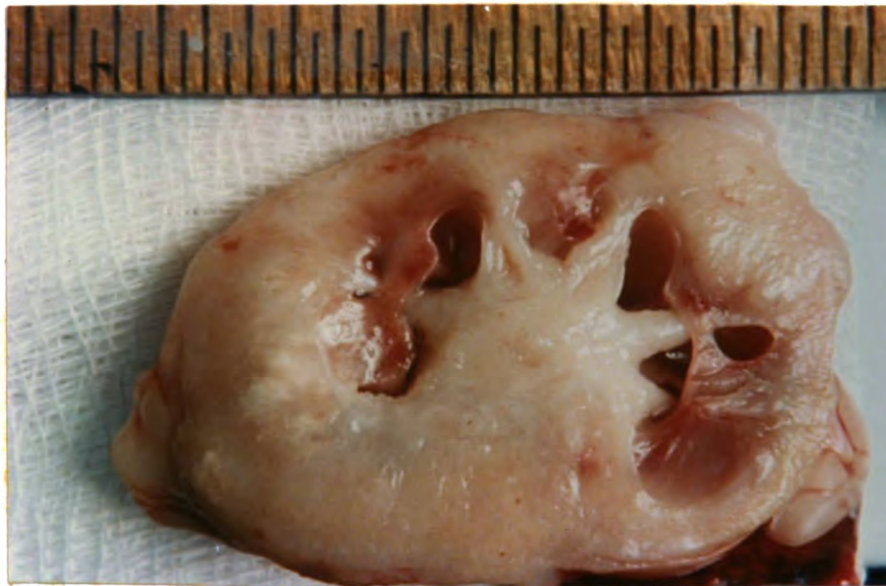


Figure 35. Malignant lymphoma, reticulum cell type, which has replaced normal kidney parenchyma.

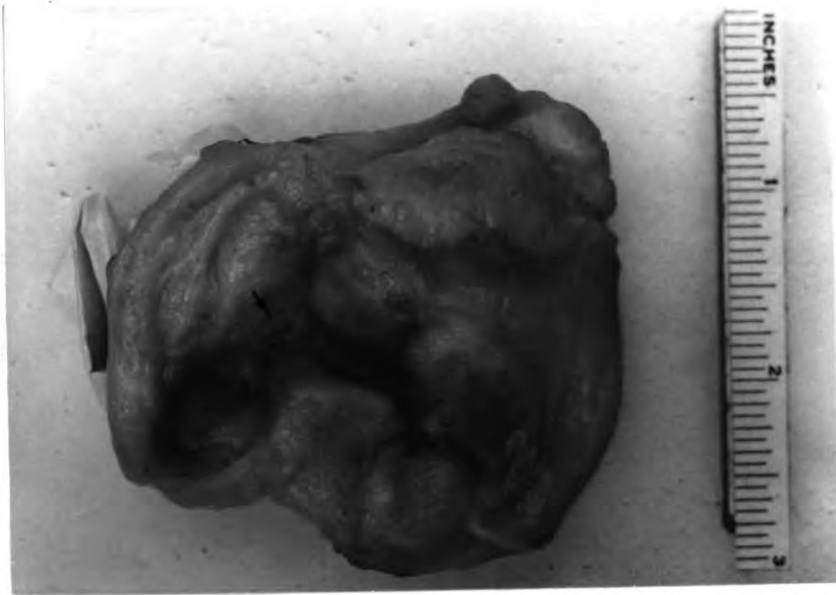


Figure 36. Malignant lymphoma. Annular thickening of small intestine due to infiltration of lymphoid cells. Arrow indicates lumen.

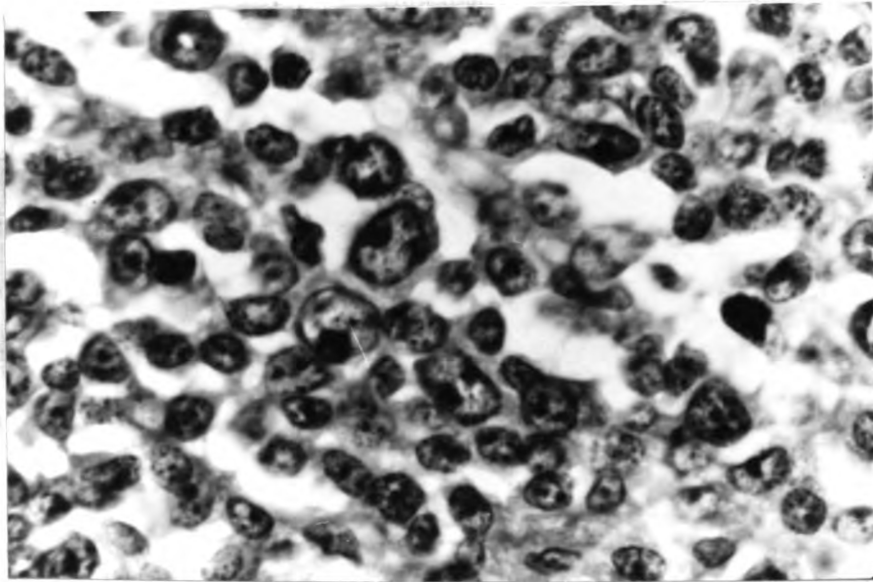


Figure 37. Malignant lymphoma, reticulum cell type. Note the extreme variation in size of the cells. Hematoxylin and eosin, x 750.

The cells were in sheets, with scant to moderate stroma. With a reticulum stain, bundles of reticulum could be seen enclosing individual cells or small groups of cells (Figure 38). When in organs such as the kidney, the sheets of tumor cells had isolated and replaced the normal architecture (Figure 39).

Lymphosarcoma type: The cells of the lymphosarcoma type of malignant lymphoma could usually be identified as lymphocytic or lymphoblastic, but because both types or intermediate forms often occurred in the same tumor, no attempt was made to separate them. The cells had very little cytoplasm and round to oval nuclei which were often hyperchromatic. They were much more regular in appearance than the cells of reticulum cell sarcomas, and the nucleoli, even when hyperchromic, were much smaller in size. Mitotic figures were usually numerous, although occasionally they were few in number.

The typical arrangement of cells was in a monotonous sheet with variable amounts of stroma (Figure 40). The cellular pattern varied from a loose arrangement to closely packed masses of cells (Figure 41). From an initial focus (or foci) in an organ, the lymphoid cells proliferated and eventually replaced the normal architecture. In the liver the initial cellular accumulations were in the portal areas, and in more advanced cases the parenchyma was compressed and atrophic (Figure 42). An unusual occurrence in a few cases was involvement of skeletal muscle (Figure 43).

In this series, there was 1 case similar to the giant follicular lymphoma of man. Within the node there was a proliferation of large lymphoid follicles which contained pale staining lymphoblastic cells. In addition, the node was overrun by more mature lymphoid elements and

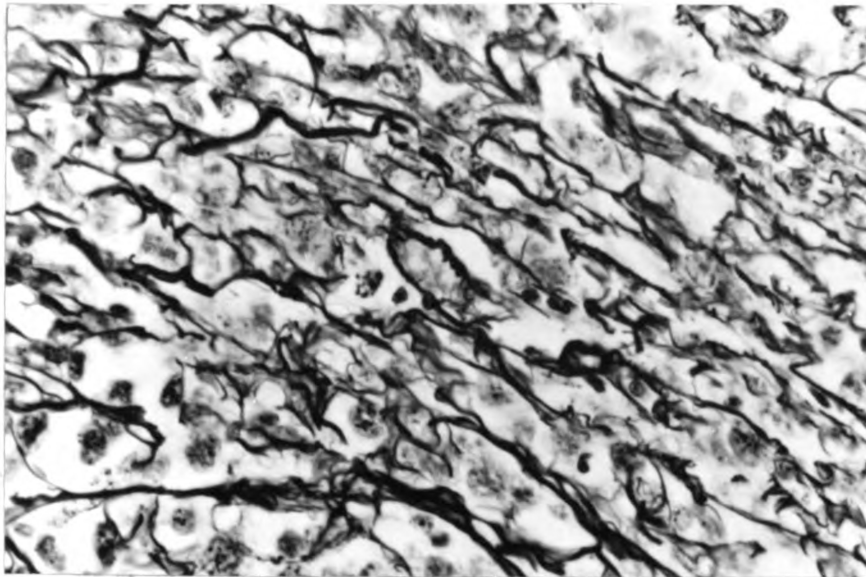


Figure 38. Malignant lymphoma, reticulum cell type. Note the reticular fibers around individual cells and small groups of cells. The same tumor as Figure 37. Lithium Silver. x 469.

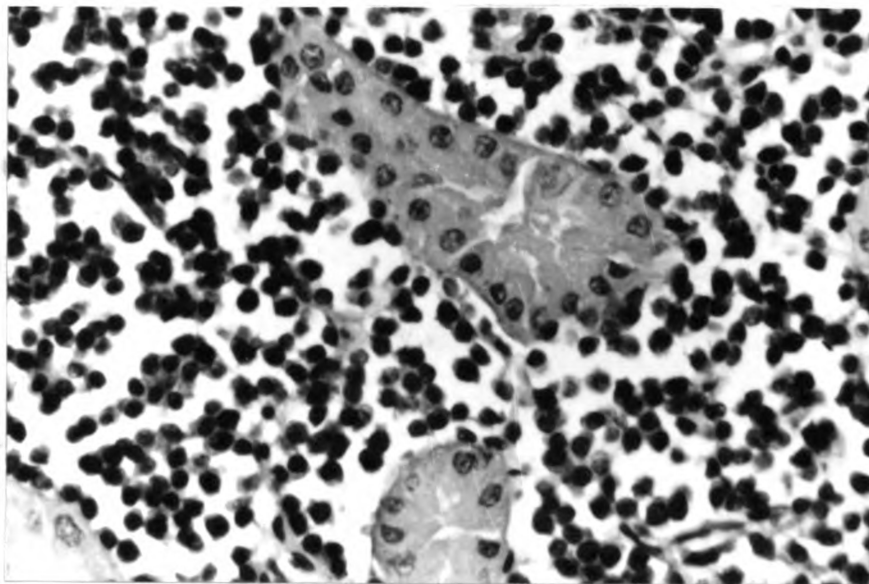


Figure 39. Malignant lymphoma, reticulum cell type, which has infiltrated the kidney. Hematoxylin and eosin. x 188.

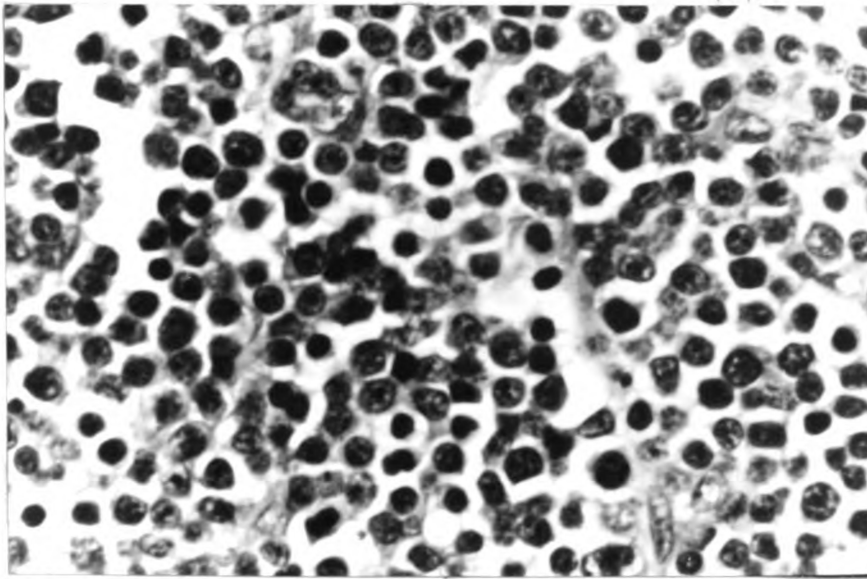


Figure 40. Malignant lymphoma. Monotonous sheets of cells with loose arrangement. Hematoxylin and eosin, x 750.

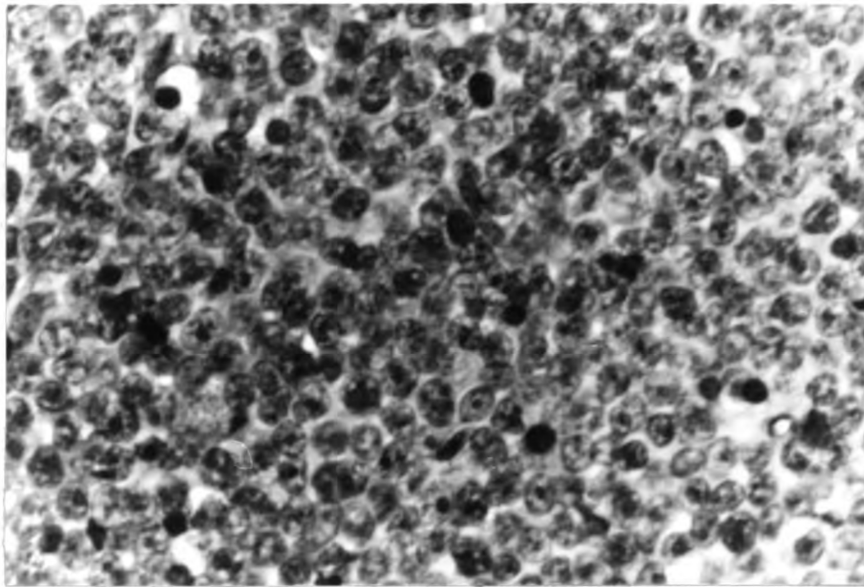


Figure 41. Malignant lymphoma. Monotonous sheet of densely packed cells. Compare with Figure 40. Hematoxylin and eosin, x 750.

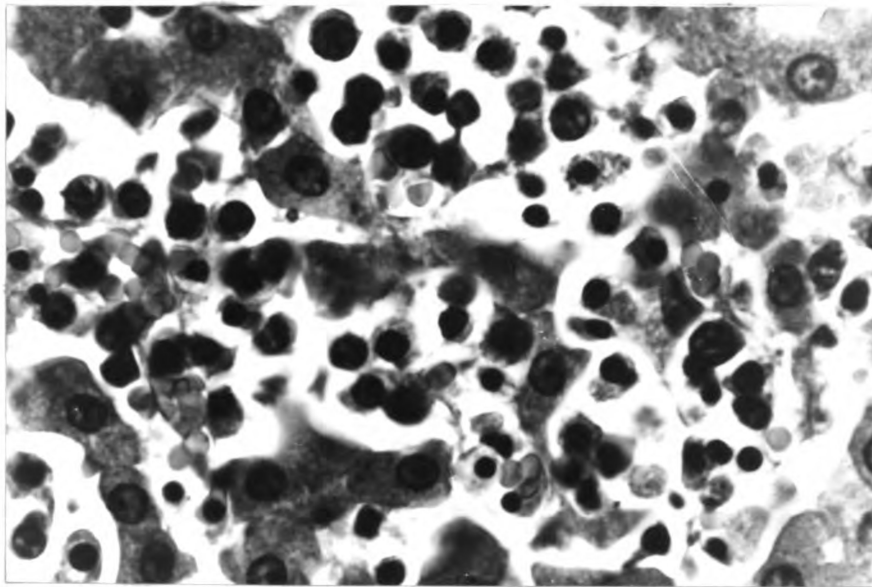


Figure 42. Malignant lymphoma. Neoplastic cells which have isolated and replaced normal liver parenchyma. Hematoxylin and eosin, x 750.

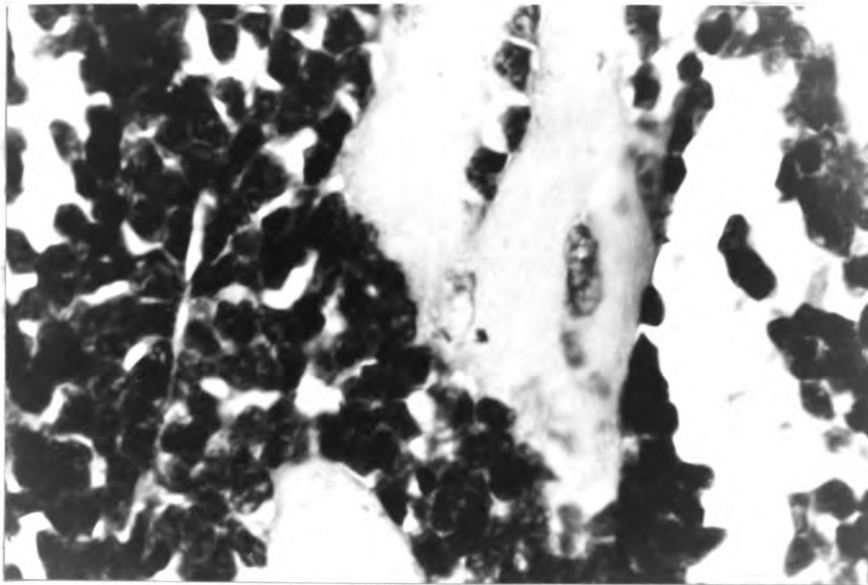


Figure 43. Malignant lymphoma. Neoplastic cells in skeletal muscle. Hematoxylin and eosin, x 750.

in several places the capsule was invaded by the neoplastic cells.

Undifferentiated Sarcoma. Gross: These tumors were all from the subcutaneous areas of the body or oral cavity, except for 1 which was widespread in many organs and whose site of origin could not be determined.

Microscopic: The cells were mesenchymal, varying from spindle-shaped cells to smaller rounded cells. In some tumors, all gradations of cell type existed. No definite determination of cell type could be made.

C. Mixed Cell Tumors

Mixed Mammary Tumor. Gross: This tumor was located in the inguinal region and was reported to look like a large abscess.

Microscopic: The glandular cells were similar to those described in the mammary adenocarcinomas and were arranged in irregular acini. There was abundant collagenous tissue, and transitional areas between the collagenous fibers and osteoid material. Glandular elements were located within the osteoid material (Figures 44 and 45). There were also scattered small areas of cartilagenous material and some bone. Inflammatory changes were prominent in several areas.

Teratoblastoma. Gross: The only tumor of this type occurred as a subcutaneous mass in the shoulder region.

Microscopic: This tumor contained epithelial elements some of which resembled papillary adenoma and some of which were in solid islands. In addition there were fibrous and bony elements within the tumor.

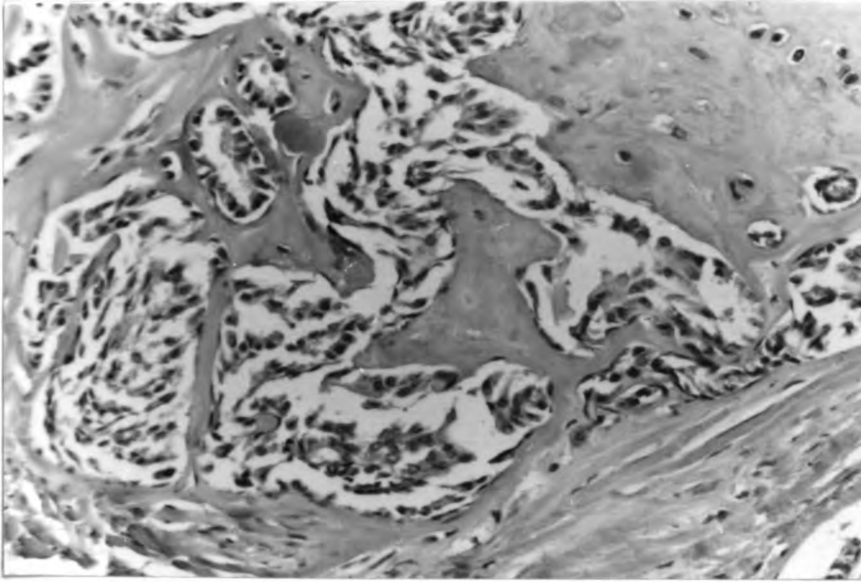


Figure 44. Mixed mammary tumor. Note glandular elements within osteoid material. Hematoxylin and eosin. x 188.

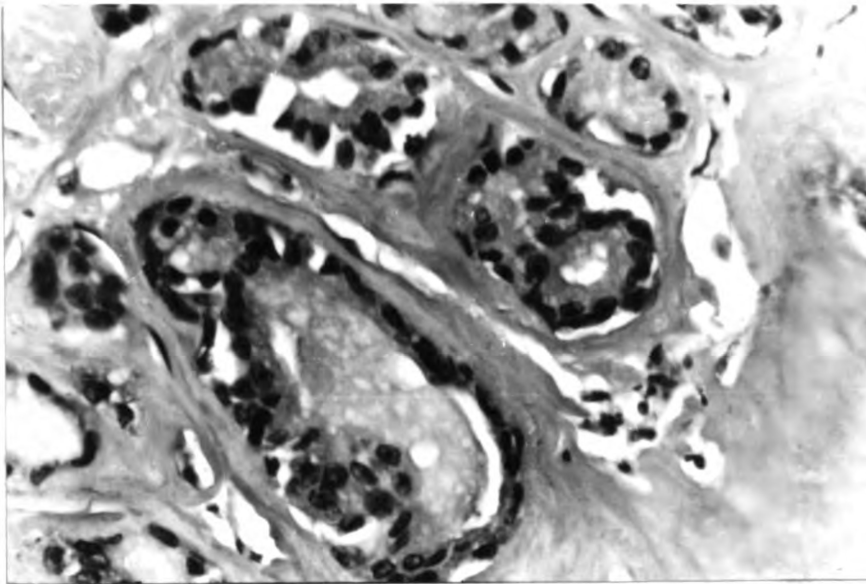


Figure 45. Mixed mammary tumor. Higher magnification of Figure 44. Note glandular acini within osteoid matrix. Hematoxylin and eosin. x 750.

DISCUSSION

A. General

Nielsen (1964) has stated that because much is known about tumors of the dog, and little about tumors of the cat, it is often assumed that they are the same in histologic appearance and biological behavior, but that such may not be the case.

The results of this study corroborate Nielsen's statement. Thirty-three different tumors were classified by cell of origin, and noticeable differences in their characteristics, as compared with tumors of the dog, occurred. These points will be brought out in the discussion of individual tumor types.

Age Incidence. The average age of the cats in this study was 7.9 years. This is lower than the average age (9.0 years) previously reported (Cotchin, 1957). One reason for this is the large increase in the number of malignant lymphoma cases within the past 15 years and the fact that malignant lymphoma is a disease of the younger cat. In addition, more cats are now kept as house pets, are probably better cared for than formerly, and receive more frequent examinations by veterinarians.

It may be that the concept of neoplasia being primarily a disease of the aged cat, as reports in the older literature indicated, will have to be re-evaluated.

Sex Incidence. Without accurate normal population data it is difficult to assess these results. Schalm (1966) said that in the normal cat population the ratio of males to females was 2:1. He does not mention the source of his data, but if it is correct the sex incidence would be significant, since it could mean that neoplasia is more frequent in the female cat.

B. Specific Tumor Types.

Certain tumors of cats are either more important or more interesting from a comparative standpoint, and only those that the author considered to be in these categories will be discussed.

Malignant Lymphoma. The results of this study are in agreement with the statements of Holzworth and Nielsen (1955), and Nielsen (1964), to the effect that malignant lymphoma is the most important neoplasm occurring in cats. This is true not only from the standpoint of total number of tumors, but also because of its degree of malignancy. Apparently no benign tumors of the lymphoid tissue have been recognized in cats.

As was previously mentioned, the apparent increase in occurrence of malignant lymphoma in the past 15 years, and the low age incidence of malignant lymphoma in cats, have contributed to the lowering of the average age of cats with tumors. Although a completely satisfactory explanation for this is not available, several factors must be taken into account. Of some importance is better clinical and pathologic diagnoses. More clinicians are familiar with malignant lymphoma and are using laboratory tests which are helpful in confirming such a diagnosis. Pathologists are also more familiar with the condition, and many tumors which may have been diagnosed

as "round cell sarcomas" a number of years ago are now being placed into the malignant lymphoma category. In addition, many tumors reported as thymomas were probably malignant lymphomas involving the thymus. The lymphoid tissues of the thoracic cavity are frequently involved in malignant lymphoma in the cat, and many of these probably originate in the thymus.

Recent reports of the apparent transmission of malignant lymphoma in cats by cell free filtrates (Jarrett, 1964b), and the demonstration of virus-like particles associated with malignant lymphoma in cats (Jarrett, 1964a), suggest another possible reason for the younger age of cats with malignant lymphoma. If a virus is responsible for malignant lymphoma of cats, it may be that early exposure is necessary, and those animals which are susceptible would then manifest the disease after a sufficient incubation period. Because of greater emphasis on preventive vaccination of kittens for infectious diseases, more young cats are made available for exposure to the presumed lymphoma virus, and instead of being removed from the population by infectious disease, they remain, only to become clinically ill with malignant lymphoma. This theory presupposes that many cats, for an as yet unknown reason, are either naturally immune or are able to surmount the initial infection and are immune in later life. These thoughts are only speculative, but such a mechanism may yet be proved.

Another interesting component of the picture of malignant lymphoma in the cat is the predominant occurrence in the viscera, with little peripheral lymph node involvement. Since there is often bilateral involvement of the kidneys, or several sites of intestinal involvement, multicentric origin is suggested. Multicentric origin might in turn suggest a carcinogen (such as a virus) which acts systemically. Why the cat has

predominantly visceral lymphoma as opposed to the common occurrence of peripheral involvement in the dog and cow is yet to be explained.

Fibroma and Fibrosarcoma. This group of tumors comprises the 2nd largest group in this series, a finding which seems to be at variance with most of the reported series, as fibrous tumors seldom have occupied this position. In addition, this is the only group having more benign than malignant tumors, a condition that has been noted previously (Cotchin, 1961). No adequate explanation can be given, but histologic examination gave the impression that few of the fibrosarcomas were very malignant. This conclusion is further supported by the fact that they rarely metastasize, tending more toward local invasion.

Mammary Gland Tumors. Mammary gland neoplasms of the cat are of interest from several standpoints. Smith and Jones (1961) stated that mammary neoplasia was common only in the dog. However, Nielsen (1964) said that mammary tumors of the cat were 2nd in importance to malignant lymphoma.

The results of this study indicate that mammary neoplasms are of considerable importance in the cat. They not only were 3rd in total number, but the majority of them was highly malignant.

Nielsen (1952b) said that spaying has no influence on mammary neoplasia of cats. This is in contrast to the condition in the dog, and more work needs to be done to substantiate this finding and to determine the reason for the apparent species difference.

Of special interest is the single mixed mammary tumor in this series. It is apparent that mixed mammary tumors are rare in the cat, especially in comparison with the fairly common occurrence of mixed mammary tumors in

dogs. As near as can be determined there are no reports of this type tumor occurring in cats.

Although the reason or reasons for this difference between the species are obscure, the myoepithelium of the mammary gland may play a predominant role. Moulton (1961) suggested that it is the myoepithelial cells which undergo metaplasia in mixed mammary tumors. Cotchin (1958a), using histochemical techniques to demonstrate alkaline phosphatase, noted the enzyme in normal canine mammary glands and in mixed mammary tumors of the dog.

A scarcity of fresh tissue from female cats has prevented the author from studying alkaline phosphatase activity in the normal feline mammary gland, but such a project should be undertaken. It is possible that either a functional or anatomical difference between the feline and canine mammary gland might explain the infrequent occurrence of mixed mammary tumors in cats.

Squamous Cell Carcinoma. The site of occurrence of the squamous cell carcinoma in cats is of interest. Nearly all in this series occurred in the oral cavity or the skin of the head. This may indicate possible carcinogenic agents or some selective mode of action of a carcinogenic agent or agents.

Although Cotchin (1956a) and other English workers (Douglas, 1951) have placed much emphasis on squamous cell carcinoma of the esophagus, in this series there was no esophageal cancer of any type. These results agree with the recent report by Brodey (1966). Cotchin considered that the high incidence of esophageal cancer might be due to ingested carcinogens, and since most of his cases were from the London area, the carcinogenic effect of air pollution should be considered.

Another factor which should be considered is the licking habit of cats. Certainly the tongue and oral mucous membranes are subject to constant low grade trauma, and potential carcinogens could easily be taken into the oral cavity.

As yet, however, there is no explanation for the differences in site of occurrence of squamous cell carcinoma in England and in America. It would seem that, unless there was a difference in carcinogenic agents, in a random population the tumors would tend to occur in similar areas of the body. This apparent geographic difference needs further study so that its significance can be accurately assessed.

Another suggested carcinogenic agent in squamous cell carcinoma of cats is sunlight (Moulton, 1961; Nielsen, 1964). Since the area around the cat's ears is more lightly furred than other areas of the body, sunlight may be of some significance, and this might explain the high incidence of squamous cell carcinoma in the head region.

Adenocarcinoma of Unknown Origin. Many of these tumors were from the abdominal cavity, and the question of the primary tumor site deserves consideration. The possibility of overlooking a primary intestinal adenocarcinoma is real, especially in a hurried or incomplete necropsy or during exploratory surgery. The primary site of an intestinal adenocarcinoma may still be small even after metastasis has occurred, and the metastatic lesion, often an enlarged lymph node or mass in the mesentery, can be more prominent than the primary. More care in performing necropsies would probably eliminate the category of adenocarcinoma of unknown origin.

Mastocytoma. Although Cotchin (1959) and Nielsen (1964) considered the mastocytoma to be rare in the cat, 13 (5%) of the total of this series were mastocytomas.

The mastocytoma qualifies as something of an enigma by several criteria. The origin and functions of the mast cell have not yet been elucidated to the satisfaction of all, some considering it to be a "tissue basophil" and others claiming that it has a separate histogenesis. Since there appears to be 2 separate entities - the cutaneous mastocytoma and the rare case of basophilic leukemia with involvement of the viscera - the theory of separate histogenesis seems plausible. As far as can be determined by this series, there was no systemic involvement in the cases of cutaneous mastocytoma.

Considering the clinical behavior and histologic appearance of both canine and feline mastocytomas, some doubt could be cast on their status as true neoplasms. In many of the tumors studied, the loose arrangement of the cells resembled an inflammatory type reaction. The ever-present eosinophils, which may be attracted by histamine, are usually considered a component of allergic or sensitivity reactions.

The possibility of something stimulating an initial inflammatory response which, for reasons as yet undiscovered, may progress into neoplasia cannot be overlooked.

Basal Cell Carcinoma. Nielsen (1964) pointed out that the basal cell carcinoma of the cat differed from that of the dog in 2 respects. In the cat they occurred all over the body instead of primarily the head region, and microscopically they usually formed small islands of cells with distinct stroma surrounding them, instead of serpentine strands and cords of cells, as in the dog.

The results of this series tend to confirm Nielsen's observations. Unfortunately, no indication of the possible mechanism causing the species difference is readily forthcoming.

Adnexal Carcinoma. Although only 2 tumors classified as adnexal carcinoma are present in this series, they are of interest from a comparative standpoint.

The adnexal carcinoma is a fairly frequently occurring neoplasm in young dogs and is considered to originate from the epithelium of hair follicles or the basal layers of the epidermis (Langham, 1966), and the cells that make up this neoplasm resemble the cells of the histiocytoma and the transmissible venereal tumor of dogs. When it occurs in the skin of the dog, this neoplasm has been called the extragenital transmissible venereal tumor. It has also been called an histiocytoma (Langham, 1966). A recent report by Nowell (1965) notes that in counting the chromosomes of the cells of the transmissible venereal tumor of dogs there were only 59 instead of the usual 78. This technique has apparently not been applied to the cutaneous neoplasm.

The transmissible venereal tumor has not been known to occur in cats, and this observation suggests that the adnexal carcinoma is truly a separate entity. Many possibilities exist for fruitful research into the adnexal carcinoma as it occurs in the cat.

Tumors of the Male Genital System. There were no tumors of this system in the Michigan State University collection. There are apparently only 3 well documented cases in the literature. Although Meier (1957b) suggested that early castration may be a factor, many male cats live to advanced age without being castrated. In comparison with the dog, the relative lack of testicular tumors in cats is an apparently valid species difference.

SUMMARY AND CONCLUSIONS

This study of the neoplasms of cats was done with emphasis on sex and age incidence, and a complete histologic description of tumor types. The major results of this study were as follows:

1. The average age of cats in this series was 7.9 years, which is younger than the average age of cats with tumors in previous reports.
2. Slightly more males than females were affected, but significant conclusions could not be drawn without normal population data.
3. The majority (72%) of the neoplasms of the cat was malignant.
4. The most common neoplasms in terms of total numbers were the malignant lymphoma, tumors of fibrous tissue, mammary tumors, and the squamous cell carcinoma.
5. A single mixed mammary tumor was noted, although no reports of this neoplasm occurring in cats were noted in the literature.
6. Although most of the neoplasms of the cat were similar in histologic appearance to those of other species, there was a difference in the histologic characteristics of the basal cell carcinomas of the cat.

Several conclusions were drawn from this study:

1. More such studies are necessary in order to obtain a clearer picture of the natural occurrence and characteristics of neoplasms of cats, and to indicate which tumors are most important and deserve more research.

2. More accurate records must be kept, in order to have more valid data. Practicing veterinarians should be encouraged to furnish complete histories with all surgical and necropsy specimens they submit.

3. Malignant lymphoma and mammary gland tumors were considered the most significant neoplasms of cats in this series.

4. While neoplasms of the cat have much in common with neoplasms of other species, there are also many unique aspects of their biological behavior and occurrence which warrant further investigation.

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