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JUAN A. DEL REGATO, M. D., *Editor*

CONTENTS

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TUMORS OF THE SOFT TISSUES

THE most remarkable feature of these CANCER SEMINARS is the unusually high order of performance which is kept year after year; there is no post-graduate teaching conference in the continent that equals them, and indeed many other conferences are now being patterned after them. Those of us who have been privileged to participate in these educational exercises look upon them as significant advances in post-graduate teaching. For this reason, I have asked that these remarks of mine be printed as an introduction.

I deem it a privilege to have been asked again, by the Penrose Cancer Hospital, to participate in this CANCER SEMINAR. The fact that we will be sitting at the feet of Doctor A. P. Stout adds significance to the occasion. It is also a privilege to have Doctor Eugene Bricker with us, for his originality and contributions to surgery of cancer are widely appreciated.

This time, I have accepted a risky assignment; no one can gainsay this, for the interpretation of soft tissue densities is among the most difficult in radiodiagnosis. But we are participating in a teaching conference, rather than in a contest, and thus, at the risk of serious mistakes that I shall unquestionably make, I am willing to participate and contribute what I can; for these CANCER SEMINARS are dedicated to improve the rapport between radiologists and pathologists. Our dependence from each other has been repeatedly demonstrated here and, as a result, better understanding between our disciplines has ensued.

That we acknowledge our limitations as radiologists does not diminish the importance of our role in the diagnosis of these tumors. In our opinion, our function does not end when we demonstrate the presence of an abnormality; we must strive to make a histopathologic diagnosis, no matter how difficult or unreasonable this may appear, at times. Forced to think in terms of tissue diagnosis, the radiologist must remain intimately familiar with the different possibilities which he endeavors to differentiate; in so doing, he avoids slothful thinking and extracts the best of his means.

PHILLIP J. HODES, M. D.
September, 1960
Philadelphia, Pennsylvania

This CANCER SEMINAR was attended, in Colorado Springs, by 419 radiologists, pathologists and surgeons, on November 7th, 1959. It was repeated in San Juan, Puerto Rico, on March 16th, 1960, under the sponsorship of the Puerto Rico Society of Pathologists and thanks to the efforts of its president, Doctor Raúl Marcial-Rojas. On that occasion, Doctor Charles E. Eckert, Professor of Surgery at the Medical School of Albany, New York, was the third speaker. Excerpts from the San Juan discussion have been incorporated in these proceedings.

1. *Juvenile Fibromatosis of the Mastoid Region*

Contributed by A. O. Severance, M.D., Asa Beach, M.D., Dean Jones, M.D., San Antonio, and J. V. Blake, Jr., M.D., Floresville, Texas

THE PATIENT was a 16-month-old boy in February, 1959, when his parents called attention to an elevated mass behind the right ear; it had been noticed two months after birth and had grown considerably. On examination, the tumefaction measured 6 x 4 cm; it was hard and smooth and lay over the right mastoid. The hemoglobin was 10 grams per cent and there were 12,900 white cells per cubic mm.

Dr. Hodes: The roentgen examination of the mastoid and the adjoining soft tissues reveal the following: (a) a small soft tissue mass lifting the pinna of the ear, (b) normal mastoid development with no superimposed evidence of mastoid engorgement, (c) a small well defined bone defect in the squamosal portion of the temporal bone, (d) no distinctive abnormalities in the soft tissue mass.

Because there was no evidence of mucous membrane engorgement in the mastoid, one can exclude with reasonable confidence active inflammatory disease as the cause for the slowly growing tumor mass. A history of tumor growth for fourteen months plus the rather sharply outlined bone defect are manifestations of a rather slowly growing tumor. Of all primary soft tissue tumors arising in this portion of the head in infants, the rhabdomyosarcomas are most common.

Dr. Hodes' impression: A slowly growing malignant tumor: 1. RHABDOMYOSARCOMA. 2. FIBROSARCOMA.

Roentgenologic Impressions Submitted by Mail:

Various benign tumors	34
Dermoid, epidermoid	18
Fibroma	15
Various malignant tumors	15
Hematoma	11
Fibrosarcoma	9
Others	18

Dr. Hodes: No one could gainsay the possibility of a benign tumor: the bone erosion plus the clinical history of progression seem to militate against this. The manner in which the bone was eroded did not suggest epidermoid; the latter lies in the diploe and bulge the inner and outer tables of the skull. The possibility of fibroma cannot be entirely excluded. There is no history of trauma and the progressive nature of the soft tissue mass, since the age of two months, was not consonant with the diagnosis of hematoma.

Dr. Regato: Dr. W. P. Stampfli, of Denver, as well as Dr. Genene Baker, of Colorado Springs, offered a diagnostic impression of fibroma. Dr. Paul Swenson, of St. Paul, Minn., suggested fibrosarcoma. Dr. Robert L. Stein, of San Francisco, preferred neurofibroma.

Operative findings: In February, 1959, the lesion was excised; it was rubbery but non-encapsulated. The tumor had invaded the bone and the duramater. The cut surface was gray-white in color with areas of punctate hemorrhage.

Dr. Stout: This is obviously a fibrous tumor. The cells are all well differentiated and there are plenty of collagen and reticulin fibers between them. This feature is somewhat variable for in some places the cells are more closely placed than elsewhere. The tumor seems well supplied with capillaries. It is obviously an infiltrating tumor because there are striated muscle fibers quite widely separated by tumor tissue. I have only been able to detect one mitotic figure in my Seminar slide but in an earlier one sent me by Dr. Severance I found a few more. None of the cells appears to me to be anaplastic.

Whether one chooses to classify this case as a fibromatosis, as I have done, or a differentiated fibrosarcoma, seems to me purely a matter of taxonomy for, clinically, there is no difference in biological behavior. Both tend to infiltrate surrounding tissues but neither ordinarily will metastasize; I say ordinarily because in either case there is about a one percent chance of metastasis. Whether mitoses can be regarded as an indicator of malignancy I have not yet learned. I tend to be more suspicious if there are many mitoses but, with a growth of this sort, I cannot say whether or not this is justified.

It may be of interest to record the number of cases in our files that have been classified as fibromatoses. Exclusive of pseudosarcomatous fasciitis and keloid, there is a total of 640 cases. Of these, 165 were in children from birth through fifteen years of age. Of all these juvenile cases I know of only one that metastasized. However, some of these children have died or lost extremities because of unchecked infiltrative growth and there have been a few infants born with multiple fibromatoses that survived only briefly after birth because of the involvement of many viscera and bones as well as the superficial soft tissues. About 10 percent of cases have multiple fibromatoses of limited extent. This CANCER SEMINAR case is of great interest because it has invaded the underlying bone and reached the dura. This of course, is most serious because it must be questionable if the excision has removed all of the tumor. A recurrence in the dura may very well be fatal.

Fig. 1 — Roentgenogram of the mastoid region showing soft tissue mass and small bone defect.

Dr. Stout's diagnosis: FIBROMATOSIS (Juvenile).

Histopathologic Diagnoses Submitted by Mail:

Juvenile fibromatosis (colli-desmoid)	95
Fasciitis	7
Low grade fibrosarcoma	53
Rhabdomyosarcoma	8
Others	25

Dr. Regato: With variations in nomenclature, most of the experts agreed to a diagnosis of juvenile fibromatosis. Dr. Dorothy Russell, of London, Dr. Rupert A. Willis, of Leeds, and Dr. Raffaele Lattes, of New York, submitted low-grade fibrosarcoma or so-called aggressive fibromatosis.

Dr. Bricker: We must admit that this is a relatively rare lesion and it behooves us to keep it in mind in considering the nature of all soft tissue tumefactions in children. Excision was adequate and well done. If I were handling the case, I would try to get a microscopic diagnosis before and then plan the surgical approach accordingly.

C. Eckert, M.D., Albany, New York (in Puerto Rico): The surgeon is in the position of a responsible clinician who has to utilize all clinical information which is available in making a decision to approach a tumor of this sort: there is no history of trauma; the slow increase in size is of great importance for this is not in keeping with the course of events in a hematoma.

This lesion was elevating the ear: it was also eroding bone and the surgeon had to decide whether or not he was going to be exceedingly radical and remove a portion of the mastoid process and, conceivably, a portion of the ear. In my own opinion, the best way of making this decision is to have a more certain diagnosis to begin with; so I think a biopsy is very helpful before deciding what treatment should be done. I judge that this particular tumor did not invade the skin, so the sacrifice of a large portion of skin would not probably be necessary in the surgical approach. The decision of whether or not a frozen section should be done is one that depends on the local preferences of the pathologist. I don't think that there is a tremendous urgency in establishing the diagnosis and proceeding at once to removal. Therefore, while I am perfectly happy to have a frozen section done, I would most prefer to hear the pathologist say he would like to look at the paraffin blocks, and perhaps do special stains, and to await this information before carrying out the definitive operation.

Dr. Stout: I know of an instance of a child, who had multiple fibromatosis; he was an infant of seven months when first seen with a fibromatosis of one toe and it was amputated. About eight months later, another growth appeared on a toe of the opposite foot and the toe was amputated. Then the growth appeared on other toes of one foot and eventually the foot was amputated. The child by that time was about three years old and the mother had become weary of successive amputations. The tumor grew into the soft tissues of the remaining foot, including the plantar surface without interference with the activities of the child. The tumor seems now, at age twelve, to be relatively quiescent.

In soft tissue tumors, I heartily support what has been said about biopsy before treatment. Many of these tumors are difficult enough to diagnose on paraffin sections; it would be my opinion that diagnoses would be more accurate if you took the biopsy and then waited for a paraffin section before going ahead with the definitive treatment. Mistakes can be made, perhaps more easily with frozen sections of these tumors than in many other conditions.

A. O. Severance, M.D., San Antonio, Texas: The surgeon who operated on this patient found that the tumor had invaded the skull and the dura mater. I had considerable trouble trying to differentiate between a fibromatosis with some areas that were very cellular with quite a few mitotic figures, and fibrosarcoma. Postoperative radiotherapy was

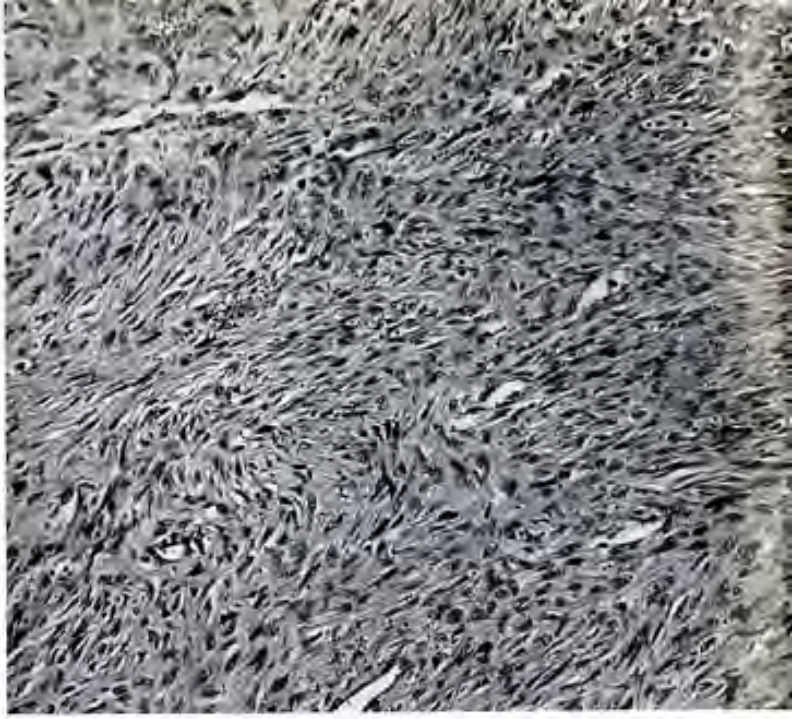


Fig. 2. — Fibromatosis with well differentiated cells and many collagen fibers.

advised by our local surgeon and myself, but the family and Dr. Stout were against it. There is at this time, no evidence of recurrence in spite of the operative findings.

L. Lowbeer, M. D., Tulsa, Oklahoma: Before Dr. Stout pointed out that these lesions do not metastasize, most of them were diagnosed as fibrosarcomas and, if they occurred in the extremities, many were sacrificed unnecessarily.

Dr. Hodes.: In these films, I called attention to the fact that there was erosion of bone: this is one of the things that bothered me.

B. Eisman, M.D., Denver, Colorado: I would like to know what the relationship is between this lesion and the plantar fibromatoses: if this is the same tumor, what percentage of the entire series has occurred on the sole of the foot?

Dr. Stout: It is the same lesion. The fibromatoses in different parts of the body have previously received various names (desmoplastic tumors, etc.) but the proportion is small. Out of the one hundred and sixty-five cases that I have collected, I don't think there would be more than ten plantar fibromatoses and not one of these was malignant; they have all been controlled when the whole plantar fascia was removed, but, if not, almost all recurred locally. The growth might stop spontaneously. I don't know whether it is a good idea to spread this information, but spontaneous arrest was certainly observed in some of the cases that the late Dr. Stevenson followed.

M. Wheelock, M.D., Chicago, Illinois: I cannot conceive that these lesions are similar to plantar fibromatoses, Dupuytren's contractures and Peyronie's disease. We see many Dupuytren's contractures in our hospital; I do not recall seeing one of them recur. I have never seen a plantar fibromatosis recur and I do not recall ever seeing a Peyronie's disease recur. Supposedly, Peyronie's disease, Dupuytren's contractures, and plantar fibromatoses are associated with epilepsy. I wonder whether or not these other fibromatoses are. Has Dr. Stout followed any of these patients with fibromatoses coli into adulthood to see whether they did have greater tendency towards the development of Dupuytren's, Peyronie's, plantar fibromatosis and possibly in women, after pregnancy, desmoid tumors of the abdomen? How many of these individuals that have been followed have tended to recur or have shown definite tendency to malignancy?

I am sure that most of the pathologists have to do frozen sections and we do have to commit ourselves; we have not seen any unnecessary amputations. Usually we play it

cautiously and, unless we are absolutely certain that the lesion is malignant, we prefer to wait for the permanent sections and the special stains.

We do have a case of palmar fibromatosis, or Dupuytren's, in a child who was first operated when about two years of age; he has been operated on three times in the past five years and it continues to recur; it has not extended into bone.

Dr. Stout: Although the histological picture varies, in different parts of the body and from one individual to another, to me they are all benign fibrous growths. I thought that the common name of *fibromatosis* would be appropriate rather than the multiple names that are now being used for them. You have to remember that you see relatively few plantar fibromatosis in children; it must be a very rare lesion. As for a fibromatosis in the palmar fascia in a child, I think that is still rarer.

It's a long time between childhood and middle age and I have not lived long enough to be able to follow these cases for that length of time. You have to raise sons and grandsons in the medical profession to follow on after you die in order to accumulate enough information. These tumors are unpredictable in their behavior. I don't think you can lay down any rule and expect them to follow that rule; some of them will go on and some of them will stop.

In regard to frozen section diagnoses, it seems to me that you only make a positive diagnosis when it is obvious. Under those circumstances, I would be willing to do so. But how often is it so obvious? You can't make a sure diagnosis fairly frequently; I suggest that you get to work on those surgeons and train them to wait for the paraffin sections.

M. Garcia-Palmieri, M.D., San Juan, Puerto Rico: I would like to ask Dr. Hodes if bone erosion is always a sign necessarily of bone invasion?

Dr. Hodes: I think one can tell the difference between bone invasion and bone erosion if you have an adequate examination. This looked like erosion to me.

Subsequent history: Dr. J. V. Blake of Floresville, Texas, reported the boy in good condition in June, 1960.

References

Konwaler, B. E., Keasebey, L., and Kaplan, L.: Subcutaneous pseudosarcomatous fibromatosis (Fasciitis). Am. J. Clin. Path., **25**: 241-252, 1955.

Prior, J. T. and Sisson, B. J.: Dermal and fascial fibromatosis. Ann. Surg., **139**: 453-467, 1954

Shnitka, T., Asp, D. M., and Horner, R. H.: Congenital generalized fibromatosis. Cancer, **11**: 627-639, 1958.

Stout, A. P.: Tumors of the soft tissues. Atlas of tumor pathology. Sect. II, fasc. 5. Washington, D. C., A.F.I.P., 1953.

Stout, A. P.: Juvenile fibromatoses. Cancer, **7**: 953-978, 1954.

2. Benign Solitary Fibrous Mesothelioma of the Pleura with Hypoglycemia

Contributed by J. O. Boley, M.D., Kansas City, Kansas

THE PATIENT was a 55-year-old lady in October, 1958, when she developed mental difficulties, temporarily relieved by the administration of sugar. In the course of a subtotal pancreatectomy for relief of these symptoms, a tumor was felt above the right side of the diaphragm. The serum calcium, potassium, phosphorus and chlorides were all within normal limits; the blood-urea-nitrogen was 6 mg per cent and the blood sugar was 20 mgs per cent.

Dr. Hodes: The roentgen examination of the chest revealed the following: (a) a large soft tissue tumor occupying the lower and posterior portion of the right hemithorax, intimately connected with the pleural surfaces as well as with the right hemidiaphragm, (b) no abnormalities within the soft tissue tumor mass, and no other abnormalities in this patient's thoracic cage.

There is no question but that the patient's hypoglycemia must be connected with the presence of the pulmonary mass. Because the pancreas was operated upon, one must consider the possibility of metastatic pancreatic cancer. However, metastatic pancreatic cancer usually is a more disseminated process with multiple small foci distributed throughout both lung fields rather than a single large solitary focus. In metastatic pancreatic cancer too we have observed very peculiar distention with air of the thoracic esophagus. This is clearly defined in the lateral and oblique projections and in our experience, has only been associated with metastatic pancreatic cancer. In this patient this peculiar abnormality was not present.

The possibility that the lung might be a huge hamartoma was entertained; this was excluded because we have never seen a hamartoma so large. In view of the marked hypoglycemia, one could not escape the possibility of a pulmonary lesion being ectopic insulin secreting pancreatic tissue of congenital origin. We have never seen such a tumor, yet the hypoglycemia forces one to toy with this unique concept.

Dr. Hodes' impression: 1. An insulin secreting MALIGNANT LUNG TUMOR. 2. ECTOPIC PANCREAS with malignant change.

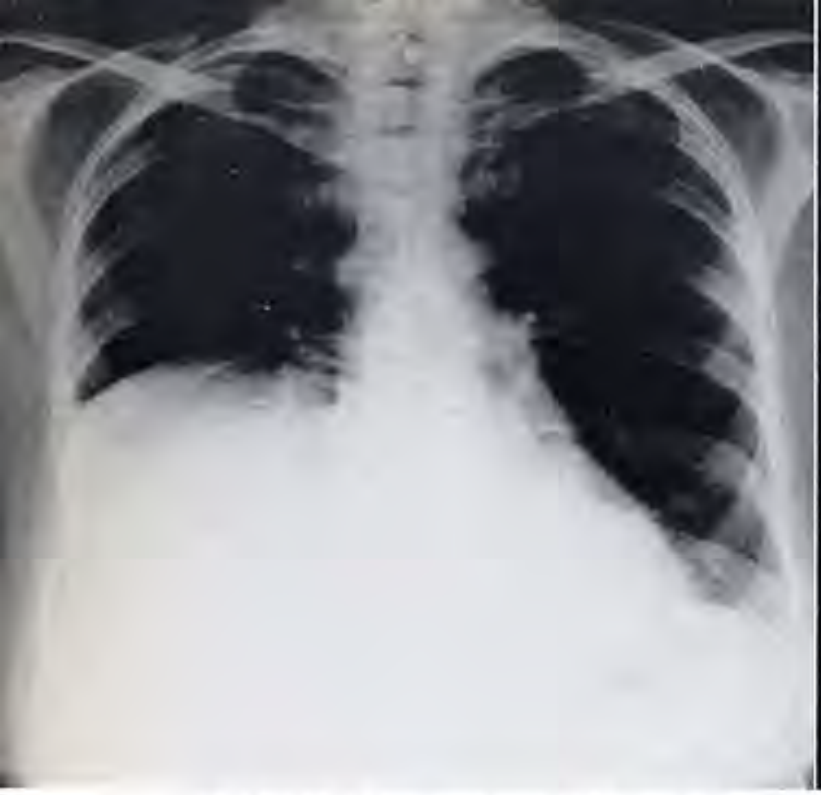
Roentgenologic Impressions Submitted by Mail:

Neurofibroma	24
Metastatic islet-cell tumor	15
Mesothelioma	13
Diaphragmatic tumor	9
Bad pre-operative work-up !	1
Others	42

Dr. Hodes: This lesion was not in the posterior mediastinum where neurofibromas usually are found; or do neurofibromas cause hypoglycemia. The possibility of a mesothelioma was considered clinically and radiologically, but because of the absence of effusion and thoracic pain, this diagnosis was not seriously considered. A diaphragmatic tumor was not considered because they usually present below the diaphragm as well as above the diaphragm and this would have been recognized at operation; in addition, a diaphragmatic tumor probably would have displaced the liver caudad.

Dr. Regato: Dr. Frederick A. Rose, of Cleveland, offered a diagnostic impression of metastatic islet-cell tumor. Dr. Benjamin Felson, of Cincinnati, Dr. Emanuel Salzman, and Dr. Robert McCarver, Jr., of Denver, all submitted mesothelioma.

Operative findings: In January, 1959, a thoracotomy was done: the tumor was adherent to the diaphragm and to the pleural surface of the lower lobe of the lung; it was excised. The mass weighed 1,000 grams, it was apparently encap-



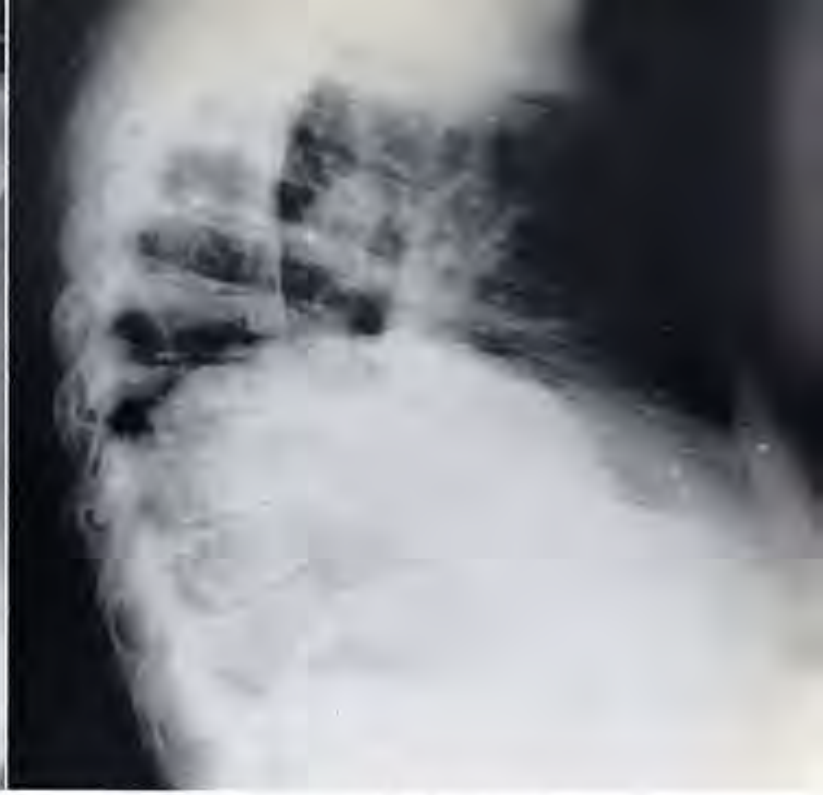


Fig. 1 and Fig. 2 — Soft tissue tumor of the lower and posterior portion of the right hemithorax above the diaphragm.

sulated and coarsely lobulated. The cut section was orange yellow in color with areas of hemorrhage.

Dr. Stout: This tumor is predominantly fibrous. It must be noted however, that the character of the tumor varies markedly from one field to another. Toward the outer zone the collagen fibers predominate, the cells vary from spindle shape to rounded and there are many capillaries and larger vessels scattered through at haphazard. The surface here is covered by a single layer of slightly swollen cells suggesting mesothelial cells. Further from the surface the more fibrous layer gives way to a more cellular one where the cells are predominantly spindle-shaped and grow in interlacing bands. There are also mitoses in this area. Passing through this more cellular zone one comes again to a broad zone of patternless fibrovascular proliferation.

This case is extremely interesting, first because of the morphology of the growth and its explanation, and second because of the possible relationship of this tumor to the hypoglycemia. The major portion of this tumor with its "patternless pattern" and its covering of mesothelial cells is characteristic of a fibrous mesothelioma. Since it was a large tumor in the right hemithorax, was covered with mesothelial cells and apparently gave no symptoms referable to the lungs, it can hardly be anything else but a solitary benign fibrous mesothelioma growing outward from pleural surface into the pleural space. What makes this tumor especially interesting morphologically is the central zone of tissue resembling differentiated fibrosarcoma with mitoses. This suggests a malignant change in the tumor. I do not take this too seriously, however, because among 72 cases classified as benign solitary fibrous mesotheliomas of the pleura I have only seen two others that showed this change and I am not informed that either of them metastasized. There is one arising in the pelvic peritoneum that recurred and had peritoneal implants. It may be of some interest to you to see recorded the distribution and classification of the mesotheliomas on record in the Laboratory of Surgical Pathology of Columbia University as of September, 1959 (Table I).

Of equal importance in this case is the relationship of this tumor to hypoglycemia. For some years now it has been realized that extrapancreatic and extrahepatic tumors may be the cause of hypoglycemia when the pancreas and liver are free from any evidence of an etiological factor. The tumors as far as I am aware have not been epithelial but have always been of mesenchymal origin. In addition to this case we have six other tumors on record in our Laboratory that have been associated with hypoglycemia. Four of them have been reported by various authors. There has been some doubt about the diagnosis expressed in some publications but in my opinion three of them were mesotheliomas, two were hemangiopericytomas and one was a fibrosarcoma. Together with this present case therefore we have four cases of mesothelioma associated with hypoglycemia. Among all of the many bizarre examples of human hormonal activity this extraordinary relationship between occasional extrapancreatic mesenchymal tumors and the occurrence of hypoglycemia seems to me one of the most mysterious. I presume someday

TABLE I

Mesotheliomas Recorded in the Laboratory of Surgical Pathology, Columbia University, 1919-1959

		Benign						Malignant					
		Solitary			Diffuse			Solitary			Diffuse		
	Total	Fibrous	Mixed	Tubular	Fibrous	Mixed	Tubular	Fibrous	Mixed	Tubular	Fibrous	Mixed	Tubular
Pleura	131	59	5	7	3	0	1	26	1	3	13	2	11
Peritoneum	114	13	0	38	1	1	3	7	1	8	4	2	36
Pericardium	12	0	0	1	1	1	3	1	0	0	2	0	3
	257	72	5	46	5	2	7	34	2	11	19	4	50

an explanation will be found but I am sure that at the present time I know of no plausible explanation for it.

Dr. Stout's diagnosis: Benign solitary FIBROUS MESOTHELIOMA of pleura (with hypoglycemia).

Histopathologic Diagnoses Submitted by Mail:

Fibrous mesothelioma	97
Fibrosarcoma	42
Leiomyosarcoma	8
Hemangiopericytoma	8
Others	16

Dr. Regato: Dr. Isaac Costero, of Mexico City, and Dr. Fred Stewart, of New York, and Dr. Fiol, of San Juan, Puerto Rico, also submitted a diagnosis of benign fibrous mesothelioma. Dr. André Pagès, of Montpellier, France, offered "fibrome lamellaire". Dr. Rober Horn, of Detroit, and Dr. Morgan Berthrong, of Denver, were worried by the mitoses. Dr. Carlo Sirtori, of Milan, made a diagnosis of leiomyosarcoma; he explained that retroperitoneal muscle tumors are usually invasive and may metastasize, but that the histological picture may be deceptive.

Subsequent history: The contributor reported that a quantitative analysis of the glycogen utilization by muscle of this tumor revealed a "significant" quantity whereas other tumors tested showed no such effect. The patient was reported relieved of hypoglycemia in September, of 1959: there was no evidence of recurrence.

Dr. Bricker: Surgeons frequently are at the mercy of surgical pathologists; in this situation I have to admit that I have to accept the surgical pathologists' diagnoses, interpretations, prognosis, and everything else. I think that one could palpate a tumor through the diaphragm as he slid his hand up over the dome of the liver; it would be possible to suspect it at the time, but it would be quite possible to miss it also unless it were large. But this one, I would imagine the surgeon could feel it rather easily, yet the presence of the tumor should have been recognized before operation. Perhaps Dr. Stout will tell us, what is the mechanisms of the hypoglycemia? Is it related to hyperinsulinism or is it some other mechanism? And I wonder if there is any differential diagnostic test to be used in the working up of a patient with hypoglycemia that might help one suspect that it might not be due to overfunction of islet cells.

Dr. Stout: In some of these cases, the hormones seem to be definitely formed in the growth because when the growth was removed, the hypoglycemia disappeared; when the tumor recurred, it came back again and when the recurrence was removed, it went away again. That applies to the case reported by Porter and Frantz, an undiagnosed tumor which to my mind, was a hemangiopericytoma. It has been possible once or twice to obtain chemically an active hormone out of the tumor tissue; generally, the trial has failed either because they didn't anticipate that they were going to look for it or because they were slow in getting around to it, or perhaps because it wasn't there. As far as I know, it is just a straightforward hypoglycemia that cannot be differentiated from the islet cell tumor of the pancreas, clinically.

Dr. Regato: These patients' hypoglycemia should be explained either because the tumor itself consumes a greater amount of glycogen or because it produces an insulin-like substance that stimulates a greater consumption of glycogen in the periphery of the body, or because the tumor produces insulin.

L. Lowbeer, M.D., Tulsa, Oklahoma: To my knowledge, there has been only one case reported in which insulin or insulin-like substance was found in such a tumor, a pleuromesothelioma (August). Prior to that, it was believed that these tumors, which are all very large, required a great deal of glucose.

M. Berthrong, M.D., Denver, Colorado: I would like to ask Dr. Stout if stains for the pancreatic islet granules have been applied to this group of tumors?

Dr. Stout: Not in the cases I had a chance to examine. We don't know how to manipulate the granule stains in the islet cells; in Germany, they say they can.

D. L. Alcott, M.D., San Jose, California: A few cases like this were reported from the Cleveland Clinic (Skillern); as I recall, they did granulation stains on them and reported that one case was positive; on that finding they felt that these were ectopic pancreatic islet cell tumors.

F. Buschke, M.D., San Francisco, California: I would like to ask Dr. Stout whether the other tumors with hypoglycemia had a location related to the sympathetic nervous system and whether the hypoglycemia could be due to this involvement (Seckel).

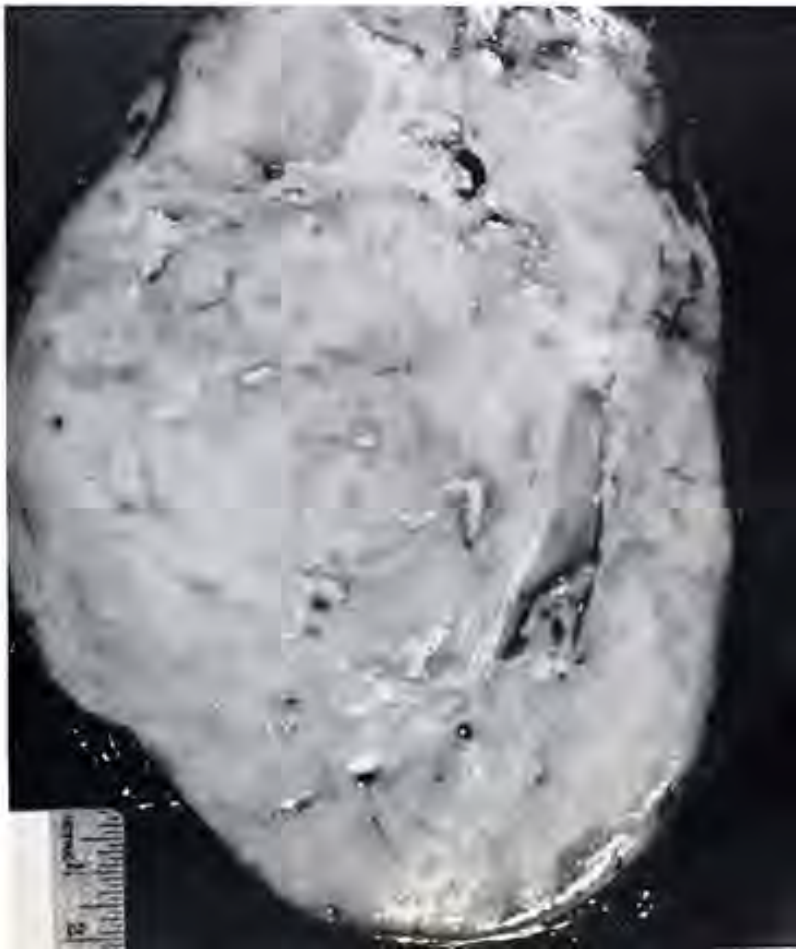
Dr. Stout: This tumor was altogether inside the pleura and this kind of a tumor does not infiltrate; I would guess that this one did not have any such relationship.

E. Murphy, M.D., Mexico City, Mexico: The history reads: "In the course of a subtotal pancreatectomy . . .", from that sentence, I judge that the surgeon did take out a part of the pancreas. We have conjectured, but have not said whether or not there was a tumor of the pancreas.

H. Elmendorf, Jr., M.D.: There is a case remarkably similar to this reported in the Annals of Surgery (Miller). In that tumor, they demonstrated insulin by the consumption of glucose by the diaphragm of the rat. In another case of a large retroperitoneal tumor, the tissue was examined several hours after death, they thought that the insulin was probably destroyed by autolysis.

J. O. Boley, M.D., Kansas City, Kansas: This is the case that was reported in the Annals of Surgery. Practically all the pancreas was removed but the pathologist was unable to find any tumor: the surgeon somewhat in desperation, got his hands above the liver and felt the diaphragm. Later the chest roentgenogram was taken. The tumor did not have

Fig. 3 — Encapsulated mass with small areas of hemorrhage.



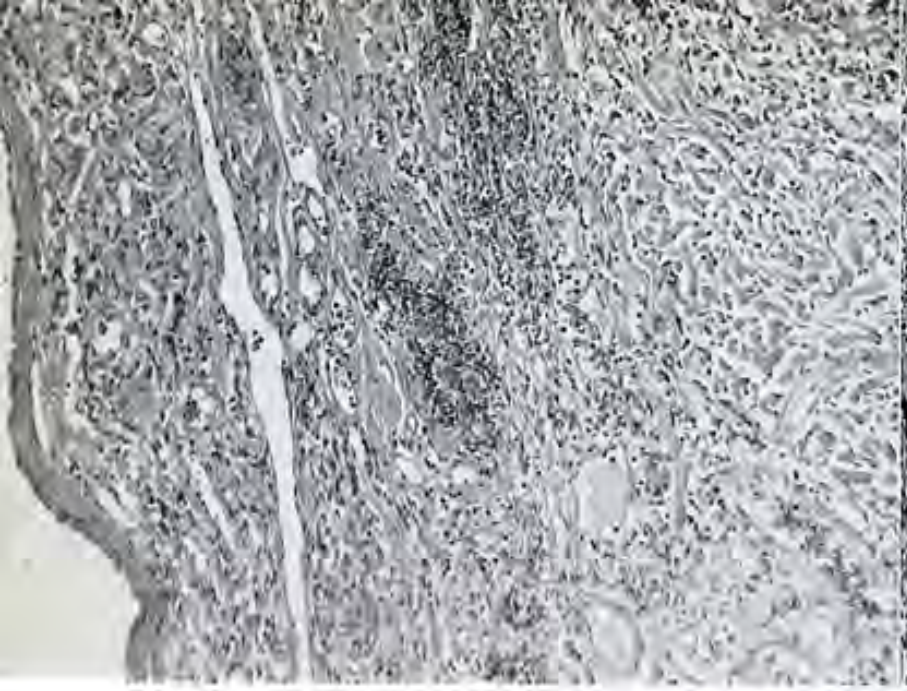


Fig. 4 — Fibrous mesothelioma with haphazard arrangement of cells, fibers, and vessels.

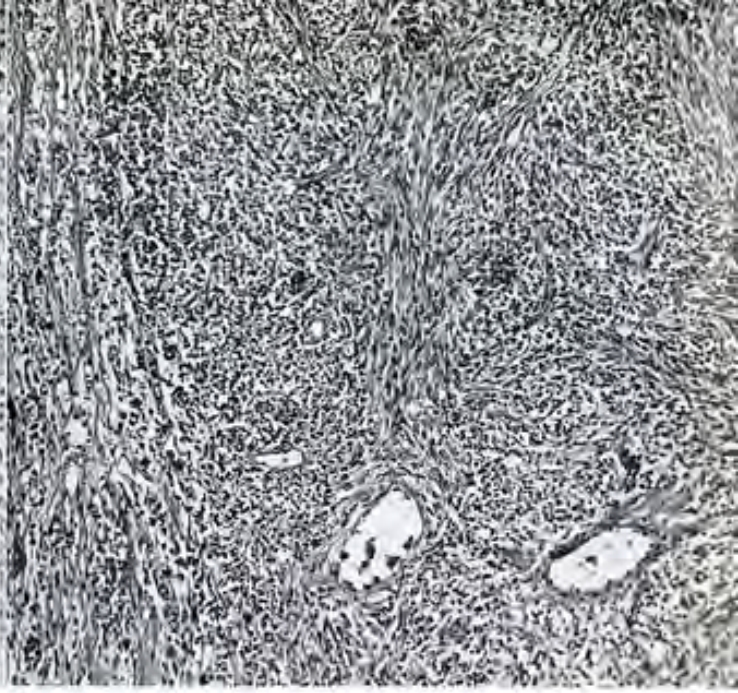


Fig. 5 — Deeper and more cellular part of mesothelioma.

insulin in it. It produced a glucose utilization as shown by the animal study.

I. Costero, M.D., Mexico City, Mexico: From a histologic point of view, mesotheliomas interest me among most tumors because of my work in the field of diseases grouped under the name of collagen diseases. Mesotheliomas offer an opportunity for the adequate study of collagen in tissue cultures. (Dr. Costero delighted the audience by the projection of photomicrographs with various stains including del Rio-Hortega stains to demonstrate different facets of collagen formation by mesotheliomas.)

C. Eckert, M.D., Albany, New York (in Puerto Rico): It is more common to have insulin producing tumors of the pancreas as causes of hyperinsulinism, but, on the other hand, there have now been reported a total of 12 cases like this and there must be many others that are not reported: so we are going to be considering this possibility more and more in the future. I used to think that fibrous mesotheliomas of the pleura were very rare tumors, but in the last three years, in Albany, we have had four. Certainly it is not as rare as I thought.

Dr. Hodes: Were these asymptomatic tumors, how large were they? Two things we look for in these patients: pain and some effusion. The more cases we see the less frequently we see these symptoms.

C. Eckert, M.D., Albany, New York: None of these four cases had symptoms which we could attribute to the tumor. They were found on routine chest roentgenograms.

Dr. Stout: In the cases that I have observed, of this benign fibrous type of mesothelioma, the patients generally had no symptoms at all and the tumor was discovered by chance. Sometimes the tumors are enormous, occupying half of the hemithorax, and these people didn't even have a cough or any kind of symptom.

T. M. Peery, M.D., Washington, D.C. (in Puerto Rico): We have run into other secondary effects of neoplasms of which I was totally unaware. One is *polycythemia* which occurs with leiomyomas of the uterus, another is *hypoproteinemia* that occurs with giant rugal hypertrophy of the stomach. If we applied more laboratory procedures to some of these neoplasms we could learn of some of these associations which may help us diagnose them.

Dr. Regato: There is also the association of *anemia* or *polycythemia* with kidney tumors.

V. M. Arean, M.D., Gainesville, Florida (in Puerto Rico): These neoplasms obviously do not produce insulin but insulin-like substances.

F. Reyes, M.D., San Juan, Puerto Rico: We have a case of a patient who died in hypoglycemic shock and at autopsy she had a huge nodular liver-cell carcinoma.

M. Garcia-Palmiere, M.D., Santurce, Puerto Rico: There is a report in the Archives of Internal Medicine (McFadzean) on a series of twenty-seven patients with primary hepatomas, a third of which had hypoglycemia.

M. Lougheed, M.D., Montreal, Canada (in Puerto Rico): I would like to ask Dr. Stout the incidence of calcification in these fibromesotheliomas.

Dr. Stout: I think it is very rare. I can only remember one in which there was demonstrable calcification roentgenologically. I think, occasionally, there are small foci in the tumor that don't show up roentgenologically. The fibrous mesotheliomas that project out into the pleural cavity or into the fissures without invading the lung, are almost invariably benign tumors. There is a malignant variety of fibrous mesotheliomas which invades the lungs and I imagine that they have been largely called sarcomas; but they are definitely fibrous mesotheliomas, as has been shown by tissue culture.

M. Garcia-Palmiere, M.D., San Juan, Puerto Rico: A case was presented at one of our conferences which turned out to have a retroperitoneal fibrosarcoma with hypoglycemia; there was extensive calcification visible on the roentgenograms.

R. Cox, M.D., San Juan, Puerto Rico: I have seen two of these fibrous mesotheliomas invade the chest wall so deeply in the lung that they are essentially unresectable. Has any one treated them with radiations?

M. Friedman, M.D., New York City (in Puerto Rico): I have irradiated approximately twenty pleural mesotheliomas; doses required are 4,000 to 5,000 roentgens (tumor dose) in about five to seven weeks. The great difficulty is the technical one of administering this dose to the peripheral thoracic cavity without giving the patient a radiation pneumonitis. The best way to approach the problem is to have the surgeon remove the entire lung first and decorticate the parietal pleura, then follow that with irradiation.

P. Lovett, M.D., Wichita, Kansas (in Puerto Rico): We have a patient with mesothelioma of the abdomen that had required some 120 abdominocentesis in the course of two years; it was ultimately treated with radioactive gold and he has remained well for seven or eight years with no fur-

ther abdominocentesis. In another case of mesothelioma following several postoperative recurrences, I tested the sensitivity of a subcutaneous nodule: after a single dose of 300 roentgens there was detectable reduction of the mass on the second day, and on the third day, it was completely gone; we could find no traces in a week. We treated another postoperative recurrence in a Chinese woman more than a year ago; we didn't carry the dose to such a high level as Dr. Friedman; we stopped in the order of 3,500 roentgens in a period of about eight weeks and she is all right.

References

August, J. T. and Hiatt, H. H.: Severe hypoglycemia secondary to a non-pancreatic fibrosarcoma with insulin activity. New Engl. J. Med., **258:** 17-20, 1958.

Dockerty, M. B.: Tumor Seminar, Case 11, Hypoglycemic tumor of kidney. Texas J. Med., **54:** 237-238, 1958.

Holten, C.: Hypoglycemia-inducing tumor resembling spindle-cell sarcoma. Acta Med. Scand., **157:** 97-102, 1957.

Howard, J. W. and Davis, P. L.: Retroperitoneal hemangiopericytoma associated with hypoglycemia and masculinization. Delaware Med. J., **31:** 29-34, 1959.

McFadzean, A. J. S. and Tse Tse, Y.: Hypoglycemia in primary carcinoma of the liver. AMA Arch. Intern. Med., **98:** 720-731, 1956.

Miller, D. R., Bolinger, R. E., Janigan, D., Crockett, J. E., and Friesen, S. R.: Hypoglycemia due to nonpancreatic mesodermal tumors. Ann. Surg., **150:** 684-696, 1959.

Nesbit, K. A., Boswell, J. T., DeJesus-Gonzales, M. A., and Sarkisian, S. S.: Malignant mesothelioma associated with hypoglycemia. Amer. J. Clin. Path., **30:** 148-157, 1958.

Porter, M. R. and Frantz, V. K.: Tumors associated with hypoglycemia, pancreatic and extra pancreatic. Amer. J. Med., **21:** 944-961, 1956.

Scholz, D. A., Woolner, L. B., and Priestley, J. T.: Spontaneous hypoglycemia associated with fibrogenic tumor: report of two cases. Ann. Intern. Med., **46:** 796-807, 1957.

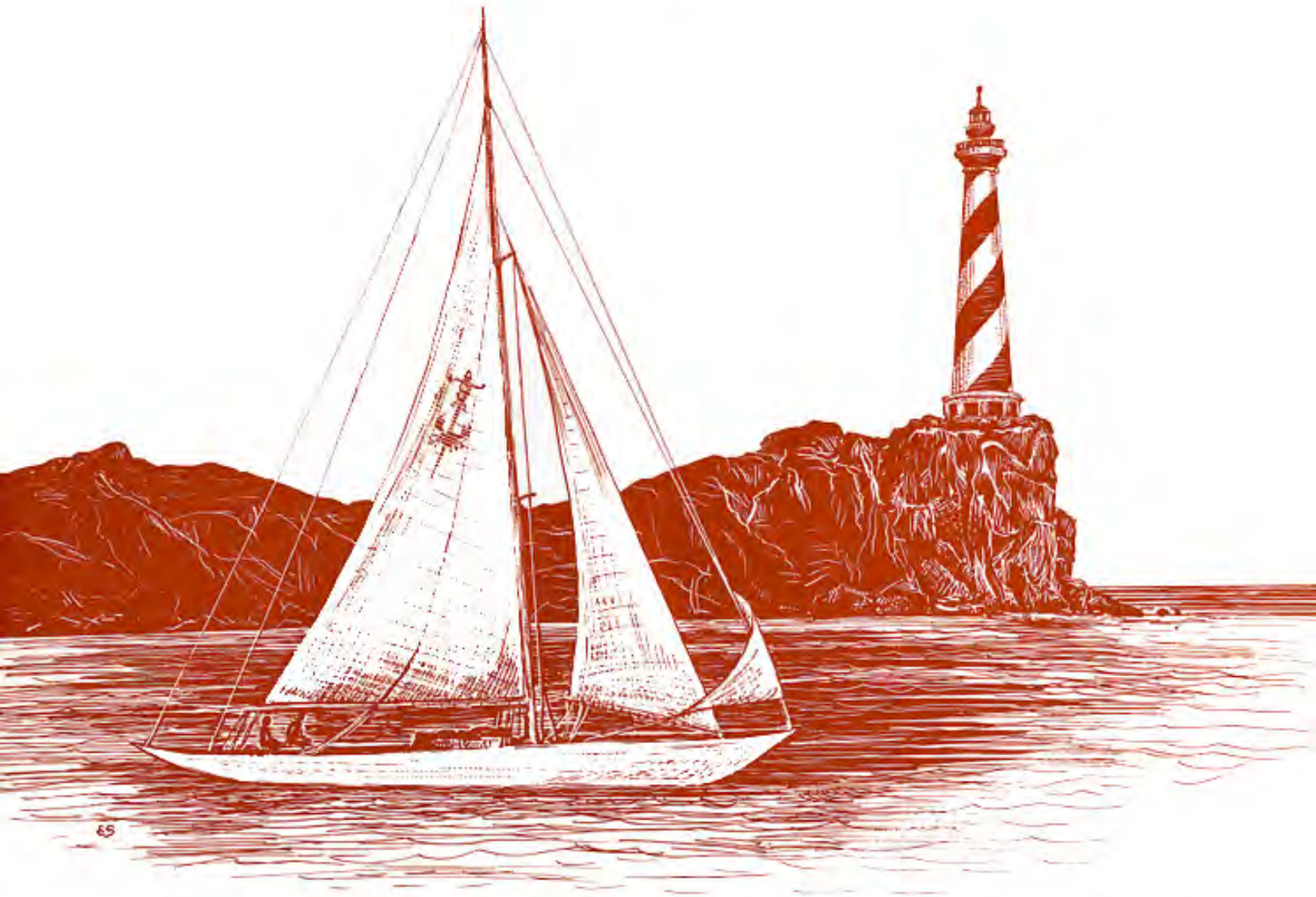
Seckel, H. P. G.: Post mortem glycogenolysis in hyperinsulinism and glycogen disease. J. Clin. Invest., **18:** 723, 1939.

Sellman, J. C., Perkoff, G. T., Null, F. C., Kimmel, J. R., and Tyler, F. H.: Hypoglycemia associated with massive intra-abdominal mesothelial-cell sarcoma. New Engl. J. Med., **260:** 847-852, 1959.

Silvis, R. S. and Simon, D. S.: Marked hypoglycemia associated with non-pancreatic tumors. New Engl. J. Med., **254:** 14-17, 1956.

Skillern, P. G., McCormack, L. J., Hewlett, J. S., and Crile, G. Jr.: Hyperinsulinism due to islet-cell tumors simulating sarcoma; a report of two cases of large tumors composed of round and spindle cells associated with hypoglycemia. Diabetes, **3:** 133-140, 1954.

Stout, A. P.: Les mesothéliomes de la plèvre, du peritoine et du péricarde. Sem. des. Hop. Paris (Arch. d'Anat. Path.) **30:** A115-A119, 1954.



3. Malignant Tumor of the Mediastinum (Dysgerminoma?)

Contributed by A. L. Ingerick, M.D., Colorado Springs, Colorado and
Alexis E. Lubchenco, M.D., Denver, Colorado

THE PATIENT was a 27-year-old woman in May, 1958, when she complained of cough, dyspnea, and pain in the left side of the chest. She was six months pregnant. Her hemoglobin was 9.4 grams per cent and there were 19,000 white cells per cubic mm. Bronchoscopy revealed occlusion of the left main stem bronchus apparently by extrinsic pressure. Bronchial washings were negative for neo-plastic cells.

Dr. Hodes: The roentgen examination of the chest revealed the following: (a) a large soft tissue mass of uniform density behind the heart in the left lower lobe, (b) no abnormalities in the surrounding lung, (c) the margins of the mass were sharp and clear-cut and no calcific debris or lipoid elements were discernible within the mass, (d) there was no evidence of pleural reaction.

It would be rare indeed for a patient 27 years of age with negative bronchial washings to have a primary bronchial carcinoma. It would be equally unusual to find an active inflammatory lesion of the lung so clearly demarcated and without changes in the perifocal lung. The history of pain, cough, and dyspnea all suggest the presence of an aggressive pulmonary tumor.

According to the history, this patient was pregnant; there exists the possibility, however, that instead of being pregnant the patient had a uterine tumor, perhaps even a choriocarcinoma. Were this the case, the solitary pulmonary lesion could be a solitary "cannon-ball" metastatic focus. If the patient were truly pregnant, there is no reason why the pulmonary lesion might not be metastatic from a primary tumor arising in the ovaries, the fallopian tubes, or in the wall of the uterus itself.

Solitary pulmonary sarcomas occur. The latter may be benign or malignant arising from any of the tissues normally encountered in lung including fat, fibrous tissue, etc. Primary lymphosarcomas of the lung have also been described including such unusual regions as the "benign" solitary pulmonary sarcoma, classically a homogeneous lesion which lies within the lung parenchyma.

Dr. Hodes' Impression: MALIGNANT TUMOR of the lung: 1. Primary pulmonary SARCOMA. 2. Metastatic CHORIOCARCINOMA.

Roentgenologic Impressions Submitted by Mail:

Neurogenous tumor	17
Teratoma	16
Mediastinal tumor	15
Bronchial cyst	13
Sequestration of lung	10
Choriocarcinoma	6
Others	35

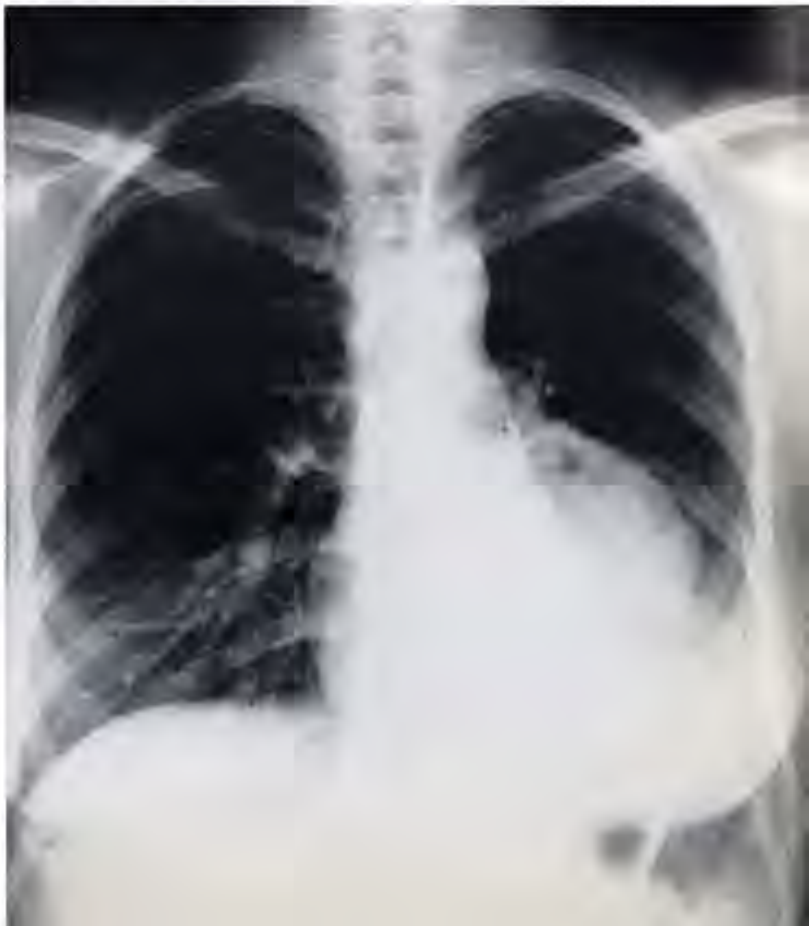
Dr. Hodes: Neurogenic tumors are more commonly situated in the posterior mediastinum; not infrequently they are associated with changes in the overlying bone. Teratomas commonly lie in the midline and contain teeth, fat, etc. Bronchial cysts usually are not this large and far more commonly lie toward the periphery. Any pulmonary mass which is sharply demarcated might prove to be sequestration; usually, however, they are more dense and commonly reveal secondary infection.

Dr. Regato: Dr. P. Swenson, of St. Paul, Minnesota, and Dr. A. Tucker, of Cleveland, suggested a sequestrated lung; Dr. B. Felson preferred a sarcoma of the lung and Dr. J. M. Dennis, of Baltimore, a neurogenous tumor. Dr. V. J. Fish, of San Francisco, offered teratoma and Dr. W. P. Stampfli, of Denver, chorioepthelioma.

Operative findings: In June, 1958, a thoracotomy was done, a tumor was found in the left lower lobe; a lobectomy with removal of hilar nodes was carried out. On cut section the tumor appeared encapsulated and measured 7 cm in diameter.

Dr. Stout: This tumor is composed of cords of moderately large rounded cells which occasionally are large enough to have three nuclei. The cells in the cords are not associated with any fibers but there are delicate fibrovascular septa separating the cords one from another producing an almost organoid effect. The cells show no evidence of secretory activity, there are no intracellular granules—indeed the cytoplasm is so scanty and inconspicuous that it is hard to detect. I could not find any mitoses after searching 35 high power fields. The tumor seems encapsulated. In the capsules and

Fig. 1 — Large, soft tissue mass behind the heart.



outside of it there are a great many blood and lymphatic vessels. Some veins and lymphatics contain tumor cells.

If this tumor lay behind the heart it was probably in the posterior mediastinum and since it pressed upon a bronchus it must have been relatively large. It does not look like any of the neurogenous tumors of the posterior mediastinum. The somewhat organoid arrangement might suggest non-chromaffin paragangiloma but the cells are quite different. I can't seriously consider reticulum cell sarcoma or any of the other malignant lymphomas. Since it is possible to find malignant teratomas in the posterior mediastinum (Schlumberger) and since one element of a malignant teratoma can outgrow all of the others and appear to be the only tumor type, we might suggest that that has occurred here. If this is so, we must suggest what kind of a tumor it is. Could it be either seminoma or dysgerminoma? It does not look like either of these tumors for almost invariably there is more tissue containing lymphocytes between the cell cords. If we exclude those two tumor types we also exclude the possibility of this tumor being a thymoma of the seminoma type situated in the posterior mediastinum. Iverson recognizes this as a thymoma type and we have three such cases in anteriorly placed thymomas. It will also exclude the possibility that this is a metastasis from a dysgerminoma of the ovary. Speaking of metastases recalls to my mind the case of granulosa cell tumor of the ovary, metastatic to the mediastinum, which was in the Third Annual Penrose Cancer Seminar in 1931 (Rigler). But this present case does not suggest a granulosa cell tumor.

We have not exhausted the possibility of an undifferentiated carcinoma arising in a misplaced teratoma and obliterated by it nor have we excluded the possibility that this is a metastatic tumor. It might be a metastasis from a malignant melanoma or an undifferentiated carcinoma from some focus in the body but I am at a loss to know from whence. Beyond these suggestions I have nothing pertinent to offer.

Dr. Stout's diagnosis: MALIGNANT TUMOR (type?) of mediastinum.

Histopathologic Diagnoses Submitted by Mail:

Dysgerminoma (seminoma)	44
Choriocarcinoma	23
Malignant lymphoma	23
Ganglio-, neuro-, sympathicoblastomas	22
Embryonal rhabdomyosarcoma	12
Undifferentiated carcinoma	12
Teratoma	3
Others	30

Dr. Regato: Dr. Fred Stewart, of New York, submitted a diagnosis of ganglionic neuroblastoma; Dr. J. French, of Ann Arbor, offered malignant paraganglioma. Dr. Font-Menéndez, of Havana, favored sympathicogonioma. Dr. Alvin O. Severance, of San Antonio, preferred malignant granular-cell myoblastoma. Dr. Morgan Berthrong, of Denver, proposed sub-coelomic mesenchymal sarcoma. Dr. Lauren Ackerman, of St. Louis, Dr. Leo Lowbeer, of Tulsa, and Dr. Luis E. González, of San Juan, Puerto Rico, offered metastatic dysgerminoma.

R. Horn, M.D., Detroit, Michigan (by mail): Probable embryonal rhabdomyosarcoma; I try hard not to make this diagnosis on slight provocation and in this instance I can not find cross-striations. One alternative is a mixture of dysgerminoma with embryonal carcinoma.

Subsequent history: In August, 1958, the patient's baby was delivered by Cesarean section. In September, 1958, she expired. Postmortem examination revealed that the pelvis was occupied by a single large mass adherent to the walls; that this was an ovarian mass could not be proven beyond doubt. There were extensive pulmonary metastases and also metastases to the bones and adrenals, most viscera being actually replaced by tumor.

M. Berthrong, M.D., Denver, Colorado: At the autopsy, this mass occupied a large area of the pelvis, both ovaries

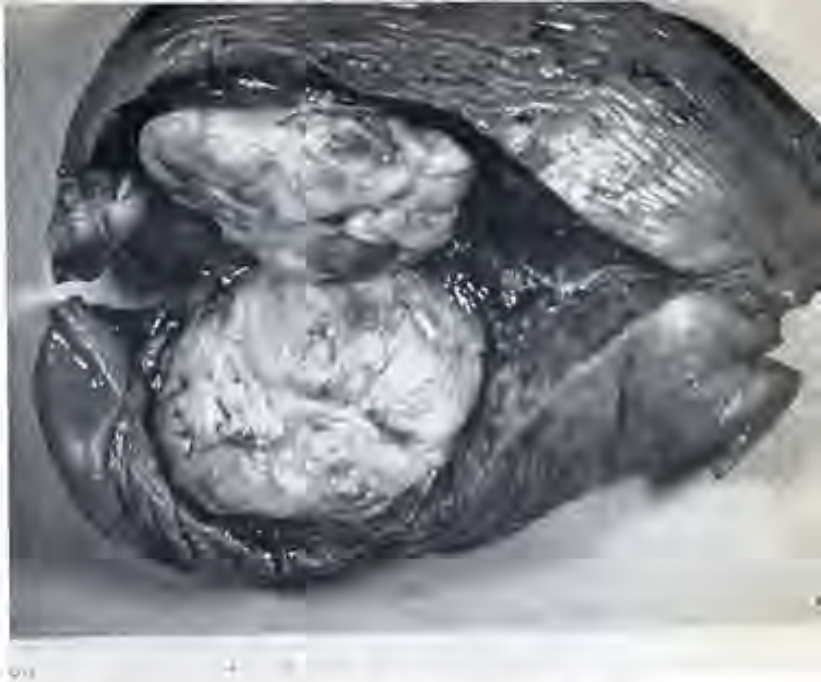


Fig. 2 — Well delineated tumor within lower lobe of left lung.

were involved by it, but it was our feeling that perhaps they were involved secondarily: we couldn't rule out the possibility of a primary in the ovary, but we thought that it was perhaps more likely from the broad ligament or some other area in the pelvis. The uterus was completely free of tumor. The microscopic appearance of the tumor was much the same everywhere, although in some areas there were many more of those giant cells. There were no gland spaces formed anyplace and no teratomatous elements. We tried to make it a choriocarcinoma but found it impossible to do so. Dysgerminoma? We never found small cell infiltration of any consequence along with the tumor cells. We wonder if this could be a subcoelomic tumor.

Dr. Bricker: I suppose this patient was examined throughout her pregnancy and nothing abnormal was palpated in her pelvis; I wonder if the diagnosis was suspected or made at the time of the Cesarean section. I do agree with the pulmonary resection done at six months pregnancy in order to determine the nature of the lesion and to rid the patient of it; it might have been a much more favorable lesion.

M. Wheelock, M.D., Chicago, Illinois: Two of the members of our faculty are on the Ovarian Tumor Registry and for the past ten years, we have been able to see these tumors as they come through. I can recall absolutely no case in that group which even compares with this. Dysgerminoma can be associated with pregnancy and a woman can carry her pregnancy all the way through with the dysgerminoma: I have seen three cases of it. I weighed the possibility of a choriocarcinoma, and I thought that in the periphery there were cells that looked like histioblasts. But when I summed it all up, I assumed that the tumor originated in the posterior mediastinum and, on the basis of the widespread distribution of the metastases as well as the histologic picture, I made a diagnosis of sympathicoblastoma; I don't think that I can be convinced that it isn't.

C. Anthony, M.D., Denver, Colorado: We examined this tumor when it was removed from the lung and we called it a leiomyosarcoma. At the time that the Cesarean section the obstetrician did not find anything in the pelvis: he found a slight thickening of the left broad ligament but the ovaries were free at that time.

Dr. Stout: Under these circumstances, I would revise the possibility that the tumor *is* a dysgerminoma but I do not feel sure enough to do more than suggest it.

R. Marcial-Rojas, M.D., San Juan, Puerto Rico: I submitted a diagnosis of dysgerminoma for the reason that she was 27 years of age, she was pregnant and the tumor looked

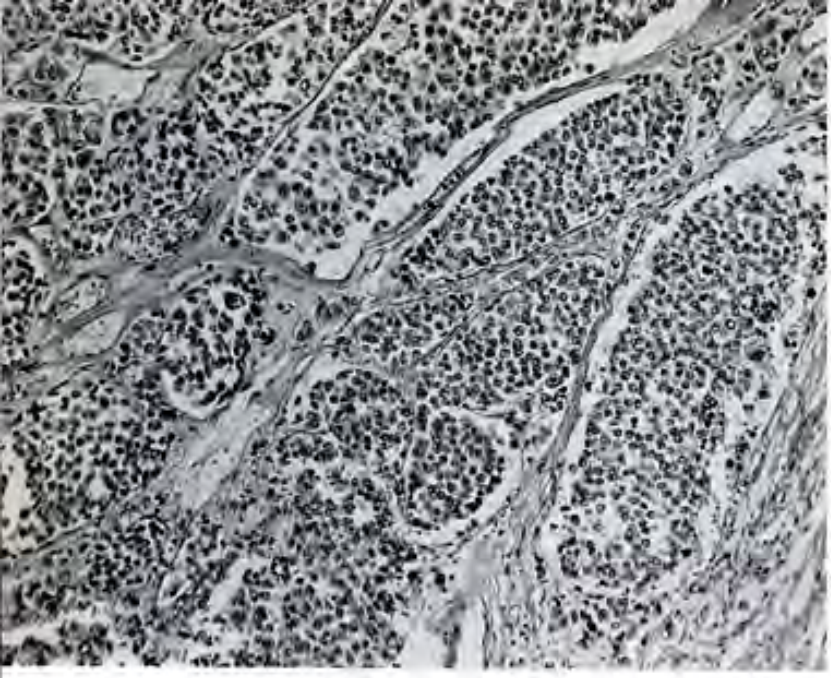


Fig. 3—Clearly defined cords of cells suggesting dysgerminoma.

somewhat like a metastatic dysgerminoma. I found out from the literature that the most frequent ovarian tumor associated with pregnancy is dysgerminoma.

C. Bagshaw, M.D., San Francisco, California (in Puerto Rico): Whenever we have been faced with a single tumor in the lung which appears as though it might be a metastatic lesion, we have uncovered other smaller metastases by doing laminagrams of the chest on both sides. It is surprising how many small metastases can be seen by doing laminography that can't be seen on plain films.

Dr. Hodes: Even better than that is the use of high voltage roentgenograms.

References

Ober, W. B. and Black, M. B.: Neoplasms of the subcoelomic mesenchyme. AMA Arch. Path., 59: 698-705, 1955.

Iverson, L.: Thymoma. A review and reclassification. Amer. J. Path., 32: 695-719, 1956.

Rigler, L. G.: Metastatic granulosa cell tumor. Cancer Seminar, 1: 83-84, 1952.

Schlumberger, H. G.: Tumors of the mediastinum. Sect. V., Fascicle 18, Atlas of Tumor Pathology, Armed Forces Institute of Pathology, 1951, Washington.

4. *Liposarcoma of the Retroperitoneal Space*

Contributed by C. Alexander Helwig, M.D. and Emmet N. McCusker, M.D.
Halstead, Kansas

THE PATIENT was a 51-year-old lady in February, 1955, when she noticed a mass in her right flank. Examination revealed a tumor 10 x 12 cm in diameter in the right upper abdominal quadrant; the hemoglobin was 10 grams per cent and the hematocrit 37 per cent; NPN was 34.5 mg per cent, and the sedimentation rate was 106 mm.

Dr. Hodes: The roentgen examination of the abdomen revealed the following: (a) the hepatic flexure and proximal half of the transverse colon are depressed by a soft tissue mass in the right upper abdomen, (b) the right ureter is displaced medially; it also reveals encroachment upon it anteriorly, (c) the iliopsoas muscle is fairly well outlined above; its details are obliterated along the lower half, (d) the tumor mass is dense and somewhat irregular in configuration. It does not have the smooth contour of a cyst; nor is it as round as a cyst, (e) the tumor itself is very dense and contains a liberal amount of fibrous tissue and perhaps even nerve tissue. No calcific abnormalities are noted within the tumor mass to suggest necrosis or phleboliths.

This is an obvious tumor arising in the lower portion of the retroperitoneal structures; it has displaced the ureter medially yet at the same time reveals evidence of encroachment upon the ureter along its anterior surface. The manner in which it has displaced the hepatic flexure and the transverse colon is consistent with the presence of a retroperitoneal tumor. The incidence of retroperitoneal tumors being almost twice as high in women as in men, this also is consonant with the presence of a retroperitoneal mass.

Dr. Hodes' impression: A MALIGNANT RETROPERITONEAL TUMOR extending well anteriorly into the abdomen: 1. FIBROSARCOMA. 2. LIPOSARCOMA with a great deal of fibrous tissue within it.

Roentgenologic Impressions Submitted by Mail:

Retroperitoneal sarcoma	40
Neurogenous tumor	11
Renal tumor	10
Various benign tumors	15
Various malignant tumors	9
Others	16

Dr. Hodes: Neurogenous tumors are more commonly situated closer to the spine and not infrequently affect bone. A retrograde study of the right kidney revealed no evidence of intrinsic disease. The presence of a mass plus the anemia and rapid sedimentation all suggest a malignant tumor rather than a benign one.

Dr. Regato: Dr. B. Felson, of Cincinnati, Dr. A. Tucker, of Cleveland, and Dr. Paul M. Kroening, of San Francisco, all submitted retroperitoneal sarcoma. Dr. E. Salzman, of Denver, qualified it as retroperitoneal liposarcoma.

Operative findings: In February, 1955, the patient was surgically explored: a large retroperitoneal mass was found attached to the lower pole of the right kidney; the tumor and the kidney were both removed. The tumor measured 6 x 8.5 cm, it was firm and was covered by a fibrous capsule; cut section revealed a yellowish color. A necrotic lymph node was removed from the vicinity of the ligamentum gastrocolicum. Post-operative roentgentherapy was administered: 1,000 roentgens were delivered to the skin of each of two large right upper abdominal fields in about two weeks.

Dr. Stout: This lesion is composed of fibrous tissue, normal adipose tissue and a great many large cells with frequent pyknotic nuclei found both among the fat cells and in the fibrous areas. Some of these cells have vacuoles both in the cytoplasms and sometimes in the nuclei. Rarely there are minute myxoid areas in the fat. Mitoses were not detected by me.

I like to classify a tumor such as this as a liposarcoma of the well differentiated type. If the whole tumor is composed of similar tissue, metastasis need not be expected. However, the tumors of this sort are usually large and tend to show progressive infiltrative growth, hence excision is usually inadequate and local recurrence is common following attempted removal. Further, one can have no assurance without multiple sections that some other part of the tumor may not have a more malignant aspect and give rise to meta-

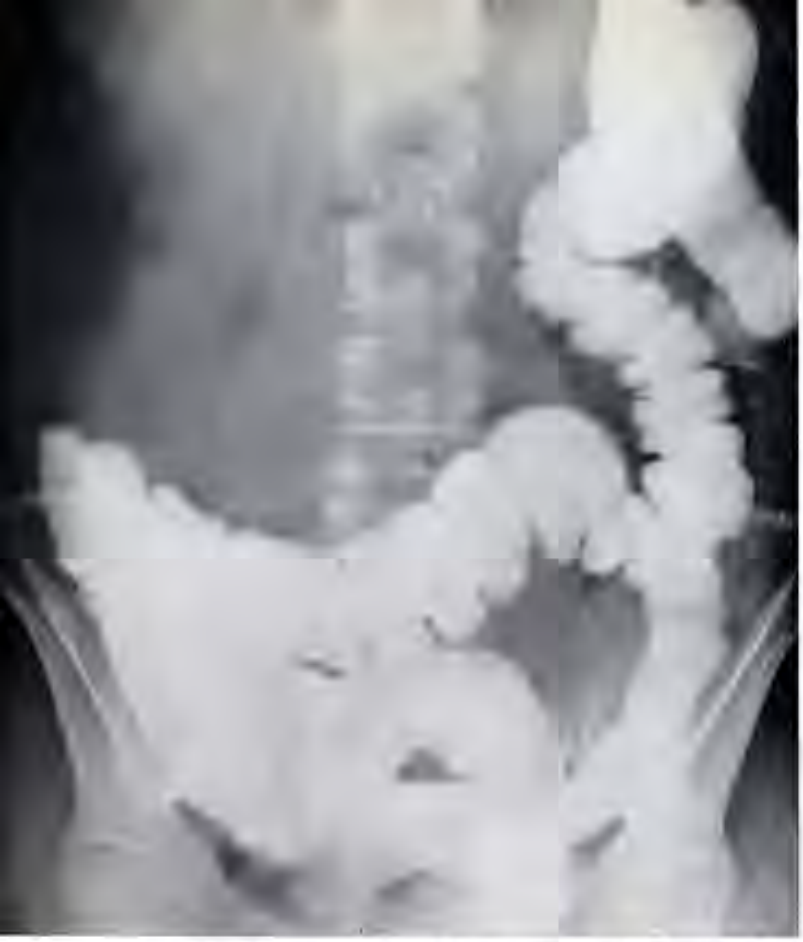


Fig. 1 — Soft tissue mass of right upper abdominal quadrant displacing hepatic flexure.

stases. For these reasons, I think it is well to call these tumors differentiated liposarcomas rather than fibromyxolipoma or some similar compound label signifying that the tumor is benign. Such tumors are common in the retroperitoneum and it is well known that the perirenal region is a favorite site for them to be found.

Dr. Stout's diagnosis: LIPOSARCOMA (differentiated).

Histopathologic Diagnoses Submitted by Mail:

Liposarcoma	92
Fibrosarcoma	23
Rhabdomyosarcoma	14
Malignant mesenchymoma	13
Others	27

Dr. Regato: Dr. Carlo Sirtori, of Milan, and Dr. Estéban Moreno, of San Juan, also made a diagnosis of differentiated liposarcoma. Dr. R. Hirtzler, of Yugoslavia, submitted a diagnosis of fibroliposarcoma. Dr. F. Bang, of Copenhagen, offered hemangioendothelioma invading fat tissue. Dr. Rupert Willis, of Leeds, preferred fibrolipoma.

Subsequent history: By April, 1956, the patient presented a recurrent mass beneath the surgical scar. In October, 1956, roentgentherapy was administered again in the form of 1,500 roentgens in about two weeks to the skin of each of two large right upper abdominal fields. In March, 1957, the tumor had grown, an additional short series of roentgentherapy was instituted apparently without result for the patient was operated again in May, 1957. Four large masses were removed which measured 28, 23, 13, and 5 cm in their respective greater diameter; they had smooth surfaces and were apparently encapsulated; the cut surface revealed a grayish-white to yellowish color.

In August, 1958, the patient appeared free from recurrence but had vaginal bleeding. A carcinoma of the cervix was diagnosed and treated by roentgentherapy and curietherapy. In July, 1959, the patient appeared in good health and without evidence of recurrence or metastases.

Dr. Bricker: Retroperitoneal tumors are an interesting and distressing group. The frozen biopsy is extremely helpful if it can show, without equivocation, that it is a carcinoma or a lymphosarcoma and not a fibrosarcoma or a liposarcoma. This may distinctly help in the surgical approach to the lesion; then we are faced with the problem of trying to determine exactly how extensive the lesion is. Sometimes, the limits of the tumor are extremely poorly defined. Liposarcomas, in particular, do not always present with a semblance of encapsulation; they can be diffuse and it may be impossible to tell exactly just how far one should go. Some of them can be resected with a fair degree of satisfaction.

Should all patients who have a liposarcoma resected from the retroperitoneal space, even though it appears to be a satisfactory resection, be submitted to postoperative irradiation? There is no question that they are sensitive, many of them quite sensitive, to irradiation. I rather feel one should irradiate because the adequacy of resection is so uncertain. In that regard, I think the surgeon should keep in mind that he would do well to mark the limits of the tumor during the course of the operation by means of silver clips, for this could be a distinct help to the radiotherapist in determining how to plan the radiotherapeutic approach.

L. Lowbeer, M.D., Tulsa, Oklahoma: An interesting sidelight to these tumors is that they can grow to a tremendous size and at the same time maintain their metabolism of the malignant fat cells at the expense of the normal fat cells of the body so that there are cases on record when the tumor weighed far more than the rest of the patient. Since some of them are radiosensitive, if a diagnosis has been established, preoperative irradiation has been frequently used to make them operable.

Dr. Regato: There is also a question of how the radiotherapy is administered. In this instance, the initial treatment consisted of rather small amounts of radiations; as a consequence, there was recurrence and the treatment had to be repeated; this carries disadvantages, for radiotherapy cannot be repeated indefinitely. It is better to plan one single treatment with a larger dose and with the certainty that all of the tumor is included in the field, rather than give a few roentgens as a gesture to an inadequately planned field.

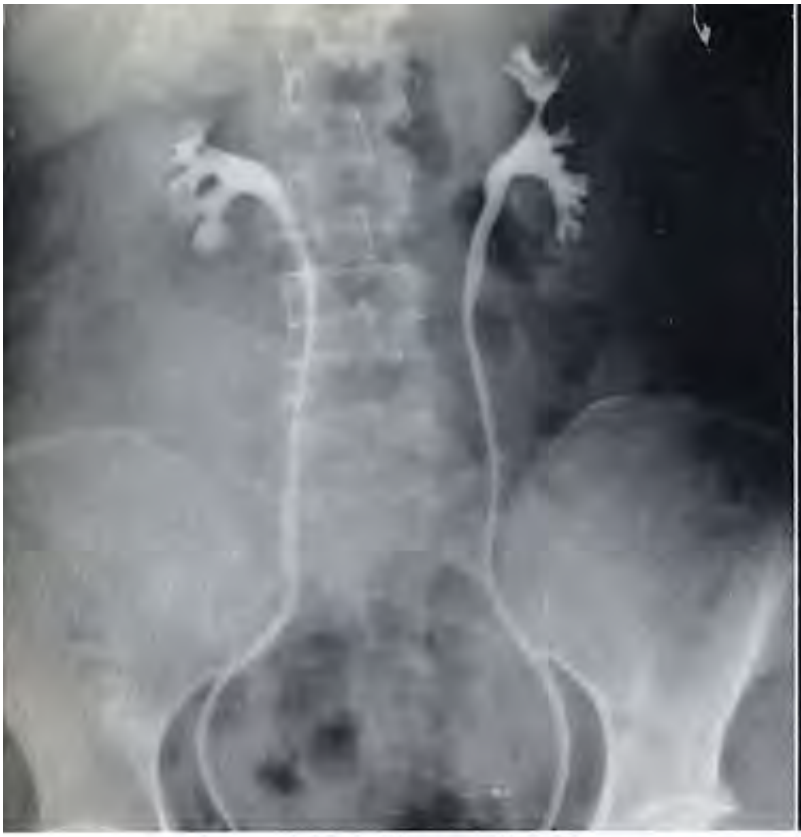
E. Salzman, M.D., Denver, Colorado: I called this a liposarcoma on the basis of the roentgenograms. What made me suspect this tumor as a liposarcoma was its bulkiness; it has been my experience that the bulkiest retroperitoneal sarcomas are liposarcomas. I would like to ask Dr. Stout whether this clinical impression has any validity.

Dr. Stout: Yes. Aside from the lymphoblastic tumors, lipomas and liposarcomas predominate; then come leiomyosarcomas, leiomyomas, rhabdomyosarcomas, and fibrosarcomas. We have very few fibrosarcomas; the impression that fibrosarcomas and neurogenic tumors are common is due to the general tendency to call almost anything a fibrosarcoma.

M. Wheelock, M.D., Chicago, Illinois: A physician of our staff, who found himself somewhat overweight, decided to reduce. As a result of his reduction, he found a tumor in his abdomen, which, on exploration, proved to be a liposarcoma invading the colon and kidney. Apparently, weight reduction does not decrease the size of a liposarcoma!

E. Valentine, M.D., Denver, Colorado: I am a little confused about this case: I ran across a report of a case which I am sure is this same one (Waller); this was a retroperitoneal xanthogranuloma with associated visceral esonophilic granuloma. Dr. Stout is credited with having seen the slides and concurred in the diagnosis. I'd like to have an explanation.

C. A. Hellwig, M.D., Halstead, Kansas: I didn't expect that discussion. However, everything that Dr. Valentine said is true. I saw those large xanthoma cells and I remembered a paper by Oberling, so I sent Dr. Oberling and Dr. Stout the slides and they thought it was a xanthogranuloma. I sent the slides to five or six other pathologists and I got very



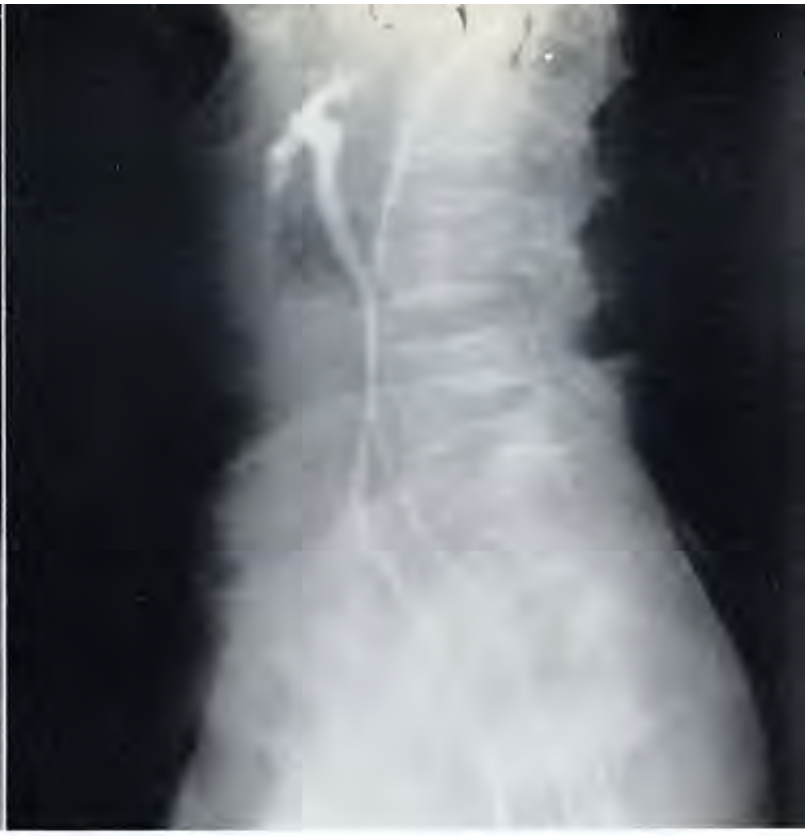


Fig. 2 and Fig. 3 — Medial displacement of right ureter.

different diagnoses, some were liposarcomas, others fibrosarcomas, others lipomas and so on until the patient had a recurrence which appeared as unquestionable liposarcoma.

Dr. Stout: I can only say that I do not see how *anyone* could have diagnosed this as a xanthogranuloma since the section showed only fibrous tissue enclosing masses of adipose tissue in which there are a few foci of microscopic fat necrosis.

C. Lockhart, M.D., Springfield, Missouri: I'd like to ask Dr. Regato if he would be discouraged by the size of a liposarcoma in that he would rather have the surgeon remove it, if possible, and then treat postoperatively, or would he be likely to treat it originally as he would a lymphosarcoma of the same size.

Dr. Regato: We consider liposarcomas as tributaries of surgical treatment. Our views on radiotherapy of liposarcomas are vague; they are based on evidence of cases of liposarcoma which recurred following surgery and were controlled by radiotherapy. On the basis of these observations, I think it is well justified to irradiate a patient postoperatively when one has reason to believe that there has been some tumor left behind. When this is done, the irradiation should be directed to the entire potential area of residual disease and the amounts of radiation given should be sufficient to sterilize a malignant tumor, not wishful-thinking amounts. I would think that removal of a bulky differentiated liposarcoma may be desirable before irradiation. The case of lymphosarcomas is entirely different. There, no matter what the bulk, radiotherapy is capable of doing the entire job more efficiently without interference by surgery, other than for histopathologic confirmation.

Fig. 4 — Large mass attached to lower pole of right kidney.

H. F. Elmendorf, Jr., M.D., San Antonio, Texas: Do you treat only those patients in whom you feel there has been some some liposarcoma left? Do you treat them immediately or do you wait for the recurrence to make itself evident?

Dr. Regato: The amount of radiations to be given would not be justified as a routine postoperative procedure; it is only justified if one feels pretty strongly that tumor might have been left behind. The irradiation should follow surgery after a reasonable postoperative lapse of one or two weeks.

Dr. Bricker: The only chance of curing a liposarcoma, in my opinion, is by its removal without ever encountering the surface of the tumor; if the surface of the tumor is encountered during the course of the operation, the chance of recurrence is almost certain. Any large liposarcoma from the retroperitoneal space is, per force, inadequately excised and recurrence can be expected. I know of no case of large liposarcoma in this area which has been cured by resection.

F. J. Buschke, M.D., San Francisco, California: I should like to mention one patient in whom roentgentherapy apparently accomplished a long-term control of surgically unmanageable liposarcoma. This patient had an attempt at surgical removal but the tumor was found infiltrating diffusely and involving a large portion of the soft tissues of the thigh. I treated this patient in October, 1944: she was treated through divided upper and lower fields to the entire thigh. In 1947, she developed a relatively soft mass in the left supraclavicular fossa. This was removed and was proved to

Fig. 5 — Gross appearance of recurrent liposarcoma.

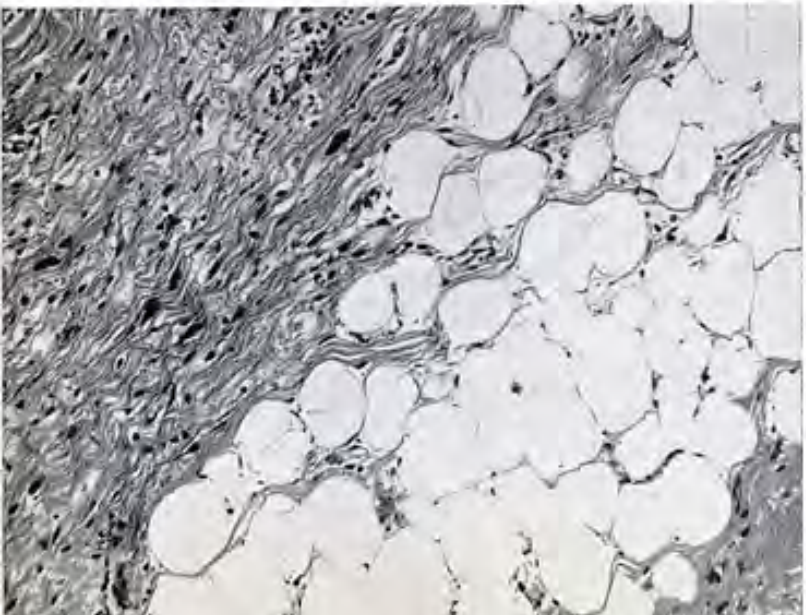
be liposarcoma. The area was treated with 200 kv, 4,300 r (skin) in 22 days. There was a very slow regression of the tumor which was still palpable three months after treatment, but finally it disappeared. In December 1945, a pelvic mass was found but this one proved to be a pregnancy which was carried to term. The child is now 13 years of age, and the mother remains in excellent condition without demonstrable recurrence in thigh or supraclavicular area.

C. Eckert, M.D., Albany, New York (in Puerto Rico): Retroperitoneal tumors imply a saga of frustration, because, though the majority of them appear to be nicely encapsulated tumors, they may be intimately associated with certain viscera or vital structures such as segments of the aorta or the vena cava; the usual story is one of local persistence in some and metastases in others. The "shoehorn technique" is the term we have applied to the surgical removal of many of these tumors, because the relationship to the parietes and to the vital structures preclude anything resembling a true cancer operation.

I have had experience personally with two xanthogranulomas; neither showed tendency to become liposarcomas.

M. Friedman, M.D., New York City, New York (in Puerto Rico): Xanthogranuloma, which is most analogous to lipoid histocytosis of bone, has a spectrum of clinical, histologic and radiosensitive pictures; on the whole, they tend to be moderately radiosensitive. Some are extremely radiosensitive, a single dose of 250 roentgens can knock them out, the more aggressive varieties may require larger doses, 2,000 to 2,500 roentgens. On the other hand, liposarcomas which, to begin with, defy the law of Bergonie and Tribondeau, have a range of necessary tumor lethal dose of radiations ranging from about 3,000 roentgens up to 10,000 roentgens. In other words, an occasional one is extremely radioresistant. I would suggest for retroperitoneal sarcomas, massive tumor doses before the operation because you can do that without irradiating the intestines.

Fig. 6 — Bizarre appearance of differentiated liposarcoma, suggesting xanthogranuloma.



J. J. Nickson, M.D., New York City, N.Y. (in Puerto Rico): Liposarcomas do tend to be quite radiosensitive and I would like to support the position that if there is any question of the surgical removal, these patients should receive the benefit of moderately vigorous irradiation. Most of them will respond but there is a group that do not. In general, after 4,000 roentgens these tumors remain quiescent, in our experience; but while the tumor is radiosensitive, it is not radiocurable; they are leisurely but in the end they kill the patient by distant dissemination.

C. Eckert, M.D., Albany, New York (in Puerto Rico): Liposarcoma in an extremity is an entirely different problem than in the retroperitoneal space where these tumors may attain tremendous size. The area of possible recurrence is really enormous which is an additional limiting factor to adequate radiation therapy. I have never seen any evidence that radiation therapy has affected the course of retroperitoneal liposarcoma.

T. M. Perry, M.D., Washington, D. C. (in Puerto Rico): I wonder if you would comment on the possibility that the changes in appearance of this tumor might be radiation induced?

Dr. Stout: I have never seen this effect achieved by radiotherapy.

W. Rider, M.D., Toronto, Canada (in Puerto Rico): I think that radiotherapy has something to offer many of these patients. All of these patients warrant a course of irradiation and I think it very important to irradiate them through a wide field, covering practically the whole abdomen and to as high a dose as one can justify without risk of hemopoietic or bowel damage.

F. C. Chu, M.D., New York City, New York (in Puerto Rico): At the Department of Radiotherapy in Memorial Center, we treated 23 patients with liposarcoma. The dosage varied from 100 roentgens in one day to 5,100 roentgens in 50 days. We found objective responses in approximately 80 per cent, except for one myxoliposarcoma. The average duration of the objective response was nine months with range from one month to five years. In other words, we found liposarcoma quite radiosensitive; the dosage we recommend should be about 2,000 roentgens.

Editor's note: After the Seminar, Dr. Stout reviewed the slide submitted to him in 1956. He concluded that it was unfortunate that the tissue selected then did not show the real lesion but rather an appearance like that of case Number 6 of this CANCER SEMINAR.

In February, 1960, this patient again presented a recurrent mass which was apparently encapsulated and was removed; it weighed over 3,000 grams.

References

Ackerman, L. V.: Tumors of the retroperitoneum, mesentery, and peritoneum. Sect. IV, Fascicle 23 and 24, Atlas of Tumor Pathology, Armed Forces Institute of Pathology, 1954, Washington.

Holtz, F.: Liposarcomas. Cancer, 11: 1103-1110, 1958.

Pack, G. T. and Tabah, E. J.: Primary retroperitoneal tumors. Study of 129 cases. Surg., Gynec., & Obstet., 99: 209-231, 313-341, 1954

Schick, A. and Rogers, L. S.: Liposarcoma. Case reports and discussion of its pathology, diagnosis and treatment. Amer. J. Roentgenol., 80: 799-806, 1958.

Stout, A. P.: Tumors of the soft tissues. Sect. III, Fascicle 5, Atlas of Tumor Pathology, Armed Forces Institute of Pathology, 1953, Washington.

Waller, J. I., Hellwig, C. A., and Barbosa, E.: Retroperitoneal xanthogranuloma associated with visceral eosinophilic granuloma. Cancer, 10: 388-392, 1957.

5. *Benign Mesenchymoma of the Kidney*

Contributed by Fred Dick, Jr., M.D. and Russell W. Blanchard, M.D.,
Waterloo, Iowa

THE PATIENT was a 50-year-old female in December, 1958, when she complained of sudden lower abdominal pain which appeared while she was pushing a cart; she was a known epileptic. On examination, there was a large, firm abdominal mass; the temperature was 104 degrees F; the culture of urine was negative.

Dr. Hodes: The roentgen examination of the abdomen revealed the following: (a) the left ureter is displaced laterally, (b) there is obvious encroachment and distortion of the lower half of the left kidney due to intra-renal disease; the outline of the lower half of the kidney is not discernible and blends imperceptibly with the surrounding tissues, (c) the left psoas muscle is clearly demonstrated; indeed its outline is unusually brilliant.

Whatever the nature of the abdominal mass, the presence of fever and abdominal pain coming on during exertion suggest hemorrhage and necrosis. Also to be considered is the history of epilepsy for there are abdominal abnormalities which may be associated with cerebral disease.

There is no question but that this patient must have a retroperitoneal tumor because of the manner in which the left ureter has been displaced. The fact that the psoas muscle shadow is seen so brilliantly suggests the retroperitoneal mass is either composed of fat or is a mesenchymoma. Both lesions notoriously do not interfere with the appearance of the psoas muscle fascial planes even though they arise and actually affect the latter. Mesenchymomas are particularly prone to develop as large retroperitoneal masses extending into the abdomen from the retroperitoneal space which radiographically seems intact. Such a tumor might well involve the kidney causing its distortion and minor displacement.

That the abnormality is primarily renal seems very probable also because primary renal tumors may extend into the retroperitoneal area displacing the ureter. This happens less often in primary renal tumors than in mesenchymomas. Also suggesting primary renal disease is this patient's epilepsy. Tuberous sclerosis, commonly associated with epilepsy, not infrequently is associated with bizarre renal tumors.

Dr. Hodes' impression: A MALIGNANT TUMOR involving the left kidney and retroperitoneal structures: 1. ANGIOLIPOSARCOMA of the left kidney with extension. 2. RETROPERITONEAL MESENCHYMOMA invading the lower pole of the left kidney.

Roentgenologic Impressions Submitted by Mail:

Ruptured aneurysm	25
Retroperitoneal lymphoma	24
Various benign lesions	20
Retroperitoneal sarcomas	13
Retroperitoneal benign tumors	12
Others	11

Dr. Hodes: There is no roentgen evidence of an aneurysm (calcified aorta); nor would the ruptured aneurysm explain the intra-renal mass. Retroperitoneal lymphomas commonly cause obliteration of the psoas muscle; also this would leave unexplained the intra-renal mass.

Dr. Regato: Dr. B. Felson, of Cincinnati, offered ruptured hamartoma of the kidney; Dr. David Gould, of Denver, Dr. Paul Swenson, of St. Paul, Minnesota, Dr. Frederick A. Rose, of Cleveland, and Dr. Paul M. Kroening, of San Francisco, all suggested aneurysm of the aorta, ruptured or dissecting; Dr. R. R. Deffenbach, of San Francisco, offered retroperitoneal abscess.

Operative findings: In December, 1958, the patient was operated upon: a large, irregular, lobulated, retroperitoneal mass was found, apparently involving the mesentery and small bowel. The mass was formed by large cystic areas with necrotic lining, containing fluid; it was impossible to remove all of the mass and postoperative roentgentherapy was considered.

Dr. Stout: The section shows a mass made up of adipose tissue both normal and with areas of fat necrosis, a good deal of young fibroblastic tissue, a few smooth muscle bands intermingled with the fat, and a variety of capillaries and larger venous tubes scattered through at haphazard. Along one border is a long line of smooth muscle bundles evidently belonging to a vein, the ureter or the kidney pelvis. The tissue covering it is loose textured and fibrous with many capillaries and is thrown up into folds. There is no epithe-

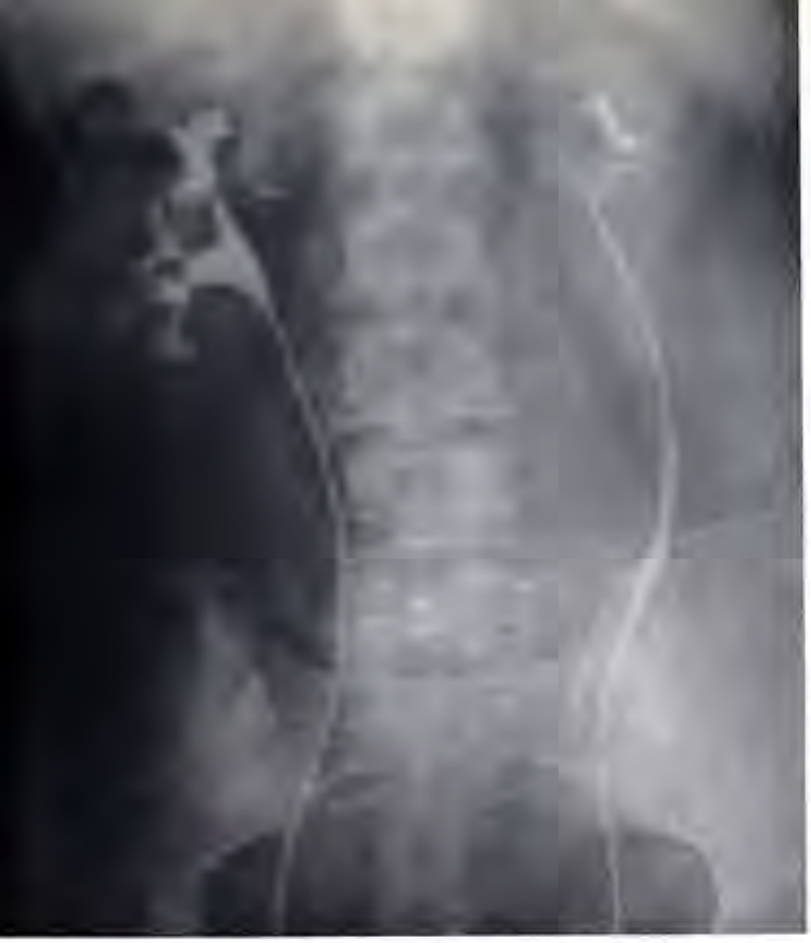


Fig. 1 — Lateral displacement of left ureter and distortion of lower half of left kidney.

lium on the surface and although the surface cells are flattened they cannot be definitely recognized as endothelial cells. A little fibrin is adherent to this surface in places. The whole complex is thrown up into unequal papillary folds. The opposite extremity of the tissue is covered with granulation tissue also thrown up into folds and heavily infiltrated with polymorphonuclear leucocytes.

Trying to interpret this histological picture from the clinical story without further knowledge of the roentgenological picture or the findings at operation forces one to canvass the possibilities. There is nothing to suggest a liposarcoma. The lesion might be a perinephric or juxta-pelvic abscess with surrounding fat necrosis. This would account for the granulation tissue and the fibroblasts and fat necrosis as reaction to the abscess. This would fail to account for the few stray bands of smooth muscle away from the surfaces. Can this be one of the benign mesenchymomas (so-called angiomyolipomas) of the kidney? Although this case has the ingredients they are not arranged in proper formation. There should be striking groups of thick-walled blood vessels and there should be more smooth muscle. I have seen five cases of this peculiar tumor of the kidney, one of them bilateral. I think it is unlikely that this is another example. There are, however, ordinary benign mesenchymomas of the kidney composed of the three elements of fat, vessels and smooth muscle so that perhaps this might be such a case. The other possibilities are a chronic perirenal abscess involving the tissue adjacent to the pelvis or an infected lipoma with fat necrosis.

Dr. Stout's diagnosis: BENIGN MESENCHYMOMA OF KIDNEY.

Histopathologic Diagnoses Submitted by Mail:

Inflammation, repair, etc.	36
Lymphangioma	33
Xanthogranuloma	28
Liposarcoma	23
Fibrolipoma	8
Angio-, myo-, lipoma	8
Benign mesenchymoma	7
Others	7

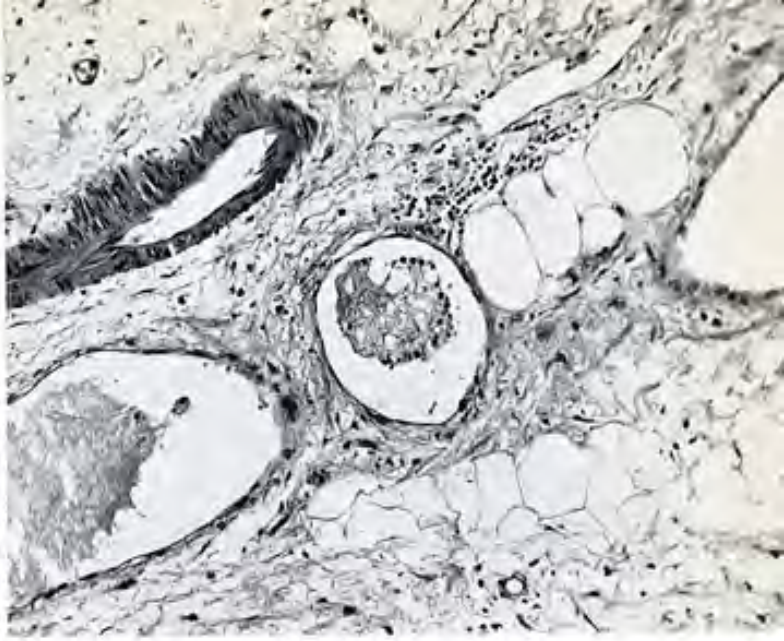


Fig. 2 — Benign mesenchymoma showing smooth muscle, fat, and vessels.

Dr. Regato: Dr. H. K. Giffen, of Omaha, also made a diagnosis of mesenchymoma. Dr. R. Hirtzler, of Yugoslavia, offered cavernous lymphangioma. Dr. Morgan Berthrong, of Denver, also chose a retroperitoneal lymphangioma with chylous granulation. Dr. Carlo Sirtori, of Milan, diagnosed hemangioma. Dr. L. Lowbeer, of Tulsa, and Dr. M. B. Dockerty, of Rochester, preferred sclerosing retroperitonitis and granuloma. Dr. Fred Collier, of Birmingham, Alabama, submitted lymphangio-endothelioma.

Subsequent history: In January, 1960, the patient appeared well, had gained weight and presented no complaints. The physical examination revealed no abnormalities and she had had no epileptic attacks.

Dr. Bricker: This case exemplifies the quandry that can face a surgeon who is trying to remove such a tumor and how very helpful it would be if a definitive diagnosis could be forthcoming while the operation is in progress. We realize that it is often impossible to know, but frequently we take a tremendous risk with the patient and one is always uneasy, in the course of an operation of this sort, trying to determine whether or not the risk is justified. If we are able to prove that it is a lymphoma, then we are not justified in taking the big risk for what can be only a palliative result. One could be greatly relieved to know that he was dealing with a benign process. I don't know anything about this type of tumor; I am intrigued by it. It was left in and I wonder, though it has a microscopic appearance of a benign tumor, what can be anticipated for this patient. It seems to me that a benign tumor will persist and grow large enough to have the same effect as a malignant one. Dr. Regato, you said you were consulted regarding radiotherapy. Have you felt that there was any indication for it in this type of tumor? Any reason to expect it to respond? And what does Dr. Stout think about the ultimate prognosis with this tumor when it is not removed in its entirety?

Dr. Regato: I certainly do not know that radiotherapy would be of any value in this case, but I am more concerned with the fact that if this patient were to receive radiotherapy, she would have to receive it over a large area including both kidneys and that means some definite risk. We have advised that this patient be followed for evidence of recurrence and then reconsider. I think that perhaps a small amount of radiations in some of these cases might be justified as an anti-inflammatory agent, but whether this will help the patient or not, I do not know.

Dr. Stout: I have never known one of these to recur, but I say this without having any proper follow-up. It has never come to my attention. My inclination in this case

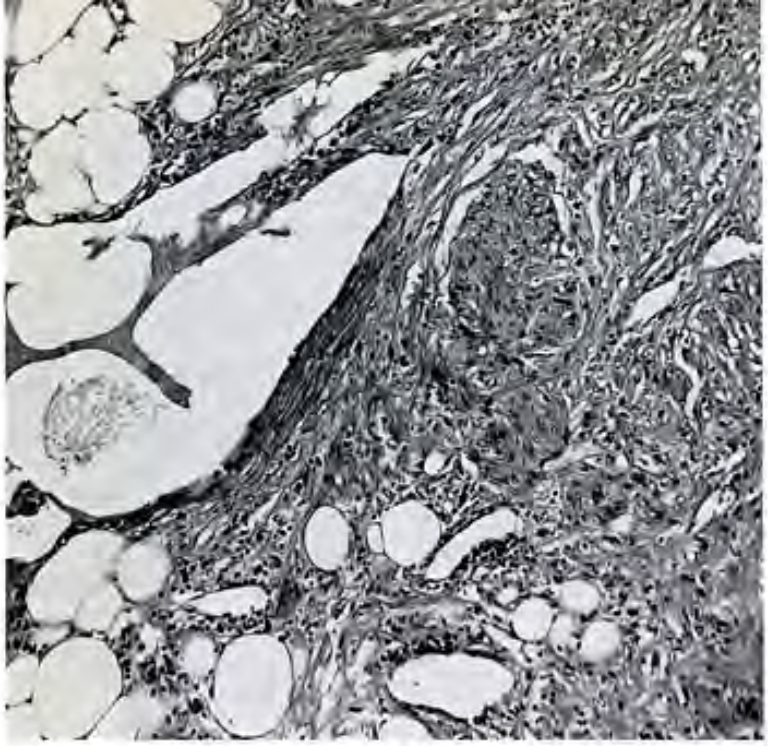


Fig. 3 — Benign mesenchymoma showing vessels, fat, and myxoid tissue.

would be to do nothing because I think the chances are at least even, that though some of it was left behind, it may not continue to grow.

H. C. Allen, M.D., St. Louis, Missouri: I have a case in which one kidney was removed with this tumor and then, very rapidly, the tumor appeared on the opposite side and involved the other kidney. The woman has been living with non-protein-nitrogen of about 80 mgr per cent, transfused about once a month for the last four years.

Dr. Stout: I recall having seen one bilateral instance but I don't recall the follow-up details.

J. W. Pickren, M.D., Buffalo, New York: Without the history, I made the diagnosis of benign mesenchymoma. Then along comes the history of sudden pain, fever, and so forth, so I ended with an abscess. I wonder, Dr. Stout, what did you do with the history in this case?

Dr. Stout: Well, I looked at the slide before I read the history and probably I was considerably prejudiced! I thought there were two interesting features in the section. One of them seemed to show that the tumor was adherent to the pelvic tissues and the pelvic tissues were full of inflammatory cells. And along another border, opposite to the border where I thought the pelvic tissues were, that they must have ripped off the side of a vein. I couldn't interpret it any other way. But I still thought after reading the history, that one could account for the symptoms of apparent infection as a secondary phenomenon to the growth of the tumor. I still thought it was a tumor.

M. Berthrong, M.D., Denver, Colorado: As it so often happens when slides are processed from the different paraffin blocks available, not all slides had enough of the significant lesion. Some of the slides showed a great deal of inflammation, a great deal of foam cells and reaction to some sort of an injury and even acute, almost abscess-like inflammation. The various slides show slightly different things: those large venous-like spaces were scattered, but here and there throughout the whole specimen they did have smooth muscle in the lining and there was smooth muscle elsewhere in the mass. Our interpretation of the entire picture was that it was a lymphangioma, connected in some way to the chyle's lymph; when the patient was pushing her cart, she may have ruptured some of these and instituted a very intense reaction to chyle that produced the multiple pictures.

C. Eckert, M.D., Albany, New York (in Puerto Rico): I think this case must have presented tremendous problems to the surgeon who took care of it. First of all, the microscopic appearance of a benign lesion was not really in keeping with the operative description of involvement of small intestines, of the mesentery, nor with the radiographic suggestion of either origin from the kidney or invasion of the kidney. The tumor was not completely removed; under these circumstances it is a wise idea to place a few silver clips as markers to outline the area where tumor has been grossly left behind for this may be of some help in the administration of radiotherapy.

Dr. Regato: We appreciate this thoughtfulness of the surgeon when radiotherapy may be contemplated; placing metal clips in the extreme limits of the potential tumor area contributes considerably to the reduction of the size of the field which is to be used in subsequent irradiation.

This patient had been considered for possible radiotherapy, but mostly because the diagnosis of liposarcoma had been suggested. In view of the diagnosis of a benign condition, we have advised only that the patient be followed closely.

Subsequent history: Dr. C. P. Addison, of Waterloo, Iowa, has reported that the patient was last seen in August, 1960; she has gained ten pounds in weight, is working as an auxiliary nurse and appears well.

References

Cibert, J., Durand, L., and Riviere, C.: Les compressions uretérales par sclerose du tissu cellulo-adipeux péri-uretéral ("periuretérites primitives"). J. Urol., Paris, **62**: 705-733, 1956.

Hawk, W. A. and Hazard, J. B.: Sclerosing retroperitonitis and sclerosing mediastinitis. Amer. J. Clin. Path., **32**: 321-334, 1959.

Miller, J. M., Lipin, R. J., Meisel, H. J. and Long, P. H.: Bilateral ureteral obstruction due to compression by chronic retroperitoneal inflammation. J. Urol., **68**: 447-451, 1952.

Ormond, J. K.: Bilateral ureteral obstruction due to envelopment and compression by an inflammatory retroperitoneal process. J. Urol., **59**: 1072-1079, 1948.

Oppenheimer, G. D., Nairns, L. and Simon, N.: Radiotherapy in the treatment of non-specific inflammatory obstruction of the ureter. J. Urol., **67**: 476-478, 1952.

Tweeddale, D. N., Dawe, J. D., McDonald, J. R. and Culp, O. S.: Angiolipoleiomyoma of the kidney. Cancer, **8**: 764-770, 1955.

6. *Retroperitoneal Xanthogranuloma*

Contributed by Donald L. Allott, M.D. and James J. McCort, M.D.,
San Jose, California

THE PATIENT was a 73-year-old man in March, 1958, when he had several episodes of hematemesis; there was no pain but he had lost twenty pounds of weight in the past year. There was a history of a similar episode in 1943. On examination, there was a palpable firm and fixed mass in the left upper quadrant of the abdomen. The blood pressure was 60/40 and the patient appeared anxious and weak.

Dr. Hodes: The roentgen examination of the abdomen revealed the following: (a) displacement of the stomach upward with extrinsic encroachment upon its greater curvature, (b) a large retroperitoneal soft tissue mass involving the area normally occupied by the body of the pancreas extending into a much larger mass in the left side of the lower abdomen, (c) evidence of reflex ileus of the descending duodenal loop as well as of the horizontal limb of the duodenum, due to the retroperitoneal mass; the jejunal and ileal loops are also affected by the mass which must lie in the mesentery and is adherent to the small intestine, (d) the left ileopsoas muscle is partially obliterated; the upper half of the right is also indistinct, (e) the abdominal masses are dense and their outline somewhat irregular and there are no changes in the adjoining bone.

Among other abnormalities this patient must have a gastric lesion. He bled on two occasions at an interval of fifteen years. Perhaps a long standing gastric ulcer has now undergone malignant degeneration.

The extensive changes throughout the abdomen suggest disseminated metastatic disease. Whereas, gastric cancer usually does not cause this type of small bowel distortion or masses of this size, there is a possibility that the gastric lesion is of an unusual type, perhaps a superficial spreading carcinoma superimposed upon an old gastric ulcer which has extended beyond the involved organ.

Fig. 1 — Large space-occupying, soft-tissue mass in left lower abdomen and upward displacement of the stomach.

Dr. Hodes' impression: A malignant abdominal disease. 1. GASTRIC CANCER with superficial spreading disease involving the retroperitoneal structures and mesentery. 2. Gastric cancer associated with some other form of invasive retroperitoneal and mesenteric disease.

Roentgenologic Impressions Submitted by Mail:

Pancreatic carcinoma with metastasis	13
Duodenal carcinoma with metastasis	12
Gastric carcinoma with metastasis	7
Various malignant tumors	23
Various benign lesions	18
Others	10

Dr. Hodes: Carcinoma of the pancreas is a very distinct possibility; it would account for the patient's weight loss, but these lesions are usually more painful. Primary carcinoma of the duodenum usually arise along the lateral margin of the duodenal loop; the lateral margin in this individual is unaffected. Nor have we seen a primary duodenal cancer associated with such disseminated metastatic disease. The only benign process we could think of was "alligator mesentery" or chronic mesenteritis; this is an extremely rare disease which usually puckers the mesentery and gut.

Dr. Regato: Dr. Robert R. McCarver, Jr., of Denver, suggested lymphoma; Dr. Robert L. Stein, of San Francisco, preferred carcinoma of the duodenum. Dr. B. Kaufman, of Cleveland, and Dr. Genene Baker, of Colorado Springs, made a diagnosis of carcinoma of the stomach with omental metastases.

Operative findings: On March 8th, 1958, at laparotomy, a mass 10 x 15 cm was found within the mesentery, apparently infiltrating the wall of the fourth portion of the duodenum. The tumor was removed with the duodenum and twelve inches of the jejunum; the wall of the small intestine appeared infiltrated as far as the submucosa. A 3 cm ulceration of the fundus of the stomach was found and a simple removal of this part of the gastric wall was done; a splenectomy was also carried out. The gastric lesion was an adenocarcinoma.

Dr. Stout: This is a vascular granulomatous lesion heavily infiltrated with polymorphonuclear neutrophiles and histiocytes most of which are foamy and no doubt contained lipids. The lesion appears sharply circumscribed and there is a remarkable uniformity of morphological features throughout the sections.

This appears to me to be a xanthogranuloma. In my experience there are two varieties of xanthomatous masses which one may encounter in the abdominal cavity and thorax. One of them is a more purely granulomatous lesion, vascular and with many foam cells. Usually there are not nearly as many polymorphonuclear leucocytes as in this case. They are found generally in the retroperitoneal space, mesentery, in and around the kidney and in the posterior mediastinum of adults over 30 years. They sometimes infiltrate the kidney or intestine. The etiology is unknown to me but I have always supposed they were inflammatory rather than neoplastic. A second type variously called xanthofibroma, xanthofibrosarcoma or xanthogranuloma is much more like a neoplasm in appearance for it is made up of large numbers of fibroblasts together with variable numbers of foamy xanthomatous cells. These tumors also are large and appear

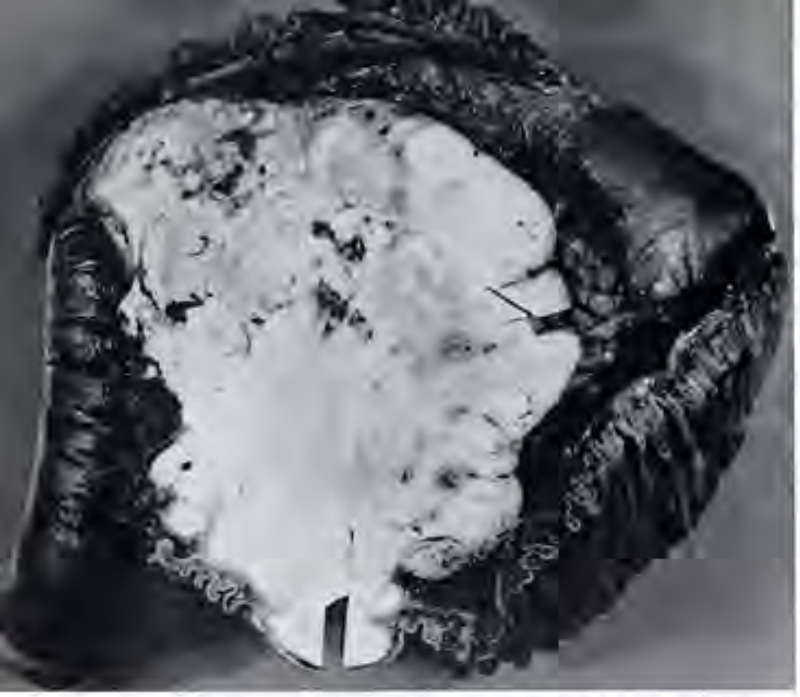


Fig. 2 — Cut section of mesenteric mass infiltrating the fourth portion of the duodenum.

in the same places as the other type. The original cases reported by Oberling were more fibrous than granulomatous. Both varieties may recur after attempted excision. It has been shown that occasionally they may be associated with multiple xanthomatosis but this is rare. It is not always easy to distinguish them from liposarcoma especially in a biopsy.

Our experience with these tumors includes 18 cases in the retroperitoneal space, mesentery and perirenal areas and four in the mediastinum. Five of these were predominantly fibrous, 12 were predominantly granulomatous like the present case, and one was mixed. We have not attempted to get follow-ups on these cases but we have learned that two of them recurred locally after attempted excision. Just what the relationship of these tumors may be to the fibrous xanthomas of the soft tissues we do not know. Since it is possible for the latter to become malignant and metastasize, it will not be surprising if a malignant example of one of these tumors should some day come to light.

Dr. Stout's diagnosis: 1. RETROPERITONEAL XANTHOGRANULOMA. 2. CARCINOMA OF STOMACH.

Histopathologic Diagnoses Submitted by Mail:

Xanthogranuloma, histiocytosis	57
Hodgkin's	30
Various malignant tumors	29
Various benign lesions	18
Bad, by any other name!	1
Others	18

Dr. Regato: Dr. V. Pardo, of Havana, Cuba, and Dr. Lauren V. Ackerman, of St. Louis, also diagnosed this lesion as xanthogranuloma. Dr. Frank Vellios, of Indianapolis, made a diagnosis of Hodgkin's granuloma; Dr. R. A. Keffler, of Lubbock, Texas, offered Letterer-Siwe's disease. Dr. André Pagès, of Montpellier, France, preferred eosinophilic granuloblastoma (Bolck).

Subsequent history: Following intervention, the patient's general condition deteriorated rapidly and he expired.

An autopsy revealed severe arterionephrosclerosis and failed to uncover any evidence of residual tumor in the abdominal cavity; in particular there was no residual tumor in the stomach, no metastatic lymph nodes, no liver metastasis.

Dr. Bricker: I don't know whether or not the surgeon could feel a pancreatic tumor or a normal pancreas. If this had been found to be cancer of the pancreas, I would not have tried to remove it; microscopic examination of the tissue might have established that the lesion was a bizarre type of xanthogranuloma, that is, an inflammatory lesion of some sort, not a tumor; I have seen it treated by radiation therapy after inadequate resection and it exhibits a rather marked radiation sensitivity. Malignant tumors, in this region, are practically never amenable to satisfactory surgical excision. Now, combine this lesion with the big ulcer in the stomach which turns out to be carcinoma and I give up! One would have to be there to know how to solve an insolvable problem.

Dr. Hodes: What was the peculiar appearance of the stomach due to? Was that just extrinsic pressure? Was the stomach plastered to the mass?

D. L. Alcott, M.D., San Jose, California: It was apparently extrinsic pressure: there was no continuity with the mass.

H. F. Elmendorf, Jr., M.D., San Antonio, Texas: Dr. Regato, would you comment on the radiosensitivity of this type of lesion?

Dr. Regato: There is some reason to believe that xanthogranulomas are radiosensitive and, since they are not malignant lesions, it is possible that the amounts of radiations necessary to make them regress is not excessive, or prohibitive, for the other organs to be irradiated.

C. Eckert, M.D., Albany, New York (in Puerto Rico): It is important to emphasize that an elderly man who has a large, fixed abdominal tumor should be explored and an absolute diagnosis established; a vast number of things can produce this type of picture. Large retroperitoneal lymphomas can do many bizarre things, including infiltrating the stomach and giving rise to ulcerations and hemorrhage. We have one example of this type: a man was cachectic, several house officers felt he was inoperable, that nothing should be done. A biopsy was done, it was a lymphoma; he was treated and seven years later he was still alive and well.

Dr. Regato: On the basis of these experiences (Cases Number 4 and 6), the next time I hear of a patient, particularly an elderly patient, with a xanthogranuloma, I am going to ask that the accompanying malignant tumor be found.

R. Marcial-Rojas, M.D., San Juan, Puerto Rico: There are cases in which droppings from tumors have been blamed for producing certain reactions in the areas draining these tumors. Is there a possibility that these mucinous tumors of the stomach may produce some abnormal proteins and that in draining the area into the nodes, this type of granuloma may result?

Dr. Stout: I don't know; xanthogranulomas in different peritoneal regions are extremely uncommon; in the course of fifty years, we collected about twenty of them. It would be hard for me to think of any relationship between the two lesions.

R. Cox, M.D., San Juan, Puerto Rico: I would like to ask if there is any relationship between xanthogranuloma and the extra-active eosonophilic granuloma group of diseases. I noted there were several diagnoses of eosonophilic granulomas and Letterer's-Siwe's included in the list.

Dr. Stout: All attempts to relate the two have failed as far as I know. I can only say that we are very far from understanding tumors, in general and in particular, and there is an enormous amount to be learned. I have been in medicine for fifty odd years and during that time I have learned a lot; I am not discouraged because we still have lots of things we don't understand. If you wait awhile and grow old you will find that some of the tough problems of the past are finally solved. It is always a great satisfaction to me, when I encounter something that I don't know, to live on; suddenly in some future time, somebody comes and tells me what it is, and then, I'm made happy for the moment.

C. Eckert, M.D., Albany, New York (in Puerto Rico): The questions that are unanswered represent problems which some inquiring mind should approach, from an experimental

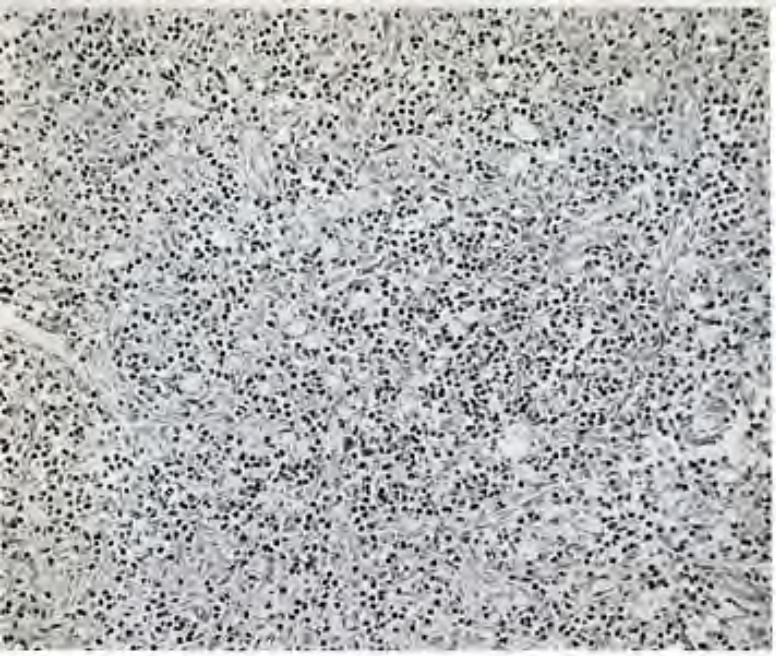


Fig. 3 — Xanthogranuloma with many histiocytes.

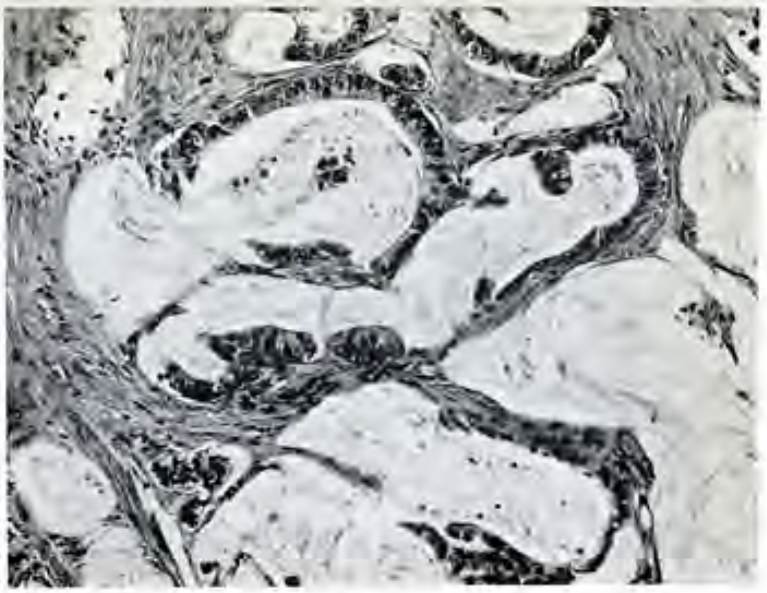


Fig. 4 — Adenocarcinoma of the stomach.

standpoint, in an effort to setup a model of some type which will provide answers. We class problems in terms which may satisfy many people, but, in labeling them, we simply cover a vast zone of our ignorance. It is important that we recognize that even though we are able to categorize certain problems in terms of their relationships to other similar ones, they may still be completely unanswered problems. Xanthogranuloma is one of the unanswered problems. We don't even know if it is neoplastic, whether it is metabolic, whether it represents a hypersensitivity response such as Dr. Marcial-Rojas suggested, although this does not seem particularly likely.

References

Botck, F.: Die Granuloblastome des Magens. Zum Aufbau von Geswulsten aus Komplexen gestaltlichen Einheiten. Beitr. path. Anat., 110: 635-660, 1949.

Donhauser, J. L. and Bigelow, N. H.: Primary retroperitoneal tumors. AMA Arch. Surg., 71: 234-238, 1955.

Duval, F.: Primary retroperitoneal tumors. J. Fac. Radiol., 9: 204-210, 1958.

Scanlan, D. B.: Primary retroperitoneal tumors. J. Urol., 81: 740-745, 1959.

7. Juvenile Extraskeletal Chondrosarcoma of the Thigh

Contributed by Thomas D. Brower, M.D., Pittsburgh, Pennsylvania

THE PATIENT was a 3-year-old girl in March, 1956, when a painless mass was noticed in the right thigh; it did not appear adherent to the bone or to the skin. It was slightly tender; there was no lymphadenopathy.

Dr. Hodes: Roentgen examination of the lower extremity revealed the following: (a) a large soft tissue mass arising within the muscle mass, (b) all normal muscle fascial planes have been distorted, (c) the adjoining femur is normal.

Any mass developing in muscle with evidence of aggressiveness must be considered rhabdomyosarcoma even though various adnexas of this tumor may exist.

Dr. Hodes' impression: A malignant soft tissue tumor: 1. RHABDOMYOSARCOMA. 2. FIBROSARCOMA.

Roentgenologic Impressions Submitted by Mail:

Rhabdomyosarcoma	38
Fibrosarcoma	13
Various other sarcomas	21
Benign tumors	15
Various benign lesions	12

Dr. Regato: Dr. Benjamin Felson, of Cincinnati, wrote that this is "obviously" a granular cell myoblastoma. Dr. John M. Dennis, of Baltimore, Dr. David Gould, of Denver, Dr. Robert L. Stein, of San Francisco, and Dr. Emanuel Salzman, of Denver, all made a diagnosis of rhabdomyosarcoma.

Operative findings: On April 16th, 1956, resection of the quadriceps muscles was done. In the groin, the tumor appeared to have extended close to the origin of the resected muscles, but there was no adherence to bone. The tumor was firm in consistency and measured 6 x 5 x 5 cm; on cut section it presented a gelatinous appearance.

Dr. Stout: This bizarre tumor appears to be composed largely of chondroblastic tissue. There are frequent zones of fibrocartilaginous matrix in which the small rounded cells are set often as single units without, or occasionally with, a capsule and sometimes in groups or cords. But there are also areas where the cells are spindle shaped, arranged in cords and are accompanied by fibers. These have the appearance of fibroblasts. Elsewhere the cells are jumbled together without any identifying characteristics. The tumor has invaded striated muscle and extends between the muscle fibers forcing them apart.

The major portion of this tumor is chondroblastic; the only question in my mind is to decide whether it is purely chondroblastic or whether there are any other tumor types recognizable beside the fibroblastic elements. After a good deal of study, I have concluded I can recognize none and that this must be a juvenile chondrosarcoma.

In 1953 Verner and I published a paper dealing with chondrosarcoma in soft tissues. Among the seven cases was one in the shoulder region of a boy 18 years old that had been present for eight years. There was only one other case in the literature at that time; a chondrosarcoma in the nasopharynx of a 16 year old boy that metastasized to the lungs and killed (Wirth). Since that time we have accumulated in the Laboratory of Surgical Pathology of Columbia University five more cases in young children. Some of these closely resembled the present case. The pertinent available

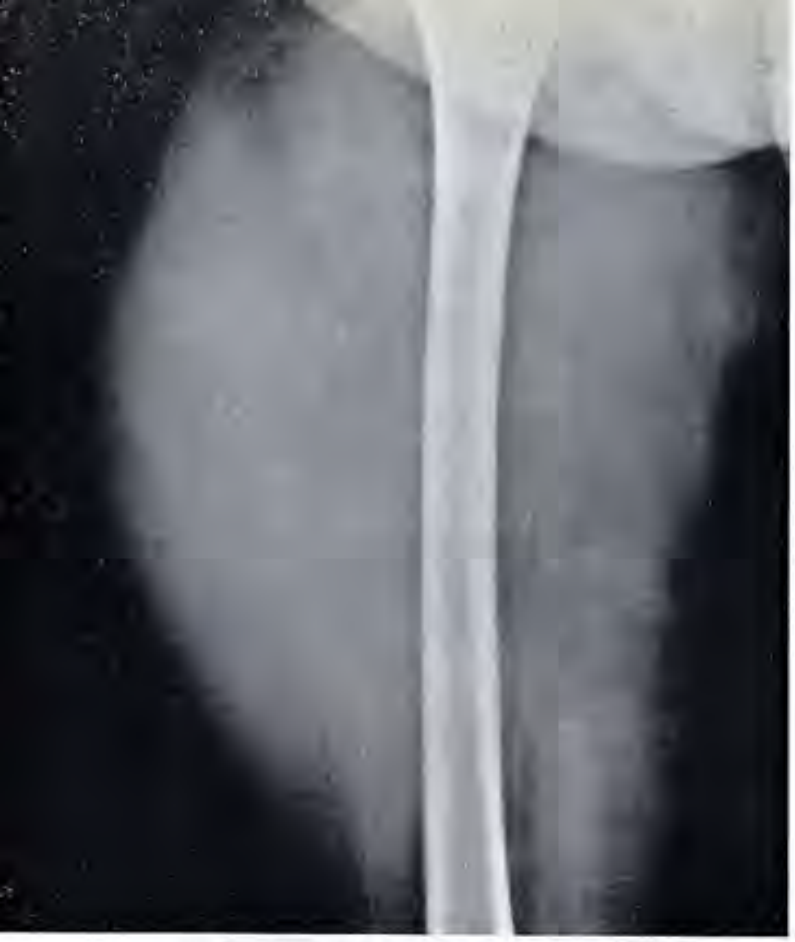


Fig. 1 — Large, soft tissue mass of the muscles of the thigh.

information about these cases is included in Table II. This information is necessarily sketchy because I have not had an opportunity to investigate these cases further. They suggest, however, that chondrosarcoma of the soft tissues does occur in children and that it can behave as a malignant tumor. I am not acquainted with any other case reports of chondrosarcoma of the soft tissues in children.

Dr. Stout's diagnosis: CHONDROSARCOMA, juvenile.

Histopathologic Diagnoses Submitted by Mail:

Hemangioendotheliosarcoma	42
Rhabdomyosarcoma	30
Malignant mesenchymoma	20
Malignant lymphangioendothelioma	15
Chondrosarcoma	12
Synovial sarcoma	12
Fibrosarcoma	10
Others	17

Dr. Regato: Dr. Jose A. Carro and Dr. Rosa Fiol of San Juan, also made a diagnosis of chondrosarcoma. Dr. E. H. Soule, of Rochester, Dr. Frank Vellios, of Indianapolis, and Dr. Robert Horn, of Detroit, offered rhabdomyosarcoma; Dr. Horn added that he *could* demonstrate cross striations but admitted the right of others to doubt it. Dr. Alvin O. Severance, of San Antonio, also made a diagnosis of extraosseous chondrosarcoma.

Subsequent history: Four months after operation there was evidence of pulmonary metastases. In October, 1956, she expired. No autopsy was done.

Dr. Bricker: In the abdomen, because the patient is under anesthesia or because of the limited effectiveness of frozen section and other factors one might have to reach a decision without biopsy; but with tumors of the extremities, there is no reason for not obtaining a preoperative diagnosis within four or five days, after consultation with the various pathologists, in order to plan definitive operation. I would recommend it for all soft tissues tumors of extremities. A tumor in the region of a major nerve trunk or major vascular bundle should be identified very carefully through a minimal incision, and incisional biopsy.

In a patient such as this, with a suspected sarcoma with no roentgenologic evidence of pulmonary metastases and no palpable liver then the first operation should be aimed at cure; and the cure in this case can only be obtained by hemipelvectomy. There is no chance of completely removing a sarcoma in that area by anything less than by hemipelvectomy distasteful as we might consider the operation. Often an appearance of mobility or of superficiality is misleading.

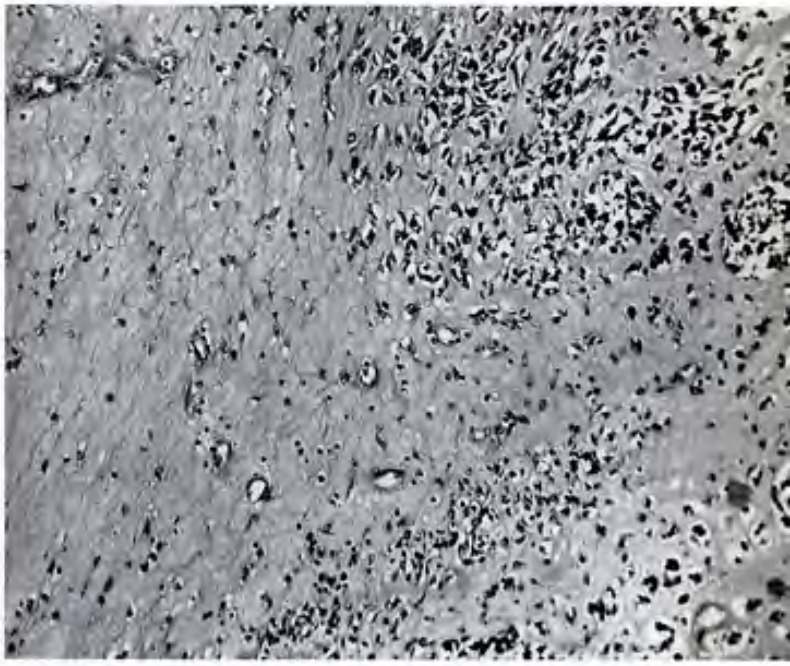


Fig. 2 — Chondrosarcoma of the soft tissues.

TABLE II
Extraskeletal Chondrosarcoma in Children

P. & S. No.	Sex	Age at Onset	Age at Diagnosis	Anatomical Site	Size	Treatment	Result
45064	M	1½	2½	Forearm	4x2.5	Excision	?
42631	M	?	3	Midline of neck, post.	?	Excision	Recurred
52565	F	?	3	Quadriceps Ext. thigh	12x9x3	Excision	?
59163	F	14	16	Thigh	20x15	Excision	Died, Lung Met.
61122	M	?	8	Dome of bladder	?	Excision	?

H. Braunstein, M.D., Cincinnati, Ohio: I would like to challenge the implication that the distinction between a chondrosarcoma and a rhabdomyosarcoma is a question of popularity or usage. I think that the clinical course is a most important distinction and bears out that this is not likely to be a chondrosarcoma. I think the concept of an embryonal rhabdomyosarcoma best fits this particular case; the prognosis of these lesions is dismal and the patients invariably die from six months to a year after the diagnosis is established.

Dr. Stout: I can only say that we have now a collection of 150 cases of juvenile rhabdomyosarcomas and none of them look like this. That collection includes all the different varieties described by Horn and Riopèlle as well as some that they didn't describe. I can't bring myself to call this a rhabdomyosarcoma; you have to credit some other malignant tumors besides rhabdomyosarcomas with metastasizing, for they do.

R. Marcial-Rojas, M.D., Santurce, Puerto Rico: I didn't see any calcification and I thought that calcification was extremely frequent in chondrosarcomas. What is the incidence of calcifications in extraosseous chondrosarcoma?

Dr. Stout: In my experience, it is almost as frequent as in chondrosarcomas of bone.

C. Eckert, M.D., Albany, New York (in Puerto Rico): There is little basis for predicting the course of a given lesion. The critical features seem to be the histologic pattern of a tumor and the anatomic area in which the tumor lies. A small tumor in the lateral portion of the thigh is an entirely different problem than a tumor of the same size occurring high in the groin, because of the relationship of the groin to the principal blood vessels as well as to the nerve supply of the extremity. To do an adequate removal of these tumors the surgeon should never see the tumor during the course of its removal; if he sees the tumor, it is likely that the removal has been inadequate. In other instances one may decide, because of the location and the histologic pattern that an amputation is justified. In this case, it would appear that the operation done was inadequate although perhaps it did not alter the outcome.

Dr. Regato: An inadequate operation should not be done because of lack of proper diagnosis or to avoid a biopsy, the harm of which is only theoretical. On the other hand, it should also be said that no biopsy should be undertaken unless the surgeon who is doing the biopsy is ready to proceed with the proper treatment that is indicated, and unless the relatives and the patient are aware of the possible issues and have agreed to them in advance. It is painful to see a patient who has had a biopsy go around "shopping" for weeks, sometimes months, to different centers only because he had agreed to have a biopsy in one institution but was not aware of the possibilities of definitive treatment or would not have it at that institution. Under those circumstances, it is preferable not to biopsy.

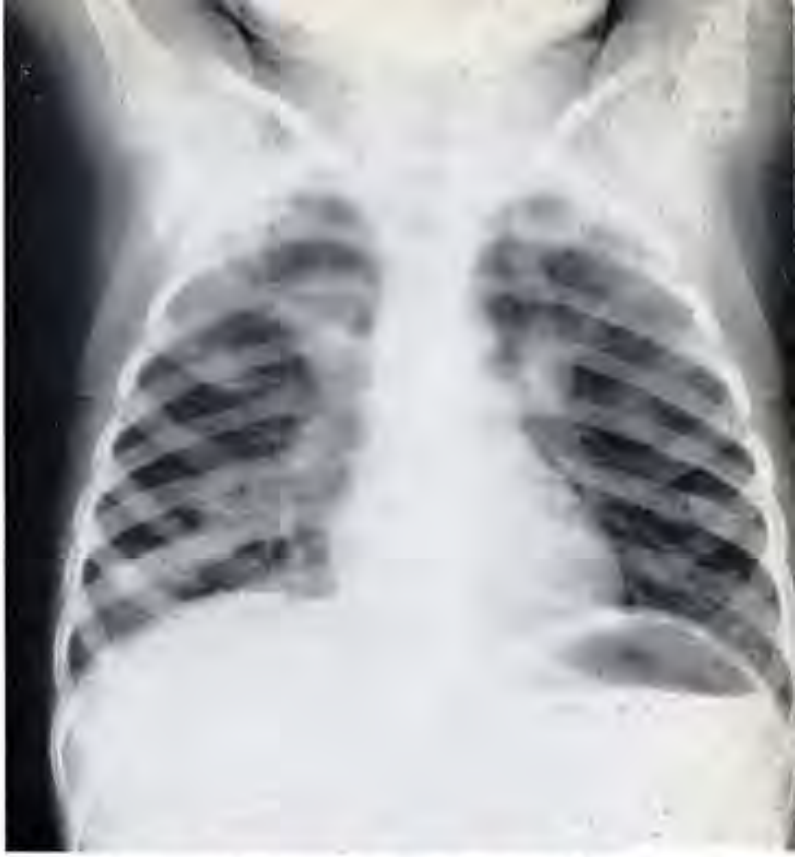


Fig. 3 — Pulmonary metastases from primary tumor of the thigh.

C. Eckert, M.D., Albany, New York (in Puerto Rico): These points are very important. To do a biopsy on any tumor, regardless of its nature, without being prepared to carry out definitive treatment, is absolutely wrong. Having an understanding with the family about the various possibilities is also of importance.

References

Horn, R. C. and Enterline, H. T.: Rhabdomyosarcoma: a clinicopathological study and classification of 39 cases. Cancer, **11**: 181-199, 1958.

Stobbe, G. D. and Dargeon, H. W.: Embryonal rhabdomyosarcoma of head and neck in children and adolescents. Cancer, **3**: 826-836, 1950.

Stout, A. P.: Tumors of the soft tissues. Sect. II. Fascicle 5, Atlas of Tumor Pathology, Armed Forces Institute of Pathology, 1953, Washington.

Stout, A. P. and Verner, E. W.: Chrondrosarcoma of the extraskeletal soft tissues. Cancer, **6**: 581-590, 1953.

Wirth, J. E. and Shimkin, M. B.: Chrondrosarcoma of the nasopharynx simulating juvenile angiofibroma. AMA Arch. Path., **36**: 83-88, 1943.

8. Malignant Mesenchymoma of the Thigh

Contributed by Albert J. Miller, M.D. and Robert S. Young, M.D.,
Pueblo, Colorado

THE PATIENT was a 52-year-old lady in February, 1958, when she gave a history of pain in the left thigh of several months duration. There was no history of trauma. A diffuse mass was palpable on the posterior aspect of the left thigh.

Dr. Hodes: A roentgen examination of the thigh revealed the following: (a) an ill-defined soft tissue mass involving the muscles, (b) the soft tissue fascial planes are distorted, (c) calcific debris of minor degree within the tumor mass, (d) cortical thickening of bone at the level of the tumor (apparently reactive adult bone and not tumor bone).

This is a primary soft tissue tumor arising in the muscles of a thigh which is obviously malignant because of the manner in which it has distorted the normal fascial muscle planes. Of considerable interest is the bone reaction in the femur at the level of the soft tissue mass. The mass itself is not intimately related to the area of bone reaction; the latter lies at a distance from the mass which is of considerable significance. Cortical response to irritative muscle processes are not unusual in the presence of fibrosarcoma. There exists the possibility that the tumor may be of nerve, fat or muscle origin rather than fibrous tissue origin. The calcific debris suggests the presence of necrosis, yet old phleboliths in an angiomatous tumor might cause similar densities.

Dr. Hodes' impression: A malignant soft tissue tumor: 1. FIBROSARCOMA. 2. RHABDOMYOSARCOMA.

Roentgenologic Impressions Submitted by Mail:

Parosteal fibrosarcoma	38
Osteomyelitis	13
Osteoid osteoma	9
Various malignant tumors	12
Others	9

Dr. Hodes: The cortical reaction to the presence of the soft tissue tumor was not the reaction of sarcomatous bone; the bone here demonstrated seemed mature. The cortical response is not compatible with osteomyelitis; the periosteitis caused by infection does not produce bone of this adult variety. This patient has a primary soft tissue tumor mass; furthermore, the nature of the cortical thickening does not suggest the more localized lesion of osteoid osteoma.

Dr. Regato: Dr. W. P. Stampfli, of Denver, and Dr. Walter G. Gunn, of San Francisco, also made a diagnosis of fibrosarcoma. Dr. B. Kaufman, of Cleveland, proposed osteoid osteoma.

Operative findings: In February, 1958, a surgical exploration was done. Extending over the middle third of the posterior aspect of the femur, there was a very firm soft tissue lesion; specimens of soft tissue and bone were removed for biopsy. A diagnosis of chondrosarcoma was rendered on the basis of which Dr. Young proposed a disarticulation. The patient refused and she was then referred to the Penrose Cancer Hospital for further study. We wished to have the patient accept a disarticulation but made some histopathologic consultations for moral support, and started on a course of radiotherapy in the meantime. We received a long letter from Captain W. M. Silliphant, M.C., USN, Director of the Armed Forces Institute of Pathology, (AFIP Ac. No. 853626) from which the following are the most pertinent excerpts:

"Despite these handicaps (lack of details as to previous trauma and its character) the staff believes that the lesion has arisen in soft tissue and produced secondary periosteal hyperostosis . . . the degenerative forms are clusters of round nuclei, foci of pseudo-giant-cell muscle degeneration and regions of nuclear proliferation of semi-agonal nature (such as occur in inadequate circulation) . . . The most dangerous-looking areas are the foci of atypical regeneration or proliferation composed of large polyhedral cells with abundant clear cytoplasm fairly closely packed together. Careful analysis . . . suggests that this is another form of proliferation on the part of the muscle caught in the scar tissue . . . Mitotic activity and variation of size and staining reaction of the type expected in a malignant tumor cannot be found . . . There are close-packed large cells which resemble and raise the question of possible metastatic tumor . . . Because of these cells and of the periosteal reaction, *consideration may perhaps be given to the wisdom of a wide local resection* . . . The overall picture suggests a reaction such as follows injury or trauma, with compensatory and atypical proliferation and degeneration . . . somewhat similar to post-inflammatory pseudo-tumors of the pleura . . . The material will be coded as *pseudo-sarcomatous hyperplasia* arising in association with a desmoid-like repair . . . *The staff believes that the lesion is probably benign*: Dr. Ackerman is in agreement with all members of the staff in this viewpoint." (Italics are ours.)

Dr. Regato: The AFIP staff added some curious remarks as to the danger that radiations might "activate" the suspicious cells, whatever they were, in the *"direction"* of a malignant tumor, and recommended that *"radiotherapy should be halted"*. Hoping that their histopathologic judgement was better founded than their radiobiologic lucubrations, we decided to continue radiotherapy, for if the lesion was benign there were chances that radiotherapy would be beneficial; not having a certainty as to the possible malignant nature, we could not ask the patient to accept a disarticulation. She received 4,500 roentgens in 26 days to a field 9 x 23 cm on the anterior aspect of the left thigh, with our Cobalt ^{60} teletherapy unit from March 6th to March 31st, 1958. The pain disappeared, the patient gained seven pounds in weight but the induration persisted on the posterior aspect of the thigh.

Towards the end of August, 1958, there was evident increase in the size of the mass with limitations of motion, pain recurred and collateral circulation appeared. A disarticulation of the thigh was then accepted by the patient and carried out on September 24th, 1958. A fusiform, 8 cm thick, mass appeared to run the course of the femoral artery and vein which were imbedded in it. Cross section revealed a gray mass flecked with yellow and blending with remnants of muscle. The femoral artery was completely thrombosed in the center of the mass. The tumor was found extending to the limits of the specimen and it was also present in lymph nodes neighboring the femoral artery. The slides distributed to the participants in this CANCER SEMINAR were processed from the disarticulation specimen.

Dr. Stout: This tumor is very hard to describe because the histological features vary greatly in different areas and none of them is sufficiently clear cut to permit proper recognition. There are areas where bizarre rounded cells show vacuoles of varying sizes usually one to a cell and this suggests liposarcoma. But it is hard to be sure that these areas are not adipose tissue invaded by undifferentiated tumor cells. There are other areas where the tumor cell

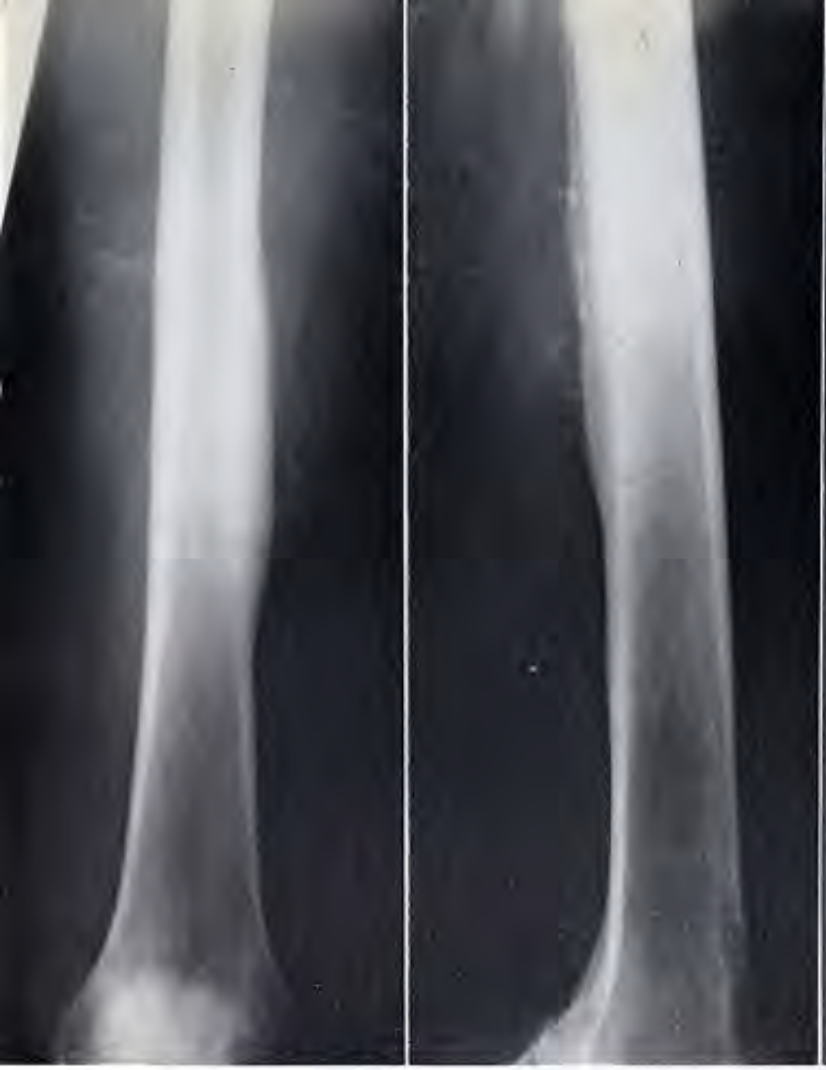


Fig. 1 and Fig. 2—Front and lateral view of the femur showing cortical thickening and some calcific debris within soft tissue mass.

Fig. 3 — Cut section of soft tissue tumor of the thigh.

cytoplasm is strongly acidophile suggesting that these are rhabdomyoblasts. But there are no cross striations and again one wonders if the acidophile cytoplasm may not represent a degenerative phenomenon. There is some true bone in one section with motheaten trabeculae and also a little proliferated osteoid but this is not neoplastic bone. Elsewhere the tissues sometimes vaguely suggest neoplastic osteoid but without sufficient differentiation to permit one to be sure. I considered the possibility that the whole tumor might be a parosteal osteogenic sarcoma but there is not enough assured differentiation to permit that diagnosis. With such uncertainty I have felt compelled to classify this as an undifferentiated malignant mesenchymoma.

I have come to the conclusion that the term malignant mesenchymoma has to be stretched further than when I first studied the mixed mesenchymal tumors. There is a differentiated form which is composed of two or more malignant tissue types, in addition to fibrosarcoma, in which the types can be recognized. That was the original variety. Now I encounter tumors like the present one in which there are suggestions of varying malignant mesenchymal types but without sufficient differentiation for the tumor types to be named with assurance. If one does not call them undifferentiated malignant mesenchymoma, the only alternative is to classify them as malignant undiagnosed mesenchymal tumors which is a neoplastic *limbo* or Gehenna from which nothing can rescue them.

That the malignant mesenchymoma is not a very uncommon tumor type in my roster of mesenchymal tumors is indicated by the fact that we have 243 malignant mesenchymomas recorded in the Laboratory of Surgical Pathology of Columbia University; fifty-six of these were in children. Dr. Artemis Nash and I have just commenced a study of them in connection with the extended study of mesenchymal tumors in children in which I am at present engaged.

Dr. Stout's diagnosis: MALIGNANT MESENCHYMOMA.

Histopathologic Diagnoses Submitted by Mail:

Rhabdomyosarcoma	76
Liposarcoma	37
Parosteal sarcoma	30
G. O. K. !	1
Others	20

Dr. Regato: Dr. Fred Stewart, of New York, offered rhabdomyosarcoma and predicted that someone will call it a granular-cell myoblastoma: Dr. Mark Wheelock of Chicago did! Dr. Robert R. Rember, of Denver, also made a diagnosis of malignant mesenchymoma.

Subsequent history: Following operation, the patient regained considerable weight. In November, 1958, she presented left sided pleural effusion; later she developed right plural effusion, edema of the right lower extremity and phantom pain of the left thigh. On March 16th, 1959, she expired.

Autopsy revealed that the tumor extended directly upward along the left iliac vessels and the psoas muscle, which was almost entirely replaced by tumor. There were numerous nodular masses in the liver, lungs, para-aortic lymph nodes, pancreas and pericardium; it was not found in the bone marrow, the adrenals, the spleen, nor kidneys.

Dr. Bricker: Malignant soft tissue tumors of the thigh cannot be predicted in extent; they extend along fascial planes but one has no way of recognizing this during physical examination or at operation. No one dislikes a hemipelvectomy more than I, but in lesions of the thigh, if one

wants to be sure of getting proximal to tumor, one should very seriously weigh the advantages and disadvantages of doing radical amputation.

Tumors of the medial aspect of the thigh can be hidden for sometime, particularly in obese women: a liposarcoma can grow to the size of a grapefruit before she even notices it. In young people who have firm thighs, difficult to palpate deeply, tumors arising in the region of Hunter's canal can cause venous obstruction and swelling of the leg which are not promptly explained. When a tumor is recognized and it appears limited, one should resist the tendency to do so-called "shelling-out" operations for these tumors are rarely truly encapsulated. One never knows, but it is likely that many of these tumors metastasize in the interval between inadequate removal and eventual clinical recurrence and before definitive treatment is instituted.

A. M. Miller, M.D., Pueblo, Colorado: I saw this specimen originally in February, 1958, and at that time I felt that there were cells present in a rather sclerotic-appearing stroma; these cells were a little bit more scattered at that time however, and the first impression I had was that of a metastatic carcinoma of the breast. But then, after seeing the roentgenograms, learning that there were no other masses and that the patient had complained of pain in this area for about a year before biopsy was taken, I felt that one good possibility to consider was a parosteal chondrosarcoma. I suppose, in retrospect, I can say that I wasn't entirely a fool since the fools are where angels fear to tread.

M. Wheelock, M.D., Chicago, Illinois: I want to find out why I was wrong—so I am going to ask Dr. Stout if he will be kind enough to say why he thinks this is definitely not a malignant granular cell myoblastoma.

Dr. Stout: I couldn't see any cells with granules, such as granular-cell myoblastomas have. There are two varieties of malignant granular-cell myoblastomas. In one, the tumor originally used to be called malignant organoid granular cell myoblastoma; now it's called alveolar cell sarcoma, and malignant paragranuloma. Incidentally, I think that the qualification of alveolar is wrongly used here; alveoli are tubes and those who use the adjective here actually mean to designate solid cords. A good friend of mine, Dr. Riopèlle, of Montreal, uses this term; he gave me twelve reasons for its use and I rejected them all! I still use the term granular-cell myoblastoma for the organoid type. This was certainly not the organoid type. The other variety is that in which the granular-cell tumor, without the organoid arrangement of its cells, becomes malignant. As far as I know, there are only seven or eight such cases recorded; they differ from the ordinary organoid myoblastoma by their somewhat larger nuclei and nucleoli; that's about the only difference. I didn't think of myocell granuloblastoma here because I didn't see any granules that I recognized as such and because of what I thought were different varieties of malignant tumor tissues.

L. Lowbeer, M.D., Tulsa, Oklahoma: I should like to know what the metastases looked like microscopically. In some of these malignant mesenchymomas, the primary tumor may be predominant like rhabdomyosarcoma or liposarcoma, but the recurrence or metastasis may be predominantly osteogenic sarcoma. How was it in this case?

M. Berthrong, M.D., Denver, Colorado: The metastasis in the lymph nodes which were present in the resection specimen were of the large epitheloid type or of the large myoblast type, or whatever they were, but none ever showed striations and none appeared clearly granular. They never assumed any specific pattern. Wherever the tumor was present in the autopsy material, it was similar: where it extended in soft tissues it had the more fibrous stroma and spindly cells. We never found any truly bone formation in any of our sections. In the metastases we found no striations,

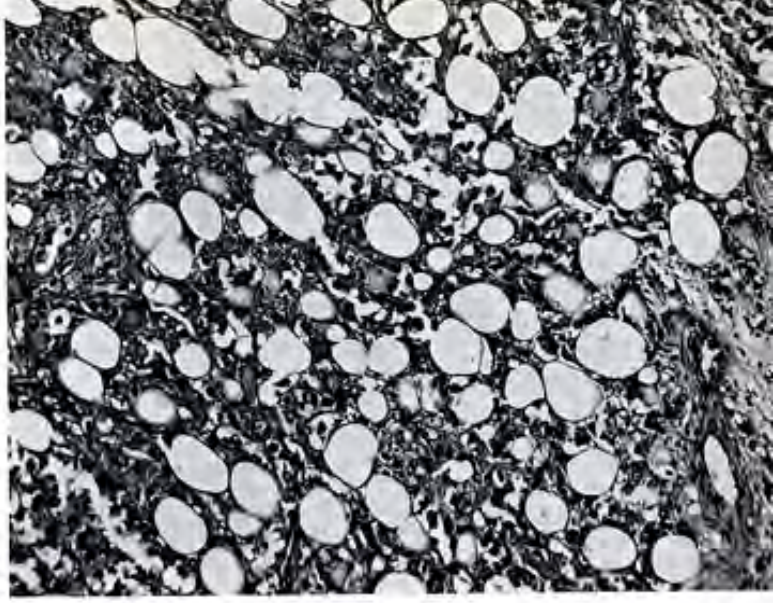


Fig. 4 — Lipoblastic part of malignant mesenchymoma.

no bone formations, and no organoid pattern to help us make a diagnosis.

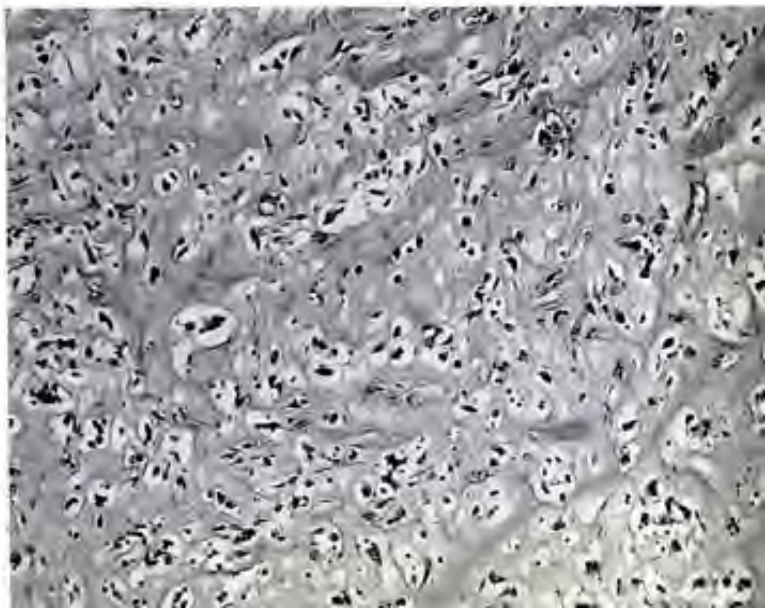
All of our attempts to do special stains were very disappointing. The amount of fat in the tumor was surprisingly small. Throughout the tumor, those round, obviously mature, fat droplets, were fat: but in what was clearly tumor cells, the fat was remarkably sparse; so much so, that we decided that we could not under those circumstances, consider a liposarcoma. This was true also in the metastases. The lymph nodes looked so much like epithelial structures that we considered melanoma and did some special stains which were also negative. We ended up with a diagnosis of undifferentiated alveolar soft part sarcoma, whatever that is!

Dr. Hodes: I would like to know how many hemipelvectomies Dr. Bricker has done and what they have accomplished?

Dr. Bricker: I have done only four hemipelvectomies: one patient is a long term survivor for fibrosarcoma; the others have all died. I tend to avoid hemipelvectomy. With certain types of tumor that are more favorable, that is, the large tumors attached to the bony pelvis with less degree of malignancy and lesser extension by lymphatics or blood stream, the results of the operation are much better. There are enough favorable results to justify it, provided one feels that the entire mass of tumor can be removed.

C. Eckert, M.D., Albany, New York (in Puerto Rico): I would assume from the description that this was a real biopsy and not just a half-hearted one. Had the correct diagnosis been made the eventual outcome in this particular case might not have been changed because this is a highly

Fig. 5 — Osteogenic focus in malignant mesenchymoma.



malignant tumor which has very bad behavior. Had you realized that this tumor ascended along the femoral vessels, it is quite possible that a hemipelvectomy might not have been recommended. We know that hemipelvectomies have been done for highly malignant tumors that have not altered the course of events at all; on the other hand, they have salvaged some potentially metastasizing tumors of lesser degree of malignancy. I think it is rather important that this operation be reserved for cases in which there is some hope of salvage rather than to simply apply it because you realize that no other operation can circumscribe this tumor.

Dr. Stout: Some tumors like chondrosarcomas of the upper end of the femur and upper end of the humerus are worth treating radically because they can possibly be saved and they couldn't be saved with anything short of that. But, osteogenic sarcoma in a child, I just don't think is worth doing.

Dr. Regato: I know of one instance of a young woman who had a chondrosarcoma of the proximal part of the femur which had grown to such a tremendous size that the patient was cacheetic. She weighed 103 pounds when admitted to have a hemipelvectomy, the specimen weighed 52 pounds so that she actually weighed less after operation than what was removed from her. She rapidly regained weight; she was the mother of small children and has continued to live now with a prosthetic appliance and in perfect happiness.

References

Barber, J. R., Coventry, M.D., and McDonald, J. R.: The spread of soft tissue sarcomata of the extremities along peripheral-nerve trunks. J. Bone Joint Surg., **39-A:** 534-540, 1957.

Bowden, L. and Booher, R. J.: The principles and technique of resection of soft parts for sarcoma. Surgery, **44:** 963-977, 1958.

Christopherson, W. M., Foote, F. W. Jr., and Stewart, F. W.: Alveolar soft-part sarcomas; structurally characteristic tumors of uncertain histogenesis. Cancer, **5:** 100-111, 1952.

Clark, R. L., Martin, R. G., White, E. C., and Old, J. W.: Clinical aspects of soft-tissue tumors. AMA Arch. Surg., **74:** 859-870, 1957.

Ewing, M. R. and Harrison, C. V.: Mesenchymoma. Brit. J. Surg., **44:** 408-414, 1957.

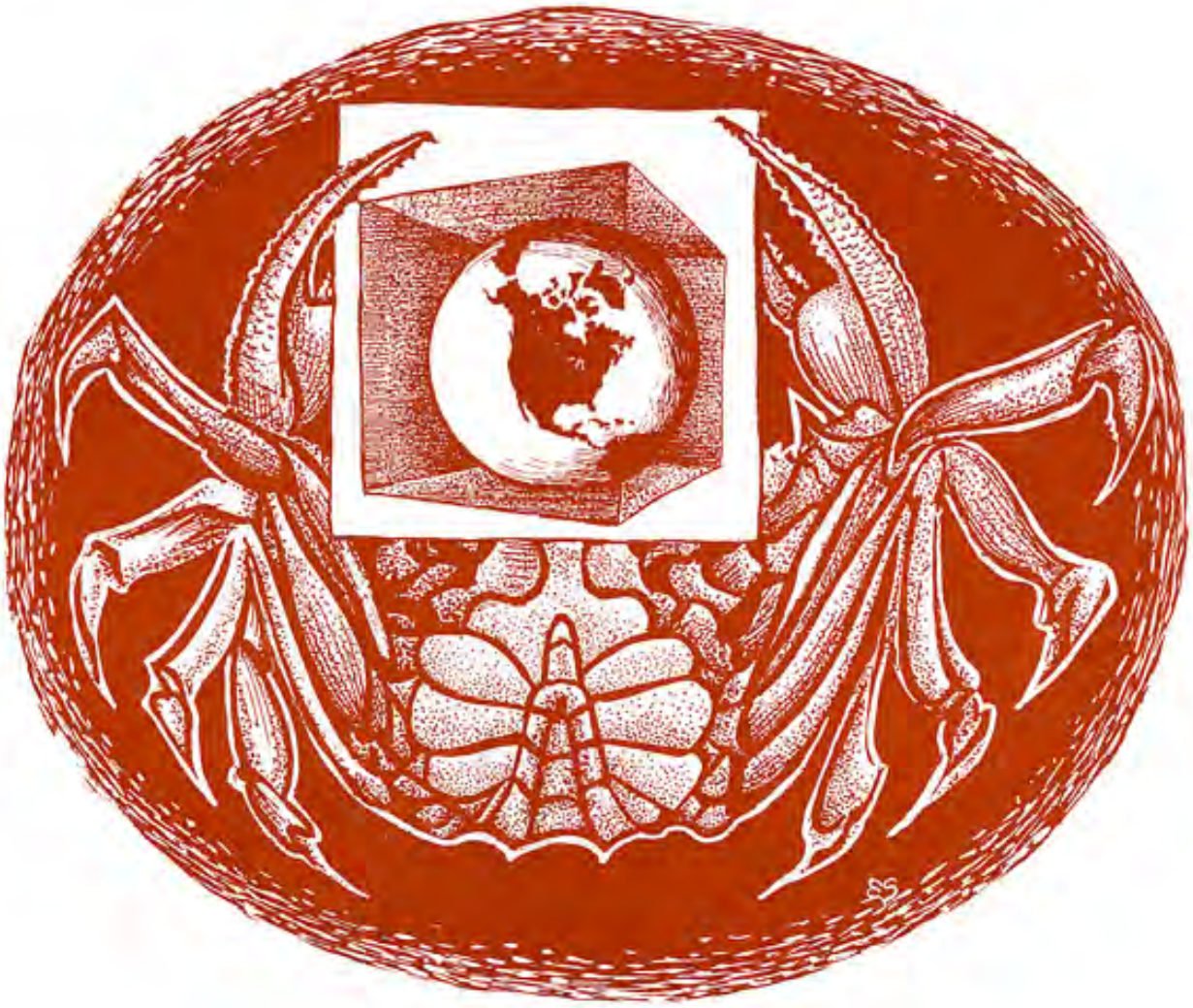
Haggart, G. E., Johnston, D. O., and Creeden, F.: Supervoltage radiation for sarcomata of the pelvis and lower extremities. J. Bone Joint Surg., **40-A:** 870-876, 1958.

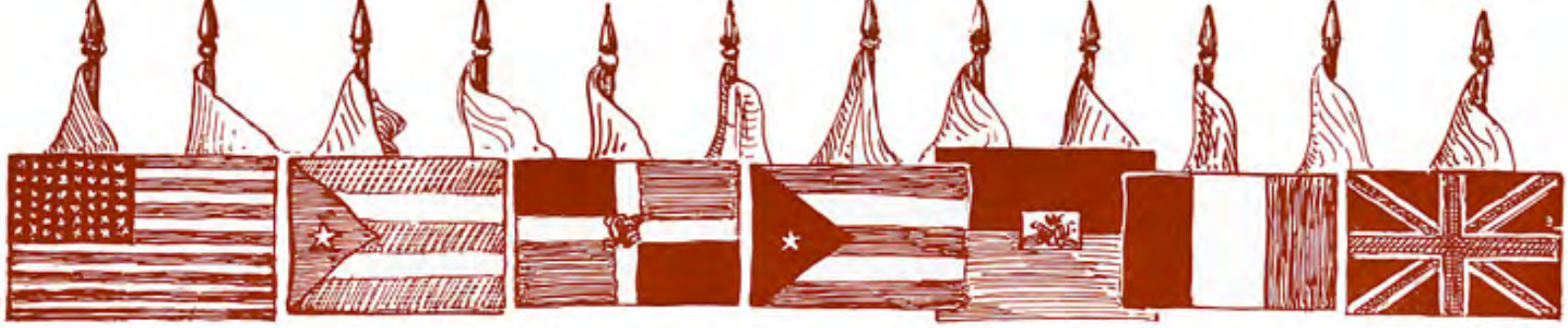
Kipkie, G. F., and Huast, M.D.: Malignant mesenchymoma (Haemangioblastomyxomatous variety) in a five-year-old boy. Canad. Med. Ass. J., **81:** 179-182, 1959.

Pack, G. T.: Major exarticulations for malignant neoplasms of the extremities: interscapulothoracic amputation, hip-joint disarticulation, and interilio-abdominal amputation. A report of end results in 228 cases. J. Bone Joint Surg., **38-A:** 249-262, 1956.

Riopèlle, J. L. and Thériault, J. P.: Sur une forme meconnue de sarcome des parties molles; le rhabdomyosarcome alvéolaire. Ann. d' Anat. Path., **1:** 88-111, 1956.

Stout, A. P.: Mesenchymoma, the mixed tumor of mesenchymal derivatives. Ann. Surg., **127:** 278-290, 1948.





9. Extensive Post-Traumatic Fat Necrosis of the Thigh Simulating a Malignant Tumor

Contributed by Henry C. Stoll, M.D., Brooklyn, New York, and
Ru-Kan Lin, M.D., Buffalo, New York

THE PATIENT was a 56-year-old man in September, 1957, when he gave a history of trauma to the left thigh fifteen months previously, followed by increasingly severe pain and loss of weight. On examination, the perimeter of the left thigh was 15 cm greater than that of the right. The enlargement was diffuse and tender to palpation. There was marked anemia and 38,000 white cells per cubic mm; the bone marrow was normal.

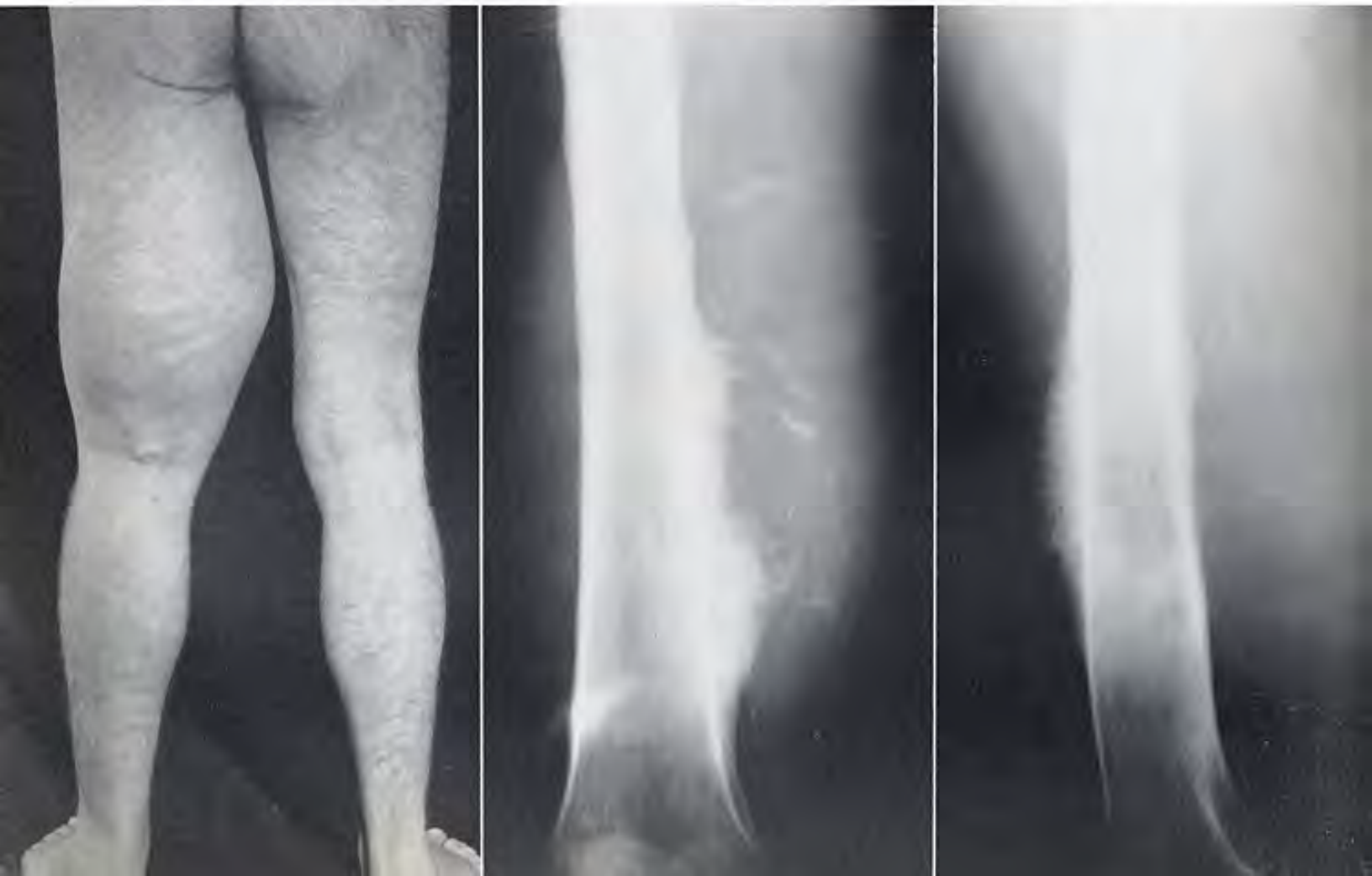
Dr. Hodes: Roentgen examination of the thigh revealed the following: (a) a large soft tissue mass within the thigh which appears to be very well demarcated, (b) the bone is dense, the outline is sharply demarcated, and one can see abortive Haversian systems within the bony debris. There are no changes within the medullary portion of the bone; nor is the endosteal segment of the cortex altered at the affected level, (c) in the soft tissues the bone debris on close examination looks like adult bone rather than malignant tumor bone.

The history of trauma plus the leukocytosis suggests that this patient has had hemorrhage which is now secondarily infected. The possibility that a soft tissue tumor mass of malignant origin has undergone necrosis cannot entirely be excluded however.

The cortical response to the overlying soft tissue mass militates strongly against an actively growing and aggressive tumor. The cortical reaction is compatible with adult bone;

Fig. 1 — Diffuse enlargement of the thigh.

Fig. 2 and Fig. 3—Front and lateral view of the femur showing marked cortical reaction and no medullary changes.



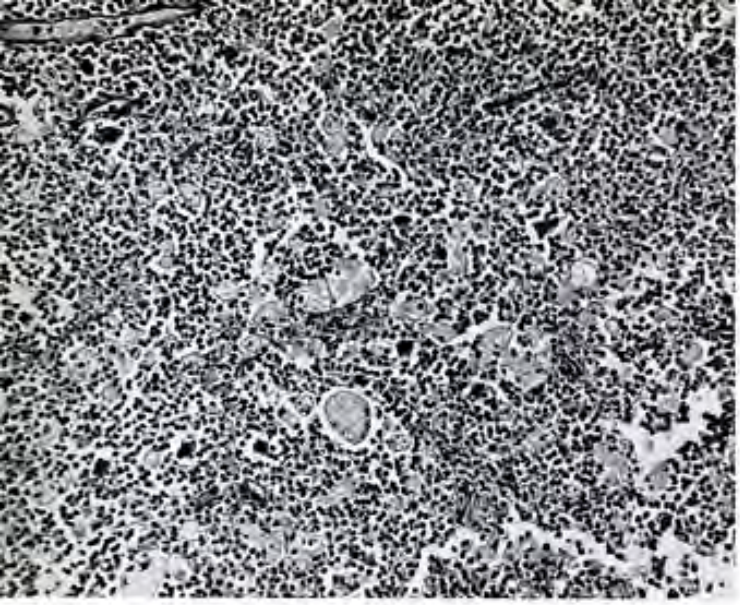


Fig. 4—Liposarcoma (?) masquerading as infected fat necrosis.

this is not the periostitis of malignant disease. The buttress of bone along the lower edge of the periosteal reaction is not as laminated as one expects in aggressive bone tumors. We have great difficulty reconciling this adult appearance with the history of trauma; perhaps the patient had trauma in the past which caused the abnormalities now seen and the current episode is a second traumatic incident superimposed upon the site of the old injury.

Dr. Hodes' impression: A BENIGN PROCESS with hemorrhage and secondary infection: 1. MYOSITIS OSSIFICANS with secondary necrosis. 2. Old foreign body reaction with recent hemorrhage and infection.

Roentgenologic Impressions Submitted by Mail:

Osteosarcoma	40
Parosteal fibrosarcoma	19
Chondrosarcoma	12
Various malignant tumors	18
Others	15

Dr. Regato: Most of the radiologic experts submitted an impression of malignant tumor.

Operative findings: In October, 1957, a surgical exploration was carried out. A large specimen, 10 x 7 x 4 cm was removed; the lesion appeared to invade the muscles and to cause periosteal reaction; on cut section the mass was soft, yellow in color, presenting a cauliflower-like appearance with areas of necrosis.

Dr. Stout: This section appears to be a very loose textured granulomatous lesion with its meshes widely distended and filled with huge numbers of polymorphonuclear neutrophiles and many foamy histiocytes. There are also scattered giant cells containing several nuclei. Some of the latter have large nucleoli, and a few show mitotic figures. No normal adipose tissue is detected, nor is any evidence of lipogenesis found. There are large areas of necrosis.

This appears to be a large mass of fat necrosis which has probably become infected because of the huge numbers of polymorphonuclear neutrophiles. Such a condition of fat necrosis and infection might follow or be associated with trauma with or without hemorrhage. Since there are no traces of old or new extravasated blood or blood pigment, hemorrhage seems unlikely. The necrosis and infection might have affected a pre-existing lipoma or liposarcoma. There is no evidence to suggest lipoma but the giant cells with mitoses might suggest a liposarcoma. This seems unlikely to me because giant phagocytic histiocytes may have large nucleoli and show mitoses without being malignant lipoblasts. The more probable explanation of this lesion seems to me to be infected traumatic fat necrosis.

Dr. Stout's diagnosis: INFECTED FAT NECROSIS.

Histopathologic Diagnoses Submitted by Mail:

Xanthogranuloma, histiocytosis	31
Liposarcoma	23
Osteomyelitis	20
Eosinophilic granuloma	18
Malignant tumors	22
Others	24

Dr. Regato: Dr. Leo Lowbeer, of Tulsa, suggested malignant lipid reticulo-endotheliosis or infected post-traumatic liposarcoma. Dr. R. Abell, of Ann Arbor, Michigan, was in favor of the former. Dr. M. B. Dockerty, of Rochester, suggested infected *grade 4* malignant neoplasm, possibly metastatic hypernephroma.

Subsequent history: Because of the uncertainty of the diagnosis, the patient refused an amputation and insisted on a trial of radiotherapy. From December 11, 1957 to January 17, 1958, he received an estimated dose, in the center of the lesion, of approximately 6,000 roentgens in five weeks. There was considerable reduction in the size of the mass and subjective relief. Towards the end of 1958, the patient developed an ulceration of the irradiated teguments which was excised and skin-grafted successfully. In January 27, 1959, an amputation was done because of severe hemorrhage. No tumor was identified in the specimen.

Dr. Bricker: I have seen three young patients who came to us after trauma with hematoma, followed by gradual resolution and by distortion with puckering of the skin suggesting a tumor. The parents were very distraught, the pediatrician very worried, but I didn't biopsy any of those. I thought that it was fat necrosis, followed by scarring. They have gone on with some distortion of skin but it appears to be lessening as time passes.

A. J. Miller, M.D., Pueblo, Colorado: Can this be called a xanthogranuloma?

Dr. Stout: I suggested a resemblance of this lesion to xanthogranuloma. I thought that it was different in this respect: the mass was largely due to the inflammatory cell infiltrate and to the extensive fat necrosis that seemed to have occurred. That seemed to me to make it different from the xanthogranuloma of the retroperitoneal space which did not show much or any necrosis.

H. C. Stoll, M.D., Brooklyn, New York: This case was originally seen with this large mass in the thigh 18 months after initial injury and about one year after he had first been hospitalized; he was quite a diagnostic problem. The clinicians felt that his leg was practically useless but the patient refused amputation, and insisted on a trial of radiotherapy. His leg became very large and they decided on a biopsy. When they did the biopsy, they didn't know where to stop and kept going down until they reached the bone and decided to quit. We weren't able to help them very much; either on frozen section or on permanent section. The slide was rather widely circulated; we couldn't offer any real assurance that it was malignant or benign.

J. W. Pickren, M.D., Buffalo, New York: This patient subsequently had an amputation: the mass persisted and eventually eroded into the femoral artery and caused massive hemorrhage; and the only way we could stop the hemorrhage was to ligate the femoral artery.

R. Cox, M.D., San Juan, Puerto Rico: In Case Number 4, that turned out to be a liposarcoma, as well as in this case, the slide showed some bizarre nuclei. Do you see bizarre cellular changes in well substantiated xanthogranulomas?

Dr. Stout: Bizarre giant-cells with big knotted nuclei always suggest to me that you are probably dealing with a liposarcoma, not just a benign lesion.

References

Oberling, C.: Retroperitoneal xanthogranuloma. Amer. J. Cancer, 23: 477-489, 1935.

10. *Pseudosarcomatous Fasciitis of the Thigh*

Contributed by RALPH FABGOTSTEIN, M.D., and ROBERT S. YOUNG, M.D.,
Pueblo, Colorado

THE PATIENT was a 13-year-old boy in April, 1959, when he complained of a gradually increasing, painless mass in the left thigh. On examination, the mass was slightly tender and firm and was situated in the upper half of the posterior aspect of the thigh.

Dr. Hodes: The roentgen examination of the thigh revealed the following: (a) a soft tissue mass which is fairly well outlined along its periphery and apparently arises in the muscles, (b) the adjoining femur is not affected, (c) calcific debris deposited within the soft tissue mass, the calcific debris suggesting calcifying tendinitis rather than bone.

The manner in which the fascial planes were distorted suggested the presence of an old inflammatory or neoplastic soft tissue mass. The clinical findings suggest tumor rather than infection. The general roentgen appearance of the soft tissue mass was consonant with a slowly growing malignant process arising within the muscles or neighboring soft tissues. The calcific debris within the soft tissue mass might well be an important lead in the differential diagnosis. The fact that soft tissue tumors undergo necrosis, infection, with ultimate deposition of calcific debris is a consideration. This could happen within ordinary fibrosarcomas, rhabdomyosarcomas, lipomas, liposarcomas, etc.

In view of the nature of this conference one is inclined to think of the less usual soft tissue masses. And because Dr. Stout is involved I am inclined to believe that perhaps this is an example of a hemangiopericytoma. This tumor is connected with Dr. Stout's name. Whereas, other portions of the body may be affected, the lesion tends to occur more commonly in the extremities. Also, the calcific described within hemangiopericytoma is not unlike that demonstrated by this individual.

Dr. Hodes' impression: A malignant soft tissue tumor: 1. HEMANGIOPERICYTOMA. 2. LIPOSARCOMA with necrosis.

Roentgenologic Impressions Submitted by Mail:

Hematoma	19
Myositis ossificans	15
Hemangioma	13
Neurofibroma	12
Malignant tumors	21
Others	22

Dr. Hodes: There was no history of trauma, yet this does not militate against a diagnosis of hematoma. The peculiar calcific debris within the tumor mass could be found in areas of hemorrhage or myositis ossificans. Hemangioma is a distinct possibility, but the absence of altered growth in the adjoining bone and because the calcific debris did not look like phleboliths we did not consider this diagnosis seriously. Neurofibromas could look like this and may contain calcific debris.

Dr. Regato: Dr. Benjamin Felson, of Cincinnati, also submitted an impression of hemangiopericytoma. Dr. Robert L. Stein, of San Francisco, submitted hematoma. Dr. Paul Swenson, of St. Paul, Minnesota, Dr. David Gould and Dr. Emanuel Salzman, of Denver, preferred calcifying hematoma.

Operative findings: In June, 1959, a hard, apparently well encapsulated but adherent mass was removed: it was within the muscle, not attached to the fascia; on cut surface it was gray-pink in color and presented cystic areas.

Dr. Stout: This sharply circumscribed tumor of the thigh must have extended to the fascia covering the muscle for it appears to be attached to it. The major portion of it consists of dense fibrous tissue arranged in bands with thick collagen fibers accompanying the cells. There are a number of irregularly spaced focal nodules of calcification in this dense and sometimes whorled area. In several focal areas the tumor suddenly changes to a very loose textured myxomatous growth. There are a fair number of capillaries scattered through; they are inconspicuous except in the myxoid areas. The foci of calcification are striking because the surrounding cells have a stellate arrangement as if the calcified material had replaced the center of some kind of a tubercle but surely not a tuberculous one.

This is indeed a peculiar lesion and I cannot recall having seen anything exactly like it. The foci of calcification are especially puzzling. Disregarding them for the moment, this lesion seems to me more like a case of pseudosarcomatous fasciitis than anything else. The fibrous tissue inter-

Fig. 1 — Soft tissue mass with light calcific debris.

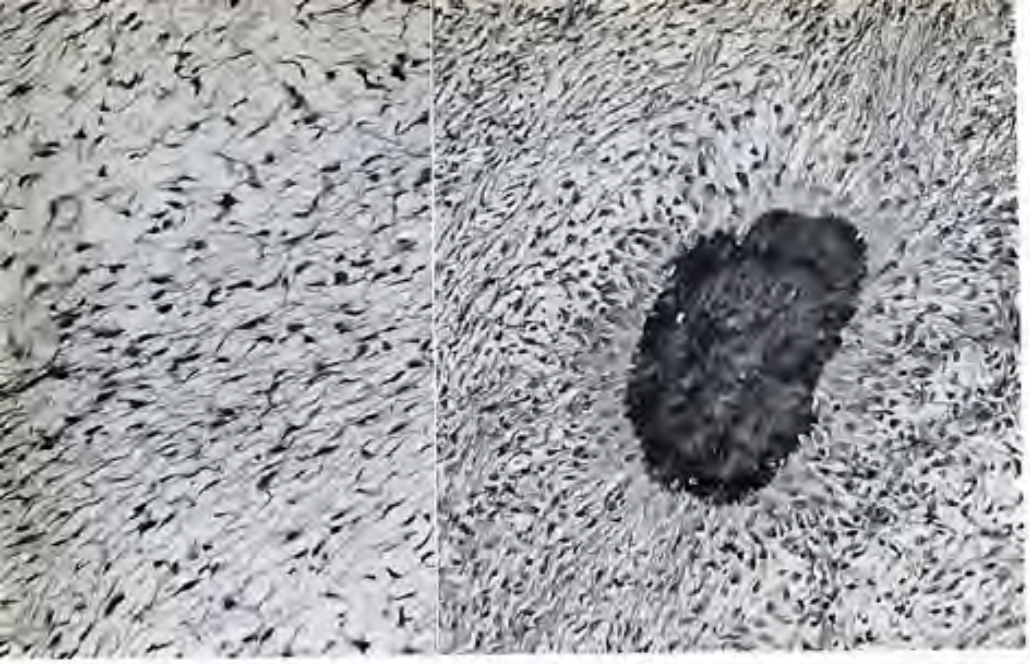


Fig. 2 and Fig. 3 — Pseudosarcomatous fasciitis with myxoid fibroblastic proliferation and peculiar focus of calcification.

mingled with the myxomatous areas are very suggestive. We are not told how long this lesion has been present but because of the calcified foci it would seem probable it had been for a period of several months or a year. One must remember that most pseudosarcomatous fasciitis cases are removed within a period of a few days to three months. This long duration might account for the absence of inflammatory cells which are so common in early cases and for the density of the fibrous tissue and absence of mitoses. In any event, I can think of no other explanation for this case.

As of September 1959, we have recorded 63 cases of pseudosarcomatous fasciitis in the Laboratory of Surgical Pathology of Columbia University. These have the following distribution:

63 Cases of Pseudosarcomatous Fasciitis

Upper Extremity	32	Lower Extremity	16
forearm	22	thigh	11
arm	10	leg	4
		foot	1

Head and Neck	5
Anterior Chest	6
Back	2
Vulva	1
Inguinal Region	1

We have follow-ups for only a few cases. One of them recurred apparently following incomplete excision, none is known to have metastasized. Almost all were subcutaneous but attached to the deep fascia. Two were attached to the deep fascia but were intramuscular. Eight were in children.

Dr. Stout's diagnosis: PSEUDOSARCOMATOUS FASCIITIS OF THIGH.

Histopathologic Diagnoses Submitted by Mail:

Ossifying fibroma	47
Myositis ossificans	34
Fibrosarcoma	20
Myxofibroma	17
Fascial fibromatosis	16
Neurilemoma	6
Fasciitis	3
Others	27

Dr. Regato: Dr. L. V. Ackerman, of St. Louis, also made a diagnosis of fasciitis. Dr. M. B. Dockerty, of Rochester, offered calcifying leiomyoma. Dr. André Pagès, of Montpellier, France, and Dr. E. H. Soule, of Rochester, offered calcifying fibroma. Dr. John D. Bauer, of St. Louis, and Dr. N. Navarro-Roca, of Santiago de Cuba, preferred myxofibroma.

Subsequent history: In July, 1959, a wider excision of the tissues of the affected area was carried out. No residual tumor was found.

The patient was last seen in August, 1959, when he was asymptomatic and appeared well-healed with full range of motion.

R. Fargotstein, M.D., Pueblo, Colorado: Dr. Young told me that the tumor was surrounded by muscle and was not attached to the fascia.

Dr. Bricker: I would have biopsied this lesion, and then decided whether or not I would operate on it as a malignant lesion. If the tumor was in a critical location, lying in close proximity to the femoral artery or a nerve and one found that it was indeed a malignant tumor, one would have been in a much better position to choose planes for dissection.

Dr. Stout, how sure do you feel at the present time that trauma never causes malignant tumors of soft tissues?

Dr. Stout: I don't see how you can ever prove that trauma causes anything. I can easily understand that a small tumor being traumatized, with the tissue about it damaged, might grow out and its growth be accelerated. I don't know of any proof of any case in which trauma caused a sarcoma.

R. G. Vernon, M.D., Dubuque, Iowa: Is there any indication that the patient's age is of any significance in the diagnosis of fasciitis?

Dr. Stout: Eight of our 63 cases were in children, the majority were in adults and the oldest as I recall, was about sixty. But the commonest age for them to occur is in young adults, I think.

C. Eckert, M.D., Albany, New York (in Puerto Rico): I would say that the right thing was done and possibly for the wrong reasons. The location of this tumor should have been favorable for adequate local removal regardless of its histologic pattern, but information about the histologic pattern would have led to adequate local removal and this would have been the end of it. The procedure of excising a tumor locally and then re-excising the area is perhaps the most difficult technical maneuver that you can imagine, because the actual outlines of this field are very poorly defined, once the tumor has been removed.

References

Konwaler, B. E., Keasbey, L., and Kaplan, L.: Subcutaneous pseudosarcomatous fibromatosis (fasciitis). Amer. J. Clin. Path., **25**: 241-252, 1955.

Sherwin, R. P. and Friedell, G. H.: Pseudosarcomatous fibromatosis (infiltrative fasciitis): Report of two cases. Boston Med. Quart., **10**: 49-51, 1959.

II. *Villonodular Synovitis of the Knee with Bone Involvement*

Contributed by PAUL E. MCMASTER, M.D. and MASON HOLT, M.D.,
Beverly Hills, California

THE PATIENT was a 45-year-old professional football player in February, 1953, when he complained of increasing discomfort of the right knee. There was a history of trauma 18 years previously.

Dr. Hodes: The roentgen examination of the affected knee revealed the following: (a) bone erosion medullary in origin arising primarily in the metaphyseal portion of the tibia, (b) the bone defects are sharply demarcated and obviously benign, (c) the adjoining joint seems unaffected.

This patient was injured 18 years previously. The bone defect alone is compatible with primary bone tumor. Single antero-posterior projections reveal no abnormalities within the knee joint. Thus, with the old history of trauma and the presence of benign bone resorption immediately adjacent to the injured site with increasing discomfort and soft tissue swelling the most probable diagnosis is villonodular synovitis.

Dr. Hodes' impression: A benign para-articular process: VILLONODULAR SYNOVITIS.

Roentgenologic Impressions Submitted by Mail:

Brodie's abscess	19
Giant-cell tumor	13
Chondroblastoma	12
Pigmented villonodular synovitis	9
Various benign lesions	32
Others	13

Dr. Hodes: The absence of bone reaction at the site of the lesion militates against infection. Giant-cell tumors usually are not centrally placed. Chondroblastoma is a distinct possibility which was considered, but we were inclined to set the possibility aside: the patient was rather old, and chondroblastomas usually lie closer to the articular joint cartilage.

Dr. Regato: Dr. Robert P. Spurck, Dr. Bertram L. Pear, and Dr. Robert McCarver, Jr., all of Denver, also submitted a diagnosis of pigmented villonodular synovitis.

Subsequent history: For three years, the patient continued to present a swelling and local tenderness. By 1956, the flexion of the knee was limited and fluid was aspirated.

In March, 1956, a surgical intervention revealed an extensive cavity filled with sanguinous fluid and communicating with the joint; it was curetted and filled with bone chips. An additional area in the lateral condyle of the femur was also curetted. A leg cast was applied. The patient was last seen in February, 1959, at which time he had no complaints and the roentgenogram showed healing of cystic areas.

Dr. Stout: The tissue appears to be a portion of synovial membrane and thickened capsule. Owing to extensive former hemorrhages, the synovial membrane has been greatly thickened and thrown up into villous projections. It is filled with many histiocytes most of which have phagocyted hemosiderin. There are many capillaries and areas of fibrosis. Further away from the synovial surface there are collections of foam cells.

This appears to be a characteristic example of villonodular synovitis of the knee joint that has probably resulted from repeated old injuries and hemorrhages. I can detect no evidence of neoplasm. It is impossible to tell the significance of the radiolucent area in the proximal end of the tibia from an examination of this section. I am quite happy to use the term villonodular synovitis in this case because it is obviously a reaction of the synovial membrane to something which has caused repeated hemorrhages. The first case comparable to this histological picture I ever saw occurred over 50 years ago in the knee joint of a hemophiliac and the villous processes that formed were the longest and most striking I have ever seen. When the same term is used for a solitary nodule with many giant and foam cells occurring in the capsule of a joint and without any villous formations, it seems to me like a different kind of lesion and I am still prone to adhere to the old term of giant cell tumor. One term that I refuse to use for it is synovioma or benign synovioma. There is no proof at all that synovial cells enter into its composition as they do into the synovial sarcoma.

If by any chance this is tissue removed from within the tibia I can only suppose it must be the result of an old intraosseous hemorrhage but that seems extremely unlikely to me.

Dr. Stout's diagnosis: VILLONODULAR SYNOVITIS of knee joint.

Histopathologic Diagnoses Submitted by Mail:

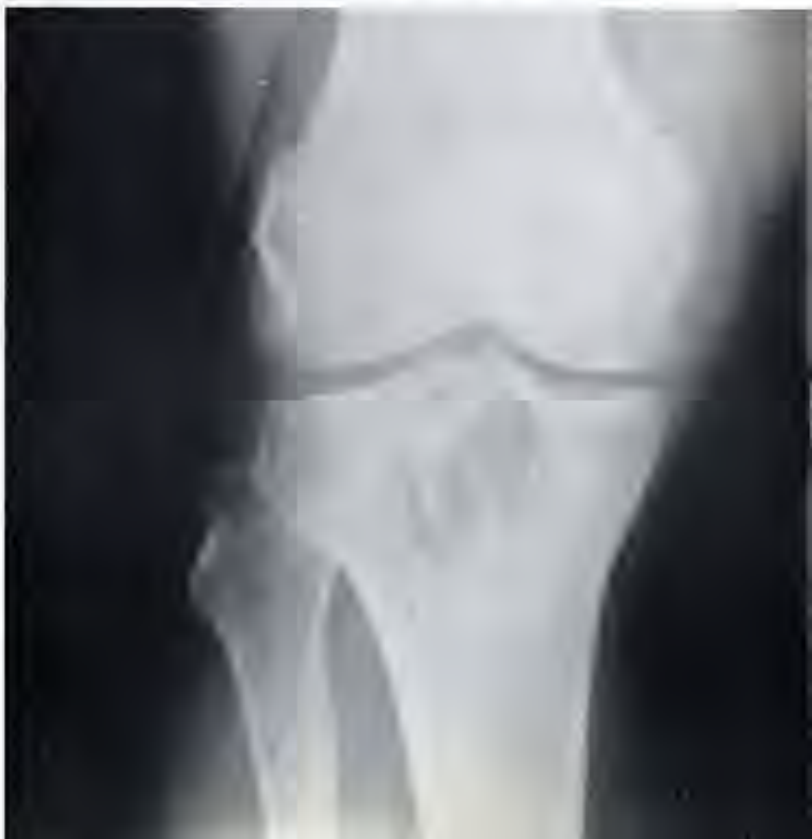
Villonodular synovitis	108
Giant-cell tumor	18
Organized hematoma	10
Don't quote me!	1
Others	24

Dr. Regato: Most of the experts agreed in the diagnosis of pigmented villonodular synovitis.

A. Harrell, M.D., St. Louis, Missouri: If one would have followed Dr. Bricker's suggestion and biopsied this lesion, wouldn't it have been better to give it roentgentherapy?

Dr. Regato: Radiotherapy has been advocated in the treatment of villonodular synovitis and they have been irradiated successfully. Dr. Milton Friedman has had experience with these lesions.

Fig. 1 — Medullary bone erosion in metaphyseal position of the tibia.



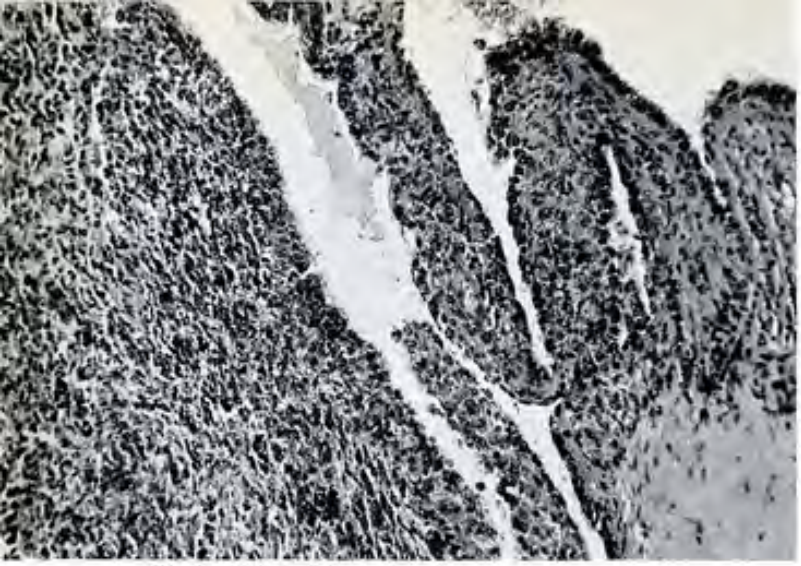


Fig. 2 — Villonodular synovitis.

M. Friedman, M.D., New York, New York (in Puerto Rico): Primary pigmented villonodular synovitis is often amenable to radiotherapy with tissue doses of 2,000 to 3,000 roentgens. In a primary lesion, uncomplicated by underlying pathology of adjacent bones, irradiation may be the treatment of choice. The prognosis is best in young adults with primary pigmented villonodular synovitis wherein the symptoms are only of a few months duration and the synovium alone is involved. The prognosis is poor in older patients or in lesions of several years duration. One less common form of pigmented villonodular synovitis is associated with a tendon sheath and invaded adjacent bones. It is amenable to larger doses of irradiation than conventional pigmented villonodular synovitis.

Other diseases, such as degenerative arthritis or traumatic degeneration of a meniscus, may occasionally evoke a secondary proliferative response of the synovium resembling a pigmented villonodular synovitis. These lesions are generally not improved by irradiation.

C. Eckert, M.D., Albany, New York (in Puerto Rico): Perhaps I haven't come in contact with the same variety of conservative orthopedists. I don't know actually how many of these lesions can be anticipated to regress spontaneously; if there is sufficient number, then I think observation is good. In this case, the patient's course was one of progression rather than regression.

Dr. Regato: Dr. Friedman believes that a rather large dose is necessary. I don't necessarily agree with him, because in inflammatory or benign conditions, very often a small amount of radiation does it or nothing does it. In the treatment of malignant lesions, the larger the dose the greater the chance of sterilizing it by means of radiations. But we must bow to the man who has the experience.

M. Lougheed, M.D., Montreal, Canada (in Puerto Rico): I don't have any great experience myself but we have had a few cases and have given doses in the order of 1,200 to 1,500 roentgens over two or three weeks. I wonder if that was homeopathic or whether or not better results could be achieved by giving more.

Dr. Regato: I think that that is a good approach. Beyond that, it would not be justified particularly since this can be well done by other means. I think your approach would be cautious and adequate.

W. Rider, M.D., Toronto, Canada (in Puerto Rico): I have had the opportunity of seeing some of these patients treated, in Edinburgh; most of them were diagnosed as giant-cell tumors. I think the high doses that Milton Friedman talks about are quite necessary. We had a policy of treating all of these patients by radiotherapy. Our experience was that under 3,000 roentgens in the middle of the lesion in a three-week period was too low. The majority of these patients did very well and we treated a lot of patients who had previously had surgical intervention and the insertion of sterilized sequestra.

Dr. Regato: I wish only to point out that many of these cases, wherever bone involvement was present, used to be misdiagnosed as benign giant-cell tumors and treated as such; as a consequence larger doses were administered. If Dr. Stout would render a diagnosis of benign giant-cell tumor, I would be in favor of larger doses of the order mentioned by Drs. Friedman and Rider.

References

Breimer, C. W. and Freiberger, R. H.: Bone lesions associated with villonodular synovitis. Amer. J. Roentgenol., **79:** 618-629, 1958.

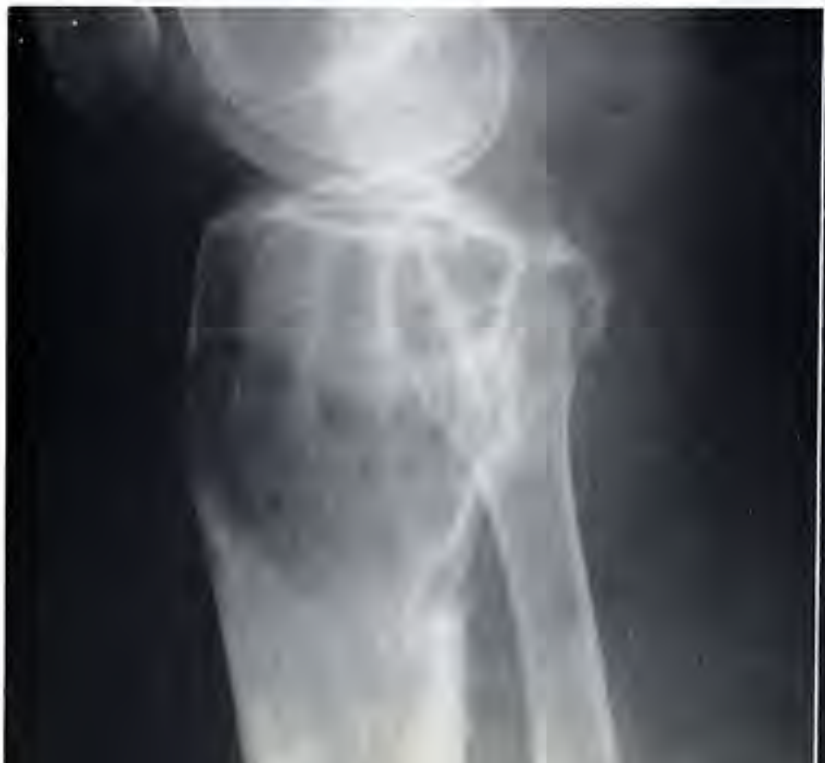
Friedman, M. and Schwartz, E. E.: Irradiation therapy of pigmented villonodular synovitis. Bull. Hosp. Joint Dis., **18:** 19-32, 1957.

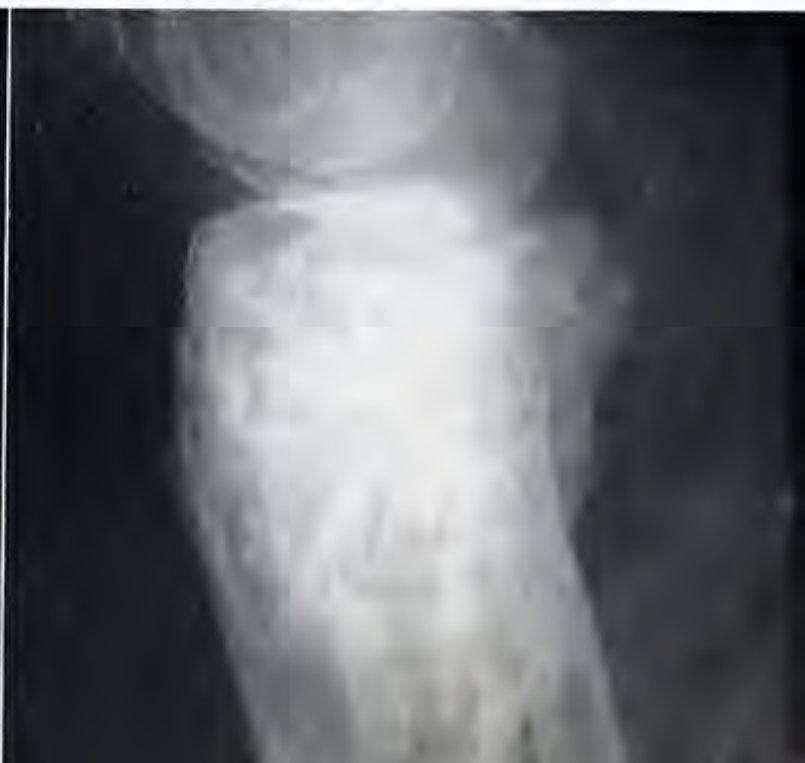
Lewis, R. W.: Roentgen diagnosis of pigmented villonodular synovitis and synovial sarcoma of knee joint. Radiology, **49:** 26-37, 1957.

Sherry, J. B. and Anderson, W.: The natural history of pigmented villonodular synovitis of tendon sheaths. J. Bone Joint Surg., **37-A:** 1005-1011, 1955.

Fig. 3 — Roentgenogram, in 1956, showing progression of bone erosion.

Fig. 4 — Roentgenogram, in 1959, showing recalcification after curettement and insertion of bone chips.





12. *Leiomyosarcoma of the Leg*

Contributed by L. Bruce Ellis, M.D., St. Louis, Missouri and John C. Lemon, M.D., Colorado Springs, Colorado

THE PATIENT was a 53-year-old man in April, 1957, when he presented a swelling of the lower half of the right leg following trauma received 18 months previously. On examination, there was a rubbery mass adherent to the deep structures at the junction of the middle and lower thirds of the right leg and measuring 4 x 6 x 10 cm in diameter. The serum calcium was 10 mg per cent; phosphorus was 1.5 mg per cent and the alkaline phosphatase was 2 Bodansky units.

Dr. Hodes: The roentgen examination of the lower limb revealed the following: (a) a soft tissue mass arising in the inter-osseous space, (b) the mass is more dense than the adjoining soft tissues, (c) erosion of bone is clearly demonstrated at the site of the soft tissue mass, (d) of unusual interest is the fact that the tibia and fibula were similarly affected.

The clinical nature of the tumor a "rubbery mass adherent to deep structures" suggests a slowly growing process which must be due to a tumor rather than infection. The nature of the bone erosion is also consonant with pressure erosion due to a slowly growing tumor rather than the result of low-grade chronic inflammatory disease. The multiple lobulations along the bone seem of unusual significance. One must postulate the presence of a tumor mass which is multi-lobulated else the very unusual nature of the cortical erosion could not be explained.

The direct resorption of cortical bone indicates some element of pulsation within the mass. Totally inert and inactive soft tissue masses do not cause pressure erosion; the element of pulsation is responsible for the defect. In neurofibromatosis, however, the bone defects more often are the result of interference with growth rather than bone resorption. The increased density of the soft tissue mass suggests a liberal admixture and an abnormal amount of fibrous or nerve tissue. The tumor, arising in the inter-osseous region, could be of nerve tissue origin. Major nerves lie in this portion of the lower limb, they are slowly growing tumors which are "rubbery" and may be associated with direct cortical atrophy.

Because of the history of trauma, the possibility of an aneurysm was considered; aneurysms rarely cause this scalloped bone erosion; there was no clinical evidence of aneurysm either.

Dr. Hodes' impression: A slowly growing malignant soft tissue tumor: 1. MALIGNANT NEURILEMOMA. 2. FIBROSARCOMA, fairly well vascularized.

Roentgenologic Impressions Submitted by Mail:

Neurofibroma	24
Arterio-venous fistula	21
Osteomyelitis	10
Fibrosarcoma	10
Various malignant tumors	18
Others	15

Dr. Hodes: The character of the bone resorption militates against arteriovenous fistula. Nor can one see in the perifocal soft tissues large blood vessels leading to the very dense tumor mass. The character of the cortical erosion militates against infection; chronic infection should cause cortical proliferation rather than cortical atrophy.

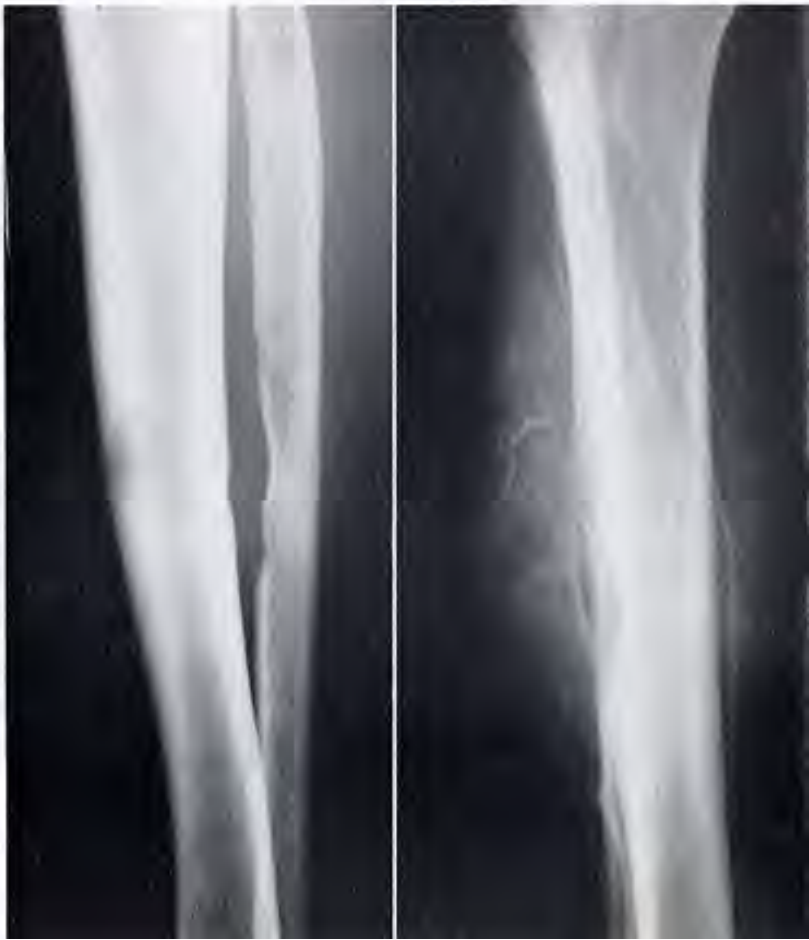
Dr. Regato: Dr. Bertram L. Pear, of Denver, and Dr. Genene Baker, of Colorado Springs, suggested neurofibromatosis. Dr. Paul Swenson, of St. Paul, Minnesota, offered an arterio-venous aneurysm. Dr. E. Salzman, of Denver, and Dr. Robert L. Stein, of San Francisco, preferred a fibrosarcoma.

Subsequent history: An arteriorgram revealed that the tumor was rather vascular, and suggested a malignant tumor. A biopsy was done.

Dr. Stout: In the areas where the tumor tissue appears best preserved, the tumor cells are elongated and arranged in bundles which interlace. The nuclei are blunt-ended and show some tendency to palisade. The cytoplasm is acidophile, fibrillated and there are many variously sized cytoplasmic vacuoles suggesting degenerative changes. As one passes out from the better preserved areas the tumor cells become more bizarre, are often large, and the nuclei have large acidophile inclusion bodies. Still further out the tumor becomes much more fibrous and only an occasional bizarre tumor cell remains in a dense relatively acellular fibrous stroma. Mitoses are present but are infrequent. The tumor is sparsely vascularized. With Masson's trichrome stain myofibrils are demonstrated in the elongated cells.

This tumor has the characteristics of a leiomyosarcoma. In spite of the many bizarre cells, I do not believe this is a

Fig. 1 — Bone erosion affecting both the tibia and fibula. Arteriogram showing increased vascularity.



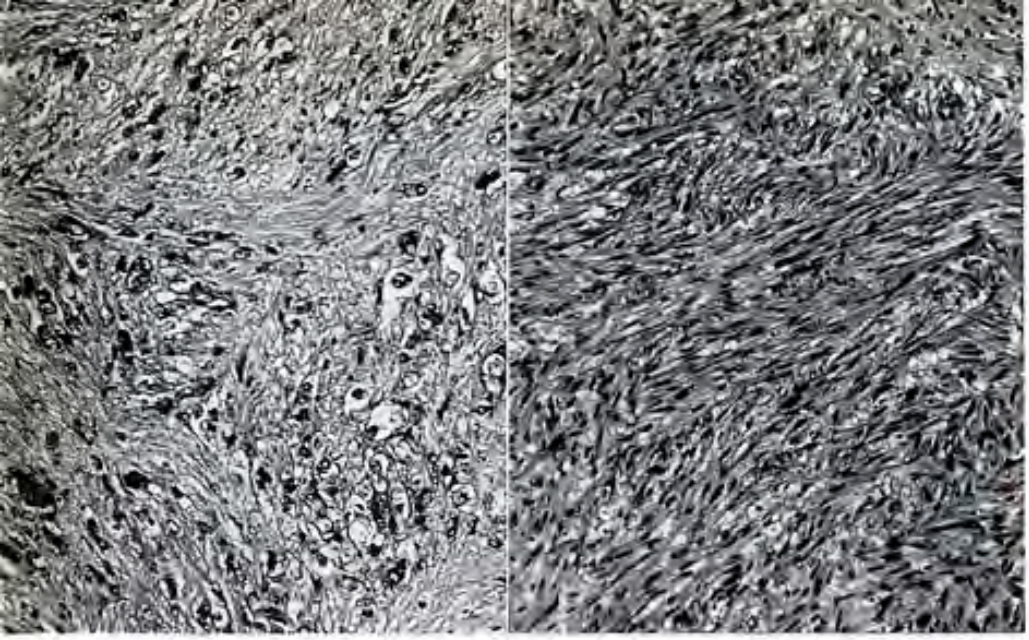


Fig. 2 and Fig. 3 — Leiomyosarcoma with well differentiated and poorly differentiated areas.

very malignant tumor if one can judge of its biological characteristics from the small fragment available for study, because there are very few mitoses; not more than 1 in 20 high power fields in my section. Since this is a leiomyosarcoma and probably primary in the leg, the changes in the bone must be due to pressure or invasion of the tibia or else must be independent of the tumor.

Leiomyosarcomas of the superficial soft tissues must be very rare for there are extremely few reports of them in the literature. Hill and I by 1957, found records of 36 cases excluding the retroperitoneal region, the mediastinum, and viscera. Females were affected twice as frequently as males. While the tumors were most frequent after 60 years of age (40%), all ages were affected including four cases in children. (Altogether we now have six cases of leiomyosarcoma in children; the sites of involvement are the scalp, forearm, leg, foot, tongue and vagina.) The results of treatment showed that about 50 per cent died or were last seen alive with metastases. Only four were known to have lived symptom-free more than five years after treatment without clinical evidence of tumor. Perhaps the most remarkable case in this group developed beneath the plantar fascia of the foot of a 15-year-old colored girl. She lived 22 years after excision then had a lung metastasis removed and died a few months later with metastases in the lung, brain and ileum. There was never any local recurrence.

Dr. Stout's diagnosis: LEIOMYOSARCOMA.

Histopathologic Diagnoses Submitted by Mail:

Leiomyosarcoma	39
Fibrosarcoma	32
Neurosarcoma	20
Malignant schwannoma	17
Rhabdomyosarcoma	16
Other sarcomas	15

Dr. Regato: Dr. N. F. C. Gowing, of London, also made a diagnosis of leiomyosarcoma. Dr. Sumner Wood, of Baltimore, offered pleomorphic fibrosarcoma. Dr. Fred Stewart, of New York, and Dr. Luis E. Gonzalez, of San Juan, Puerto Rico, favored rhabdomyosarcoma. Dr. Dorothy Russell, of London, and Dr. Morgan Berthrong, of Denver, offered malignant schwannoma. Dr. Isaac Costero, of Mexico City, preferred malignant neurilemoma.

Subsequent history: The patient presented evidence of early pulmonary metastasis and for this reason was submitted to roentgentherapy: in April-May, 1957, a series of irradiations were given, totaling 4,000 roentgens ("in depth") in 29 days. Following this, the lungs also were irradiated. In July, 1958, the patient's liver was enlarged and also was irradiated. In March, 1959, the patient expired. No autopsy was done.

I. Costero, M.D., Mexico City, Mexico: Malignant neurilemoma was my diagnosis, but if there are myofibrils in the trichromic stain done by Dr. Stout, this is, of course, a leiomyosarcoma.

J. K. Frenkel, M.D., Kansas City, Kansas: I wonder if Dr. Hodes would care to explain why there is pressure atrophy at the fibula and thickening in the cortex of the fibia. Is there biologic reason that would explain this finding?

Dr. Hodes: Usually you will not have pressure erosion unless you have pulsation. Solid tumor laying right next to a piece of bone will not produce erosion but if it is vascularized, the pulsation, like increased intracranial pressure produces erosion.

C. Eckert, M.D., Albany, New York (in Puerto Rico): It would have been very difficult to do a local removal and control this tumor. I would think from the films and extent to the lesion that an above-the-knee amputation would have been the site of election in this particular case. An assiduous search for metastases is very wise before you proceed with an amputation. We have done arteriorgrams in a number of highly vascular lesions and they offer considerable help, at times, in defining the source of blood supply to the given tumor and enable you to do a better job technically.

Dr. Hodes: Equally as informative is the fact that you may have no increased vessels or the way that they present themselves.

W. Rider, M.D., Toronto, Canada (in Puerto Rico): Are there very many metastatic hazards involved in angiography?

C. Eckert, M.D., Albany, New York (in Puerto Rico): You are doing arterial puncture at a considerable distance from the tumor and you are simply injecting a radioopaque material which circulates under slightly increased pressure through the tumor; I don't believe that this is going to be particularly conducive to an increase in the rate of metastases. I have no reason to think so, at any rate.

References

Stout, A. P. and Hill, W. T.: Leiomyosarcoma of the superficial soft tissues. Cancer, 11: 814-824, 1958.

13. *Malignant Mesenchymoma of the Ankle Region*

Contributed by ELEANOR H. VALENTINE, M.D., Denver, Colorado

THE PATIENT was a 48-year-old man in August, 1957, when he gave a history of a slow growing mass in the left ankle. It had been present for one year. On examination, the tumor appeared cystic: it measured 7 cm in diameter; it did not interfere with movements.

Dr. Hodes: The roentgen examination of the ankle revealed the following: (a) the bones and joints of the ankle were perfectly normal, (b) the soft tissue mass is fairly well demarcated and seems to lie outside of the ankle joint, (c) a few faint calcific deposits within the soft tissue mass.

Well localized para-articular soft tissue masses always suggest tumors of "synovial" origin arising from adjacent tendon sheaths or bursae; these tumor masses characteristically are all delineated. Whereas, they may present within the joint space most of the tumor mass lies beyond the confines of the latter.

Dr. Hodes' impression: A malignant soft tissue tumor arising in para-articular structures: 1. SYNOVIAL SARCOMA. 2. BENIGN SYNOVIOMA.

Roentgenologic Impressions Submitted by Mail:

Synovial tumor	31
Benign tumor	22
Synovial cyst	9
Malignant tumor	9
Benign lesion	18

Dr. Regato: Dr. F. A. Rose, of Cleveland, suggested xanthoma of the tendons. Dr. John M. Dennis, of Baltimore, offered synovial cyst. Dr. Bertram L. Pear, of Denver, and Dr. Victor J. Fish, of San Francisco, preferred synovioma.

Operative findings: In August, 1957, a surgical exploration revealed that the tumor invaded between the tendons and communicated with the joint surfaces; it could not be totally excised but part of the tumor was removed for biopsy. One week later, a below-the-knee amputation was carried out. The tumor consisted of rubbery tissue predominantly fibrous but with gelatinous necrotic and hemorrhagic areas.

A diagnosis of synovial sarcoma was made. The slide was submitted to the Armed Forces Institute of Pathology where a diagnosis of chondrosarcoma was rendered. Dr. Valentine submitted the slide to Dr. Stout (P. and S. 59138) who answered thus:

"In cases in which pathologists differ from the AFIP, I cannot always agree with the AFIP diagnosis. In this case of yours I must agree with them. I believe this is a characteristic chondrosarcoma of the soft tissues. One might suspect this possibility from the gross description for the tumor is called "nodular" and "pale, lobulated and somewhat gelatinous" on cut section. This fits a chondrosarcoma but no synovial sarcoma in my experience has had a comparable gross appearance. Microscopically the tendency of the tumor to grow in balls and nodules is striking. Only occasionally can one find a hint of matrix or myxoid tissue but they are there and the majority of the cells are rounded and differentiation is poor enough so that no capsules have been formed. . . . This tumor does not have the characteristics of a synovial sarcoma. I will not make that diagnosis unless I have proof of the intermingling of fibrosarcoma-like cle-

Fig. 1 — Soft tissue mass of the ankle.

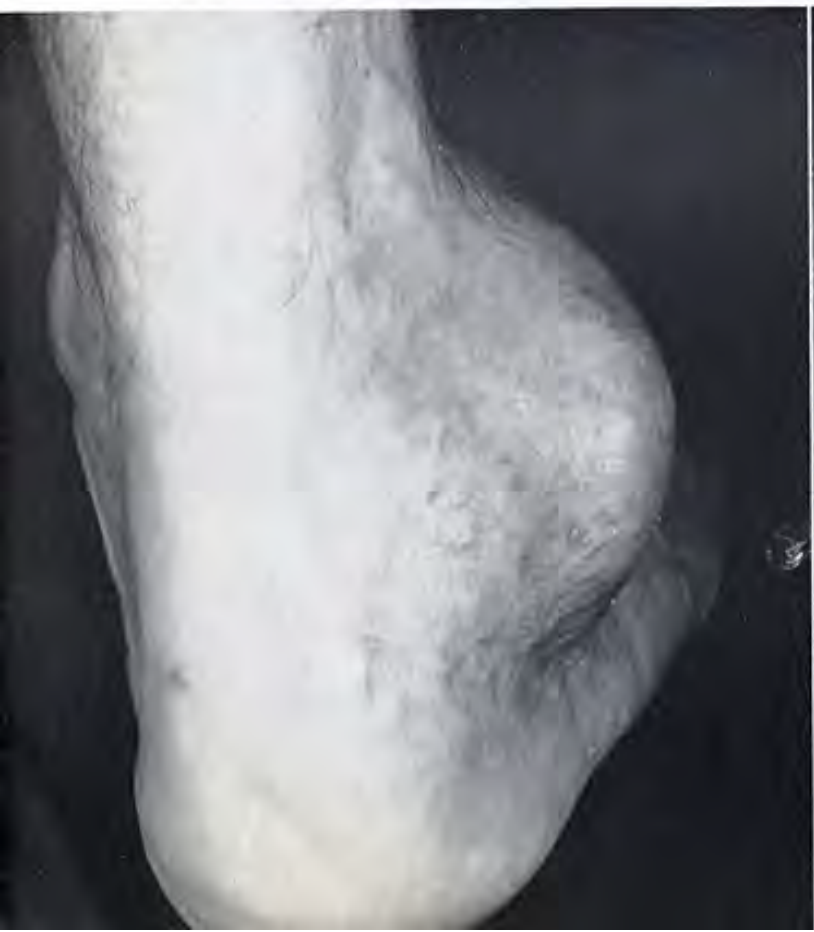
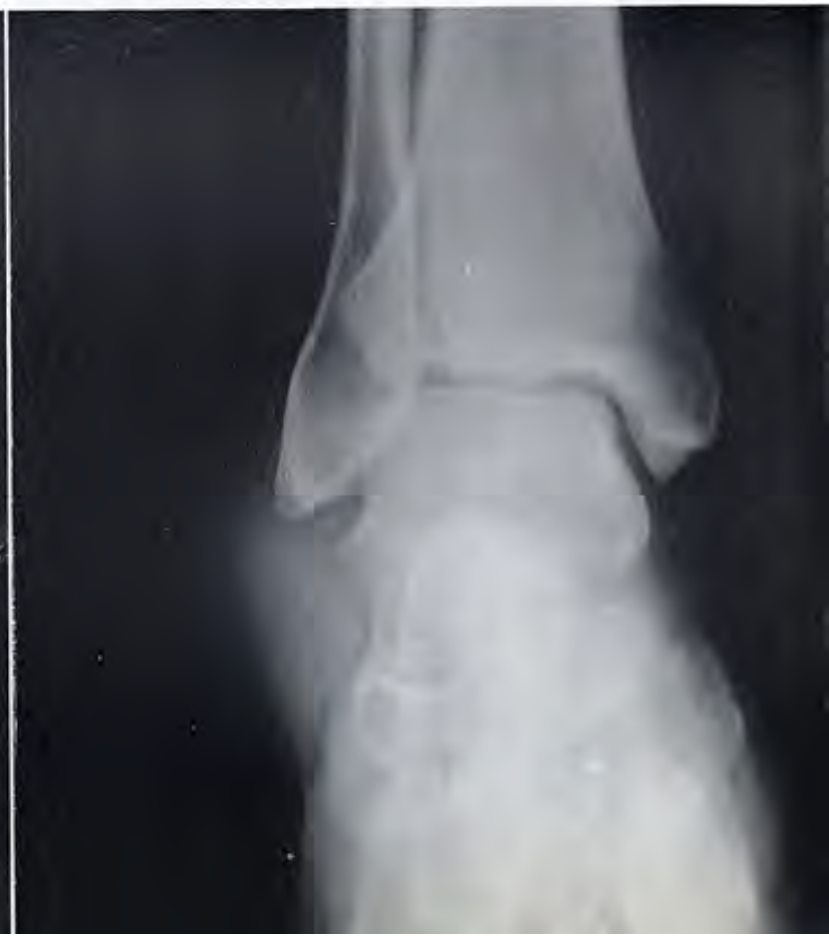


Fig. 2 — Soft tissue mass not affecting the bones.



ments with cords, slits or tubes of synovioblasts. Consequently, I have the opinion that synovial sarcoma is really a very rare tumor."

(At the SEMINAR, Dr. Stout was not aware that he had been previously consulted about this case. See Dr. Stout's final note at the end of the discussion.)

Dr. Stout: This tumor is characterized by the presence of a great many vague spaces, some slit-like and others larger. Lining the walls of these spaces and partly filling the lumens are many large polygonal cells. These are not all confined to the lining and lumen of the spaces but are sometimes found in the fibrous tissue outside. The picture is further complicated by the presence of a number of capillary and larger vessels in the stroma which are lined by normal endothelial cells. Mitoses are rare. A Laidlaw silver reticulin stain shows that while the cellular masses outside the slit-like and other spaces are relatively free from reticulin fibers, they are not entirely so (P. and S. 64450).

A tumor such as this raises the question in diagnosis between synovial sarcoma and malignant hemangioendothelioma. I do not believe this is a synovial sarcoma because the tissue between the slits looks like ordinary fibrous tissue and not fibrosarcoma, but also because there are a few reticulin fibers among the tumor cells. Such fibers should appear only in the fibrosarcomatous elements and not among the synovioblastic elements. I favor a diagnosis of malignant hemangioendothelioma because the endotheliobblasts often both heap up in the lumens and also invade the surrounding stroma. Our experience with this uncommon malignant tumor runs to some 110 cases. Fifty of these were scattered through the deeper soft tissues of the body, 19 were in bones, 2 were in peripheral nerves and 2 sprang from veins. The other regions involved included: spleen—8, liver—3, female breast—13, uterus—1, penis—2, upper respiratory system—3, pleura—2, mediastinum—1, diaphragm—1, and metastases from undetermined sites—3. Fourteen of the 110 cases were in children less than 16 years of age. The malignant hemangioendothelioma is generally very malignant, metastasizes easily and widely and is usually fatal. However, not all of them do this; some grow much more slowly and may not metastasize at all. Tumors of this sort are uncommon and large groups of them have not been published with proper follow-up information, so the actual incidence of metastases is not known to me. Of one thing I think one can feel assured: the malignant hemangioendothelioma does not arise from the relatively common benign hemangioendothelioma which is so frequently found in children.

Dr. Stout's diagnosis: MALIGNANT HEMANGIOENDOTHELIOMA.

Histopathologic Diagnoses Submitted by Mail:

Synovial sarcoma	130
Benign synovioma	12
Chondrosarcoma	9
Malignant hemangioendothelioma	7
Others	5

Dr. Regato: Dr. André Pagès, of Montpellier, France; Dr. J. French, of Ann Arbor, and Dr. Edward Murphy, of Mexico City, offered a diagnosis of synovial sarcoma. Dr. R. R. Rember, and Dr. H. L. McCaffey preferred chondrosarcoma. Dr. R. A. Keffler, of Lubbock, Texas, made a diagnosis of malignant hemangioendothelioma.

Subsequent history: The patient was last seen in March, 1959, when he appeared well except for a 2 cm left inguinal node. He refused biopsy or further follow-up.

B. Eiseman, M.D., Denver, Colorado: This patient was urged time and time again to come in; he came to the hospital day before yesterday: he has a firm mass, 1.5 cm in diameter in his left groin. We intend to remove this in a radical groin dissection.

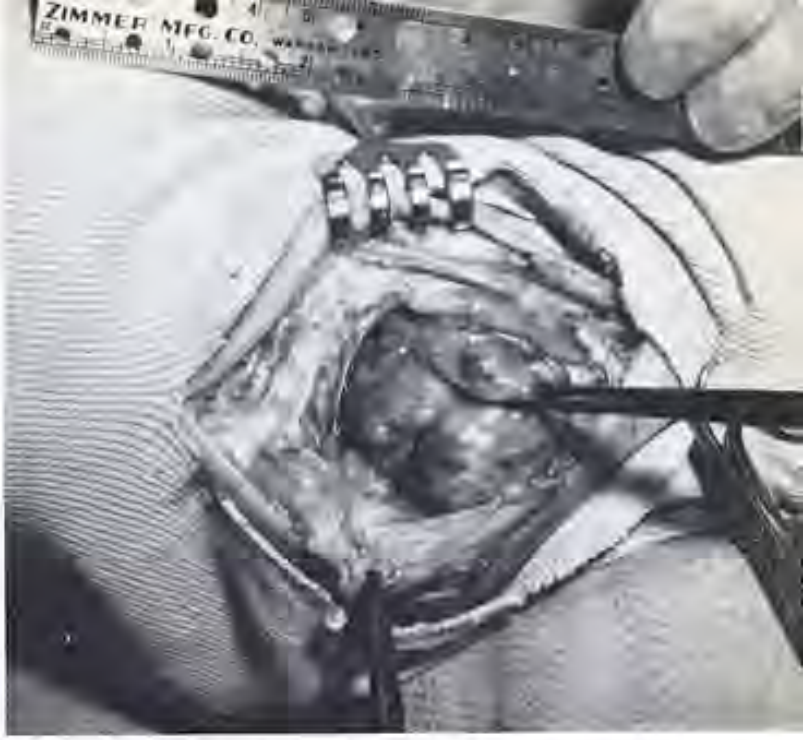


Fig. 3 — Tumor developing between tendons.

Dr. Bricker: The facts of this case substantiate our suspicion that surgical pathology is not an entirely exact science.

L. Lowbeer, M.D., Tulsa, Oklahoma: We have seen a case which seems to combine the features which have been reported now and those which were reported before. This was a middle-aged man who, perhaps for about ten years, developed a huge tumor in the popliteal fossa. This tumor was removed. It was sent to the Armed Forces Institute of Pathology for consultation and a diagnosis was rendered of a chondrosarcoma. However, the tumor had two components: the spaces were lined with synovial-like cells such as this one, and in between was the stroma which looked like that of a chondrosarcoma, with cells surrounded by halo and embedded in a chondro-myxoid-matrix. I favored a synovial sarcoma or a synovial tumor where the synovial cells converted themselves not into fibroblasts but into chondroblasts.

B. Eiseman, M.D., Denver, Colorado: May I ask Dr. Bricker if he would consider anything more radical than a groin dissection on this patient, presuming that this is metastatic tumor in the left groin?

Dr. Bricker: I would do an ilio-femoral dissection which starts up in the abdomen and takes the iliac nodes. You certainly want a group of negative lymph nodes proximal to your positive one. I don't think it is justified to do a hemipelvectomy as a procedure aimed at controlling lymphatic spread.

C. Eckert, M.D., Albany, New York (in Puerto Rico): The ability to control a tumor of this sort by local removal is zero and therefore, an amputation should be carried out. I would say that the worst thing that could be done is to biopsy a tumor in the way this tumor was biopsied, that is, by removing various and sundry areas of it from between tendons. The fact that a lymph node metastasis appeared may be of importance. Synovial sarcoma metastasizes to regional lymph nodes with perhaps the greatest frequency. But certainly, it would be difficult to call it synovial sarcoma without the typical clefts and cells.

We have one case comparable to this that was an actual synovial sarcoma. Amputation offers a certain degree of curability.

Dr. Stout: I would approve of a local removal in cases of synovial sarcoma that are small enough and in such a situation that you could excise them without entering the tumor field. But if you can't expect to do that, then I would agree to amputation. Our results in adults with *real* synovial

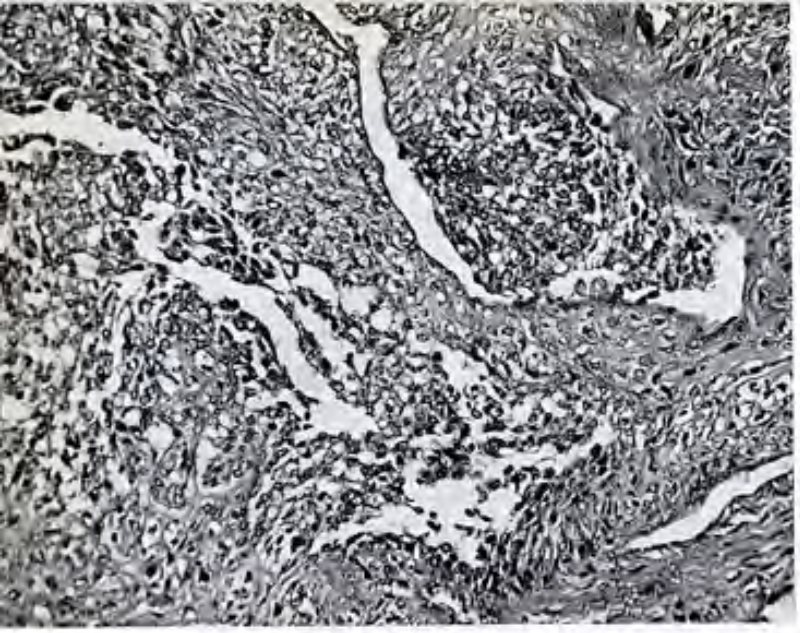


Fig. 4 — Area of malignant mesenchymoma suggesting hemangioendothelioma.

sarcoma have been so gloomy that I get discouraged; the few cases in adults of synovial sarcoma that did survive happened to be just as often treated by local excision as they were by amputation. I think that there is some degree of biological variation in the character of these tumors, which we can't recognize histologically. Therefore, it is extremely difficult to formulate any rule to apply to all cases of synovial sarcoma.

J. Kuzma, M.D., Milwaukee, Wisconsin (in Puerto Rico): I would like to ask Dr. Stout if, in the lesions which he calls malignant synovioma, the fibrosarcomatous stroma ever undergo retrogressive change showing sclerosis and losing its sarcomatous picture? If that were so, that might explain the interpretation of synovial sarcoma in the last case.

Dr. Stout: I don't see how you could ever tell that, because you remove it and it isn't there anymore and it hasn't the chance to undergo that change. I can't recall having seen such a change take place, but maybe it does. I can't answer that question.

J. Kuzma, M.D., Milwaukee, Wisconsin (in Puerto Rico): I would assume such, on the basis of the variation in the appearance of the tumor from one part to the next. I think that I have seen extreme variations of tumor areas in other types of tumors, like myosarcomas.

Dr. Stout: We are handicapped in making observations of synovial sarcomas because, after all, they are very rare tumors and nobody can see many of them. There are an awful lot of phonies circulating around because of this habit of calling anything that you want to, a synovial sarcoma; that dilutes the whole business.

Editor's note: In November, 1959, a radical excision of the iliac, hypogastric, inguinal and femoral nodes was carried out. There was a single node, less than 1 cm in diameter, just inside the inguinal ligament which contained tumor. Dr. Stout saw these slides and concluded to the diagnosis of malignant mesenchymoma (P. and S.64818).

Dr. Stout: This case is a very good example of the hazards of trying to evaluate a case from a small portion of it. Obviously the tumor had differing histological appearances in different sections and at different times. The metastasis in a lymph node is ample proof of its malignancy. It was of course a great surprise to me to learn that I had seen this tumor before and had attached a very different diagnosis to it, namely chondrosarcoma. Now that I have reviewed the five slides previously sent to me, I appreciate how the error came about. When one encounters a confusing histological picture, it is only natural to try to find a single tissue type name for it, since the great majority of malignant tumors of the soft tissues are single cell type tumors. Originally after struggling to do this I observed one area where there was suggestive atypical cartilage and I also observed that the tumor tended to form nodules in its growth, so I decided to call it a chondrosarcoma. But this neglects other areas which will not fit chondrosarcoma; some are vascular, some might even be rhabdomyosarcomatous. Therefore I will now suggest that this tumor is a malignant mesenchymoma which releases one from the necessity of forcing all the varied growth patterns into a single category.

References

Stout, A. P.: Hemangio-Endothelioma: a tumor of blood vessels featuring vascular endothelial cells. Ann. Surg., 118: 445-464, 1943.

Stout, A. P.: Mesenchymoma, the mixed tumor of mesenchymal derivatives. Ann. Surg., 127: 278-290, 1948.

Strickland, B. and Mackenzie, D. H.: Bone involvement in synovial sarcoma. J. Fac. Radiol., 10: 64-72, 1959.

14. *Metastatic Melanoma (?) of a Metatarsal Bone*

Contributed by MARK M. BRACKEN, M.D. and C. RICHARD PERRYMAN, M.D.,
Pittsburgh, Pennsylvania

THE PATIENT was a 68-year-old lady in July, 1956, when she complained of a painful swelling of the left foot. On examination, there was a fluctuant, apparently inflammatory, tumefaction overlying the fifth metatarsal bone giving the impression of a thrombosed vein.

Dr. Hodes: The roentgen examination of the affected foot revealed the following: (a) obvious early bone destruction, cortical in origin, lying within the metaphyseal zone, (b) the neighboring joints and bones show no abnormalities, (c) periosteal proliferation and advanced bone destruction at the site of the lesion, (d) large perifocal soft tissue mass blending imperceptibly with the adjoining tissues.

Under ordinary circumstances the most common cause for localized bone destruction arising within the medulla of one of the small bones of an extremity is metastatic disease, inflammatory or neoplastic. If the lesion were inflammatory one would have expected changes in the perifocal articulating surfaces and bones.

Because we believe the abnormality started within the medullary canal of the affected metatarsal bone, at the metaphysis, we are faced with considerable difficulty in explaining it. Thus we are disposed to postulate that the patient's history is incomplete and that at some time in the past this patient stepped upon a sharp foreign body which drove adjoining soft tissues into the medulla of the metatarsal affected. Such an abnormality may subsequently be associated with metaplasia and malignant degeneration. We feel constrained to re-emphasize the fact that under other circumstances the first possibility considered roentgenographically would have been metastatic malignancy or a primary bone tumor among which would be included reticulum cell sarcoma and plasmocytoma.

Dr. Hodes' impression: 1. Malignant degeneration of ECTOPIC TISSUE with metaplasia. 2. METASTATIC TUMOR. ,

Roentgenologic Impressions Submitted by Mail:

Osteomyelitis	19
Inflammatory lesion	15
Various benign lesions	18
Malignant tumors	30
Metastatic tumor	16
Plantar wart	1

Dr. Hodes: Active infection severe enough to cause this much bone destruction and periostitis would most certainly affect the neighboring articulating surfaces and neighboring bones. In this individual the latter were not present.

Dr. Regato: Dr. Benjamin Felson, of Cincinnati, offered a diagnosis of aneurysmal bone cyst. Dr. Walter G. Gunn, of San Francisco, Dr. David Gould, of Denver, Dr. Norman Glazer, of Cleveland, and Dr. Genene Baker, of Colorado Springs, all suggested metastatic tumor.

Operative findings: In August, 1956, with a diagnosis of osteomyelitis, an incision and drainage was done; bacterial cultures were negative. In September, 1956, the roent-

Fig. 1 — Early cortical bone destruction in the proximal metaphysis of the fourth metatarsal bone.

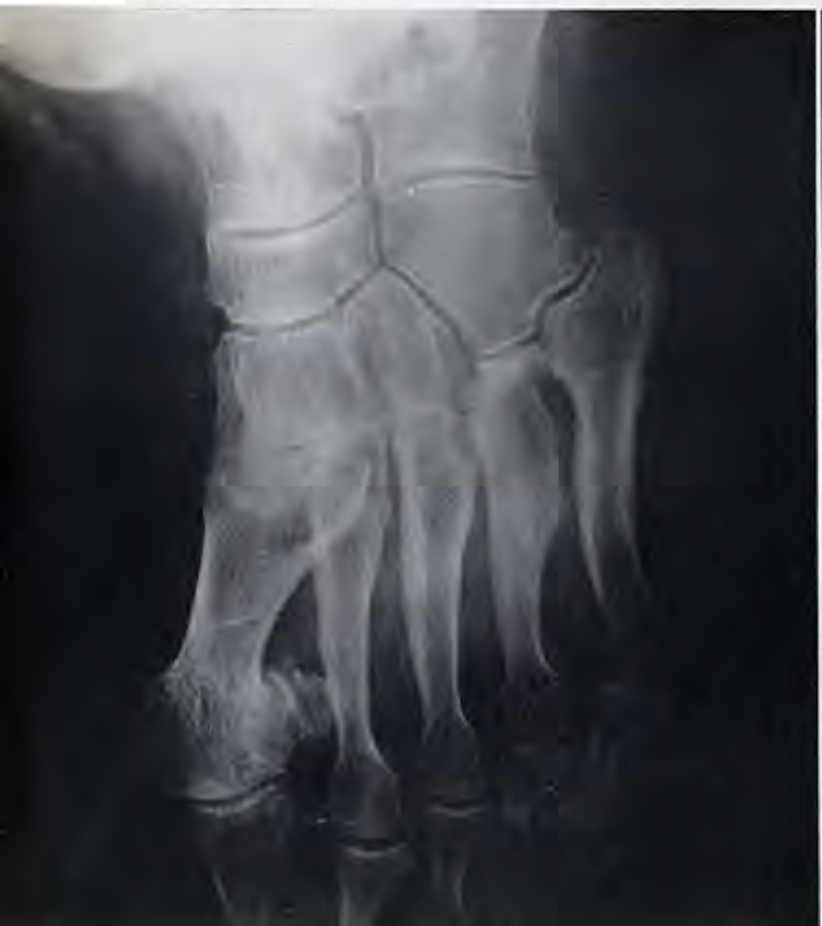
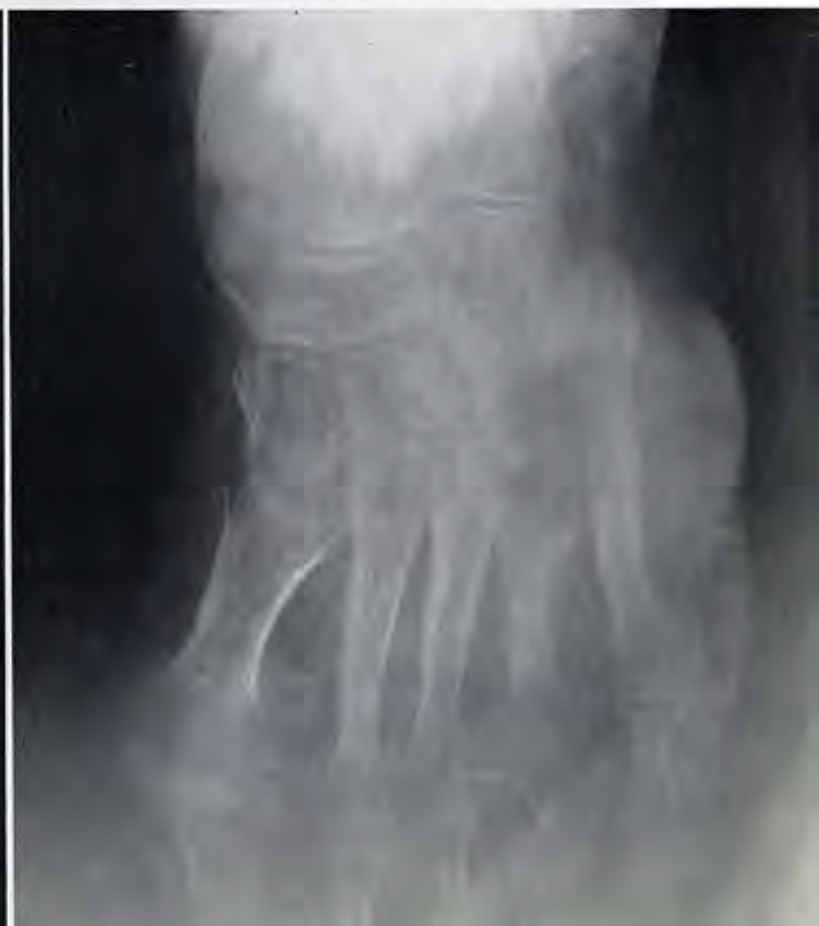


Fig. 2 — Further destruction of metatarsal bone.



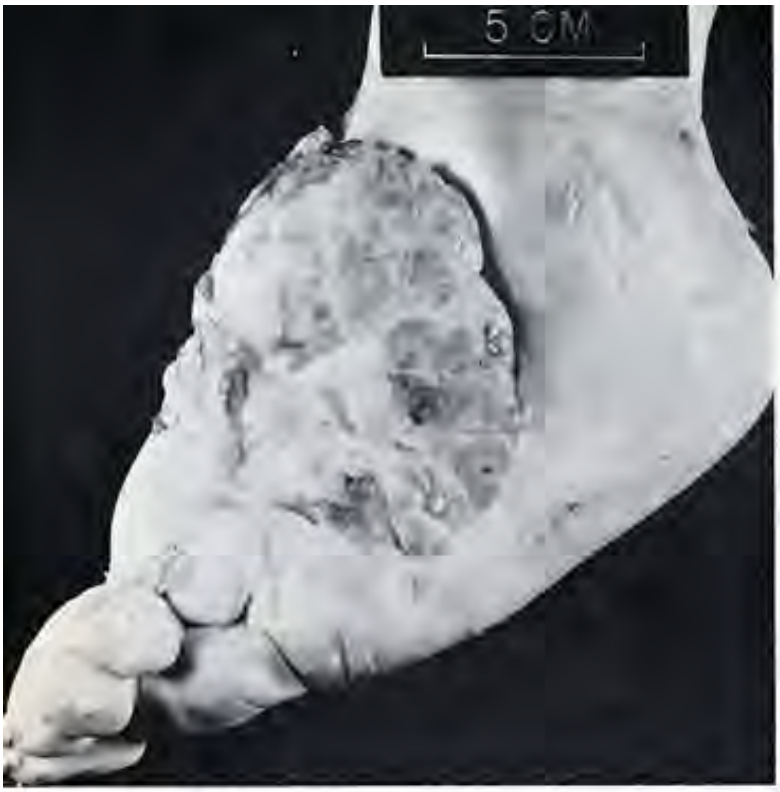


Fig. 3 — Gross appearance of ulcerated tumor.

genogram showed further destruction of the fourth metacarpal bone. The second, third, fourth, and fifth metatarsals were excised together with a tarsal bone. The patient refused immediate amputation, but by March, 1957, the foot had not healed and the tumor was growing around the wound: a below-the-knee amputation was done.

Dr. Stout: This tumor is composed of short cords and groups of large irregularly rounded cells showing much anaplasia and some mitoses. The individual cells do not cohere and are not associated with any fibers. The cell cords are separated by delicate fibrous septa. The individual cells show no evidence of secretional activity that I can detect. A few cells have large intracellular vacuoles which gives them a signet ring aspect but the vacuoles appear empty suggesting that they probably contained lipid rather than mucin. I have been unable to detect any intracellular granules.

It seems very unlikely to me that this is a primary tumor. I cannot believe it is a juvenile type of rhabdomyosarcoma. I can think of no primary bone tumor which would look like this, nor does it seem probable that it is a carcinoma derived from the skin adnexae nor a primary malignant melanoma. It seems much more probable that it is a metastatic malignant melanoma or carcinoma. My first choice would be metastatic malignant melanoma from some occult source. The morphological picture would fit this and we have seen so many metastatic malignant melanomas without any discovered primary focus that I feel inclined to suggest it whenever the morphological picture is compatible. If not that, then metastatic carcinoma. Possibilities are giant-cell carcinoma of lung, carcinoma of pancreas, ovary, kidney, adrenal and probably other sites. Since it has been put into this SEMINAR, the chances are good that it is some rare type that I won't think of, so I shall stop guessing any more.

Dr. Stout's diagnosis: Metastasis of MALIGNANT MELANOMA (?).

Histopathologic Diagnoses Submitted by Mail:

Reticulum cell sarcoma	45
Metastatic tumor	38
Plasmacytoma	20
Myeloma	11
Rhabdomyosarcoma	10
Je ne sais pas-oma!	1
Others	25

Dr. Regato: Dr. Lauren V. Ackerman, of St. Louis, and Dr. Mark Wheelock, of Chicago, called this a plasma-cell myeloma. Dr. Morgan Berthrong, of Denver, preferred a reticulum-cell sarcoma but called attention to the plasma-cell appearance. Dr. M. B. Dockerty, of Rochester, and Dr. N. F. C. Gowing, of London, also favored plasma-cell myeloma. Dr. V. Pardo, of Havana, suggested metastatic melanoma. Dr. Carlo Sirtori, of Milan, submitted a diagnosis of "cytoblastoma" which he defined as a tumor so cytologically malignant that it has lost the features of the tissue of origin; he feels that such tumors may later be more definitely diagnosed.

Fred Stewart, M. D., New York City, New York (by mail): Superficially, this suggests dysgerminoma but isn't. We considered an unusual plasmacytoma; also a tumor of which we have a few examples and we are not sure what to call: it occurs in the small bones of the foot first, alter in multiple bones within the extremity of origin.

Subsequent history: Following operation, there was slough of the stump and a left inguinal adenopathy. No inguinal biopsy was done. The groin was irradiated with a Cobalt ^{60} unit: a total of 5,000 roentgens were administered in 34 days.

In January, 1960, the patient was reported in good health and without evidence of metastasis.

M. M. Bracken, M. D., Pittsburgh, Pennsylvania: There has been no recurrence of the enlarged nodes in the inguinal region.

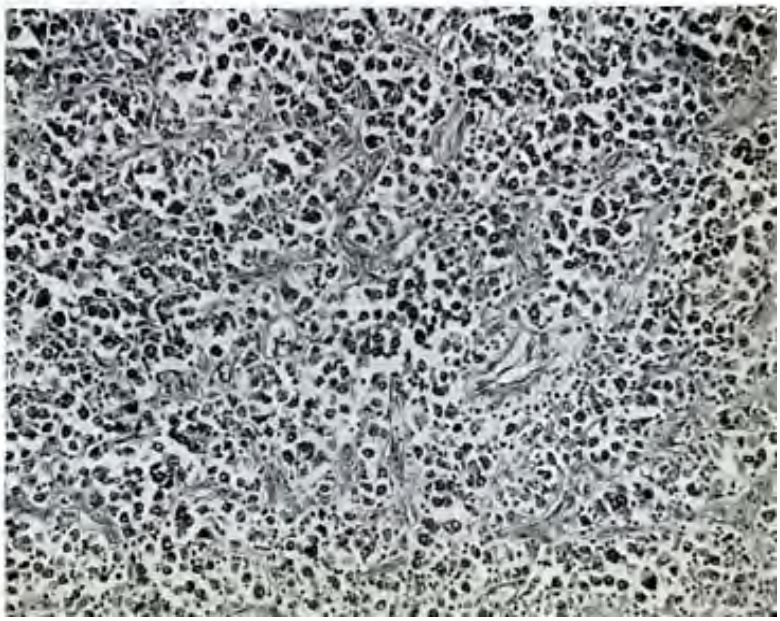
Dr. Bricker: I assume that the breakdown in the stump was simply a complication of surgery and not associated with the nature of the tumor. One can't help wondering, in view of the disparity of opinions regarding the nature of the tumor on the foot, whether an early histological diagnosis followed by a trial of radiotherapy might not have been justified. I would have felt justified in advancing this because some of the histologic opinions pointed to radiosensitive lesions and because the patient refused amputation.

M. Wheelock, M. D., Chicago, Illinois: Is there anything in the clinical data which would substantiate a diagnosis of plasmocytoma: enlarged spleen, electrophoretic studies, or any alteration of the total proteins? Was there a known history of a malignant melanoma somewhere?

M. M. Bracken, M. D., Pittsburgh, Pennsylvania: No.

F. J. Buschke, M. D., San Francisco, California: Irradiation might have given us an answer for the differential diagnosis between a plasmocytoma and a melanoma.

Fig. 4 — Cords of epithelial tumor suggesting malignant melanoma.



15. *Chondrosarcoma of the Foot*

Contributed by A. O. Severance, M.D. and Hugo F. Elmendorf, Jr., M.D.,

San Antonio, Texas

THE PATIENT was a 44-year-old man in November, 1956, when he complained of a tumefaction developing between the second and third toe of his right foot; it was painless and it had been present for three years but there had been more rapid growth following trauma in the past six months. On examination, the mass measured 2.5 cm, appeared fluctuant and non-tender.

Dr. Hodes: The roentgen examination of the foot revealed the following: (a) a well delineated soft tissue mass of unusual density; (b) there were no abnormalities in the adjoining bones.

The density of the soft tissue mass suggest the possibility of the presence of pigment within the tumor. Among the more common pigmented tumors found on feet is melanoma and melanosarcoma. The possibility of an angiosarcoma (Kaposi) was considered, but the fact that the lesion was solitary plus its unusual density seemed to favor melanoma. Also, the history of a slowly growing mass which suddenly revealed rapid growth suggested melanoma rather than a Kaposi tumor.

Dr. Hodes' impression: A highly malignant soft tissue tumor: 1. MELANOSARCOMA. 2. KAPOSI SARCOMA.

Roentgenologic Impressions Submitted by Mail:

Fibroma	21
Synovial cyst or tumor	15
Fibrosarcoma	10
Giant-cell tumor of tendons	9
Hemangioma	8
Others	27

Dr. Regato: Dr. Paul Swenson, of St. Paul, Minnesota, and Dr. E. Salzman, of Denver, offered a diagnosis of fibrosarcoma.

Operative findings: In November, 1956, a partial amputation of the right foot was carried out. The tumor was removed with the second and third metatarsals and corresponding toes. The tumor was rather soft and non-encapsulated; it appeared completely removed; the cut section revealed a gray to yellowish color with areas of hemorrhage.

Dr. Stout: The section shows that this tumor lies very close to the epidermis. It is composed largely of small rounded cells set in a loose matrix containing an exceedingly fine meshwork of reticulin fibers. Occasionally this approaches the appearance of a fibrocartilaginous matrix. Most of the cells lie naked in this stroma but very occasionally a cell seems enclosed in a capsule. There are a moderate number of mitoses. At one side the tumor merges with granulation tissue containing various kinds of inflammatory cells. There are an unusual number of large plump fibroblasts, some hemorrhage and many phagocytes filled with blood pigment.

The dominant lesion here appears to me to be a chondrosarcoma. The only other possibility that might be considered, in my opinion, is fibrosed myxoma. But the cells are not stellate but rounded and since some of them seem to be in capsules, I cannot believe this tumor is a myxoma. I have been puzzled by the peculiarly cellular granulation tissue at one side of the main tumor. I have wondered if it could be neoplastic; either altered chondroblasts or a different tumor element making this a mesenchymoma. But after prolonged study I must confess that I cannot recognize this as anything more than very cellular granulation tissue. I have already discussed chondrosarcoma in connection with Case 7. I can only say that this case seems to me to be definitely malignant and capable of metastasis.

Fig. 1 — Soft tissue developing between toes.

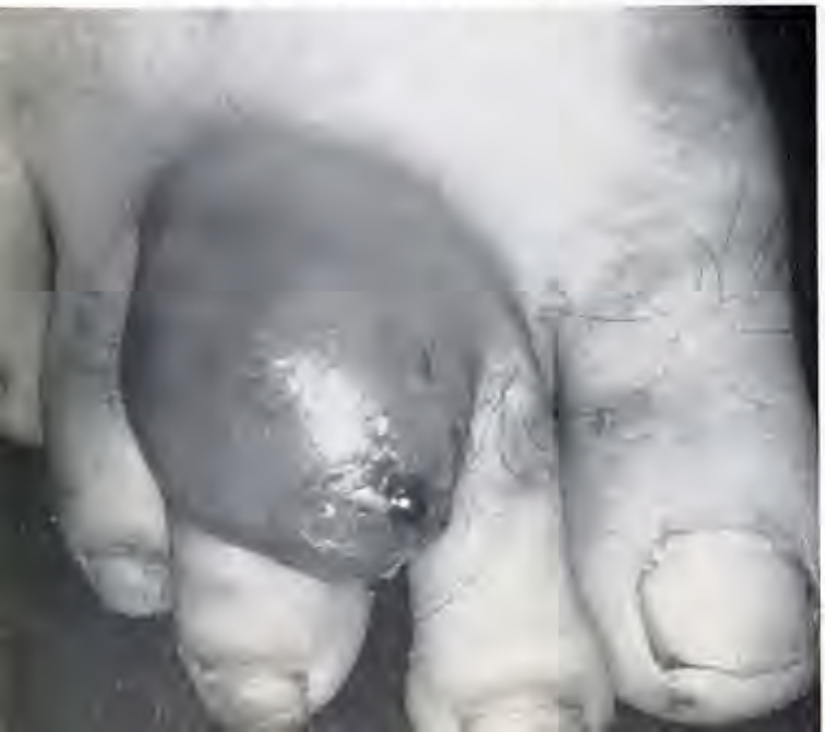
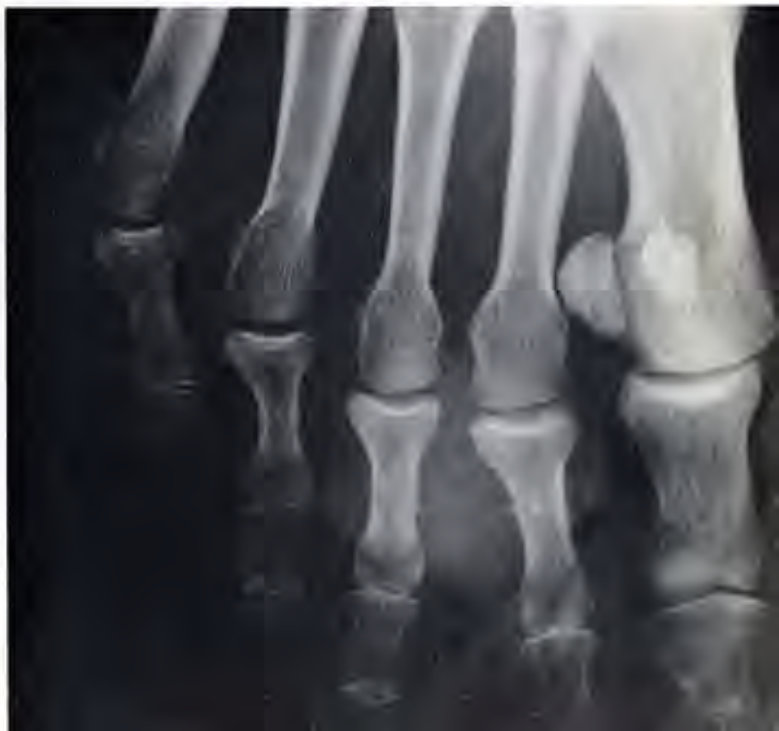


Fig. 2 — Well delineated soft tissue mass without abnormalities of bones.



Dr. Stout's diagnosis: CHONDROSARCOMA.

Histopathologic Diagnoses Submitted by Mail:

Angiosarcoma (Kaposi's)	14
Embryonal rhabdomyosarcoma	13
Synovial sarcoma	12
Neurosarcoma	12
Chondrosarcoma	11
Hemangiopericytoma	10
Malignant mesenchymoma	10
Myxosarcoma	9
Malignant schwannoma	8
Fibromyxoma	7
Neuroglioma	6
Liposarcoma	6
Neurilemoma	5
Melanoma	4
Boy- Were these tough!-	1
Others	14

Dr. Regato: Dr. Fred Collier, of Birmingham, Alabama, also submitted chondrosarcoma. Dr. Morgan Berthrong, of Denver, thought that this case should give Dr. Stout an opportunity to discuss hemangiopericytomas. Dr. F. Foote, of New York, made a bet that Dr. Stout will call this a mesenchymoma. Dr. R. Font-Mer.ández, of Havana, not Dr. Stout, made a diagnosis of malignant mesenchymoma.

Subsequent history: The patient was last seen in January, 1960, more than three years after treatment: there was no evidence of recurrence or metastasis.

A. O. Severance, M. D., San Antonio, Texas: In the middle of September, the patient came to my office and I saw the foot myself. There is no recurrence and the foot looks pretty good. He says he can use it except at the end of a hard day; as a day laborer, he gets a little tired.

M. Berthrong, M. D., Denver, Colorado: I saw lots of rather spindly cells that seemed to radiate around small vessels. I am going to send this slide to Dr. Stout and see if it would have warranted a discussion of hemangiopericytoma.

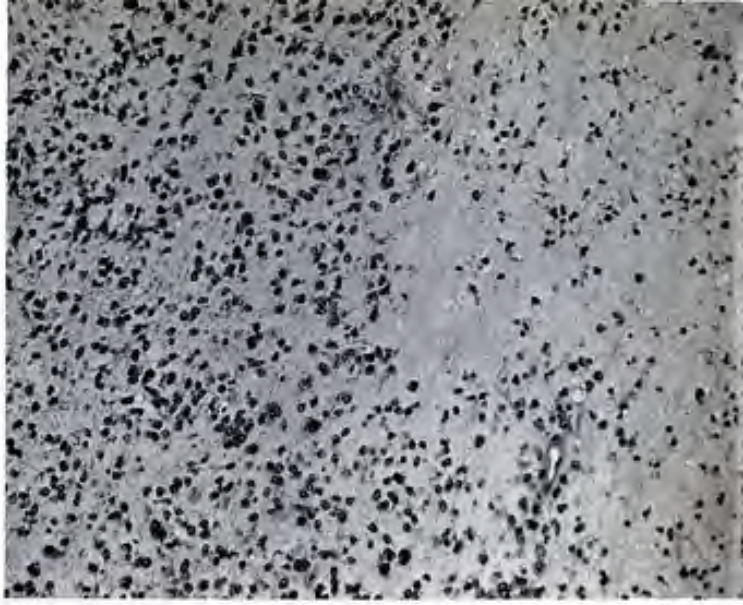


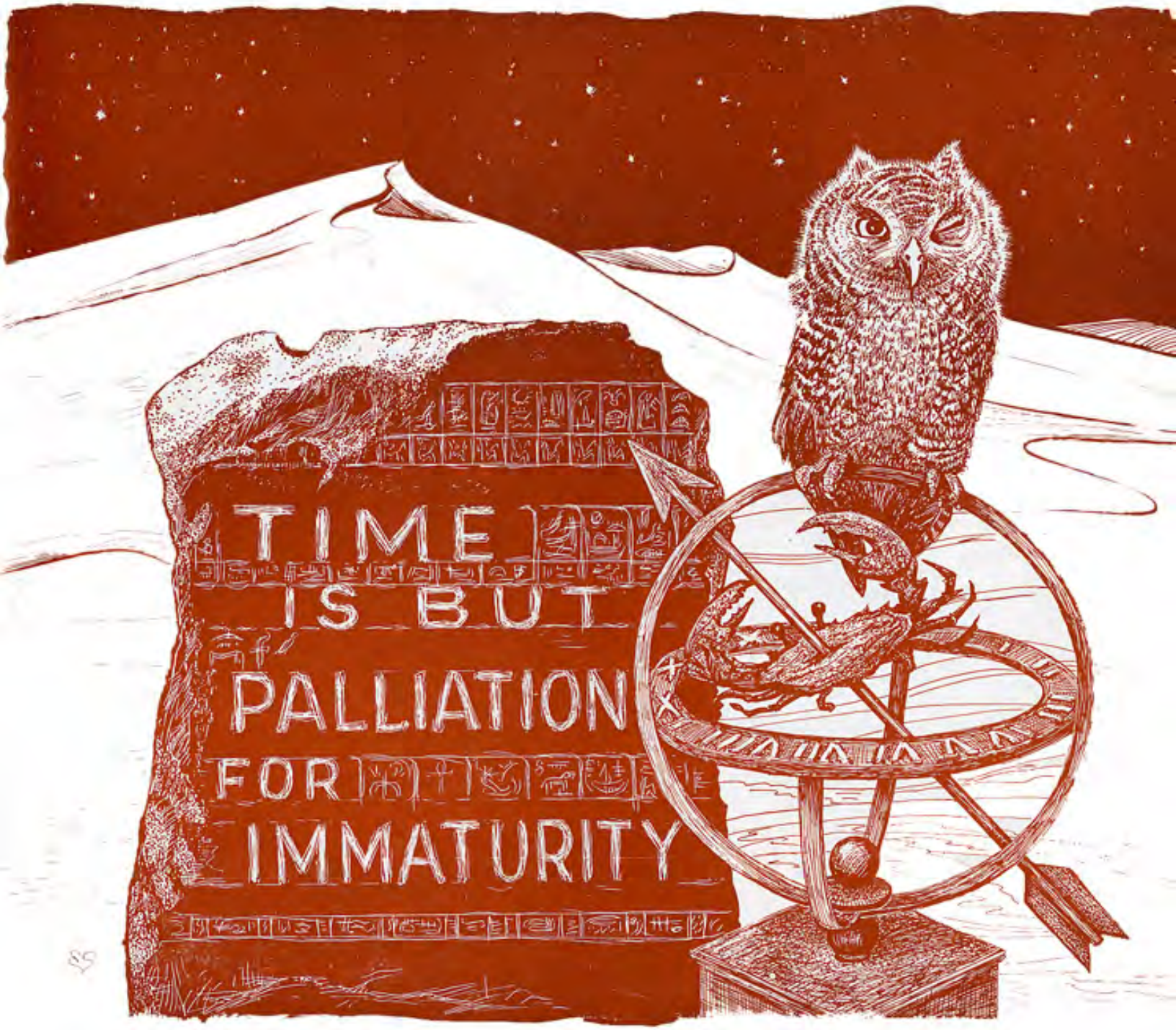
Fig. 3 — Chondrosarcoma.

M. Wheelock, M. D., Chicago, Illinois: Certainly the way the tumor bulged above the surface, the cross section, the hemorrhage, the spindle form, the multiple types of cells, could fit a diagnosis of dermatofibrosarcoma protuberans; also this could be a malignant mixed tumor of the skin, something comparable to ones seen in salivary glands.

Dr. Regato: That's what Dr. Ackerman called it, a salivary gland tumor type.

C. Eckert, M. D., Albany, New York (in Puerto Rico): I can't argue with success; the patient is well three years later and this is certainly successful. The question of partial amputation of the foot as a means of establishing the diagnosis and providing treatment at the same time is one that is possibly open to debate: to leave a weight-bearing surface is certainly a fairly good approach to the problem.

EDITOR'S NOTE:



Penrose Cancer Hospital

Sisters of Charity

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Pathologist

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Chairman of the Penrose Hospitals' Liaison Committee

Our Guest Speakers

PHILIP J. HODES, M. D., Professor of Radiology, Jefferson Medical College, Philadelphia, Pennsylvania. Doctor Hodes graduated from the University of Pennsylvania in 1931; he is Consultant in Radiology to the Armed Forces Institute of Pathology and is well known because of his activities in the field of education and for his contributions to academic radiology. Doctor Hodes was the guest of the Penrose Cancer Hospital.

ARTHUR P. STOUT, M. D., Emeritus Professor of Pathology, Columbia University and Consultant to the Francis Delafield Hospital of New York City. Doctor Stout graduated from Columbia University in 1912; he is well known as the Dean of American surgical pathologists and one of the foremost world authorities in pathology of tumors. Doctor Stout was the guest of the College of American Pathologists.

EUGENE M. BRICKER, M. D., Associate Professor of Surgery, Washington University Medical School, St. Louis, Missouri. Doctor Bricker graduated from Washington University in 1934; he was Chief Surgeon of the Ellis Fischel Cancer Hospital and is known for his originality and contributions to the surgery of cancer. Doctor Bricker was the guest of the Penrose Cancer Hospital.

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