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TUMORS OF THE SOFT TISSUES

Arthur Purdy Stout, M. D.

ARMED FORCES INSTITUTE OF PATHOLOGY

ATLAS OF TUMOR PATHOLOGY

Section II—Fascicle 5

TUMORS OF THE SOFT TISSUES

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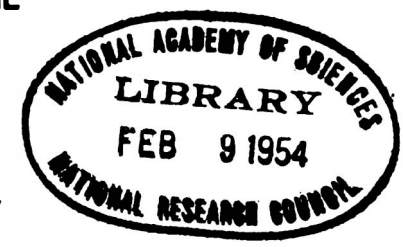

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• Arthur Purdy Stout

TUMORS OF THE SOFT TISSUES

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TUMORS OF THE SOFT TISSUES

INTRODUCTION

In order that one may understand the tumors that arise in the soft tissues of the body, it is necessary to take cognizance of certain facts. If the tumors of the epidermis and the ectodermal structures of the skin and those of the lymph nodes are excluded, all of the neoplasms develop from two primitive sources: the mesoderm and the neurectodermal tissues of the peripheral nervous system. From the primitive mesenchyme come the supportive and reticuloendothelial tissues and their corresponding tumors, and from the neurectoderm come the schwannian sheath, possibly the endoneurium, and conceivably the perineurium, which in turn form the prototypes of most of the tumors of the peripheral nerves. If the various tumors developing from these tissues reproduced their prototypic tissues in pure form, albeit in various stages of differentiation, recognition would be relatively simple. Unfortunately this is not always the case, and it is these aberrations which result in the formation of the metatypical conglomerations that are so difficult to recognize. It is well known that the repair which follows injury takes place by the proliferation of fibroblastic cells primarily, accompanied by endothelial proliferations forming capillaries. No other tissues with the exception of Schwann cells reproduce themselves with the same facility. It need not surprise us, therefore, to find that many tumors, especially the malignant ones, show a tendency in greater or less degree to produce fibroblastic elements. This may be carried to such an extent that these transformed areas are histologically indistinguishable from fibrosarcomas; or the metaplasia may be incomplete so that, for example, lipoblasts, leiomyoblasts, or rhabdomyoblasts may retain their distinguishing characteristics while at the same time acting as fibroblasts and producing connective tissue fibers. Indeed in one tumor, the synovial sarcoma, this is invariably the case. It is always made up of two elements inextricably intermingled.

This tendency to form multiple tissues is sometimes carried much further, so that one tumor may be compounded of several more or less differentiated tissues without the predominance of any one type. In this fashion is produced the mixed mesodermal tumor or mesenchymoma, which is seen in both benign and malignant examples. The best known benign form consists of an admixture of adult fat, blood vessels, and smooth muscle in varying quantities. Malignant mesenchymomas may have an admixture of as many as five

different cellular types in the same tumor. The combinations formed are almost endless and no two of these strange tumors are ever exactly alike. Inevitably one is reminded of mixed tumors and teratomas in which are found admixtures of both epithelium and tissues resembling the derivatives of the mesenchyme. These latter develop in certain definite situations such as the salivary glands, the male and female genitourinary systems, and the breast; and in regions where congenital malformations of development are apt to occur, such as the sacral region. The mesenchymomas may be found in these areas, but they also develop in other situations such as the thigh, where teratomas are unknown.

One might expect that tumors of certain types would arise in areas where corresponding varieties of tissue are normally found, but this is by no means necessarily the rule. It seems to hold for tumors of schwannian and other neurectodermal cells; and of course since connective tissue, fat, and vascular elements including smooth muscle are almost universal, there need be no surprise if tumors composed of their cells are encountered almost anywhere. On the other hand, striated muscle, bone, and cartilage are restricted in their distribution; yet malignant tumors composed of rhabdomyoblasts, osteoblasts, and chondroblasts in pure or compound form can develop in situations where normally such tissues are never found.

While the ordinary hematoxylin and eosin stain properly carried out after good fixation will suffice to permit recognition of many of these tumors if one is thoroughly familiar with their vagaries of growth, it will not do for all and must be supplemented in some cases by differential fiber stains, adequate silver reticulin impregnations, and stains for special substances like lipoid, mucoid or hyaluronic acid, hemosiderin, melanin, elastic tissue, amyloid, and nerve fibers. If in addition one can call upon the aid of tissue culture, obscure tumors can sometimes be elucidated, because in most instances, no matter how anaplastic, explanted tumor cells will grow in vitro with sufficient resemblance to their normal prototypes to permit recognition. At the present time this aid is not available in most laboratories, and there are very few individuals capable of the proper interpretation of differential tissue growth.

Even with all our knowledge about tumor cells and their growth in vivo and in vitro, there are still a few tumors which can be recognized and named, the exact nature of which remains obscure. Prominent among these is the tumor originally called myoblastic myoma but now better known as the granular cell myoblastoma or myoma. This was originally believed to be a myoblastic tumor. Considerable doubt arose as to the truth of this assumption, because embryonal myoblasts do not have granules in them, and because the tumor sometimes grows in places where striated muscle is never found. It has been suggested that these are tumors of histiocytes (Martin), of granular cell fibroblasts (Pearse), that they are tumors induced by parasites (Gullino), that they are tumors of Schwann cells (Fust and Custer), that some of them are paragangliomas

(Smetana and Scott), and that they are forms of granular myolysis of muscle and not tumors at all (Roffo). Tissue culture has shown that the cellular outgrowth in vitro most nearly resembles striated muscle but does not account for the intracellular granules, so that the tumor's exact nature remains a mystery.

The failure properly to label the soft tissue tumors, especially the malignant ones, has led to a great deal of confusion regarding the distribution, relative frequency, and relative malignancy of many of them. This has been largely responsible for the fact that mesenchymal tumors of the soft tissues of the extremities, especially the malignant ones, are the least understood and probably the most inadequately treated of all tumors.

While the tumors of bone, bone marrow, and peripheral nerves will not be dealt with in detail in this fascicle because there are separate fascicles devoted to them, it should be remembered that the nerve tumors grow in the soft tissues, and certain tumors of bone, notably the fibrosarcoma of the periosteum and Ewing's sarcoma, secondarily invade and may form larger tumor masses in the soft tissues than in their tissue of origin.

If one is quite familiar with the usual distribution, relative frequency, and gross growth characteristics of the soft tissue tumors, it is sometimes possible to make a more or less accurate diagnosis on physical examination alone: The surface hemangiomas are familiar to all and the deep hemangiomas or benign vascular mesenchymomas involving muscle often contain phleboliths, which give a characteristic roentgenogram; lipomas of the skin forming pedunculated growths, and lipomas of the subcutaneous tissues forming soft, diffuse, and sometimes multiple masses are generally identifiable; the slow-growing multinodular so-called dermatofibrosarcoma protuberans has an appearance not often assumed by other tumors; if a tumor is deep, bulky, and nodular, often it proves to be a liposarcoma; if it starts deeply and grows into the skin producing a projecting, dark red, fungating mass, it may be a rhabdomyosarcoma; if it produces a fusiform swelling, movable from side to side but not in the long axis of the extremity, it is apt to be a nerve sheath tumor, whether or not there is any interference with function or sensation; and if it is a subungual lesion producing attacks of paroxysmal pain, it will almost surely prove to be a glomus tumor. But these examples and a few others that can be added to them cover a relatively small proportion of the soft tissue tumors; and even the examples given in most instances may be imitated by something else, so that in a vast majority of instances, indeed it would be safer to say in all cases, accurate diagnosis depends upon histologic examination.

In order to give a comprehensive picture of the neoplasms of the soft tissues, it will be necessary to enumerate not only the malignant and benign neoplasms but also the tumor-like lesions about which there is some uncertainty as to whether or not they are neoplasms. In each instance a succinct note will describe the important facts concerning each lesion. It is difficult to know

Table I

7,337 BENIGN MESENCHYMAL TUMORS*

Surgical Pathology Laboratory, Columbia University
Feb. 1, 1906—Sept. 1, 1951

Tumors	Number of tumors in subgroupings	Total number of tumors
Fibromatoses		1,596
Fibromas	1,144	
Keloids	390	
Desmoids	19	
Cases of Peyronie's Disease	0	
Cases of Palmar and Plantar Fibromatoses	31	
Cases of Fibromatosis Colli	5	
Cases of Progressive Myositis Fibrosa	7	
Benign Myxomatoses		646
Ganglions	643	
Cases of Localized Myxedema	3	
Xanthomatoses		783
Xanthomas and Xanthelasmas	189	
Multiple Xanthomatoses	9	
Fibrous Xanthomas**	187	
Xanthogranulomas	17	
Histiocytomas	9	
Giant Cell Tumors	322	
Fat Necrosis Tumors***	50	
Lipomatoses		****2,411
Benign Myomatoses		338
Leiomyomas	217	
Rhabdomyomas	1	
Granular Cell Myoblastomas	120	
Benign Angiomatoses		1,236
Hemangiomas	885	
Hemangiomatoses	34	
Cirsoid Aneurysms	6	
Venous Racemose Aneurysms	9	
Benign Hemangioendotheliomas	41	
Benign Hemangiopericytomas	74	
Glomus Tumors	83	
Lymphangiomas	104	
Benign Tumors of Bone and Cartilage		123
Osteomas	76	
Osteochondromas	9	
Chondromas	6	
Cases of Myositis Ossificans	23	
Cases of Myositis Ossificans Progressiva	9	

*All skeletal tumors, all benign lymphomas, and leiomyoma of uterus are omitted.
**Includes sclerosing hemangiomas.
***So-called traumatic fat necrosis.
****Includes 6 cases of hibernoma.

7,337 BENIGN MESENCHYMAL TUMORS—Continued

Tumors	Number of tumors in subgroupings	Total number of tumors
Benign Synoviomas		2
Mixed Tumors of Skin		21
Benign Mesenchymomas		48
Benign Mesotheliomas		58
Blue Nevi		75
Total		7,337

Table II

1,349 MALIGNANT MESENCHYMAL TUMORS*

Surgical Pathology Laboratory, Columbia University

Feb. 1, 1906–Sept. 1, 1951

Tumors	Number of tumors
Fibrosarcoma	403
Myxoma	99
Liposarcoma	262
Leiomyosarcoma	117
Rhabdomyosarcoma	112
Malignant Granular Cell Myoblastoma	4
Malignant Organoid Granular Cell Myoblastoma	12
Malignant Hemangioendothelioma	34
Malignant Hemangiopericytoma	32
Kaposi's Sarcoma	43
Lymphangiosarcoma	7
Osteogenic and Chondrosarcoma (extraskeletal)	13
Synovial Sarcoma	38
Malignant Mesenchymoma	78
Malignant Mesothelioma	40
Reticulum Cell Sarcoma	27
Plasmocytoma	28
Total	1,349

*All skeletal tumors, lymphosarcomas, and neurogenous tumors are omitted.

where to draw the line in such an enumeration, since there are a good many infections—for example, tuberculosis, sarcoid, syphilis, rheumatic nodules, etc.—which can produce gross lesions closely resembling neoplasms but which can be identified on microscopic examination. These have been omitted.

It is also difficult to know what to exclude from the term "soft tissues." Broadly interpreted it could mean everything except the bones. It is customary, however, to exclude all the organs, epithelial-lined tubes, the epithelial structures of the skin, the bone marrow, and the lymph nodes. This leaves the remaining tissues covering the bones of the head, neck, trunk, and extremities, as well as the internal soft tissues. Most of the latter will be dealt with in other fascicles, but for the sake of completeness the distribution of some of these soft tissue tumors in the abdominal and thoracic cavities and in the orbit will be touched upon. The benign and malignant tumors will be considered separately.

Although the writer has dealt with all of the benign and malignant tumors of mesenchymal derivation with which he is familiar both personally and by repute, the reader need not expect to find here recorded all of the tumor forms that can grow. There are many cases of undiagnosed tumors in the files of every laboratory of pathology awaiting future study and recognition. This is true particularly of many puzzling varieties which develop in infancy and childhood. Tissue culture and meticulous cytologic and histochemical techniques no doubt will eventually lead to the clarification of these mysteries.

In order that the reader may have some conception of the relative numbers of the different varieties of growths to be discussed in this fascicle it may be stated that there have been recorded in the Laboratory of Surgical Pathology of Columbia University during the 45½ years from February 1, 1906, to September 1, 1951, 8,686 tumors and tumor-like lesions of the soft tissues of which 7,337 were benign (table I) and 1,349 malignant (table II). It must be emphasized that almost all of the diagnoses have been made on surgical material and that doubtless the malignant tumors are heavily overweighted because many of them come from other institutions and there is a much greater tendency to request consultations on malignant than on benign tumors. It is useful, however, to know something about the relative frequency of the different tumor types in a sequence such as this.

FIBROMA DURUM

(Figures 1 and 2 are from the same case)

Figure 1. A small nodule in the skin of the shoulder. The patient, a 35-year-old man, had noticed this symptomless mass for some months. This is a cross section of the entire nodule which lies inconspicuously in the corium, interdigitating with and slightly thickening the normal corium. × 35. A. F. I. P. Acc. No. 218822–1.

Figure 2. Higher magnification showing the proliferated fibroblasts. At the margin, these form strands which lie between the normal thick collagenous fibers of the corium. × 226. A. F. I. P. Acc. No. 218822–2.

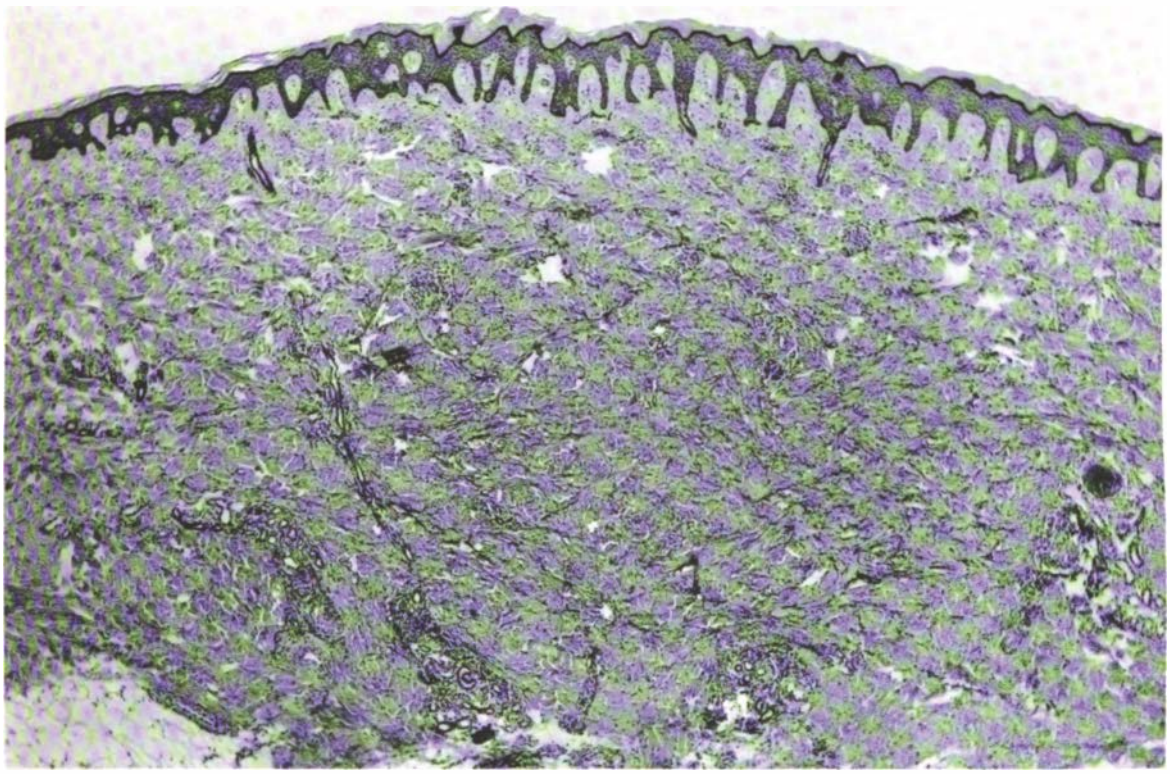


Fig. 1

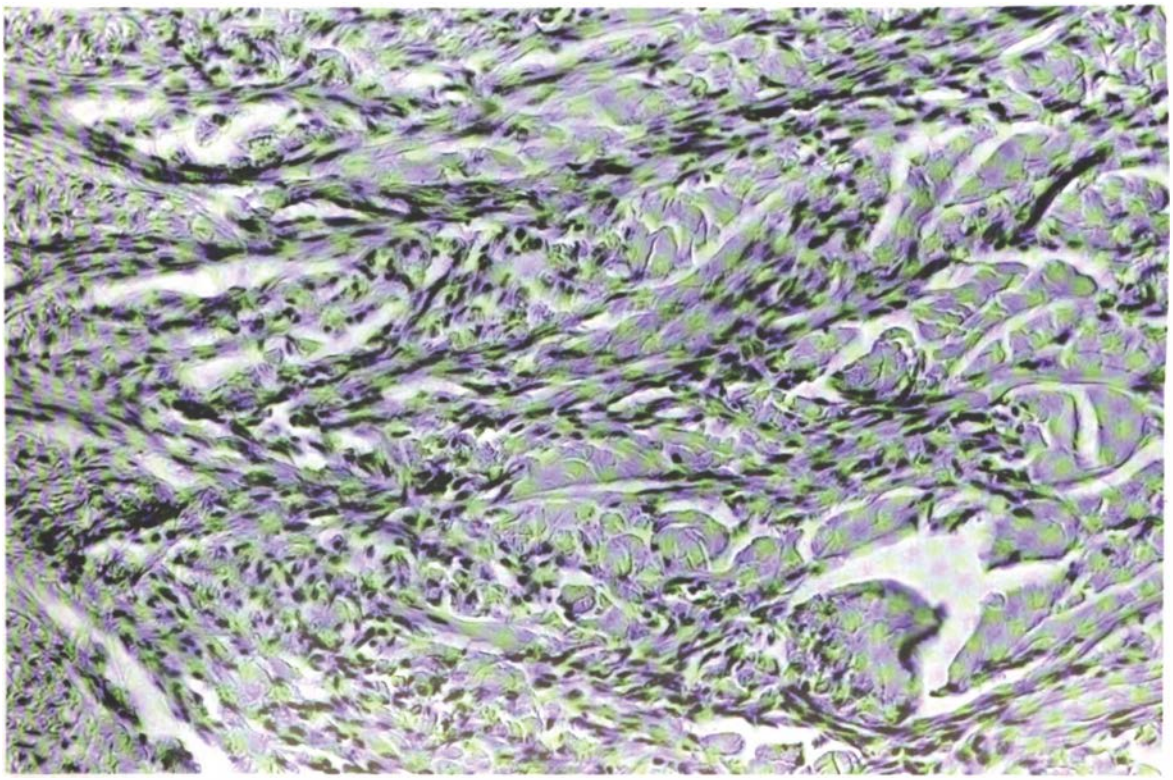


Fig. 2

PLATE I

DESMOID TUMOR

A. Desmoid tumor. Cut surface. Married woman, 33 years old, with a 2-year-old child and pregnant for the second time. The nodule had been present in the lower end of the rectus abdominis muscle for one year. It measured 5 × 3 cm. and was excised with some surrounding muscle after quick frozen section diagnosis of desmoid tumor. No recurrence after two years. A. F. I. P. Acc. No. 218822–C1.

FIBROUS XANTHOMA

B and C. Xanthoma of the scalp in an 11-month-old infant girl. It was first noticed in the occipital region at two months and attained a diameter of 8 mm. Chemical analysis proved that the lipoid was cholesterol. (See fig. 8.) A. F. I. P. Acc. Nos. 218822–C5 and C6.

KELOID

D. Keloid. Cut surface. A Negress 33 years old had an abdominoperineal operation for carcinoma of the rectum two years before. Subsequently there was keloidal thickening ot the abdominal cicatrix. A. F. J. P. Acc. No. 218822–C2.

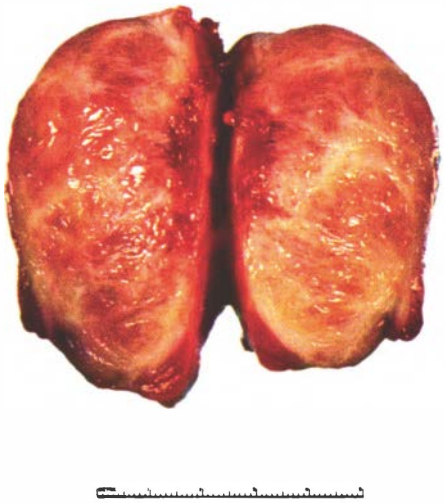
PLANTAR FIBROMATOSIS

(Plate I–E and figure 3 are from the same case)

E. Dupuytren's contracture (pseudoneoplastic type) of plantar fascia. A 16-year-old girl had a nodular thickening of the plantar fascia without contracture. Five years before, the sole of the foot had been lacerated, cauterized, and later the cicatrix was excised. After a symptomless interval of three years, a nodule was excised elsewhere from the plantar fascia. It reappeared and ramified widely in the plantar fascia, all of which was excised. The photograph shows a section through the fascia. The diffuse growth can be easily distinguished from the more regular fascial sheath. A. F. I. P. Acc. No. 218822–C3.

GANGLION

F. Ganglion of leg. Woman, 35 years old. A symptomless lump had been noticed in the calf of the left leg for five months. It measured 8.5 × 3 × 2 cm. and was excised from its bed deep to the gastrocnemius muscle in the midline 5 cm. caudad to its origin. It contained a mucoid, colorless fluid (hyaluronic acid) in a unilocular cavity. No recurrence after two years. A. F. I. P. Acc. No. 218822–C4.



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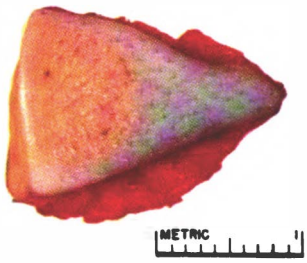

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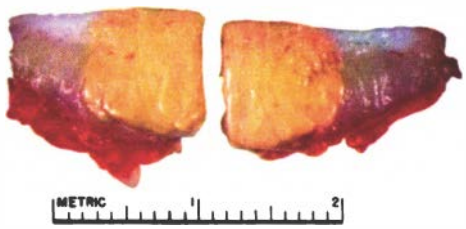

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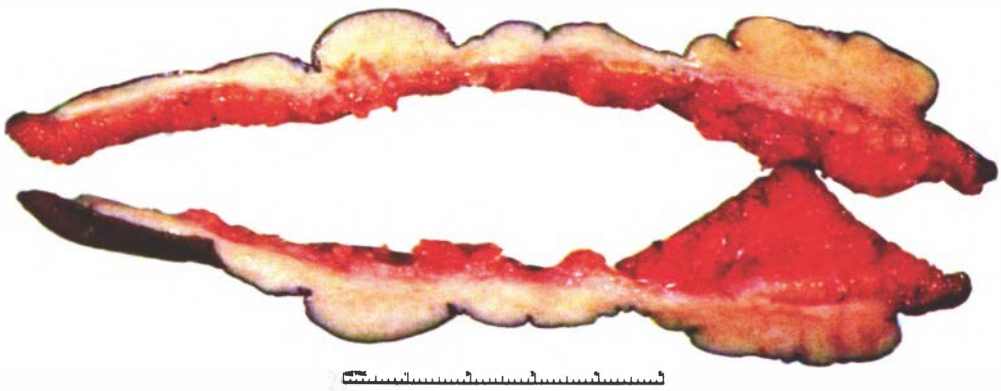

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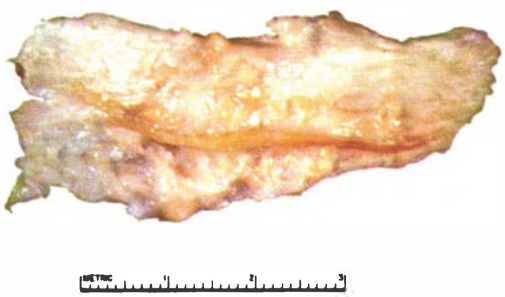

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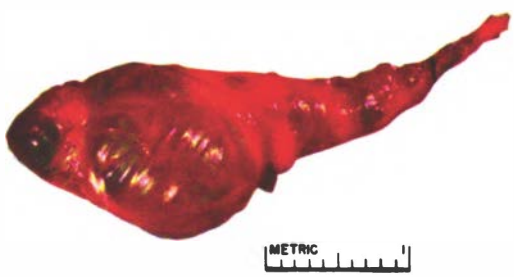

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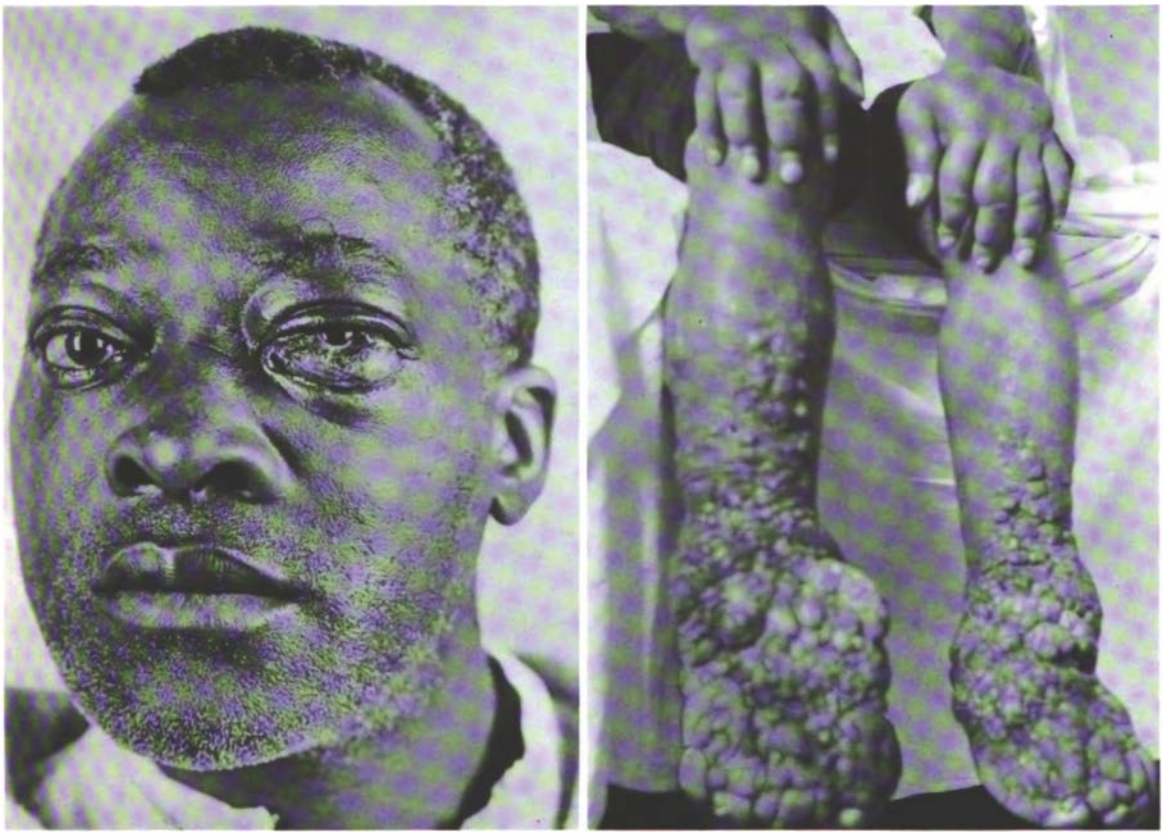
PLATE I



A B

Fig. 5

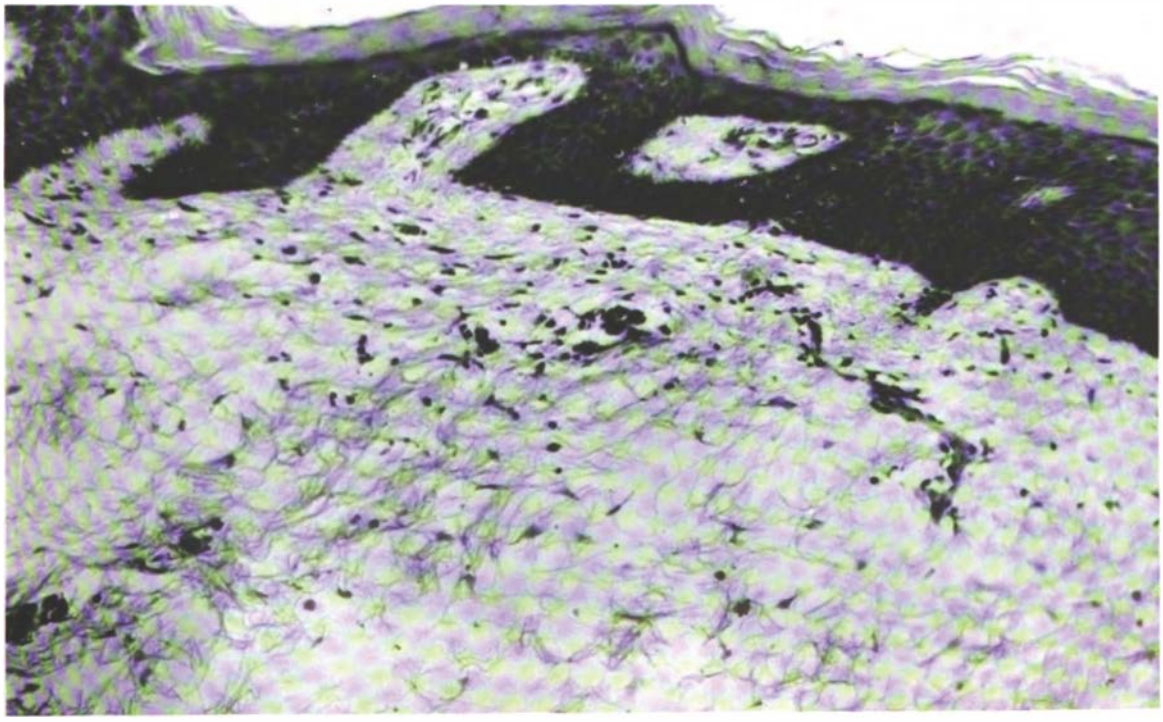
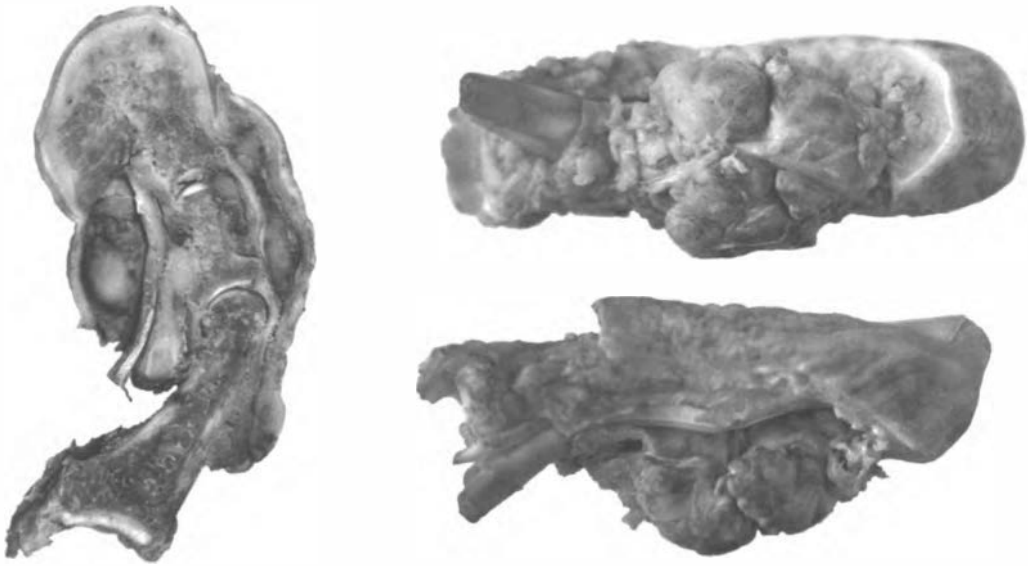


Fig. 6

XANTHOMATOSES

Figure 7. Xanthomatous giant cell tumor from the finger of a 28-year-old woman with hypercholesteremia and multiple xanthomatosis of both upper extremities. There are many foam cells and lens-shaped cholesterol clefts with surrounding multinucleate, phagocytic, syncytial masses. × 226. A. F. I. P. Acc. No. 218822–7.

Figure 8. Xanthoma (juvenile type). The ovate 1.6×1 cm. orange nodule was removed from the scalp of an 11-month-old infant girl (pl. I–B, C). It was circumscribed and confined to the skin. Chemical analysis showed a high cholesterol content of the tumor. The many foam cells containing the ester are supported by a fibroblastic framework. × 602. A. F. I. P. Acc. No. 218822–8.



A B

Fig. 12

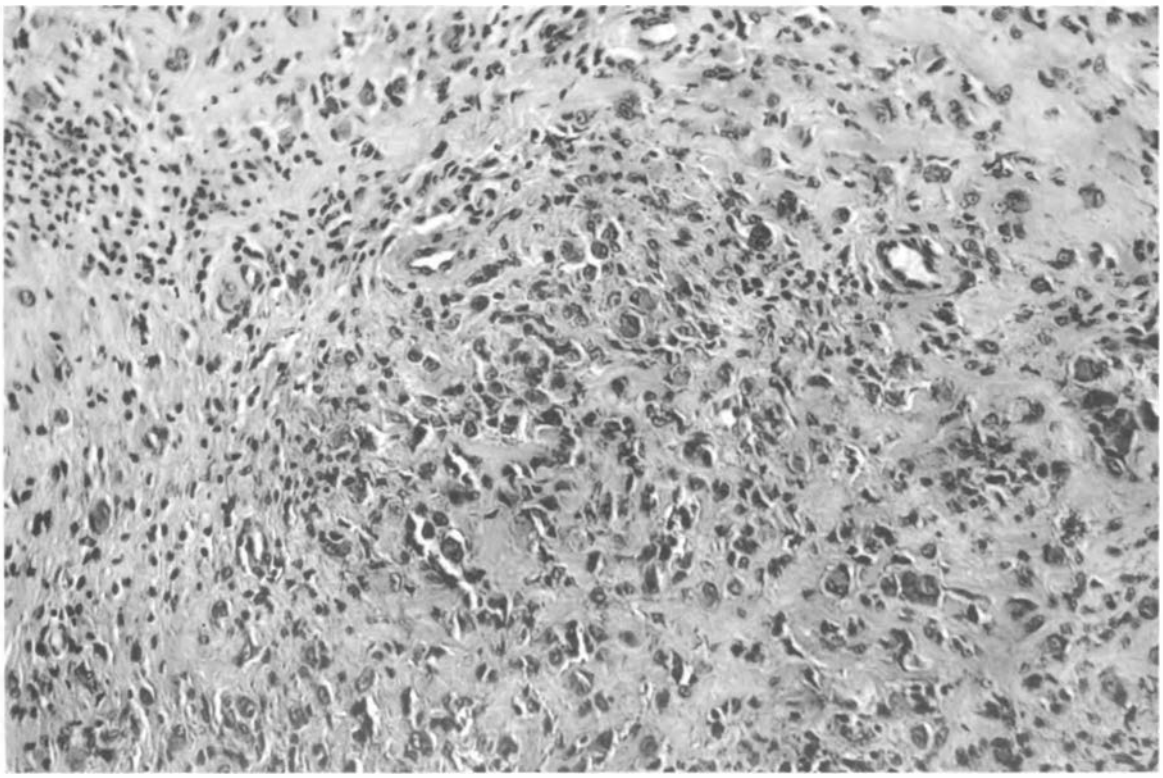


Fig. 13

PLATE II

HIBERNOMA

A. Hibernoma of axilla. An encapsulated mass 8×5×2 cm. was removed from beneath the latissimus dorsi muscle of a 32-year-old man who had been aware of its presence for only three weeks. The cut surface was light brown. This photomicrograph of tissue stained with Scharlach R shows the organoid arrangement of the rounded lipoblasts. A. F. I. P. Acc. No. 218822–C7.

GIANT CELL TUMORS

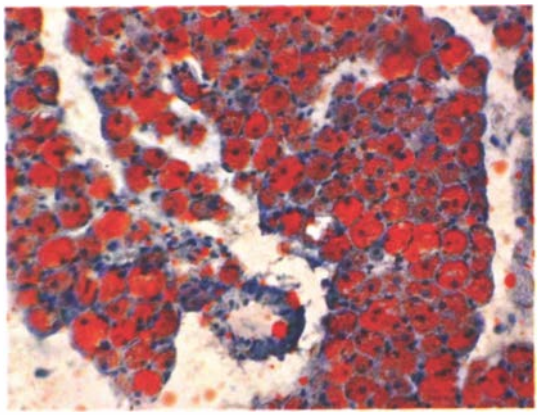
B. Giant cell tumor of ulnar bursa. A painful swelling had been present in the palm of the left hand of this 15-year-old girl for two months. This 15×12 mm. encapsulated tumor was removed from the ulnar bursa to which it was attached. No recurrence after two years. A. F. I. P. Acc. No. 218822–C8.

GRANULAR CELL MYOBLASTOMA

C and D. Granular cell myoblastoma. Man 35 years old. The nodule was in the left scapular region and had been first noticed 18 months before. The photographs show the lesion involving the skin and subcutaneous tissue. The nodule measures 13×14×17 mm. A. F. I. P. Acc. Nos. 218822–C9 and C10.

VENOUS HEMANGIOMA

E and F. Venous hemangioma of chest wall. This 4×3×1.5 cm. nodule was removed from the subcutaneous fat of the chest wall of a 19-year-old woman where it had been present for years. It is made up of a congeries of anastomosing blood-containing vessels with smooth muscle in their walls. A. F. I. P. Acc. Nos. 218822–C11 and C12.



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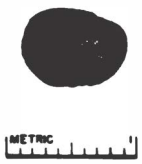

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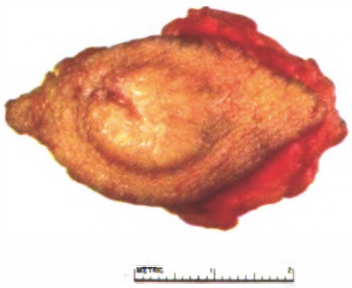

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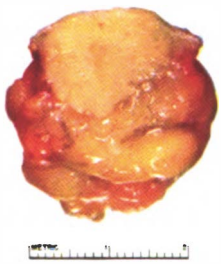

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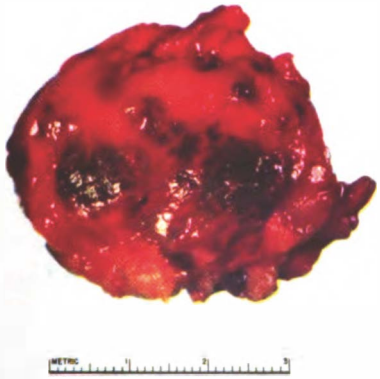

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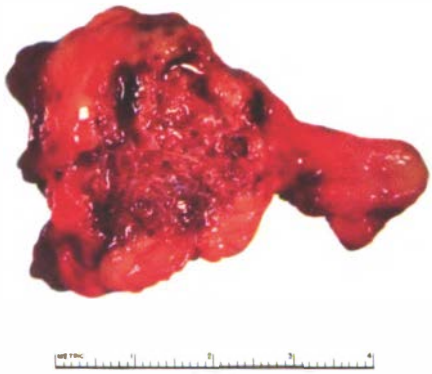


F

PLATE II

strated relationship to nerves, and the cause of the pain is unknown. These painful lipomas probably have no relationship to adiposis dolorosa (Dercum's disease), which is characterized by painful, diffuse fatty infiltration associated with asthenia and psychic disturbances. When lipomas grow in the skin itself, they become pedunculated and, if not removed, may attain a remarkable size. Examples of these are found in the perineum (fig. 15) and upper inner surface of the thighs, where they may hang down to the ground, and in the occipital region, where the tumor may hang down to the waist and appear like a sack. Lipomas are found in or around muscles and tendons; attached to tendon sheaths; in the knee joint, where the fat may collect beneath the synovial lining in swollen villous projections to form the so-called **lipoma arborescens** (fig. 16); in the mesentery, and in the omentum or peritoneum; in the retroperitoneum, where tumors of fantastic size may develop especially in the perirenal zone; and in the mediastinum—in fact, there are no areas in the soft tissues where lipomas have not been reported.

Some lipomas have areas of increased vascularity with occasional spindle or stellate lipoblasts in inconspicuous numbers. These probably represent growth centers. They are found only by chance in casual sections. The fatty tumors associated with capillary and venous vascular proliferations and areas of smooth muscle, which are usually found in deeper situations, especially in striated muscle, are mixed mesodermal tumors or mesenchymomas. They are referred to here because the fat elements may predominate so that grossly they may resemble pure lipomas. The lipomas of the suprarenal medulla, called **myelolipomas** because they contain bone marrow, seem to be a specialty of that site alone.

Some fatty tumors are made up in part of adult fat cells and in part of an embryonal, sticky, myxoid tissue containing spindle and stellate lipoblasts and signet ring cells—an appearance seen in the developing fat of the embryo and for a short time after birth. Such tumors have often been called **myxolipomas, lipomyxomas, myxofibrolipomas,** etc., and are considered benign. They differ from the ordinary lipoma, however, because they grow by infiltration and are difficult to eradicate except by very wide excision. For that reason it has seemed preferable to this writer to classify them as differentiated liposarcomas even though they do not metastasize.

Seemingly, lipomas of adult form undergo malignant transformation into liposarcomas only with the greatest rarity. This writer has seen only one unquestionable example of such transformation, although variations in the degree of differentiation of a liposarcoma may tempt one to suspect it.

Hibernoma

This name has been applied to a rare subcutaneous tumor composed of congeries of large foamy cells, each distended with multiple lipoid-filled

MULTIPLE SYMMETRICAL LIPOMATOSIS

Figure 14. Multiple symmetrical lipomatosis in a 48-year-old chronic alcoholic teamster. Swellings first appeared 15 years before on the back of the neck and spread gradually to the front and chest. Other swellings then appeared on the abdomen, back, arms, and thighs in symmetrical arrangements. There was no familial history of lipomas. The sella turcica was slightly smaller than normal. Normal-appearing fat was removed from the neck to improve the appearance. A. F. I. P. Acc. No. 218822–14.

LIPOMA

Figure 15. Pedunculated lipoma of the thigh. At the age of 19 years, this man first noticed a small lump on the upper inner aspect of the right thigh. It grew slowly to reach its present size after four years. It was composed of adipose tissue with one small cyst due to necrosis. A. F. I. P. Acc. No. 218822–16.

Figure 16. Lipoma arborescens of knee joint. A mass of villi filled with fat was removed from an arthritic knee joint of a 55-year-old woman. A. F. I. P. Acc. No. 218822–15.

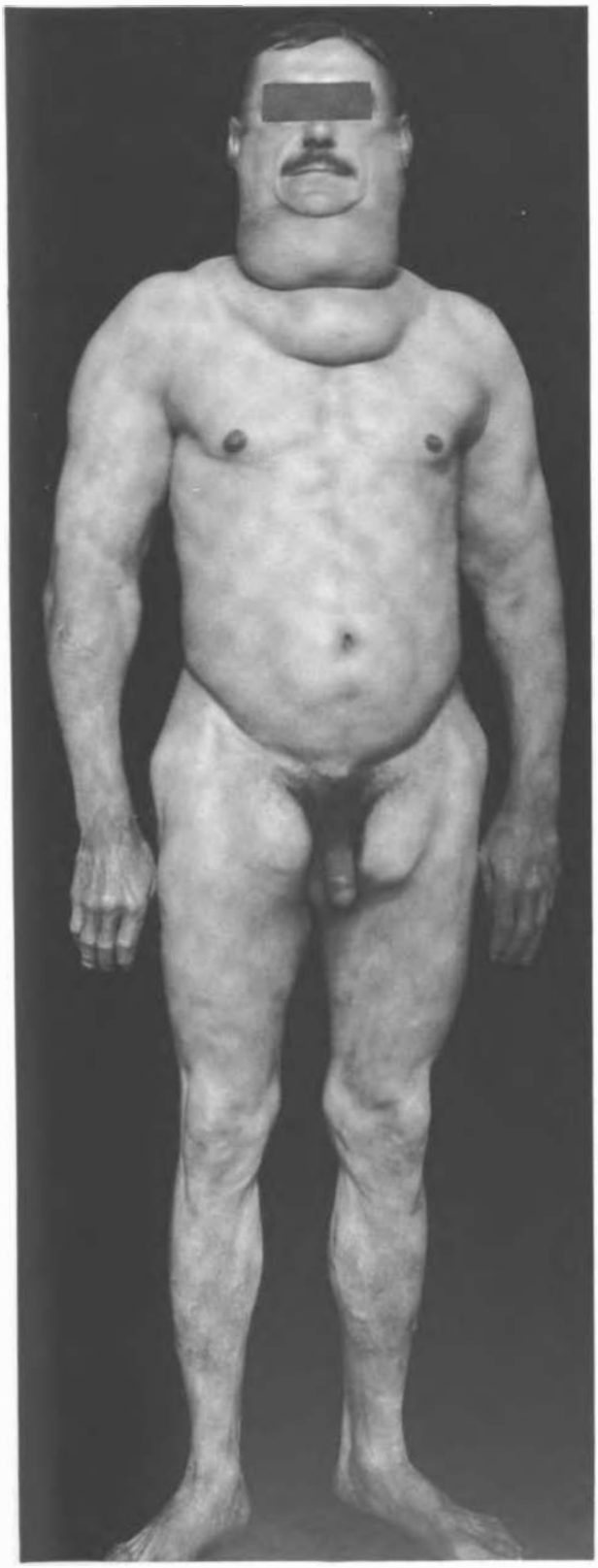


Fig. 14

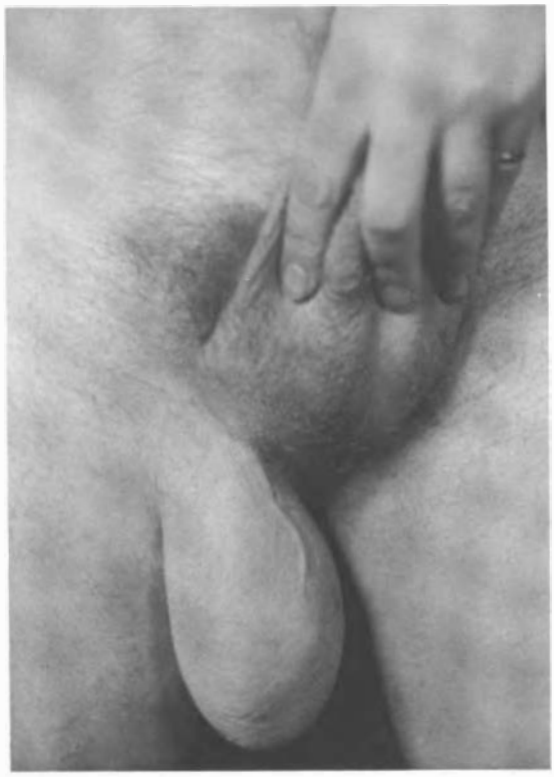


Fig. 15

Fig. 16

vacuoles. Tumors of this type have a definite lobulated arrangement simulating the appearance of the hibernating organs of certain animals. They have been found in the thigh, the popliteal space, the back, the neck, the axilla, the abdominal wall, and the mediastinum. They grow slowly, may attain a diameter of 20 cm., and are not known to become malignant (pl. II–A).

BENIGN TUMORS OF MUSCLE

Leiomyoma

SYNONYMS AND RELATED TERMS: Angiomyofibroma; dermatomyoma; fibroleiomyoma; fibromyoma; myofibroma; myofibroma lymphangiectaticum; myoma; painful subcutaneous tubercle; solitary superficial leiomyoma; subcutaneous leiomyoma; superficial leiomyoma; telangiectatic fibromyoma; vascular leiomyoma.

Outside of the uterus and gastrointestinal tract, leiomyomas are rather uncommon but are most frequent in the skin and subcutaneous tissue. There are two varieties: (1) **superficial leiomyomas,** composed almost exclusively of smooth muscle, which are probably derived either from the smooth muscle of the arrectores pilorum or the smooth muscle of the skin in the genital zones; (2) **vascular leiomyomas,** which apparently arise from the smooth muscle of blood vessels. The latter are very vascular. They may be solitary or multiple, rarely grow to a large size, and are rather richly innervated. Either variety may occasion attacks of paroxysmal pain, a peculiarity not shown by smooth muscle tumors in other parts of the body (figs. 17–19). When multiple they are not commonly scattered in a haphazard fashion over all the body surface but are more apt to be grouped together in one particular area or zone. Malignant changes in skin leiomyomas are unknown. Elsewhere, leiomyomas are very uncommon in the soft tissues and are found only rarely deep in the subcutaneous tissue and in the broad ligament, retroperitoneal tissues, mesentery, omentum, mediastinum, and orbit. There appears to be no clear-cut separation between vascular leiomyomas and venous hemangiomas, so one has to select the name depending upon the amount of smooth muscle outside the tumor vessels. The vascular leiomyoma can be distinguished from the hemangiopericytoma with spindle cells by the presence of myofibrils in the former. It suggests a close relationship between the smooth muscle cell and the pericyte.

The smooth muscle cells, which interlace in bundles to form the leiomyoma, closely resemble normal smooth muscle cells but they are generally somewhat larger, and not every one of them seems to contain myofibrils, although most of them do. The benign tumors show very few mitoses and often none can be found if only one section is made. Very occasionally such an apparently benign growth, especially the larger ones situated in the broad ligament, retroperitoneal area, and mediastinum, will metastasize. (See Leiomyosarcoma, p. 88.)

Rhabdomyoma

It is questionable whether or not there occurs a truly benign tumor made up of differentiated rhabdomyoblasts outside the heart. The whole question will be discussed under Rhabdomyosarcoma, but here it can be said that in the tongue and other voluntary muscles a few such small, differentiated tumors have developed which have not recurred or metastasized during rather short periods of observation following removal.

Granular Cell Myoblastoma

SYNONYMS AND RELATED TERMS: Abrikossoff's tumor; embryonal rhabdomyoblastoma; epulis of newborn; "granular cell neurofibroma"; granular myoblastoma; myoblastic myoma; myoblastoma; "pleomorphic-cell sarcoma."

It is probable that no tumor at the present time has aroused more interest and greater differences of opinion than the mysterious granular cell tumor which is most frequently called granular cell myoblastoma. Although sporadic cases have been recorded under various names at least since 1854, it was first described as an entity by Abrikossoff in 1926. He called it a myoblastic myoma and believed it was a neoplasm of striated muscle cells. The distribution of the tumor is wide and peculiar. Tables I and II show that there are records of 136 of these tumors in the Surgical Pathology Laboratory of Columbia University if one includes 16 malignant examples. These have the following distribution: extremities 31, trunk 30, head and neck 8, multiple in skin 2, tongue 29, gums 6 (congenital epulis of newborn), breast 9, larynx and trachea 5, bladder, uterus, orbit, perianal region and appendix 2 each, and solitary examples in the floor of the mouth, esophagus, stomach, omentum, retroperitoneum, and vulva. The tumors are generally small and rarely attain a diameter greater than 6 cm. (pl. II–C, D). While many of the tumors lie in striated muscle, there are just as many more which do not. This has led many authors to doubt their origin from myoblasts, and some of the alternative hypotheses are recorded on page 8 of the Introduction. Particularly it has been doubted that the so-called organoid variety (fig. 21) is myoblastic because it differs histologically from the more common type. The writer still adheres to the myoblastic hypothesis because of the tissue culture studies of Murray, who has grown both varieties in vitro and who concludes "that granular-cell-myoblastoma cultures bear a greater resemblance to cultures of various forms of skeletal muscle, normal and neoplastic, than to cultures of other tissue types to which their origin has been attributed." Until more convincing arguments for another origin are advanced, the writer will continue to adhere to the myoblastic hypothesis (fig. 22).

MICROSCOPIC. The benign tumors are composed of masses of rather large polygonal cells with small deeply stained nuclei and voluminous cytoplasm, distinguished by the presence of many fine granules that are usually acidophile (fig. 20). The spacing of these granules is such that in low power magnifi-

VASCULAR LEIOMYOMAS

Figure 17. Vascular leiomyoma of the leg. Negress 45 years old. For two or three years she had noticed the tumor, which was always tender to touch and occasionally painful. × 33. (Figure 7, case 8 from Stout, A. P. Solitary cutaneous and subcutaneous leiomyoma. Am. J. Cancer, 29: 435–469, 1937.) A. F. I. P. Acc. No. 218822–17.

Figure 18. Vascular leiomyoma. A tumor 2.2×1.5 cm. was present on the leg of a 55-year–old man for 15 years. When touched it became hard and prominent. The tumor is composed of blood vessels with smooth muscle in their coats, and there is additional unrelated smooth muscle in the stroma shown at lower left. × 226. A. F. I. P. Acc. No. 218822–18.

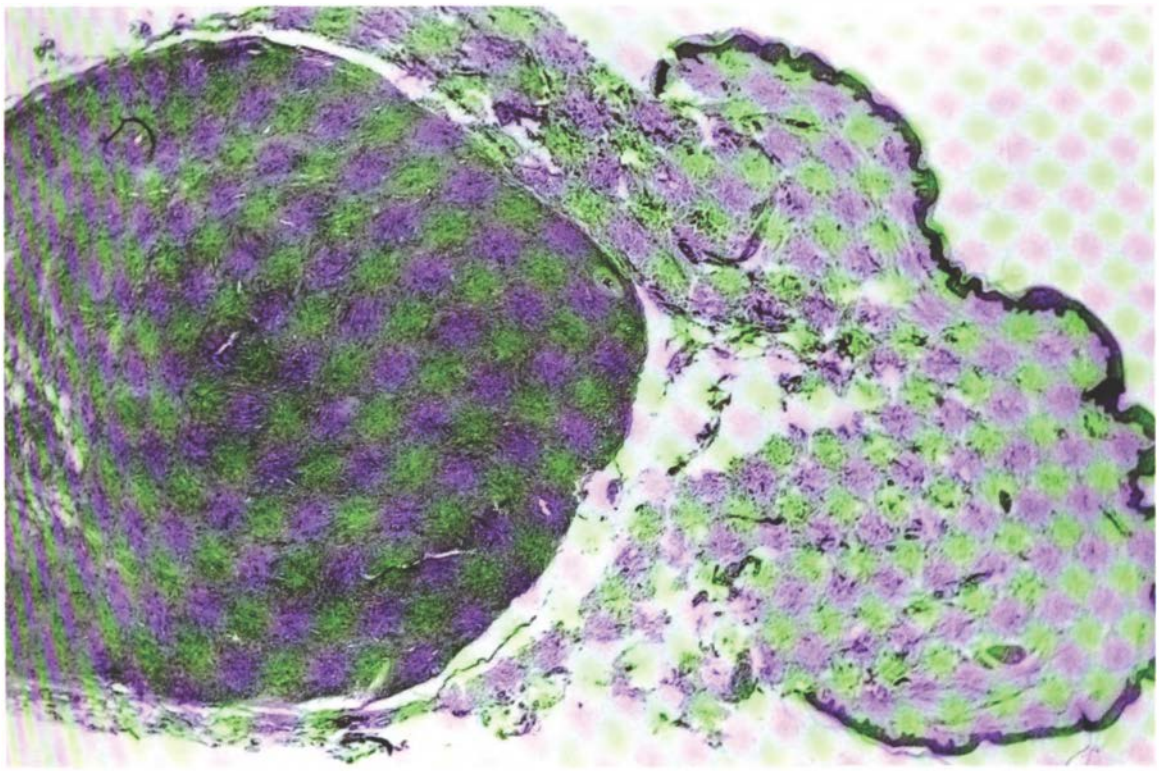


Fig. 17

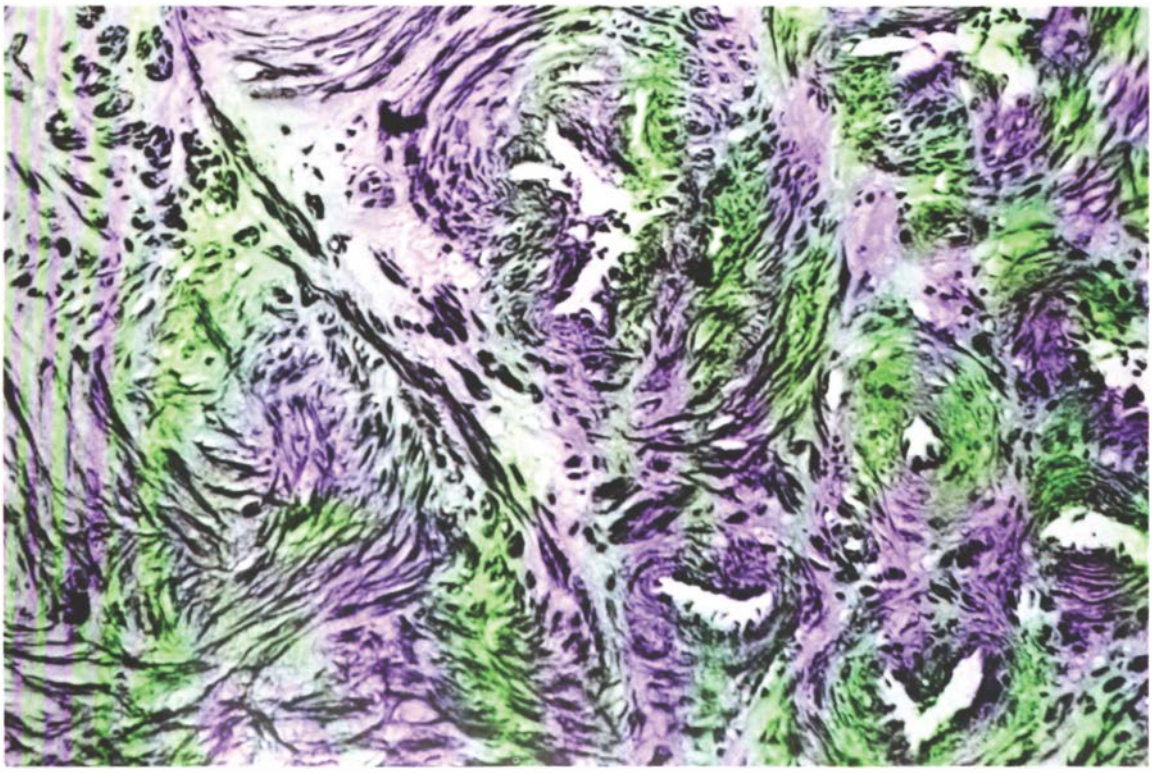


Fig. 18

VASCULAR LEIOMYOMA

Figure 19. Vascular leiomyoma. A 1.5×1 cm. painless lump was present for five years in the palm of a 60-year-old man. During the last three months it became tender and red. The tumor is composed of many vessels with smooth muscle in the walls and additional unrelated smooth muscle at the periphery of the tumor. This is a Laidlaw modification of a Gros-Bielschowsky silver impregnation showing the numerous bundles of nerve fibrils in the tumor. × 226. A. F. I. P. 218822–19.

GRANULAR CELL MYOBLASTOMA

Figure 20. Benign granular cell myoblastoma. This is one of some 15 subcutaneous nodules scattered over the back, arm, thigh, face, tongue, cheek, and lip, varying from 1 to 11 cm. in diameter. They had been present for 18 years in a 31-year-old Negress. The cells are characteristic with voluminous cytoplasm containing fine acidophilic granules, and the nuclei are small. There are dense fibrous septa supporting the tumor cells. × 226. (From case 4 reported by Powell, E. B. Granular cell myoblastoma. Arch. Path., 42:517–524, 1946.) A. F. I. P. Acc. No. 218822–20.

Figure 21. Malignant granular cell myoblastoma of thigh (organoid type). Girl, 18 years old. A tumor the size of a lemon was removed from the thigh muscles, where its presence had been noted for six months. This illustrates the endocrine architecture of some of these tumors, producing a striking pattern consisting of balls of rounded granular cells separated by delicate septa containing capillaries. (Figure 4 from Horn, R. C., Jr., and Stout, A. P. Granular cell myoblastoma. Surg., Gynec. & Obst., 76: 315–318, 1943.) A. F. I. P. Acc. No 218822–21.

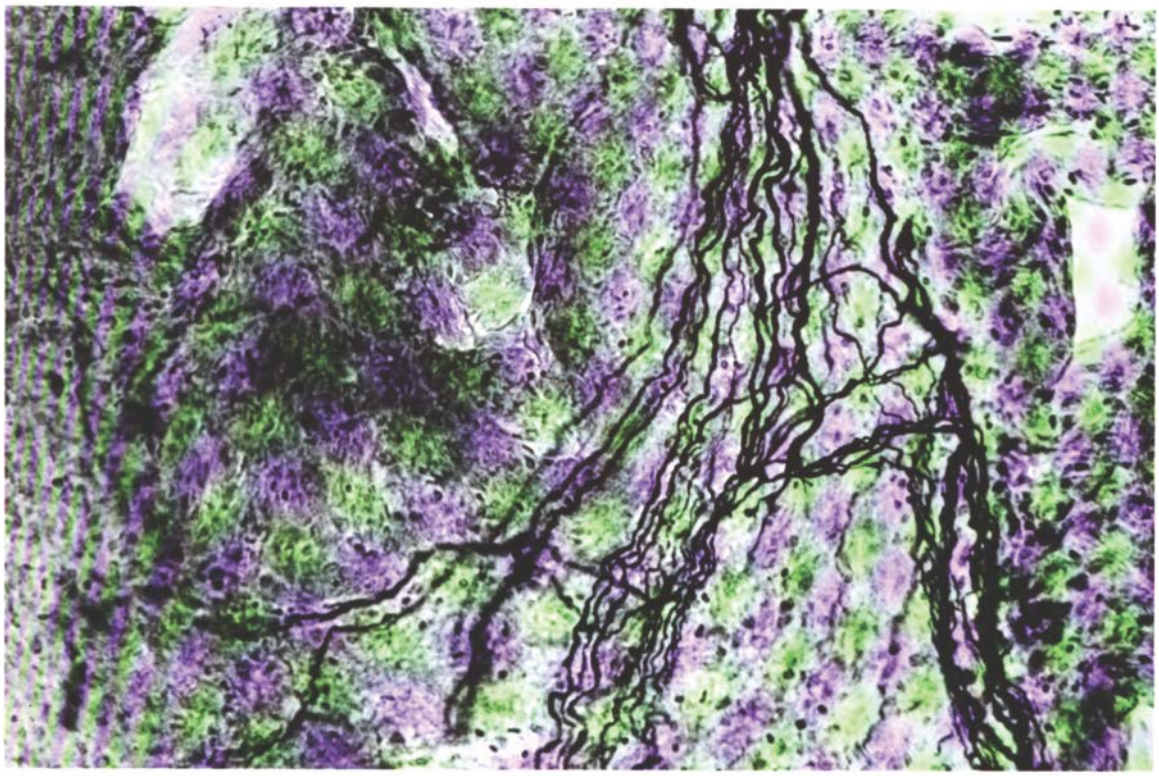


Fig. 19

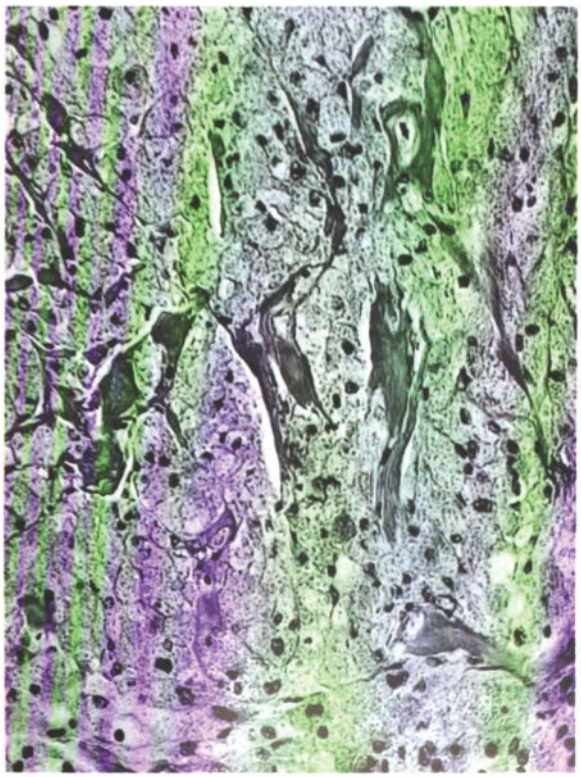


Fig. 20

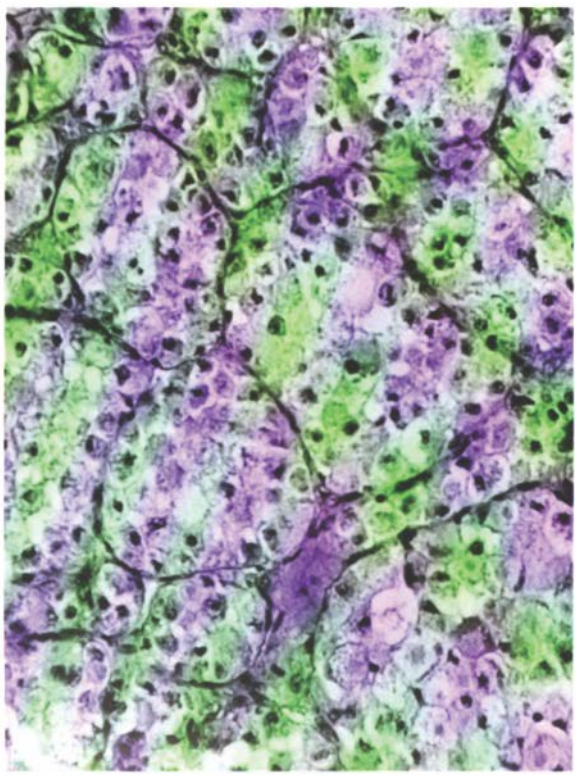


Fig. 21

cation the cell may appear foamy as if it were a xanthomatous histiocyte. But higher magnification will quickly convince one that there are either no vacuoles or only sporadic ones in occasional cells, and fat stains are usually entirely negative. The cells have fairly distinct cell membranes and may appear inside nerve sheaths, and if in the skin or squamous mucosae may penetrate into the papillary layer. If this occurs, a peculiar response to the presence of the granular cells may cause the squamous cells to proliferate and invade downward into the tumor, forming keratinized pearls. It is important to know about this in order not to confuse it with squamous cell epithelioma, which it resembles, because it is not a malignant process (fig. 23).

The great majority of these tumors are benign and will not recur unless incompletely excised. However, it must be noted that four tumors in the Columbia series with this relatively benign appearance have behaved like malignant tumors and metastasized, so that one cannot make the sweeping statement that tumors with the classic morphology of the common accepted form of granular cell myoblastomas are always harmless. The specialized tumor variously called organoid granular cell myoblastoma and paraganglioma will be described later in the section on Malignant Granular Cell Myoblastoma, since it is a malignant tumor.

BENIGN ANGIOMATOSES

Hemangiomatoses

SYNONYMS AND RELATED TERMS: Angioendothelioma; angioma; angiokeratoma; angioma pigmentosum atrophicum; hemangioendothelioma; benign hemangiopericytoma; erectile tumor; gemmangioma; granuloma pyogenicum; hemangioendothelioblastoma; nevus anemicus; nevus araneus; nevus flammeus; nevus vasculosus; plexiform angioma; racemose aneurysm; spider nevus; telangiectasis, hereditary; vascular nevus.

A majority of the vascular tumors are found in the skin, where they often appear at birth or in the early postnatal months and years. They assume a variety of appearances, many of which have received descriptive names from the dermatologists. This phase of the subject will be dealt with in Fascicle 7, "Tumors of the Cardiovascular System." Here will be described only the histopathologic appearance of vascular tumors, the way in which they grow, and a somewhat more detailed account of the much less common, deeply placed neoplasms.

The capillaries are composed of a lining of endothelial cells, a supporting sheath of reticulin fibers and cells, and certain cells scattered at intervals over the outer surface of the sheath, which have been called pericytes by Zimmerman and Rouget cells by some histologists. The nature of these cells is uncertain, but it is probable that they have long processes that extend along and wrap around the capillary with contractile powers so that its caliber can be changed by them. These cells and their processes normally can be demonstrated only

by a special silver technique. Veins and arteries have smooth muscle and elastic tissue replacing the pericytes.

Vascular tumors are named according to their composition. If a tumor is made up of capillaries alone, it is called a **capillary hemangioma** (fig. 24). The ordinary capillary hemangioma has no definite pattern; the capillaries are arranged at haphazard. If they are widely dilated, the tumor is called a **cavernous hemangioma.** Sometimes capillaries sprout from larger parent vessels to form lobulations, producing a growth somewhat like hyperplastic granulation tissue. If this occurs spontaneously beneath an intact epidermis or mucosa without known cause, it has been called by the dermatologists a granuloma pyogenicum—a term without merit or significance, since it has no primary relationship to pus or infection. This writer prefers the term **capillary hemangioma, granuloma type,** for these growths (fig. 25). If the vascular tumor has vessels with thicker walls containing smooth muscle cells, it is called a **venous hemangioma** (pl. II–E, F, fig. 26).

Sometimes the capillary hemangiomas in infants show a proliferation and doubling or even tripling of the endothelial layer. This may be called a **benign hemangioendothelioma** (or **infantile hemangioendothelioma,** fig. 27) to distinguish it from the malignant form. In somewhat similar fashion the pericytes may heapupas rounded or spindle-shaped cells just outside of the reticulin sheath, giving rise to the **benign hemangiopericytoma** (pericytoma, perithelioma; fig. 28). To distinguish surely between these two varieties, it may be necessary to do a silver reticulin impregnation in order to be sure that the proliferated cells are outside the reticulin sheath in the territory of the pericytes and not inside it with the endothelial cells.

The best known form of hemangiopericytoma is the **glomus tumor** (angioneuroma, angioneuromyoma, glomangioma, neuromyoarterial glomus, painful subcutaneous tubercle, Popoff tumor, subcutaneous glomal tumor, tumor of neuromyoarterial glomus). This interesting growth first accurately described by P. Masson is most commonly found beneath the finger nails, but has also been reported in many other situations, both superficial and deep. Almost all of the reported tumors have been associated with attacks of paroxysmal pain and often with disturbances of the sympathetic nervous system. It is an interesting fact that glomus tumors in the fingers are much more common in females, while elsewhere they are more frequently found in males. The tumors are made up of a congeries of thick-walled blood vessels with vast numbers of nonmyelinated nerve fibers between them. The vessel walls are thickened by the presence of several layers of apparently rounded cells, usually with a clear zone around the nucleus, which Murray and Stout by a method of tissue culture have identified as pericytes (figs. 29–34). The glomus tumor is benign, and very rarely recurs after excision, although occasionally it may do so.

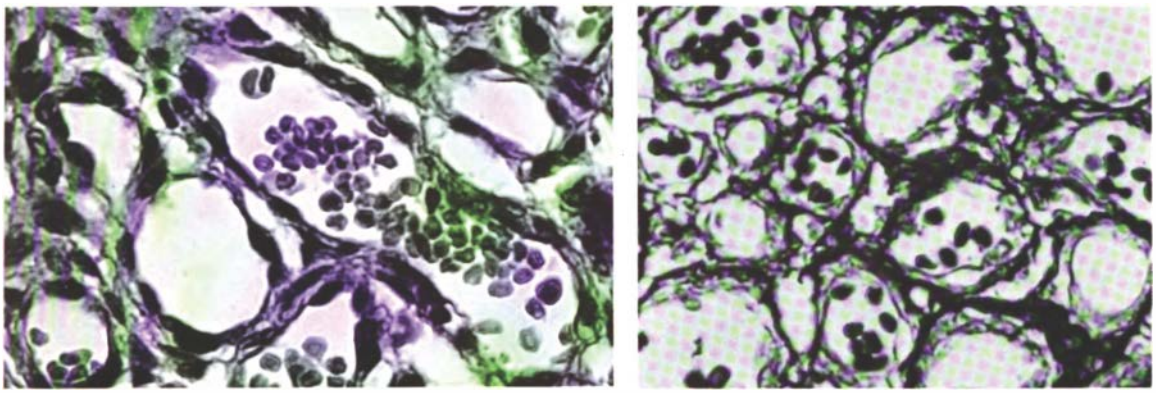
CAPILLARY HEMANGIOMA

Figure 24. Capillary hemangioma appearing as a congenital bright red nodule in the skin of the forearm. This had grown to a size of 2.2 × 1.7 cm. when it was excised at the age of six months. A: The tumor is made up of a solid mass of capillaries with prominent endothelial lining cells. There is no special proliferation of either endothelial cells or pericytes. B: A Laidlaw silver reticulin impregnation shows the vascular reticulin sheaths. A. F. I. P. Acc. No. 218822–24.

Figure 25. Capillary hemangioma, granuloma type (granuloma pyogenicum) of the thigh. A soft, solid, pink, pedunculated growth 5 mm. in diameter, without bleeding or erosion, was removed from a 36-year-old man. The photomicrograph shows a cross section of the entire growth, which is made up of vague lobules of capillaries beneath an intact epidermis. A. F. I. P. Acc. No. 218822–25.

VENOUS HEMANGIOMA

Figure 26. Venous hemangioma of peroneus muscle. A 19-year-old girl had a thickening of the leg since birth. Roentgen ray showed spots of calcification in this lesion. A diffuse hemangioma infiltrated the whole length of the belly of the peroneus muscle, which was excised. The photomicrograph shows scattered muscle fibers separated by blood vessels, some of which have smooth muscle in their walls. × 226. A. F. I. P. Acc. No. 218822–26.



A B

Fig. 24

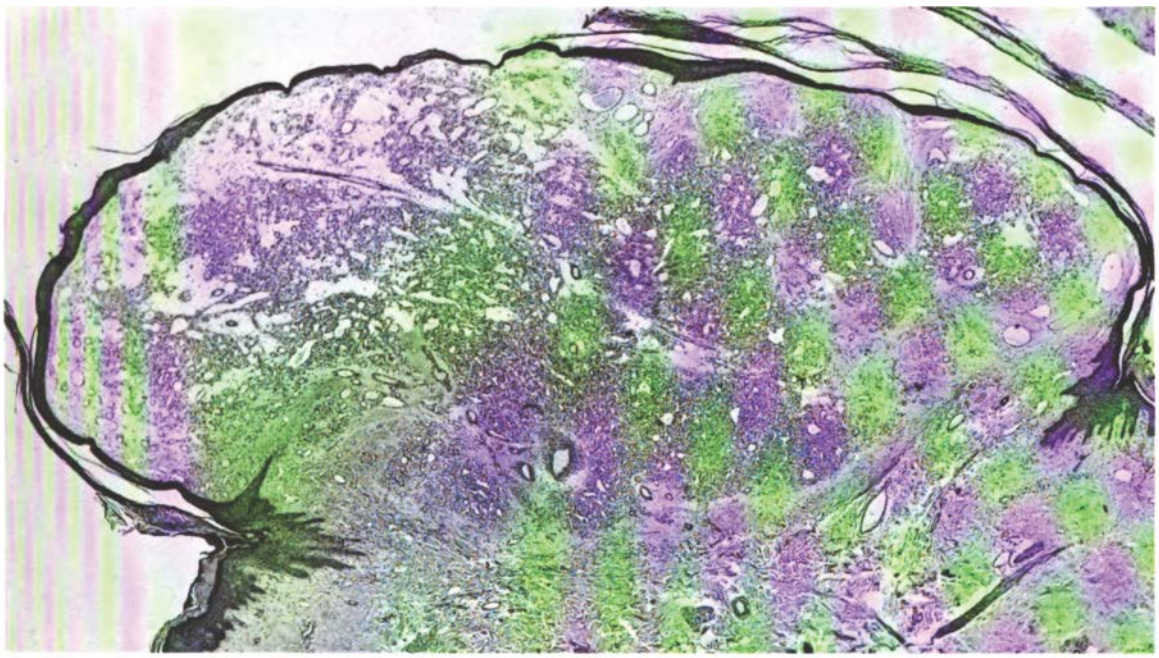


Fig. 25

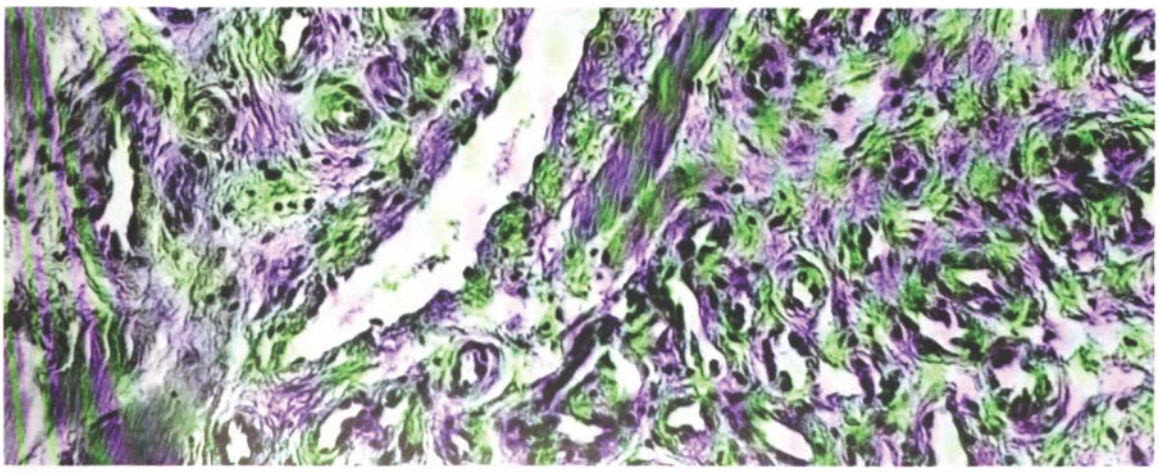


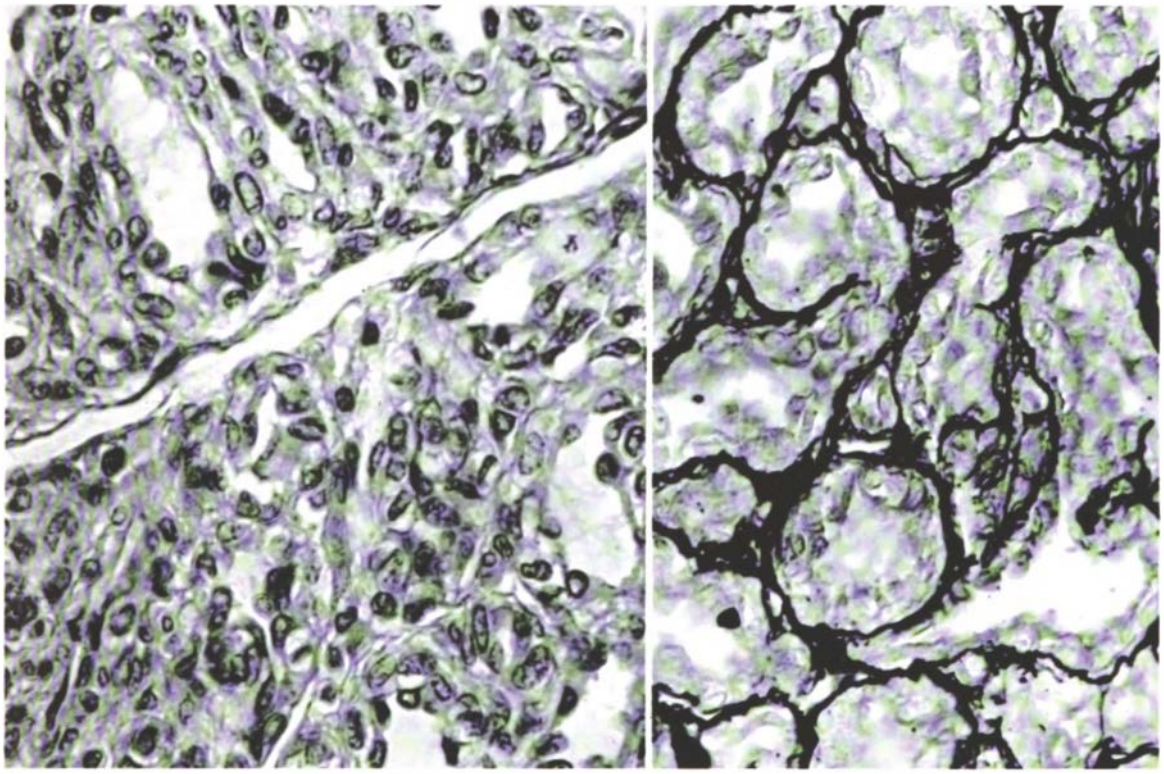
Fig. 26

BENIGN HEMANGIOENDOTHELIOMA

Figure 27. Benign hemangioendothelioma of infancy. This infant girl was born with a small red spot in the parietal region. It had enlarged to a diameter of 1 cm. at the age of three months when it was removed. The photomicrographs show: (A) a proliferation of cells, which has sometimes obscured the vessel lumens; (B) a Laidlaw silver reticulin impregnation which outlines the capillary sheaths and indicates that all of the cellular proliferation is inside them and therefore endothelial. × 525. (Figure 5–A from Stout, A. P. Hemangio-endothelioma: a tumor of blood vessels featuring vascular endothelial cells. Ann. Surg., 118. 445–464, 1943.) A. F. I. P. Acc. No. 218822–27.

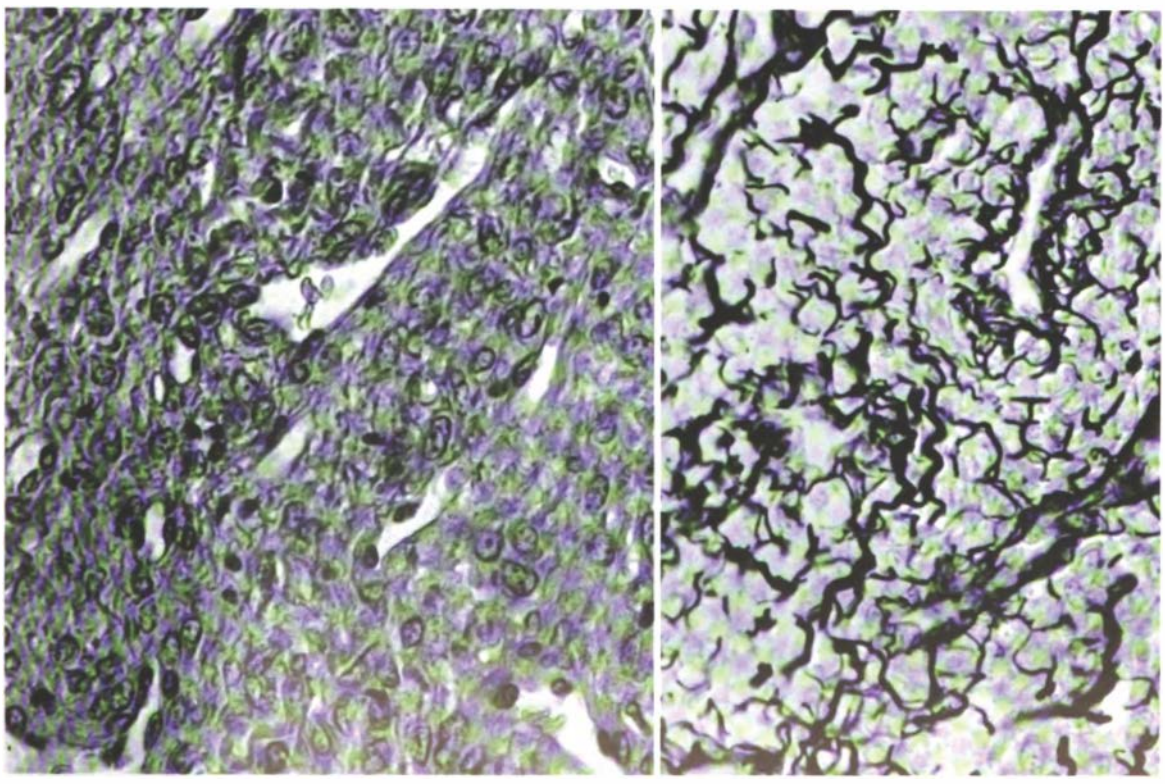
BENIGN HEMANGIOPERICYTOMA

Figure 28. Benign hemangiopericytoma. A 7×5×3 cm. tumor present for seven years in the mons pubis of a 43-year-old woman. It was very vascular when excised. There was no recurrence after six years. A: This shows the capillaries lined with normal endothelial cells with the tumor cells packed in tightly about them. B: In a Laidlaw silver reticulin impregnation the capillary sheaths are clearly defined. All of the tumor cell proliferation is outside of these sheaths. × 515. A. F. I. P. Acc. No. 218822–28.



A B

Fig. 27



A B

Fig. 28

GLOMUS TUMOR

Figure 29. Subungual glomus tumor (paucivascular type of Masson). Five years after this 31-year-old woman crushed her right middle finger in a door, a dark red spot was excised from beneath the nail because of paroxysmal pain. The tumor recurred and four years later it was again excised. There was a defect in the phalanx into which the encapsulated tumor fitted. This photomicrograph shows the arrangement of cords of pericytes separated by very loose-textured tissue. Very few vascular lumens can be seen. × 226. A. F. I. P. Acc. No. 218822–29.

Figure 30. Subungual glomus tumor. Cajal impregnation, showing the rich plexus of delicate axis cylinders, which occupies the loose-textured spaces found between the masses of pericytes. A. F. I. P. Acc. No. 218822–30.

Figure 31. A: Explant from a glomus tumor 24 days in vitro. A branching form is adopted by "epithelioid cells" from the cell masses surrounding capillaries. Formalin fixation; modified Bodian silver impregnation. B: A pericyte with lateral branches contracted from the heart of a 43-year-old man. After Zimmermann, 1923. (Figure 4, from Murray, M. R., and Stout, A. P. The glomus tumor; investigation of its distribution and behavior, and the identity of its "epithelioid" cells. Am. J. Path. 18: 183–203, 1942.) A. F. I. P. Acc. No. 218822–34.

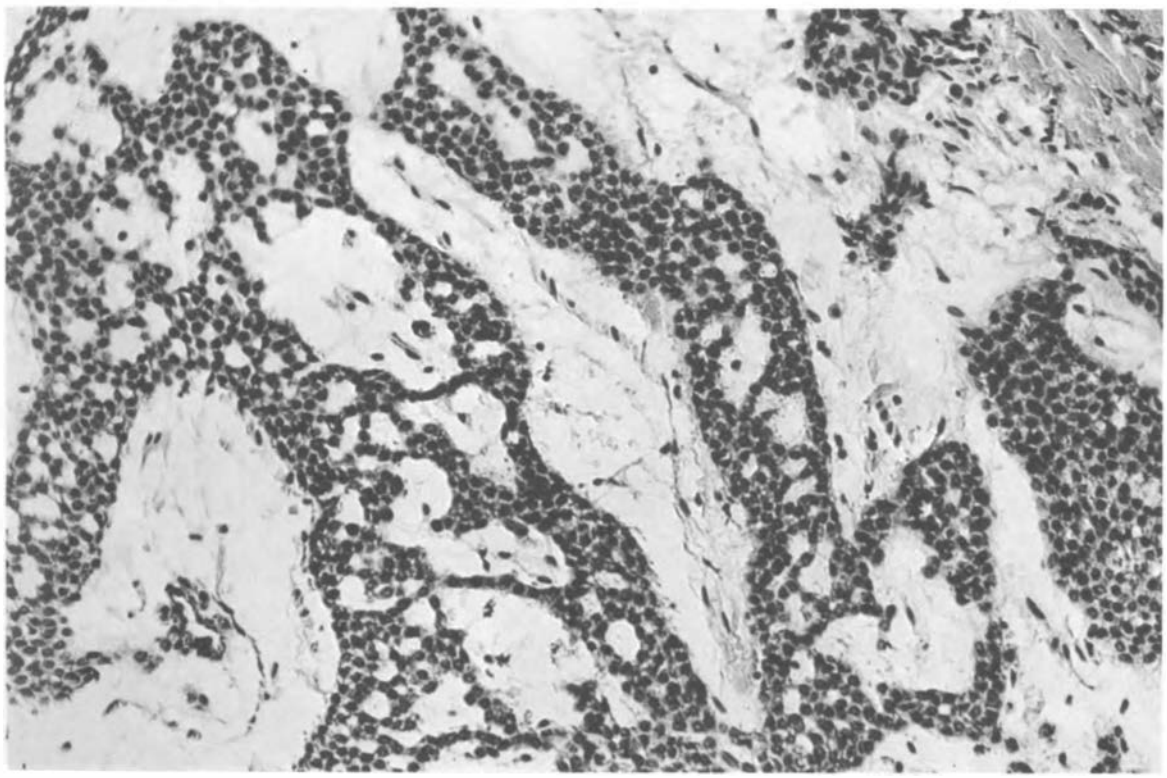


Fig. 29

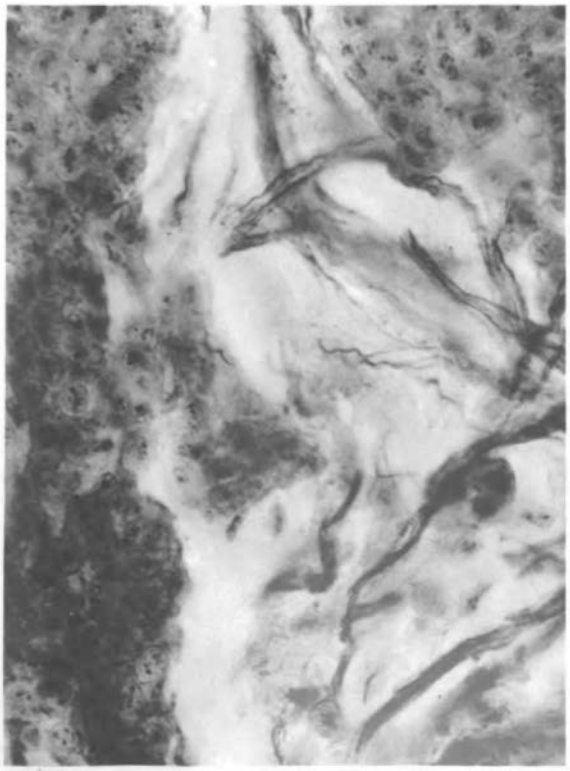
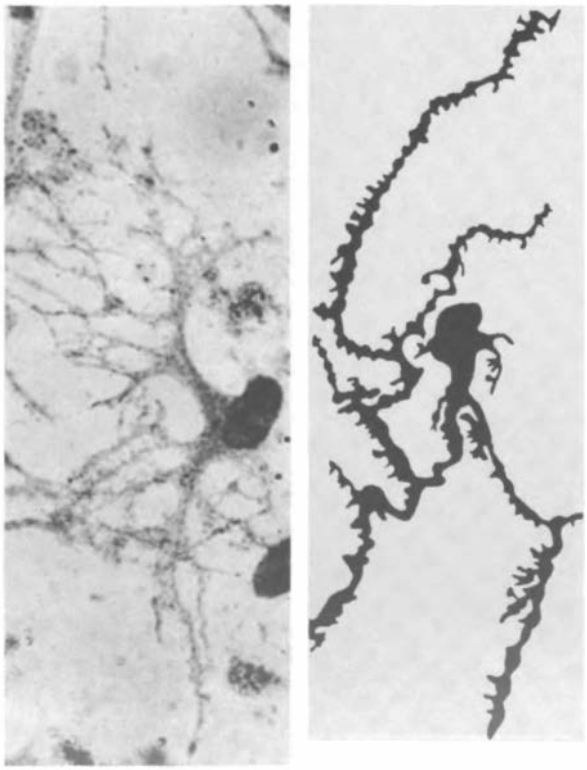


Fig. 30



A B

Fig. 31

GLOMUS TUMOR

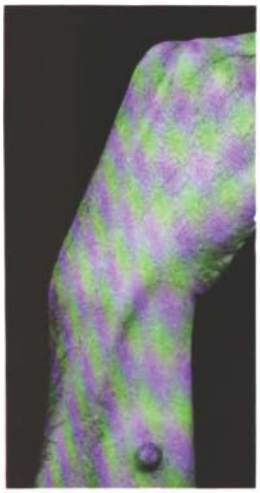
(Figures 32–34 are from the same case)

Figure 32.* **A and B. Glomus tumor of the forearm of a 65-year-old man. The tumor had been present and stationary for 43 years. During the two months preceding removal it had increased in size and was painful when hit. A. F. I. P. Acc. No. 218822–31.**

Figure 33.* **A low power photomicrograph of the tumor illustrated in figure 32. This is Masson's vascular form of glomus tumor. A. F. I. P. Acc. No. 218822–32.**

Figure 34. Higher magnification of one of the tumor vessels of the case illustrated in figures 32 and 33. The vessel has a small lumen lined with normal endothelial cells. It has a muscular coat with pericytes surrounding it and intermingled with the smooth muscle cells. (Figure 6 from Stout, A. P. Tumors of the neuromyo-arterial glomus. Am. J. Cancer, 24: 255–272, 1935.) A. F. I. P. Acc. No. 218822–33.

***Figures 32 and 33 are figures 4 and 5 from Stout, A. P. Tumors of the neuromyo-arterial glomus. Am. J. Cancer, 24: 255–272, 1935.**



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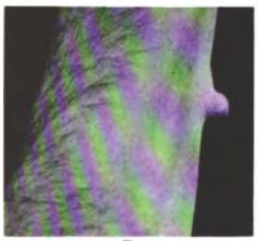


B

Fig. 32

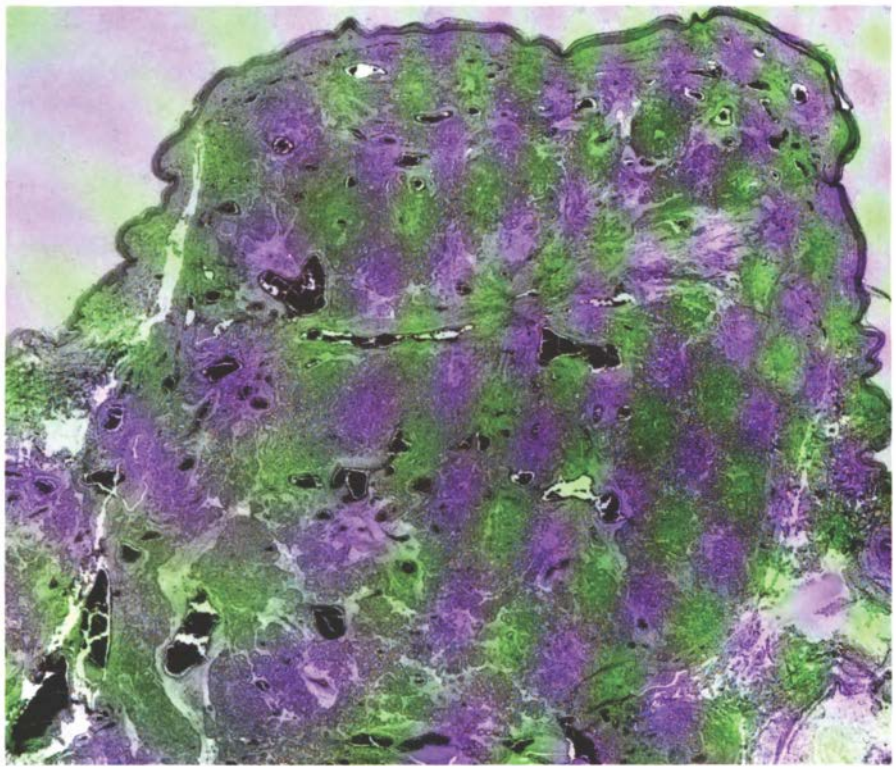


Fig. 33

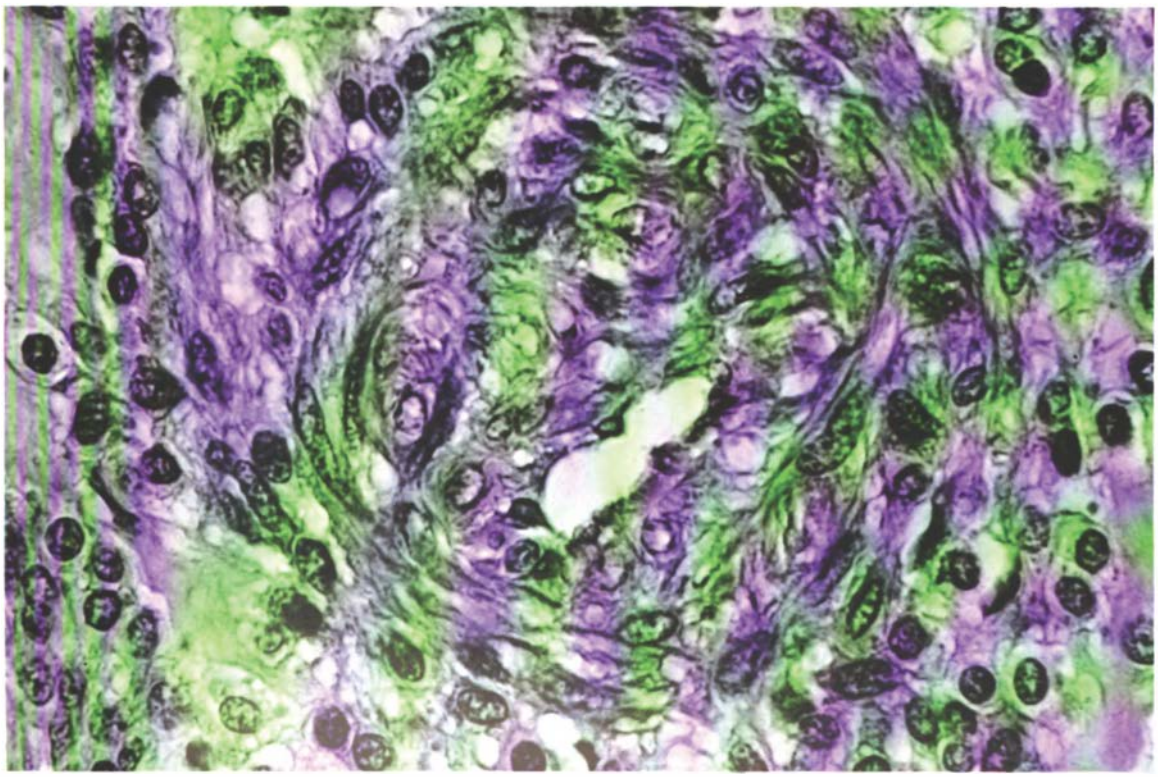


Fig. 34

The hemangiopericytoma does not always assume the organoid appearance of the glomus tumor. Usually the pericytes in rounded or elongated form are packed in tightly around the capillaries, so that there is no intervening space containing nerve fibers. Some hemangiopericytomas approximate the appearance of venous hemangiomas, except that the spindle-shaped cells oriented around vascular lumens have no myofibrils. Others with rounded cells oriented outside the reticulin sheaths of capillaries somewhat resemble glomus tumors, but differ because they are not organoid and grow progressively by infiltration. Between these two extremes, all gradations are found. This suggests the possible relationship of the pericyte to the smooth muscle cell. The tumors grow slowly and painlessly to a larger size than that attained by the glomus tumors. While generally benign, a few have proved malignant and will be dealt with again with the sarcomas.

Capillaries are not always the sole component of a vascular tumor. As pointed out in the sections dealing with lipomas and leiomyomas, a tumor may be made up of a mixture of fat, smooth muscle, and blood vessels, both capillary and venous. Such compound tumors are benign, generally deeply seated in or around voluntary muscles, and may be called benign mesenchymomas (see Benign Mesenchymoma). During development, various malformations of blood vessels can occur, which may only become apparent in adult life. In this way the **cirsoid aneurysm** may develop, consisting of a congeries of arterial vessels collected in one area, generally in the head end of the body; the **venous racemose aneurysm**, or aneurysmal varix, a similar collection of venous structures, may be found in any part of the body. Finally, the formation during development of one or more congenital arteriovenous fistulas may result in or at least be accompanied by a proliferation of capillaries in an extremity or elsewhere, a sort of **diffuse angiomatosis** leading to overdevelopment of an extremity or part and profound nutritional disturbances including gangrene.

All of the above described vascular lesions are benign. It is improbable that any of them give rise to the rare examples of malignant angiomatous tumors that arise de novo. The congenital capillary hemangiomas not infrequently disappear spontaneously. This is not true of the granuloma pyogenicum, hemangioendothelioma, hemangiopericytoma, or other benign vascular tumors.

Lymphangioma*

SYNONYMS AND RELATED TERMS: Cavernous lymphangioma; cystic lymphangioma; hygroma cysticum colli; simple lymphangioma.

Proliferations of lymphatic vessels are far less common than those formed of blood vessels. As a rule they do not form definite tumors but consist of

*Well illustrated in Fascicle 7, "Tumors of the Cardiovascular System."

diffuse proliferations in the tongue, mouth, skin, fingers, or elsewhere in the extremities, the neck, inguinal region, and mesentery. They generally stem from embryonal segregations of lymphatic vessels, which may start to proliferate before birth or at any time after it. In one form, the proliferation may result in the production of gigantic overgrowth of the affected part—tongue, finger, or even an entire extremity. In another form, dilation of the lymphatics may lead to the formation of **lymphatic cysts.** These occur especially in the neck, where the lesion is called **cystic hygroma (hygroma cysticum colli).** They also occur in the mesentery, where such cysts may produce intestinal obstruction. The cystic lymphangiomas of the neck are generally found in young children and tend to extend downward behind the clavicle into either the mediastinum or the axilla or both. Usually there is a single large cyst with proliferated lymphatic vessels about it, but multiple cysts are not unknown. The growth of lymphangiomas is generally self limited. After the initial period of proliferation, growth generally ceases and does not recommence. However, there is no definite rule, and growth may start again after a long period of inactivity. So far as this writer knows, malignant tumors do not arise from lymphangiomas (figs. 35, 36). The cystic lymphangiomas of the neck may reach such a large size as to be disfiguring and to press upon large vessels and embarrass circulation. They present a difficult problem, for their total removal may be hazardous.

Both lymphangiomas and blood vessel tumors may be multiple, and growths composed in part of lymphatic vessels and blood capillaries may be found.

OTHER BENIGN TUMORS

Benign Tumors Composed of Cartilage or Bone

It seems to be well established that the extraskeletal formation of bone can take place about almost any group of mesenchymal cells, provided there can be mobilized at the site the proper concentration of mineral salts, enzymes, a flexible pH, and an adequate blood supply. Whether or not the local cells control this complicated, physiochemical interaction is unknown. Bone sometimes is formed in granulation and scar tissue, and in calcified areas of necrosis or degeneration if they happen to be invaded by granulation tissue, but these processes need never be confused with neoplasms. Tiny balls of trabeculated bone with normal bone marrow are found occasionally in the skin, usually in connection with pigmented moles but sometimes as independent formations. They may even grow to a size sufficient to make them palpable, as has been reported by Hopkins. These may be called **osteoma, osteochondroma,** or **chondroma** depending on composition.

The best known of the tumor-like growths is the so-called **solitary myositis ossificans.** This consists of a formation of bone, or bone and cartilage, between

LYMPHANGIOMA

Figure 35. Lymphangioma (cystic hygroma) of lateral neck of a 13-year-old boy. At the age of 10 years a swelling first appeared in the supraclavicular fossa. After a year and a half, an attempt to excise it failed. Then a large cystic swelling lay beneath the trapezius and lower sternomastoid muscle and extended behind and below the clavicle. The photomicrograph shows multiple and sometimes cystic lymphatic vessels with foci of lymphoid tissue. × 22. A. F. I. P. Acc. No. 218822–35.

Figure 36. Lymphangioma (cystic hygroma). For seven months a 16-year-old girl had a cystic swelling 4.5 × 3 cm. in the right submaxillary region. It was removed from beneath the deep fascia, and there was no recurrence after four years. It consisted of one large cyst about the periphery of which these dilated lymphatic vessels had proliferated. × 226. A. F. I. P. Acc. No. 218822–36.

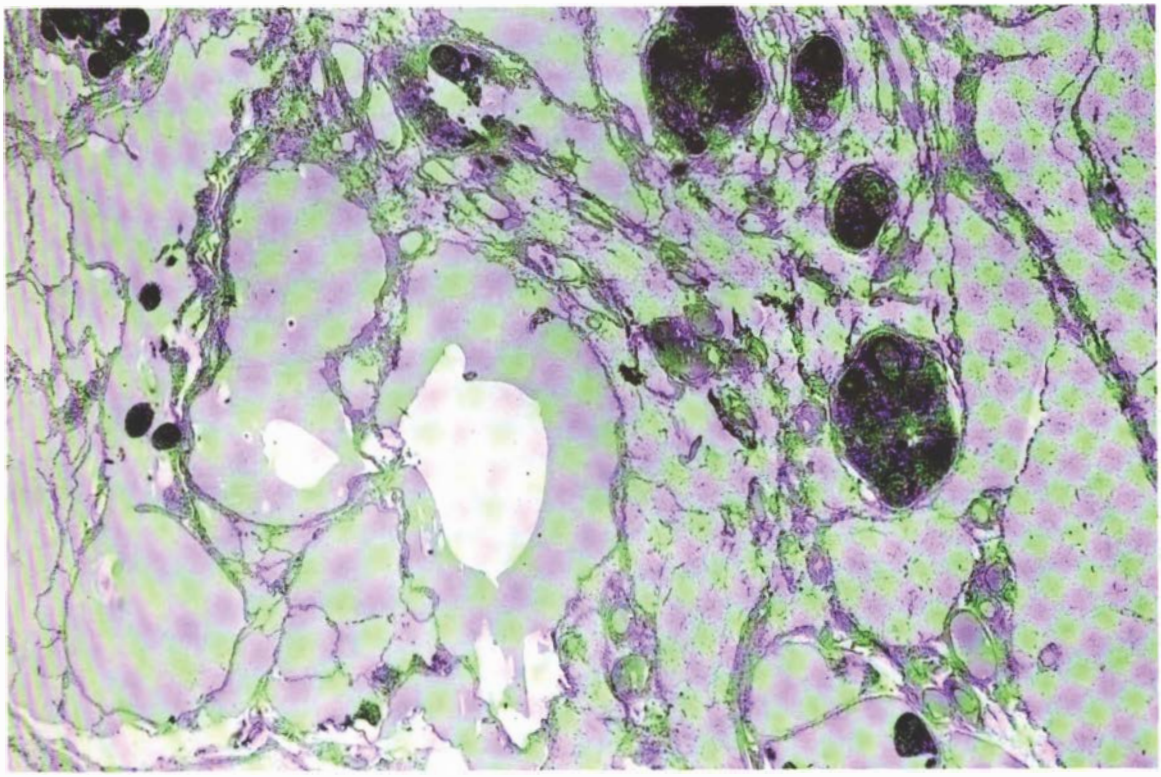


Fig. 35

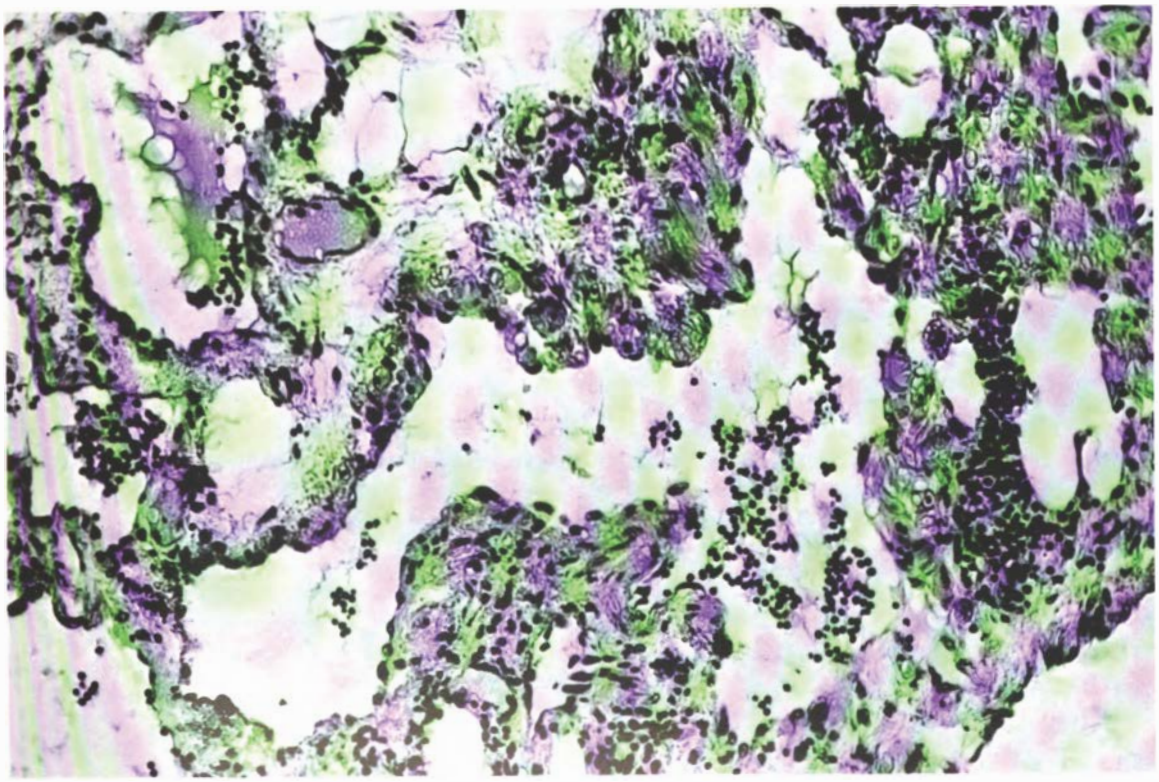


Fig. 36

the separated fibers of voluntary muscle, with the gradual disappearance of the muscle by pressure necrosis. These masses may attain a size of 10 cm. or even more. Some of them are attached to bone, but many are entirely independent formations in the muscle. Less than half the cases have a history of trauma, and it is certain that these latter cases are not due to torn and misplaced periosteum, although it is conceivable that some kind of pathologic change in the muscle precedes their development. Growth is generally self limited, and it is questionable whether or not a true malignant neoplasm has ever developed from one of them (fig. 37). Geschickter and Copeland have described a lesion which can be confused with cases of myositis ossificans attached to bone. They propose the name parosteal osteoma for it; the term is unfortunate, since the tumor is malignant while the name osteoma connotes a benign tumor. Generally this tumor can be distinguished histologically from simple myositis ossificans because there is some degree of atypism in the formation of the bone trabeculae and the fibroblastic stroma and because the bony growth is not interdigitated with the striated muscle fibers. **Progressive myositis ossificans** is a congenital disturbance of the formation of fibrous tissue including bone and osteoid in and adjacent to the muscles. It is much like progressive myositis fibrosa in distribution, except that bone and osteoid are formed in some areas of proliferation. Whether or not it ever progresses to the formation of a true malignant neoplasm remains uncertain, since so few cases have been reported.

Benign Synovioma

SYNONYMS AND RELATED TERMS: Fibroendothelioma of joint; synovialoma; synovioendothelioma.

Very occasionally one or more tumor-like nodules have been found in the capsule of the knee joints. These are made up of a stroma of adult fibrous tissue and many devious, sinuously twisted slits lined by prominent but otherwise normal synovial cells. Whether or not these are simply localized hyperplasias of synovial tissue or true neoplasms is unknown. The synoviomas are morphologically distinct from the so-called villonodular synovitis or giant cell tumor of joints. All that can be said is that they reproduce exactly, but in adult, differentiated form, the structural composition of the synovial sarcoma, and that they are benign (fig. 38).

Mixed Tumor

SYNONYMS AND RELATED TERMS: Adenochondroma; adenomyxochondrosarcoma; chondrocarcinoma; cylindroma; endotheliosarcoma; fibromyxoendothelioma; mixed tumor (salivary gland type); myxofibroepithelioma; myxopleomorphic epithelioma; pleomorphic adenoma; pleomorphic salivary adenoma.

Although they will be dealt with in Fascicle 11, "Tumors of the Salivary Glands," and Fascicle 2, "Tumors of the Skin and Accessory Structures," it seems wise at this juncture to point out that mixed tumors, similar to those

found in the salivary glands, are occasionally encountered in the skin of almost any part of the body. In addition to their epithelial elements, these tumors may have myxoid tissue and cartilage forming part of them. The favorite hypothesis supposes that these tumors arise from sweat glands and that the mesenchymal elements are metaplastic products of the epithelium (fig. 39).

Benign Mesenchymoma

SYNONYMS AND RELATED TERMS: Benign mixed mesodermal tumor; choristoma; hamartoma.

This is a convenient term intended to describe the benign mixed mesodermal tumors. One might use the names choristoma or hamartoma for such growths, but there has been so much mystery and confusion connected with these names that the more restricted terms, "mixed mesodermal tumor" or "mesenchymoma," seem more suitable. Reference has already been made under the sections dealing with the Lipomatoses, Leiomyoma, and Hemangiomatoses to the tumors made up of these three elements in varying proportions. The most common site for them is in subcutaneous tissue or in or around voluntary muscles. The presence of fibrous tissue as one element in a tumor is so frequent that it seems wise not to call a tumor mesenchymoma if it is composed of fibrous tissue and only one other element, such as fat or smooth muscle, but to reserve the term for any tumor made up of two or more mesenchymal elements other than fibrous tissue. It is a term included here among the benign tumors for convenience. The malignant variety is far more important.

Benign Mesothelioma*

The lining cells of the peritoneum, pleura, and pericardium are usually referred to as mesothelial cells; consequently it is quite proper and desirable to call the tumors that are formed from them mesotheliomas. They are extraordinarily versatile cells; they secrete hyaluronic acid, which permits opposed surfaces to glide smoothly one upon the other without friction, and Maximow has shown by tissue culture that they can act as fibroblasts and form connective tissue fibers. When irritated they sometimes swell up, multiply, and form crypts and tubes beneath the surface. It is rare for them to form tumors. When they do, it appears that one variety reproduces the microscopic aspect of irritational tubes and crypts, and another forms peculiar fibrous growths with a unique histologic aspect.

The peritoneal cells covering the male and female genital organs, specifically the uterus, tube, canal of Nuck, epididymis, and cord seem to produce small, firm tumors, **benign mesothelioma of the genital tract,**** composed of multiple tubes lined by swollen and vacuolated cells, which secrete a mucoid

*See Fascicles 23 and 24 (in one volume), "Tumors of the Retroperitoneum, Peritoneum, and Mesentery."

**See section on Adenomatoid Tumors, pp. 127–136, Fascicle 32, "Tumors of the Male Sex Organs."

MYOSITIS OSSIFICANS

Figure 37. The photomicrograph has been made from a biopsy of a mass in the vastus lateralis of an 80-year-old woman. It shows differentiated cartilage and osteoid, which has extended between small groups of muscle fibers. × 226. A. F. I. P. Acc. No. 218822–37.

BENIGN SYNOVIOMA

Figure 38. Benign synovioma of knee joint. A 17-year-old girl had had swelling of the knee joint for 18 months. At operation a tumor occupied the entire suprapatellar pouch. It was markedly cystic. There was no recurrence 30 months after excision. The growth is composed of innumerable cavities lined with hyperplastic synovial cells and a differentiated stroma infiltrated with many inflammatory cells. × 190. A. F. I. P. Acc. No. 218822–39.

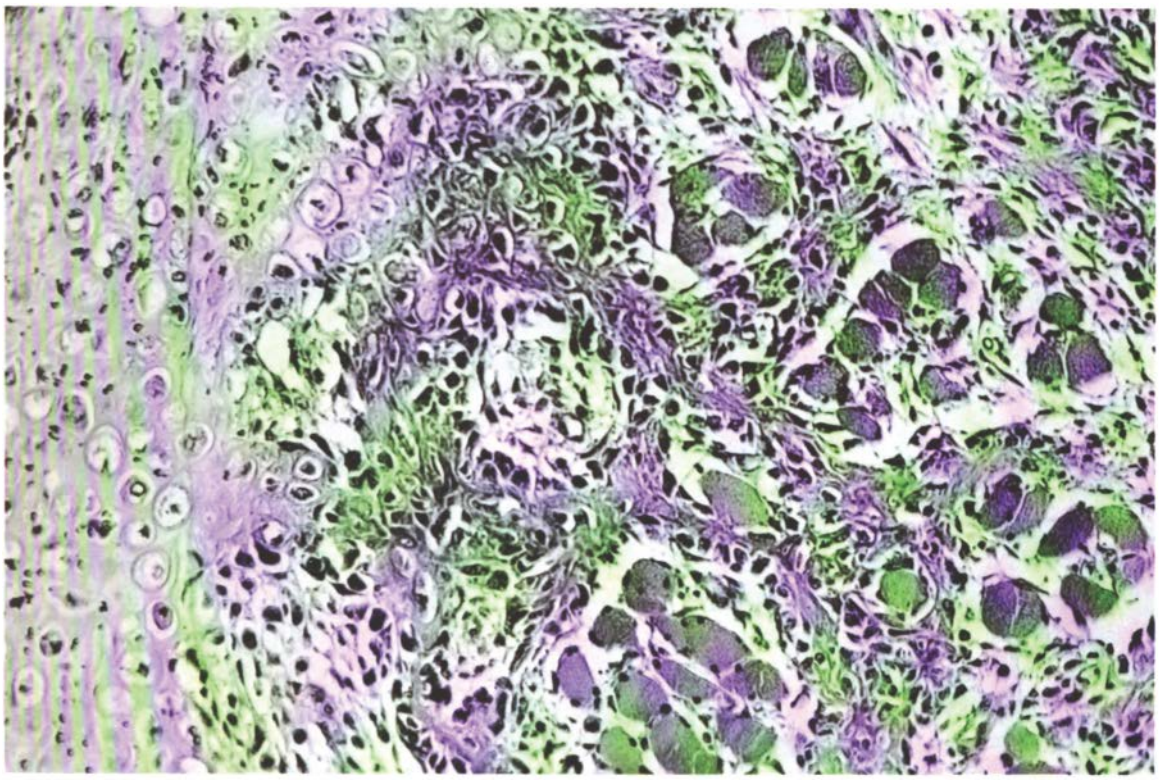


Fig. 37

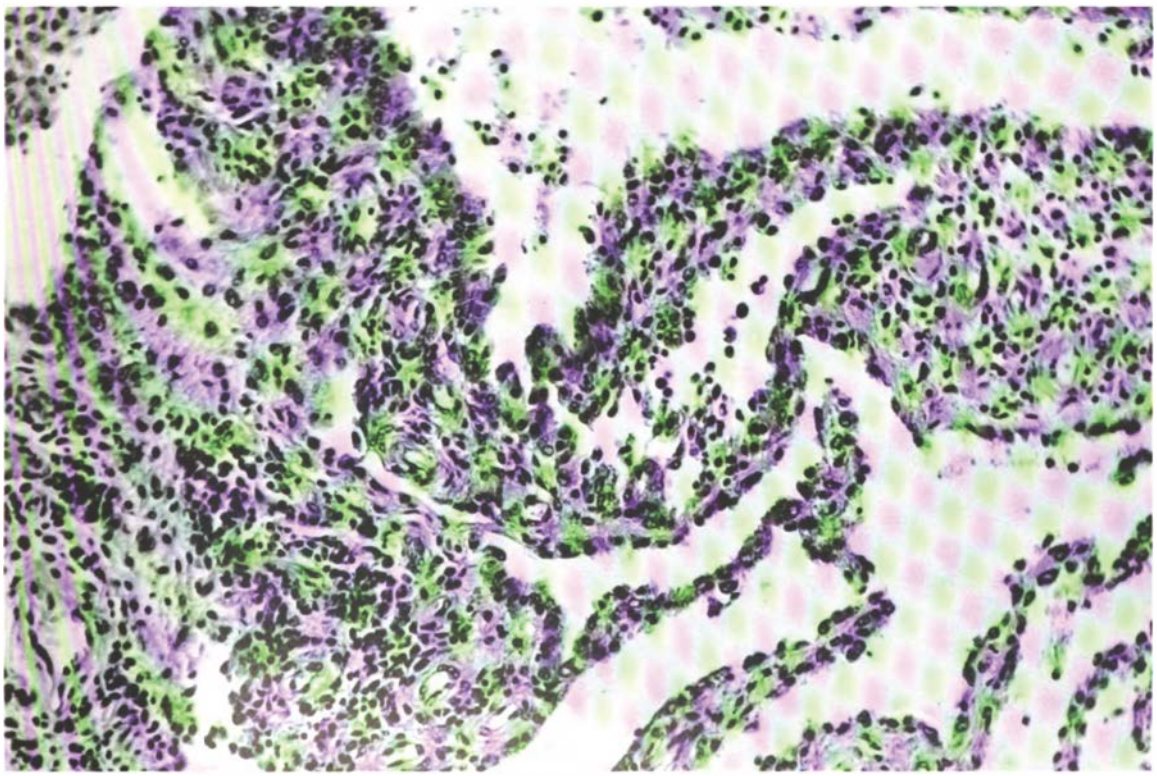


Fig. 38

material and are set in a fibrous stroma that may or may not have an admixture of smooth muscle fibers. Masson, Riopelle, and Simard, and later Evans, independently noted the strong resemblance of these tumor cells to peritoneal mesothelium and proposed to call them benign mesotheliomas. Although other authors, notably Golden and Ash, have hesitated to accept this explanation, the substitutes proposed are vague and unconvincing. Certainly the growths are not lymphangiomas, and to call them adenomatoid is descriptive but ineffectual. This writer is in agreement with the hypothesis that they are mesotheliomas. They generally remain small and are almost always benign (fig. 40).

The vast majority of examples of the **benign solitary fibrous mesothelioma** have been found in the pleura, although the writer found one in the peritoneum. In the pleura these hard tumors grow to a large size, project into the pleural space or an interlobar fissure, and are generally symptomless. They are composed of spindle-shaped cells, collagen and reticulin fibers, and blood vessels which grow without any definite growth pattern so that whereas in one area the cells may be closely placed, immediately adjoining areas may be almost acellular. The blood vessels show the same inconstancy of arrangement. In spite of this, the cells do not appear anaplastic. Such disorderliness and lack of organized pattern sets this tumor apart from all other fibrous growths and makes it relatively easy to recognize. All reported cases of this sort have been solitary and encapsulated. Recently the writer has seen a diffuse fibrous growth thickening the entire visceral and parietal pleural surfaces on one side which exactly simulated the histologic appearance of the solitary tumors. Apparently, therefore, there exists a **diffuse form of benign fibrous mesothelioma.** The reasons for supposing that these fibrous tumors are derived from mesothelial cells are based upon the observation of Murray that the cells of a malignant variant of a solitary mesothelioma grew mesothelial cells when explanted in vitro and upon the observations of Maximow that normal mesothelial cells can behave like fibroblasts in vitro.

Blue Nevus

The characteristics of the blue nevus necessary for its diagnosis are that it is a fibrous growth resembling a skin fibroma that does not touch the epidermis or extend into the papillary layer, contains varying numbers of elongated, strap-shaped, often stellate melanoblasts, and has no ordinary mole cells. It has been assumed that this is a mesodermal melanoblastoma in contradistinction to the ordinary mole that is ectodermal, but Masson has pointed out his belief that the blue nevus is a tumor derived from Schwann cells, which in this instance are capable of acting as melanoblasts; although in the ordinary type of pigmented junctional nevus no melanoblasts are produced by the schwannian component, but all descend from the epidermis. The tumor appears blue because the brown melanin is viewed through a thin film of epidermis and

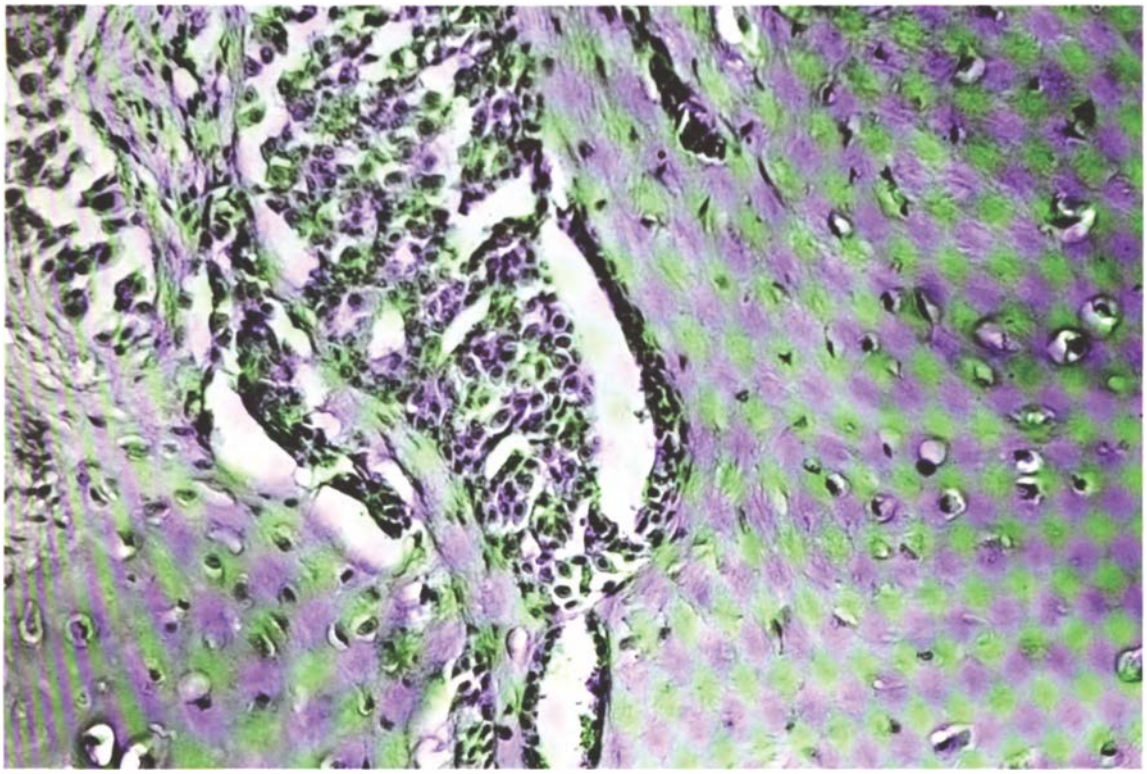


Fig. 39

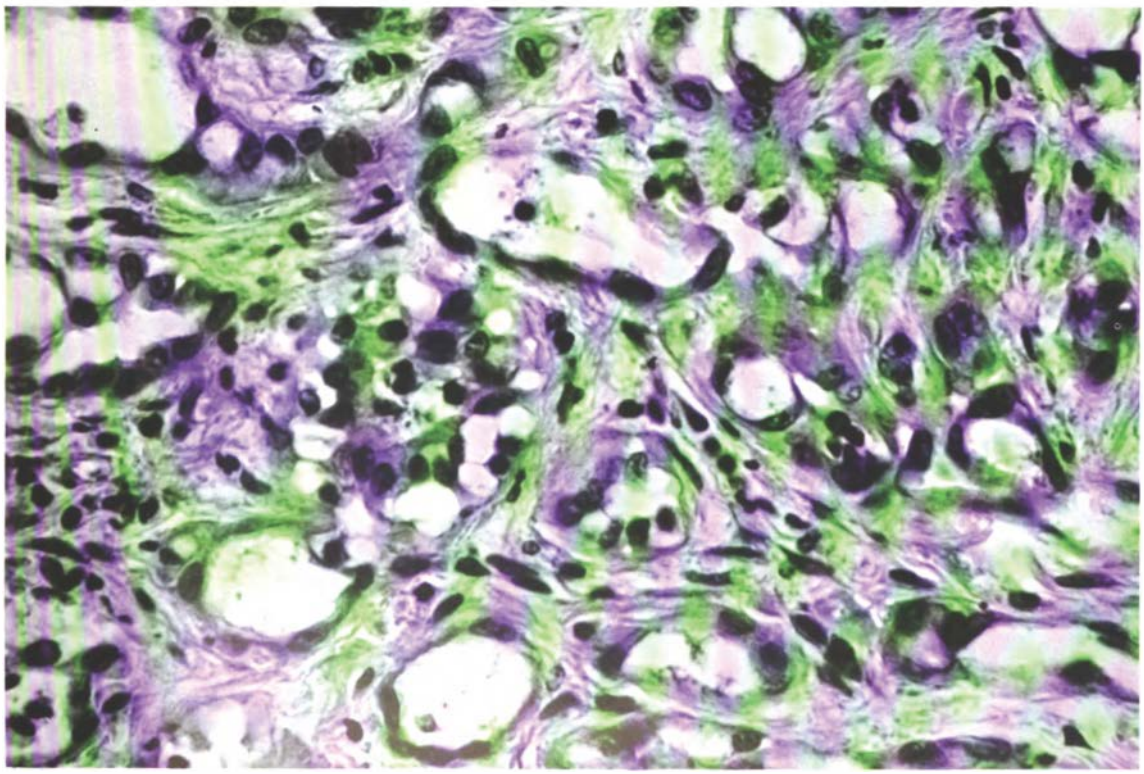


Fig. 40

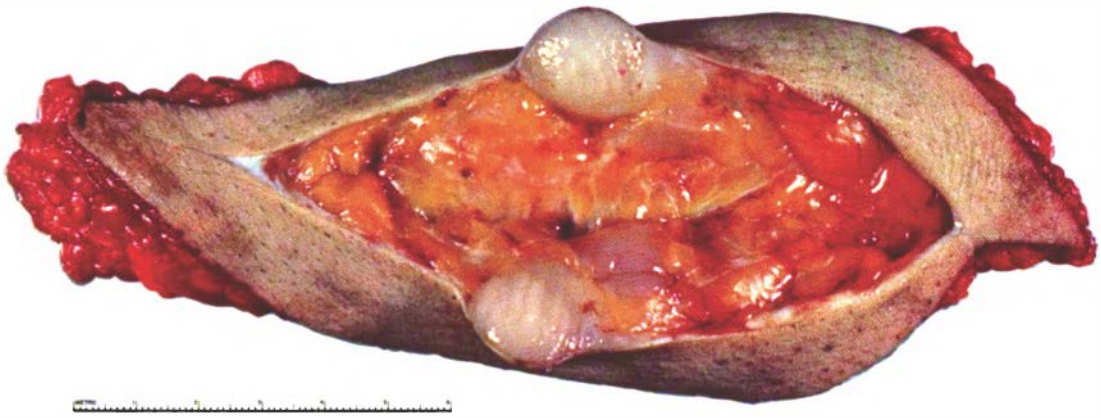
PLATE III

FIBROSARCOMA

A. Fibrosarcoma of abdominal wall extending into the subcutaneous fat. A cutaneous mass had been present in the suprapubic region of this 46-year-old man for 15 years. During the past four months there was rapid increase in size but it did not recur following this wide excision. Histologically the tumor is well differentiated. A. F. I. P. Acc. No. 218822–C13.

MYXOMA

B and C. Myxoma of arm. A 43-year-old man had this 6 × 2.5 cm. soft encapsulated mass of one year's duration removed from the arm close to the ulnar nerve. Ten months before, after biopsy, a lymphosarcoma of the proximal half of the stomach was treated by radiotherapy. There was no recurrence of either tumor five years after the arm operation. A. F. I. P. Acc. Nos. 218822–C17 and C18.



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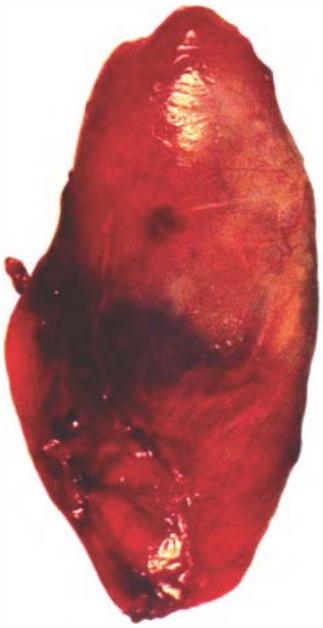

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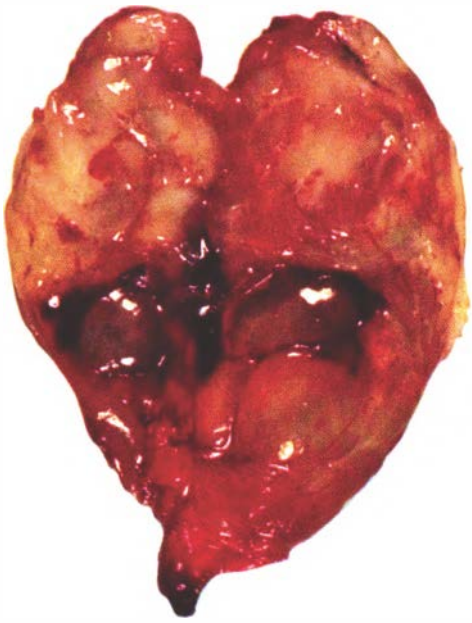


C

PLATE III

Fig. 43

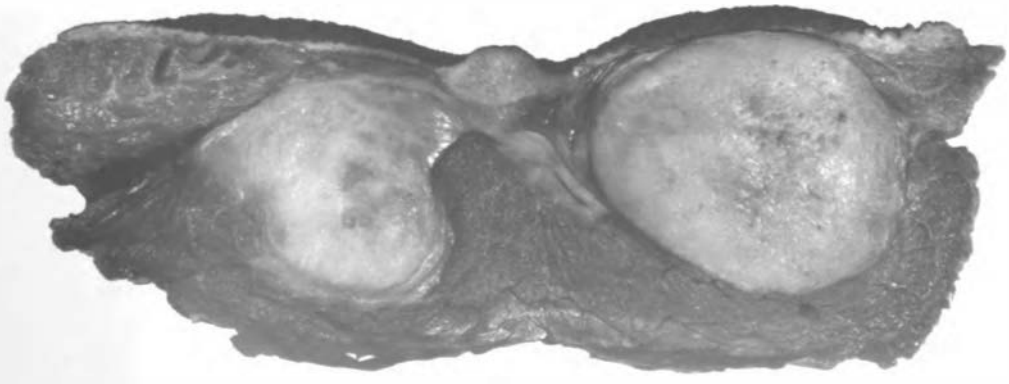


Fig. 44

FIBROSARCOMA

(Figures 45 and 46 are from the same case)

Figure 45. Fibrosarcoma in a 37-year-old woman. During the past 20 years there had been five excisions and a little radiotherapy of a recurring tumor of the calf. Eventually there was a mid-thigh amputation and dissection of metastatic inguinal nodes. She died a year later with pericardial effusion due to myocardial metastases. The tumor still has a relatively adult appearance of its fibroblasts with many intercellular connective tissue fibers but a rather high mitotic rate, which is indicative of malignancy. × 511. A. F. I. P. Acc. No. 218822–45.

Figure 46. Metastasis in inguinal lymph node from the case shown in figure 45. A. F. I. P. Acc. No. 218822–46.

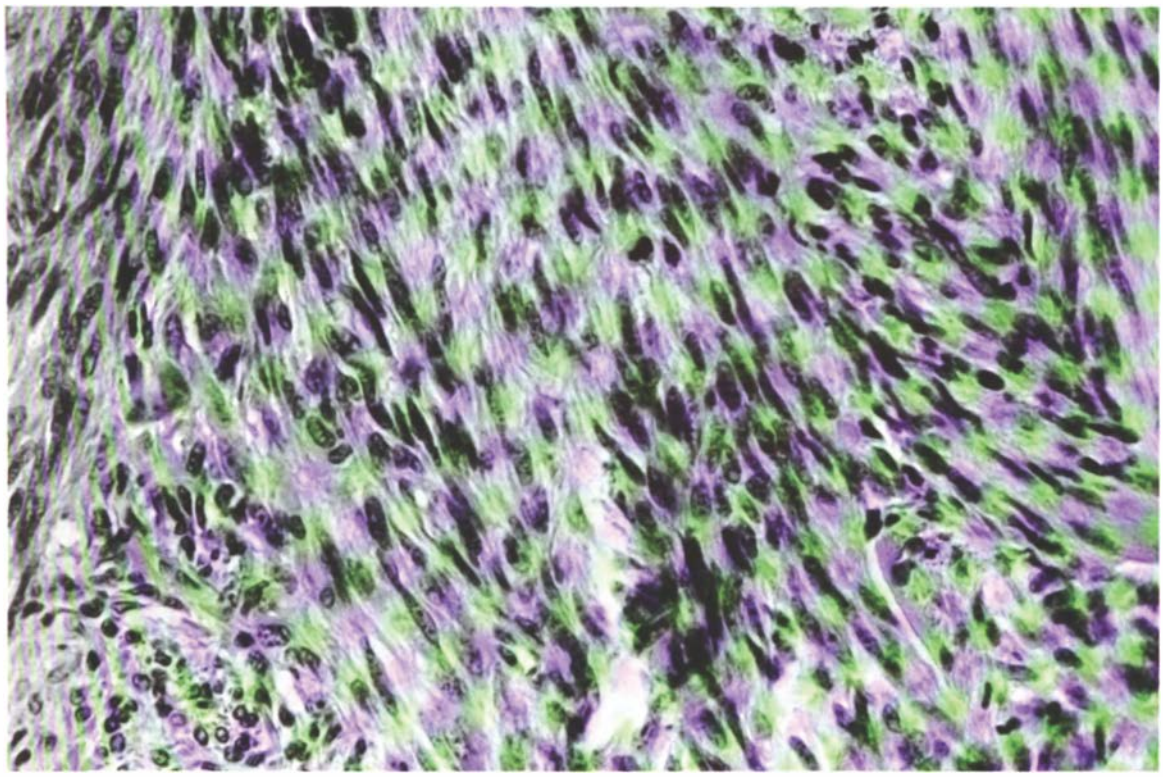


Fig. 45

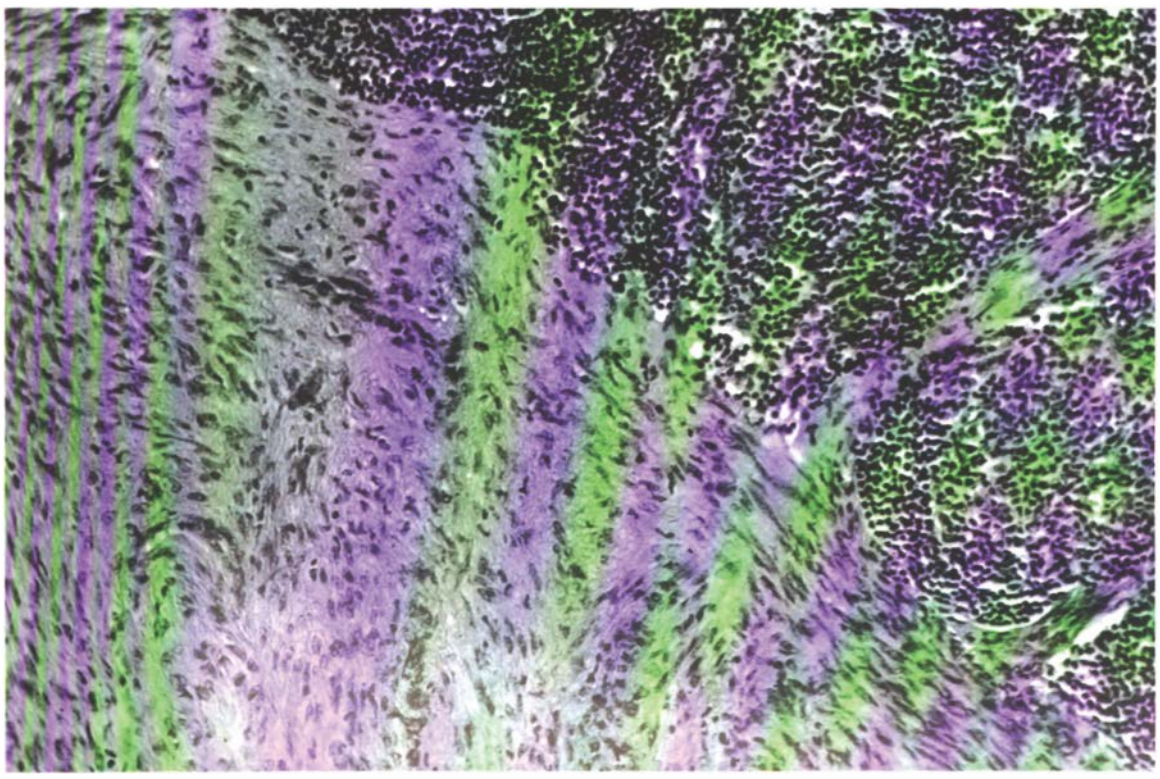


Fig. 46

FIBROSARCOMA

Figure 47. Explant in vitro from a differentiated fibrosarcoma of the chest wall. The pattern of interlacing bands characterizing the fibrosarcoma is retained to some degree in the outgrowth of characteristic fibroblastic cells. Eighteen days in vitro. Helly's fluid; Delafield's hematoxylin. A. F. I. P. Acc. No. 218822–47.

MYXOMA

Figure 48. This photomicrograph is characteristic of a myxoma. Stellate cells are surrounded by mucoid hyaluronic acid, which stains red or pink with mucicarmine. The cells and hyaluronic acid are enclosed within a delicate meshwork of reticulin fibers. The quantity and density of the connective tissue vary not only in different tumors but in different parts of the same tumor. A. F. I. P. Acc. No. 218822–48.

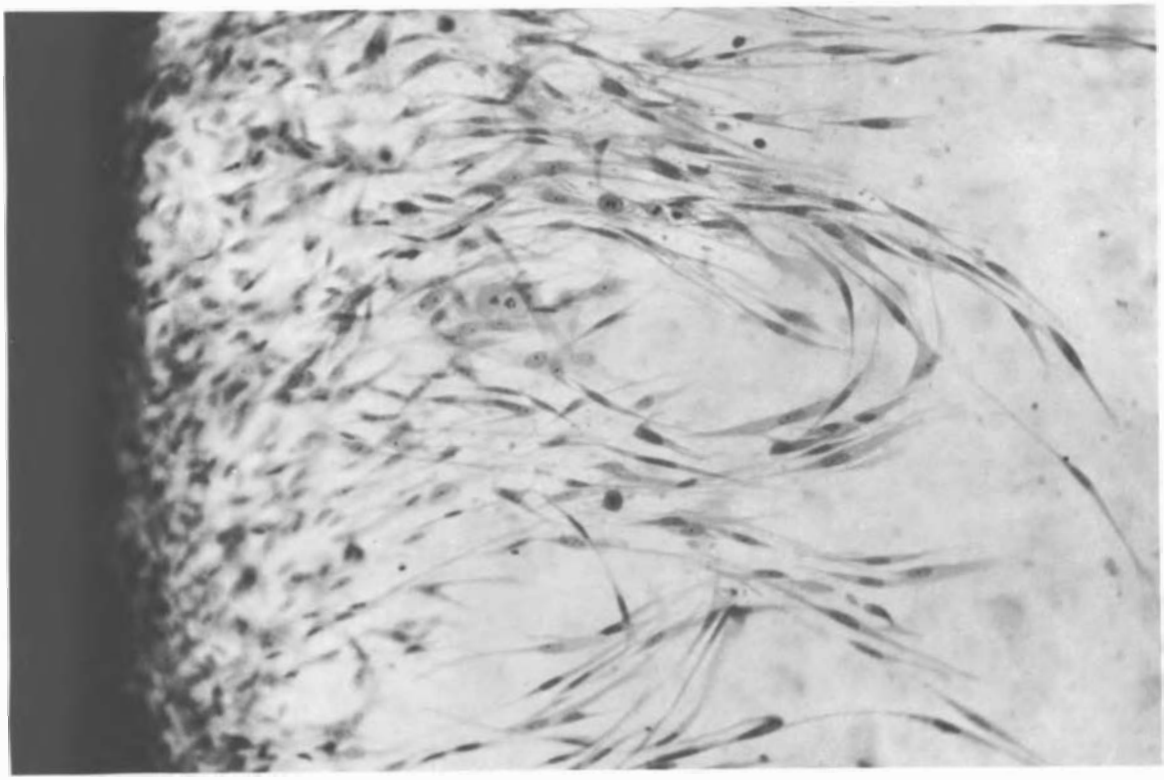


Fig. 47

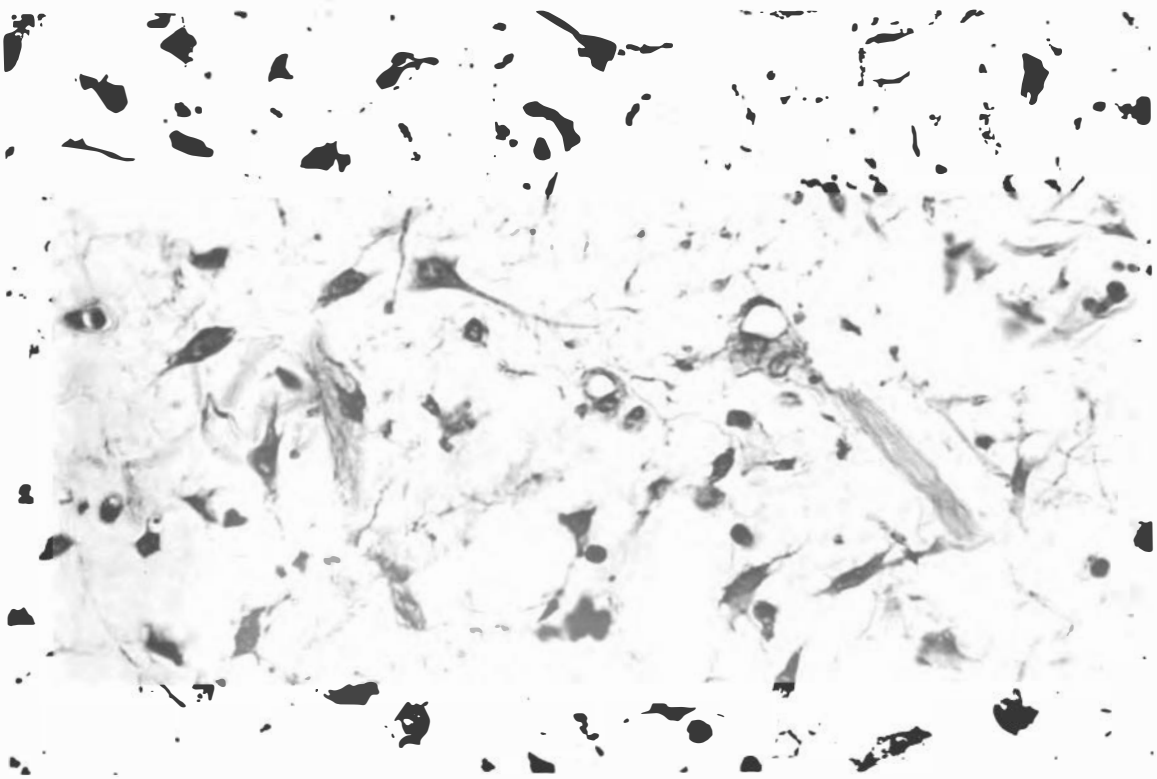


Fig. 48

LIPOSARCOMA

Figure 49. Differentiated liposarcoma of thigh in a 46-year-old woman. The tumor is composed in part of adult fat cells, and intermingled among them are lipoblasts which are immature, being spindle-shaped or forming small signet rings set in a slimy mucoid stroma. × 530. A. F. I. P. Acc. No. 218822–49.

Figure 50.* Liposarcoma of thigh in a 55-year-old woman who died 42 months after excision of the tumor. The tumor had recurred following excision and had resisted radiotherapy. It shows mixed lipoblastic activity: (A) the growth resembles myxoid, vascular, embryonal fat of the common type, while (B) the lipoblasts are rounded and closely packed together imitating the appearance of brown fat. A. F. I. P. Acc. No. 218822–50.

*Figures 49 and 50 are figures 7 and 11 from Stout, A. P. Liposarcoma, the malignant tumor of lipoblasts. Ann. Surg., 119: 86–107, 1944.

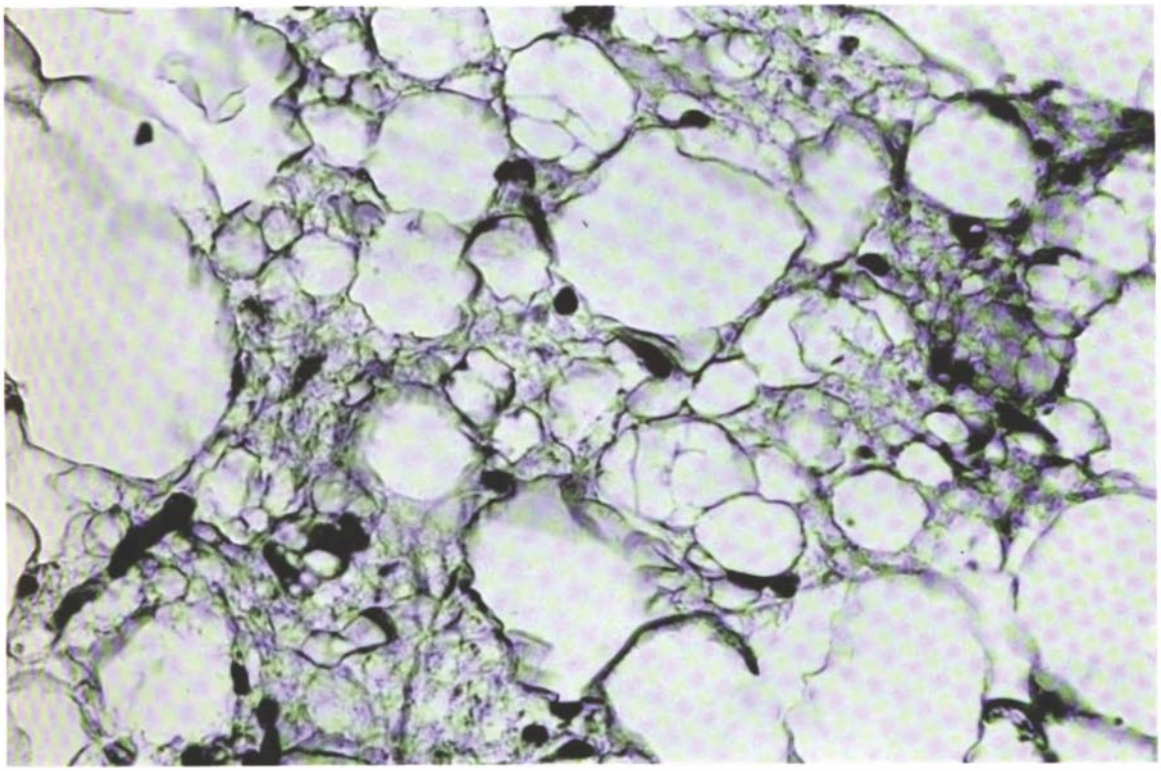
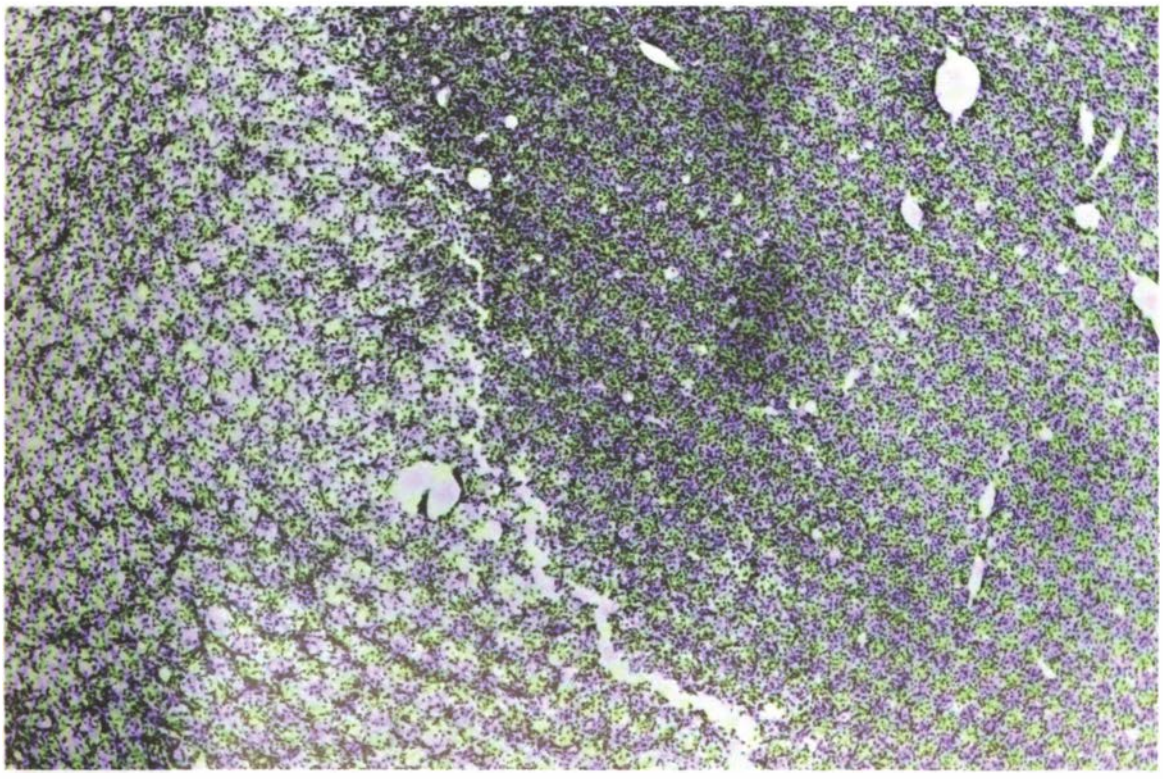


Fig. 49



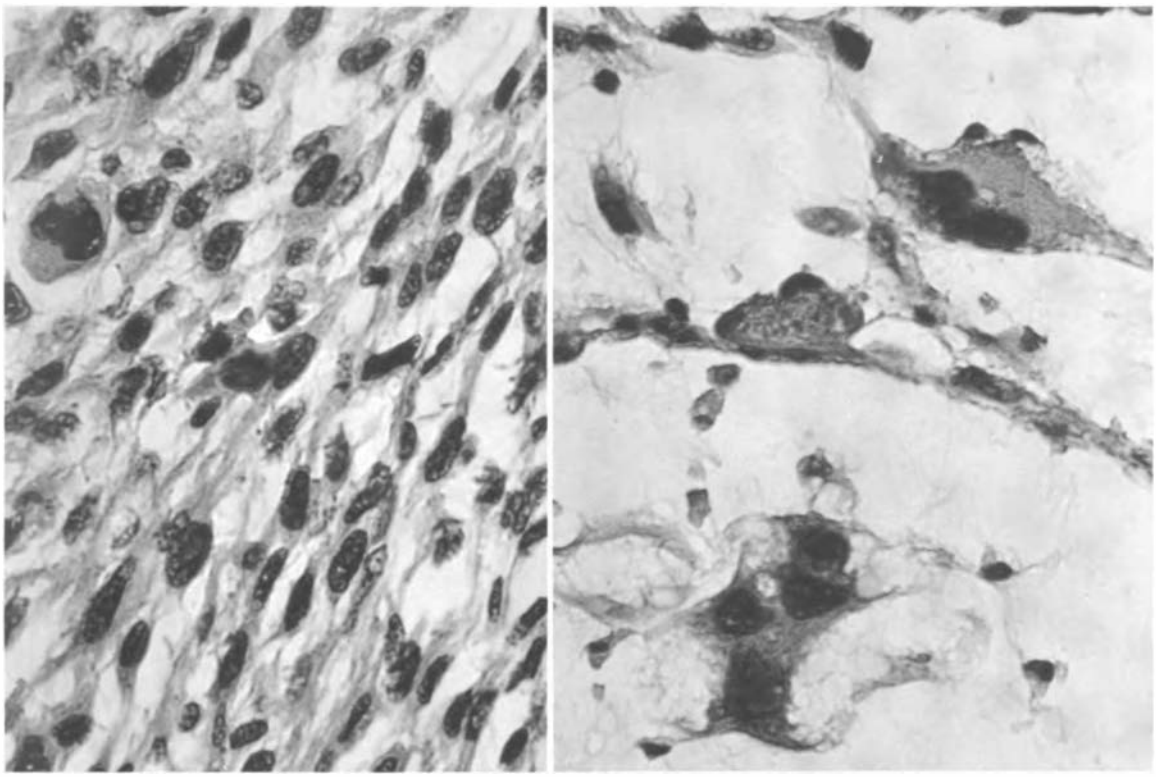
A B

Fig. 50

Figure 51.* A large tumor from the axilla of a 55-year-old man. The composite picture shows lipoblasts from different parts of the same tumor. A: Here they form bundles of spindle-shaped cells of varying sizes, which might be mistaken for myoblasts. B: The bizarre giant cells with foamy cytoplasm betray the true nature of the neoplasm. × 530. ("B" is also in figure 2 from Stout, A. P. Sarcomas of the soft parts. J. Missouri M. A. 44: 329–334, 1947.) A. F. I. P. Acc. No. 218822–51.

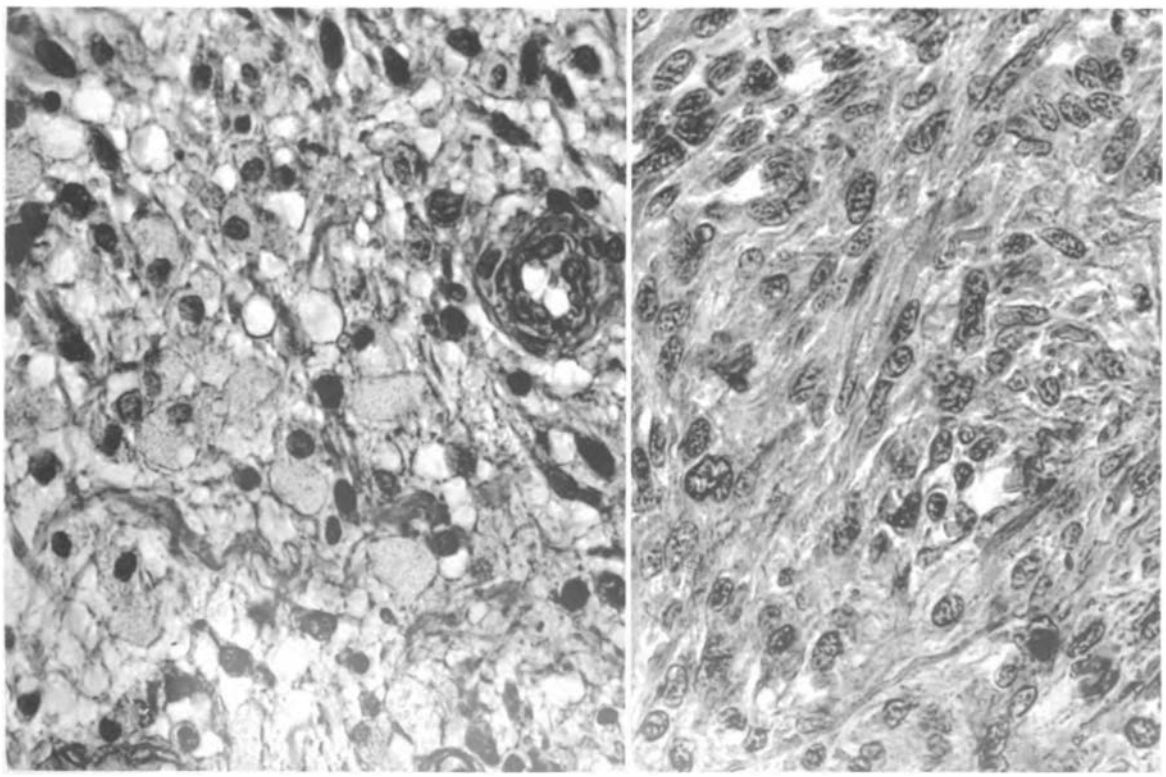
Figure 52.* Large tumor in the thigh of a 32-year-old man. It recurred after excision and resisted radiotherapy: the patient died with lung metastases 67 months after the first excision. This is a complex tumor imitating the appearance of a fibrosarcoma (B) but showing rounded and spindle-shaped, foamy lipoblasts (A). × 530. A. F. I. P. Acc. No. 218822–52.

*Figures 51 and 52 are figures 9 and 14 from Stout, A. P. Liposarcoma, the malignant tumor of lipoblasts. Ann. Surg., 119: 86–107, 1944.



A B

Fig. 51



A B

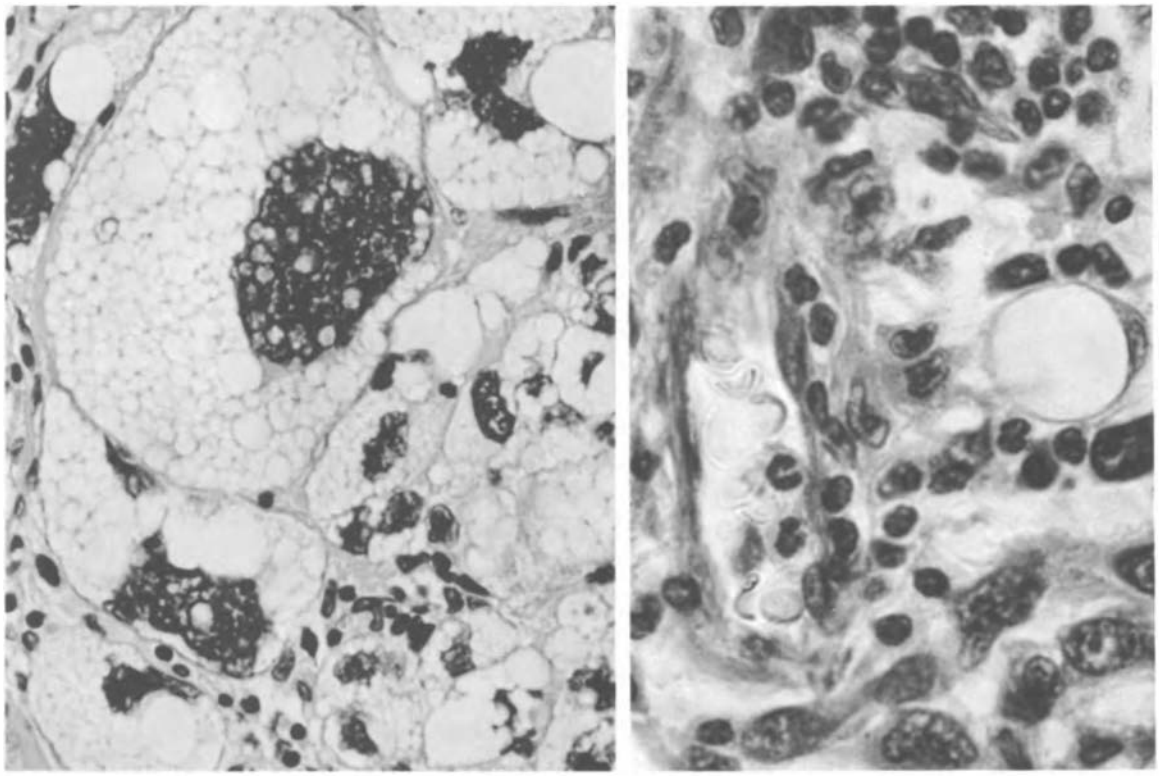
Fig. 52

LIPOSARCOMA

Figure 53. Detail picture showing lipoblasts from two different liposarcomas. A: This shows huge lipoblasts with the vacuoles in the cytoplasm producing indentations in the nuclei. × 540. B:* There are many undifferentiated anaplastic lipoblasts, but the signet ring cell betrays the true nature of the neoplasm. × 630. ("A" is figure 13 from Stout, A. P. Liposarcoma, the malignant tumor of lipoblasts. Ann. Surg., 119: 86–107, 1944.) A. F. I. P. Acc. No. 218822–53.

Figure 54.* Explant from a metastasis in the upper arm of a tumor of the elbow region. (See figure 53–B.) Embryonic lipoblasts of characteristic aspect. Seven days in vitro. Zenker's fluid; fuchsin-ponceau-aniline blue. A. F. I. P. Acc. No. 218822–54.

*Figures 53–B and 54 are figures 3 and 5 from Murray, M. R., and Stout, A. P. Characteristics of a liposarcoma grown in vitro. Am. J. Path., 19: 751–763, 1943.



A B

Fig. 53

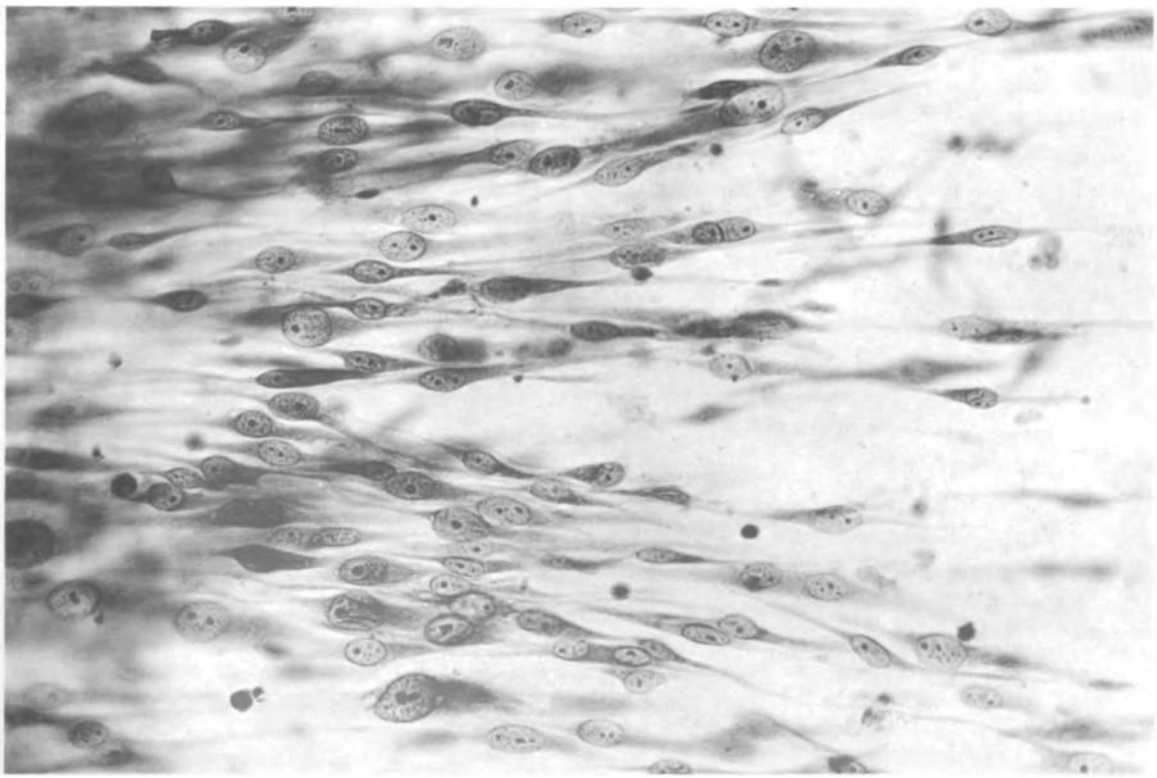


Fig. 54

to be cautious in making a diagnosis of metastatic tumor when multiple tumors appear in unusual sites.

Since only small superficial tumors 4 cm. or less in diameter have proved curable by radiotherapy, excision or amputation is the treatment generally selected. To be successful it must pass several centimeters beyond the palpable tumor on all of its aspects, deep as well as superficial.

MALIGNANT TUMORS OF MUSCLE

Leiomyosarcoma

SYNONYMS AND RELATED TERMS: Malignant leiomyoma; metastasizing leiomyoma; myosarcoma.

Malignant tumors of smooth muscle have been infrequently reported except in the uterus, broad ligament, and gastrointestinal tract. When the writer published a study of sarcomas of the soft tissues in 1946, 13 cases of leiomyosarcoma were included. A check of the files of the Surgical Pathology Laboratory two years later showed a total of 25 cases, 16 of which came from the Presbyterian Hospital. These were divided as follows: retroperitoneum 15, omentum 1, broad ligament 1, orbit 1, abdominal wall 1, gluteal region 1, thigh 1, leg 2, arm 2. Sixteen of these were females and the mean age was 50.9 years, with an age spread from 24 to 79 years.

GROSS. In the retroperitoneal area, these tumors generally grow to a large size and form nodular, firm, brownish yellow masses with areas of necrosis or hemorrhage, or both, reaching a diameter of more than 20 cm., so that weights of more than a kilogram are not uncommon. They grow at varying rates of speed, but are almost invariably fatal in the retroperitoneum because of wide extension, with involvement of neighboring organs and a high metastatic rate to the liver, peritoneum, and lungs. In the extremities and torso, leiomyosarcomas are rare, as evidenced by a total of only seven cases in the Columbia University collection. Only one of these cases involved the skin (of the arm); the rest were subcutaneous or deeper. Although usually quite circumscribed so that complete excision has been accomplished, usually without local recurrence, blood-borne metastases to the lungs and elsewhere are known to have occurred in four of the cases from two to five years after excision. Of the other three, one (in the skin of the arm) was not followed; and the cases involving the thigh and the leg were free from signs of tumor nine years respectively after excision and after postoperative roentgen therapy.

MICROSCOPIC. Leiomyosarcoma is composed of long, spindle- or strap-shaped cells accompanied by some straight reticulin fibers which are arranged in interlacing bundles. While in most tumors the cells and nuclei are somewhat larger than simple leiomyocytes, and do not vary much in relative size, occasionally giant forms are found with a single nucleus or multiple bizarre nuclei. The cells usually show some intracytoplasmic myofibrils, although this is not always

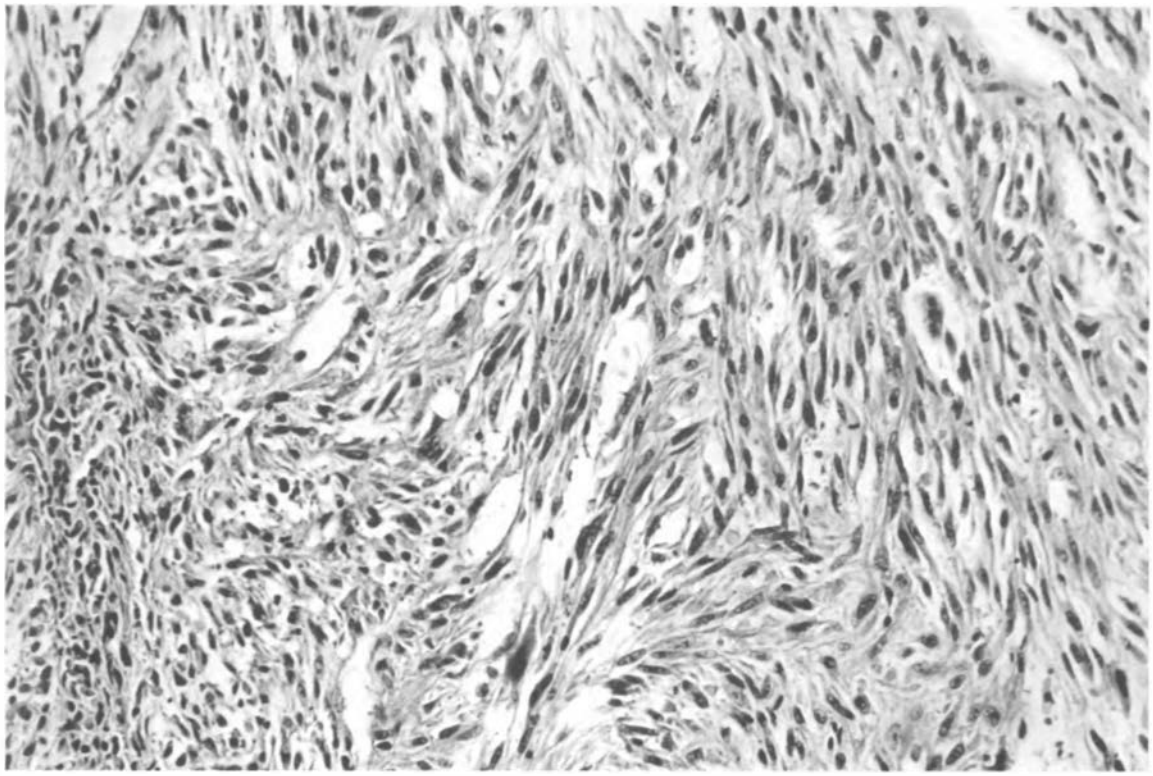


Fig. 55

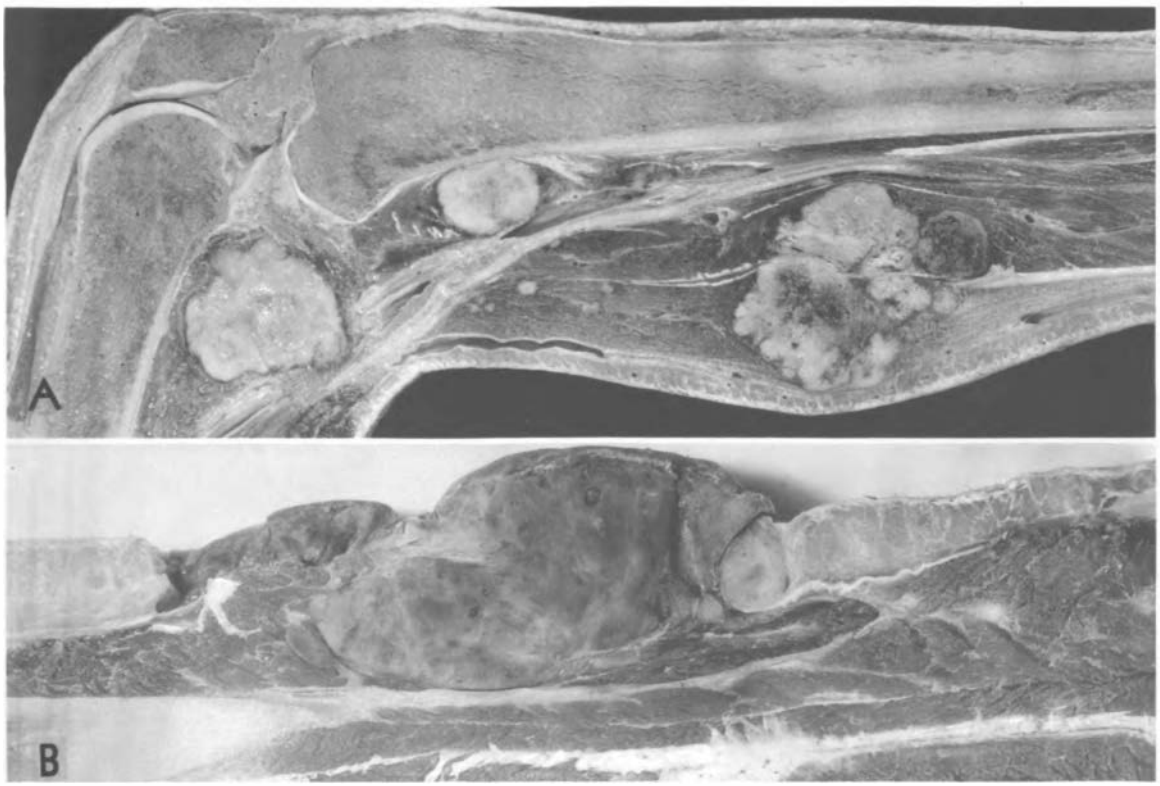
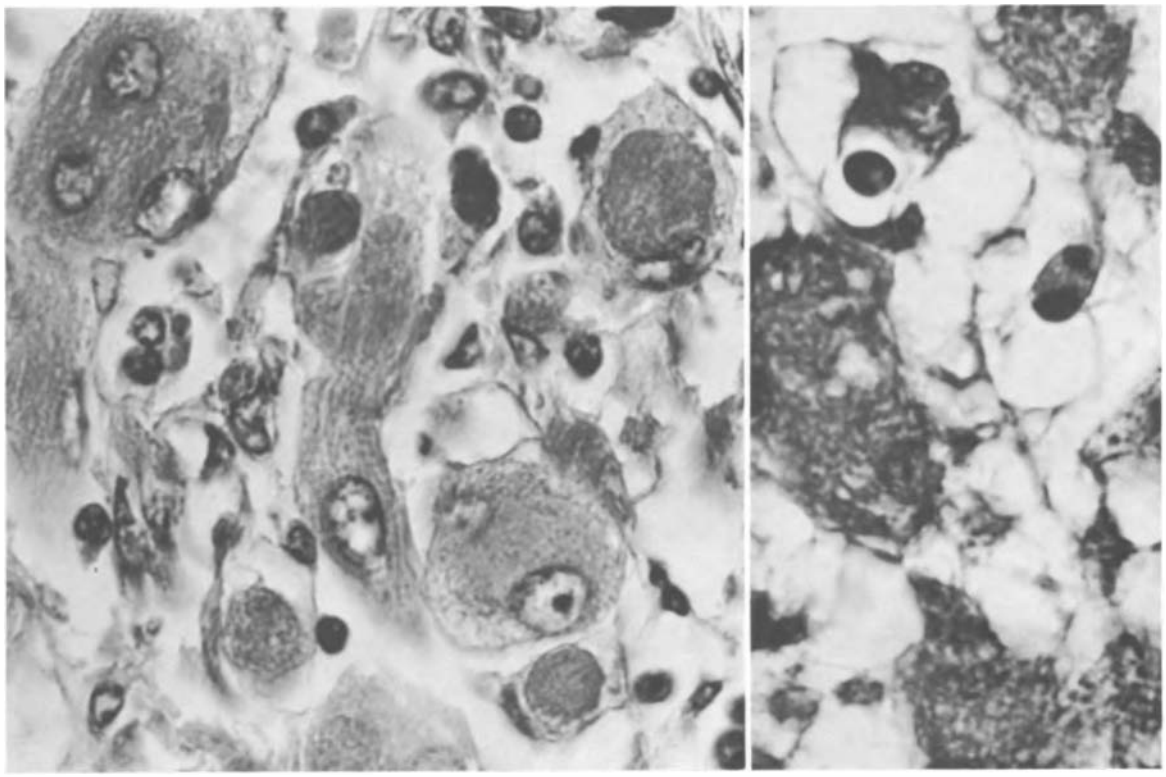


Fig. 56

RHABDOMYOSARCOMA

Figure 57. Rhabdomyoblasts from two partly differentiated malignant tumors show cross striations and vacuoles which presumably had been filled with glycogen. × 1240. A. F. I. P. Acc. No. 218822–57.

Figure 58. Rhabdomyoblasts from two different malignant tumors show variations in shape and size. The high magnification is necessary to demonstrate indistinct cross striations. × 1240. (Figures 11 and 13 from Stout, A. P. Rhabdomyosarcoma of the skeletal muscles. Ann. Surg., 123: 447–472, 1946.) A. F. I. P. Acc. No. 218822–58.



A B

Fig. 57

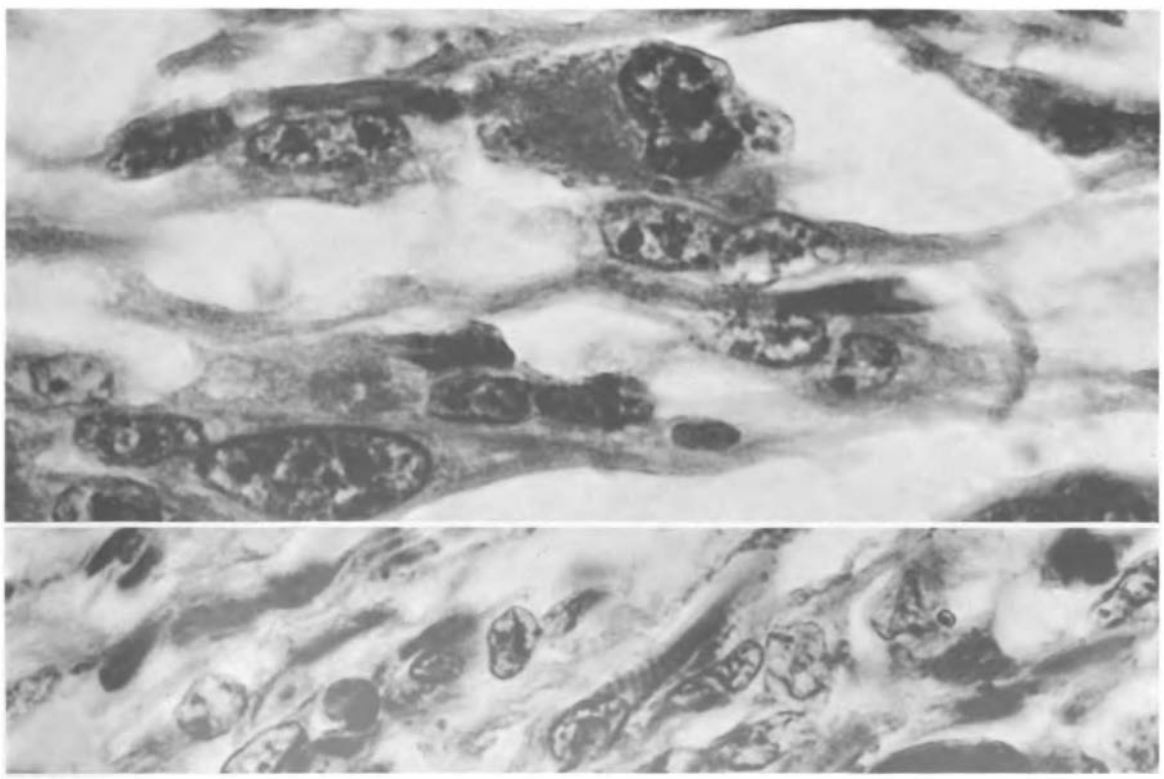


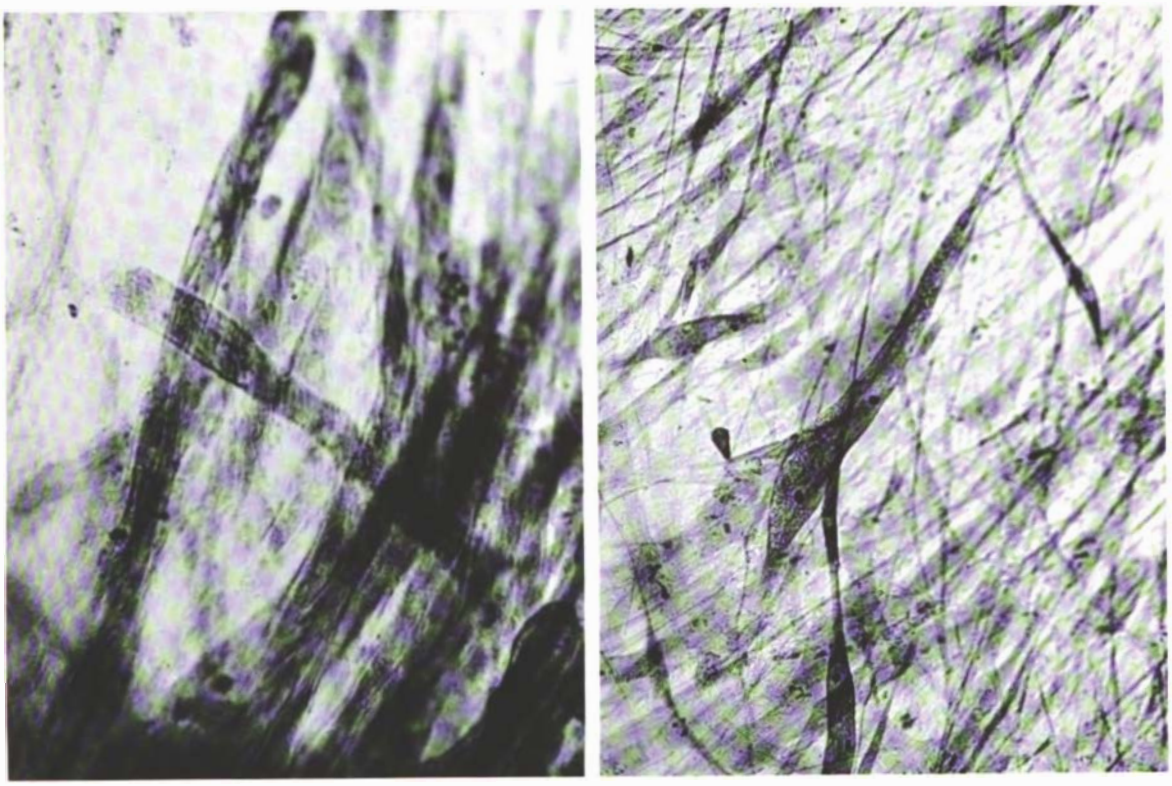
Fig. 58

RHABDOMYOSARCOMA

Figure 59. Explant in vitro from a malignant tumor of the gastrocnemius muscle. A: The outgrowth approximates the appearance of normal striated muscle ribbons. Nine days in vitro. B: These ribbons are bizarre with vesicular nuclei and high nucleocytoplasmic ratio. Forty-seven days in vitro. Zenker's fluid. Phosphotungstic acid hematoxylin. A. F. I. P. Acc. No. 218822–59.

MALIGNANT GRANULAR CELL MYOBLASTOMA

Figure 60. Malignant granular cell myoblastoma, involving the urinary bladder of a 31-year-old man, causing painless hematuria for 11 days with frequency every hour. The tumor filled the right iliac fossa and merged with the wall of the bladder. It recurred following excision and metastasized widely; death followed 17 months after the first operation. The cells have the characteristic, voluminous cytoplasm filled with acidophilic granules. The nuclei appear relatively somewhat larger than the small nuclei of benign tumors, and they have somewhat more prominent nucleoli. × 600. (Case reported by Ravich, A., Stout, A. P., and Ravich, R. A. Malignant granular cell myoblastoma involving the urinary bladder. Ann. Surg., 121: 361–372, 1945.) A. F. I. P. Acc. No. 218822–60.



A B

Fig. 59

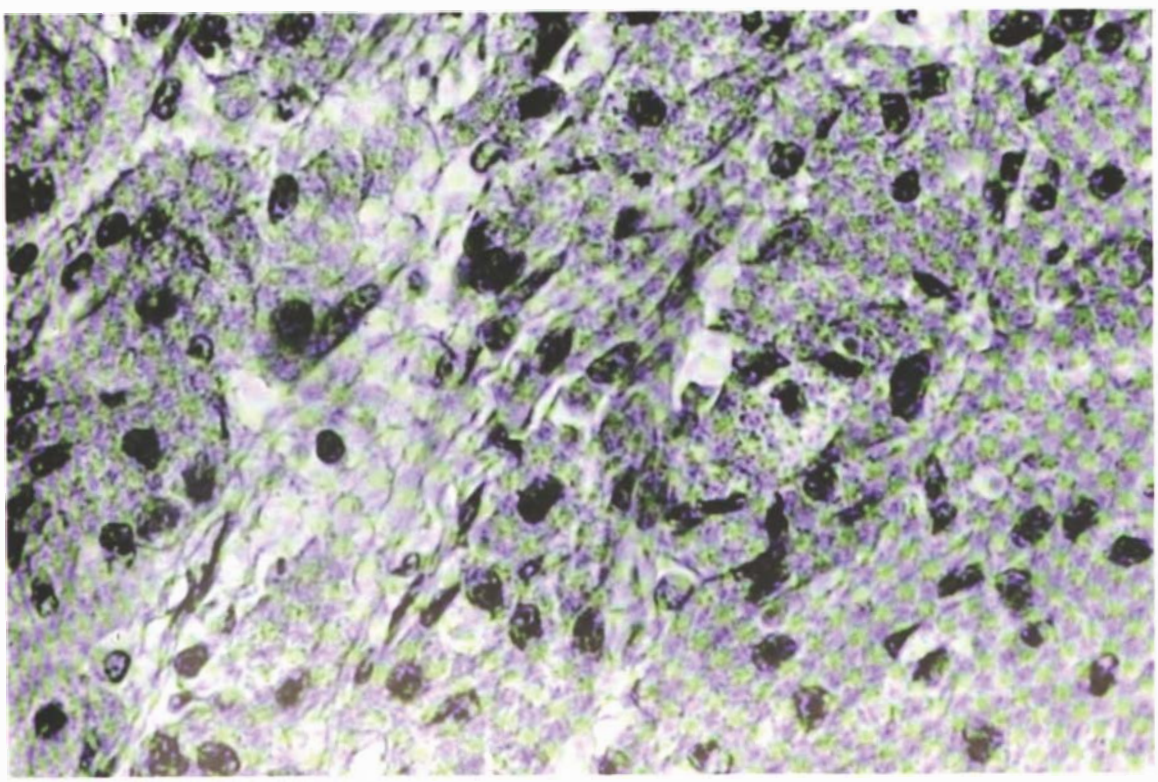


Fig. 60

The question of whether or not any of the better differentiated tumors composed of rhabdomyoblasts in skeletal muscles can be considered as benign growths similar to those found in heart muscle is undecided. Since the latter are not infrequently associated with tuberous sclerosis, kidney tumors, and cysts, they have been regarded as congenital malformations. When they are found in skeletal muscles, they may grow slowly without metastasis, but they infiltrate and so may be difficult to eradicate. It seems safer, therefore, to classify all striated muscle tumors of the soft tissues as rhabdomyosarcomas. Too few cases have been studied to permit any definite statement about the best form of treatment, or about the efficacy of radiotherapy as an adjuvant or replacement for surgery. One can only indicate that the ideal to be sought is wide removal or destruction of the tumor well outside of its palpable limits at as early a time as possible in the course of the disease.

Malignant Granular Cell Myoblastoma*

SYNONYMS AND RELATED TERMS: Malignant myoblastoma; polymorphous sarcoma; malignant nonchromaffin paraganglioma; alveolar soft part sarcoma; granular cell myoblastoma with organoid structure.

When Abrikossoff published his second paper amplifying the description of the tumor which he called myoblastic myoma, he recorded four different varieties: (1) the typical form made up of round, egg-shaped, or elongated "myoblasts" from 20 to 25 microns long with granules but without longitudinal or cross striations; (2) a variation of the first type in which some cells show longitudinal or cross striations; (3) a hypertrophic form with cells from 40 to 160 microns and sometimes multinucleated. These three groups are all composed of granular cells, and according to him all are benign tumors; (4) a malignant form in which the myoblasts are not granular but assume atypical aspects and vary in size, so that the tumor resembles a polymorphous sarcoma. He had had no personal experience with this group but cited the case of von Meyenburg as an example of it. The addition of this fourth group was very unfortunate, because almost certainly it is composed of rhabdomyosarcomas, while the first three groups composed of granular cells are of uncertain origin, and their outstanding characteristic is the presence of acidophilic granules in the cytoplasm.

The malignant varieties of the granular cell tumors assume two different forms. In the less common one the morphology of the tumor closely resembles the benign type, but the cells may have somewhat larger nuclei (fig. 60). The other and somewhat more common variety is quite different. The larger cells are gathered together in masses or balls outlined by delicate fibrous septa in which capillaries course. The cells have more hyperchromatic nuclei, the

*See also Alveolar Soft Part Sarcoma in Fascicles 23 and 24 (in one volume), "Tumors of the Retroperitoneum, Peritoneum, and Mesentery."

cytoplasm while granular may be somewhat vacuolated, and some cells may contain lipoid (fig. 21). The tumor thus is strikingly organoid in appearance and only resembles the benign forms because its cells are granular. It is small wonder that many authors (Smetana and Scott; Christopherson, Foote, and Stewart) refuse to accept this tumor as a relative of the benign granular cell myoblastoma. Whatever one believes about its cellular origin, every one agrees it is a malignant neoplasm which often metastasizes. Most of these tumors have been found in the striated muscles especially of the extremities.

ANGIOSARCOMATOSES

In comparison with the benign tumors, the number of malignant ones is minute. In their growth they reproduce features that characterize the benign tumors. In all of them, capillary tubes are formed, but the cells that play a dominant role are not always the same; in some it is the endothelial cells, and these are best indicated by the name "malignant hemangioendothelioma." In a second smaller group it appears to be the pericytes—hence the name "malignant hemangiopericytoma." A complex vascular growth consisting of capillaries and fibrosarcoma-like cells in symbiosis characterizes Kaposi's disease. It is uncertain whether or not this is a true neoplastic process; nevertheless, it seems impossible to avoid reference to it in any consideration of malignant vascular tumors. It is possible that the smooth muscle of veins and arteries may give rise to leiomyosarcoma, since the smooth muscle of veins can produce benign leiomyomas; but proof of this is exceedingly difficult to obtain, for when such a tumor is found attached to a large vessel, there is no sure way of proving whether it sprang from or invaded it. Finally, rare malignant tumors featuring lymphatic endothelioblasts and called lymphangiosarcomas have been described.

Malignant Hemangioendothelioma

SYNONYMS AND RELATED TERMS: Angiofibrosarcoma; hemangioblastoma; hemangioendotheliosarcoma; hemangioendotheliosarcoma.

In 1943 when the writer published a study of this tumor type, he was able to assemble 18 cases recorded in the Laboratory of Surgical Pathology of Columbia University, only 9 of which involved the soft tissues. Three years later only 3 more cases involving the soft tissues had been added, and at the present writing (September 1951) there is a total of 34 cases with the following distribution: liver 1; spleen 4; breast 5; bone 4; uterus, pharynx, pleura, corpora cavernosa penis, and sciatic nerve 1 each (i. e., 19 cases outside of the soft tissues); orbit 1; upper eyelid 1; neck 4; trunk 3; upper extremity 2; lower extremity 4 (i. e., 15 cases in the soft tissues). It would thus appear to be one of the rarer varieties of soft tissue sarcomas.

GROSS. A majority of the benign forms of this tumor are found in the skin of infants and young children, but the malignant varieties develop in the

muscles or other deep tissues of older children and adults of all ages and both sexes. Swelling is the only symptom as a rule. If it approaches the surface, its vascularity may be apparent from the red or blue color; generally, however, it is only when it is approached surgically that its great vascularity can be appreciated, and in some cases where endothelial proliferation has obstructed the blood channels, one may have no true conception of the nature of the growth from its gross appearance.

MICROSCOPIC. This aspect is usually striking. There will be a congeries of atypical capillaries with a marked tendency to frequent anastomosis, lined by swollen, anaplastic endothelioblasts, which are either rounded or elongated and sometimes heaped up so as partly to fill the lumen (fig. 61). With any good silver reticulin impregnation, it will be possible to observe the vascular pattern to the best advantage. The tumor cells will lie inside of the delicate reticulin sheath that encloses each vessel (fig. 62), and this will serve to distinguish the tumor from the hemangiopericytoma (fig. 63), where the vessels have a normal endothelial lining, and the tumor cells are all outside of the reticulin sheath. When the tumor cells have overgrown the entire field so that in ordinary stains the nature of the tumor is obscured, the silver reticulin impregnation may still show the basic vascular pattern by emphasizing the reticulin sheaths of the capillaries. Confirmation of the nature of the cells composing such a tumor may be gained if tissue culture can be done (Murray and Stout). One would expect blood-borne metastases from a tumor in which the tumor cells are formed inside of a blood vessel and are in actual contact with the circulating blood, and such indeed is the case. It should be noted, however, that sometimes the metastatic foci are slow in manifesting themselves and occasional metastases take place through the lymphatics to the regional nodes as well as through the blood stream.

Some authors have described what they choose to call "benign metastasizing hemangioma." The writer does not believe in such a tumor form. He has examined the slides of the cases reported by Wollstein and by Robinson and Castleman and has found that the freely anastomosing capillaries were lined with only a single layer of swollen, hyperchromatic endothelioblasts. After these studies and after reviewing all case reports of so-called metastasizing hemangioma, he has concluded that all of them can be interpreted either as multiple foci of the benign form of the hemangioendothelioma of infancy or as a failure to recognize the malignant nature of an adult hemangioendothelioma. Two different neoplasms have sometimes been erroneously confused with the hemangioendothelioma. Metastases of hypernephroid carcinoma in which tubules are formed, lined with swollen clear cells, occasionally show red blood cells filling most of the tubules. It need only be noted that endothelioblasts never have a clear cytoplasmic zone surrounding the nucleus. The chorionepithelioma not infrequently makes spaces filled with red blood cells

KAPOSI'S SARCOMA

(Figures 64 and 65 are from the same case)

Figure 64. A 67-year-old woman with a few purplish nodules on the foot and one on the dorsum of the hand measuring 7×5 mm. This was excised and is shown in this photograph. × 22. A. F. I. P. Acc. No. 218822–63.

Figure 65. Detail from figure 64. The proliferated tissue consists of capillaries, many of which are inconspicuous, because they are intermingled with more easily apparent, spindle-shaped fibroblastic cells resembling those seen in a fibrosarcoma. × 310. A. F. I. P. Acc. No. 218822–64.

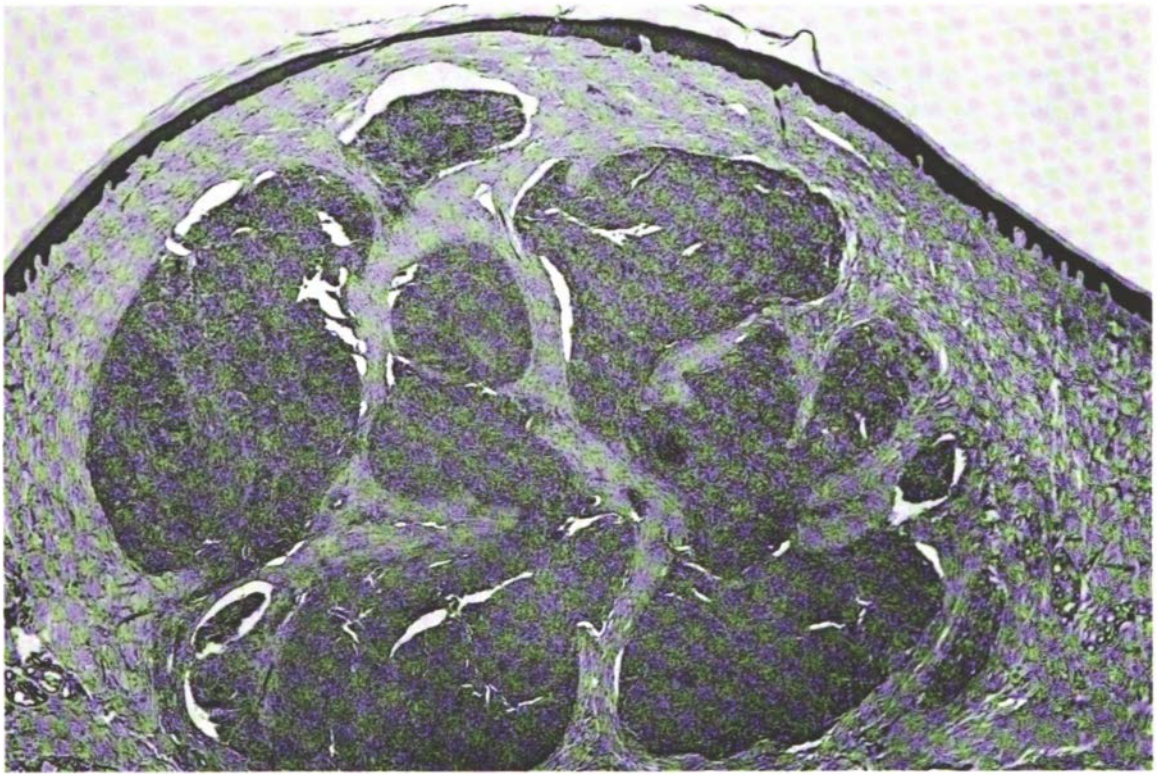


Fig. 64

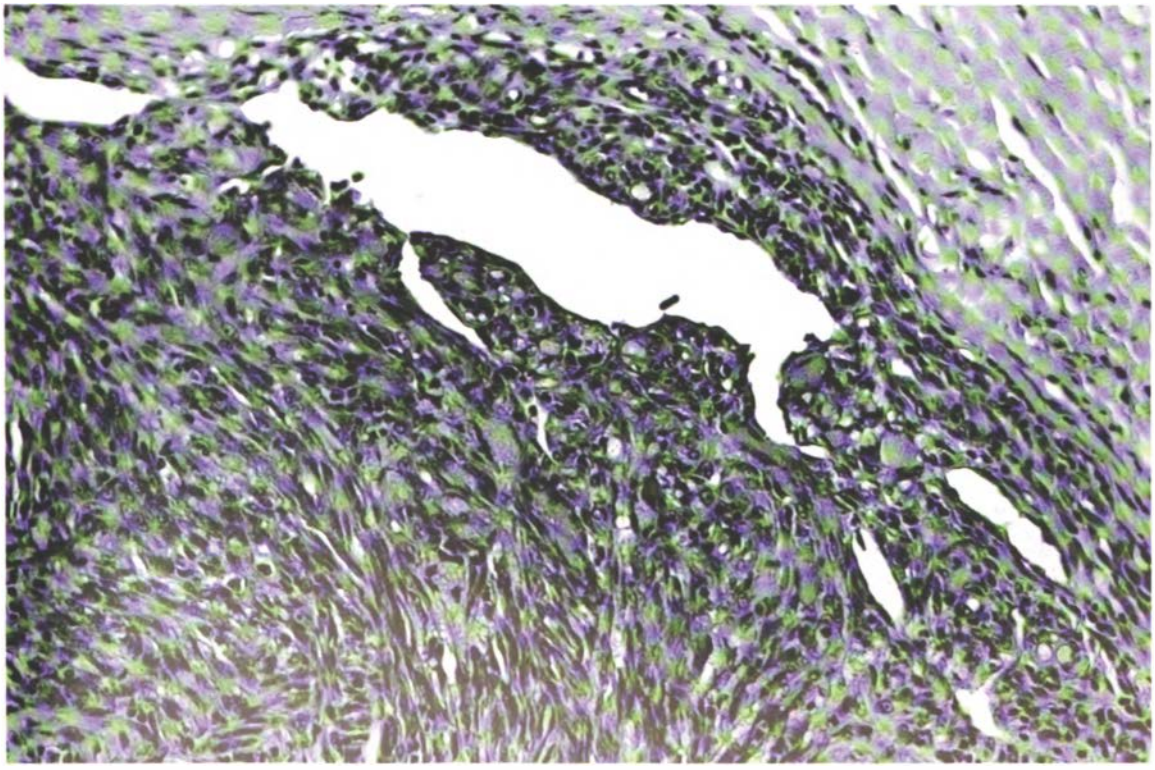


Fig. 65

MALIGNANT LYMPHOID AND RETICULOENDOTHELIAL TUMORS

Lymphosarcoma

SYNONYMS AND RELATED TERMS: Malignant lymphoblastoma; malignant lymphoma.

The vast majority of lymphosarcomas of the soft tissues arise in lymph nodes. Since these are dealt with in another fascicle,* they will not be discussed in this one. These aside, however, there are certain lymphosarcomas that seemingly are primary in the skin and orbit, because they may manifest themselves in those places alone or, if followed by involvement of other parts of the body, there may be a long interval of time before this phenomenon takes place. If only a short interval of time elapses between skin or orbit involvement and the appearance of lymphosarcoma elsewhere in the body, one is justified in rejecting the lesion as primary, because any lesion in the skin is noticed almost as soon as it appears, whereas deeper lesions if painless easily escape notice for a relatively long time. In the skin, lymphosarcoma generally forms an area of thickening or nodularity with a reddish hue as a rule, although occasionally it may be pallid and semitranslucent. All of the common histological varieties, **giant follicle lymphosarcoma, lymphocytic cell lymphosarcoma,** and **reticulum cell lymphosarcoma** have been recorded. It is extremely difficult to learn of the degree of malignancy and the cure rate following radiotherapy or excision of primary lymphosarcoma of the skin and orbit, because no adequate reports of large groups of cases followed over a long period of time are in existence. There is some indication that about half of the cases remain free from other evidence of tumor for more than five years.

Reticulum Cell Sarcoma

SYNONYMS AND RELATED TERMS: Clasmatocytic lymphoma; histiocytic lymphoma; monocytoma; reticulocytoma; reticulothelial sarcoma; stem cell lymphoma.

One other member of this rather heterogeneous group, although rare, deserves special attention at this point. A malignant tumor composed of cells identified as probable reticuloblasts is found on rare occasions in the deeper soft tissues involving subcutaneous tissues and muscles or their sheaths. It has apparently no connection with bone marrow, lymph nodes, or skin; it does not form follicles or lymphocytic tumor cells; and it has been presumed, faute de mieux, that the origin is from cells of the reticuloendothelial system, since these are ubiquitous. If this is correct, it is proper to call the tumor reticulum cell sarcoma (figs. 66, 67), which serves to distinguish it from the more familiar reticulum cell lymphosarcoma of lymphatic tissue origin. Whatever the name, it seems to be an entity, occurring in the deep soft tissues and behaving as a fully malignant metastasizing neoplasm.

*Fascicle 8, "Tumors of the Hematopoietic System."

RETICULUM CELL SARCOMA

(Figures 66 and 67 are from the same case)

Figure 66. Reticulum cell sarcoma of scapular region. A 23-year-old woman developed a painless lump on the left shoulder, which in a year reached a size of 9×7×2 cm. Without trauma it bled into itself. When biopsied it was very vascular and composed of soft, yellow-tinted, solid tissue mixed with old blood. A. F. I. P. Acc. No. 218822–74.

Figure 67. Photomicrograph of tumor shown in figure 66. It is composed of solid masses of cells resembling reticuloblasts without any lipoid content and supported by a vascular framework. Following radiotherapy with roentgen ray, the tumor disappeared, and there was no recurrence after 11 years and 4 months. (Figure 2 from Stout, A. P. Sarcomas of the soft parts. J. Missouri M. A., 44: 329–334, 1947.) A. F. I. P. Acc. No. 218822–73.

PLASMA CELL TUMOR

Figure 68. Plasmocytoma of inframammary region of a 71-year-old man. This was a rapidly growing nodule which had increased in 20 days from a 6 mm. red spot to a diameter of 2.5 cm. and a thickness of 5 mm. with ulceration. There was no bone involvement by roentgen ray. Following excision and skin grafting, nodules appeared in the donor site, at the site of excision, and in one naris. This illustration shows the solid massing of characteristic plasma cells, which vary somewhat in size. × 1130. (From Stout, A. P., and Frerichs, J. B. Plasmocytoma of inframammary region. [Tumor Seminar.] J. Missouri M. A., 46: 275–277, 1949.) A. F. I. P. Acc. No. 218822–72.

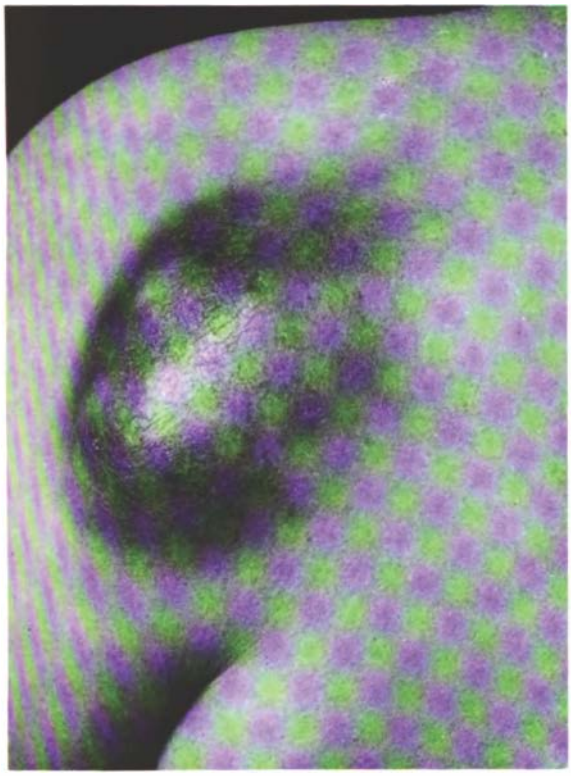


Fig. 66

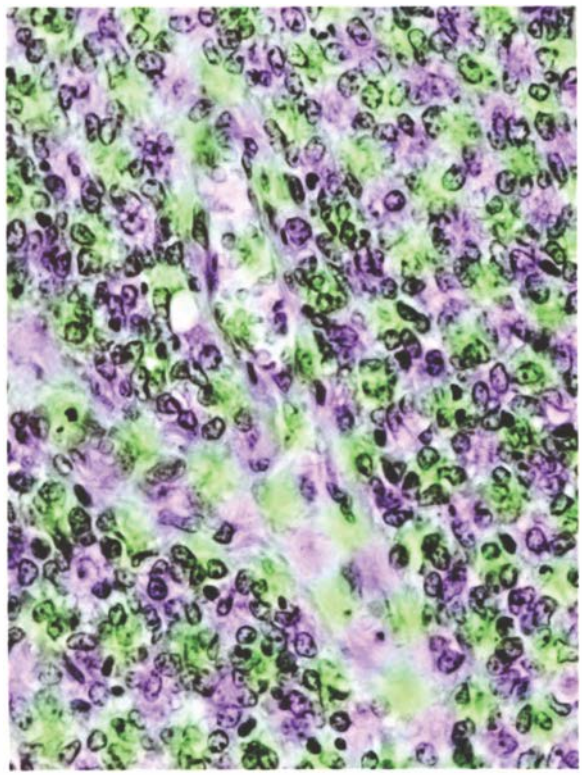


Fig. 67

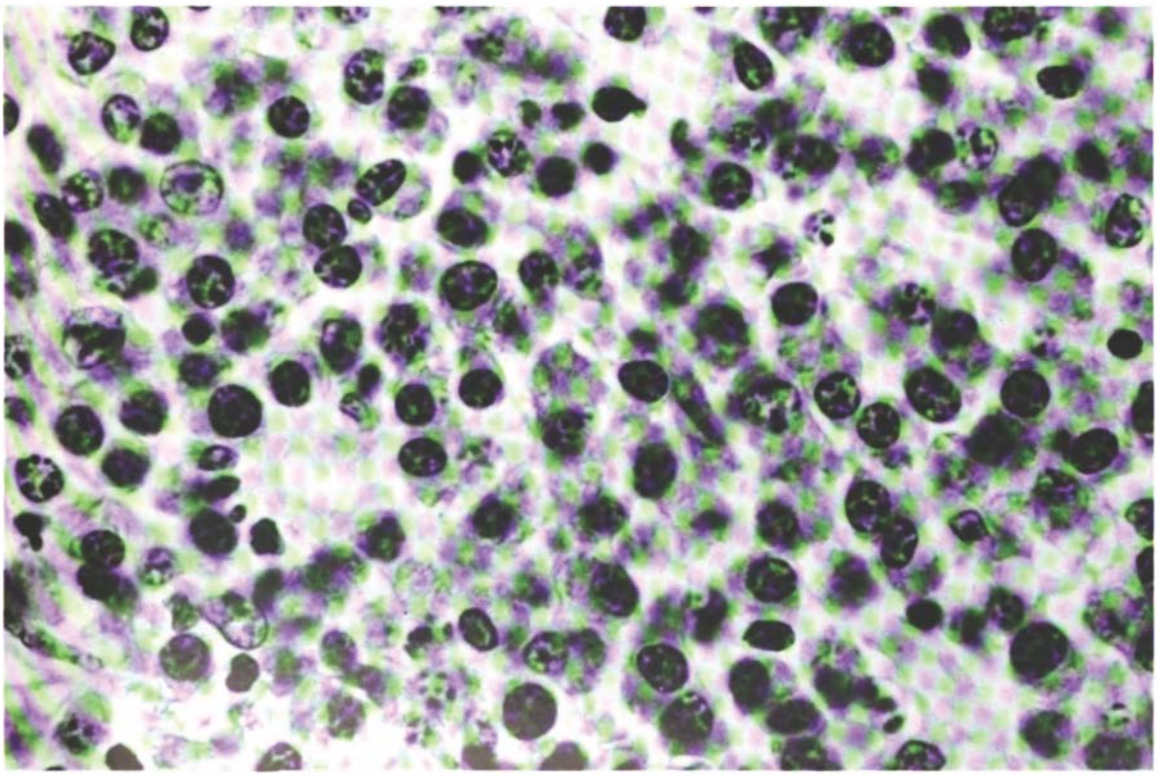


Fig. 68

Mycosis Fungoides

SYNONYMS AND RELATED TERMS: Fibroma fungoides; granuloma fungoides.

Possibly the peculiar and obscure disease known as mycosis fungoides is related in some way to the lymphosarcoma. It, too, manifests itself generally in the skin by the formation of multiple reddish patches of thickening due to the infiltration of the corium by a variety of lymphocytic and lymphoblastic cells, instead of in the guise of one of the three more characteristic lymphoblastic tumors previously mentioned. Like "Kaposi's disease," it is uncertain whether or not mycosis fungoides is a true neoplasm. It runs a long course lasting years and may eventually involve the viscera with fatal results.

Plasma Cell Tumor

SYNONYMS AND RELATED TERMS: Lymphocytic myeloma; plasmacytoma; plasmasarcoma; plasmocytoma; solitary myeloma.

Plasma cell tumor has been reported in the skin and mediastinum, according to Hellwig. Frerichs has called to the writer's attention one case (Stout and Frerichs) that developed primarily in the corium and subcutaneous tissue of the chest wall (fig. 68). These are presumably primary growths and not extensions or metastases from plasma cell myeloma in the bone barrow. The neoplastic plasmocytoma can be distinguished from the plasma cell granuloma, because the tumor is composed solely of plasma cells to the exclusion of all others save for a very delicate fibrovascular supporting framework, while the granuloma has an admixture of other types of inflammatory cells among the preponderant plasma cells. Almost all of the extramedullary plasmocytomas have been found in the upper air and food passages, the middle and external ear, the conjunctiva and lids, and the gastrointestinal tract down to and including the anus. Their occurrence in the soft tissues is a curiosity observed only once by the writer.

OTHER MALIGNANT TUMORS

Osteogenic Sarcoma and Chondrosarcoma

SYNONYMS AND RELATED TERMS: Chondroma myxomatodes; chondroma sarcomatodes; chondro-osteosarcoma; "malignant aneurysm"; osteoblastic sarcoma; osteoblastoma; osteocarcinoma; osteochondromyxosarcoma; osteochondrosarcoma; osteogenic fibromyxosarcoma; osteoid sarcoma; osteolytic sarcoma; sarcoma osteogenicum; sclerosing osteosarcoma; telangiectatic osteosarcoma.

Obviously no bone or cartilage is found normally in the soft tissues. Nevertheless, by a process of metaplasia both bone and cartilage of a differentiated aspect can be formed occasionally in healing wounds and cicatrices, in connection with areas of calcification which become secondarily invaded by granulation tissue, and in the peculiar condition called myositis ossificans. This means that cells of mesenchymal origin, which have differentiated functionally along other lines, may find themselves transformed into osteoblasts under proper conditions of pH, vascularity, and local concentration of ferments and bone

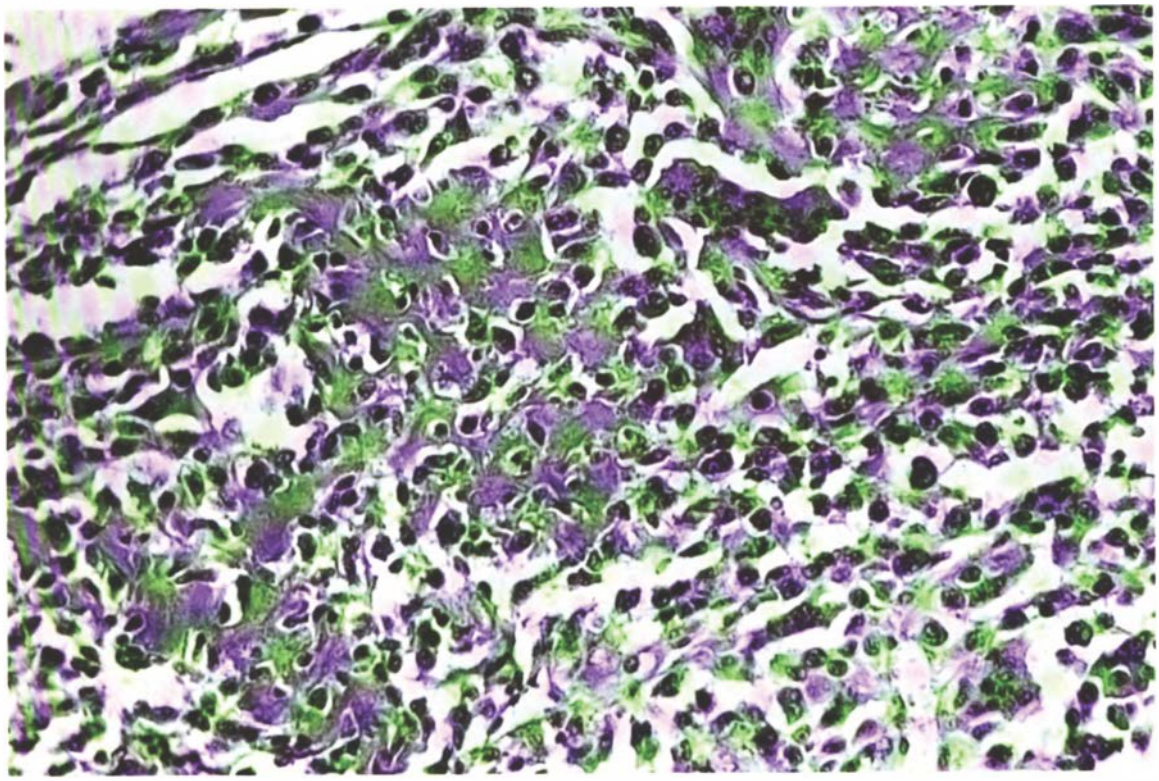


Fig. 69

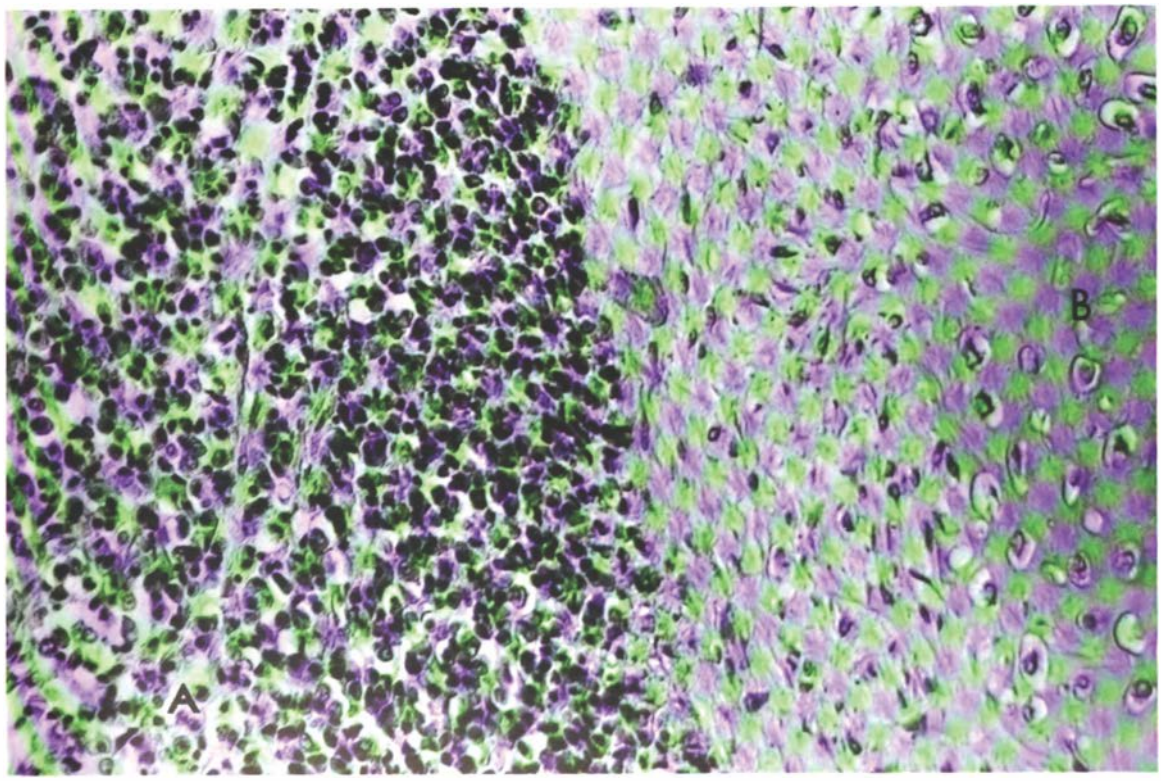


Fig. 70

SYNOVIAL SARCOMA

(Plate V–B and Figure 72 are from the same case)

Figure 71. A 27-year-old man had a mass in the antecubital fossa for four years. Following biopsy a high amputation was done. He remained well for nine years, then lung metastases appeared and he died almost ten years after amputation. The photograph shows the position and relationships of the tumor, which was close to but did not invade the joint. (From figure 2 in Haagensen, C. D., and Stout, A. P. Synovial sarcoma. Ann. Surg., 120: 826–842, 1944.) A. F. I. P. Acc. No. 218822–67.

Figure 72. A large tumor was present for one year in the thigh of a 44-year-old man. High amputation was done shortly after an attempt at local excision failed. He died with lung and bone metastases after 22 months. This tumor was not in contact with any joint (see pl. V–B). A: The tumor tends to form glandlike spaces with synovioblasts and with a fibrosarcoma-like tissue between. B: A Laidlaw silver reticulin impregnation shows the reticulin fibers in the spindle cell zones. × 680. (Figure 5 from Haagensen, C. D., and Stout, A. P. Synovial sarcoma. Ann. Surg., 120: 826–842, 1944.) A. F. I. P. Acc. No. 218822–66.

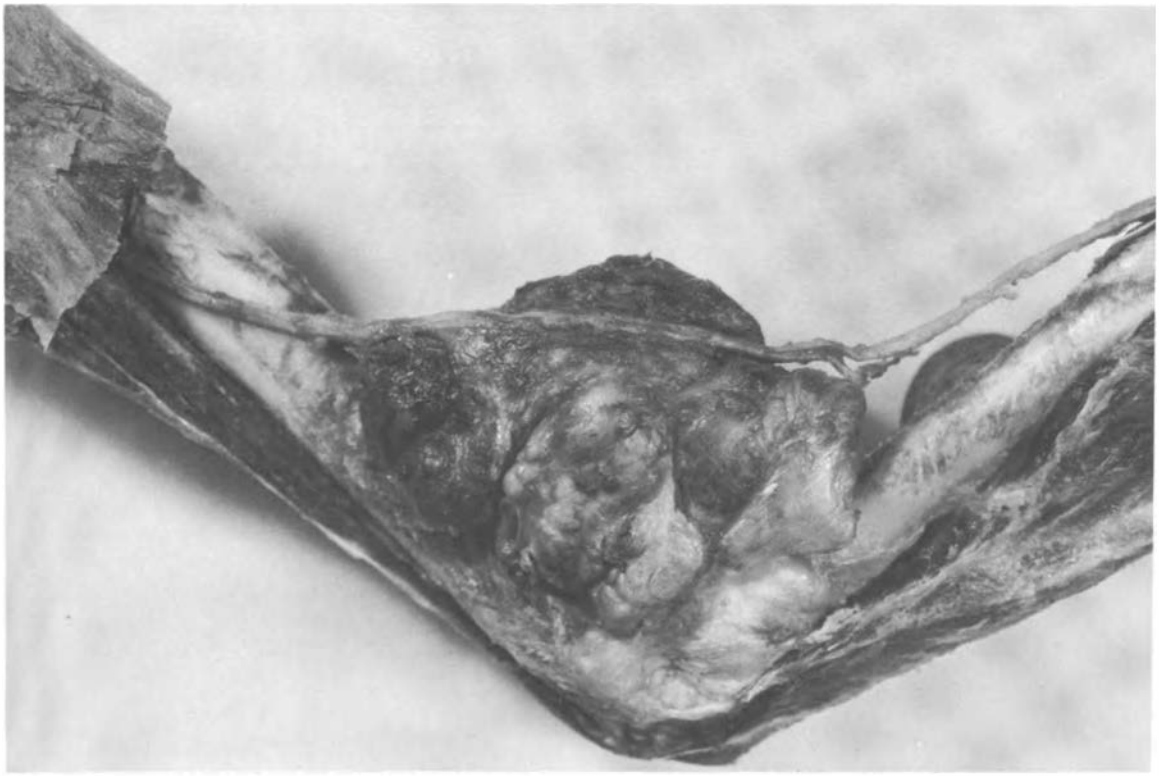
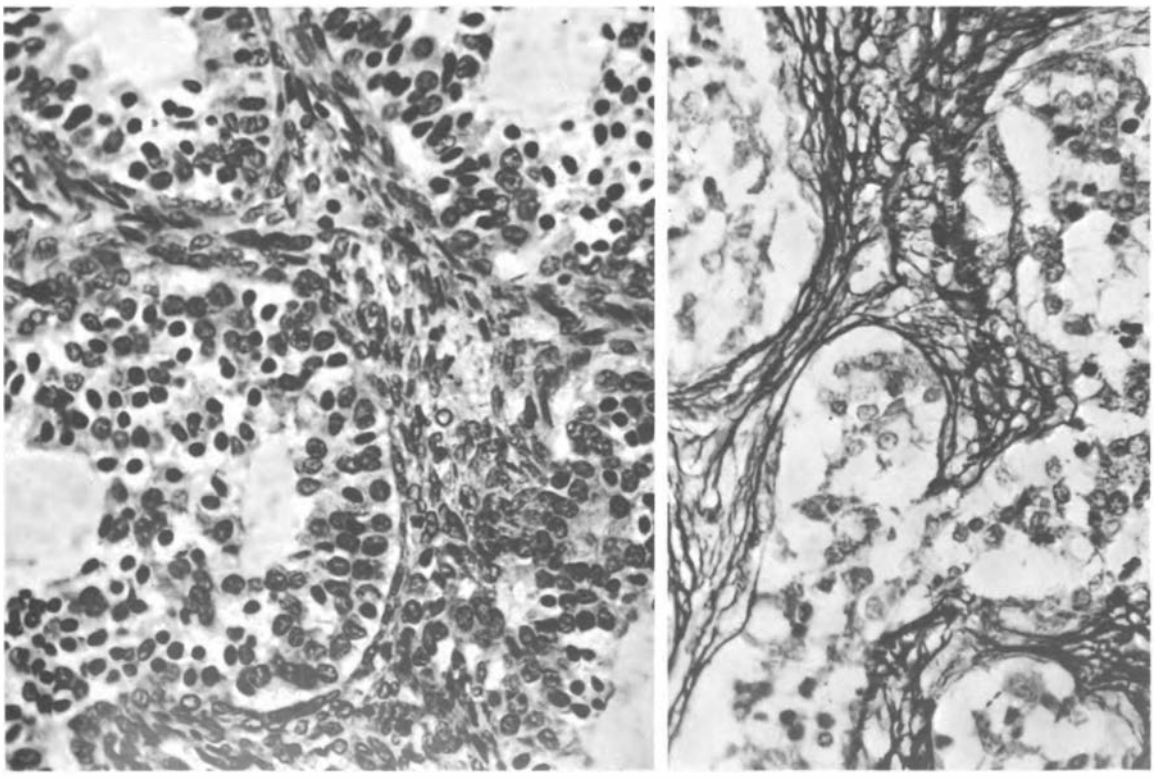


Fig. 71



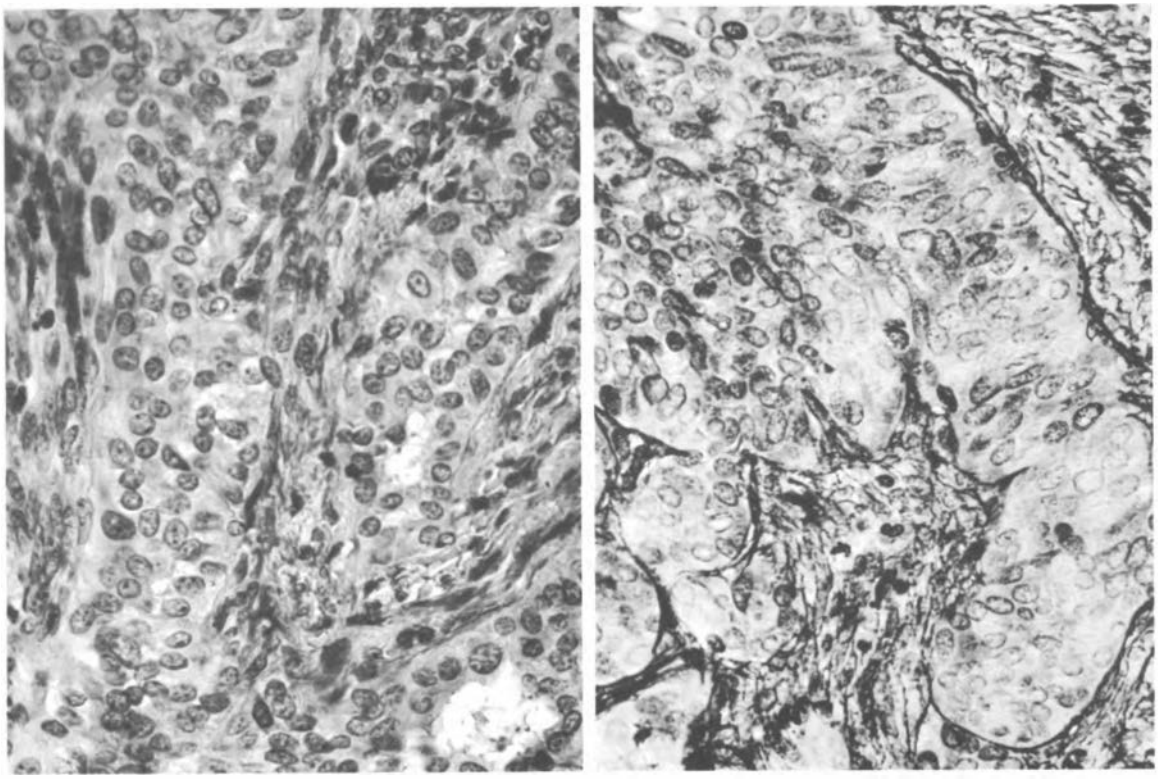
A B

Fig. 72

SYNOVIAL SARCOMA

Figure 73. Synovial sarcoma. A tumor in the groin of a 19-year-old man was removed after 15 months of growth. He died with lung metastases five years and four months after operation. A: In this tumor the synovioblasts grow in solid cords with little tendency to form slits or gland-like spaces. B: A Laidlaw silver reticulin impregnation shows the reticulin fibers, which lie between the spindle-shaped cells, and the complete absence of fibers among the synovioblasts. × 680. (Figure 4 from Haagensen, C. D., and Stout, A. P. Synovial sarcoma. Ann Surg., 120: 826–842, 1944.) A. F. I. P. Acc. No. 218822–68.

Figure 74. Explant in vitro from a malignant metastasizing tumor of the thigh. The outgrowth consists of spidery cells, which characterize normal synovial outgrowths in culture. The normal cells often have more processes. Zenker's fluid; Harris' hematoxylin. (Figure 4 from Murray, M. R., Stout, A. P., and Pogogeff, I. A. Synovial sarcoma and normal synovial tissue cultivated in vitro. Ann. Surg., 120: 843–851, 1944.) A. F. I. P. Acc. No. 218822–69.



A B

Fig. 73

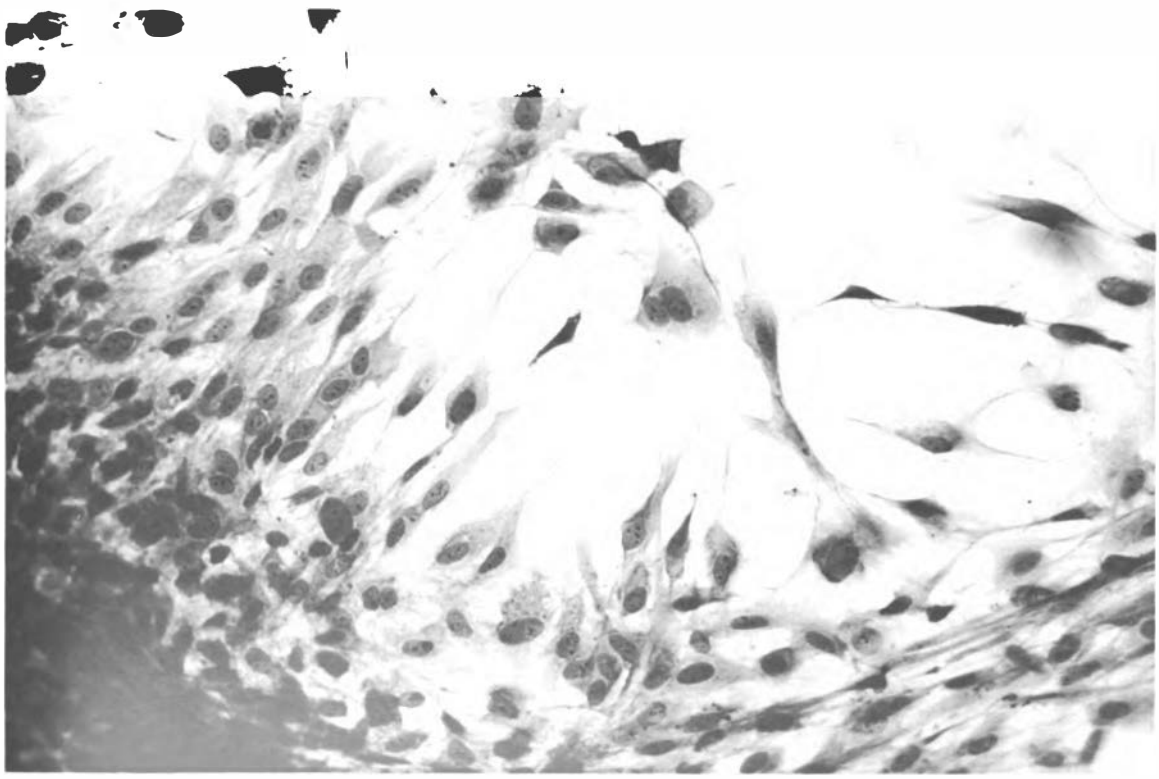


Fig. 74

by treatment may be accounted for in part perhaps by the fact that the mean duration of symptoms before curative treatment was attempted was 2.6 years.

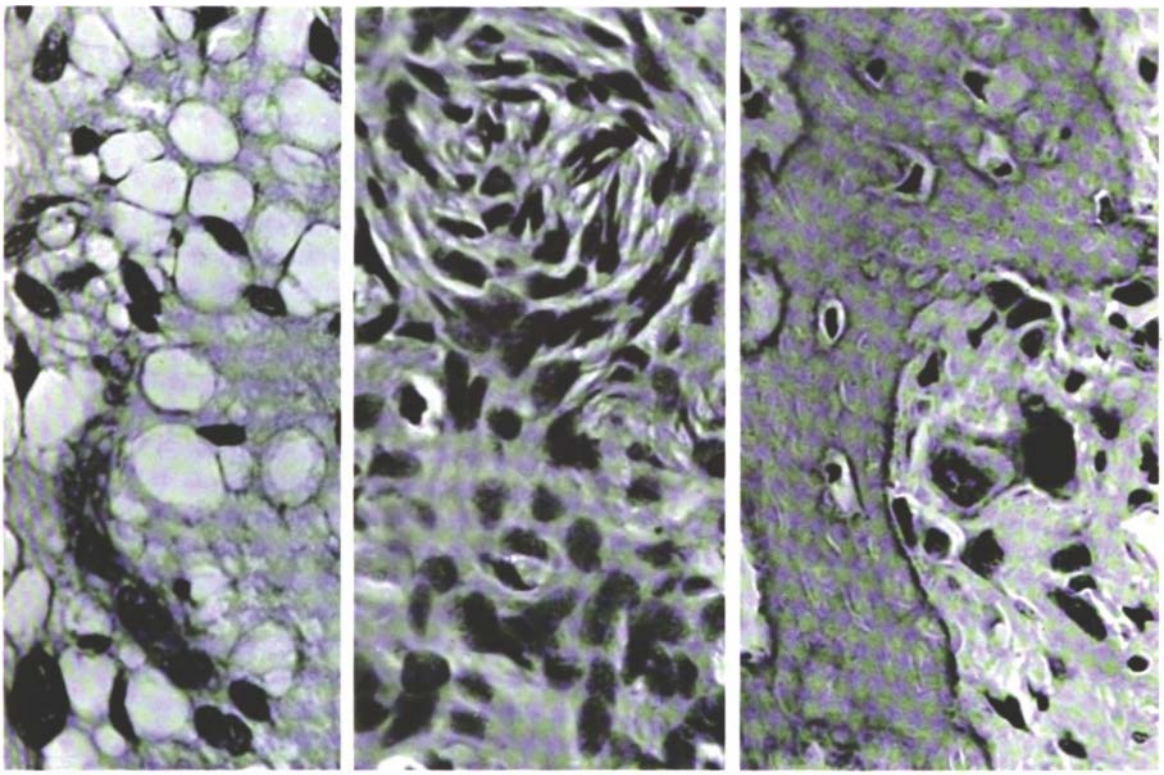
GROSS. These are solid and often sharply circumscribed tumors (fig. 71, pl. V–B), which occasionally show spotty areas of calcification demonstrable by roentgen ray examination (Lewis).

MICROSCOPIC. The pattern is very striking, for the tumors are composed of two histologically differing tissue types inextricably intermingled. One, which may be referred to as the synovioblastic element, is made up of fairly large polygonal or sometimes cylindrical cells that grow in cords tightly packed together. Frequently these cells are oriented around slits or short tubes lending the tumor an adenomatous aspect. This is enhanced by the fact that the cells lining these spaces may secrete a mucoid material which is stained red by mucicarmine. Actually the material is hyaluronic acid, and the supposed "glands" are simply abortive attempts by the synovioblasts to form synovial structures. Between these cells there are no connective tissue fibers; but between the cords of synovioblastic tissue are areas filled with spindle-shaped cells with delicate reticulin fibers wrapped about them, which have the aspect of fibrosarcoma (figs. 72, 73). Both types of tumor cells are always present but in greatly varying amounts so that sometimes one dominates the picture and sometimes another. On explantation in vitro, the only cells that proliferate exhibit the growth characteristics of synovial tissue (fig. 74), so it may be that cells of the supposed fibrosarcomatous areas are in reality synovioblasts masquerading as fibroblasts; but this remains an unsolved problem.

Malignant Mesenchymoma

SYNONYMS AND RELATED TERMS: Botryoid sarcoma; capsuloma of kidney; enchondromyxohemangiosarcoma; embryonal myoblastoma; embryonal rhabdomyoblastoma; endothelioma; fibrosarcoma, embryonal type; hemangioblastomyxoma; lipomyxosarcoma; malignant mixed mesenchymal tumor; mesenchymal mixed tumor; multiple mesenchymal hemendotheliomata.

This term has been applied to those tumors of the soft tissues of mesenchymal origin which are composed of tumor cells differentiating into two or more unrelated malignant forms. Since most of the tumors of mesenchymal derivation may have fibrosarcomatous areas, this form is not recognized as a separate one in evaluating tumors. It has been shown that synovial sarcomas always have a fibrosarcomatous element, and liposarcoma and rhabdomyosarcoma not infrequently. But an exception is made if fibrosarcoma is found associated with a neoplastic form such as lymphosarcoma in a conjunction that has never been reported for the latter tumor type. Nor does the presence of adult differentiated bone or cartilage in the framework of a malignant tumor, such as the liposarcoma, indicate that it is another malignant element. But when tumors are composed of two or more unrelated malignant elements, such as for instance a tumor of the rectus femoris muscle in which were recognized leiomyosarcoma, osteogenic sarcoma, chondrosarcoma, reticulum cell sarcoma,



A B C

Fig. 75

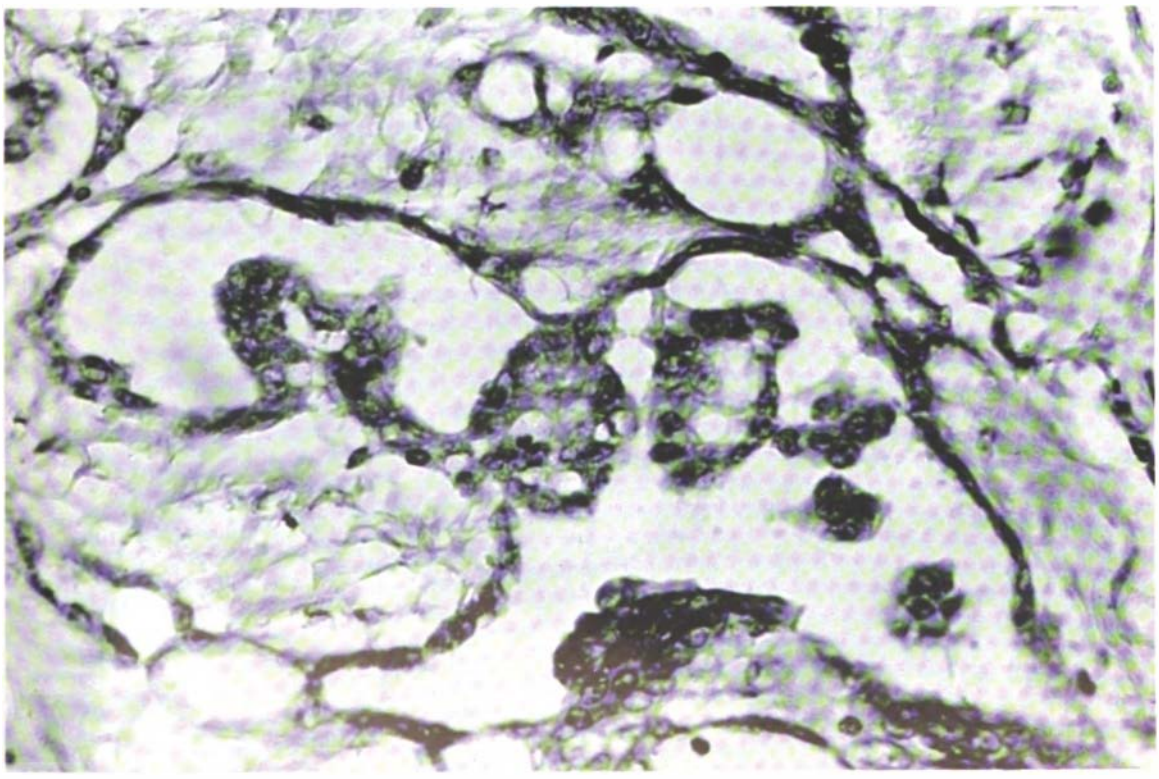


Fig. 76

MALIGNANT MESOTHELIOMA

Figure 77. Malignant mesothelioma of pleura. Explant in vitro. The outgrowth consists of cells with rather fibrous cytoplasm, which form membranes and tongues characteristic of normal mesothelial tissue in vitro. Seven days in vitro. Zenker's fluid; phosphotungstic acid hematoxylin. (Figure 3 from Stout, A. P., and Murray, M. R. Localized pleural mesothelioma. Arch. Path., 34: 951–964, 1942.) A. F. I. P. Acc. No. 218822–71.

MELANOSARCOMA (?)

Figure 78. For seven years a 36-year-old man had a 4×2×0.7 cm. tumor, deep in the corium on the dorsum of the foot. There has been no recurrence eight years after the tumor was excised. The growth is composed of interlaced bands of fibers and fibroblasts scattered among which are stellate melanoblasts with long processes. Masson-Fontana stain. × 441. (Figure 2 from Stout, A. P. Sarcomas of the soft parts. J. Missouri M. A., 44: 329–334, 1947.) A. F. I. P. Acc. No. 218822–75.

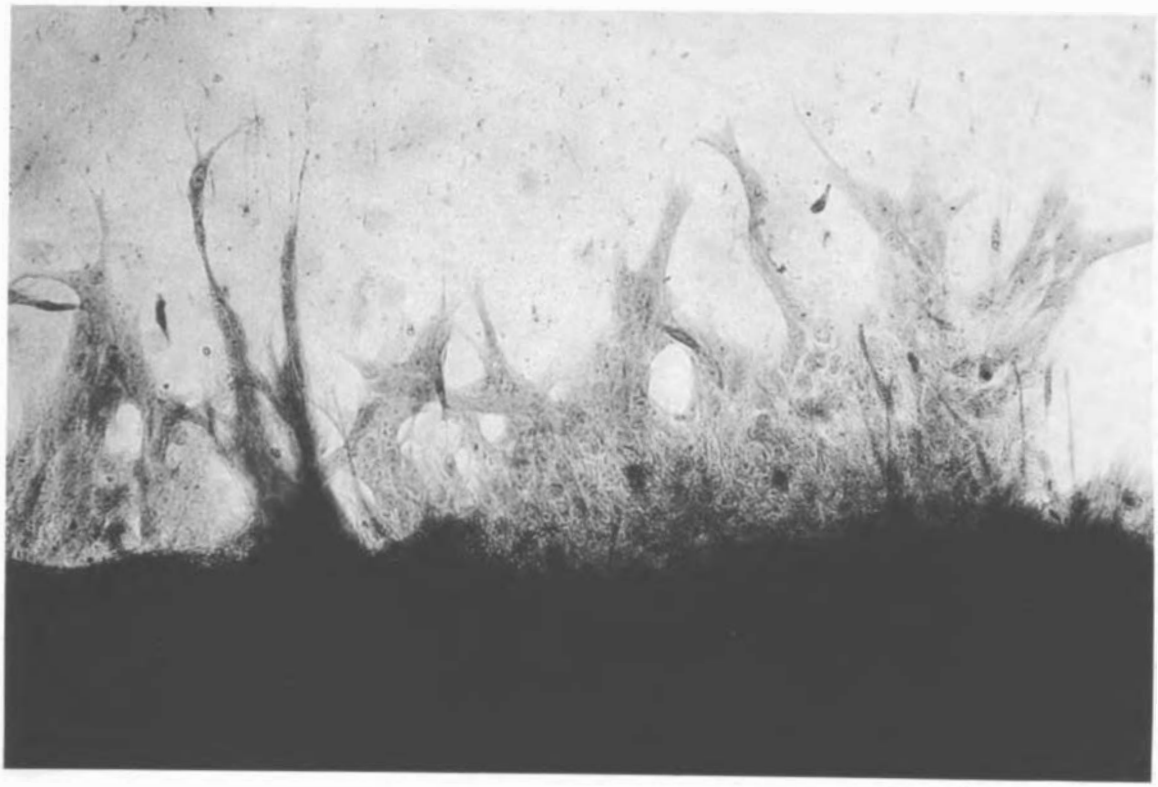


Fig. 77

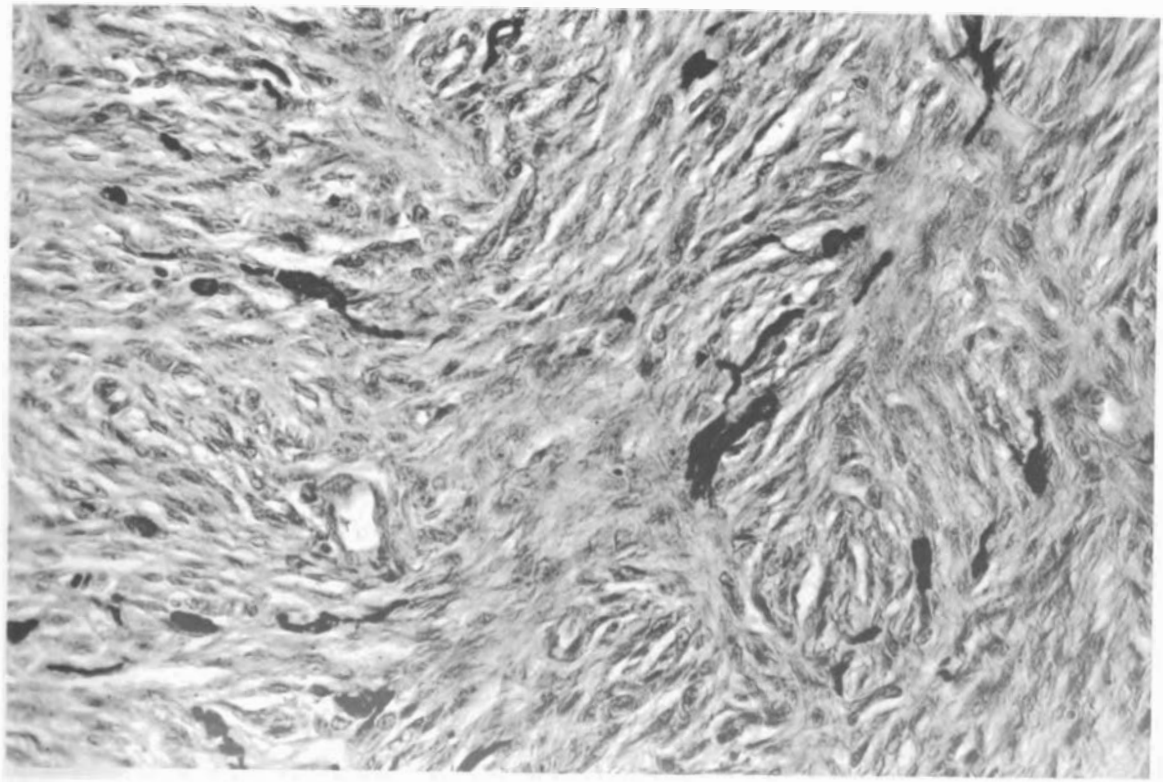


Fig. 78

DIAGNOSIS AND TREATMENT

The foregoing summary of the various benign and malignant tumors of the soft tissues, to which must be added the information contained in Fascicle 6, "Tumors of the Peripheral Nervous System," in Fascicle 3, "Melanotic Tumors of the Skin," and in Fascicle 2, "Tumors of the Skin and Accessory Structures," makes it abundantly clear that proper diagnosis and treatment demand accurate knowledge and understanding of an almost bewildering variety of tumors. While some of the benign surface tumors can be recognized clinically, the vast majority of the deep tumors cannot. It is beyond the scope of this fascicle to give in detail the treatment of benign tumors. Since the benign tumors seldom assume malignant characteristics, it is rare for them to become a menace to life. But it is altogether different in regard to the malignant tumors that are often fatal and alas very often ineffectually treated. For this reason the problems of diagnosis and treatment will be briefly discussed.

The best chance of curing the malignant tumors of the soft tissues lies in the hands of the therapist who makes the first attempt. If this attempt fails, the chances that subsequent attempts will succeed are enormously reduced no matter how radical they may be. Unless the therapist is thoroughly familiar with all of the different varieties of tumor he may encounter and the proper form of treatment for each one, he will be well advised if he makes a thorough clinical study of the case and calls his pathologist into consultation from the start. The pathologist will be in a better position to interpret the biopsy if he knows in advance all about the clinical features of the case, and if he properly fulfills his functions, he will be prepared to advise the surgeon about the probable behavior and the best form of treatment of any tumor encountered.

No treatment should be undertaken without biopsy, so that the therapist can proceed armed with knowledge. Without this information, treatment is usually not radical enough, but sometimes it can be more drastic than is necessary. The biopsy must be interpreted by the pathologist. If it is possible to make a diagnosis by frozen section, this may be done and the appropriate treatment instituted at once. The writer has seldom found it possible to be sufficiently accurate from a frozen section and prefers to have treatment delayed a day or two until a paraffin section properly stained can be studied If this technique is used, it is important to have the biopsy taken with the utmost care to prevent smearing tumor cells into the wound, and as small and dry a wound as possible should be sought. The treatment selected will be surgery rather than radiotherapy in the majority of cases. If the surgeon is informed by the

pathologist of the exact nature of the malignant tumor, its method of growth, which is almost always by insidious infiltration, the probability of metastasis, and the chances of cure if the primary growth is removed, he is then armed with the necessary knowledge to enable him to decide whether it is possible to succeed by sacrifice of local tissues, or if an extremity is involved whether amputation will be necessary. If the surgeon is to succeed, he must be instructed in the principles of cancer surgery, which strives to remove a tumor by passing everywhere through normal tissues so that the knife never touches the tumor. The surgeon must think first of removing the tumor and undertake to repair the damage only after this has been done.

With this preamble the potentialities of the various tumors can be briefly reviewed. For purposes of treatment, they can be considered in groups.

Group 1. Tumors of the highest malignancy that call for the most drastic surgical treatment, such as:

Undifferentiated fibrosarcoma
Undifferentiated liposarcoma
Leiomyosarcoma with many mitoses
Rhabdomyosarcoma
Malignant hemangioendothelioma
Malignant lymphangiosarcoma
Synovial sarcoma
Osteogenic sarcoma
Chondrosarcoma
Malignant mesenchymoma

Group 2. Tumors that are malignant because of infiltrative growth, but do not metastasize, such as:

Skin fibrosarcoma
Myxoma
Differentiated liposarcoma
Melanosarcoma

Group 3. Tumors that are malignant and metastasize but cannot definitely be distinguished from their benign forms, such as:

Malignant granular cell myoblastoma
Malignant hemangiopericytoma

Group 4. Tumors that are usually better treated by radiotherapy, such as:

Lymphosarcoma of the lymphocytic and giant follicle type
Mycosis fungoides
Kaposi's sarcoma
Reticulum cell sarcoma

Group 5. Tumors about which insufficient information on results of different forms of treatment is available, such as:

Plasma cell tumor

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