PRIMARY SPONTANEOUS TUMORS OF THE TESTICLE AND SEMINAL VESICLE IN MICE AND OTHER ANIMALS

XII, STUDIES IN THE INCIDENCE AND INHERITABILITY OF SPONTANEOUS TUMORS IN MICE

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Tumors of the testicle would seem to be uncommon in mice, for we have been unable to find even a single case reported in the literature, although they have been described in other species of lower animals. Thus, among 103 primary tumors observed by McCoy (1) among 100,000 rats killed in plague work, there was one described as an "angiosarcoma" of the testicle, without further details. Other series of tumors in wild rats (Woolley and Wherry (2), Beatti (3)) do not record cases of testicular tumors. Caspar (4) says:

Carcinomas of the testicle, often described in horses and dogs, form sometimes soft, sometimes hard tumors, in which not rarely single portions are formed differently. Through mucoid and colloid degeneration of the cell nests, cysts with gelatinous contents may be formed.

Infiltration along the spermatic cord and lymph-node metastases are often observed. Horses appear especially to develop testicular tumors, particularly if we consider the relatively small number of old animals that have not been castrated. In Japan, where this operation is less often performed than in Europe, equine testicular tumors are most abundant. Thus Kimura records the finding of 49 such growths among 142 tumors observed in 77,224 slaughtered horses. This may be compared
with the figures given in the census statistics on the mortality from cancer in the registration area of the United States, which shows that of 52,420 cases of malignant tumor there were but 121 recorded as arising in the testicles, or 2.3 per thousand; as 21,282 of the cancer cases were males, the proportion of testicle tumors is 5.8 per thousand of all tumors in males. Kimura studied in detail 12 specimens of equine "orchidoblastomas" varying in size up to 7500 grams weight; all were unilateral, and in at least five cases there were metastases in the spermatic cord and the inguinal and lumbar lymph-nodes. He describes their anatomic characteristics as follows:

1. Tumors usually develop without altering the normal shape of the testis. The albuginea is somewhat thickened, showing more or less engorgement of blood-vessels on its surface and expanding with the growth of the tumor, and may continue to enclose it even when of large size.

2. Generally the entire glandular portion of the organ is replaced by new growth, but sometimes the atrophied deep brownish glandular portion may remain under considerable compression at the peripheral part.

3. The tumor consists of nodules, which vary considerably in size and are generally surrounded and separated by strands of fibrous tissue in varying amount.

4. On section the cut surface of the tumor parenchyma is of medullary yellowish gray-white colour and of soft or somewhat firm consistence, whilst here and there creamy yellowish red-gray islets which represent the softened necrotic areas, and various-sized irregular deep red hemorrhages can be seen, so that these figures give an almost marble-like appearance.

5. The spermatic cord and the inguinal and lumbar lymph-nodes are frequently apt to become involved, and distant metastases perhaps may occur (dissemination in the peritoneal cavity).

Microscopical examination

1. Corresponding with the macroscopic appearance, bands of fibrous tissue are seen traversing the section in all directions. These vary in width and divide the parenchyma into islets of various sizes and shapes, giving an alveolar appearance.
2. The tumor cells are roughly polyhedral, spheroidal, or ellipsoidal in shape, the cytoplasm stains in general feebly with eosin and appears homogeneous or slightly granular, varying in size from 11 μ to 35 μ in diameter.

The nuclei are of three kinds, according to their shape, size, and staining qualities.

(i) Spheroidal or short ellipsoidal, deeply stained small nuclei with invisible nucleoli.

(ii) Ellipsoidal large nuclei with vacuolar appearance, in which only the nuclear membrane and nucleolus have taken on the stain, and the latter stains bright red with eosin (usually only one, sometimes two or three in number).

(iii) Nuclei which show intermediate characters between (i) and (ii).

The size of these nuclei varies from 6.5–16 μ in diameter. Multinuclear cells with strikingly large cytoplasm and a circular arrangement of their nuclei about a central lumen are numerous in all cases. Mitotic figures are abundant in the tumor cells, most of them being bipolar, though figures with three, four, or more poles, and cells with irregular distribution of chromosomes are not infrequently met with.

Generally the tumor cells are rich in glycogen, but only a small amount of fat is to be seen; there are small areas of haemorrhage and necrosis in the tumor parenchyma, and the fat can be shown circumscribed especially in the latter, in sections stained with Sudan III.

3. Traversing the section in all directions and cutting up the parenchyma into islets, the fibrous stroma gives off finer strands—sometimes only a few fibers—running in towards the peripheral portion of the enclosed parenchyma from the main circumferential band; but the tumor cells lie along the walls of the alveoli without intimate connection with them and are packed together without fibrillar intercellular substance, so that not all the tumor cells are intermingled with the fibrous stroma. The stroma represents more or less round-cell infiltration, which mostly consists of lymphocytes; and reactive proliferation of the connective tissues may sometimes be seen. Elastic fibers appear generally in small amount.

4. In the atrophied residual glandular portion, spermatogenesis is usually not visible; only one case among four with surviving glandular tissue showed spermatogeny. The cells in the atrophic seminiferous tubules greatly resemble tumor cells morphologically. Interstitial tissue and membrana propria of the seminiferous tubules are in general
increased, and masses of granular cells in the interstitium (Zwischen-zellen) appear atrophic.

As compared with these observations in Japan, Sticker (6), in his compilation of the European literature on the occurrence of tumors in the lower mammals, reports that of 298 malignant tumors in horses, but 11 were in the testicle; in cattle, of 110 tumors none were in the testicle, and there were none among the recorded neoplasms of sheep (7 cases), of cats (7 cases), or of swine (7 cases). But of 766 tumors in dogs, 18 were in the testicle. Of 305 cases of bovine tumor observed in the slaughter house at Glasgow, according to Trotter (7), there was none in the testicle. Undoubtedly these figures give an entirely false impression as to the frequency of testicular tumors in the lower animals, since so few old, uncastrated horses, cattle, swine, or sheep come to the slaughter houses, where most of the neoplasms are detected. According to Caspar (4) a testicular cancer has been observed in a cat by Leiserling, metastases having been found in the mesentery of the transverse colon. A case of carcinoma of the bovine testicle is mentioned without details by Murray (8), and Williams (9) says that in the ass sarcoma of the testicle has been described; he also mentions the occurrence of tumors in the testis of swine, but without citing the origin of these reports. Wolff (10), in his compilation of the literature, refers to several cases of testicular tumor in dogs and horses, but records none in mice or other animals. He refers to the case, reported by Axe, of a tumor arising in an ectopic testicle in a pony, and several other cases in the literature suggest that in dogs and horses, as in man, the ectopic testicle is especially likely to undergo malignant transformation.

One of us (H. G. W.) has observed two cases of primary tumor of the testicle in dogs, which, because of the infrequency of recorded cases in the literature, are briefly described here, as follows:

Case I. A pure blooded Pomeranian, age five and one-half years, was brought to the laboratory by Dr. J. W. Walker, in order that a growth involving the right testicle might be removed by operation.
This growth had been noticed at least two years before and had grown very slowly. The operation was done under anesthesia; the animal recovered and is now in apparently perfect health three years after the operation. No metastases could be palpated in the groin or elsewhere. The animal had been suffering from extensive loss of hair for some time before the operation, but after it the normal coat was restored. The growth was about 3 x 2 x 2 cm., involving the body of the testicle as an encapsulated nodule and leaving a compressed remnant of testicle tissue at one side. There was no infiltration, and the epididymis was not involved.

Microscopically it shows irregular coarse lobules with heavy fibrous tissue trabeculae, packed full of large cells with little cytoplasm and pale vesicular nucleus closely resembling the spermatogonia. The capsule is very dense and contains a few islands of tissue cells. Despite the heavy fibrous tissue the cells do not seem to be compressed. In the residual testicle tissue there is some spermatogenesis going on. This seems to represent an unusually benign, slow-growing type of the usual large cell tumor of the testicle.

Case II. A mongrel fox terrier dog, apparently moderately old, was killed in the course of experimental work in the Department of Physiology of the University of Chicago, and an autopsy was performed by Dr. A. B. Luckhardt. The right testicle, which was within the scrotum, was replaced by a tumor about 6 cm. in diameter, entirely contained within the tunica albuginea, and not adherent to the surrounding tissues. No metastases could be found in the regional nodes or elsewhere. The prostate, however, was swollen, and irregular in shape and consistence, and contained a purulent fluid. The left testicle lay within the inguinal canal and was decreased in size to about one-half the normal dimensions, although the epididymis was apparently normal. Nothing is known of the history of this animal, but it was striking in that the teats resembled those of a bitch that has nursed repeatedly.

Microscopically the tumor resembles the usual type of alveolar carcinoma seen in human cases (fig. 1). The cells are large, consisting chiefly of a large vesicular nucleus; the stroma is heavy and coarse, and divides the tumor not only into alveoli but also into lobules; only in a few areas is it cicatricial. Mitoses are abundant. A striking peculiarity in this tumor is the tendency of the cells in some alveoli to form long cords parallel to each other and at right angles to the basement membrane, producing an unusual effect of palisade arrangement.
Sections through many parts of the tumor show no residue of testicle tissue, and no teratomatous elements. The prostate shows an extensive round cell interstitial infiltration, with numerous polymorphonuclear leucocytes within the tubules. The atrophied ectopic testicle shows an epididymis resembling that of the preadolescent testicle, while the testicle itself consists of ill-defined tubules with ordinarily but a single row of irregular cells near a thickened basement membrane, although the center of the tubules contains much protoplasmic debris which is often pigmented. The stroma is moderately increased, but Leydig's cells are not conspicuous. Several of the tubules are full of large deeply staining cells resembling those of the tumor of the opposite testicle. These give the impression that in these isolated atrophic tubules neoplastic proliferation is beginning to arise independently.

In other species of animals, although castration is not commonly practiced, testicle tumors are rare. The reviews of the literature on spontaneous tumors of birds and fowls by Joest
and Ernesti (11), and by Pentimalli (12), mention only three
testicular tumors. One was a teratoma replacing the testicle of
a chicken, described by Winokuroff (13) and the other two were
cases of sarcoma of the testicle in parrakeets (Palaenoris
Eupatrius?), reported by Fox (14). One of these was bilaterally
symmetrical, probably derived from the testicle, and described
as a large round cell alveolar sarcoma; the other was unilateral,
and undoubtedly arose in the testicle. In his extensive autopsy
experience with wild animals Fox has found no case of tumor
of the testicle, nor could we find any such cases in the literature,
unless we include the instance recorded by Pick and Poll (15)
of a cystoma testis with carcinomatous areas and a secondary
nodule, which occurred in the testicle of a Japanese giant
salamander (Kryptobranchus japonicus).

From such descriptions of the histological findings of the
testicular tumors of lower animals as are found in the literature,
and which are mostly meagre, these growths seem to present
the same characteristics as those observed in man. The pre-
vailing type is those tumors of large polyhedral cells in alveolar
arrangement, which are often described as alveolar sarcoma or,
when the normal relation of the tumor cells to the nutritive
vessels is conspicuous, angiosarcoma. Lymphoid infiltration of
the stroma is also commonly described in animals as well as in
human tumors. Ewing (16), in his critical review of testicular
neoplasms, says of the human material: "The commonest tumor
of the testis is an embryonal carcinoma, alveolar or diffuse, with
polyhedral or rounded cells and often with lymphoid stroma."
This statement holds equally well for the testicular growths of
animals as described in the literature. Ewing also states:
"These tumors are probably one sided developments of terato-
mata," an origin which is not suggested by those authors who
describe animal tumors, although Caspar (4) quotes Kitt as
saying that chondromas are found repeatedly in the testes of
horses; on the other hand, Kimura does not even mention the
occurrence in horses of tumors suggesting a teratomatous char-
acter. Furthermore, Frank (17), in his discussion of the hist-
togenetic origin of testicle tumors, concludes that the typical
large cell tumors are not derived from teratoid tumors, but from spermatogonia. Kimura, in his study of equine material, also came to the conclusion that these tumors are derived from the epithelium of the seminiferous tubules.

TESTICULAR TUMORS IN MICE

In 19,000 autopsies on mice of the Slye stock we have found 28 tumors arising in the testicle. These figures, it should be emphasized, apply to mice living a natural life and reaching as great an age as it has been possible to make them attain by the best of care and the most rigorous hygienic precautions; all died natural deaths, without having undergone any experimental interventions or manipulation. Of the 19,000 about one-half were males. Statistics have not yet been compiled as to the total number of tumors arising in male mice, although they are much less common than in females, most abundant being tumors of the lung, subcutaneous tumors, sarcomas, tumors of the testis, and adenoma of the liver. As we have pointed out in previous papers, the great predominance of females among tumor mice, observed and emphasized by other writers, depends solely upon the frequency of mammary tumors. Excluding these and other sex gland tumors, we find an approximately equal distribution. Thus, in our published lung tumor series (18) of 160 cases there were 42.6 per cent in males, and 57.4 per cent in females; in 28 liver tumors (19) there were 50 per cent in each sex; in 8 cases of cancer of the stomach (20) also, equal numbers were observed in each sex. Sarcomas are more abundant in female mice than in males in the ratio of 2 to 1 because the mammary gland is a common site of sarcomas (21). The tumors of the testicle offset in large measure the tumors arising in the ovary.

That we have obtained so large a number of tumors of the testicle is explained by the fact that all these tumors, with one exception (7308), occurred in the mice in a single strain, No. 90, and its hybrid derivatives. This exceptional case was not a typical testicular growth, but a spindle cell sarcoma. As has
been emphasized in previous papers, not only the tendency to develop cancer depends on the ancestry of the mice, but also the localization of tumors in special organs or tissues (see Slye (22)). Had not this particular strain been developed, hybridized extensively, and followed for several years, there would have been but a single case of testicle tumor to record, and that a sarcoma. We may mention the fact that some forms of growth observed in other laboratories seem to be relatively infrequent in the Slye stock, e.g., the keratinizing type of lung tumors described by Tyzzer and Haaland, and the preputial gland adenomas observed especially in Bashford’s laboratory. As material accumulates this tendency of certain tumors to occur in certain strains of mice becomes more and more distinct; this has its counterpart in human pathology—e.g., the uterine fibroids of the negro, and the repeatedly described predominance of tumors of certain viscera in certain families.

Most of these new growths of the testis are essentially benign in character, developing very slowly, rarely ulcerating, generally distinctly limited by the tunica albuginea, and in no case with distinct remote metastases (fig. 2). Some cases have remained under observation for as long as eight months, and in only a few instances have they seemed to be the cause of death, through urinary retention or ascending suppurative nephritis (5 cases), local necrosis and suppuration (3 cases), or hemorrhage (3 cases). They have varied in size from about 5 mm. in diameter to one 30 by 23 by 23 mm., the larger tumors usually showing much necrosis, although not often infected because of the protection afforded by the intact tunica albuginea. Contrary to the experience with other species, no case has been observed in an ectopic testicle, a malformation that seems to be rare in mice. As with other tumors, these growths do not appear until the mice are of middle age or older; the youngest animal in this series was 9 months old when the tumor was first seen and died when 14 months old; the oldest was 3½ years at death, the tumor having been under observation for eight months.

Four tumors seemed to result directly from trauma, appearing in mice while under observation because of injuries to the genital
organs received in fighting. One of these was a typical spindle cell sarcoma (3117) which arose at the site of a bitten wound of the testicle, while simultaneously a similar sarcoma arose in a

![Image](image-url)

**Fig. 2. Primary Tumor of the Right Testicle of a Mouse, Showing the Gross Appearance Usual in These Cases**

The lower pole of the tumor is necrotic. It is entirely encapsulated and there are no metastases. Microscopically this was a typical "mesothelioma" or "orchidoblastoma" as shown in figures 3 and 5.
wound on the back. Of the other three, two were of the usual large cell type (3561 and 8145) while one (585) again was a spindle cell growth. It is, of course, impossible to tell how many of the other 24 tumors followed trauma.

Several instances of simple cyst formation, probably secondary to trauma, have not been included in this series.

**FIG. 3. SHOWING THE TYPICAL CYTOLOGICAL CHARACTERS OF MOST OF THE TUMORS OF THIS SERIES.** (X 480)

At the lower edge of the field is a blood-space, showing the direct relation of blood and tumor cells, without distinguishable vessel wall.

Microscopically the great majority of these tumors are all of one structure (fig. 3), which is entirely typical and characteristic. These typical growths are composed of large rather pale and delicately architectured cells. The nuclei are vesicular, often markedly so, with the chromatin in coarse granules and not uniformly arranged. There is an abundant cytoplasm, staining faintly, usually with well defined margins and of polygonal
outline unless compressed into flattened or spindle shaped cells (fig. 4). Mitotic figures are fairly abundant in some specimens, but never extremely numerous; pycnosis and karyorrhexis are frequently seen. Commonly there is a tendency for the cells to be arranged in cords, as in liver tissue, and an alveolar structure is often distinct although never very well developed. As with all mouse tumors, the stroma is seldom so dense as in corresponding human tumors. Usually the tumor is extremely vascular, with large blood channels (fig. 5), the walls of which are often composed solely of tumor cells, although sometimes the vessels have definite fibrous walls; hemorrhages are frequent, and in many sections old pigment and cholesterol masses indicate the site of former hemorrhages. Cells with atypical and giant nuclei are common, and multinucleated cells are often found. Sometimes tubule-like structures are present, but these cannot
be identified as typical "rosettes" such as have been described in human testicular neoplasms. Multipolar and other abnormal forms of mitosis have occasionally been seen.

Necrosis is present to greater or less degree in most of the specimens, and in some nearly all the tumor is necrotic, as if strangulated by the dense capsule. Often the necrosis is uniformly distributed in those cells more remote from the blood spaces, leaving about each vessel a zone of living tumor cells so that the resulting picture resembles a "hemangiosarcoma," often quite characteristically (fig. 6). This recalls the fact that a common diagnosis of testicular tumors in man is "angiosarcoma."

In every case the original testicle tissue has been almost or quite completely destroyed, so that only occasionally can the

![Fig. 5. Showing the General Histological Features Characteristic of Most of the Tumors of the Mouse Testis. (× 110)](image)

The intimate relation of tumor cells to blood-spaces is a striking feature.
remains of a single isolated seminiferous tubule be found. Most often the tubules are only indicated by a partly calcified tubular outline, identified solely by the sperm heads which persist in the lumen. If more tubules remain they are generally compressed against the capsule, often heavily pigmented. The capsule of the testicle always persists, and although usually invaded, it is perforated only in a few instances; occasionally the capsule

contains what seem to be lymph-vessels filled with plugs of tumor cells. When seminiferous tubules remain for comparison, it is usually apparent that the typical tumor cells have much the same structure as some of the cells of the tubule, the spermatogonia.

The stroma is usually scanty and very delicate, so that large areas often show no evidence whatever of stroma elements.
When best defined it divides the tumor cells into indistinct alveoli, and frequently shows an abundance of small lymphoid cells. In many instances clear cyst-like spaces are found without any distinct lining, but giving the impression of resulting from softening and absorption of the tumor, rather than from cyst formation. Blood pigment is often found in phagocytic cells in the stroma and capsule.

Five of the tumors present a histological structure resembling sarcoma, but in three of these, at least, it is probable that the sarcomatous appearance is merely the result of flattening of the cells by pressure. This assumption is supported by the finding, in some of the sarcoma-like tumors, of cell areas resembling the more usual type of testicle tumors, and by the occasional presence, in the ordinary tumors, of areas of spindle cells that are undoubtedly the result of local pressure, e.g., beneath the capsule. These tumors would seem to correspond to the type of tumor often found in the human testicle and commonly diagnosed as alveolar sarcoma or angiosarcoma. One of them (10062), however, presents so much finely divided intracellular golden pigment, without evidence of old hemorrhage as a source of this pigment, that it may possibly represent a tumor derived from the interstitial cells of Leydig, for tumors of such origin have been described in man.

Of the remaining two, one is a typical spindle cell sarcoma which has been described in our paper on sarcoma in mice (case 3117). This mouse was bitten on the back and on the genitals. From each of these sites arose a typical spindle cell sarcoma. The genital tumor seemed to arise from and replace the testicle. Both neoplasms developed at the same time, and seemed to be independent, primary, spontaneous tumors. This mouse also had an adenoma of the liver. The fifth tumor (fig. 7) also seems to be a typical spindle cell sarcoma (7308), in which no persisting elements of testicle can be found; at one point it has grown through the capsule, so that the growth is bilobed. Mallory's connective tissue stain supports the interpretation of the growth as a true sarcoma, the individual cells lying in and evidently producing a matrix of collagenous fibers.
This tumor is especially interesting as being the only growth occurring in an animal not derived from strain 90.

It is a matter for comment that we have found no example of the teratoid type of tumor that is so common in the human testicle. In not a single section have we found a trace of heterologous tissue elements that might suggest a teratomatous origin. Twice we have found simple cysts, apparently resulting from traumatism and subsequent absorption of the testicle elements. Indeed, in these 19,000 autopsies which have furnished so rich a tumor material, we have found but a single instance of true teratoma, and this arose in the ovary. We have made complete serial sections of three of these testicular tumors, without finding any teratomatous elements. This evidence would seem to us to indicate that, at least in the mouse, the orchidoblastomas do not ordinarily arise in teratomas, which have been

**FIG. 7. SPINDLE CELL SARCOMA ARISING WITHIN THE TESTICLE OF A MOUSE. (X 480)**
maintained by some to be the common origin of the similar tumors in man. The histological evidence of the similarity of the tumor cells to the spermatogonia would seem to support Frank's view that these neoplasms arise from the epithelium of the seminiferous tubules.

In view of the extremely heterotypical structure of these growths, the total absence of metastases in this series is surprising, especially as metastasis is so extremely extensive and early in the structurally similar tumors of man. And in other mammals, also, metastases are described from testicular tumors, especially in the horse.

One case alone (9441) showed involvement of both testicles, the structure of each growth being the same. In our first canine case, however, the animal showed no recurrence three years after orchidectomy, and the second had developed no visible metastases when autopsied. Several of our sections of mouse tumors show what appear to be plugs of tumor cells in the lymph-channels, while the blood-spaces are commonly lined with naked tumor cells, apparently offering every opportunity for extensive metastasis. Nevertheless, close inspection of the lung sections has failed to show even the retrogressing tumor cell emboli which are so often found in the lung in connection with abdominal carcinoma, as pointed out by M. B. Schmidt.

In but five cases was the tunica albuginea definitely perforated by macroscopic growths. One of these, however, showed very extensive formation of secondary nodules (7870), there being several large tumors outside the testicle (fig. 8). Here the growth consisted of six contiguous nodules, each distinct and enclosed in a capsule. Histologically all these nodules are of similar structure, characterized by an unusually large amount of lipoid material and many necrotic areas. So far as structure is concerned this tumor does not seem to be more malignant than other tumors that do not show the multiple nodules. In one case (2753) the growth extended along the spermatic cord, so that the mass resembled a hernia.

As noted in previous studies of special types of tumors in mice, animals with one tumor are likely to exhibit a growth of
some other sort, apparently more often than would be explained by the law of probability. With testicular tumors the co-existence of other neoplasms would not be expected to be so frequent as was observed with the tumors previously described (lung tumors, liver tumors, sarcomas) because the commonest of all tumors in mice, the mammary carcinoma, does not often

Fig. 8. Tumor of the Left Testicle With the Production of Several Local Metastatic Growths, But No Remote Metastasis
occur in males. Nevertheless, among our 28 cases of tumor of the testis we find the following seven instances of multiple tumor formation: One mouse with a subcutaneous spindle cell sarcoma and an adenoma of the liver; three with papillary adenomatous growths arising in the lung; two with osteosarcomas, one arising in the thigh (16370), the other in the subcutaneous tissues near the fore leg (8745). In still another mouse there was a subcutaneous growth in the neck of such a character that a diagnosis has not been made (5037). This growth was about 1 cm. in diameter and 2 to 3 mm. thick, consisting of a mass of cells with strongly basophilic cytoplasm, of a finely granular, "ground glass" character, resembling that of plasma cells. The nuclei, however, are centrally located and have not the characteristic chromatin arrangement of the plasma cell nucleus. The cell boundaries are distinct, and the cells tend to form long rows and strings, recalling the structures sometimes seen in the so-called "lymphangioma hypertrophicum." It is probable that this growth is a true neoplasm, but as long as its nature remains undecided its neoplastic character cannot be definitely determined. The character of the cells is such as to make it improbable that it is a metastatic growth. The occurrence of multiple primary new growths in no less than 25 per cent of these male tumor mice is striking evidence of the existence of a predisposition to tumor formation.

SARCOMA OF THE SEMINAL VESICLE

In the literature on tumors of the lower mammals we have found mention of but one instance of a neoplasm arising in the seminal vesicles. Such growths are also rare in man, Ceelen (23) in 1912 having been able to find reports of but five cases of carcinoma and one of sarcoma, to which he added a case of fibromyoma. We have not been able to find records of any other human or animal cases, except that described by Flexner and Jobling (24) as "originally regarded as a sarcoma; probably a teratoma, from which an adeno-carcinoma was developed." This tumor, which has been used extensively in transplantation,
was found in a white rat, as a tumor "the size of a walnut" attached to the left seminal vesicle, without production of metastases. It was first described as a polymorphous sarcoma, but with included glandular elements. In the course of transplantation the carcinomatous elements developed and replaced the sarcomatous structures, becoming established as an adeno-carcinoma by the twenty-eighth generation.

Fig. 9. Primary Sarcoma of the Seminal Vesicle of a Mouse. (× 110)

Note the numerous giant cells, and the polymorphous character of the tumor cells.

A single case of primary tumor of the seminal vesicle has been observed in one of the mice examined in this laboratory (15443). This animal died of pneumonia, and autopsy disclosed the left seminal vesicle constricted at a point midway of its length, with the tip shrunken. The remainder of the organ is distended into a mass 10 by 8 by 8 mm., rather soft, but containing no fluid. The right seminal vesicle is similarly con-
stricted, but there is no tumor tissue and the tip is merely dis-
tended with yellow secretion; the rest is in shape like the left, but slightly smaller and yellow in color. There were no meta-
static growths to be found. The testicles seem normal, and the kidneys show a slight nephritis. Microscopically the lumen of the right vesicle is found to be distended by a solid cellular growth, limited by the somewhat thickened peritoneal coat and the remains of the muscular coat, except at one point where these structures have been penetrated by the neoplasm. Only a few small groups of columnar epithelial cells remain to represent the original mucosa. The tumor is composed of spindle cells of varying size, but mostly larger than in the usual spindle cell sarcoma (fig. 9). There are also many multinucleated cells, and numerous enormous single cells with a single giant nucleus, sometimes undergoing asymmetric direct division. Thin-walled blood-channels and blood-spaces lined only by unmodified tumor cells are abundant. There are no hemorrhages or necrotic areas, but some cystic spaces full of plasma. This is a typical large polymorphous celled sarcoma. Nothing was found to indicate a teratomatous or carcinomatous character, such as was observed in the Flexner-Jobling rat tumor, yet the fact that theirs was at first diagnosed as a polymorphous cell sarcoma is suggestive. In our case no transplantation experiments were attempted.

SUMMARY

Among 19,000 mice dying natural deaths and examined post mortem, about one-half of which were males, 28 instances of primary tumor of the testicle were found. Most of these resembled in all essential features the tumors that arise in the testicle of man and other animals, consisting of cells closely resembling the epithelium of the seminiferous tubules, arranged in an alveolar structure. Despite great vascularity and a markedly atypical structure, no remote metastasis was observed, although in one case a series of six contiguous independent nodules was formed, and one case showed bilateral testicular tumors. Two of the growths seemed to be true spindle cell sarcomas, one arising at the site of a wound. Three of the typical "or-
chidoblastomas" also followed trauma. No evidence could be obtained that any of these tumors had arisen in a teratomatous growth, and no cases of teratoma have been observed.

One case of polymorphous cell sarcoma of the seminal vesicle of a mouse is described, apparently the second case of a tumor of this organ reported in a lower animal.

Two cases of primary spontaneous tumor of the testicle in dogs are described.

With the exception of one sarcoma, all the 28 neoplasms of the mouse testis occurred in the members of a single strain of mice and its hybrid derivatives, thus substantiating the statement that heredity influences the incidence of tumor development in different organs or tissues. This fact also probably explains the absence of any recorded cases of tumor of the testis in mice from other laboratories.

REFERENCES

(3) Beatti: Semana med., 1917, xxiv, 643.
(7) Trotter: Jour. Comp. Path. and Therap., 1911, xxiv, 1.