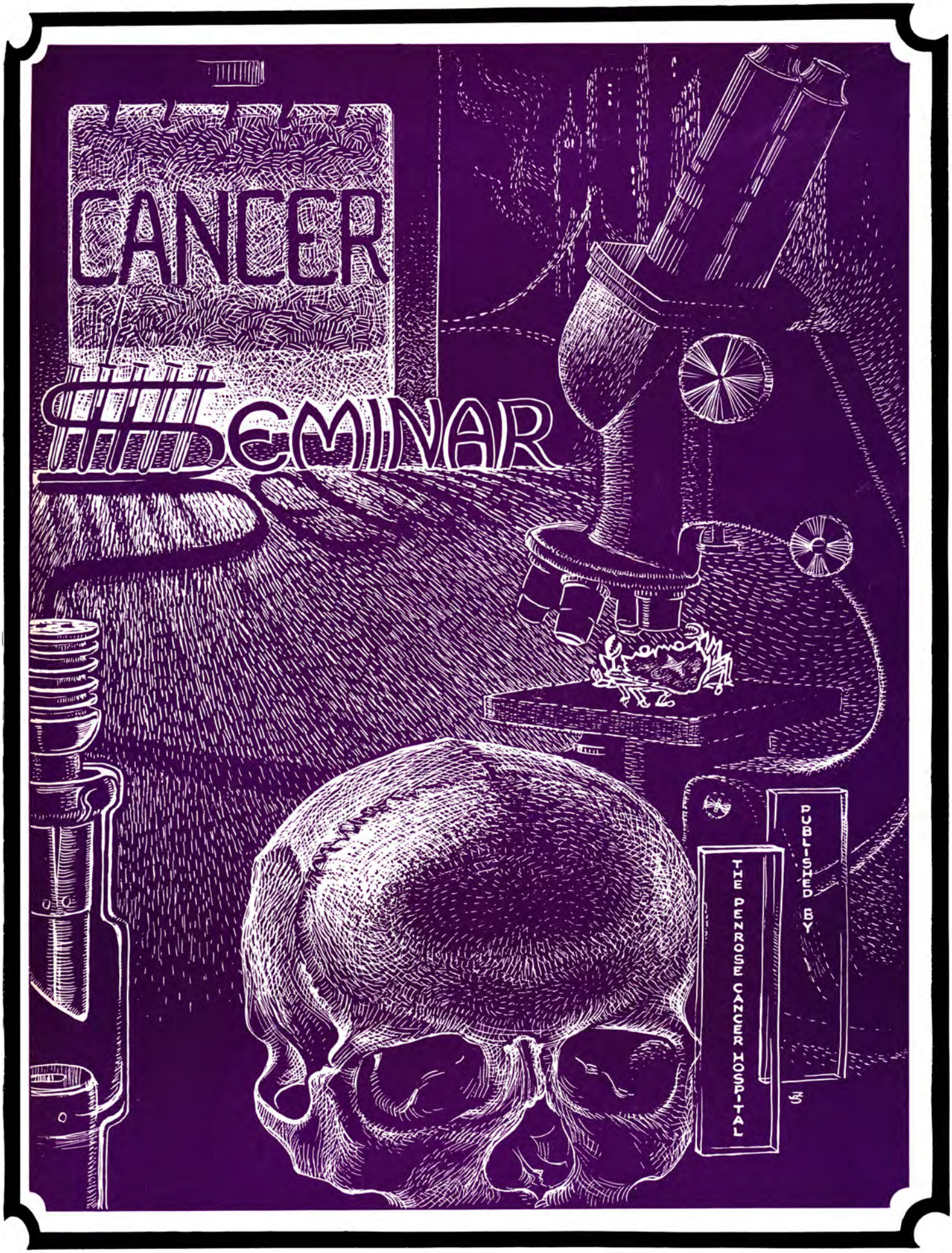
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JUAN A. DEL REGATO, M. D., *Editor*

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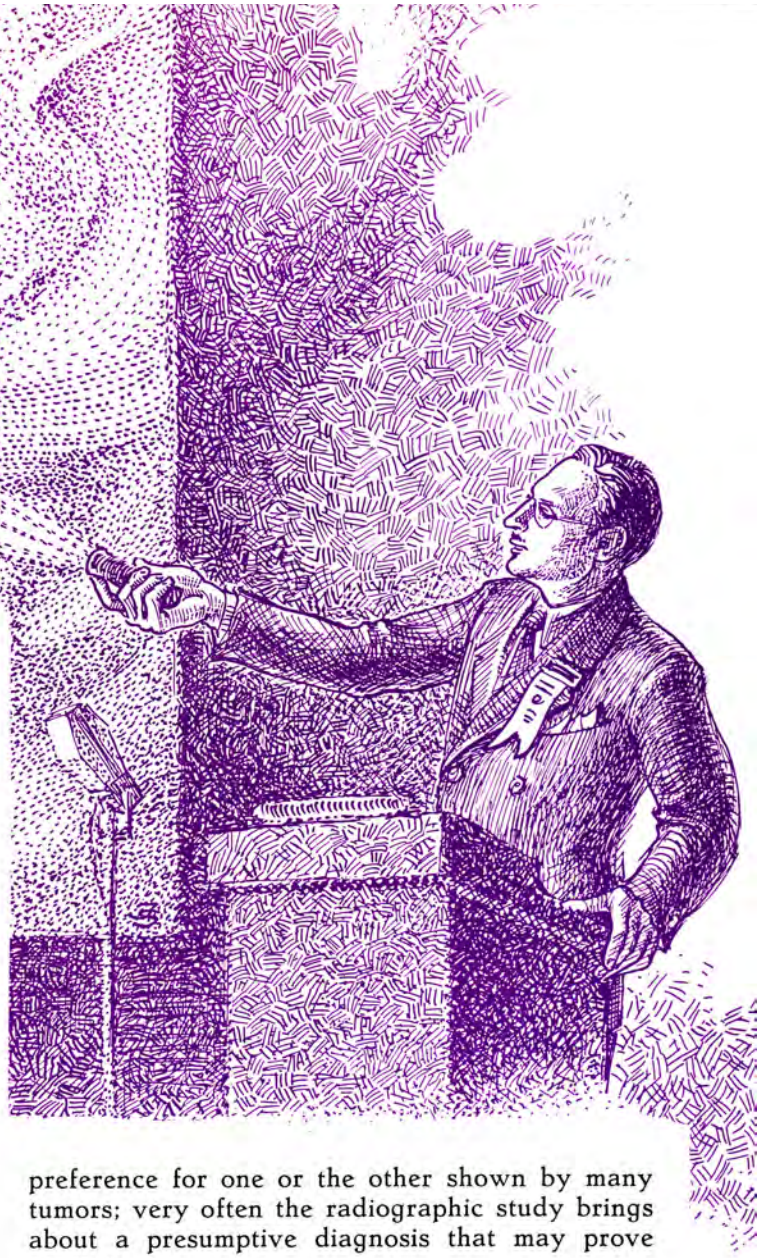
BONE TUMORS



THE SUCCESSFUL treatment of most bone tumors depends, as is often the case of any other neoplasms, upon the establishment of an early diagnosis. But bone tumors are among the most difficult to diagnose accurately, for they do not always repeat their character and have to be differentiated from congenital, trophic or traumatic deformities, from endocrine, circulatory or metabolic disturbances, from parasitic or inflammatory lesions, etc.

Information obtained through a detailed clinical history may be helpful in the diagnosis; however, such information is often limited to the knowledge of the patient's age, to the presence or absence of local pain and of a tumefaction, and to the patient's estimate of the duration of these symptoms; indeed, the history may prejudice an otherwise clear situation.

Physical findings are sometimes helpful in the differentiation of inflammatory lesions and benign and malignant tumors, but more often the physical examination contributes little of value.

Laboratory examinations sometimes aid in affirming a presumptive diagnosis or serve to eliminate one of the diagnoses in consideration, but chemical changes of the blood and urine are neither frequent nor specific and more often they fail to contribute to the diagnosis.

The radiographic examination of the diseased bone contributes a rather precise set of informative data: The point of origin, the exact location, the relation of the lesion to the medullary and cortical structures and the presence or absence of osteolysis or bone formation. The radiographic examination should be, of course, exhaustive, utilizing different projections and planigraphy; in addition, this examination should be complemented by the investigation of the condition of the chest and of other bones. The establishment of the exact location of the tumor, in the diaphysis, metaphysis or epiphysis may in itself suggest a diagnosis of probability by virtue of the definite preference for one or the other shown by many tumors; very often the radiographic study brings about a presumptive diagnosis that may prove correct.

That we assert this much is to imply that in a certain proportion of cases the histopathologic study of the lesion may prove the possibility of a roentgenologic diagnosis under certain circumstances, but it does not mean that a radiologic diagnosis is always possible.

The histologic study of the lesion is the last measure of information that is available before making a therapeutic decision; it is sometimes remarkably enlightening, sometimes simply corroborating, and sometimes incapable of offering a clear solution. Much of the strength of histopathology stems from the fact that it can compound all of the previously obtained information (the history, physical examination, laboratory and radiographic examinations) with the morphologic study, and express it in the form of a summary diagnostic conclusion. In many bone tumors a purely morphologic diagnosis may not be possible, but the histopathologic findings often gain stature when clinical and laboratory data are added.

Radiology and pathology are not antagonists, yet the lack of preciseness of radiology and the limitations of morphology have invited argument on the relative merits of each procedure and emphasis on their competitive aspects. Dr. J. F. Brailsford, a respectable British authority on the subject of bone tumors, takes the position that histopathologic diagnoses and morphologic classifications are vague and unreliable and that in final practical consideration it is essential to establish only whether a lesion is benign or malignant. Brailsford believes that this may be done by the careful appraisal of the clinical data and other available information, by the radiographic study, and in some instances by the changes that may take place during a period of observation; he is certain of the dangers of biopsy and is not troubled by delay since he has never seen early treatment result in cure of an osteogenic sarcoma.

Brailsford's defamers assert that radiology lacks the finesse of the histologic criteria, that four-fifths of a vertebra must be destroyed before radiographic discernment is possible, and that a method of examination so grossly handicapped could hardly be regarded as a means of differential diagnosis, allowing for intellectual excesses; they note that the Bone Tumor Registry records a greater proportion of biopsies among the living than among the dead patients; they affirm that histology is the most reliable source of diagnosis, that erroneous diagnoses by a trained pathologist are extremely infrequent and that, anyway, experience places the microscope several notches above the roentgen tube.

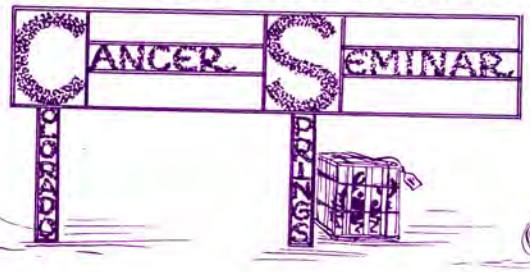
We feel that it is important to accept the interdependence of our means, and that to reach an early diagnosis, all information must be put to work in order to be able to decide upon the institution of proper therapeutic measures. It is as temerarious to amputate a limb on a purely morphologic impression as it is to procrastinate and pretend to solve the delicate matters of treatment of these lesions on the basis of clinical and radiographic observation. Most decisions to be made are not necessarily dramatic nor are all forms of therapy necessarily mutilating. The early histologic confirmation of the nature of a lesion may lead to conservative treatment, radiotherapeutic or surgical, with greater possibilities of success. Let us admit that biopsies of bone lesions are not always without danger; biopsy should be done when all other forms of information have been exhausted; the procedure should be carried out with all due precautions and should only be done when the therapeutic eventualities have been discussed and the conditions of adequate treatment are immediately available.

This Seminar was organized for the exclusive purpose of studying a small number of bone lesions. Photographic copies of the roentgenograms and clinical summaries of fourteen problem cases were submitted to approximately 120 radiologists; over 120 sets of histopathologic slides and the same clinical summaries were submitted to pathologists. The natural limitations of this exercise made it impossible to provide the radiologists with numerous roentgenograms; for the sake of brevity our clinical summaries contained no mention of negative laboratory examinations or other negative findings; but, except in one case, at the request of the contributor, no information was purposely withheld from the participants; the information given contained all available data at the time of the examination. The diagnoses submitted by mail by radiologists and pathologists were presented with each case; several study groups submitted the various diagnoses of their members. Subsequent details of the developments in each case, of unquestionable value toward the diagnosis, were given in the course of the discussion. We were fortunate in obtaining the disinterested cooperation of many authorities in the fields of radiology and pathology; their diagnoses or comments were introduced in the discussion. The radiologists were handicapped by the lack of several roentgenographic views and most of the radiologic opinions were submitted as impressions, rather than categoric diagnoses which, indeed, it was not often possible for them to be.

The 160 surgeons, pathologists, and radiologists who attended this Cancer Seminar at the Broadmoor Hotel on September 9, 1950, were presented with the expert dissertations of our guest speakers: Philip J. Hodes, M. D., Professor of Radiology, University of Pennsylvania, and L. V. Ackerman, M. D., Professor of Surgical Pathology and Pathology, Washington University. An opportunity was offered to everyone to challenge the experts and to enlighten others with the product of their own experience. The College of American Pathologists graciously co-sponsored the Seminar. We are thankful to all for the success of the Seminar.

It was not our purpose to prove anybody right or wrong. We are interested only in the educational value of these exercises and in what there is for us to learn from each other. We hope that this discussion confirms the weaknesses of the lone rangers and shows once more the interdependence and fruitfulness of the cooperation of Radiology and Pathology.

J. A. del Regato, M. D.
Colorado Springs, September 1951.



1. *Monostotic Fibrous Dysplasia of the Tibia*

Contributed by L. V. ACKERMAN, M. D., St. Louis, Missouri

THE PATIENT was a young man 25 years of age, who in August 1949 developed a skin eruption, accompanied by pain, on the lower half of his legs. There was no history of trauma and there was tenderness on palpation. Serum calcium and phosphorus, as well as the alkaline phosphatase, were found within normal limits. The roentgenogram showed a translucent area of the tibia; copies of this film were sent to the participants. A biopsy specimen was removed from the tibia from which the slides distributed were prepared.

Radiologic Diagnoses Submitted by Mail		Histopathologic Diagnoses Submitted by Mail	
Fibrous dysplasia	66	Fibrous dysplasia	84
Benign bone cyst	36	Osteitis fibrosa	12
Osteitis fibrosa	14	Osteoid osteoma	9
Giant cell tumor	10	Osteofibroma	3
Neurofibroma	10	Chondrofibroma	3
Eosinophilic granuloma	8	Periosteal proliferation	3
Syphilis	4	Osteogenesis benigna	1
Osteomyelitis	8		
Seven other diagnoses	12		

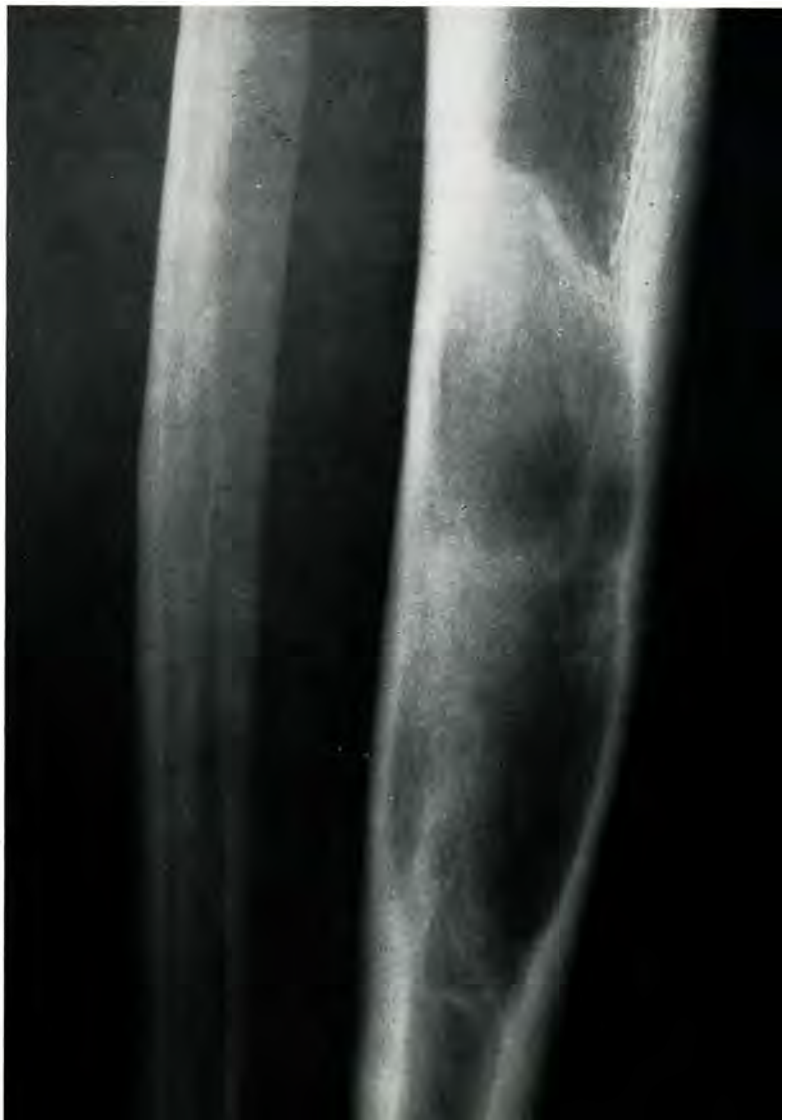
Dr. Hodes: This is a monostotic lesion which is cystic and trabeculated, involving the mid portion of the shaft of a long bone and obviously causing some increase in the width of the bone. As the result of the expansion of this cystic lesion, there is evidence of atrophy of the cortex with no evidence of periosteal reaction. The normal medullary trabeculation is displaced by a multi-loculated cystic process, which is very sharply demarcated and is obviously benign. The proximal and distal limits of this polycystic lesion are clearly defined. There is no associated soft tissue mass. The lesion has occurred in an elderly individual and lies well away from the epiphyseal end of the bone; these facts militate against its being an ordinary cyst. There is no history of trauma that would suggest a hemorrhagic cystic process. The lesion is far too large for the ordinary cystic lesions seen in neurofibromas of bone.

Dr. Hodes' diagnosis: MONOSTOTIC FIBROUS DYSPLASIA.

Dr. Ackerman: The lesion has a characteristic microscopic pattern of fibrous dysplasia. It consists of connective tissue and metaplastic bone spicules growing near blood vessels. Focal areas of this fibrous tissue undergo metaplasia to cartilage. The osseous metaplasia is most apparent close to pre-existing bone. In small areas resorption of the bone by osteoclasts results in the formation of small cysts (Schlumberger). Lichtenstein believes the cyst formation follows hemorrhage, or is due to softening of cellular connective tissue.

Fibrous dysplasia frequently occurs in older children and young adults. It is most commonly localized in the rib, femur, tibia, and maxilla; in the tibia the lesion commonly affects the shaft. It is uncommon in the pelvis, vertebral column, small bones of the hand and feet; in any of these bones it produces a sharply delineated destructive focus and the transition from normal to abnormal bone is often abrupt (Schlumberger). In the involved bone, particularly in the rib, there may be expansion of the bone with thinning of the

Fig. 1—Roentgenogram of the bones of the right leg showing a multiloculated lesion of the tibia.



cortex and on cut section there is a gritty sensation and a grayish-yellow color. According to Schlumberger, the monostotic process bears no relation to the syndrome described by Albright in which there are multiple bone lesions, areas of pigmentation, endocrine dysfunction, and precocious puberty in females. Lichtenstein believes that transition between the monostotic and polyostotic form occurs. According to Schlumberger, this lesion does not become malignant.

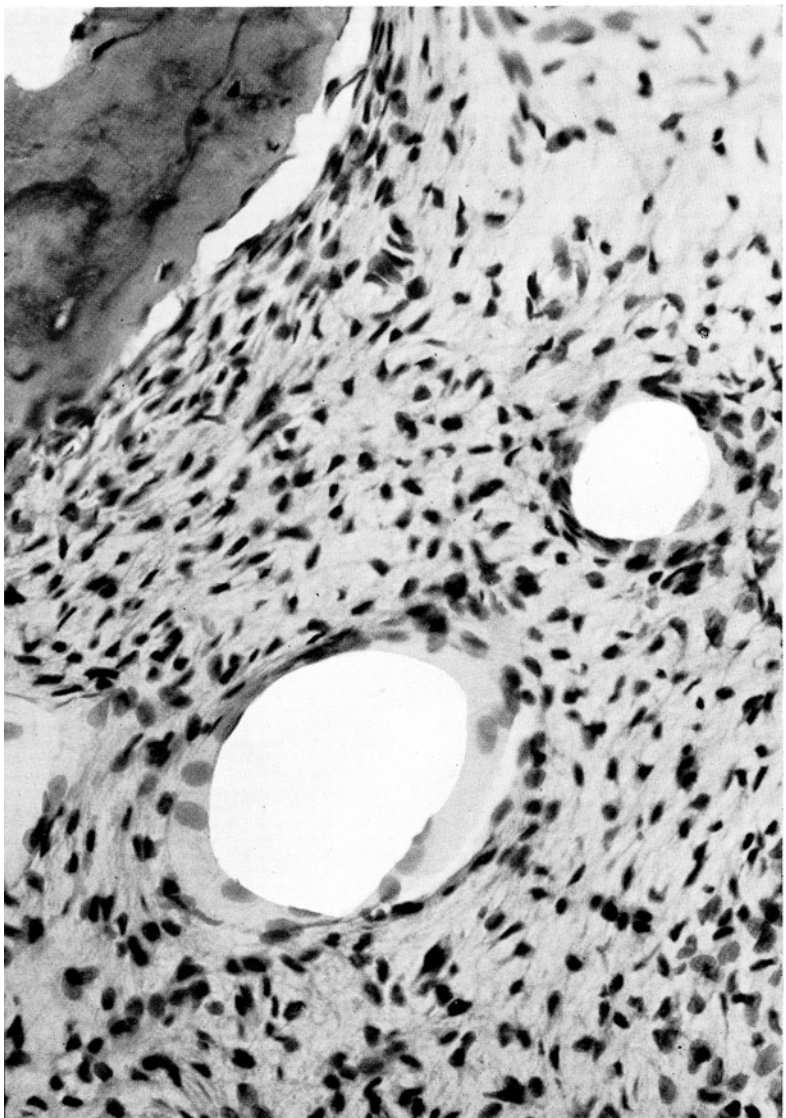
Dr. Ackerman's diagnosis: FIBROUS DYSPLASIA.

Arthur Purdy Stout, M. D., New York, New York, (by mail): This section shows a plexiform pattern of young osteoid or bone which is well differentiated but has many cells within the lacunae. The spaces between are filled with a young myxoid fibrous tissue with many stellate cells resembling mesenchyme. There are a moderate number of capillaries devoid of blood. There are very few osteoclasts or other evidences of bone destruction.

There is no history of trauma. I shall, therefore, exclude simple callus. If this is the tissue from that lucent area, the trabeculae probably represent osteoid. If so, we seem to be dealing with an area of dysplasia within the bone which one can call either fibrous or osseous dysplasia. I will call this lesion fibrous dysplasia.

Subsequent history: The patient was treated by curettement and introduction of bone fragments in the bone cavity; he is well at present.

A. M. Ginzler, M. D., Bridgeport, Conn.: Dr. Jaffé has accepted the idea that these lesions may become malignant, and I believe he has seen one or two such cases.



William H. Bauer, M. D., St. Louis, Mo.: The important question as yet unanswered is whether this monostotic lesion represents a variant, dwarfish type, of the polyostotic fibrous dysplasia or merely a reaction to irritation, or an ossifying fibroma or a reparative stage of a giant cell node. Unquestionably, some instances of monostotic fibrous dysplasia were demonstrated to be an early stage of polyostotic fibrous dysplasia. However, I believe that those monostotic cases which remain limited should not be regarded as a variant of the polyostotic type, nor should the remarkable resemblance of these two lesions be used to infer identity.

This polyostotic disease is of polyglandular origin and classically reveals segmented lesions in many bones, melanotic pigmentation and sexual precocity, previously observed in females and recently observed in males also. The pigmentation and sexual prematurity are not a constant finding.

Our studies indicate that the osseous lesions commence in the Haversian systems with osteoclastic destruction of the bone followed by gradual fibrous transformation of the marrow. Though osteoclastic destruction is the predominant feature, deposition of irregularly calcified bone trabeculae rimmed by wide osteoid zones has been observed. Bizarre fibrous bone trabeculae coated by wide osteoid layers were observed in loose fibrous tissue, the main vascular spaces of which were surrounded by a broad ring of transudate. Occasionally, the fibrous tissue became very dense and produced rounded accumulations of collagen. This collagen material in scattered areas became the core of fibrous bone formation. In two cases we have observed there was large accumulations of erytherocytes surrounded by many giant cells in the fibrous marrow; a few groups of foam cells appeared in the tissue. (Dr. Bauer illustrated his discussion with color photomicrographs.)

LeRoy Sante, M. D., St. Louis, Mo.: Just one word about the radiographic aspect of these lesions. I do not think that these cyst-like lesions originate in the medullary canal. The roentgenologic evidence would suggest that they originate within the cortex, and I think that this is a good differential point in their differentiation from bone cyst and other bone tumors. Their origin within the cortex perhaps explains why there is not the same degree of uniform expansion that there is in ordinary bone cysts and other types of expanding lesions. In other words, if we define, for our own understanding, expansion of the bone as being symmetrical enlargement of the shaft of a bone from some slowly enlarging lesion in the medullary canal, then such intracortical lesions would not be true expansion. This might be called irregular expansion, or irregular enlargement, but it is not true symmetrical expansion. This is a point then, I think, that is quite characteristic; at least we thought so from the experience which we had with the cases discussed by Dr. Bauer. The pressure of these intracortical cystlike areas upon each other gives the appearance of oval areas of enlargement extending up and down the shaft, which is quite characteristic of fibrous dysplasia.

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Fig. 2 — Photomicrograph (X400). Note fibrous area without mitotic activity; such areas are easily overdiagnosed as fibrosarcoma.

Reticulum Cell Sarcoma of the Femur

Contributed by T. W. Blake, M. D., P. Lund, M. D., and F. Buschke, M. D., Seattle, Wash.

THE PATIENT was a young woman 16 years of age, who first noticed a pain in the right thigh while doing a Russian dance in September 1949. Three months later a soft tissue swelling was noticed on the lower half of the thigh, posteriorly. On examination the tumor measured 10 x 12 cm in diameter, was not apparently fixed to the bone, and there was no inguinal adenopathy. The roentgenogram revealed the presence of a large soft tissue tumefaction with moderate periosteal reaction; this was the roentgenogram submitted to the participants in the Seminar. A generous specimen was removed for biopsy from which the slides distributed to the pathologists were cut.

Radiologic Diagnoses Submitted by Mail		Histopathologic Diagnoses Submitted by Mail	
Periosteal fibrosarcoma	64	Synovioma	54
Soft tissue sarcoma	40	Bone sarcoma	12
Osteogenic sarcoma	20	Soft tissue sarcoma	21
Synovioma	10	Ewing's tumor	12
Ewing's	8	Hemangiopericytoma	8
Chondrosarcoma	8	Reticulum cell sarcoma	6
Four other diagnoses	12	Neuroblastoma	3
		Lymphangioma	3

Dr. Hodes: This is a dense, well circumscribed soft tissue mass which has a sharply defined border and pushes before it the fascial and muscle planes; it seems to spring from the metaphyseal portion of the periosteal segment of the bone, without causing any change in the width of the neighboring bone. There is periosteal proliferation with new bone being laid down in perpendicular and parallel manner and the cortex of the bone shows pressure atrophy as a result of this soft tissue mass. We can find no roentgenologic manifestations of destruction of the medullary portion of the bone or the inner portion of the cortex at the affected site.

This does not look like a primary bone tumor. It appears to be a tumor arising in the periosteum or periosteal soft tissues but is secondarily affecting the outer layers of the cortex. Its density suggests it may be of fibrous, nervous or muscle tissue content. It is obviously a tumor, and in view of the changes in the bone it is evidently malignant.

Dr. Hodes' diagnosis: PERIOSTEAL FIBROSARCOMA.

Dr. Regato: Dr. Brailsford, of Birmingham, suggested than an aneurysm should be ruled out in this case.

Dr. Ackerman: The section shows masses of tumor cells which have rather large vesicular nuclei, their nucleoli are inconspicuous. The cytoplasm is pale pink, and cytoplasmic outlines are not well defined. The reticulum stain demonstrates large amount of reticulum winding around individual cells and running between them. These findings suggest that this lesion is a reticulum cell sarcoma. Stout believes that the histogenesis of Ewing's tumor and a reticulum cell sarcoma of bone are similar. However, Parker and Jackson point out that the cells in this tumor are larger than the cells in a Ewing's tumor, the nucleoli are more prominent, and the pink cytoplasm is more conspicuous.

Dr. Ackerman's diagnosis: RETICULUM CELL SARCOMA.

Arthur Purdy Stout, M. D., New York, N. Y., (by mail): The tumor is made up of rounded cells with deeply stained nuclei sometimes moulded by pressure into an oat shape. They are often oriented around capillaries with thick walls. Here, they are well nourished but further away they have apparently died and undergone autolysis leaving open spaces between the capillaries with their sheaths of cells—the old-fashioned parithelial arrangement. The tumor infiltrates the dense fibrous tissue and appears inside the lumen of one vein.

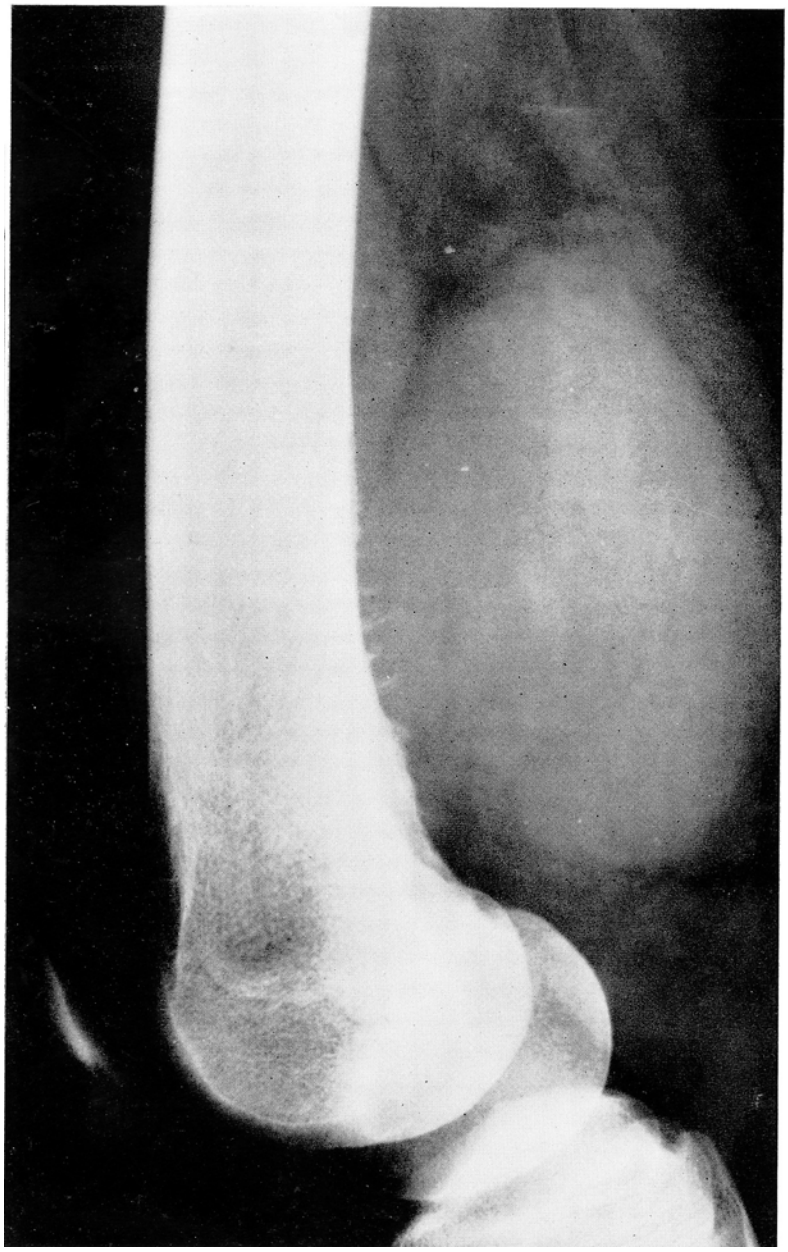
This is not any of the common tumors of the soft parts. I would reject the possibility of synovial sarcoma and the orientation about blood vessels makes me reject a reticulum cell sarcoma of the soft parts. One could not exclude the

possibility of metastasis from sympathicoblastoma. The patient's age and the marked orientation about blood vessels make this unlikely; a Ewing's tumor can involve such a small part of the cortex of a bone, while at the same time a huge soft part tumor can be formed. My suggestion for this case is a Ewing tumor.

Subsequent History: From January to March, 1950, the patient was submitted to a series of roentgentherapy; the tumor showed rather marked radiosensitivity. A dose of approximately 2200 roentgens (on skin) was administered in 32 days to each one of three fields (15 x 10 cm) directed to the soft tissue mass in the lower thigh; approximately 2700 roentgens were administered in 21 days to each one of two fields (10 x 12 cm) directed to the upper part of the thigh. These treatments were given with an equipment of 400 kv; tumor regression was noticeable the 33rd day. The mass had entirely disappeared at the end of two months.

Mark Wheelock, M.D., Chicago, Illinois: I made a diagnosis of synovioma and such was also the diagnosis of ten other men who studied the slide in Chicago; none even

Fig. 1 — Roentgenogram showing large soft tissue mass and periosteal proliferation of the cortex of the femur.



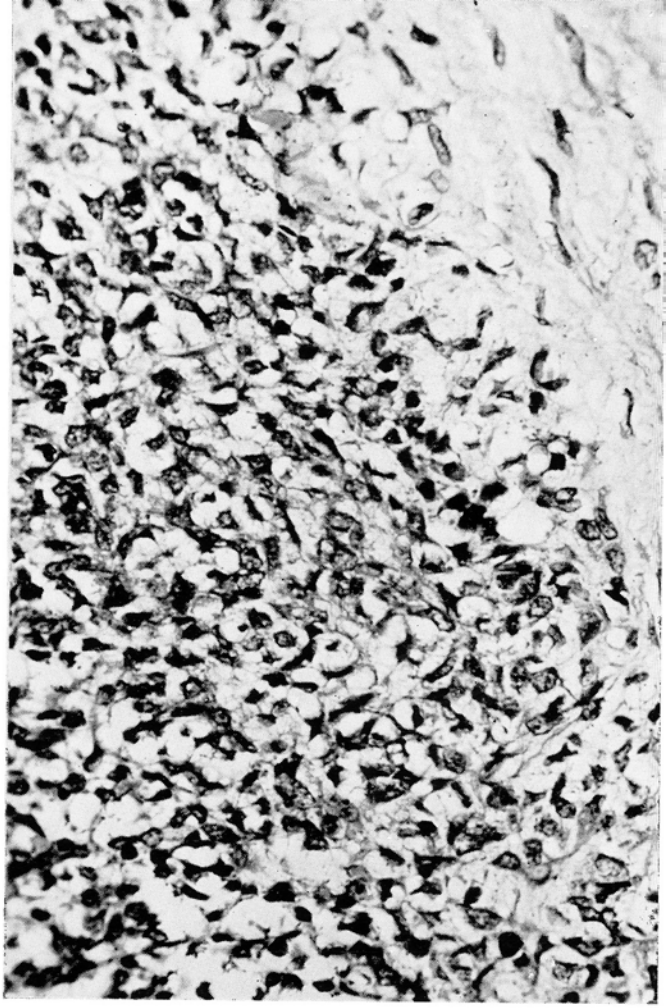


Fig. 2—Photomicrograph (X400). Reticulum cell sarcoma. The cells are large with vesicular nuclei and pale cytoplasm. The reticulin stain shows rather large amount of reticulun winding around individual cells.

mentioned the possibility of reticulum cell sarcoma; I can't see it at all myself. We have been reviewing a series of several hundred lymphomas from several Chicago hospitals; I can't recall one single case of solitary, localized, reticulum cell sarcoma of any caliber arising in a region like this one; we had subcutaneous, orbital, tonsilar lymphomas of small size, but there were always other lesions either in other regions or in the lymph nodes. Personally, I still think it is a synovioma; the papillary character of the tumor is consistent with that diagnosis. I do not think that the case is closed, for this patient may live for several years and eventually die of whatever it is. May I say that I thought that pathologists were agreed that the reticulum stain was a useless procedure in the diagnosis of these tumors.

William H. Bauer, M.D., St. Louis, Mo.: I based my diagnosis of a synovioma on the papillary and only occasionally solid pattern of polygonal, epithelium-like cells of a tumor found in the close vicinity of a joint. It seems to me that the moderate amount of reticulin shown in the projected slide is not indicative of a reticulum cell sarcoma. The reticulum cell sarcoma occurs within the long bones, whereas the tumor apparently developed outside the bone.

William B. Dublin, M.D., Fort Logan, Colo.: May I request that Doctor Ackerman dispose a little more specifically of the papilliferous projections into spaces in this tumor.

Dr. Regato: I believe that the radiosensitivity of the tumor militates against the diagnosis of synovioma. May I add that Dr. Ackerman was not informed of the radiosensitivity of this tumor any more than the other participants; he

was provided, however, with unstained slides and did his own reticulin stains.

The statement has been made that synoviomas are very poorly radiosensitive. Haagensen and Stout concluded that irradiation is "singularly futile" in the treatment of synoviomas and stated that they had been unable to find any clear evidence that irradiation was even of palliative value. However, in a recent paper of Pack and Ariel, two cases of synovial sarcoma are reported that were controlled by radiotherapy and the statement is made that roentgentherapy "has offered good palliation" in others.

Dr. Ackerman: I'm sorry that all those pathologists in Chicago thought this was a synovioma. I have seen reticulum cell sarcomas form voluminous masses. I saw no areas which had the real papillary character and which is found in synoviomas. I think that the reticulum pattern has something to do with the diagnosis of a tumor. I have found it so in angiosarcomas, the lesion called hemangiopericytoma and even in synoviomas.

William B. Dublin, M. D., Fort Logan, Colo.: I should like to ask Dr. Ackerman what his experience has been with reticulum in synovioma; in my experience the sarcomatous phase of the tumor will show reticulum between tumor cells, whereas the mesothelial phase or cell nests will not, and therefore one may find more or less blank spaces alternating with well impregnated areas; an evaluation of this feature may be worthwhile in this case.

Dr. Ackerman: I agree that with the reticulum stain there is an apparent mixture of elements in synovial sarcomas. I wish to point out that several of the cases reported by Jackson and Parker were single focus lesions, which responded to treatment and remained well for many years.

Dr. Regato: It should be of interest to all that Fred Stewart of New York, Charles Geschickter of Washington, and Rupert Willis of Leeds, all made a diagnosis of synovioma. Henry L. Jaffé of New York commented that he would hesitate in accepting a diagnosis of synovioma but would consider one of Ewing's tumor. Charles Oberling of Paris, who originally described reticulum cell sarcomas, thought that this tumor should belong in that group if the silver stains confirmed its identity. Brachetto-Brian of Buenos Aires also thought this to be a reticulum cell sarcoma.

A commentary appears pertinent: the radiographic impressions were overwhelmingly favorable to the types of tumor that would have led to drastic surgical intervention or to abstension; the majority of histopathologic diagnoses, though different, would have also led to radical surgical treatment; only the minority of the histopathologic diagnoses pointed to the possibility of conservative radiotherapeutic management.

(In January 1951 this patient presented extensive, rapidly growing mediastinal and pulmonary metastases; she expired in February having presented no peripheral adenopathy. Autopsy was not done. Ed.)

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3. *Eosinophilic Granuloma of the Femur*

Contributed by L. V. ACKERMAN, M. D., St. Louis, Mo.

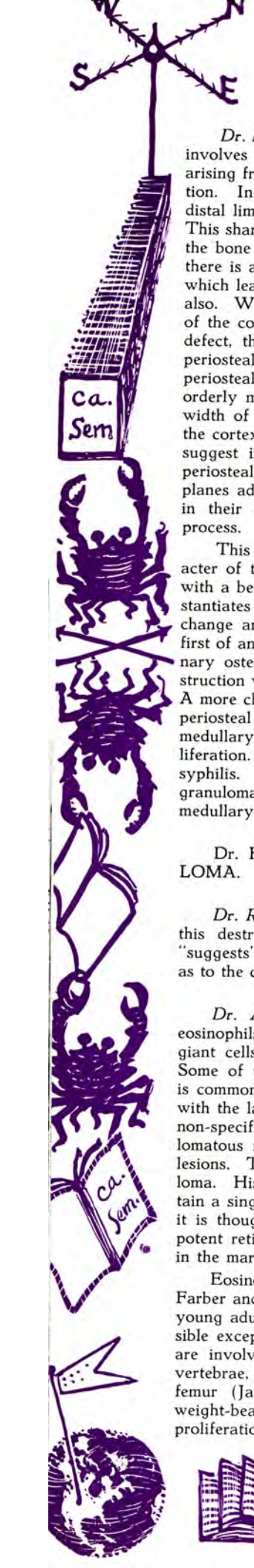
THE PATIENT was a boy 9 years of age who in August 1948 fell from a tree but had no immediate complaints; a week later there was pain in the left thigh and limping. The white cell count was slightly elevated but the differential was normal. A roentgenogram taken in October 1948 showed a destructive lesion in the subtrochanteric area of the left femur; copies of this roentgenogram were sent to the participating radiologists. Roentgenograms of other bones showed no abnormalities. The femur was explored and a specimen was removed; sections of this specimen were sent to the participating pathologists.

Radiologic Diagnoses Submitted by Mail

Ewing's tumor	72
Osteogenic sarcoma	16
Chondrosarcoma	10
Reticulum cell sarcoma	4
Osteomyelitis	36
Eosinophilic granuloma	20
Fibrous dysplasia	6
Seven other diagnoses	20

Histopathologic Diagnoses Submitted by Mail

Eosinophilic granuloma	105
Lymphoma	5
Ewing's tumor	3



Dr. Hodes: This is apparently a monostotic lesion which involves the metaphyseal portion of the bone, apparently arising from the medulla, and producing considerable destruction. In spite of this bone destruction, the proximal and distal limits of the medullary defect are sharply demarcated. This sharp delineation is more marked in the proximal end of the bone defect than in the distal end, but in the latter site there is an abrupt change in the character of the trabeculae which leads one to believe that it is sharply demarcated here also. Whereas there is some destruction of the inner layers of the cortex of the bone at the site of the main medullary defect, there is considerable new bone proliferation due to periosteal activity. This is a uniform and diffuse type of periosteal activity and the new bone is laid down in a very orderly manner. As a result of periosteal proliferation, the width of the femur is definitely increased. At no place in the cortex has there been produced a definite bone defect to suggest infiltration by tumor. The appearance is that of periosteal reaction to an irritant. The soft tissue fascial planes adjoining the main bone defect are a little decreased in their definition suggesting an associated inflammatory process.

This does not look like a tumor. The well defined character of the medullary defect indicates that we are dealing with a benign process. The orderly periosteal reaction substantiates this impression. In view of the marked medullary change and the obvious new bone proliferation, one thinks first of an inflammatory or granulomatous process. An ordinary osteomyelitis producing this amount of medullary destruction would by this time have broken through the cortex. A more chronic low grade osteomyelitis producing this much periosteal reaction would not have caused such widespread medullary destruction without more medullary new bone proliferation. We are given no indication that this patient has syphilis. The findings are compatible with a low grade granuloma arising in the reticuloendothelial system in the medullary portion of the bone.

Dr. Hodes' diagnosis: EOSINOPHILIC GRANULOMA.

Dr. Regato: Dr. Brailsford, of Birmingham, stated that this destructive medullary lesion with periosteal reaction "suggests" a primary malignant tumor of bone; he inquired as to the condition of the patient's chest.

Dr. Ackerman: The sections show large masses of eosinophils separated by numerous foam cells; multinucleated giant cells are not rare and mitotic figures are infrequent. Some of the cells exhibit phagocitic activity, and necrosis is commonly encountered. The large number of eosinophils with the large reticuloendothelial cells effectively rules out a non-specific osteomyelitis and the absence of typical granulomatous reactions rules out tuberculosis and other related lesions. The picture is obviously one of eosinophilic granuloma. Histiocytes which are found in this lesion may contain a single nucleus, but may also have two or more nuclei; it is thought that these histiocytes are derived from multipotent reticulum cells in the adventitia of the blood vessels in the marrow; hemosiderin pigmentation is not unusual.

Eosinophilic granuloma of bone, first reported by Otani, Farber and Jaffé, is seen mainly in children, adolescents, and young adults; it can involve almost any bone with the possible exception of those of hands and feet; if multiple bones are involved, very frequently those affected are the ribs, vertebrae, cranial vault, and particularly the humerus and femur (Jaffé and Lichtenstein). Fractures may occur in weight-bearing bones, resulting in considerable periosteal proliferation which may result in a roentgenologic suspicion

Fig. 1 — Destructive lesion of the metaphyseal end of the femur; note sharply demarcated limits.

of Ewing's tumor; since the response to irradiation has often been dramatic, some of these cases have been erroneously reported in the past as cured cases of Ewing's sarcoma.

Dr. Ackerman's diagnosis: EOSINOPHILIC GRANULOMA.

Subsequent history: 1200 roentgens (measured on skin) to each one of three fields directed to the lesion; other details not known. Patient was well until March 1950, when a mass appeared in the region of the scar inside the irradiated area. Biopsy revealed recurrence of eosinophilic granuloma. He was again treated by roentgentherapy: a calculated dose of 1600 roentgens was delivered to the tumor in eight days. The patient is at present well and has shown no other lesions elsewhere.

Dr. Regato: The diagnosis of "eosinophilic granuloma" has now become very popular among pathologists. As repeatedly pointed out by many, "eosinophilic granuloma" is not a disease entity, but only a phase in the histologic aspect of a clinical syndrome usually referred to as Hand-Schuller-Christian disease. According to Engelbreth-Holm, the natural history of this condition includes four phases: (1) a proliferative phase with histiocytic proliferation and accumulation of eosinophils, (2) a granulomatous phase with increase of blood vessels and fibrils, reticular cells, histiocytes, eosinophils and giant cells, (3) a xanthomatous phase with

isolated foam cells, and (4) a fibrous, healing phase. The "eosinophilic granuloma" becomes but an early stage in the syndrome.

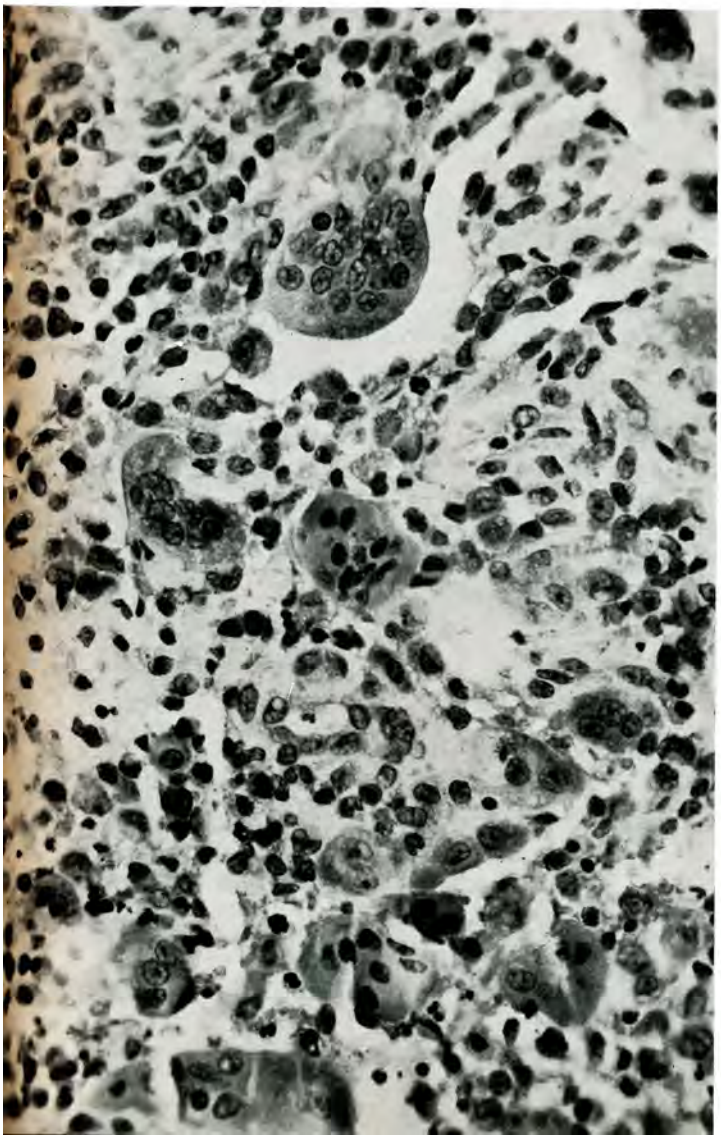
Balint Orban, M. D., D. D. S., Colorado Springs, Colo.: I have seen in recent years three cases of eosinophilic granuloma which were diagnosed by soft tissue biopsy of gingival tissues; usually these patients complain of painful swelling of the gingiva, extensive ulceration, or lack of wound healing following extraction of teeth. The roentgenologic appearance of the bone in these cases was very much like that of periodontal diseases (periodontosis). One of these cases later developed a lesion of the scapula; another had other lesions of the maxilla, clavicle, scapula, and humerus, and the third one had a lesion of the temporal bone. All these cases were controlled by roentgentherapy.

Anthony F. Rossitto, M. D., Wichita, Kans.: Would you describe the pain present in this case?

Dr. Regato: Dr. Ackerman, who contributed this case, states that the pain was mild.

Dr. Rossitto: I believe that one cannot make a diagnosis of these lesions on the basis of the roentgengram alone; the presence or absence of pain is important in the differential diagnosis. I have had a patient who presented the same roentgenologic appearance, but the pain became excruciating and the child was unable to walk. We made a diagnosis of Ewing's sarcoma and administered radiotherapy; the pain disappeared after the third day of irradiation; bone regeneration occurred, and healing was complete. Eighteen months later the child developed a metastatic lesion of the spine, again with severe pain; death ensued six months later.

Fig. 2—Photomicrograph (X400). Eosinophilic granuloma; note numerous eosinophils, macrophages and giant cells.



Raymond R. Lanier, M. D., Denver, Colo.: I have had an opportunity to observe at the University of Chicago two cases of eosinophilic granuloma, one in a girl seven years of age and the other in an adult 26 years old; in both cases there were skin and bone lesions and in both there was local pain. One of the cases appeared to originate in the hypopharynx and showed response to roentgentherapy, but later lesions appeared in the bones of the skull and other parts of the skeleton. The second case had its first lesion in a rib and later other lesions developed in the vulva, anal ring, and skull. We felt that this was a generalized disease and that sooner or later subsequent lesions would develop.

Dr. Regato: Has any member of the audience seen a recurrence following radiotherapy of the so-called eosinophilic granuloma? Obviously, the matter of adequacy of the treatment, including dosage, should be analyzed in such instances.

Marcus J. Smith, M. D., Santa Fé, N .M.: We had a very interesting case at the University of Minnesota; the nature of the lesion was obscure, and over the period of years the histologic diagnoses ranged from reticulum cell sarcoma to transitional stages of multiple myeloma and Ewing's sarcoma. When I first saw the case, the diagnosis was changed to eosinophilic granuloma, probably because at that time this condition was becoming recognized. The patient had geographical defects of the bones of the skull and other bones, which responded nicely to radiotherapy; there were numerous recurrences over a period of 15 to 17 years.

LeRoy Sante, M. D., St. Louis, Mo.: We have treated three patients who had multiple involvement of numerous bones by eosinophilic granuloma. All three of these patients are well; their lesions have regressed and they have remained well, one for more than ten years. After roentgentherapy, we have observed reformation of bone but have also observed an advancement of the lesions at its edges. I think that this is not actually a recurrence but rather that the area of apparent extension may not have been covered in the field of irradiation.

Dr. Regato: In this case a respectable number of roentgenologic opinions suggested an ominous prognosis; the performance of a biopsy revealed a morphology readily recognized and leading to a successful conservative treatment.

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4. *Osteogenic Sarcoma (Low Grade) of a Rib*

Contributed by RICHARD E. JOHNSON, M. D., Columbia, Mo.

THE PATIENT was a man 27 years of age who in 1940 complained of pain in the dorsal region. A roentgenogram revealed a cystic lesion expanding the eighth rib. This was the roentgenogram submitted to the participants in the SEMINAR. In 1941 an excision was done of a portion of this rib 6 cm. in length containing the lesion; the slides submitted to the participants were cut from this specimen.

Radiologic Diagnoses Submitted by Mail		Histopathologic Diagnoses Submitted by Mail	
Bone sarcoma	46	Osteogenic sarcoma	54
Chondrosarcoma	32	Chondrosarcoma	6
Metastatic tumor	18		
Myeloma	18	Osteoid osteoma	27
Osteochondroma	14	Fibrous dysplasia	3
Ewing's tumor	12	Healing bone or foreign body reaction	4
Angiosarcoma	4	Osteoid tissue forming tumor	1
Ten other diagnoses	20	Aneurysmal bone cyst	1

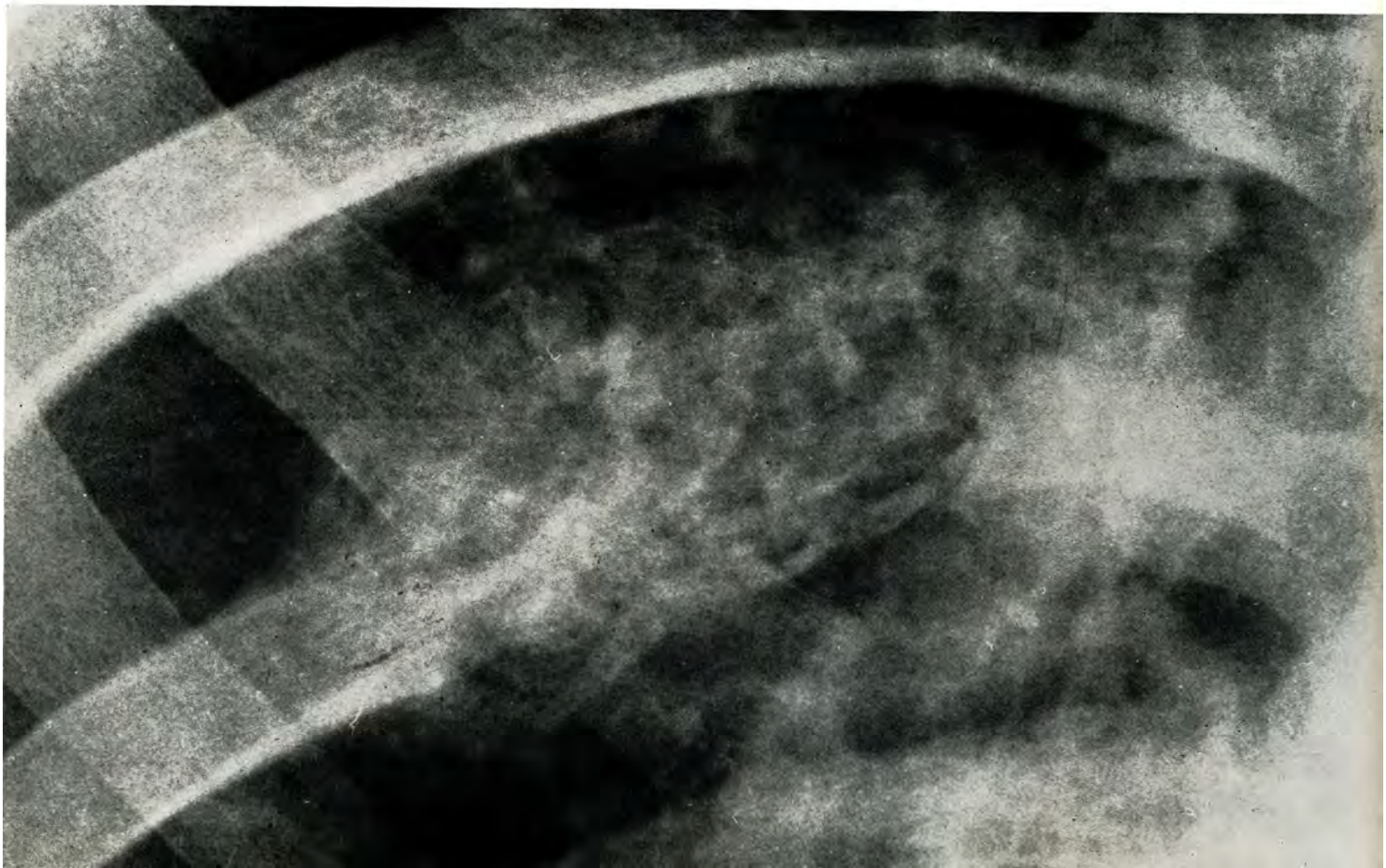
Dr. Hodes: This apparently is a monostotic lesion, although the proximal portion of the ribs below the affected rib seems somewhat deossified. The process is medullary in origin. It has caused remarkable expansion of the rib in a somewhat asymmetrical manner. In spite of the apparent well demarcated character of the bulbous mass, the bony margin of the lesion is definitely irregular in texture and apparently has broken through the cortex at multiple points, but in spite of this, I can find no associated soft tissue masses around the bone. The tumor mass within the rib has a very granular appearance suggesting multiple islands of calcified cartilage, osteoid, or both. The lateral margin of the bone defect in the rib is fairly well demarcated. However, there is a definite change in the trabecular pattern of the apparently normal segment of the rib where the trabeculae are abnormally coarse and showing definite reactive changes. In addition a classical Codman's cuff is evident at the lateral margin of the bony mass.

This is obviously a tumor. Apparently, too, in view of its medullary origin, this is a bone tumor. The irregularity of the periphery of the bulbous lesion, the peculiar stippled appearance of the medullary portion, and the Codman's cuff all attest to the malignancy of the process. Whether this is a cartilaginous tumor or bone tumor remains to be differentiated. In view of the fact that cartilaginous tumors occur a little more commonly in the ribs, that these tumors in the ribs often appear benign while in fact they are malignant, and also in view of the fact that cartilage has more growth potentiality than ordinary bone tissue, I would favor a cartilaginous neoplasm.

Dr. Hodes' diagnosis: CHONDROSARCOMA.

Dr. Regato: A radiographic diagnosis of chondrosarcoma was also rendered by Drs. Brailsford of Birmingham,

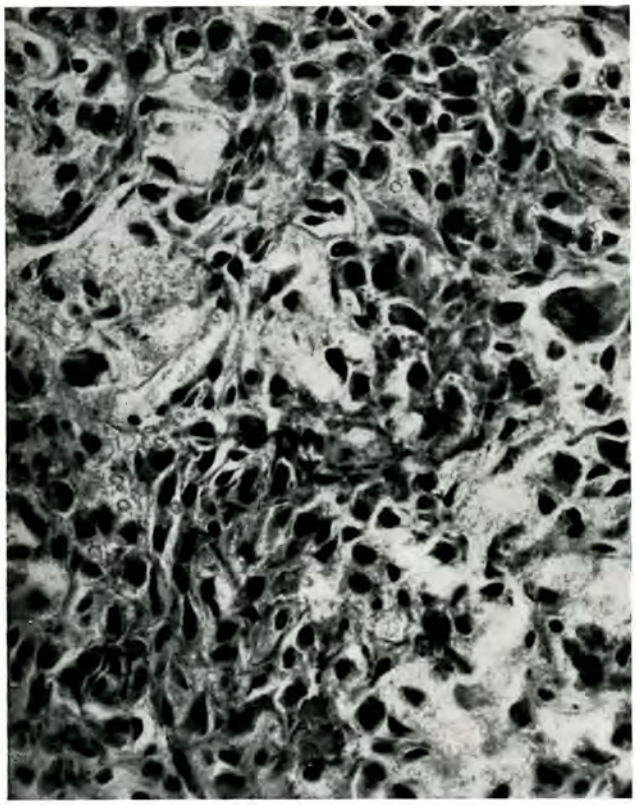
Fig. 1—Expanding lesion of the rib with stippled appearance of the medullary region.



LeRoy Sante of St. Louis, Albert Ferguson of Boston, and G. Esguerra of Bogotá; the possibility of an angioma of the bone was suggested by Dr. L. Goin of Los Angeles.

Dr. Ackerman: Microscopically, this lesion shows an extremely variable pattern. It appears to be well vascularized and there are numerous endothelial-lined dilated vascular spaces. Between these spaces and also forming islands there are cellular areas consisting of cells apparently coming from bone-forming mesenchyme. This extremely cellular tissue shows considerable nuclear variation, passes into areas where there are small islands of osteoid tissue. The cells between these islands show no evidence of increased mitotic activity, but there appears to be some regularity in the formation of the osteoid. There are a few osteoclasts present. This lesion is rare; we have seen only one other which occurred in a young male, it was thought to be non-malignant and was designated by Jaffé as an ossifying fibroma and by Stout as a benign unclassified lesion of bone. It would be difficult

Fig. 2—Photomicrograph (X400). Biopsy of 1942: cellular area with variable sized nuclei but no osteoid.



microscopically to designate this as frankly malignant. Details of subsequent history known to us have influenced our opinion.

Dr. Ackerman's diagnosis: OSTEOGENIC SARCOMA (LOW GRADE).

Arthur Purdy Stout, M. D., New York, New York (by mail): Very few remnants of the original bone of the rib remain because of an extensive destructive tumor growth. This is extremely variable in its appearance but in many places it seems to form a kind of atypical osteoid, sometimes with extremely anaplastic cells. I can only think of osteogenic sarcoma when I see this picture. I cannot think of any other lesion, benign or malignant, which could produce it.

Dr. Regato: A diagnosis of fibrous dysplasia was submitted by Dr. R. Willis of Leeds; Dr. Fred Stewart of New York felt that probably this was an osteoid osteoma, and Dr. Henry L. Jaffé of New York also considered the case as probably a benign borderline lesion, between osteoid osteoma and ossifying fibroma.

Subsequent history: In 1942 this patient experienced a recurrence of pain; an extrapleural resection of the sixth, seventh, and the eighth rib was done. It was recognized at operation that tumor had been cut through, parts of it were curetted out, and the region was cauterized with zinc chloride paste; a histopathologic diagnosis of osteochondroma was then rendered. The patient was followed for six consecutive years without showing any evidence of recurrence; a roentgenogram of the chest taken in 1947 showed no abnormalities. In November 1948, three months after the last examination at which he had presented no abnormalities, he suddenly developed a syndrome of obstruction of the superior vena cava; his chest was explored and the superior mediastinum was found replaced by a partially calcified mass that could not be resected; only a biopsy was done. Symptoms gradually subsided and in March 1950 he was entirely symptomless and had no apparent change in the mediastinal mass as seen in the roentgenogram.

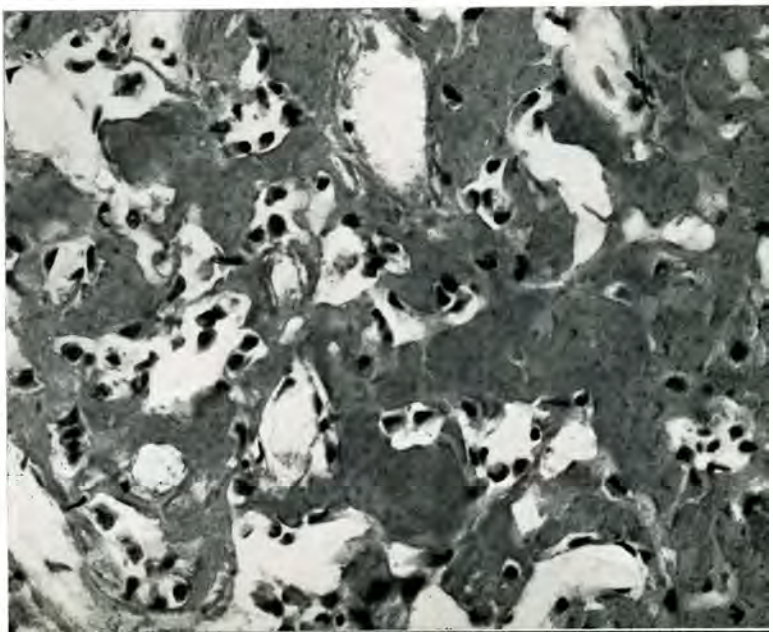
William H. Bauer, M. D., St. Louis, Mo.: My diagnosis was osteogenic sarcoma, perhaps superimposed on a so-called "monostotic fibrous dysplasia"; this would reconcile the benign looking areas of the tumor with the malignant ones.

Wesley Johnson, M. D., Colorado Springs, Colo.: The possibility of hemangioma of the bone was suggested. The hemangioma of bone presents three radiologic appearances; sunburst effect as usually seen in flat bone, soap-bubble effect usually seen in long bones, and the striated course parallel or vertical strias as seen in vertebrae.

Ernst A. Schmidt, M. D., Denver, Colo.: Twenty years ago we saw a similar case diagnosed as osteogenic sarcoma of the occipital bone; the patient was given roentgentherapy and remained well five years afterward. The slides of this case were shown to Dr. Ashoff, who was visiting in this country; he made a diagnosis of osteogenic sarcoma of what he called fibrotic type and used an analogy with fibrotic tuberculosis in reference to that case. Perhaps this corresponds to what Dr. Ackerman calls low grade.

Dr. Regato: It may be noted that in this case most radiologists favored a malignant lesion while a surprisingly high proportion of pathologists considered this lesion as benign; the clinical evolution of the case points frankly towards local malignancy.

Fig. 3—Photomicrograph (X400). Biopsy of 1948: Questionable fibrosarcoma; note osteoid formation that was not observed in previous biopsy.

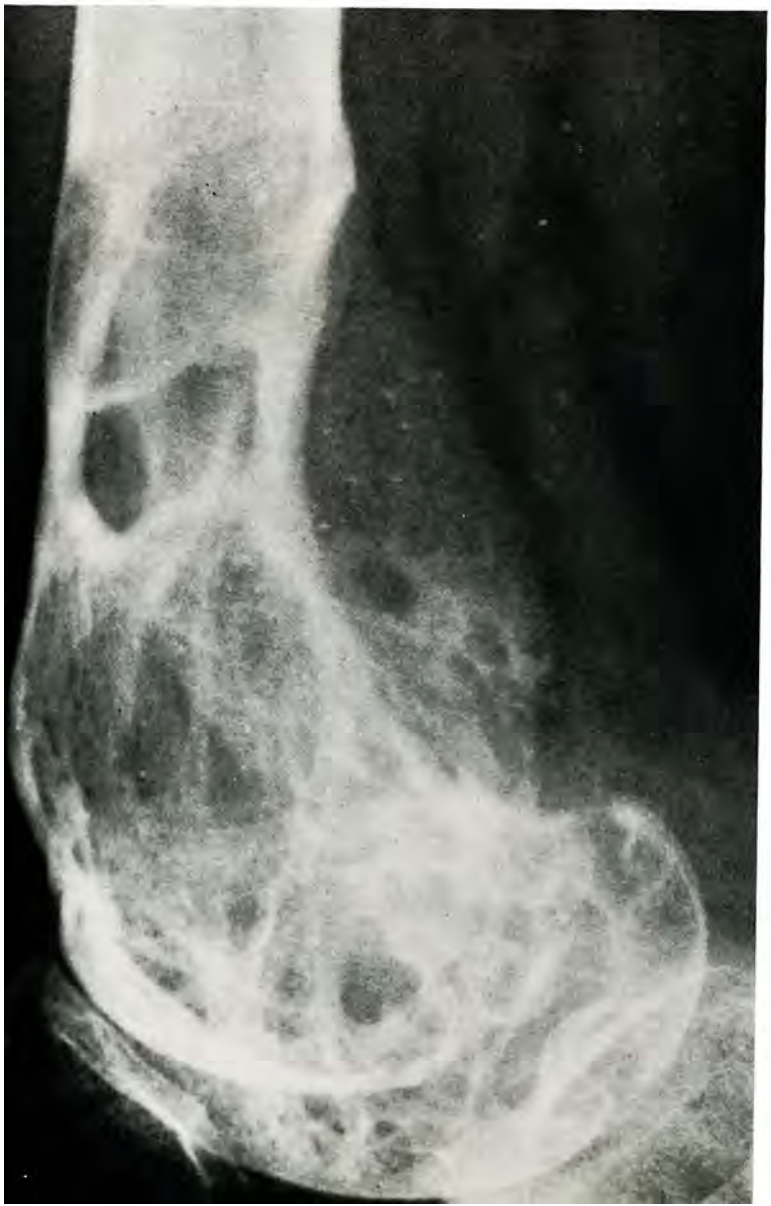


5. *Fibrosarcoma (?) of the Femur*

Contributed by L. V. ACKERMAN, M. D., St. Louis, Missouri

THE PATIENT was a woman 20 years of age in 1947 when she complained of progressive loss of motion of one knee; a roentgenogram had then revealed a lesion of the distal end of the femur; a biopsy was reported as showing a giant cell tumor. The patient continued to complain of pain and progressive loss of motion of the right knee until February, 1950, when a roentgenogram showed a cystic-looking lesion replacing the epiphysis and involving the metaphysis of the distal end of the femur; copies of this film were sent to participants. Serum calcium and phosphorus and alkaline phosphatase were normal. The slides of previous biopsy were obtained but they consisted of shreds of poorly stained tissue. A surgical exploration and curettement was done from which the slides distributed were prepared.

Fig. 1 — Multiloculated lesion of the epiphysis of the femur producing definite expansion of the bone; no evidence of periosteal reaction.



Radiologic Diagnoses Submitted by Mail	
Giant cell tumor	66
Chondroma or chondrodysplasia	14
Fibrous dysplasia	8
Hydatid cyst	6
Malignant giant cell tumor	20
Chondrosarcoma	16
Sarcoma	10
Ten other diagnoses	20

Histopathologic Diagnoses Submitted by Mail	
Osteogenic sarcoma	30
Fibrosarcoma	12
"Neurogenic" sarcoma	1
Fibrous dysplasia	24
Osteitis fibrosa	18
Fibroma	12
Osteoid osteoma	6
Giant cell tumor with cysts	2

Dr. Hodes: This is a monostotic multi-loculated lesion involving the epiphyseal portion of the bone and apparently arising in the medulla. It has extended into the metaphysis and partially into the diaphyseal portion of the bone and produced definite expansion of the bone. There is no evidence of periosteal reaction; cortical bone atrophy is present. Evidence of extension of the disease beyond the normal confines of the bone is manifest in the posterior portion of the distal femur. A soft tissue mass extends well beyond the bone; calcific debris seem to be distributed throughout this soft tissue mass, but they might prove to be artefacts.

This is obviously a tumor and a malignant one, in view of the soft tissue mass extending beyond the confines of the bone. The long-standing character of the lesion is attested to by the fact that there is associated soft tissue atrophy, extension of the lesion into the proximal portions of the shaft of the bone, and marked deossification in the normal bone proximal and distal to the site of the lesion. A centrally placed fibrosarcoma might conceivably produce such a lesion; yet, these are rather rare and the extent of the disease process and lack of new bone proliferation would seem to militate against the latter possibility. The medullary origin of this tumor in the epiphyseal portion of a long bone suggests that this is a giant cell tumor which has undergone malignant degeneration. The patient's age and the apparent chronicity of the process would lend further support to this diagnostic possibility.

Dr. Hodes' diagnosis: MALIGNANT TRANSFORMATION OF A GIANT CELL TUMOR.

Dr. Regato: A radiographic diagnosis of giant cell tumor undergoing malignant transformation was also rendered by Drs. P. Swenson of Philadelphia, LeRoy Sante of St. Louis and Albert Ferguson of Boston.

Dr. Ackerman: This lesion does not show giant cells but does show an extremely cellular fibroblastic tissue varying in cellularity in the different areas and made up of spindle shaped cells with even-stained nuclei; mitotic figures are rare; there is bone destruction in some areas. The process does not resemble fibrous dysplasia or giant cell tumor. A non-osteogenic fibroma usually forms an excentric defect in the metaphyseal area of the bone; the process does not have the tangled appearance of neurofibroma nor were there any other manifestations of that condition. Could this be a fibrosarcoma arising within the bone cavity from supporting connective tissue of the marrow? If it is a fibrosarcoma, it must have a low grade of malignancy for it has been present at least three years.

This material has been seen by Hatcher, who was unwilling to make a diagnosis, by Stout, who thought this was a fibrosarcoma, and by Litchtenstein, who was of the opinion that this is a low-grade fibrosarcoma.

Dr. Ackerman's diagnosis: FIBROSARCOMA (?) OF LOW MALIGNANCY.

Arthur Purdy Stout, M. D., New York, N. Y. (by mail): This is a lesion difficult for me to interpret. I am worried by the extent of the epiphyseal involvement and by the tumor-like proliferation of fibroblasts. This possibly may mean that a fibrosarcoma has developed in the dysplasia (or an osteogenic sarcoma masquerading as a fibrosarcoma). I believe, however, that this is not the case so far as this section is concerned because of the good differentiation and lack of mitoses. I shall, therefore, classify this tentatively as monostotic fibrous dysplasia of which it has many of the characteristics; I would like to believe that this is at least the basic underlying condition.

Dr. Regato: Drs. Fred Stewart, of New York, and R. Willis of Leeds also thought this to be a case of fibrous dysplasia; Dr. Leo Lowbeer of Tulsa submitted a histopathologic diagnosis of fibrosarcoma (medullary or periosteal), Doctor Brachetto-Brian of Buenos Aires, one of fibroblastic sarcoma and Dr. C. Oberling of Paris, one of fibrosarcoma with low malignancy.

Subsequent history: Amputation was considered but the patient was treated by curettement and introduction of bone fragments.

A. M. Ginzler, M. D., Bridgeport, Conn.: In the section that I had, I do not feel that there was sufficient pleomorphism or atypism of the cells to justify the diagnosis of fibrosarcoma although that diagnosis must certainly be considered. In my section there was an area of newly formed bone trabeculae. I think that this lesion represents an ossifying fibroma of bone. I do not think it represents a fibrous dysplasia.

William H. Bauer, M. D., St. Louis, Mo.: Like Dr. Ginzler, I was impressed by the large number of very well developed giant cells, cysts, and bone formation on the periphery of the tumor. I thought of a fibrous variant of, or reparative change in a giant cell tumor.

Anthony F. Rossitto, M. D., Wichita, Kansas: Was this film sent to us for study taken before or after surgery?

Dr. Regato: It was taken before curettement; only a biopsy had been done three years previously.

Mark Wheelock, M. D., Chicago, Ill.: A characteristic which I think is indicative of malignancy in this case is the fact that the roentgenologic study showed no capsule but rather an invasive appearance.

Dr. Ackerman: Dr. Hodes is of the opinion that the roentgenogram showed extension into the metaphysis and diaphysis, which I take as additional evidence of the malignant tendency of this tumor.

William B. Dublin, M. D., Ft. Logan, Colo.: It is evident that the more closely a mesenchymal tumor approaches the borderline between benign and malignant, the more difficult it becomes to form appropriate judgment; often it appears impossible to decide between malignancy and benignancy. It may be admitted that mitotic figures are quite worthless in evaluating the malignant tendency of a tumor in general, but I think that there may be an exception when the growth is composed of spindle cells (leiomyoma, fibroma, etc.). Dr. Newton Evans pointed out in one of his earliest papers that borderline leiomyosarcomas tend to show the appearance of mitotic figures; this does not always hold true, but it may be helpful. In my own study of fibroma and fibrosarcoma, of the soft tissue of the extremities, mitotic figures were easily found in the higher grades. In the low-grade and borderline lesions the finding of mitotic figures with reasonable ease (numerically, about 2 per thousand cells) indicated malignant tendency. Conversely, however, it is true that a fairly well differentiated fibroma, especially of neurogenic origin, may infrequently show unexpected invasiveness in the absence of appreciable numbers of mitotic figures.

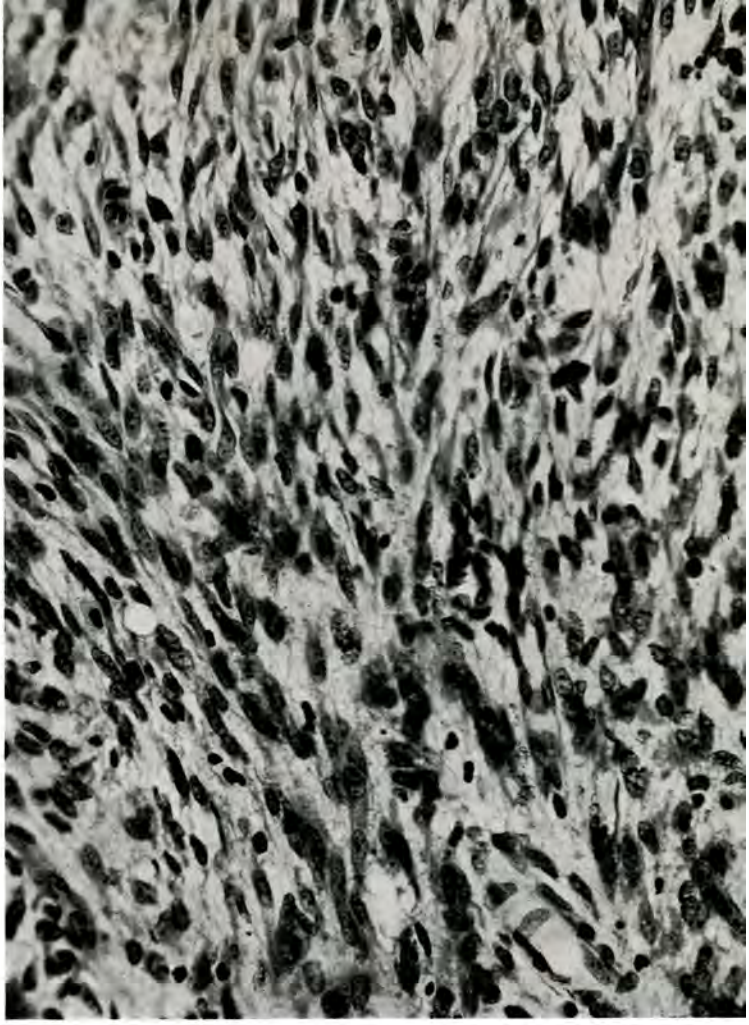


Fig. 2—Photomicrograph (X400). Questionable fibrosarcoma; extremely cellular fibrous area; no mitotic figures.

I would like to ask Dr. Ackerman for a follow-up report on whether progress has been made regarding ability to distinguish morphologically the three main types of spindle cells: the smooth muscle cell, the fibroblast, and the lemmocyte, in tumors. This was discussed in last year's Seminar and an investigative project was mentioned. Is there anything further on that?

Dr. Ackerman: When Dr. Stout first saw this case and called it a malignant tumor, he saw several slides that I submitted to him, while now he examined only one section and concluded that it is benign. This may prove the advantage of examining several sections in some cases.

I certainly agree that if mitotic figures appear in large numbers in smooth muscle tumors, they are a fairly good sign that the tumor is malignant; but if the mitotic figures are not present, we have no assurance that the tumor is not malignant, for I have seen fairly well differentiated smooth muscle tumors metastasize.

It is very difficult to be dogmatic about identification of fibroblasts and smooth muscle cells. I think that one can get to a reasonable conclusion in a fair number of tumors, particularly if they are well differentiated, by using reticulum and phosphotungstic-acid-hematoxylin stains and by taking into consideration the location and gross appearance of the tumor. In an undifferentiated sarcoma it may be impossible to determine the type of cell, but then there will be little value in the differentiation.

6. Monostotic Paget's Disease Of a Lumbar Vertebra

Contributed by ISADORE LAMPE, M. D., Ann Arbor, Mich.

THE PATIENT was a man 37 years of age who in March, 1948, first complained of lumbar pain; in March, 1949, he had severe attacks of lumbar pain that caused him to collapse; a similar episode occurred in December, 1949. A roentgenogram taken at the latter date showed a collapse of the third lumbar vertebra; copies of this film were seen by the participants. A surgical exploration revealed softening of the spinous process and lamina of the third vertebra; a specimen was removed from which the slides submitted were made.

Radiologic Diagnoses Submitted by Mail	
Metastatic tumor	24
Myeloma	28
Lymphoma	16
Hemangioma	34
Giant cell tumor	14
Paget's disease	4
Localized osteomalacia	2
Very difficult for me	1
Nine other diagnoses	21

Histopathologic Diagnoses Submitted by Mail	
Paget's disease	54
Osteotitis fibrosa	21
Fibrous dysplasia	6
Ossifying fibroma	6
Giant cell tumor	6
Tuberculosis	2
Myeloma	3
Bone sarcoma	1
What is it?	1

Dr. Hodes: The evidence indicates that this is a monostotic lesion. Deossification characterized the process and the deossification not only involves the vertebral body but also the vertebral appendages. The degree of deossification seems uniform. There is no one area in this vertebral segment which seems more affected than any other portion. There is no change in the vertebral bodies below and above the affected vertebral segment; the adjoining vertebral plates seem unaffected. There is very marked expansion of the intervertebral discs on either side of the involved vertebral body. There is no evidence of a soft tissue mass extending beyond the vertebral body as seen in the lateral projection. Of extreme importance is the apparent molding of the vertebral body which has become definitely longer, when viewed in the lateral projection, than the vertebral bodies above and below it. This bespeaks for a chronic process with gradual bone softening and molding in the shape of the bone.

This vertebral segment reveals none of the elements of infection, nor are there any changes to suggest that we are dealing with a tumor. A chondroma of the vertebra might produce this picture but chondromas are usually associated with abnormal masses. When one considers slowly progressive bone softening processes limited to one vertebral segment, one is forced to consider the possibility of monostotic Paget's disease.

Dr. Hodes' diagnosis: MONOSTOTIC PAGET'S DISEASE.

Dr. Regato: A radiologic diagnosis of localized osteomalacia was submitted by I. G. Williams of London.

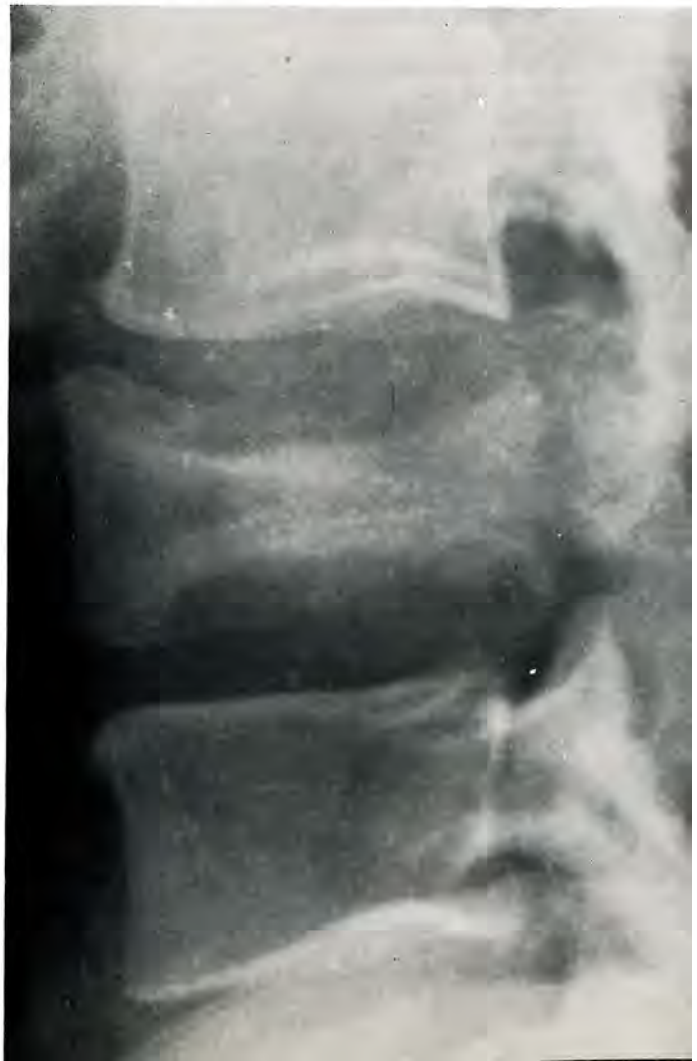
Dr. Ackerman: This is a lesion which does not show any evidence of malignant change and consists of areas of bone production and bone absorption. Osteoclasts are particularly prominent and the fibrous stroma is rather cellular. There has been new bone production and cement lines are particularly prominent. There are no signs of inflammation; tuberculosis, syphilis and other processes would have to be ruled out. This much bone resorption would be unusual in fibrous dysplasia. Could this be due to hyperparathyroidism? In extreme hyperparathyroidism there is usually formation of cysts with so-called Brown tumors and evidence of bone destruction and bone formation.

I am more willing to call this Paget's disease than any other entity for the following reasons: Paget's disease has a spotty distribution and a lumbar vertebra is one of its most common locations. The initial lesion of Paget's disease is bone-destroying but the composite picture shows both bone destruction and bone production. There is a typical evidence of both in this slide. Most important, is the increased number of cement lines within the thick trabeculae; these cement lines are completely irregular, often with tooth-like margins. Pagetoid mosaic bone can occur in polyostotic fibrous dysplasia. Uehlinger points out that in fibrous dysplasia there is invariably excentric atrophy of the cortical bone which is absent in Paget's disease. The involvement of a vertebra in fibrous dysplasia as a monostotic phenomenon would be distinctly unusual. In a listing of the common areas involved in fibrous dysplasia, Uehlinger lists femur, tibia, pelvic bones, humerus, and fibula in that order. He does not mention vertebra. Although 37 years of age is young for Paget's disease, it is perfectly within the realm of possibility.

Dr. Ackerman's diagnosis: MONOSTOTIC PAGET'S DISEASE.

Arthur Purdy Stout, M. D., New York, N. Y. (by mail): This process can fit the picture of so-called osteitis fibrosa whether it be solitary or multiple and associated with hyperparathyroidism. The underlying causes of this particular process I would not even attempt to guess without know-

Fig. 1 — Uniform deossification of a lumbar vertebra; the adjoining vertebral plates and vertebrae are not affected.



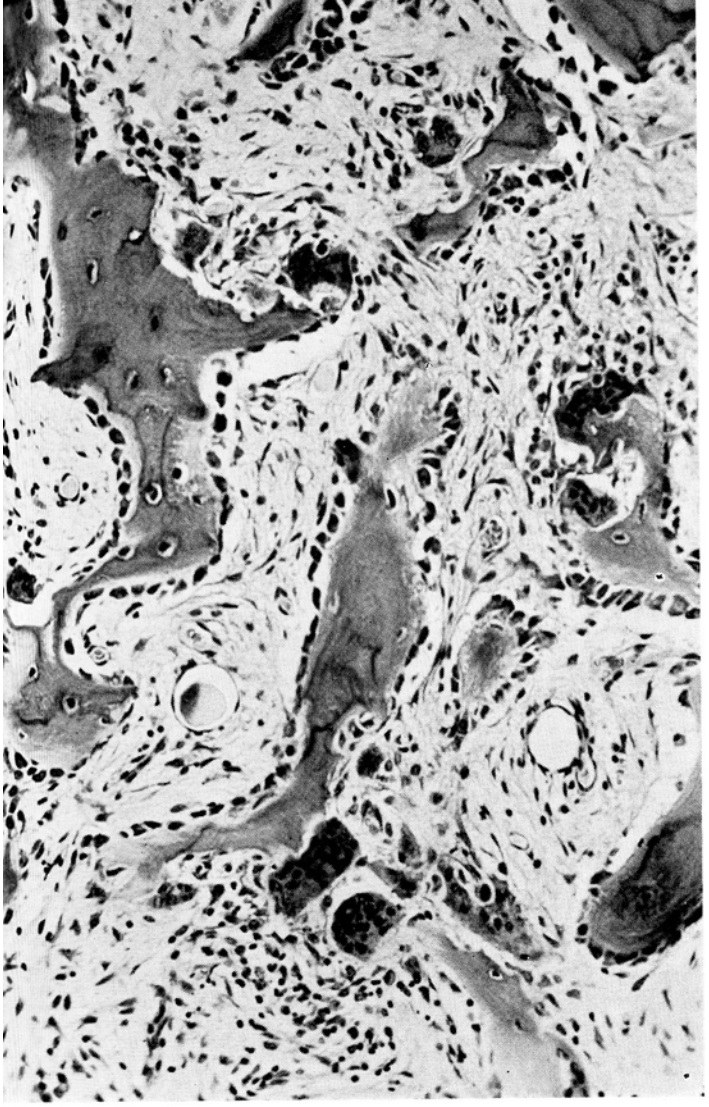


Fig. 2—Photomicrograph (X230). Paget's disease: bone destruction and bone formation with numerous multinucleated osteoclasts.

ing a great deal more about the case. Some quite different diseases might produce this histological picture, such as osteitis deformans and the soft osteomas of the facial bones and skull. I do not think it is any of these, but I could not be sure of it.

Dr. Regato: Dr. R. Willis, of Leeds, submitted a histopathologic diagnosis of fibrous dysplasia.

Subsequent history: Roentgenograms of this patient's spine, taken in March 1948, those taken in December 1949, and the more recent ones have not shown any change over a period of at least 20 months.

A. James French, M. D., Ann Arbor, Mich.: We, too, were concerned with the two possibilities that have been raised and, in addition, thought a third diagnosis warranted some consideration. Our diagnosis was not Paget's disease but fibrous dysplasia, and inasmuch as the vertebra was rarely the site involved in reported cases of fibrous dysplasia, we felt that an infarct of bone might be a third possibility. We thought of this primarily because of the reparative process present. The generalized osteogenesis that we see here, if I may use that word, in regard to the calcification of the vertebral body, suggests a more extensive process, perhaps fibrous dysplasia. We have no definite convictions. Some of us considered Paget's disease as a possibility, but we leaned more toward fibrous dysplasia, and in addition the possibility of an infarct of bone.

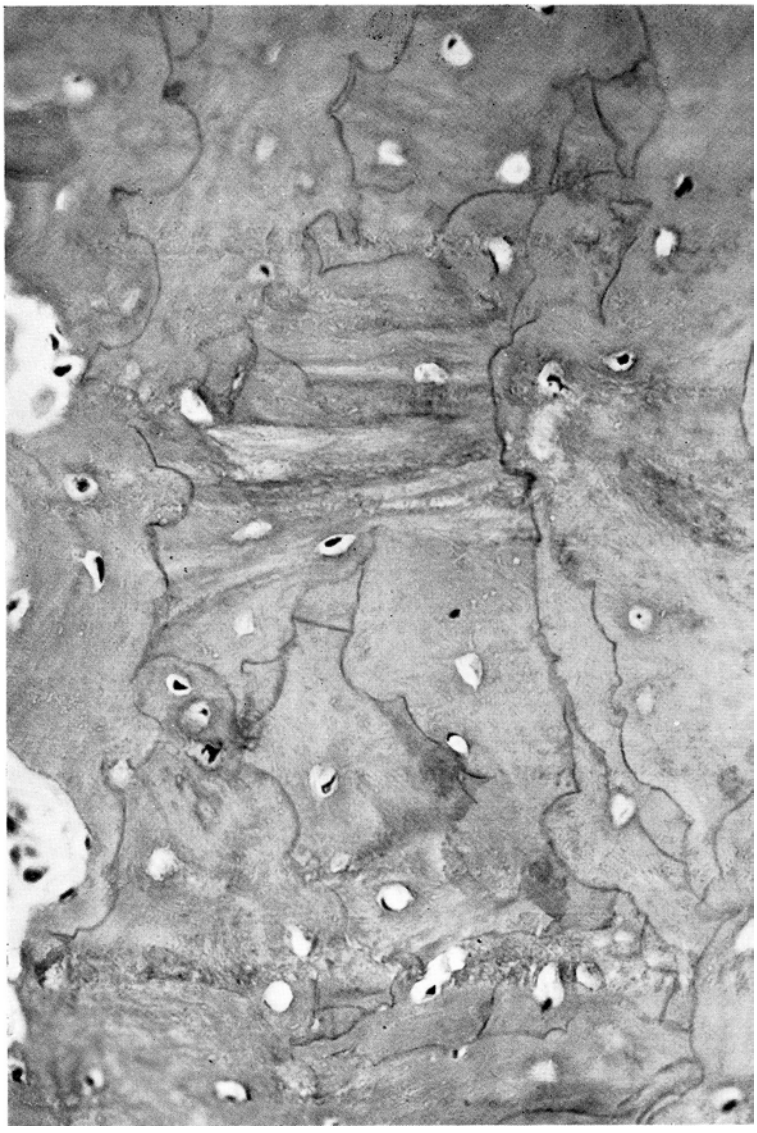
Dr. Hodes: The usual appearance of the bone infarct is not one of diffuse deossification like this.

Ernst A. Schmidt, M. D., Denver, Colo.: I am glad somebody brought up the question of osteitis fibrosa cystica in this case, as I noticed a number of pathologists have mentioned localized osteitis fibrosa cystica as a possibility. There was a time when we did not differentiate radiologically at all between Paget's disease and von Recklinhausen's disease; up to the age of 50 as a rule we called it von Recklinhausen's disease; if the process had been present for several years, or the patient was elderly, we called it Paget's disease. I would like to hear both from a radiological viewpoint and from a pathological viewpoint whether or not there may be a definite relationship between osteitis fibrosa cystica and osteitis deformans, between Paget's and von Recklinhausen's disease.

Dr. Hodes: Cystic lesions are destructive lesions. This one shows none of the markings of destruction; the bone appears to be giving away like a piece of clay that has been squeezed between two hands; also there is a definite uniformity of this change, not only in the vertebral body but also in the appendages.

K. T. Neubeurger, M. D., Denver, Colo.: About a quarter of a century ago there was no clear-cut differentiation between osteitis fibrosa and osteitis deformans, both of which were considered variants of "osteodystrophia fibrosa.". I remember an important publication on this subject which was published in the *Transactions of the German Pathological Society (Verhandlungen der Deutschen Pathologischen)* in 1926; the relationship of osteitis fibrosa to hyperparathyroidism and calcium metabolism has never been definitely established.

Fig. 3—Photomicrograph (X400). Typical mosaic with scalloped cement lines of Schmorl.



Dr. Regato: This patient's age is not a factor against the diagnosis of Paget's disease. In a series of 367 cases of Paget's disease studied by Dickson, Camp, and Ghormley, thirty cases were diagnosed in patients under 40, and fifty-five had presented their first symptom when less than 40 years of age.

Groh reported on a series of nine cases of monostotic Paget's disease, which he felt is a definite entity, not necessarily a first stage of the generalized disease. Six of Groh's nine cases had lesions of the lumbar vertebrae; one of these was diagnosed in a patient 26 years of age who complained of lumbar pain; the roentgenogram of that patient is almost identical with the one under our study and no change had been observed over a period of ten years.

A. M. Ginzler, M. D., Bridgeport, Conn.: As Doctor Ackerman pointed out so well, the section showed a marked reconstruction of this bone, and in view of this, together with the classical mosaic pattern present, it appears difficult to me to consider on a histologic basis any diagnosis other than Paget's disease. I gave some consideration to osteitis fibrosa generalisata which, in advanced cases, might show some degree of this reconstruction and mosaic pattern, but I think that I was influenced also by the age of the patient and the collapse of the vertebral body, and for these reasons gave more consideration to osteitis fibrosa than I should have on histologic grounds alone. I am very much interested and happy to learn, as I have today, that so many cases of Paget's disease can appear at that younger age.

Aside from other considerations, the point that Doctor Hodes made in his first remarks that the other vertebral bodies and other bones seen in the roentgenograms showed no changes would, I think, also speak against generalized osteitis fibrosa, since even the non-cystic areas in the latter condition will almost always show osteoporosis.

Dr. Regato: Dr. Ginzler, you may be interested in knowing that Dr. Henry L. Jaffé, of New York, who, as you know, has made a long study of osteitis deformans, offered a diagnosis of Paget's disease (acute phase) in this case.

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7. Chondrosarcoma of the Femur

Contributed by L. V. ACKERMAN, M. D., St. Louis, Mo.

THE PATIENT was a man 54 years of age with a history of injury to the right thigh five years previously. In June, 1949, he developed pain in the right thigh radiating to the knee; the pain became severe. A roentgenogram showed an osteolytic lesion of the intertrochanteric region of the right femur; copies of this film were sent to participants. There was also a non-described lesion of the fourth lumbar vertebra. In July, 1950, a specimen was removed from the head of the femur from which the distributed slides were prepared.

Radiologic Diagnoses Submitted by Mail	
Metastatic tumor	38
Bone sarcoma	16
Myeloma	12
Giant cell tumor	32
Bone cyst	14
Poor picture	2
Nine other diagnoses	24

Histopathologic Diagnoses Submitted by Mail	
Chondrosarcoma	42
Chondroma	48
Osteoid chondroma	12
Osteochondritis dessicans	1
Very bad section	2

Dr. Hodes: This is a metaphyseal lesion which apparently is limited to one bone and seems to have started in the medullary portion of the bone. It seems to have extended into the greater trochanter and has caused expansion of the proximal portion of the femur. The cortical new bone proliferation which is noted along the medial aspect of the proximal end of the femur seems unusual and important. Not very much reaction is noted around the lateral portion of the expansile lesion but some cortical reaction is present. Examination of the proximal and distal ends of the cystic process which seems multi-loculated reveals a lack of clear-cut definition of bone detail. The trabeculae seems somewhat moth-eaten, and at the distal end particularly, there seems to be some rarefaction beyond the normal contour of the cystic area. These features suggest that the lesion is an actively growing one and probably malignant. The soft tissue detail overlying this right femur is extremely poor. There is the distinct possibility that a soft tissue mass extends beyond the confines of this bone; yet, a definite point of break-through of the tumor into the surrounding soft tissues is not demonstrated.

This looks like a malignant bone tumor. The central osteosarcomas, whether sclerosing or destructive, usually do not expand bone. The cartilaginous tumors, however, do. Furthermore, the proximal femur, as well as proximal humerus, is a favorite site for this lesion.

Dr. Hodes' diagnosis: CHONDROSARCOMA.

Dr. Regato: A radiographic diagnosis of giant cell tumor was suggested in this case by Sir Graham-Hodgson and by I. G. Williams, of London.

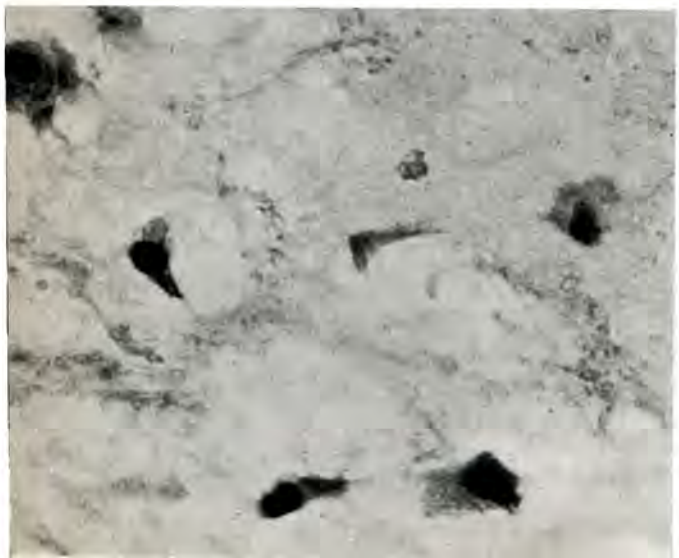

Fig. 1—Photomicrograph. Chondrosarcoma. Note plump and atypical nuclei.

Dr. Ackerman: The sections show collections of immature cartilage cells with no mitotic figures but do show plump nuclei, atypical nuclei, and double nuclei. There is also evidence of calcification. The changes described in these cells make the diagnosis of chondrosarcoma mandatory. This is not an osteogenic sarcoma, for in osteogenic sarcoma, as Jaffé has pointed out, the tumor arises directly from a sarcomatous stroma. Neoplastic osteoid is not present in chondrosarcoma. The areas of calcification which may be present give the splotchy appearance which some radiologists feel it suggestive of chondrosarcoma (Pendergrass).

The prognosis in chondrosarcoma is best the farther from the trunk the lesion is located, and the prognosis becomes extremely poor when the lesions arise in any portion of the trunk. The chondrosarcoma of the rib cage do poorly because radical resections are frequently not done and local recurrences appear. The prognosis is better in chondrosarcomas which arise from the cartilaginous cap of an exostoses than in those which arise within the bone.

Dr. Ackerman's diagnosis: CHONDROSARCOMA.

Arthur Purdy Stout, M. D., New York, N. Y. (by mail): The fragments of tissue show a cartilaginous tumor. Although a matrix has been formed in most places, the cells are not all fully adult and contained within capsules and in a few places a kind of fibrous myxoid tissue has been formed and even an occasional trabecula of osteoid. Some of the cartilaginous masses show calcification. Traces of the original bony trabeculae show aseptic pressure necrosis.

I consider this a well-differentiated form of chondrosarcoma. I do not call it a simple chondroma or enchondroma because it is not composed entirely of adult differentiated cartilage. Tumors such as this are slow to metastasize and frequently cured if completely removed by amputation or other drastic operation.

Dr. Regato: A histopathologic diagnosis of chondroma with malignant change was submitted by Dr. C. Geschickter of Washington; Dr. C. Oberling of Paris made a diagnosis of osteochondromyxoma, prognosis reserved; Dr. Fred Stewart of New York made a diagnosis of chondromyxosarcoma, low grade.

Subsequent history: This patient's lesion was thought to be localized and local excision and prosthesis were done in July 1949; post-operatively a lung abscess developed; a lobectomy was done in September, 1949; and the patient expired. The post-mortem examination revealed the presence of persistent local tumor and of pulmonary metastases, many of them subpleural. The microscopic study of the pulmonary metastases showed further dedifferentiation, and the appearance of the cells suggested fibrosarcoma.

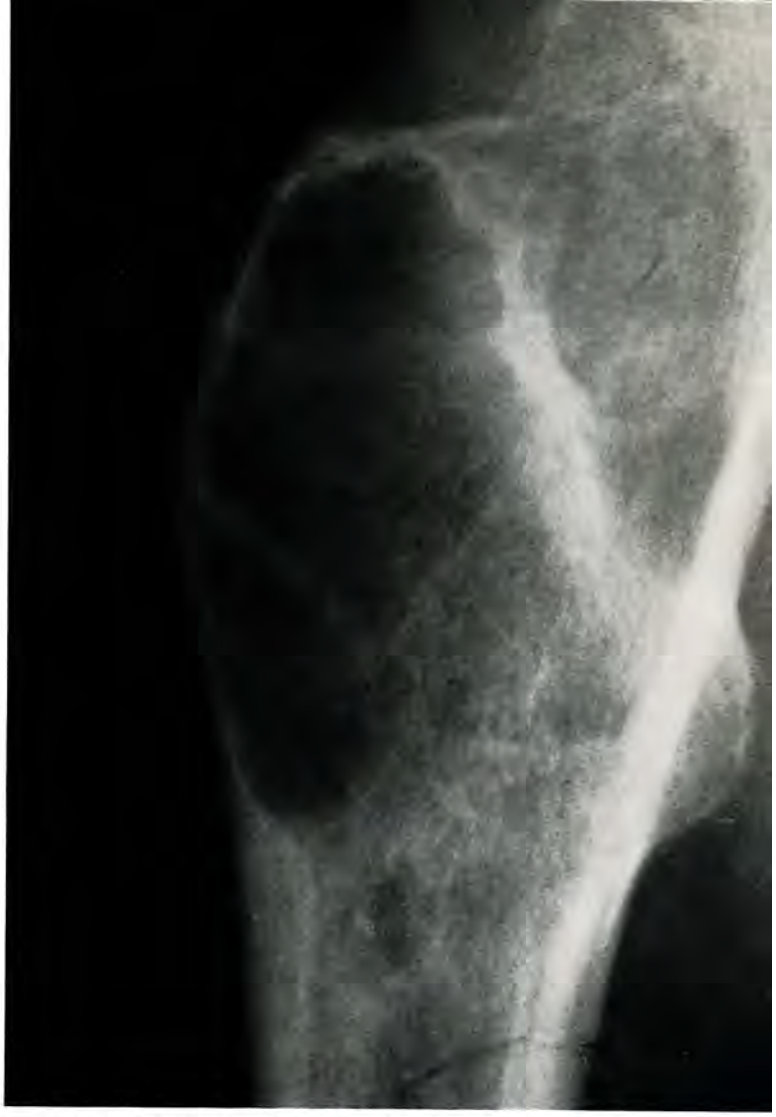

Fig. 2—Osteolytic lesion of the metaphysis of the femur with indefinite limits and some cortical new bone proliferation.

(No audience participation in the discussion of this case.)

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8. Reticulum Cell Sarcoma of the Scapula

Contributed by RICHARD E. JOHNSON, M. D., Columbia, Mo.

THE PATIENT was a man 53 years of age who in January, 1947, started to complain of headaches and noticed palpable defects on his skull. In March, 1949, a roentgenogram of the skull revealed regular osteolytic areas; this was one of the roentgenograms submitted to the participants. Biopsy done on all of the skull lesions was reported as showing bone proliferation but no tumor; no treatment was instituted. In July, 1949, pain appeared in the right arm, and a roentgenogram showed irregular osteolytic defects of the glenoid process of the right scapula; the skull defects had undergone a spontaneous regression. The patient refused to accept treatment. By February, 1950, a mass 8 cm. in diameter was palpable in the right infraclavicular region and the roentgenograms showed progressive destruction of the scapula; this was the second film, copies of which were submitted to the participants in the SEMINAR. Shortly thereafter nodules appeared under the skin of the chest. One of these was removed and sections submitted to the pathologists were cut from it.

Radiologic Diagnoses Submitted by Mail

Metastatic tumor	52
Myeloma	32
Chondrosarcoma	6
Bone sarcoma	8
Reticulum cell sarcoma	8
Syphilis	24
Xanthomatosis	14
Mycosis	12
Something bad!	1
Five other diagnoses	13

Histopathologic Diagnoses Submitted by Mail

Reticulum cell sarcoma	51
Sarcoma	27
Metastatic tumor	21
Myeloma	9
Lymphoma	6
Reticuloendotheliosis	3

Dr. Hodes: Multiple bone defects fairly well demarcated are distributed throughout the skull. The defects obviously vary in age and some are quite small and others very large. Close inspection indicates that the disease seems to arise in the diploe and extend through the outer table of the bones of the calvaria. There seems to be no tendency for the disease process to infiltrate the inner table of the skull. In the occipital region, where the large lesions are present, the inner table of the bones also is destroyed but this seems to be a very late manifestation of the disease. There are no associated soft tissue masses. In the center of the large occipital region a small island of bone is evident which in some respects suggests a sequestrum.

Extensive destruction is noted in the shoulder girdle. This destruction has affected the glenoid fossa as well as the neck of the scapula. Early infiltration of the proximal end of the humerus below the joint surface is also noted. A large soft tissue mass is associated with this obvious bone destruction. Overlying the lateral margin of the humerus is a peculiar, lace-like bone density which is very irregular and which might also prove to be a sequestrum.

The bone defects of the skull do not appear to be malignant. Their origin in the diploé and the fact that they infiltrate only the outer table suggest that we are dealing with a granulomatous process. Apparently this patient does not have syphilis. The absence of overlying soft tissue tumors militates against the ordinary inflammatory processes as well as tuberculosis. In multiple myeloma the bone defects are more sharply demarcated and they occur predominantly in the frontal and parietal bones rather than in the occipital region as is evident in this patient. Furthermore, this patient presented but very little pain clinically and his biopsy revealed no evidence of tumor tissue.

I find it difficult to relate the lesions in the skull with the lesion in the shoulder girdle. Whereas I am inclined to believe we are dealing with a granulomatous process in the bones of the calvaria, the lesion in the shoulder girdle definitely looks malignant. I attribute that dense, lacy portion

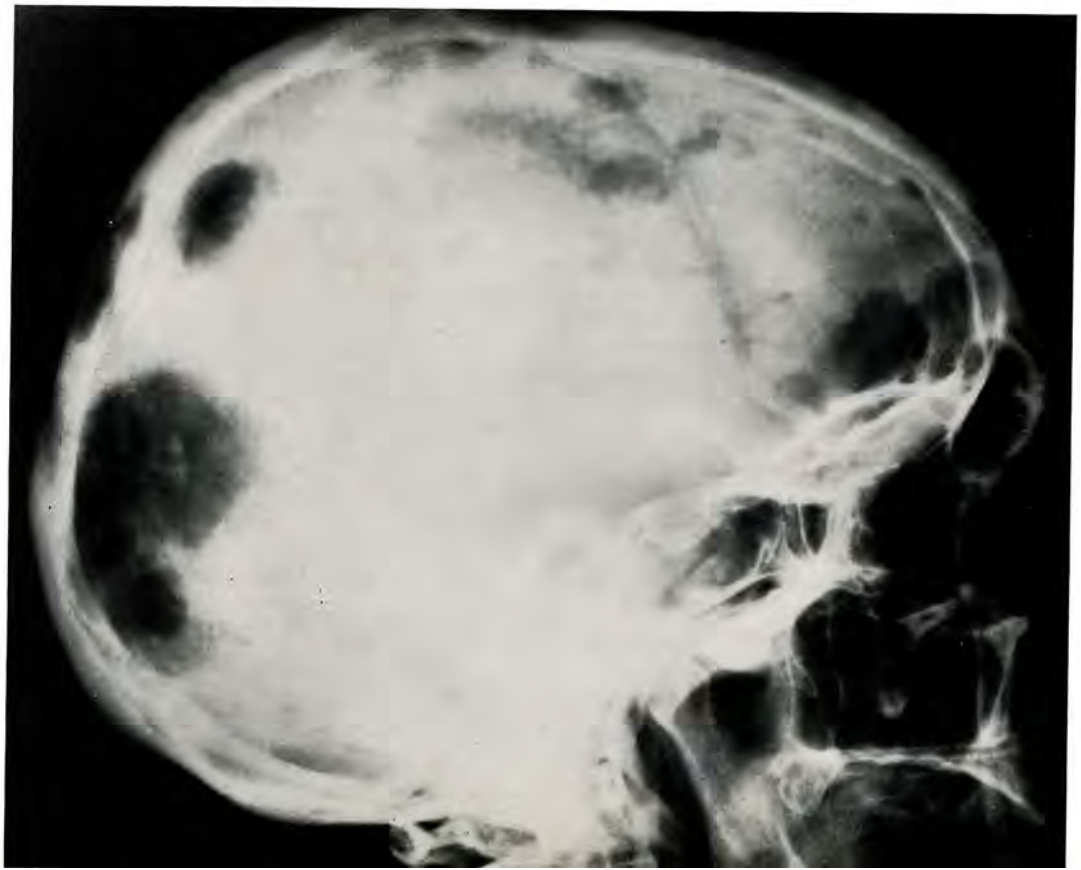


Fig. 1—Multiple fairly well demarcated defects of the skull; the lesions apparently arise in the diploe.

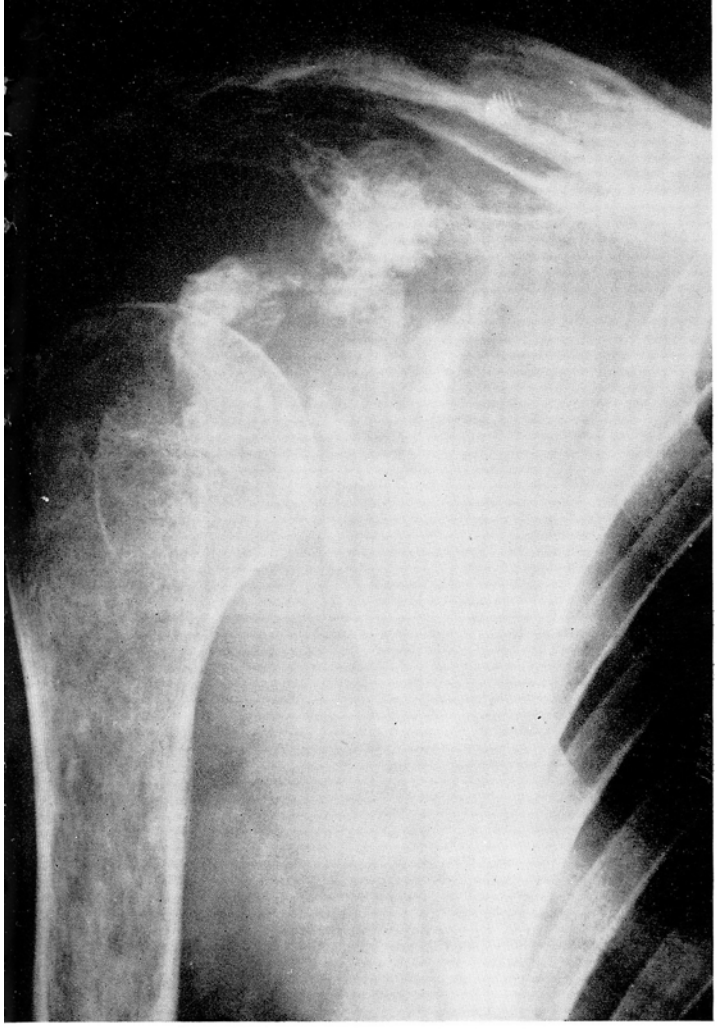


Fig. 2—Extensive destruction of the shoulder girdle.

of bone to bone sequestration as a result of the aggressive character of the tumor which has interfered with blood supply. I am inclined to believe that the lesion in the shoulder girdle has arisen in the elements of the capsular cuff. Of these, the most likely would be a synovial sarcoma. To lend further support to our impression that we are dealing with a malignancy in the shoulder girdle plus infection, the adjoining segment of the lung reveals multiple small nodules. Unfortunately, we do not have a film of this patient's lungs, but I strongly suspect that this patient may have metastatic nodules in the lung field at this time. These might prove to be unusually prominent vascular markings. Because I am loath to make two distinct diagnosis in one individual, I am inclined to believe that the shoulder girdle, in spite of its malignant appearance, will prove to be related to the lesion in the skull. Xanthomatosis would explain the picture. Perhaps an associated sarcomatous degeneration or a separate synovial sarcoma of the shoulder will prove to be present.

Dr. Hodes' diagnosis: XANTHOMATOSIS OF THE SKULL WITH MALIGNANT DEGENERATION OR SYNOVIAL SARCOMA OF THE SHOULDER.

Dr. Regato: A radiographic diagnosis of Hand-Schuller-Christian disease was also rendered by Dr. M. Sosman of Boston.

Dr. Ackerman: The section is from the soft tissue lesion and it reveals involvement which extends up to the epidermis. There are wide areas of necrosis. The microscopic pattern of tumor cells is the same as that observed in the scapula. Individual cells are somewhat variable, have large nuclei and relatively prominent nucleoli. Cytoplasmic outlines are poorly defined with pale pink cytoplasm. Mitotic figures are frequent. The reticulin stain (Wilder method) reveals extremely prominent reticulum pattern with individual wiry reticulum winding around individual cells and extending between them.

This tumor shows none of the characteristics of Hodgkin's disease, adenocarcinoma or melanocarcinoma. It has been associated with apparent spontaneous regression. The only tumor which I know which would conform to this clinical behavior and microscopic pattern is the reticulum cell sarcoma of bone. This type of tumor must be differentiated from Ewing's sarcoma. Lichtenstein has seen spontaneous regressions of skin manifestations of reticulum cell sarcomas, but not of bone lesions. A high percentage of these tumors arise from within the medulla of tubular bones and show cortical bone destruction with poorly defined borders. Periosteal reaction is often absent.

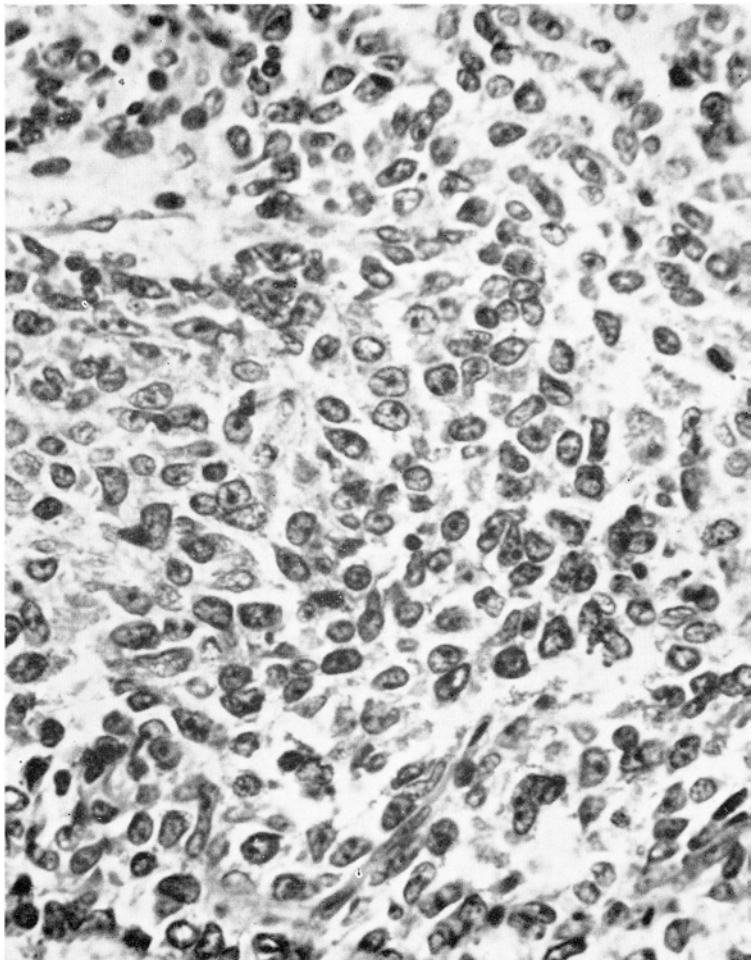
Dr. Ackerman's diagnosis: RETICULUM CELL SARCOMA.

Dr. Regato: Dr. C. Geschickter, of Washington, offered a histopathologic diagnosis of undifferentiated synovial sarcoma; Dr. D. Brachetto-Brian, of Buenos Aires, called this tumor a syncytial malignant reticuloblastoma (Reticulosarcoma).

Subsequent history: In May 1950, the patient developed severe pain and finally accepted to be treated. He received roentgentherapy directed to the right shoulder. There was immediate relief of pain and marked regression of the tumor; the entire series of treatments lasted five weeks. He was last seen in August 1950, when new subcutaneous nodules had appeared in the right axilla and breast.

Dr. Regato: The designation of reticulum cell sarcomas as a separate entity of tumors previously confused with other types is primarily due to Oberling, who in 1928 regarded the

Fig. 3 — Photomicrograph (X600). Reticulum cell sarcoma. Note prominent nuclei and nucleoli.



mesenchymal reticulum cell as the cell of origin of this tumor and felt that Ewing's tumors are but a variant in this category. Oberling's view is that the reticulum cell of the bone marrow may differentiate toward plasma cell, lymphocytic, myelocytic, monocytic, and erythroblastic subvarieties. Parker and Jackson studied, in 1939, a group of 17 cases of the Tumor Registry that had been classified as Ewing's sarcoma, osteogenic sarcoma, giant cell tumors, lymphogranulomatosis, and lymphosarcoma; they proposed that they be reclassified as reticulum cell sarcomas. This proposal was accepted by Dr. Ewing in the name of the Bone Tumor Registry, but the entity Ewing's sarcoma was retained. The situation is further confused by the consideration that reticulum cell sarcomas may arise in non-bony structures and may also be metastatic in bone. Regardless of any histogenetic dispute, it remains that the group of primary bone tumors now generally recognized as reticulum cell sarcomas has a rather benign course and a high curability, by means of adequate radiotherapy, that has never been claimed for any other form of malignant bone tumor. This fact alone commands our interest in this form of tumor. A recent review of 37 cases by Coley revealed a five-year survival of forty percent.

Richard Johnson, M. D., Columbia, Mo.: There have been several recent manifestations in this case; new lesions have appeared in the left supraclavicular region, right ilium, and intergluteal fold. All the lesions have shown marked radiosensitivity.

A. James French, M. D., Ann Arbor, Mich.: I wonder if Dr. Ackerman cares to discuss the differential diagnosis or wishes to state whether or not there is a difference in the terms reticulum cell sarcoma and reticuloendothelial cell sarcoma? This may be an academic point, but generally speaking it appears that reticulum cell sarcoma is an all-inclusive term and pathologists may not agree that reticuloendothelial cell sarcoma is a separate entity.

Dr. Ackerman: It is hard enough for me to make the diagnosis of reticulum cell sarcoma. I cannot separate it any further. I think that the diagnosis in this case was very difficult from the standpoint of being sure that you are placing it in a lymphoma group as contrasted to metastatic tumor, melanoma, etc.

Dr. Hodes: I would merely like to say that radiogically we care to place this properly among the reticuloendothelioses.

Editor's Note: When this patient was last seen, in December 1950, his general condition remained relatively good in spite of numerous new manifestations.

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9. *Metastatic Lesion of the Femur, from a Primary Carcinoma of the Kidney*

Contributed by L. V. ACKERMAN, M. D., St. Louis, Mo.

THE PATIENT was a man 55 years of age who in August, 1947, complained of pain in the right thigh. He was hospitalized in April, 1948. A roentgenogram showed an osteolytic lesion of the proximal metaphyseal area of the femur; copies of this roentgenogram were sent to the radiologists; other osteolytic lesions could be seen in the roentgenogram of the pelvis. On general physical examination a diagnosis of renal neoplasm was made and a nephrectomy decided upon; a carcinoma of the kidney was found (these details of the history were withheld at the request of the contributor). Following nephrectomy a resection of the proximal third of the right femur was done and a stainless steel prosthesis was placed; the distributed slides were cut from this surgical specimen. In spite of proficient, though anachronous surgical attempts, the patient expired in March, 1949.

Radiologic Diagnoses Submitted by Mail		Histopathologic Diagnoses Submitted by Mail	
Metastatic carcinoma	84	Metastatic carcinoma (primary kidney)	96
Metastatic tumor	18		95
Myeloma	28	Angioendothelioma	2
Osteogenic sarcoma	10	Liposarcoma	6
Chondrosarcoma	4	Osteoid osteoma	2
Eleven other diagnoses	22	Gaucher's disease	1
		Storage disease	1

Dr. Hodes: This is a polyostotic lesion which involves the proximal end of a femur as well as a portion of the ileum. The lesions are obviously of medullary origin and purely destructive in character. Their periphery is totally irregular and the appearance is that of a metastatic process. Attention is called to the coarse trabeculation of the iliac lesion which is noted occasionally in patients with malignant renal tumors.

Dr. Hodes' diagnosis: METASTATIC LESION, PROBABLY FROM A PRIMARY IN THE KIDNEY.

Dr. Ackerman: The slide shows an obvious metastatic carcinoma of the typical type arising from the kidney. This is the type of lesion which is relatively simple to diagnose on the microscopic finding. This tumor is probably most easily confused with a liposarcoma. Both of these neoplasms contain large amount of cytoplasmic fat and small amounts of glycogen. Most important differential diagnosis is the fact that the nucleus in renal cell carcinoma usually remains in the central portion of the cell, whereas the nucleus in liposarcoma is frequently compressed to a crescentic ring. Both lesions are radiosensitive. Primary liposarcomas of the bone have been reported by Stewart, but he now feels that this is a debatable entity. The diagnosis of the bone lesion is more difficult when the primary tumor is small. There is a direct correlation between the size of the tumor and its metastases (Bell), but it is not rare for small tumors, even tumors without pyelographic findings, to make themselves manifest by bone metastases first. Another property of this metastasizing tumor is its tendency to grow through the cortical bone to form a soft tissue pulsating mass. In the region of the

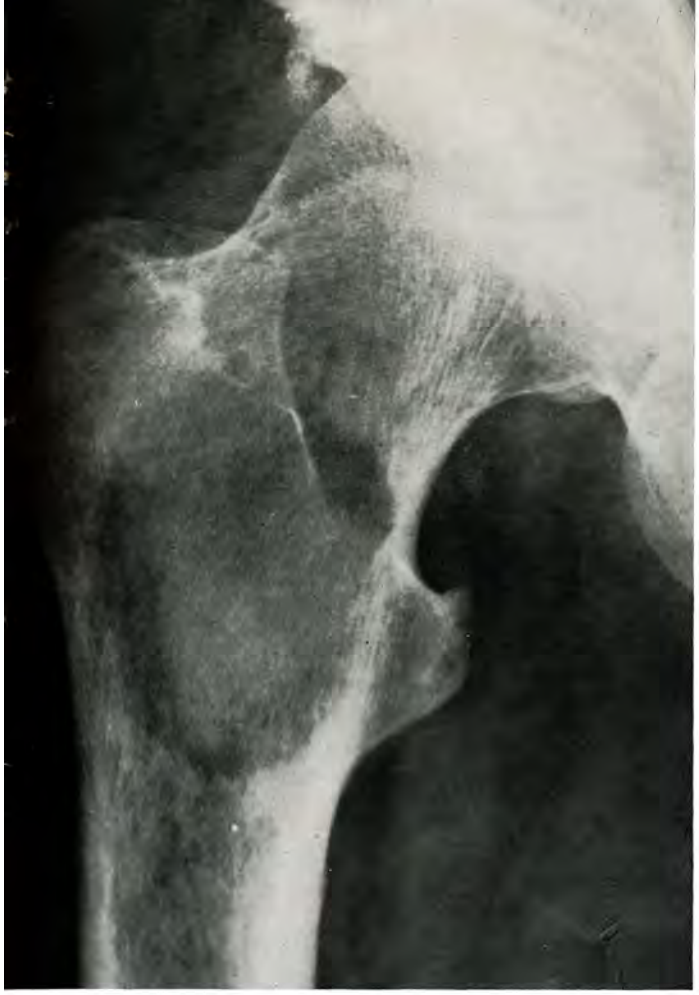

Fig. 1—Destructive lesion of the proximal end of the femur with irregular periphery.

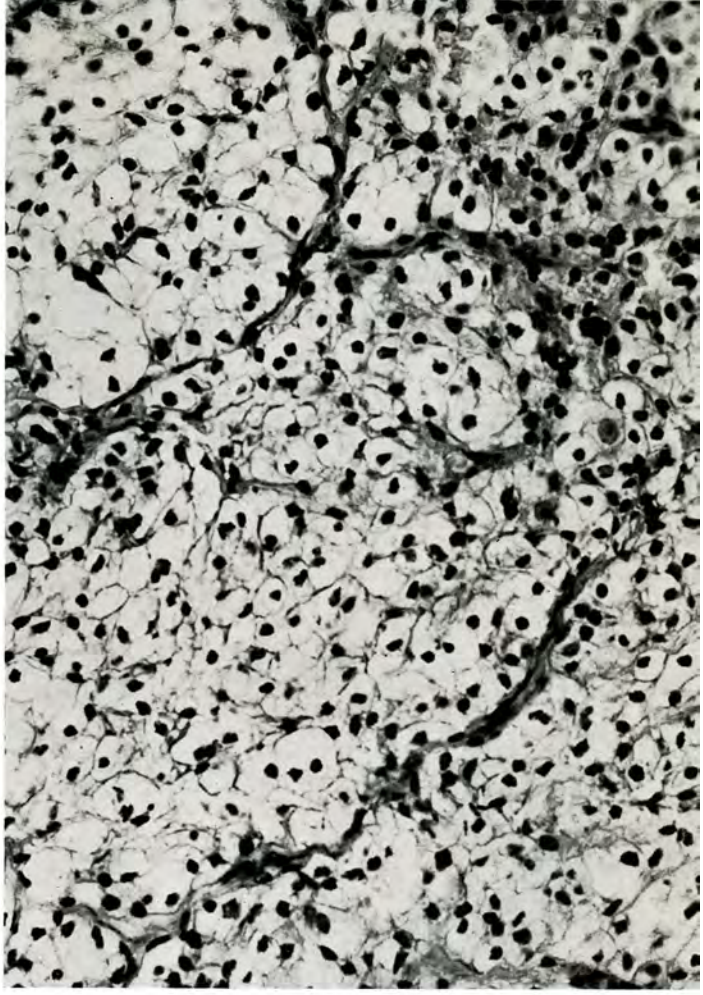

Fig. 2—Photomicrograph (X400). Metastatic carcinoma; individual cells have uniform nuclei and clear cytoplasm.

sternum the two tumors which may form such soft tissue pulsating masses are the metastatic thyroid cancer, the metastatic renal cell tumor. It is not rare for the metastasis to be apparently single (Sherman). Periosteal reaction is unusual in this entity and pathologic fractures are common.

Dr. Ackerman's diagnosis: METASTATIC CARCINOMA, PRIMARY KIDNEY.

Dr. Regato: This was the only case in the Seminar in which part of the history was concealed from the participants. In no other case was there a greater agreement among radiologists as well as pathologists on the diagnosis.

(No audience participation in the discussion of this case.)

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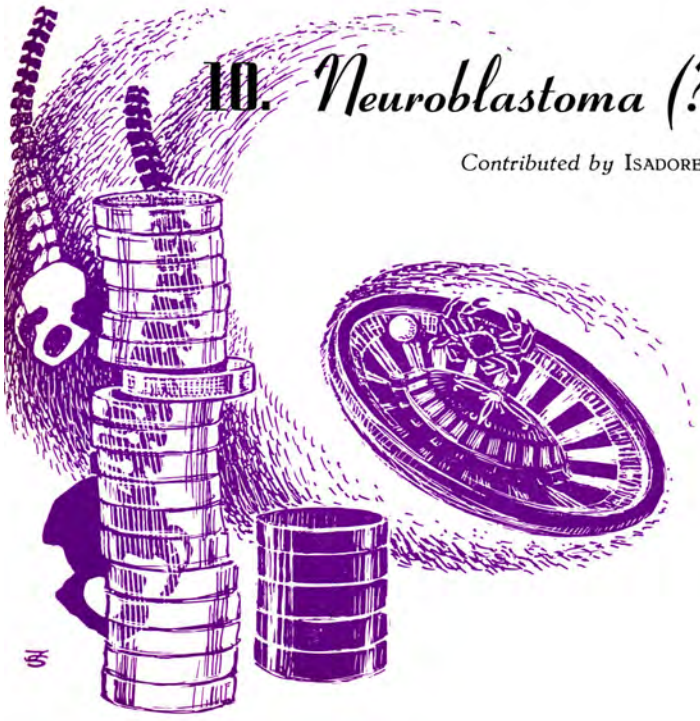


10. *Neuroblastoma (?) in a Dorsal Vertebra*

Contributed by ISADORE LAMPE, M. D., Ann Arbor, Mich.

THE PATIENT was a girl 10 years of age with a short history of pain in the dorsal region and gradual loss of sensory perception, of voluntary motion of lower extremities, and of voluntary control of urinary bladder. A roentgenogram revealed collapse of one of the upper dorsal vertebrae. In December, 1948, a decompression laminectomy was done and grayish gelatinous tissue was found occupying the epidural space. The section submitted to the participants was made from this material. A roentgenogram was taken after the laminectomy; copies of this roentgenogram were sent to participating radiologists.

Radiologic Diagnoses Submitted by Mail	
Spinal cord tumor	40
Lymphoma	22
Metastatic tumor	22
Metastatic neuroblastoma	20
Ewing's tumor	10
Inflammatory spondylitis	26
Ten other diagnoses	32

Histopathologic Diagnoses Submitted by Mail	
Metastatic neuroblastoma	48
Ewing's tumor	12
Sympathicogonioma	4
Myeloma	6
Metastatic ovarian tumor	6
Angioblastic meningioma	3
You tell me!	1
Toughest one yet	1
Others	5

Dr. Hodes: The lesion apparently is arising in the medullary portion of the vertebra and as the result of its destructive character has caused a definite loss of stature in this vertebral body. Extending well beyond the confines of the bone is a symmetrical soft tissue mass, bulbous in character and containing no calcific debris. The vertebral bodies above and below the involved segment are not affected. The vertebral plates of the adjoining vertebral bodies are perfectly normal, as are also the vertebral plates of the involved segment. The intervertebral spaces are normal. Close inspection of the vertebral body itself reveals some irregular destruction.

This obviously is not an inflammatory process. The preservation of the intervertebral disc spaces, the fact that the vertebral plates are intact, plus the absence of calcific debris in the soft tissue mass, all militate against tuberculosis. Ordinary osteomyelitis of the spine usually does not produce this much vertebral collapse, and it is more often associated with increased bone density. In addition, it is an extremely painful process. This looks like a tumor and a malignant one and it seems to have arisen in the medullary portion of the vertebral body and extended well beyond the confines of the bony segments. Whereas one might expect metastatic neuroblastoma to produce such a lesion in the spine, the fact that we are dealing with a monostotic lesion would be against this diagnosis. Osteogenic sarcoma of the vertebrae is quite rare. This would lead us to suspect the presence of a reticulum cell sarcoma. The latter can arise in a vertebral body and produce vertebral collapse and quite often are associated with marked soft tissue masses. They are rapidly growing tumors.

Dr. Hodes' diagnosis: RETICULUM CELL SARCOMA.

Dr. Ackerman: The bone apparently has been partially replaced by fibrous tissue and between the fibrous tissue, and extending beyond it there are collections of tumor cells. Individual tumor cells have variably shaped nuclei, inconspicuous cytoplasm, and the chromatin of the nuclei is fine. If this lesion had occurred in a male of 55, metastatic carcinoma, particularly from the lung, would be considered. At 10 years of age, the tumors which must be considered include lymphosarcoma, neuroblastoma, and Ewing's tumor. It would be unusual for this lesion to be the first manifestation of lymphosarcoma, but it would be possible. I am also unable to rule out neuroblastoma or Ewing's tumor. All of these lesions are extremely radiosensitive. This slide demonstrates to me the limitations of the morphologic diagnosis.

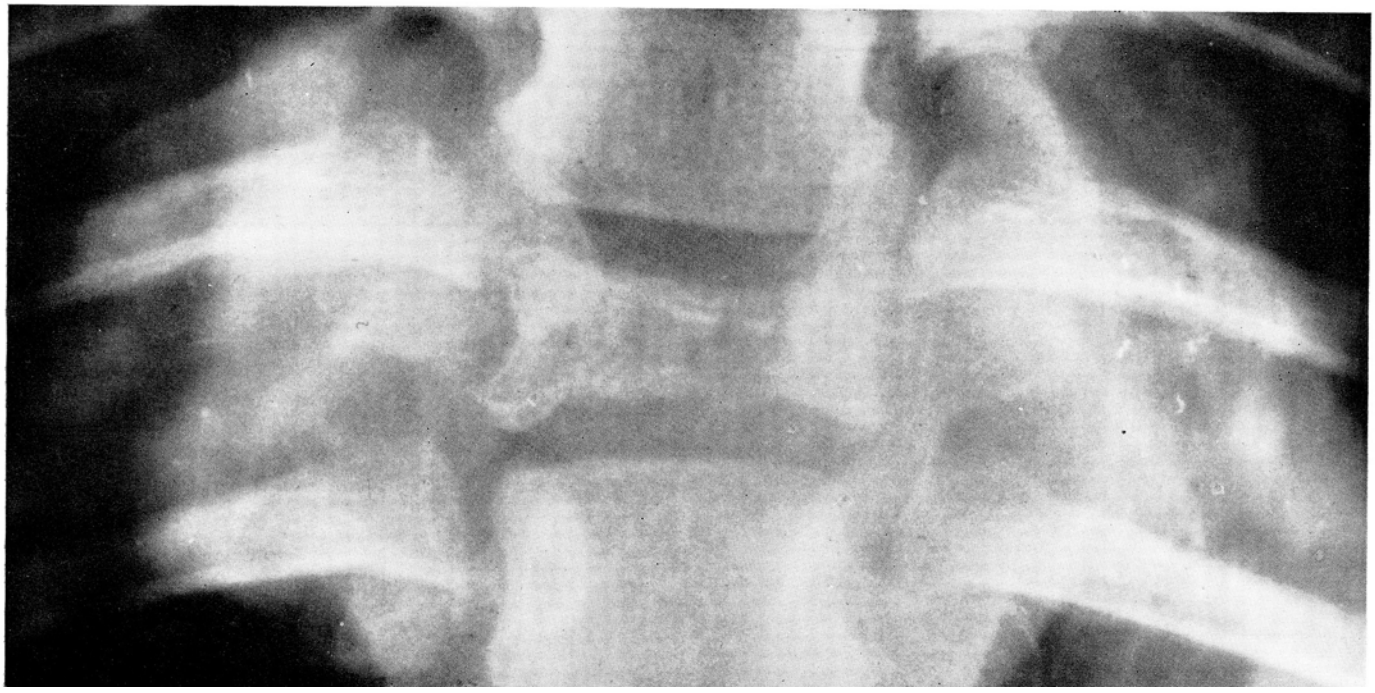
Dr. Ackerman's diagnosis: MALIGNANT, TUMOR, UNCLASSIFIED.

A. P. Stout, M. D., New York, N. Y. (by mail): The fragments of soft tissue are fibrous and quite vascular. This stroma is extensively infiltrated by strands of relatively small irregularly rounded cells with nuclei solidly blued by haematoxylin so that the nuclear architecture cannot be studied. Many of these cells are oriented about dilated vessels.

The diagnosis must lie between Ewing tumor and metastatic sympathicoblastoma. I do not know any sure way to differentiate between the two from a histological picture alone such as this one. An in vitro culture would tell because the sympathicoblastoma would promptly grow neurites while the reticuloblasts of Ewing's tumor could not do so. In the spine, a sympathicoblastoma might reach there by direct extension from the posterior mediastinum as well as by metastasis. As a pure guess (and because I have favored Ewing tumor for Case 14) I will give the nod to sympathicoblastoma for this case—I am quite prepared, however, to learn that it was a bad guess.

Subsequent history: The patient was given a course of roentgentherapy, consisting of a skin dose of 2650 roentgens administered to a field 14 x 10 cm over the diseased area in 16 days in December, 1948. The paralysis disappeared and the child remained well until October, 1949, when there was a recurrence of dorsal pain, nausea and vomiting; the roentgenogram taken at this time showed marked increase of the paravertebral involvement. A new course of roentgentherapy, consisting of a skin dose of 1500 roentgens, was delivered in 13 days to each of two fields 8 x12 cm in diameter directed to the spinal cord; anew there was a regression of the paravertebral mass. The child was able to return to school and was well in January, 1950. In May, 1950, a mass was discovered in the posterior mediastinum, and the patient was given a new course of treatments.

Fig. 1—Destructive lesion of a dorsal vertebra with collapse and symmetrical soft tissue mass.



M. Smith, M. D., Santa Fé, N. M.: Could this be consistent with Hodgkin's disease, pathologically?

Dr. Ackerman: I think that it would be consistent with it from the standpoint of radiosensitivity, but I do not think it would be consistent with the histologic appearance. Perhaps it is a neuroblastoma. That would fit quite well.

Editor's Note: This patient was last seen in November, 1950; roentgenographically, the posterior mediastinal mass was absent; the patient complained of pain in the upper dorsal region and the roentgenograms showed a metastatic lesion in the body of the fifth lumbar vertebra.

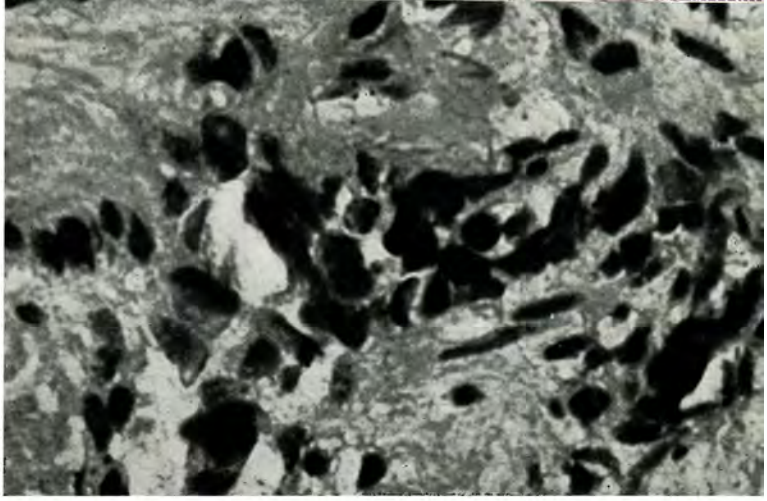


Fig. 2 — Photomicrograph. Clusters of malignant cells with heavily stained nuclei. No exact histogenetic diagnosis can be made.

II. Fibrosarcoma Arising from a Pre-existing Giant Cell Tumor of the Femur

Contributed by L. V. ACKERMAN, M. D., St. Louis, Mo.

THE PATIENT was a man 58 years of age who in September, 1948, complained of pain in the lower half of the thigh. The roentgenogram showed an osteolytic lesion involving the epiphyseal and to some extent the metaphyseal lower extremity of the femur; copies of this roentgenogram were sent to participants. A specimen was removed from which the slides sent to pathologists were prepared. (Note that these slides are not those on which the final diagnosis has been based.)

Radiologic Diagnoses Submitted by Mail		Histopathologic Diagnoses Submitted by Mail	
Benign giant cell tumor	72	Benign giant cell tumor	54
Osteitis fibrosa, bone cyst	34	Malignant giant cell tumor	48
Chondroma	12	Osteosarcoma with giant cells	2
Bone sarcoma	12		
Malignant giant cell tumor	2		
Very inadequate history	1		
Ten other diagnoses	26		

Dr. Hodes: This is a cystic and trabeculated lesion which arises in the medullary portion at the epiphyseal end of the bone, and has caused definite bone expansion. There is no evidence of cortical reaction around the expanded bone.

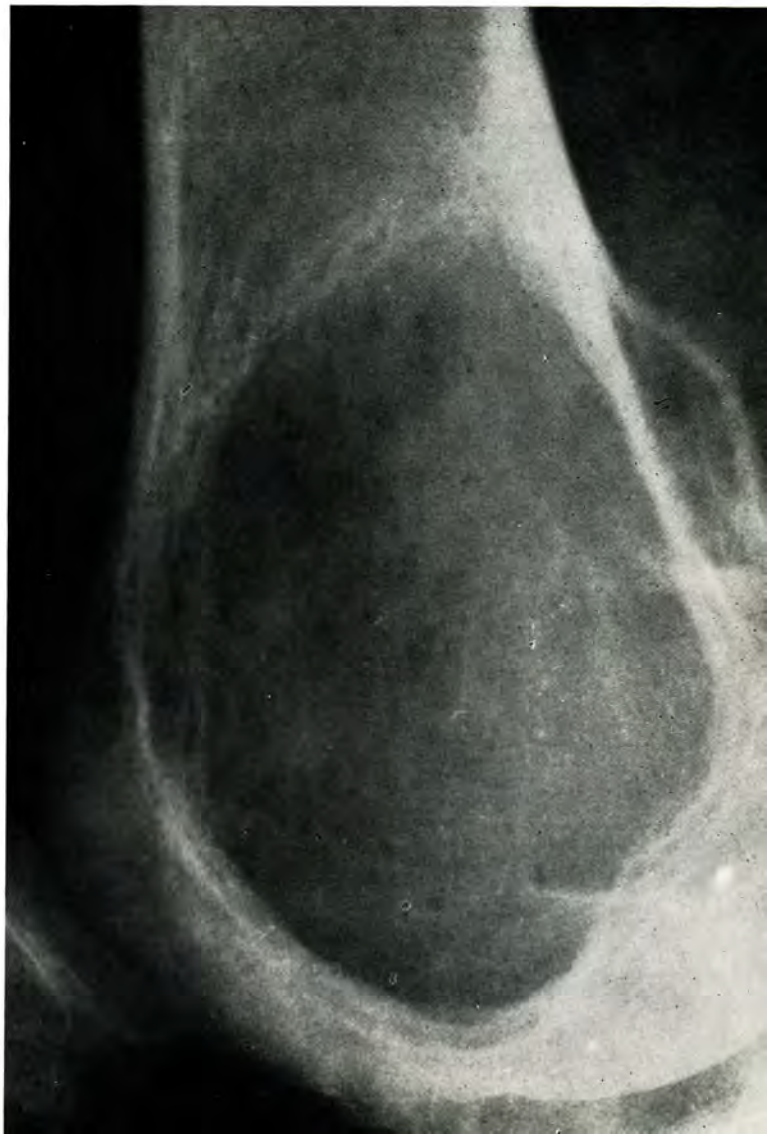
When one considers the cystic lesions arising in the epiphyseal portion of a long bone in an adult, one obviously considers first the giant cell tumors. This seems like an ordinary giant cell tumor, but the irregularity and deossification at the periphery of the proximal end of the lesion suggests that it may be undergoing very early malignant change. I am by no means certain of this but merely suspicious. Occassionally the endosteal fibrosarcomas produce such lesions, but because of the lack of bone proliferation I exclude it as a diagnostic possibility.

Dr. Hodes' diagnosis: GIANT CELL TUMOR (POSSIBLY UNDERGOING MALIGNANT TRANSFORMATION.)

Dr. Regato: A roentgenologic diagnosis of giant cell tumor undergoing malignant transformation was also submitted by Dr. P. Swenson of Philadelphia.

Dr. Ackerman: The tumor is made up of large numbers of giant cells often with innumerable nuclei and a stroma

Fig. 1—Cystic lesion of the epiphyseal end of the femur with expansion of bone but no cortical reaction.



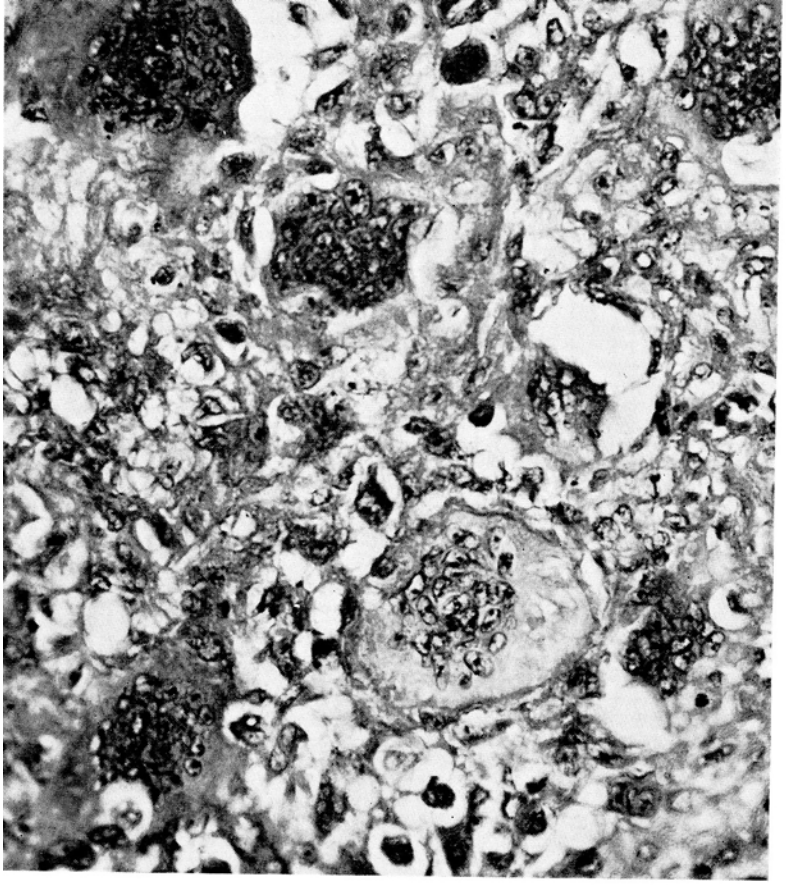


Fig. 2—Photomicrograph of first biopsy (the one submitted to participants). Appearance of giant cell tumor with prominent stroma.

which in some areas is inconspicuous and in others is extremely cellular. In the celluar areas individual cells have prominent nuclei and nucleoli; mitotic figures are relatively infrequent.

The lesion arises in an area where giant cell tumors usually occur but where chondroblastomas are also seen. In chondroblastomas, however, the basic tumor cells are polyhedral, moderate sized, with fairly large nucleus and invariably with focal areas of calcification in the cellular tumor tissue; these changes are not present here.

Dr. Ackerman's diagnosis. GIANT CELL TUMOR.

A. P. Stout, M. D., New York, N. Y. (by mail): As far as I can tell, the history, clinical findings, and this biopsy show the picture of a true epiphyseal giant cell tumor. The good differentiation of all the cells and the rare mitoses make an osteolytic osteogenic sarcoma extremely unlikely. There is also the so-called malignant giant cell tumors of bone marrow. If this exists, it is very rare, and I know of no way of differentiating it from the benign giant cell tumor.

Dr. Regato: Dr. Lent C. Johnson, of the Armed Forces Institute of Pathology, Washington, D. C., pointed out the fact that the stromal cells are two to five times normal size and also that they are producing matrix; he considered both as warnings of imminent malignant transformation, but concluded with "not malignant yet, at least in my slide." Dr. Ackerman will be surprised to learn that Dr. Brachetto-Brian, of Buenos Aires, made a diagnosis of malignant fibroblastoma arising from a giant cell tumor. A diagnosis of osteolytic sarcoma with giant cells was submitted by Dr. C. Geschickter of Washington.

Subsequent history: This patient received roentgentherapy, but no details of this treatment could be obtained. After 12 treatments a fracture occurred through the tumor. In November, 1948, the patient was treated by curettement and introduction of bone fragments. He was well until November, 1949, when a tumefaction appeared on the lateral aspect of the knee. In January, 1950, a disarticulation of the hip joint was done.

Dr. Ackerman: A study of the recurrence shows an obvious fibrosarcoma. Individual cells are fusiform in shape and show rather numerous mitotic figures. This fibrosarcoma shows strong resemblance to the stromal portions of the previous curettement. There are also a few areas in which giant cells are seen. There is no formation of neoplastic osteoid. It appears that this is a giant cell tumor which has undergone malignant transformation to become a fibrosarcoma. Such a development, although unusual, has been previously reported (Stewart, Jaffé, Finch).

Dr. Ackerman's amended diagnosis: FIBROSARCOMA ARISING IN A PRE-EXISTING GIANT CELL TUMOR.

H. B. Latourette, M. D., Ann Arbor, Mich.: I would like to ask Dr. Ackerman if he would care to comment on the possible origin of giant cells which are common parts of these tumors.

Dr. Ackerman: I have been struck by the great similarity between the nuclei lying within the stromal cells and the nuclei lying within the giant cells, and I have always felt that that is where the giant cells come from; I also agree with Jaffé that probably there is some basis for thinking that giant cell tumors come from rather early connective tissue, which is the reason why I designated this as a fibrosarcoma. I think it is unfortunate that the word giant cell tumor has been appended to this lesion because many other tumors, including osteogenic sarcomas with giant cells have been put into this category, and I think that there is such a lesion as a giant cell tumor which is a definite neoplasm and which on occasions may become malignant. We have seen three cases of giant cell tumors in which, following trauma, metastases appeared in the lung which presented the typical microscopic appearance of a perfectly benign giant cell tumor. In one instance the tumor appeared of low malignancy (Jaffé called it a grade II), and an amputation was done just below the elbow in 1939; in 1945 lung metastases were removed; in 1947 two other pulmonary lesions appeared and were removed. We do not agree that giant cell tumors can arise from the metaphysis (Cade, Willis). In Paget's disease there is a malignant sarcoma which has giant cells and which should not be designated as malignant giant cell tumor (Russell).

Mark Wheelock, M. D., Chicago, Ill.: Would Dr. Ackerman have made a diagnosis of malignant giant cell tumor on the slides that were distributed, if he had had no knowledge of the subsequent course of this case? Perhaps Dr. Ackerman recalls a case presented at a Tumor Seminar in Columbia, Mo., in the discussion of which Dr. Stout objected to the concept of a giant cell tumor becoming malignant (Stout). Regarding recommendation of therapy, are we going to continue to think that these tumors, whatever one calls them, are predominantly benign and only rarely malignant?

Dr. Ackerman: In examining the slides of the first biopsy, I cannot but think that the stroma is very active. In the case discussed at Columbia, we found a little piece of bone in one of the metastases; that bone, in my opinion, had nothing to do with the tumor, but it gave basis to Dr. Stout's objection. In our experience, these tumors are benign, but in a few instances they become malignant. I would like to ask Dr. Hodes whether or not he thinks that it is possible for giant cell tumors to become malignant following irradiation.

Dr. Hodes: I, in turn, would like to hear Dr. Regato's opinion in that respect.

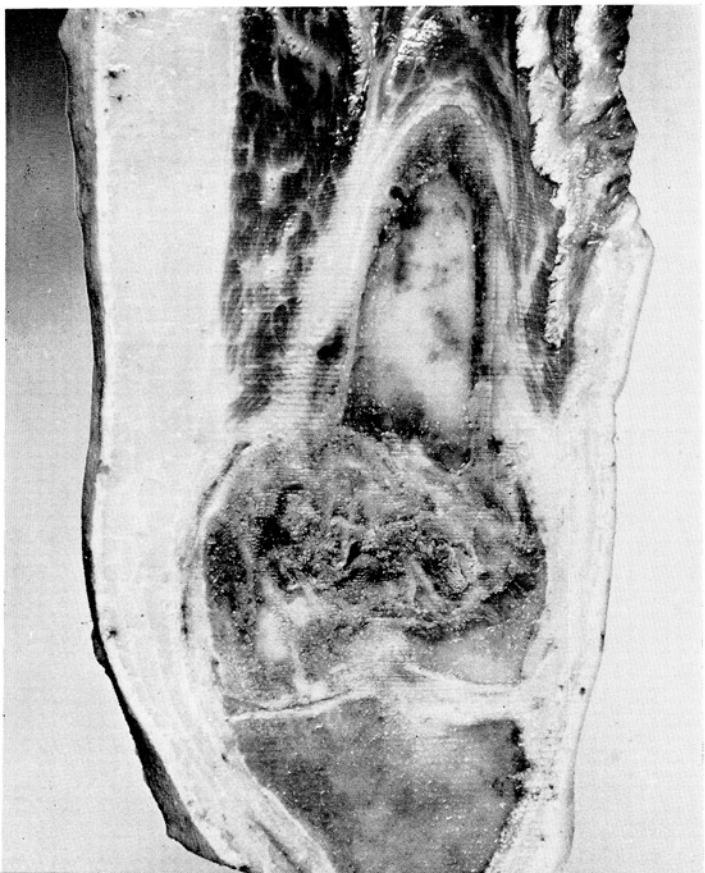
Dr. Regato: In the first place, there is a question of definition; of whether or not these cases are malignant from the start (Pierce) and whether or not so-called malignant giant cell tumors are something else (Stout). Cases considered as benign giant cell tumors have been treated surgi-

cally and later have been recognized, in their recurrence, as a malignant tumor (Leucutia); yet, we hear nothing of the cancerigenic properties of the curette or of the knife. The case in discussion was considered by many of the participating pathologists as a benign lesion, and admittedly, they would have diagnosed it later as definitely malignant; but just as many other pathologists recognized its malignant character in the biopsy performed before roentgentherapy had been administered. Did the tumor become malignant or was it malignant in the first place? It is also true that some pathologists would diagnose, as giant cell tumors, lesions that would not be acceptable as such to others, on account of more strict limitations in respect to age and location (Lichtenstein) but not because of a clearer definition of their morphology. It is perfectly possible for radiotherapy to cause the malignant transformation, just as it can produce a malignant tumor in normal bone (Cahan) but a long interval would be required following irradiation. Such cases should be rare and should not be used as a "scarecrow" to discourage patients from taking advantage of roentgentherapy whenever it is properly indicated (Buschke). The fact remains that, mostly because of the limitations of the histopathologic diagnosis of tumors, cases considered as such may not be actually benign; consequently, close follow-up should be imposed in all instances.

I. Lampe, M. D., Ann Arbor, Mich.: I would like to add that I have been impressed with the fact that in too many of the cases reported of bone tumors developing after irradiation of bone, the technique of irradiation was precisely the kind to cause a maximum of damage. On the other hand, if treatment is carried out according to modern methods, which should leave the tissues relatively unharmed, the possibility of such irradiation causing a malignant transformation should be slight.

Dr. Regato: I agree entirely with Dr. Lampe. The matter of intensity of irradiation is of great importance, as it is in the cases of carcinoma developing on irradiated skin: it is the short, intensive, pugilistic type of treatment, the type preferred by surgeons who practice radiotherapy "on the side," that is usually to blame.

Fig. 3—Gross specimen of malignant tumor that has extended out into the soft tissues and up into the marrow cavity.



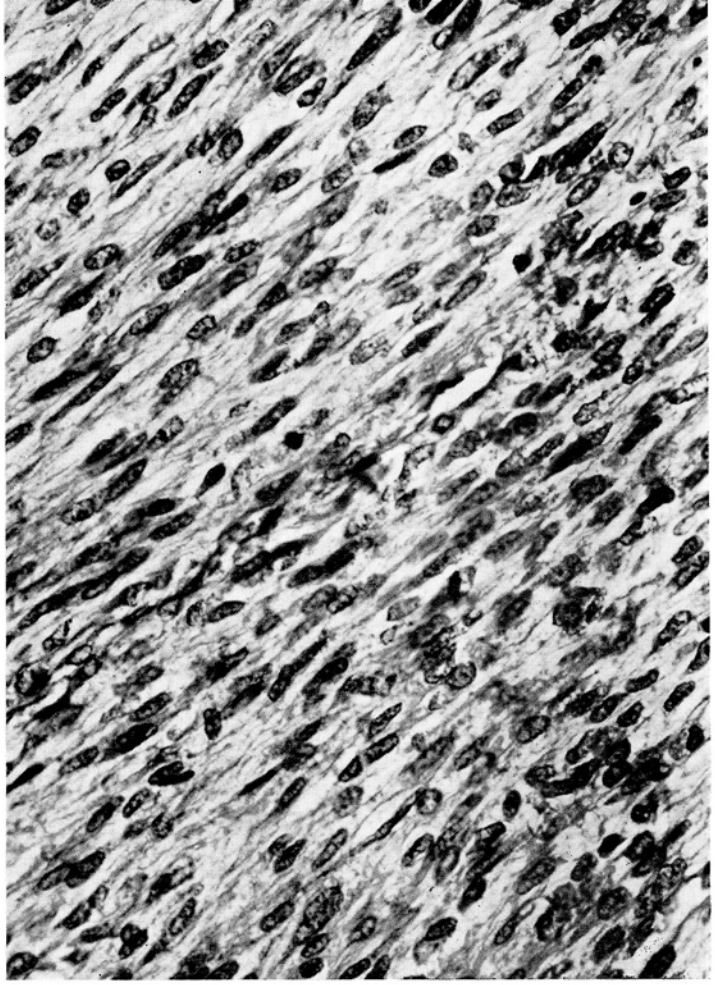


Fig. 4 — Photomicrograph (X460). Biopsy of January 1950: fibroscarcoma.

F. H. Hartshorn, M. D., Denver, Colo.: Could we have a little more specific discussion of the radiation therapy of giant cell tumors in regard to dose and the merits of radiotherapy as opposed to surgery.

Dr. Regato: We feel that roentgentherapy is definitely indicated in the treatment of giant cell tumors because of its conservative aspects; it is more adequate than curettage, and it is preferable to an amputation. We see no objection to the surgical treatment when the lesion can be excised without deformity or impairment. The technique of choice is a protracted treatment of several weeks' duration; the dosage is relatively unimportant so that large daily or total doses are not advisable.

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12. Metastatic Myeloma of the Tibia, from an Apparent Primary Lesion in the Epiglottis

Contributed by WENDELL SCOTT, M. D., St. Louis, Mo.

THE PATIENT was a man 53 years of age, who in September, 1949, presented a grape-like, red and white tumor of the laryngeal wall of the epiglottis, which was excised. There was some post-operative bleeding, and the surgeon had the impression that parts of the tumor had been left; for this reason, post-operative roentgentherapy was given to the neck. In November, 1949, he developed tenderness on the upper part of one leg, and the roentgenograms revealed an osteolytic process of the metaphyseal area of the tibia. Copies of this roentgenogram were submitted to the participants. Serum proteins were normal, and Bence Jones proteins were negative. No other skeletal lesions were found. A specimen was removed from the tibia from which the sections distributed were cut.

Radiologic Diagnoses Submitted by Mail		Histopathologic Diagnoses Submitted by Mail	
Metastatic carcinoma	60	Metastatic plasmocytoma	63
Metastatic tumor	38	Myeloma	30
Myeloma	30	Metastatic carcinoma	12
Osteogenic sarcoma	8	Lymphoma	3
Giant cell tumor	10		
Can't see soft tissues	1		
Seven other diagnoses	17		

Dr. Hodes: This is a monostotic lesion which apparently has arisen in the medullary portion of the epiphyseal end of a long bone. It is definitely osteolytic, and its periphery reveals nothing to suggest the sharply demarcated border of a benign process. Under a strong light one can see evidence of break-through of the cortex in the region of the tubercle. In addition, at this site there is definite thickening of the patellar ligament.

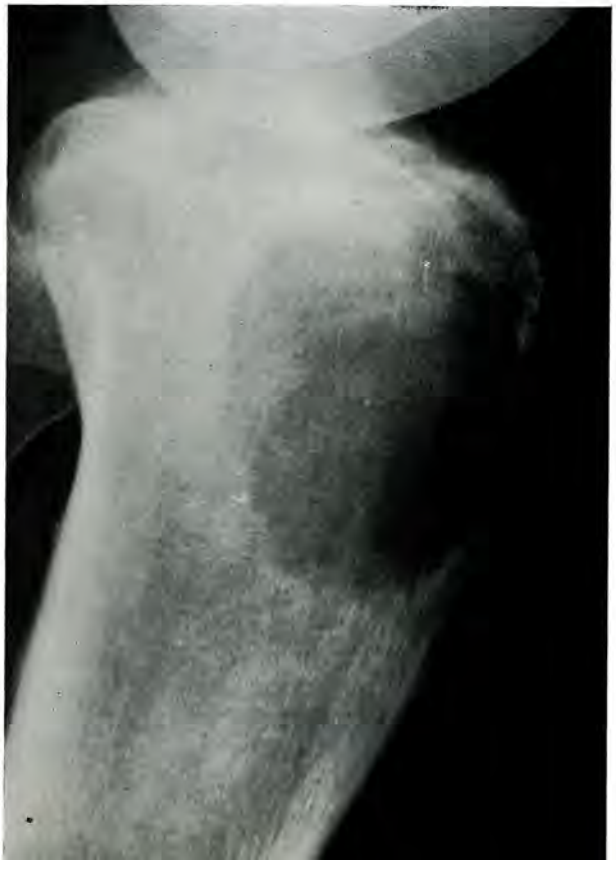
This has all of the roentgen manifestations of a malignant process. In view of the fact that this patient had a lesion removed from the epiglottis, one is inclined to connect the two and suggest that the tibial lesion, even in spite of its presence below the knee, is a metastatic epidermoid process. Faced with the possibility that the epiglottic lesion was benign, one must consider other purely bone destructive malignancies, such as osteolytic osteogenic sarcoma, chondrosarcoma, and monostotic plasma cell myeloma. The close relationship with the patellar tendon insertion, where cartilage exists, suggests that this might be a secondary chondrosarcoma. The absence of new bone proliferation would militate against this, however. A purely destructive osteogenic sarcoma could not be differentiated from an early plasma cell myeloma both of which would arise in the medullary portion of the bone, both of which would be most irregular in configuration, and both of which would not produce new bone proliferation.

Dr. Hodes' diagnosis: METASTATIC LESION FROM EPIGLOTTIC MALIGNANT TUMOR.

Dr. Ackerman: This lesion reveals a very prominent variation in size and shape of the cells. Frequently the nuclei are eccentric and the cytoplasm is pink. Cells with two nuclei are frequent, and often bizarre and giant forms are observed. This material was obtained elsewhere, but it is difficult to stain so that we do not have good nuclear detail, but at times there is a suggestive cartwheel arrangement of the chromatin. Mitotic figures are few in number, and there is no evidence of osteoid formation or acinar formation.

This patient had a lesion of the epiglottis which had a similar microscopic pattern to this and was diagnosed as a malignant plasma cell myeloma. This localization of a plasma cell tumor is unusual. It is well known that plasma cell tumors may show their first clinical manifestations in extra-medullary areas. Primary growths in the upper air passages and oral cavity have been reported, but there has been only one previous case reported from the epiglottis (Jaeger). We have seen other primary sites of localization, such as the thyroid, skin, stomach, small bowel, and mediastinum. In the soft tissue the differentiation between a primary malignant plasma cell tumor and a granulomatus mass containing numerous plasma cells may be difficult. In a malignant plasma cell tumor there are invariably broad sheaths of tumor cells supported by a delicate stroma made up mostly of capillaries and tending to replace other tissues (Rawson). Other characteristics which support the diagnosis of malignancy include atypical cells, giant multi-nucleated cells, and plasma cells with prominent nuclei. Reticulin stains show fibers dividing tumor cells into large groups. In a benign process there is usually an intermingling of plasma cells with other inflammatory cells. Invariably the plasma cells seen appear quite normal with eccentric nuclei, fine nucleoli, and the usual cartwheel arrangement of the chromatin. The presence of Russell bodies in the cytoplasm (eosinophilic hyaline droplets) of plasma cells is more often seen in a benign than a malignant process. Such granulomatous masses do not replace other tissues. If the lesion appears malignant as described above, it undoubtedly is malignant. However, in certain instances when there are broad sheaths of normal-appearing plasma cells, the differentiation between a benign and malignant lesion may be difficult.

Fig. 1—Osteolytic lesion of the proximal end of the tibia.



Dr. Ackerman's diagnosis: MYELOMA.

A. P. Stout, M. D., New York, N. Y. (by mail): This appears to be a solitary bone lesion following what I presume was a plasma cell tumor of the epiglottis. When we studied the plasmocytomas of the upper respiratory passages, Kenney and I found that only a small number of them were followed by the appearance of bone marrow lesions and that there were just as many examples of solitary bone involvement as multiple. Moreover, the disease was much less apt to proceed to a rapid and fatal termination when the bone lesion was a solitary one than when there were multiple bone lesions at the time of first diagnosis. The pharynx and nasopharynx and the gastro-intestinal tract appear to be the favored sites for the development of the uncommon cases of extra-medullary malignant plasmocytoma.

Subsequent history: The microscopic study of the laryngeal specimen has now been reported as showing a plasmocytoma. The patient was given a series of roentgentherapy to the tibia consisting of a dose of 1700 roentgens (in air) to each of two lateral fields and 600 roentgens to a posterior field (the length of the entire treatment and the size of the fields and other factors were not given.) In March, 1950 the tibial defect was found unchanged in spite of the treatments given and surgical treatment was recommended. In April, 1950, the lesion was curetted and bone fragments were introduced in the cavity. No microscopic evidence of residual tumor was found in the curettements. There was great surprise when the specimen did not show any tumor. A bone marrow study revealed increased number of plasma cells to 9 percent, indicating a possible dissemination of the disease. At the present time, the patient is carrying on normal activities.

M. Wheelock, M. D., Chicago, Ill.: How often do you see amyloid in these cases of multiple myeloma? There is so much being written about it, and we see it so rarely.

Robert Moore, M. D., St. Louis: I do not think it is frequent, but one sees an occasional example. Perhaps 1 or 2 percent of all of these may show amyloid deposits of the usual type.

C. L. Davis, D.V.M., Denver, Colo.: The moderator may recall that I submitted for consideration in the SEMINAR a spontaneous case of plasma cell myeloma in a hamster. No roentgenograms were available and consequently the case was incomplete and not acceptable. The animal showed enlarged cervical lymph nodes with involvement of the submaxillary glands, both the liver and spleen were enlarged and mottled, enlargement of the body lymph nodes and diffuse involvement of the vertebrae, particularly in the lumbar region. The tumor cells invaded the spinal canal causing pressure on the cord, resulting in posterior paralysis observed in the live animal. A blood smear made shortly after death showed a definite increase in plasma cells. In reviewing the sections from this case, Dr. Regato may recall that the histopathologic picture is indistinguishable from the human case presented here. I mention this case in the hamster because I know there is considerable research work being done on the experimental production of tumors in hamsters and this unofficial report of a spontaneous plasma cell tumor seems advisable for the information of those engaged in this type of research.

I. Lampe, M. D., Ann Arbor, Mich.: For the sake of those radiologists who made a diagnosis of metastatic tumor, I would like to know definitely if it is thought the lesion in the tibia was metastatic from the epiglottis.

Dr. Ackerman: This is the same problem that occurs in Ewing's tumor—whether it is of multiple origin or whether the tumor metastasized. It does seem a little bit unusual to have so many lesions of bone of both Ewing's tumor and plasma cell myeloma without comparable involvement of other organs, although the Ewing's tumor not infrequently goes to lung and other organs. In plasma cell tumors it is infrequent to find involved viscera, such as in the spleen, pancreas, etc. So I do not know the answer to that question.

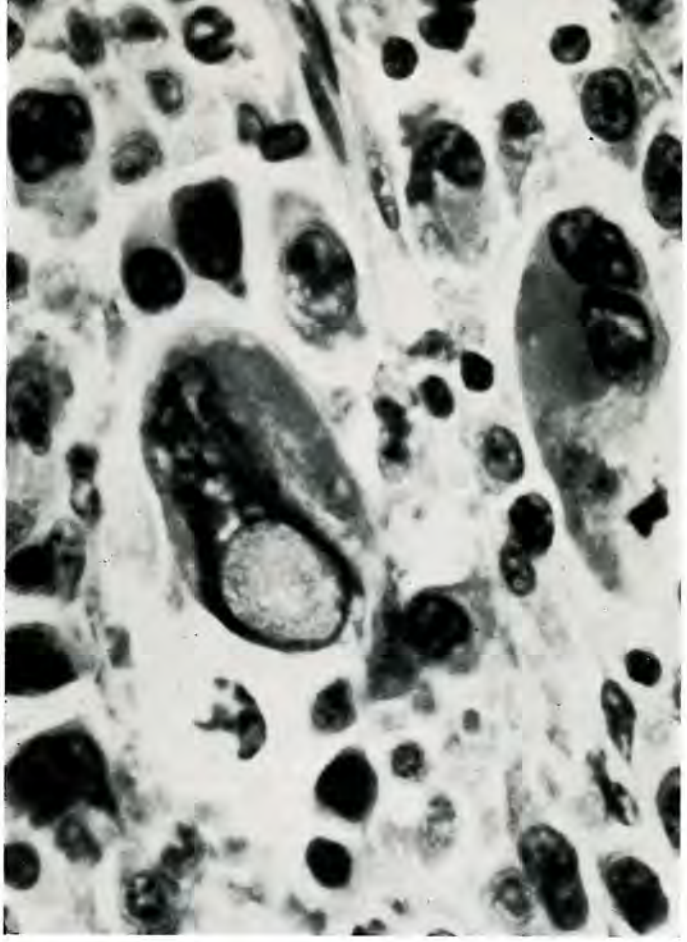


Fig. 2 — Photomicrograph. Plasma cell myeloma; note giant tumor cells concentric nuclei and multiple nuclei.

Dr. Regato: Certain tumors, like the adenocarcinomas of the breast, seem to be capable of metastasizing to regional lymph nodes and to the lungs, brain and bones. Others show predilection for certain organs or tissues for the development of metastatic colonies; it is well known that bone sarcomas do not metastasize to lymph nodes but would invariably develop metastases in the lung; carcinomas of the thyroid and prostate seem to prefer the bones as sites of metastases. In the same manner, we believe, lymphosarcomas show predilection for the lymphatic structures; and myelomas, seldom found in nodes, prefer the bone marrow. In the latter two instances the primary lesion may pass unsuspected even when the disease is widespread. Many authors admit the multicentric origin of both. We think that like other malignant tumors, myelomas originate in a region and are metastatic in others.

Robert Moore, M. D., St. Louis, Mo.: May I ask Dr. Ackerman if he agrees with Dr. Stout's opinion as expressed in his comment that the plasmocytoma of the nasopharynx is infrequently associated or followed by tumors in bones. I have had the impression, in recent years, that the longer these patients were followed the higher was percentage of involvement of bones after diagnosis of plasmocytoma in the nasopharynx.

Dr. Ackerman: The clinical duration of plasma cell tumors arising from the oral cavity or nasopharynx is often long. In those cases in which the lesion apparently began within the oral cavity, nasopharynx, or other areas, it seemed to me that a very high percentage of them later became disseminated. Also, there are certain instances in which the

patient came in with a lesion of a bone, but going into the history carefully it was discovered that the patient had had a lesion of the nasopharynx several years previously, perhaps as many as four or five years. I would certainly guard the prognosis of patients with plasma cell tumors of nasopharynx, and if I saw any tumor which arose in the nasopharynx or oral cavity which looked like this one, I would say without qualification that it was a malignant tumor which would eventually kill the patient.

(This case has also been published by Costen in the Laryngoscope. Ed.)

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13. *Cavernous Hemangiomata of the Bones of a Newborn Child*

Contributed by ISADORE LAMPE, M. D., Ann Arbor, Mich.

THE PATIENT was an infant girl 3 months of age, who for six weeks had presented a swelling of the right shoulder and a similar tumefaction of the left ankle and wrists. Roentgenograms showed osteolytic lesions with proliferative reaction in the distal end of several long bones; copies of one of these roentgenograms were submitted to the participants. A specimen was removed for biopsy from which the slides distributed were prepared.

Radiologic Diagnoses Submitted by Mail		Histopathologic Diagnoses Submitted by Mail	
Congenital syphilis	58	Hemangioma	75
Osteomyelitis	12	Fibrous dysplasia	9
Cortical idiopathic hyperostosis	8	Scurvy	8
Vitamin deficiency	8	Syphilis	6
Vitamin A poisoning	1	Synovioma	3
Metastatic neuroblastoma	28	Osteogenesis imperfecta	2
God knows what!	1	You name it!	1
Nine other diagnoses	23		

Dr. Hodes: This is obviously a polyostotic lesion which involves the humerus, both bones of the forearm and a rib. The lesion is apparently medullary in origin. It is producing considerable destruction of the medulla but the medullary destruction is well defined and sharply demarcated suggesting that it is a benign process. The disease is producing a diaphysitis, epiphysitis, metaphysitis, and periostitis. Close inspection of the zones of temporary calcification in the distal forearm reveals definite fractures in these portions of the epiphysis. The latter, plus a peculiar calcific character of the periosteal changes, suggest that this patient has had considerable sub-periosteal hemorrhage with resulting calcification of the type seen in patients with scurvy.

The character of the medullary defects suggests that this is a benign process. One's first impression would be congenital syphilis, but we are given no history of the latter. Ordinary osteomyelitis would produce more soft tissue swelling around the bony lesions. It is conceivable that tuberculosis could produce such a picture, but I would expect more bone demineralization, and I would not expect the fractures of the epiphyseal plate or the evidence of sub-periosteal hemorrhage.

The polyostotic nature of this patient's disease and the apparent tendency toward sub-periosteal hemorrhages seem to be the clues. There are none of the other manifestations of scurvy, and I therefore tend to exclude one of the metabolic diseases. One is left, therefore, with a granulomatous process arising in the medullary portion of the bone which also is affecting the lungs. All of these changes in an individual of this age lead one to suspect Letterer-Siwe disease.

Dr. Hodes' diagnosis: LETTERER-SIWE DISEASE.

Dr. Regato: Dr. Brailsford, of Birmingham, wrote that this roentgenographic appearance was likely to be called hyperostosis, but objected that this is not a diagnosis; he favored a diagnosis of inflammatory lesions in a patient with alimentary deficiency. A suggestion of luetic bone lesions came from numerous correspondents, including L. H. Garland of San Francisco, M. Sosman of Boston, G. Esguerra of Bogotá, and Sir H. Graham-Hodgson of London.

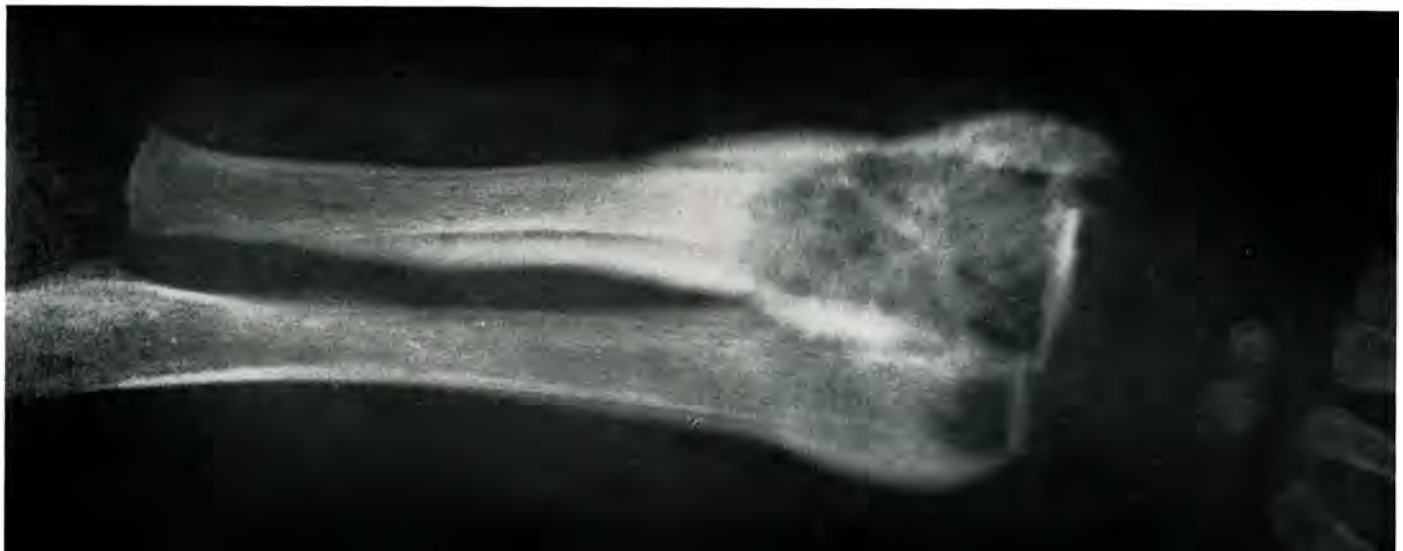

Fig. 1—Polyostotic medullary lesions of the epiphysis of long bones.

Dr. Ackerman: The section demonstrates numerous vascular channels lined by endothelium well filled with red blood cells. There is no evidence of layering of these endothelial cells which may be seen in angiosarcomas. The stromal support is made up of rather abundant cellular connective tissue. Occasionally, foam cells are seen but they are no reason to believe that this process is an expression of eosinophilic granuloma. In the section there is also evidence of some new bone formation which is probably the result of the expansion of this process. These microscopic findings appear to be entirely compatible with a hemangioma of bone.

Hemangiomas of bone, particularly of the spine, are common. Töpfer found hemangiomata in 11.9 percent of 2,154 spines examined. He emphasized that although such lesions are extremely frequent as autopsy findings, they are only rarely of any importance clinically. In 34 of his cases the lesions were multiple. The microscopic picture is typical. Grossly, there may be cystic destruction and in the long bones this may produce a loculated pattern. In the long bones it is usually located near the epiphysis. On section, the lesion may have the appearance of currant jelly. The loculations are smaller than in giant cell tumor. In bone cysts and giant cell tumor, the cortex is expanded but in hemangiomata it may be partially eroded. In the flat bones such lesions may show sun-burst trabeculations of large size, radiating from a common center with elevation but not perforation of the periosteum (Bucy and Capp). In the vertebrae there may be fracture with a compression myomalacia (Holta).

Dr. Ackerman's diagnosis: CAVERNOUS HEMANGIOMA.

Dr. Regato: A histopathologic diagnosis of hemangioma was also rendered by C. Geschickter of Washington, L. Lowbeer of Tulsa, H. L. Jaffé of New York, R. Willis of Leeds, and Brachetto-Brian of Buenos Aires. Lent C. Johnson of the Armed Forces Institute of Pathology suggested the possibility of a salmonella osteomyelitis.

A. P. Stout, M. D., New York, N. Y. (by mail): For me, this is the most difficult to interpret of all the lesions in the SEMINAR. The history fails to tell us a number of things which we should know in order to make a correct diagnosis, such as exact distribution of the lesions, state of the skin (i.e. pigmentation, neurofibromata), blood chemistry, state of the sella turcica, urine analysis, etc. The general appearance at first glance suggests to me a fibrous dysplasia. Since the lesions are multiple, one has to think of Albright's syndrome, but this I have excluded because there is no mention of skin pigmentation, no specifications about segmental distribution and no mention of sexual precocity. There is nothing in the history to point to hyperparathyroidism. I must consider this as a possibility, but I exclude it at present for lack of confirmatory evidence. If, then, this is a form of polyostotic fibrous dysplasia, it must be a non-specific one. But can it be something else? As I study the slide, my attention is directed to the large number of blood vessels which in places are crowded together. Can this be a hemangioma? I am loath to believe it because the fibroblastic tissue accompanying them is too great in amount so that the vessels do not dominate the picture. I am therefore, left in a quandary and will only suggest the possibility that this is a non-specific form of polyostotic fibrous dysplasia.

Subsequent history: The lesions continued to increase in size; there was a rapid course downhill, and the patient died. An autopsy was done: vascular lesions were found at the end of long bones and ribs; similar lesions were found in subpleural portions of lungs and retroperitoneal tissues; there was extreme myelophthisis, fibrous atrophy of the thymus, cerebral edema and eosinophilia of the lymph nodes, spleen and bone marrow.

A. J. French, M. D., Ann Arbor, Mich.: This case was

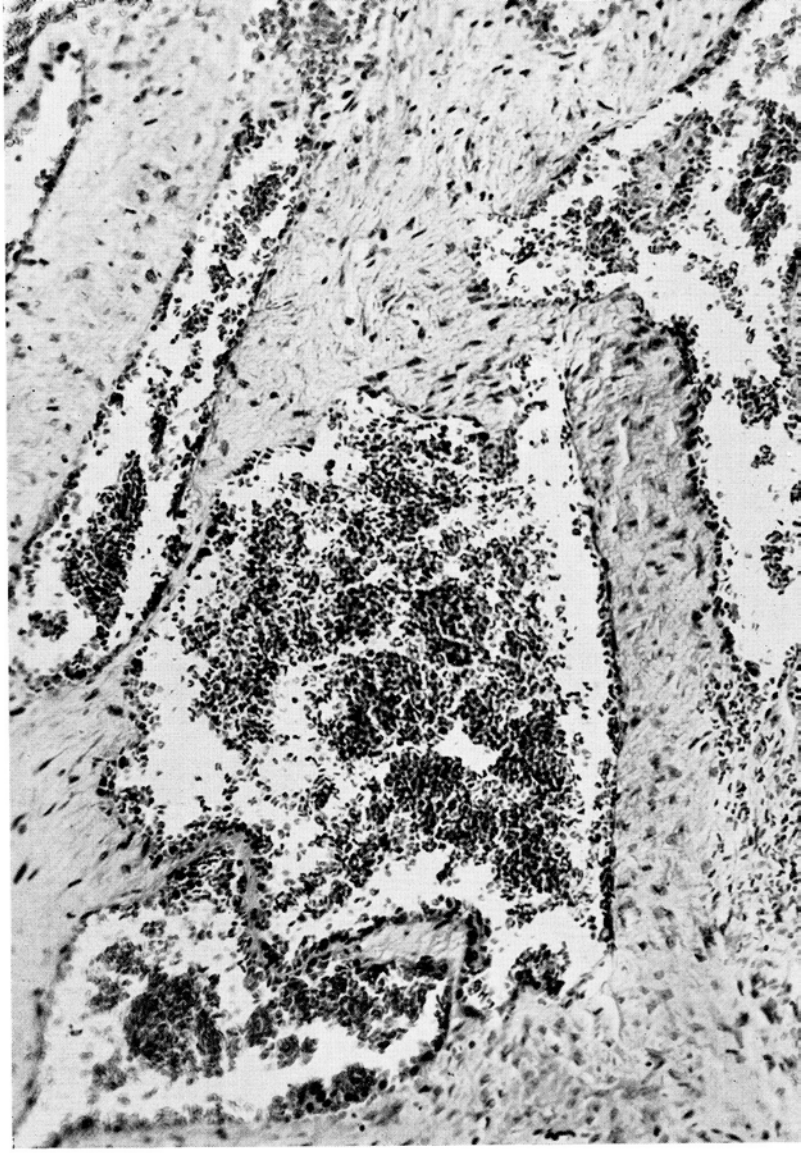

Fig. 2 — Photomicrograph. Cavernous hemangioma of bone. Note large vascular spaces filled with blood and separated by connective tissue septa.

a puzzle to us, also, and I think the two possibilities that have been raised certainly deserve further consideration. We felt that these lesions were hemangiomas occurring in multiple foci. There were hemangiomas in the pancreas as well as in the subpleural portions of the left lung and in the bones. In addition to the vascular spaces, there were cellular foci which raised the question of Letterer-Siwe disease. However, none of the other manifestations of Letterer-Siwe disease were present. There were no skin lesions. The spleen, lymph nodes, thymus, and bone marrow did not show anything that we thought was compatible with that diagnosis, so that finally we were led to conclude that it must be an example of hemangioblastoma. However, we found a little evidence of proliferating endothelial cells. We considered it to be a developmental disturbance.

LeRoy Sante, M. D., St. Louis, Mo.: I would like to ask one question: Why should such hemangiomas kill a baby?

Dr. Regato: That is a very good point, Dr. Sante. A diagnosis of hemangioma must be taken with some skepticism in this case. In the first place, hemangioma of bone is most frequently observed in vertebrae and flat bones; it is rarely found in the long bones, and very rarely multiple lesions are found. In a total of 63 cases of hemangioma of bone reported by Bucy and Capp, and later by Geschickter and Maseritz, there were only eight cases with lesions of the long bones; the youngest patient in the series was eight years

of age—so, in the second place, the young age of our patient becomes also a factor against the diagnosis of hemangioma.

W. H. Bauer, M. D., St. Louis, Mo.: My diagnosis was hemangioma associated with vitamin-deficiency, perhaps vitamin D and C. The extremely broad osteoid zones reminded me of vitamin D deficiency, while the hemorrhages could be due to vitamin C deficiency. Dr. Hodes pointed to the calcified areas parallel to the shafts of the long bones seen in the roentgenogram. These areas could result from calcification of sub- and epiperiosteal bleedings in vitamin C deficiency.

E. S. Murphy, M. D., Denver, Colo.: The question was not answered: How can hemangioma kill a patient?

A. J. French, M. D., Ann Arbor, Mich.: We did find extensive involvement of the bone. Perhaps a vitamin deficiency did exist but the blood picture of advanced anemia is a possible explanation of death.

Dr. Regato: Dr. French, do you think that the eosinophilia which was found [illegible] biopsy may point at the possibility of this being an early atypical form of xanthomatosis?

Dr. French: That is a very definite possibility.

Dr. Hodes: I find it difficult to accept multiple vitamin deficiency in an individual whose epiphyses are so singularly normal. Dr. Sante, would you agree with that?

Dr. Sante: Yes, I would agree with that. I think your diagnosis is correct.

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14. *Ewing's Tumor of the Femur*

Contributed by L. V. ACKERMAN, M. D., St. Louis, Mo.

THE PATIENT was a boy 16 years of age who in July, 1949, had a sudden onset of pain in the left hip and thigh. A biopsy had been done at another hospital and reported as showing Ewing's tumor; four roentgentherapy treatments of 250 roentgens to a large field were administered. In January, 1950, a roentgenogram showed a dense mass; copies of this film were sent to participants. Since the available biopsy was not conclusive, a new one was performed from which our slides were processed.

Radiologic Diagnoses Submitted by Mail		Histopathologic Diagnoses Submitted by Mail	
Bone sarcoma	86	Ewing's tumor	81
Ewing's tumor	22	Reticulum cell sarcoma	12
Chondrosarcoma	10	Malignant tumor	3
Osteomyelitis	18	Osteogenic sarcoma	9
Chondroma	6	Osteoma	3
Giant cell tumor	4		
Four other diagnoses	15		

Dr. Hodes: This is a monostotic lesion which affects the metaphyseal portion of the bone and appears to arise from the medulla. The normal medullary structure is being replaced by a very coarsely trabeculated pattern with multiple, fine, dense, bony spicules distributed throughout its lacework. This increased density is very irregular and suggests calcified cartilage or osteoid. The proximal and distal margins of the medullary lesion are somewhat irregular in character. Of considerable importance is the periosteal proliferation which extends well beyond the level of the medullary defect and has an "onion peel" appearance. A definite increase in the width of the bone is manifest at the level of the lesion. Whereas there is some destruction of the inner layers of the cortex at the level of the medullary disease, the general appearance of the cortex of the bone throughout this segment is one of definitely increased density associated with an increase in its thickness. At one point near the lesser trochanter considerably more cortical destruction seems present and the epiphyseal center of ossification of the lesser trochanter seems to have been displaced medially.

The densely stippled appearance of the medullary bone militates against an inflammatory process. Osteomyelitis, of the Garré type, does not produce bone stippling but rather diffuse eburnation and the medullary changes usually blend with the cortical thickening and periosteal reaction. It would seem therefore, that we are dealing with a bone tumor which the irregular medullary distribution, the displacement of the lesser trochanter, and the periosteal reaction suggest is malignant.

Centrally placed osteogenic sarcomas that have produced this much cortical reaction usually produce more destructive change in the medulla. This, however, is not good evidence against the possibility of a central sclerosing osteogenic sarcoma. The centrally placed chondrosarcomas usually produce a little more bone destruction than is evident in this femur. Because the chondrosarcomas produce cartilage, one would not expect these small stippled areas of apparent osteoid tissue (we cannot differentiate between osteoid and calcified cartilaginous tissue). In view of this patient's age, and in spite of the metaphyseal location of this lesion, we believe this is a Ewing's tumor. The short history and acute onset of pain are in keeping with this diagnostic possibility. Furthermore, early Ewing's tumors are often associated with cortical thickening and increased medullary density.

Dr. Hodes' diagnosis: EWING'S TUMOR.

Dr. Regato: A radiologic diagnosis of Ewing's tumor was also submitted by M. Sosman of Boston, and by Zuppinger of Berne.

Dr. Ackerman: The sections showed tumor cells which are uniform with small nuclei, fine nucleoli, and inconspicuous cytoplasm. They do not form reticulin, and there is good vascularization of the lesion. There is no evidence of tumor

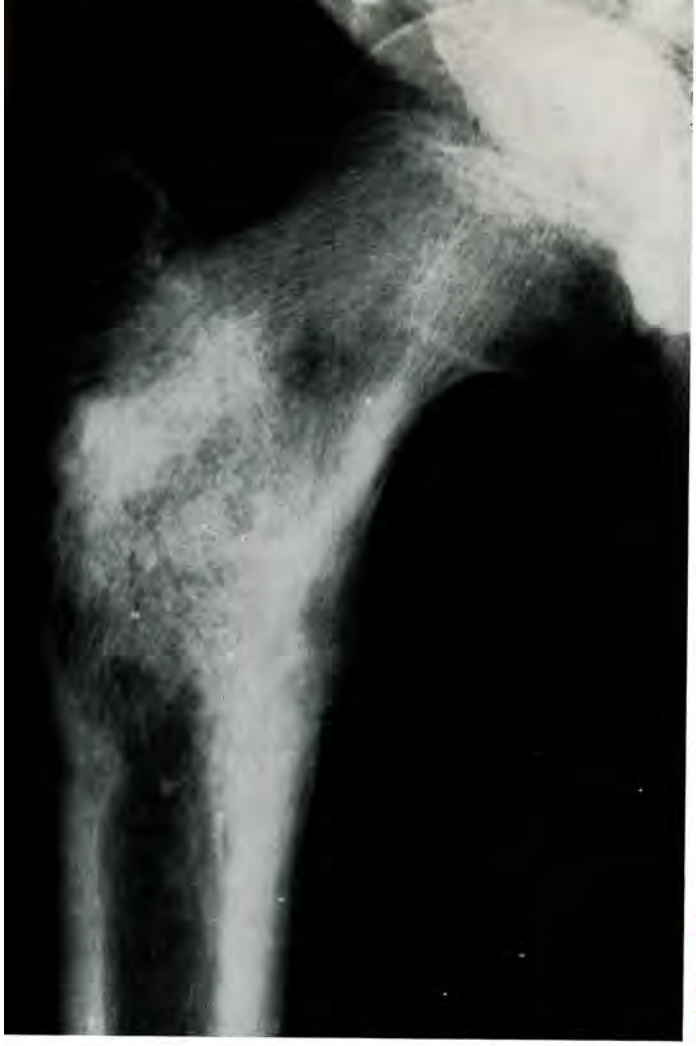


Fig. 1—Bone forming lesion of the metaphyseal end of the femur; note bone proliferation beyond confines of medullary lesion and definite increase in the width of bone.

bone. This is a malignant tumor arising from within the cells of the marrow, possibly from the young reticular cells (Stout), and it is still probably best designated as a Ewing's sarcoma.

Ewing's tumor has a tendency to regressive changes probably because of impairment of the blood supply. This results in cytologic change followed by necrosis and then by fibrosis and cyst formation; after irradiation similar changes occur but to a greater degree. A study of this irradiated tumor reveals wide areas of fibrosis in which nests of tumor cells are growing. It appears reasonable that this stromal background would probably result in failure of further irradiation. Unander-Scharin has studied these regressive changes in both treated and untreated Ewing's tumor and feels that they are only a matter of degree. He speaks of a Ewing's tumor with thick-walled vessels which he believes is radio-resistant.

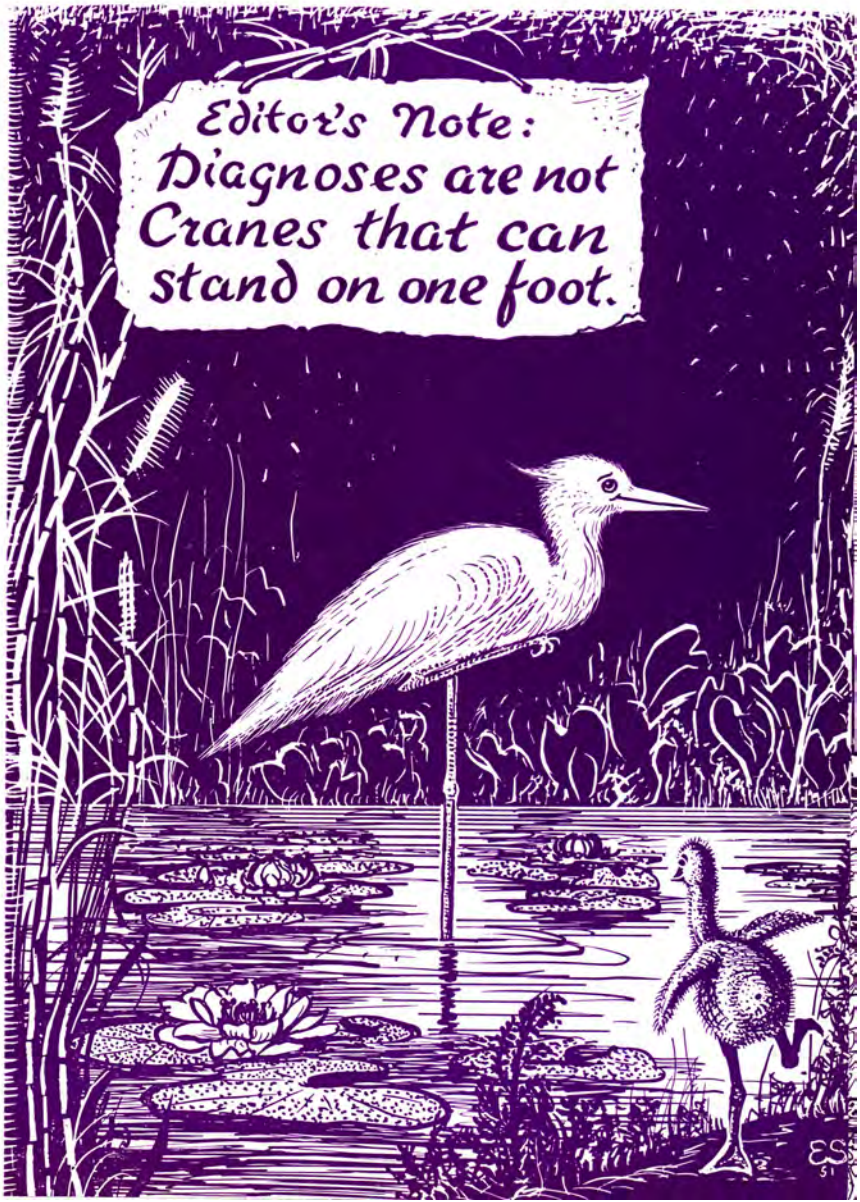
This is no doubt that this tumor mimics neuroblastoma clinically, radiologically, and pathologically. I am certain that some Ewing's tumors are metastatic neuroblastomas. However, there have been autopsy cases of Ewing's sarcoma without any evidence of adrenal involvement and there are fairly numerous examples of Ewing's tumor which have been cured by surgery or irradiation which have remained well over five years. How can the differential diagnosis between neuroblastoma and Ewing's sarcoma be made? Murray and Stout have demonstrated that tissue culture of neuroblastoma allowed neurites to grow out in less than twenty-four hours and this finding, if present, is absolutely diagnostic. True rosettes may be present in neuroblastoma, but unfortunately in the peripheral manifestations of the metastatic process in neuroblastoma, such rosettes may be absent.

The overall prognosis of Ewing's sarcoma is poor: Coley reported 73 cases treated from 1918 through 1942, of which only three cases were free of disease more than five years. It has been my impression that with increasing age, Ewing's tumors grow at a slower rate of speed and that the chances of cure are greater.

Dr. Ackerman's diagnosis: EWING'S SARCOMA.

A. P. Stout, M. D., New York, N. Y. (by mail): The two principal diagnoses to be considered are Ewing's tumor and metastatic sympathicoblastoma. The age is more in favor of Ewing's tumor, but short of tissue culture there is no absolute way to differentiate between the two. It is just barely possible, because of the above described masses resembling osteoid, that this might be an osteogenic sarcoma. The way in which the tumor penetrates along the marrow spaces near the cortex without destroying the bone is more a characteristic of Ewing's tumor than of the others, and that is the diagnosis I shall make.

Dr. Regato: Dr. R. Willis of Leeds submitted this histopathologic diagnosis: undifferentiated malignant tumor of undetermined nature. Dr. Fred Stewart of New York indicated that silver stains would be necessary to make a diagnosis of neuroblastoma; without this, he stated, one would have to "consider (1) neuroblastoma, (2) Ewing's tumor, and (3) reticulum cell sarcoma, and pray that you may be right!"



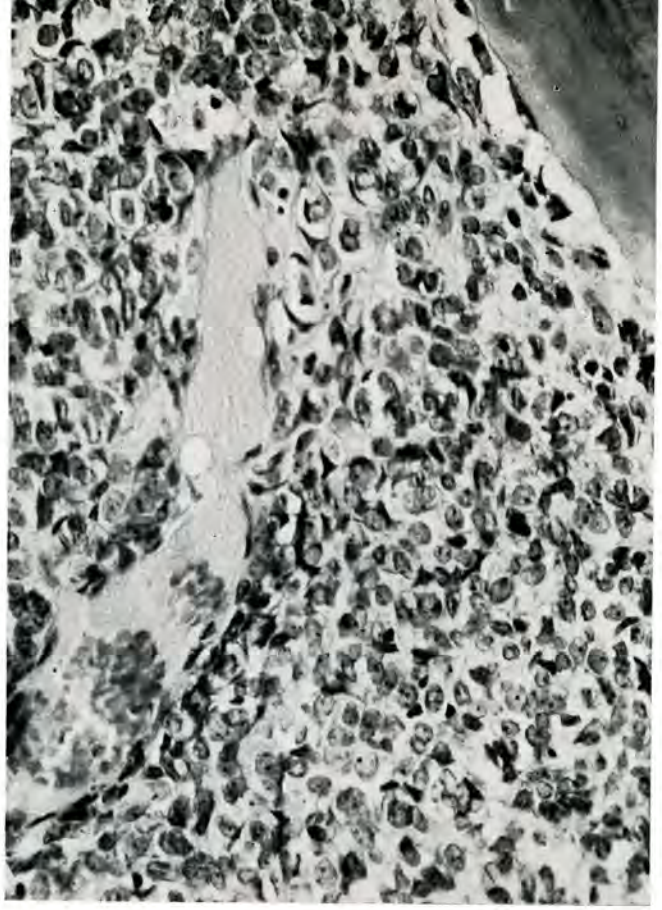


Fig. 2—Photomicrograph (X400). Ewing's sarcoma. Note uniform appearance of cells and absence of osteoid formation.

Subsequent history: In February-March, 1950, a new series of roentgentherapy was decided upon. The previous treatment had been admittedly insufficient; the patient received five treatments of 300 roentgens. In March, immediately after roentgentherapy, a disarticulation was done. The patient subsequently developed pulmonary metastases and in August, 1950, was in terminal stages.

Dr. Regato: At the present time the diagnosis of Ewing's tumor is more popular among radiologists than among pathologists. Ewing believed that the tumor that bears his name arose from capillary endothelium and was characterized by pseudo-rosettes, perithelial structures and cords of polyhedral cells lining elongated spaces.

Some pathologists, with Rupert Willis, deny the entity Ewing's tumor and believe that a good number of so-called Ewing's tumors are metastatic lesions, often metastatic neuroblastomas, whence the pseudo-rosettes (Coleville). An argument against this point of view is the reported cases of Ewing's tumor that have been cured by local treatment. I confronted Dr. Willis with this argument and he reasoned as follows: "When we recall that in the past plasmocytoma, reticulum cell sarcoma, lymphosarcoma, and various inflammatory lesions have all been mistaken for *'Ewing's sarcoma'*, we must be very cautious about taking this diagnosis when any atypical features are present." This statement referred to the atypical features of the three cases reported as cured in a paper by Coley and collaborators, and which Doctor Ackerman commented upon. Unquestionably many cases that have been reported cured of Ewing's tumor were reticulum cell sarcomas and eosinophilic granulomas.

I tend to agree with Dr. Willis. In the past we have seen false entities, such as "branchiogenic carcinomas" of the neck, "aberrant thyroid tumors" and "lymphosarcomas of lymph nodes" which were actually metastatic lesions taken for primaries.

W. B. Dublin, M. D., Fort Logan, Colo.: I also am uncertain regarding the histogenesis of Ewing's tumor. The tumor does not impregnate with reticulum stains; therefore, when we attempt to distinguish it from a neuroblastoma on such a basis, we have inconsequential results. I am sure that we have all had the experience of being unable to distinguish the cells of these two neoplasms, and of seeing others unable to distinguish them. In each case, the cell is a small, round, undifferentiated or indifferent cell. In the nervous system, until nerve-cell characteristics appear, we are dealing with the medulloblast. I am unaware, however, of evidence clearly supporting the neurogenic or medulloblastic histogenetic basis of Ewing's tumor. Neurofibroma and neurocytoma (ganglioneuroma) of bone are rare, and ganglionic tissue is not ordinarily considered a rich or prominent intrinsec element of bone.

M. Wheelock, M. D., Chicago, Ill.: I just thought you might be interested in a little story that they tell about Ewing's tumor: A University of Pennsylvania group many years ago wrote to Dr. Ewing and asked him to send some representative slides of this tumor. They tried to compare them with their cases and were unsuccessful in finding anything characteristic in Ewing's tumor. So they eliminated the markings from Doctor Ewing's slides and returned them to him asking for his diagnosis: he did not think they were cases of Ewing's tumor!

Dr. Regato: I have heard the same story, but it was connected with a Boston Hospital; could it be that the story is apocryphal?

Dr. Hodes: The authentic story is: Dr. Ewing had sent a piece of tissue from which all of our class slides were made. Some 20 odd years later he wrote asking to have some of the slides from that case because he could not find another such classic example.

R. E. Johnson, M. D., Columbia, Mo.: In my section I saw osteoid tissue around the trabeculae of the pre-existing bone. It appeared to be intimately associated with the tumor. I had the impression that it was being formed by the tumor, and I made the diagnosis of osteogenic sarcoma. Could this be attributed to the pre-operative radiotherapy?

Dr. Regato: Dr. Ackerman did not mention radiotherapy when he submitted the summary of the case; I think that he was unaware of it. Actually, the patient had received four treatments of 250 roentgens (on the skin), and it is quite probable that such treatment would not affect much the tumor, but it could have caused some regeneration of bone. Many of the radiologists were misled into a diagnosis of osteogenic sarcoma for lack of this important bit of information, and I wish to apologize to them. In the same manner the description of the radiologic appearance as a "cystic lesion", given to pathologists was also erroneous. I hope that even this error has been helpful in demonstrating how valuable any bit of information may be; I ask you to excuse us for this error, and I assure you that it was not our intention to deprive you of any information.

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Our Guest Speakers

LAUREN V. ACKERMAN, M. D., Professor of Surgical Pathology and Pathology at Washington University, St. Louis, Mo., was graduated from the University of Rochester Medical School in 1932. He is co-author of a book on *Cancer: Diagnosis, Treatment and Prognosis* and is also a noted authority on tumor pathology. Doctor Ackerman was the guest of the regional section of the College of American Pathologists.

PHILIP J. HODES, M. D., Professor of Radiology at the University of Pennsylvania Medical School, was graduated from the University of Pennsylvania, with which institution he has kept an almost uninterrupted association until the present. He is a Fellow of the American College of Radiology, Chief Consultant in Radiology to the Veterans Administration and is well known for his numerous didactic contributions to the radiological literature. Doctor Hodes was the guest of the Penrose Cancer Hospital.

CHARLES S. CAMERON, M. D., Medical and Scientific Director of the American Cancer Society, was graduated from the Hanemann Medical College of Philadelphia in 1935. Doctor Cameron's spirited leadership has given great impulse and unity to the American Cancer Society. Doctor Cameron, the guest of the Penrose Cancer Hospital, was the banquet speaker.

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