FOREWORD

The Conference this year has been enlarged to include radiological studies of the cases presented, thus making it a cancer Pathology and Radiology Conference. The Conference will be jointly conducted by Dr. Granville A. Bennett, Professor of Pathology, University of Illinois College of Medicine; and Dr. L. Henry Garland, Clinical Professor of Radiology, Stanford University.

Would you return the enclosed sheet (unsigned) giving your diagnoses (roentgenological or pathological as the case may be) as soon as possible so that these may be tabulated for use during the Conference. A duplicate sheet is enclosed for your personal copy. Following the meeting you will be sent the transcribed discussions given by Dr. Bennett and Dr. Garland. This can be attached to the clinical data sheets enclosed herewith and will complete a pathology "tumor topic" for your future reference and information.

William O. Russell, M. D.
Chairman of the Program Committee
March 15, 1952
Case No. 101

Contributor: E. W. Thurston, M. D., St. Mary's Hospital, Chicago, Illinois

R. L. Male-White-Age 20 (1950)

Clinical History

Ten months ago this 20 year old white male struck his right elbow against a ladder and had since experienced pain of a throbbing and aching nature which was worse at night. Radiological examination revealed a bone cyst of the olecranon. This cyst was opened 7 months ago with a trephine, and currettage was carried out. Bone grafts from the tibia were placed in the curretted area. Recently swelling occurred in the right elbow.

Physical Examination

The only significant physical finding was swelling in the right elbow region. Routine x-rays of skull and chest were negative.

Laboratory Findings

Results of routine hematological and urinalysis studies were within normal limits.

Roentgenological Studies

Circumscribed multilocular radiolucency in proximal end of ulna, subsequently undergoing pathologic fracture. No periosteal reaction in original film.

Treatment

On surgical exploration, soft tissues of the right elbow appeared highly vascular. The upper portion of the ulna and the olecranon process formed a shell enclosing a highly osteolytic mass of soft tissue which bled profusely. The mass was removed and the resulting cavity subjected to currettement. A vaseline gauze packing was inserted. Surgical impression was that of a highly vascular tumor.
Case No. 102

Contributor: George Milles, M. D., Augustana Hospital, Chicago, Illinois

Female-White-Age 62 (1950)

Clinical History

For over a month this 62 year old widow noted an intermittent drawing pain over the sacral area, particularly after exertion. Protracted constipation was present, and an undue amount of straining was necessary on defecation. There was no melena or vaginal bleeding, nor has any significant weight loss occurred. Menopause was 17 years ago and a hemorrhoidectomy was performed 8 years ago. The patient gave a history of polyuria.

Physical Examination

On digital examination of the rectum, there was palpated a smooth-surfaced tumor mass firmly adherent to the sacrum and extending some 10 cm. in the long axis. The posterior wall of the rectum was observed proctoscopically to bulge in the region of the palpable tumor, and the mucosa was injected. A smooth fixed mass the size of an egg was noted in the area of the cul de sac. A hernia was present in the lower right quadrant.

Laboratory Findings

Results of routine blood chemistry examinations were within normal limits except for a blood sugar level of around 285 mgm per 100 ml. Urinalysis showed 1 + sugar. Hematological and serological findings were essentially normal. Electrocardiograph showed myoccardial damage from coronary heart disease. There was an intraventricular block of the “bundle-branch” type.

Roentgenological Studies

Pelvis, Destructive lesion in distal two-thirds of sacrum. Examination incomplete. (AP stereo and lateral desirable for evaluation.)

Treatment

On surgical exploration a purplish, hard, irregularly lobulated tumor mass the size of a lemon was observed between the rectum and the sacrum. The tumor was strongly fixed to the sacrum and upper part of the coccyx, apparently involving bone or periosteum. The posterior wall of the rectum did not appear to be involved, nor did the ureters. The tumor was considered to have probably arisen from periosteum, sacrum, or presacral nerves. This tumor mass was excised, and no evidence of tumor in the abdomen could be found. A right salpingo-oophorectomy was also performed.
Gross Pathology

The specimen from the sacrum was a bosselated, finely nodular, and gelatinous mass 5.5 x 3.5 x 3 cm. Part was encapsulated with a clear transparent membrane, but a portion of the surface was bare and shaggy. This latter region of the tumor was considered to be the probable area of attachment to the sacrum. The encapsulated surface appeared tan to dusky red, while the unencapsulated portion was a mottled bright to dark red with a few yellow to grayish-yellow specks. The excised ovary was a solid mass 3 x 2 x 1.5 cm.
Clinical History

A 22 year old married white female complained of pain of gradually increasing intensity in the left side of the chest for the past 20 days. The pain was aggravated by coughing and sneezing and radiated toward the left. The patient claimed a recent weight loss of eight pounds.

Physical Examination

A "cafe au lait" spot was present over the anterior portion of the lower left chest region. Moderate tenderness was present in the midclavicular line over the 7th and 8th ribs, and a soft fixed mass was present.

Laboratory Findings

Results of routine hematological, serological, urinalysis, and blood chemistry examinations were within normal limits.

Treatment

The involved portions of the 7th and 8th ribs were resected. The tumor of the 7th rib extended through the cortex and up to the junction with the costal cartilage. The 8th rib was involved to a lesser degree. Recovery was uneventful.

Radiological Findings (Post-Operative)

A pleural reaction was present, suggesting a minimal amount of fluid in the left costophrenic angle. A moderate degree of pneumothorax was noted in the left part of the thoracic cage.
Clinical History

This 57 year old man had a rather long history of recurrent episodes of vague transitory pains in various joints, with favorable response to salicylate therapy. About five months ago he experienced recurrent attacks of dull aching pain of several days duration in the region of the left elbow. Approximately one month ago pain of an aching and throbbing nature appeared in the left elbow and became progressively more severe. There was no history of trauma.

Physical Examination

The distal end of the left upper arm was enlarged, indurated, and slightly warm. There was a slight limitation of motion.

Laboratory Findings

Routine hematological, serological, and urinalysis examinations yielded normal values. Serum phosphate and alkaline phosphatase levels were also normal. Serum acid phosphatase value was 1.4 Bodansky units, and the corrected Wintrobe sedimentation rate was 26 mm.

Radiological Findings

Left elbow. Patchy decalcification of distal 7 cm. of humerus, with periosteal calcification about distal 10 cm. of shaft; soft tissue swelling about the involved bone area.

The chest film revealed changes indicative of pneumonitis. An enlargement of the medial and posterior portions of the distal end of the left humerus was present. The diaphysis exhibited an irregular area of osteoporosis, and the periosteum of the lateral aspect of the distal portion of the shaft appeared prominent.

Treatment

One week after biopsy, amputation of the left arm was performed.
Contributor: Granville A. Bennett, M. D., University of Illinois
College of Medicine, Chicago, Illinois

D. R. Male - White - Age 15 (1951)

Clinical History

A 15 year old white male complained of progressively severe dull aching pain above the left knee for two months, and swelling of the left knee with inability to extend the leg for one month. Four x-ray treatments prior to admission to the hospital gave transient relief.

Physical Examination

The only significant physical finding was the markedly enlarged left knee with limitation of motion and fixation in a position of 165° flexion. Roentgenograms were consistent with a diagnosis of osteogenic sarcoma of the left femur.

Clinical Laboratory Findings

Significant laboratory findings were:

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Total proteins</td>
<td>4.8</td>
<td>1.9</td>
</tr>
<tr>
<td>Sedimentation rate</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>9.5</td>
<td></td>
</tr>
<tr>
<td>Phosphorus</td>
<td>4.2</td>
<td>5.4</td>
</tr>
<tr>
<td>Phosphatase</td>
<td>11.6</td>
<td>2.7</td>
</tr>
</tbody>
</table>

Roentgenological Studies

Extensive sclerosing lesion in distal one-fifth of femoral shaft with sunburst periosteal calcification on mesial and dorsal aspects of lesion and marked soft tissue swelling.

Treatment

A supracondylar amputation of the left leg was done.
Clinical History

Following an accident 16 years ago, this 36 year old man noticed a gradual swelling in the right knee. Aspirations have been performed at intervals of approximately one year. There was at no time pain, tenderness, or limitation of motion.

Physical Examination

The only significant finding was the swollen right knee.

Laboratory Findings

Results of routine hematological, serological, and urinalysis examinations were within normal limits.

Radiological Findings

A pneumo arthrogram of the right knee revealed a large, irregular suprapatellar bursa with thickened septa. There was some irregularity of the popliteal bursa. The infrapatellar bursa was practically obliterated by the irregular thickened synovia. The synovia of the inferior portion of the suprapatellar space and the popliteal bursa showed irregularity and thickening. There was no evidence of a loose joint body.

Treatment

At surgery, there were noted numerous fibrous bodies undergoing metaplasia to cartilage formation. The synovia of the anterior chamber, including the patella and medial and lateral cartilages, were removed.
Clinical History

In 1947 the patient developed pain about the left knee, anorexia, easy fatigability, and failed to gain weight. The pain disappeared after 2 or 3 months, but recurred 3 years later and was associated with swelling of the left knee and surface drainage of purulent appearing material. The knee was held in semi-flexion and was extremely tender and swollen. The patient appeared chronically ill and his femoral and inguinal lymph glands were enlarged but discreet.

Roentgenological Studies

Extensive destructive lesion involving shaft of femur at junction of middle and distal thirds. Patchy sclerosis of bone proximal and distal to destroyed areas. Marked periosteal calcification about the shaft in the region of the sclerotic bone changes. Soft tissue swelling. The prints available are technically fair.

Treatment

Following a biopsy, the left leg was disarticulated at the hip. Although immediately following the operation the patient gained weight, he died in February, 1951, with marked central nervous system signs being notable prior to death.

Gross Pathology

(None available at this time.)
Contributor: Robert C. Lyons, M. D., Wichita Falls, Texas

Female - White - Age 66 (1950)

Clinical History

A small mass developed in the region of spinous process of the left scapula two years before the patient's admission to the hospital, enlarged slowly, caused only slight discomfort, and was only slightly tender when bumped. An x-ray examination of the affected part at the time of hospital admission revealed a 'tremendous soft tissue mass overlying the left shoulder posteriorly and extending into the left axilla'. The left scapula in its inferior 1/3rd was irregularly sclerosed and from this point the mass appeared to arise.

Roentgenological Studies

X-rays show irregular destructive lesion involving distal one-fourth of left scapula with some new bone formation and with an enormous soft tissue mass posteriorly. Patient apparently very stout and technical quality of films poor. Chest x-ray negative for metastasis.

Treatment

The tumor was excised along with the inferior 2/3rd of the left scapula. Eighteen months after the first operation two recurrent tumors were removed from the operative site. To date the patient has developed no new untoward signs or symptoms and has only a mild restriction of abduction and rotation at the shoulder.

Gross Pathology

The mass initially excised was a 4.5 kg, 27 x 20 x 14 cm., firm, lobulated, encapsulated tumor adherent to attached portions of scapula. Upon section, its surfaces were glistening, translucent, soft, pale gray, friable, and contained partially liquified and hemorrhagic areas.

The recurrent tumors were similar, soft hemorrhagic and necrotic. They measured 16 x 10 x 5 cm. and 10 x 6 x 5 cm. and peripherally were composed of non-encapsulated, grey, rubbery tissue which invaded contiguous soft tissue.
Clinical History

Ten months ago this 61 year old woman had experienced pain and swelling in the toes. The swelling gradually progressed to the thighs. Tingling of the fingers and progressive stiffness of the hands had also been present. More recently joint pain was noted in the hips, back, and shoulders. There was an increasing shortness of breath and orthopnea. A weight loss of 16 pounds had occurred during the past ten months. The local physician had given gold salts therapy for rheumatoid arthritis.

Physical Examination

This obese pallid woman had a greatly enlarged, firm, smooth tongue. There was a pitting edema of the lower extremities and the lower abdominal parieties. Blood pressure was 178/104, apical pulse rate 112, and radial pulse rate 80. The right shoulder and fingers of the right hand were swollen, stiff, and restricted in motion. The liver and spleen were not palpable and the heart was not enlarged.

Laboratory Findings

Routine hematological studies yielded normal results except for a red cell count of 3.2 millions and a hemoglobin of 9 gms. The corrected Wintrobe sedimentation rate was 36 mm./hr., and prothrombin concentration was 74%. Urinalysis showed a 3 plus albumin and granular casts. Tests for Bence-Jones protein varied from 1 plus to negative. The serum protein level was 5.8 gms. % with 2.5 gms. of albumin and 3.3 gms. of globulin. Serum calcium and phosphorus were normal; the alkaline phosphatase value was 5 Bodansky units. The rate of disappearance of congo red from plasma was normal.

Electrocardiograph Findings

Auricular fibrillation noted on first examination persisted despite therapy with digitalis and quinidine.

Radiological Findings

X-rays of skull, thoracic spine and lumbar spine showed no evidence of destructive bone lesions. Changes characteristic of hypertrophic arthritis were present in the spine, hands, elbows, and shoulders.
10/26/50 Extremities. There is moderate generalized osteoporosis. Slight degenerative arthritic changes are present in the distal interphalangeal joints. There is no x-ray evidence of rheumatoid arthritis.

Skull. There are faint circumscribed radiolucencies in the calvarium, suggestive but not diagnostic of diffuse metastatic process (early carcinosis, multiple myeloma, etc.).

Chest. The heart is slightly enlarged; the aorta shows arteriosclerotic changes. There is moderate hilar congestion. The lungs are otherwise clear. The bony thorax is negative.

Subsequent chest films made up to January 1951 disclose development of right hydrothorax but no other remarkable findings.

Except for slight degenerative changes the thoracic and lumbar spine is negative.

**Treatment**

Treatment was symptomatic. Four months after the patient was first seen, she expired suddenly while undergoing a second examination.
Clinical History

A 26 year old negro laborer complained of a progressively enlarging tumor mass in the mid portion of the left arm for the past year. A sharp pain radiated from the mass to the left scapula. There was no history of associated physical trauma.

Physical Examination

The only significant physical finding was the mass in the left arm. Roentgenograms of the left arm showed a soft tissue density with irregular calcification in the mid portion. Chest films, bone survey films, and routine laboratory studies were within normal limits.

Treatment

A left forequarter amputation was done including the arm, scapula, and distal one-half of the clavicle.

Gross Pathology

The specimen consisted of a left arm, with the attached scapula and distal one-half of the clavicle. Within the biceps, and confined to it but extending into the tendinous portion of the long head of the muscle, was an ovoid tumor measuring 8 x 8 x 5 cm. The cut surface of this tumor was firm, gray-white, glistening, and marked by degenerating areas filled with clear mucoid material. The tumor was adjacent to bone, but not adherent to the periosteum and there was no extension into the scapulo-humeral joint.
Contributor: William O. Russell, M. D., M. D. Anderson Hospital, Houston, Texas; and Ira Gore, M. D., Hermann Hospital, Houston, Texas

Dr. E. W. B. Male-White-Age 59 (1950)

Clinical History

This physician 59 years of age was in general good health, until 1946, with the exception of a long history of gout controlled by aspirin and colchicine. In 1946 routine physical examination and x-ray studies revealed changes in the pelvis and right femur compatible with a diagnosis of Paget's disease.

In August 1948 there was vague onset of pain in the left mid-thigh which rapidly increased in severity. A small tumor mass developed in the region which gradually increased in size. This was considered as probably either of gouty or traumatic origin and was only observed until October 1948 when an excision biopsy of the gradually enlarging mass was made. Following the pathologic diagnosis of "Rhabdomyosarcoma" radical excision of the lateral thigh muscles was made and approximately 8000R of therapeutic x-radiation was given through 3 parts.

In August 1949 the patient developed right low back pain and right sciatic pain which was considered as possibly due to trochanteric bursitis. At this same time he developed a slight cough with occasional hynoptysis. Chest x-rays revealed a definite tumor mass in the lower lobe of the right lung and smears of bronchial secretion revealed definite tumor cells. In October 1949 right lower lobectomy was performed on which specimen a pathologic diagnosis of "Metastatic Rhabdomyosarcoma with negative glands" was given.

In December 1949 the patient suffered a spontaneous pathological fracture of the left femur. Despite traction and long caliper brace the fracture failed to unite or produce callus.

In February 1950 the right femur fractured and exploration and biopsy at the fracture site was made. The pathologic diagnosis was "Osteogenic Sarcoma". Disarticulation of the right hip joint with amputation was performed. Diagnostic x-rays of the chest subsequently showed the appearance and progressive increase of metastatic pulmonary lesions.

In May 1950 pain followed by a tumor mass appeared in the left deltoid region.

The patient followed a steadily downhill course which ended with death July 28, 1950.
Physical Examination

The pertinent physical data have been given above.

Treatment

The various orthopedic procedures and lobectomy have been outlined above. A course of nitrogen mustards given in May 1950 followed by a course of Coley's toxins administered in May 1950 were both without demonstrable effect on the pulmonary lesions. In July 1950, shortly before death, radioactive gallium was given by the Medical Division of the Institute of Nuclear Studies, which revealed uptake of gallium in the chest, right hip, and upper end of the left tibia.

Roentgenological Studies Summarized

8/10/48 Pelvis and left femur. Typical Paget's disease involving pelvis and visible portion of right femur. Probable early changes in head and neck, left femur. No soft tissue or bony lesions visible in region of clinically noted left mid thigh tumor. Note: There is soft tissue swelling proximal and medial to the middle third of the left femoral area which might be a muscle tumor, but this lies above and medial to the lead arrow visible in the film. There is no comparison view of the right thigh to permit decision as to whether this soft tissue swelling is abnormal.

6/25/49 Left femur. Patchy decalcification of distal one-half of shaft, perhaps due to disuse or radiation osteitis. Patchy periosteal calcification along lateral and dorsal distal two-thirds of shaft. Patchy decalcification of cortex on lateral aspect of middle third of shaft. This might be due to tumor invasion or infection.

12/1/49 Left femur. Fracture mid shaft.

1/20/50 Right femur. Patchy sclerosis of medulla in inferior portion of intertrochanteric area. Decalcification of cortex on mesial aspect of proximal end of shaft. Probable malignant change in Paget's. (Osteogenic sarcoma).


3/29/50 Left femur. Fracture ununited. Cortical and periosteal changes on lateral aspect of shaft more marked.

5/23/50 Chest. Extensive nodular pulmonary metastases (3 to 15 mm. diameter each).
Gross Pathology.

At autopsy no gross tumor could be demonstrated at the site of fracture in the left femur. The right pubic bone was expanded by spongy, gritty, grey tissue and a nodular mass of similar tissue was adherent to the acetabulum. The eleventh thoracic vertebra was replaced by similar tissue. Discrete nodules of firm, grey tumor were present in all lobes of the lungs. A discrete tumor mass of spongy, bloody, grey tumor 7 cm. in maximum diameter was present in the left deltoid muscle.
PROCEEDINGS OF THE
PATHOLOGY AND RADIOLOGY CONFERENCE

at the
Joint Meeting of the

SOUTH CENTRAL SECTION OF THE COLLEGE OF AMERICAN PATHOLOGISTS

ANNUAL SYMPOSIUM ON FUNDAMENTAL CANCER RESEARCH
OF THE UNIVERSITY OF TEXAS M. D. ANDERSON HOSPITAL AND
POSTGRADUATE SCHOOL OF MEDICINE

Conducted by

Dr. Granville A. Bennett, Professor of Pathology
University of Illinois College of Medicine
Chicago, Illinois

and

Dr. L. Henry Garland, Professor of Radiology
Stanford University Medical School
San Francisco, California

THE SHAMROCK
April 25, 1952
Houston, Texas
DR. RUSSELL: I should like to take this opportunity to welcome our audience to the Joint Meeting of the South Central Section of the College of American Pathologists with the M. D. Anderson Hospital for Cancer Research for a combined Pathology and Radiology Conference. The South Central Section of the College of American Pathologists includes the states of Arkansas, Colorado, Kansas, Louisiana, Missouri, New Mexico, Oklahoma and Texas.

The topic of Tumors of Bone is not only interesting to pathologists, where the problem of precise histologic diagnosis is of great importance, but to radiologists, pediatricians and orthopedic surgeons. These specialists have been invited to our conference today.

This morning I spent an hour and a half with our two speakers. I should like to emphasize, however, that this was co-ordination, not collaboration. Our conference was concerned with arranging how the material would be presented to you. Dr. Garland, for example, does not know the pathological diagnoses of Dr. Bennett and has up his sleeve several questions and cases that he wishes to present to Dr. Bennett. Likewise, Dr. Bennett has several cases and points that he will pose to Dr. Garland for opinion. We wish to emphasize again that this is an entirely impromptu presentation.

The cases will be presented as follows: (1) The clinical resume will be thrown on the screen and you will be given an opportunity to read it. (2) Dr. Garland will discuss the case and give his radiological diagnosis. Dr. Bennett will then give his pathologic diagnosis. (3) The case will then be open for general discussion and comment. (4) The tabulated diagnoses submitted by the Radiologists and Pathologists will be reviewed and discussed, first by Dr. Garland and then by Dr. Bennett.

It is my pleasure to present to you, on my right, Dr. Granville A. Bennett, Professor of Pathology and Head of the Department at the University of Illinois, Pathologist-in-Chief at the Research and Education Hospital in Chicago and a consultant to the Armed Forces Institute of Pathology. He is Past President of the Canadian and American
sections of the International Association of Medical Museums. Dr. Bennett is probably best known to pathologists as the Editor-in-Chief of Archives of Pathology. It is my pleasure to present Dr. Bennett.

On my left is Dr. L. Henry Garland, who needs no introduction to Radiologists and not much to Pathologists, since he is well known to them. He is Clinical Professor of Radiology at Stanford University, Past President of the Radiological Society of North America and a consultant to the Armed Forces Institute of Pathology.

I will ask our speakers now for their introductory remarks before the cases are presented.

DR. GARLAND: Needless to say, I feel very honored to be at the Houston Pathological meeting. It is a privilege to be here. I notice that Radiologists were paid the courtesy of labelling it a Pathology and Radiology Conference. But, I think it's really a Pathology Conference. Indeed it's one for Histopathology. Part of the reason for saying that is that the radiological material submitted to you for study is not as complete as it should be. Therefore, on several of the cases it really would be almost impossible to reach a radiological diagnosis from the evidence submitted. Secondly, in the abstracts sent out to the group, the gross description was appended to many of the cases. That, of course, is a weapon not normally in the hands of radiologists. Therefore, it may be that those who made their diagnoses after receiving the abstracts were in a more favorable position than normally exists.

Well, now, we all know that the early diagnosis of bone tumors requires many things. It requires a good clinical examination, an adequate x-ray examination, and adequate consultation with the pathologist or surgeon or both. The method of procedure is important and that, of course, is the difficult thing to teach people because bone tumors are rare. One teaches medical students about them but, by the time they are in practice, they are apt to see a maximum of only one primary bone tumor per year, and perhaps three metastatic bone tumors per year, mostly from the breast. A few, of course, will see more. The criteria for making an x-ray diagnosis of bone tumor are known to most of you. The order in which we like to teach our own students is:
First - Is there x-ray evidence of a lesion? Often you will see a film sent in to you as a pathologist or a radiologist in which there is a normal anatomical pattern. For example, a large supratrochlear foramen in the humerus may have been called a bone cyst; or a large external occipital protuberance in the skull diagnosed as an osteoma. So the first decision is, is there really x-ray evidence of a lesion. If there is, the question arises - is it most probably inflammatory, neoplastic, or metabolic? The third is, if it's probably neoplastic, is it benign or malignant?

Now the roentgenogram is unfortunately just a shadowgram. Further, it reflects the findings present at a certain day and hour only. There are few characteristic findings in the x-ray. The sunray pattern that we used to think diagnostic of malignant bone tumors has been repeatedly seen now in inflammatory lesions of bone. Periosteal lamination that was once thought to be very suggestive of Ewing's tumor; the Codman triangle and so forth have been seen by all of you in inflammatory lesions and even in some metabolic disorders.

As radiologists, we try to teach students to think of primary bone tumors from the point of view of the apparent tissue of origin; the gross anatomic tissue of origin rather than the microscopic. (See Table I) The benign lesions arising from bone are primarily the osteomas and the osteochondromas; one sees a few osteoid-osteomas. The malignant are the osteogenic sarcomas. The cartilaginous group, similarly, include the chondromas and chondrosarcomas. Chondroblastoma is listed in courtesy to those who are using that term; I have recognized none. The so-called marrow area gives rise to fibromas and giant cell tumors, and in the malignant group the myelomas, reticulum cell sarcomas, Ewing's tumor and the liposarcomas. Blood vessel tumors are similarly grouped. The chordomas and adamantinomas are difficult to list; some of them are malignant, some benign and I think some are semi-malignant.
Table I

Bone Tumors. Classification according to apparent tissue of origin:

Primary

<table>
<thead>
<tr>
<th>Bone</th>
<th>Cartilage</th>
<th>&quot;Marrow&quot;</th>
<th>Blood and Lymph Vessels</th>
<th>Other</th>
<th>Clinical Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoma</td>
<td>Chondroma</td>
<td>Fibroma, central</td>
<td>Hemangioma</td>
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<tr>
<td>Osteochondroma</td>
<td>Chondroblastoma</td>
<td>Giant cell T. ?</td>
<td>Lymphangioma</td>
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<td>Benign</td>
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<tr>
<td>Osteoblastoma</td>
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<tr>
<td>Osteogenic Sa.</td>
<td>Chondrosarcoma</td>
<td>Myeloma</td>
<td>Angiosarcoma</td>
<td>(Synoviosa.)</td>
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<tr>
<td></td>
<td>Ret. cell sar.</td>
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<td></td>
<td>Fibrosarcoma</td>
<td>Malignt.</td>
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<tr>
<td></td>
<td>Ewing's Tumor</td>
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<td>Lymphangiosa.</td>
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<td></td>
<td>Malignt. G.C.T.</td>
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<td></td>
<td>Liposarcoma</td>
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</table>

Metastatic

| Carcinoma             | Sarcoma                |
|                       | Lymphoma (Hodgkin's, Lymphosa., Leuk.) |
|                       | Neuroblastoma, etc.    |
### Table II

**Bone Tumors:** Lesions to be considered in differential roentgen diagnosis:

<table>
<thead>
<tr>
<th>Bone</th>
<th>Cartilage</th>
<th>&quot;Marrow&quot;</th>
<th>Blood-Vessel</th>
<th>Other</th>
<th>Clinical Type</th>
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</thead>
<tbody>
<tr>
<td>Paget's Dis.</td>
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<td>Fibrous dysplasia</td>
<td>Infarcts</td>
<td>Myositis ossificans</td>
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<td>Hyperostosis (adult)</td>
<td></td>
<td>Neurofibromatosis</td>
<td>Aneurysm</td>
<td>Scurvy</td>
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<tr>
<td>Hyperostosis (infantile)</td>
<td></td>
<td>Bone cyst</td>
<td></td>
<td>Parathyroidism</td>
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<tr>
<td>Leont. ossea</td>
<td></td>
<td>Eosinophilic granuloma (the liporeticularoses)</td>
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<td>Basophilism</td>
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<td>Radiation osteitis</td>
<td></td>
<td>Epidermoid</td>
<td></td>
<td>Rare Anemias</td>
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<tr>
<td>Marble bones, etc.</td>
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<td>Dermoid Cyst</td>
<td></td>
<td>Meningioma</td>
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<tr>
<td>Sclerosing osteitis</td>
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<td>Osteomyelitis (luetic, tuberculous, etc.)</td>
<td>---</td>
<td>Periostitis</td>
<td>Infectious</td>
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<td></td>
<td></td>
<td>Granuloma (sarcoid, etc.)</td>
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<td></td>
<td></td>
<td>Echinococcosis</td>
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</table>
The metastatic tumors, in clinical practice, are the more common and perhaps the more important ones. However, they are not the main subject of our conference today.

In differential diagnosis, students are asked to consider lesions in the same order as is shown in Table II.

(See preceding page)

The order of procedure which we advise is: first, a good history and physical examination. Then, adequate x-ray examination - multiple projections, including soft tissue views. It is a curious fact that a patient will have a little indigestion and a radiologist will examine him, fluroscope him, make spot films, plus multiple regular roentgenograms and end up with a diagnosis, say, of duodenal ulcer - - - a benign disorder common in intellectuals. But when he has a bone tumor to examine - a potentially lethal entity but one that might be cured by radical surgery in some cases - just two films may suffice. He should, of course, go ahead and examine the opposite extremity, the chest and, in occasional cases, other parts such as the skull.

After history, physical examination and x-rays come the other procedures as listed in Table III.
## Table III

**Bone Tumor Suspect. Procedures for Identification.**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>1.</td>
<td><strong>History</strong> and Physical Examination.</td>
</tr>
<tr>
<td>2.</td>
<td><strong>X-Rays - local.</strong> Multiple projections, including soft tissue.</td>
</tr>
<tr>
<td>3.</td>
<td><strong>X-Rays - general.</strong> Opposite extremity. Chest. In selected cases, skull, ribs, pelvis, etc.</td>
</tr>
<tr>
<td>5.</td>
<td><strong>Chemistry.</strong> Serum alk. and acid phosphatase. Calcium and P.</td>
</tr>
<tr>
<td>6.</td>
<td>Additional studies if infection present: tbc. &amp; cocci. skin tests; brucella agglutination; smear and culture, etc.</td>
</tr>
<tr>
<td>7.</td>
<td><strong>Biopsy - adequate in origin and size, and properly preserved!</strong></td>
</tr>
<tr>
<td>8.</td>
<td><strong>Consultation.</strong> With one or more radiologists and pathologists prior to radical treatment.</td>
</tr>
</tbody>
</table>

In trying to correlate roentgenograms and gross pathology, one may encounter trouble; this possibility increases with microscopic pathology. The roentgenogram reflects the gross pathologic picture of the entire tumor while the histologic slide reflects only the microscopic data from a tiny portion of the tumor. The same microscopic appearance can occur with quite different types of radiologic findings; some of the most confusing to me are the so-called fibrous dysplasias of the skull, which in one patient may be dense and in the next radiolucent.
(The speaker then illustrated with lantern slides some of the basic points in roentgen interpretation of benign and malignant primary bone tumors, using cases with complete follow-up.)

DR. RUSSELL: Thank you Dr. Garland. Dr. Bennett?

DR. BENNETT: Dr. Garland's comment on the rarity of skeletal tumors is a point well taken. However, they are so terribly important when they occur that I think it points up the need of this sort of joint conference, to bring together the Radiologists, Pathologists and Clinicians who are going to treat or manage these cases. The steps in diagnosis which he enumerated are very important too; the determination as to whether or not a tumor exists; whether it is benign or malignant; and, specifically, whether it can be managed successfully by local procedure (which in most instances it cannot) or by some operation less than a mutillating, amputating procedure. I think that the knowledge which can be gained from group consideration of these tumors is highly important.
CASE 101

A white man 20 years of age after striking his right elbow experienced throbbing and aching pain. Radiologic examination revealed a bone cyst of the olecranon process which was curetted and grafted three months after injury. Seven months later a swelling occurred in the right elbow. Highly vascular soft tissue tumor was removed at surgery.

DR. GARLAND: On the left hand side you see one of the earlier roentgenograms, showing a circumscribed, porotic lesion in the proximal end of the ulna, without visible periosteal reaction. We don't have oblique views. We assume that the other bones are negative since nothing is mentioned (but one should have visual evidence of that). Pathologists or radiologists analyzing a bone tumor should require the opposite extremity, and in some cases a lateral of the skull or an A.P. of the pelvis, and so forth. The best thing of all, of course, is to have the actual patient present so that you can examine him, palpate for a soft tissue mass, an area of increased warmth, and so forth.

The lesion has been described in the protocol as a bone cyst. That word, of course, should be dropped from the literature, since the word "cyst" to the average doctor implies something filled with fluid. It should be recorded as a radiolucent area in the bone. We don't know whether it's full of fluid, semi-solid or solid material. Is it benign or malignant? There are none of the criteria of malignancy here; the lesion is circumscribed and without visible periosteal reaction. Therefore we think it's some kind of a benign process. But, is it inflammatory or one of the so-called metabolic disorders? Well, I don't know. On first impression I wrote down (1) eosinophilic granuloma; (2) localized fibrous dysplasia; (3) giant cell tumor; and (4) synovioma. And I didn't know which one of those to pick. I was about to flip a coin when, fortunately or unfortunately, this printed record arrived with a description of excision of a very vascular lesion, so I discarded fibrous dysplasia and eosinophilic granuloma, and ended up with a diagnosis of either benign giant cell tumor or synovioma.

DR. BENNETT: When I examined the sections from the first biopsy in this case I regarded the lesion as an unusual example of an eosinophilic granuloma. There appeared to be a
great deal of organization which was believed to account for the vasoformative aspects. However, this was quite some time ago. When the material came back for re-evaluation as a part of the seminar set and particularly when I undertook to photograph it, I became less certain that this was an eosinophilic granuloma. Now, in order to recall to you what this lesion consists of, let us have the next slide projected.

You see that there are many endothelial cell lined vascular spaces. This is, in other words, a vasoformative lesion. There are, however, some clusters of eosinophiles in the lesion. (Next slide -)

In this high power photomicrograph we note loosely reticulated areas containing scattered eosinophiles and histocytic cells. The more I have studied this lesion the more convinced I have become that this vasoformative growth is not just a reparative reaction within an eosinophilic granuloma, but rather that it is actually a tumor. At the present time I conclude that this is an angio-endothelioma of bone. However I am forced to put a question mark behind my diagnosis, indicating some degree of uncertainty.

Pathologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eosinophilic granuloma of bone</td>
<td>25</td>
</tr>
<tr>
<td>Hemangioendothelioma</td>
<td>12</td>
</tr>
<tr>
<td>Hemangiosarcoma</td>
<td>6</td>
</tr>
<tr>
<td>Giant cell tumor</td>
<td>6</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>6</td>
</tr>
<tr>
<td>Osteolytic osteogenic sarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Osteitis fibrosa cystica</td>
<td>2</td>
</tr>
<tr>
<td>Fibrous dysplasia</td>
<td>1</td>
</tr>
<tr>
<td>Metastatic carcinoma</td>
<td>1</td>
</tr>
</tbody>
</table>

DR. BENNETT: In tabulating the diagnoses which were sent in, we have obtained very little help. The two principal groups of diagnoses have run about even. There were 25 who favored calling this an eosinophilic granuloma; a diagnosis which was my choice a year and a half ago. Twenty-four diagnoses favor a vascular tumor. Giant cell tumor listed by six is not justified, in my opinion. Osteolytic osteogenic sarcoma mentioned by 3 can be dismissed as erroneous interpretations.
Fibrous dysplasia and metastatic carcinoma are readily ruled out. I think it's highly important in this particular tumor to consider management. Before I pass the microphone back to Dr. Garland, I should like to remark that this patient has had a good deal of radiation therapy. Despite this, he still has the lesion.

DR. GARLAND: Thank you. May we have the slide showing the tabulation by the radiologists?

Radiologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giant cell tumor</td>
<td>22</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>5</td>
</tr>
<tr>
<td>Aneurysmal bone cyst</td>
<td>3</td>
</tr>
<tr>
<td>Eosinophilic granuloma</td>
<td>2</td>
</tr>
<tr>
<td>Osteogenic sarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Myeloma</td>
<td>1</td>
</tr>
<tr>
<td>Malig. degen. in giant cell tumor</td>
<td>1</td>
</tr>
<tr>
<td>Synovioma</td>
<td>1</td>
</tr>
<tr>
<td>Granulomatous cyst</td>
<td>1</td>
</tr>
<tr>
<td>Angiosarcoma</td>
<td>1</td>
</tr>
</tbody>
</table>

DR. GARLAND: Twenty-two thought that giant cell tumor was a likely possibility; 5 hemangioma; 3 aneurysmal bone cyst; 2 granuloma; 2 sarcoma; one myeloma; 1 each malignant degeneration in a giant cell tumor; synovioma; granulomatous cyst; and angiosarcoma. So therefore we were just like the seven blind pathologists examining the elephant. We had two separate groups of ideas and were trying to be too precise. This case exemplifies the fact that there is this broad zone in bone tumors where neither the clinical data nor the radiological (nor the histological!) data permits you to say any more than "probably non-malignant" or "probably malignant". May we have the next slide please?

This is the follow-up after radiation therapy and those two surgical approaches. The gentleman still has his ulna, he has a cortex on the dorsum of it. It's an expansile lesion, medially. This might be the response of a giant cell tumor, or an unorthodox eosinophilic granuloma. It might even be the response of an angioma. I still don't know what it is. I should like them to watch it very carefully for if there should be any evidence of cortical breakthrough, or a soft tissue mass, he ought to have his arm off - a month before the evidence appears!
DR. BENNETT: Dr. Garland has just said what I felt compelled to say over the telephone a few days ago to the pathologist who submitted this problem. His reply was, "Well, I'd like to wait until you come back from Houston. Perhaps you will learn something more down there". My personal feeling is that this probably is a progressive lesion, despite what has been done to it. Therefore it requires further treatment by whatever means are necessary to totally eradicate the process.

DR. GARLAND: Dr. Bennett, there is one important thing here, of course. And that is the precise radiation dosage and the time since radiotherapy. We know that some giant cell tumors and some angiomas will give a sluggish response (the slowest giant cell response I saw was 12 months, during which everybody was very worried). Therefore, the fact that it's behaving like this doesn't prove that local amputation or resection is essential. Do you happen to know what the dosage was and what the time interval after dosage before this film?

DR. BENNETT: I haven't any exact information on the latter. Notes given me indicate that the lesion received 3,000r and I presume from the notes that this was given within a period of four weeks.

DR. GARLAND: And probably you were not told whether that was tissue roentgens in the tumor, or 3,000r to one field in air, or 1,000r to each of three fields, etc. The expression of dosage, unfortunately, is often not precise. It should give the tumor dosage in such and such a period of days. Three thousand r air to this area in 3 months would be mild dosage, whereas 3,000r tissue in one week would be an excessive dosage. So we really don't have the facts yet. It is a bizarre tumor, not yet clinically or microscopically malignant.

DR. RUSSELL: Let's have general discussion from the audience. May we call on General DeCoursey?

GENERAL DE COURSEY (Washington, D.C.): I have no comment.

DR. SHARPE (Pasadena, Texas): Well of course these films suggested to me an aneurysmal cyst and it's entirely possible that the changes up to date are from the radiation therapy.
DR. RUSSELL: Dr. Bennett, if they won't help you out, I'm going to call on several people here. Let's call on Dr. Goforth.

DR. GOFORTH (Dallas, Texas): No comment.

DR. RUSSELL: Dr. Severance? (No comment) Dr. Mark Wheelock?

DR. WHEELOCK (Chicago, Ill.): I don't have any comment. I thought it was eosinophilic granuloma in the sections that I saw. I was just talking to Dr. Severance a moment ago. We both thought it was eosinophilic granuloma on the original slides, but we didn't see the follow-up that Dr. Bennett had. I certainly would be willing to change my own opinion and call it a neoplasm at the present time.

DR. GARLAND: Well, Dr. Bennett, if nobody will help you out, perhaps we should call it a giant cell tumor of bone. Since about 5% of these apparently become malignant, the course may be consistent.

DR. BENNETT: The trouble with that is; a giant cell tumor of bone is a tumor which can be recognized histologically. This, to my mind, is not a giant cell tumor of bone. It may behave like a giant cell tumor of bone, but histologically it bears no real resemblance to a giant cell tumor.

DR. KOENIG (Ft. Smith, Ark.): Dr. Bennett, don't you think that on the basis of morphology alone the cells forming or lining the vascular spaces seen in the sections are identical with the cells seen elsewhere in the lesion? I don't think that that can be tossed off very lightly.

DR. BENNETT: How do you interpret that?

DR. KOENIG (Ft. Smith, Ark.): Well, my diagnosis on this particular section was hemangioendothelioma, with the neoplastic group.

DR. BENNETT: That is my present diagnosis and I agree with you that the vasoformative cells represent an integral part of the neoplasm.
DR. GARLAND: What, in one short sentence, Dr. Bennett, is the difference between a hemangioendothelioma and a Ewing's tumor?

DR. BENNETT: First I would say that a Ewing's tumor is not a vasoformative lesion. Ewing's sarcoma is basically a small-celled tumor, the cells presumably arising out of undifferentiated marrow cells. One of the principal characteristics of the Ewing's sarcoma is that the cells do not have the capacity of forming intercellular substance or forming vascular spaces.

DR. GARLAND: Well is this, then, a semi-malignant tumor?

DR. BENNETT: To date this lesion has not behaved as a malignant tumor and I hope that it isn't going to acquire malignant properties. Actually I would call this an angioendothelioma, believing that it is a neoplasm which, as yet, is not a metastasizing tumor. Apparently it is capable of continued local growth and destruction of surrounding bone.

DR. RUSSELL: I think this case illustrates very well the difficulty which you run into regarding tumors of unclassifiable type. You have to take all factors into consideration, including the clinical history. That's why I like to leave the decision as to disposition of the case to the clinician after he has seen all the information available from all sources.

DR. WHEELOCK (Chicago, Ill.): I'd like to ask one question, in view of the questionable status of this case. Would there be any particular contra-indication to another biopsy? Would that be opposed by the radiologists or the surgeons; would the pathologist also be opposed to it? I think maybe additional information would be helpful and may substantiate the necessity of the amputation which has been questioned.

DR. GARLAND: Assuming that the dosage had been adequate, say 2 or 3,000 roentgens in a period of one month, and if the lesion is presently quiescent and not causing symptoms, perhaps an aspiration biopsy from one end of it would give you some valuable information.
DR. BENNETT: Well, I should dislike, in this particular instance, to place very much reliance on aspiration biopsy. The lesion is a pleomorphic growth, as you have seen within your own sections. Unless one looks over many sections from adequate samples, one can get into a lot of trouble, especially after the lesion has been treated. Perhaps another biopsy should be taken, followed by immediate resection of the lesion if the biopsy warrants it.

GENERAL DE COURSEY (Washington, D.C.): By "immediate" you mean you'd wait long enough to see a good paraffin section?

DR. BENNETT: I certainly would.

GENERAL DE COURSEY (Washington, D.C.): Do you go along with the findings of Dr. Fred Stewart at Memorial, and others, that waiting several days after most biopsies has not shown any decrease in malignant action?

DR. BENNETT: Well, I'm not aware of any substantial evidence that we lose anything by waiting long enough to obtain permanent sections. I don't know how Dr. Garland feels about it.

DR. GARLAND: Yes; I think our viewpoint on biopsies has undergone alteration in the last 20 years. But I would like to hear the experts here tell me how many of them agree with Ferguson's maturation period. Ferguson, as you know, had a better five-year survival rate in those osteogenic sarcomas which were trifled with for a year or two than those in which there was very prompt vigorous action. McDonald has interpreted that to mean that those which were trifled with for a year or two were biologically slow growing tumors and were relatively favorable, even though osteogenic; whereas those that were attacked immediately were biologically very malignant tumors and were beyond hope of cure right from the start. Now, is the temporizing in this particular case, for example, going to be all right and do the patient no harm? Maybe so; maybe biologically this is an indolent tumor. What do you think of Ferguson's "delay" data, Dr. Bennett?

DR. BENNETT: It is my thought that Dr. Ferguson's data should be interpreted by you as a Radiologist.

DIAGNOSIS: Angio-endothelioma, atypical?
CASE 102

A white woman 62 years of age noted intermittent pain in the sacral area on exertion. Rectal examination revealed a mass posterior to the rectum. At surgery, a hard, irregular, lobular mass approximately 6 cm. in diameter was apparently attached to the sacrum and upper part of the coccyx, involving the periosteum but no surrounding soft tissue.

DR. GARLAND: Our original interpretation was based on a single A.P. film and a brief history. There is a radiolucent area in segments S-4 and S-5, not very well defined. One should have stereoscopic A.P. projections, a lateral projection, and a film of the chest before attempting to express an opinion on this. Nevertheless, being invited to Houston I had to express an opinion. So, I think, #1 a chordoma, and #2 a chondroma. Chordomas in the upper and lower ends of the spine are not rare; the history is of a lesion palpable by rectal examination, and of no great pain.

DR. BENNETT: I did not take many microphotographs of this because the sections present a monotonous picture and one film is enough to tell the story. I selected this field because it shows some cartilage, top and bottom, which is from an area in the sacrum which is being invaded by the tumor, the histologic quality of which has a certain degree of resemblance to cartilage. Dr. Garland's interpretation is correct, namely, chordoma. It so happened that there was another chordoma submitted for consideration in this seminar. This lesion arose in the opposite end of the axis (base of the skull) and I did bring along a couple of microphotographs to show the remarkable degree of variation which may be observed in chordomas from time to time. Usually they look like this. Next slide please -

This is a higher power of the same specimen from the case for presentation - typical chordoma. Next slide -

Here is a lesion which is less typical, on initial study at least, in that it is a much more pleomorphic type of growth. There are many mitotic figures among these tumor cells. Next slide please -
In the higher magnification of this lesion the qualities of chordoma are less well shown than the specimen under consideration. I recall seeing, over the years, chordomas which on first sight have been misinterpreted as metastatic lesions, particularly as renal carcinomas. At times the cells can be very large and clear. Such cases are, of course, interesting. The diagnosis here is chordoma.

DR. RUSSELL: Is there discussion from the audience? (None) I should like to ask Dr. Bennett what is in the vacuoles which you see in these cells. Is it glycogen?

DR. BENNETT: In our experience it is difficult or frequently impossible to demonstrate glycogen. I don't know what the intracytoplasmic material is. Do you have any ideas?

DR. RUSSELL: I thought that Dr. George Hoss, some ten years ago, expressed the idea that in chordoma the vacuoles contained glycogen. I've always carried it in my mind but I never stained it. Did anyone ever stain the vacuoles in these tumors? (No answer) I believe we ought to do it. Is there any further discussion?

UNIDENTIFIED PARTICIPANT: What was the ovarian tumor described in this case?

DR. BENNETT: I'm sorry, but I cannot help you out on that. I made inquiry about the chordoma and secured a statement that there appeared to have been a recurrence of recent date, but I have no information about the ovarian tumor.

Radiologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chordoma</td>
<td>25</td>
</tr>
<tr>
<td>Neurofibroma</td>
<td>2</td>
</tr>
<tr>
<td>Retroperitoneal sarcoma</td>
<td>4</td>
</tr>
<tr>
<td>Osteogenic sarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Dermoid or chromaffin body tumor</td>
<td>1</td>
</tr>
<tr>
<td>Estrogenic sarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Met. Ca. from ovary</td>
<td>1</td>
</tr>
</tbody>
</table>

DR. GARLAND: The score was pretty good on this - 25 chordomas; 2 neurofibromas, which I think is acceptable; 4 retroperitoneal sarcomas - I think they were misled by the
x-ray. Dermoid and chromaffin body tumor are unlikely. The diagnosis of "estrogenic sarcoma" must have been made by a lady radiologist; metastatic carcinoma from the ovary - that may be from the gentleman who just raised his hand - so let us pass on.

**Pathologists' Diagnoses Tabulation**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chordoma</td>
<td>53</td>
</tr>
<tr>
<td>Chondroma</td>
<td>2</td>
</tr>
<tr>
<td>Middeldorf's tumor</td>
<td>1</td>
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<tr>
<td>Chondromyxoma</td>
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<tr>
<td>Primary chondromyxosarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td>1</td>
</tr>
</tbody>
</table>

**DR. BENNETT:** The pathologists likewise agreed pretty well on this case. Chordoma was named in 53 instances; chondroma in 2. When I saw that third diagnosis this morning I said, "What in the name of heaven is that?" I was told that I had missed something, that this is another name for chordoma; that Middeldorf described the tumor, or at least was one of those alleged to have described it.

**DR. RUSSELL:** This was just an impression of mine, Dr. Bennett. I'd like to have discussion from the audience, particularly the person who submitted that diagnosis, if he is present.

**DR. HERTZOG (New Orleans, La.):** I'm responsible for that diagnosis. The slide I had was a very difficult one to interpret. It was rather poor section. Middeldorf originally used that term for any pre-sacral kind of tumor and it can include neurofibromas, chordomas, and a wide variation in that term. I think the real term Middeldorf's tumor doesn't have any application any more.

**DIAGNOSIS:** Chordoma of sacrum.
CASE 103

A white woman 22 years of age complained of increasing left chest pain with moderate tenderness over the 7th and 8th ribs and palpable, soft fixed mass in this region. The 7th and 8th ribs were resected.

DR. GARLAND: On this case no films were submitted to us. The history described a patient with holes in the ribs and a pigmented spot, shall we say a "cafe au lait" spot, on the skin; one was very tempted to think of neurofibromata. On the other hand, one sees more patients with so-called polyostotic fibrous dysplasia than one sees with osseous neurofibromata. In a person of this age, the question of destruction of ribs by pleural tumor has to be considered. There were two ribs involved.

There were no anti-operative films submitted, but this morning Dr. Bennett kindly showed me the x-ray slide, which reveals two ribs with multilocular radiolucent lesions. One shows expansion of cortex; one does not. However, the latter shows cortical reaction and so-called periosteal spiculation. This type of process doesn't fit with any of the entities I've mentioned and I think here of an hemangioma or a sarcoma.

DR. BENNETT: I think this is a rather simple problem from the standpoint of histopathology. Dr. Otto Saphir felt this was a neat lesion and presented me with the blocks and with the film which is before you. We haven't seen this lesion too frequently, but we do have a few other examples which are almost identical to this one.

I took a single photomicrograph which, as you see, shows that the lesion is made up of a large number of endothelial lined spaces. In some places these are filled with blood. In other places there are small cellular masses or tubules of the capillary endothelium. Thus, it is evident that this an angioma of the rib.

DR. RUSSELL: I'd like to congratulate Dr. Garland on his diagnosis of hemangioma with the meager information available.
### Radiologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrous dysplasia</td>
<td>9</td>
</tr>
<tr>
<td>Sarcoma in Vonreclkin</td>
<td>6</td>
</tr>
<tr>
<td>Neurofibroma</td>
<td>5</td>
</tr>
<tr>
<td>Benign chondroma</td>
<td>3</td>
</tr>
<tr>
<td>Eosinophilic granuloma</td>
<td>2</td>
</tr>
<tr>
<td>Chondroma-Chondrosarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>1</td>
</tr>
<tr>
<td>Tuberculoma</td>
<td>1</td>
</tr>
<tr>
<td>Adenoma</td>
<td>1</td>
</tr>
<tr>
<td>Giant cell tumor</td>
<td>1</td>
</tr>
</tbody>
</table>

**DR. GARLAND:** These are from the radiologists; they were just based on the history and gross description, and spread all over the place. They are not based on any factual material.

### Pathologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
</tr>
</thead>
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<tr>
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</tr>
<tr>
<td>Polyostic fibrous dysplasia</td>
<td>2</td>
</tr>
<tr>
<td>Hemangioendothelioma</td>
<td>2</td>
</tr>
<tr>
<td>Hodgkin's sarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Eosinophilic granuloma</td>
<td>1</td>
</tr>
</tbody>
</table>

**DR. BENNETT:** Since the pathologists had a slide and the radiologists did not have a film, the pathologists should have won out on this case. Fifty-eight pathologists made the correct diagnosis. The two diagnoses of polyostic fibrous dysplasia are difficult to understand. Perhaps someone was overly impressed with that "cafe au lait" patch on the skin. There is nothing to support the one diagnosis of eosinophilic granuloma or the diagnosis of Hodgkin's sarcoma.

**DR. GARLAND:** Is this lesion a benign lesion, Dr. Bennett?

**DR. BENNETT:** I think that it is a benign lesion, insofar as any metastasizing qualities are concerned. However, these lesions can be extraordinarily persistent in local...
growth unless they are completely removed. You will notice that in this instance two ribs were involved. We have had other instances in which more than one rib has been involved.

DR. GARLAND: One often sees in roentgenograms of the spine, especially lateral films, vertebrae with vertical striations and they are called hemangiomas. They are frequently multiple. Do you know if that conclusion is warranted, Dr. Bennett?

DR. BENNETT: We have seen hemangiomas of the vertebra but not too frequently.

DR. HALPERT (Houston, Tex.): I think that this lesion is probably an anomaly rather than a neoplasm. Such hemangiomas as this occur frequently in the liver. Their structure is identical with this and if the radiologists see these frequently they probably are malformations which may later become exaggerated when the patient becomes older.

DR. RUSSELL: I might add, Dr. Halpert, that there is a disease in cattle, in animals which are being stuffed with high concentrates of grain when they are putting on unusual amounts of weight, in which they have breakdown of the sinusoids and formation of small hemangiomas in all parts of the liver. These go on, in some places, to become large cavernous hemangiomas and actually become infected with bacteria from the gastrointestinal tract. I think it's a good point you make for it not being a truly malignant tumor or a truly neoplastic state, but I think that there are many of them which are. Don't you, Dr. Bennett?

DR. BENNETT: Yes, I think so and I believe that the present lesion is a tumor. When one tries to define a tumor one frequently finds it has led to hopeless difficulty. However, I would make a distinction between this particular lesion and the telangiectases that you sometimes see involving bone as well as other tissues. I don't know how many of your sections showed this, but parts of the lesion in my slides were quite cellular at the periphery. Many of the capillaries had not opened up. It is true that most of the tissue which I showed in the photograph contained markedly dilated, thin-walled capillary spaces. But this was a growing lesion and one which was slowly extending through the bone, as hemangiomas frequently do.

DR. RUSSELL: What do you think the prognosis is, Dr. Bennett?
DR. BENNETT: Well I think the prognosis is excellent, provided the whole lesion was excised. That goes for a wide variety of lesions such as fibromas of bone, ossifying fibromas of bone, hemangiomas of bone; provided the lesion is totally extirpated, the prognosis is excellent. In this particular instance I conferred just recently with Dr. Saphir, who was the contributor of the case. The patient has been checked and there is no evidence of recurrence of the process. No other lesions have been discovered anywhere else in the bone.

DR. RUSSELL: Dr. Garland, I would like to ask if you would comment about roentgenotherapy in these lesions. The sensitivity of endothelium for radiant energy is well known. It would seem reasonable that you could control it with radiation.

DR. GARLAND: Well of course the small cutaneous hemangiomas of childhood are notoriously radiosensitive. Many will disappear spontaneously; the remainder are helped by radiotherapy. Now, we have treated seven cases of benign hemangioma of the vertebral body in which symptoms were apparently attributable thereto, either symptoms of pain or cord pressure from presumed or established posterior expansion. Most obtained pain relief - perhaps partly psychogenic. Some showed a little recalcification in the vertebral body. In others the vertebral body was totally unchanged. The doses were small - about 600 r tissue in 4 days, sometimes repeated at monthly intervals for three courses.

DR. HERTZOG (New Orleans, La.): Dr. Bennett, how often do hemangiomas involve multiple bones?

DR. BENNETT: I cannot give you any reliable figures. They are much more common in a single bone. Have you had any experience with it? Would you care to report it?

DR. HERTZOG (New Orleans, La.): Only one case where the question came up whether they were metastases. This one case had multiple lesions and the question came up whether they were disseminated metastases or just single isolated lesions. Histologically they were isolated lesions.

DIAGNOSIS: Hemangioma of rib.
A white man 57 years of age experienced recurrent attacks of pain in the left elbow which became progressively more severe. On examination the left upper arm was enlarged, indurated and slightly warm at its lower end. After biopsy the arm was amputated.

DR. GARLAND: Well here we have a destructive lesion involving a portion of the cortex of the humerus on its lateral aspect in its distal one-third, with quite a bit more periosteal reaction than is visible in this reproduction. In examining the original film with a hand lens and a bright light, one could detect quite a bit of periosteal reaction extending up the shaft. There is also evidence of some soft tissue swelling, but not as much as the clinical examination reported. Well, we have a destructive process with more soft tissue swelling than is common in osteomyelitis. Therefore I think first of bone tumor, and of malignant bone tumor because of the amount of destruction. My first diagnosis would be sarcoma, reticulum cell. But I wouldn't be surprised if it turned out to be Ewing's. I would be very much astonished if this turned out to be an inflammatory process or an eosinophilic granuloma.

DR. BENNETT: The initial biopsy in this case was regarded as a malignant tumor arising in bone and since there were no lesions suggestive of metastases the surgeon elected to amputate the arm.

The colored photographs before you indicate the gross appearance of the tumor. There is bone destruction and extensive invasion of the soft tissue around the lower one-third of the humerus.

These photomicrographs will recall to you the histologic features of the lesion. It is a highly cellular tumor composed of small round or oval shaped cells. In the reticulum stains there is no evidence that the tumor cells are forming intercellular substance. We have been impressed with the nuclear configuration and the granular cytoplasm in many of the tumor cells. It is my belief that this tumor has arisen from the marrow and that the cells bear a certain resemblance to myeloid series cells.
My own diagnosis is myelosarcoma.

I have been informed just recently that the patient died in another hospital in recent weeks. However, I was unsuccessful in obtaining further follow-up information before leaving Chicago.

DR. RUSSELL: Are there general discussions on this case?

DR. GARLAND: If Dr. Bennett were approached by three pathologists, all of whom diagnosed this case as reticulum cell sarcoma, would he still stand by this term myelosarcoma?

DR. BENNETT: Yes, I think I would stand by the diagnosis, unless they were armed very heavily. I will admit, however, that it is very difficult to take a single position and defend it conclusively. However, in this tumor, the cells are not doing the things that cells in a reticulum cell sarcoma should do. The slight variations in cells that we see here are not of the type which one sees in the typical reticulum cell sarcoma. Also I think that the behavior of this tumor has not been in keeping with that of a reticulum cell sarcoma. I am unable to believe that it falls within the Ewing’s group, the cytologic pattern is a bit different from that of Ewing’s sarcoma and personally I have never seen a tumor that I was willing to designate as Ewing's sarcoma in a patient of this advanced age. I whispered to Dr. Russell here a moment ago asking him if he remembered the case and whether he would care to comment on what he thinks the tumor is.

DR. RUSSELL: It was agreed, when this case was reviewed at our departmental conference, that this was a tumor of marrow origin; a myeloid tumor. I should like to bring up for a matter of general discussion the question raised by Dr. Bennett of reticulum cell sarcoma of bone, since you stated that you had not seen many which you thought were primary in bone. If that is true, I am guilty of making a wrong diagnosis probably several times. As you know, the first cases of this disease were reported by Dr. F. Parker, Jr., my former Chief at the Mallory Institute of Pathology in Boston.

DR. BENNETT: I have had little experience with reticulum cell sarcomas in bone. That was the reason I made the comment to you initially. Until that time we had not seen
a tumor in our own series of cases which we were willing to
call a reticulum cell sarcoma of bone. As a matter of fact,
in the preparation of material for a seminal in 1953 we have
found it necessary to obtain our example from the A. F. I. P.

Opinion concerning reticulum cell sarcoma varies over the country. We have had some in-
stances of tumors in childhood in which the cells have been
larger than those of the usual Ewing's sarcoma. The nu-
clear pattern has been a little bit different from that which
you expect to see in the Ewing's sarcoma. For our own
satisfaction we have sent sections from some of these cases
to other pathologists. This has not been too helpful because
the diagnoses which have come back have varied to include
both reticulum cell sarcoma and Ewing's sarcoma. It seems
evident, therefore, that opinion on just what a reticulum cell
sarcoma is is a bit varied at the present time. For those
reasons we are willing to accept as a reticulum cell sarcoma
only those tumors in which there is a certain degree of pleo-
morphism of the cells and in which there is a definite rela-
tionship between reticulum fibers and tumor cells. In in-
stances of Ewing's sarcoma and in the present case, which
I prefer to call a myelosarcoma, there is no evidence of any
intercellular substance being formed by tumor cells.

DR. RUSSELL: Now could we have general dis-
cussion on this? I'd like to ask Dr. Severance if he has any
comments.

DR. SEVERANCE (San Antonio, Tex.): I disagree with the
reticulum cell sarcoma diagnosis.

DR. HALPERT (Houston, Tex.): I don't agree with Dr.
Bennett's diagnosis, rather than that of a reticulum cell
sarcoma. I don't know, however, why we have to tread
so lightly around not calling this a plasma cell myeloma.
Actually there are a lot of plasma cells, neoplastic plasma
cells, in this tumor and along with it are all those granul-
cytes and I think it is just a matter of being a neoplasm of
marrow where perhaps the granulcylic precursors are
more numerous than in the ordinary plasmacytoma where
they overshadow the rest of it.
DR. ABBOTT (Houston, Tex.): Could you classify this tumor along with the chloromas found in other places in the body?

DR. BENNETT: With respect to what Dr. Halpert said, of course you never can argue too convincingly on the basis of a single case. However, the behavior of this tumor, the localized site, is a little different from what you expect to see from a plasmacytoma. It is an infiltrative tumor, infiltrating the soft tissues, and there was no evidence of any spread to any other part of the skeleton, and no substantiating features for plasma cell myeloma.

On the question about chloroma - I think that is a good question. This tumor did not have the color of a chloroma and there was no evidence of tumor in any other skeletal part and there were no circulating myelocytes or other cells of the myeloid series.

DR. HOUSMAN (San Antonio, Tex.): I think there is one histologic feature here which supports the diagnosis of Dr. Garland. If you look at the cells carefully, many of them have a short point, slightly bent at the tip. These have been described as being very characteristic of reticulum cell sarcoma.

DR. GARLAND: Dr. Bennett, the literature suggests that the prognosis of treated reticulum cell sarcoma, treated either by resection or by local radiotherapy, is not too bad. What's the data on the myelosarcomas?

DR. BENNETT: Well I would say that this type of tumor is so uncommon that statistical data is not likely to be helpful. I think that this is an extraordinarily uncommon tumor. I noted the cells which were referred to as having small points on them. I must say that we had many sections processed with many different stains and, while the diagnosis of reticulum cell sarcoma was regarded as a possibility on the initial study, we felt forced to give up this possibility. I think the predominant cell is a myeloid cell. For this reason it is my preference to designate the tumor as myelosarcoma and not a reticulum cell sarcoma. If it is true that reticulum cell sarcoma has a reasonably good prognosis, then I think it is important not to mix the present tumor in with that group of neoplasms.
DR. RUSSELL: If there are no further discussions, let's go to the radiological diagnoses as sent in.

Radiologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>Osteogenic sarcoma</td>
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</tr>
<tr>
<td>Fibrosarcoma</td>
<td>6</td>
</tr>
<tr>
<td>Ewing's tumor</td>
<td>4</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Synovioma</td>
<td>1</td>
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</table>

DR. GARLAND: A great many were impressed with the features of malignant tumor here, especially the physical description, so I can understand the diagnoses of osteogenic sarcoma and fibrosarcoma; Ewing's tumor also. Synovioma I don't understand. I am happy to see no diagnoses of osteomyelitis.

Pathologists' Diagnoses Tabulation

<table>
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</thead>
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<td>Malignant lymphoma:</td>
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<td>(Retic. cell, lympho. etc.)</td>
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</tr>
<tr>
<td>Myeloma:</td>
<td>15</td>
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<tr>
<td>(Myeloid, leukemia, etc.)</td>
<td></td>
</tr>
<tr>
<td>Ewing's sarcoma</td>
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</tr>
<tr>
<td>Plasmacytoma</td>
<td>3</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Osteosarcoma, pleomorphus type</td>
<td>1</td>
</tr>
</tbody>
</table>

DR. BENNETT: There was a wide range of interpretations given here and Dr. Russell took some editorial license in grouping some of the terms together. Thus we have 34 votes for a tumor of the malignant lymphoma group. Myeloma, including myeloid leukemia, runs second with 15 votes; Ewing's sarcoma came in for 5; plasmacytoma for 3; sarcoma 2; osteosarcoma, pleomorphus type for a single vote. It is evident that we haven't established any substantial agreement on designation in this case and it is my own preference to continue to regard the lesion as a myelosarcoma.

DIAGNOSIS: Myelosarcoma.
CASE 105

A white boy 15 years of age experienced progressively severe dull pain above the left knee, with swelling and inability to extend the leg. The knee was markedly enlarged and partially fixed in flexion. A supracondylar amputation was performed.

DR. GARLAND: This case is one with an extensive bone-producing lesion in the distal end of the femur, with much calcification in the soft tissues and a fairly large soft tissue mass (if you examine the films with a bright light). It looks like a primary bone tumor; it certainly looks like a malignant tumor; the label we would give it is osteogenic sarcoma. Some of our colleagues would worry about chondrosarcoma and so forth but those are refinements which I don't think the radiologist can attain with this limited data. Therefore the diagnosis is osteogenic sarcoma.

DR. BENNETT: This was a photograph showing the soft tissue swelling over the lower end of the femur. I think it is important to recognize that even with a small tumor within bone there may be a good deal of soft tissue swelling.

This is a photograph of a hemisection of the lower end of the femur. (If you will re-project the roentgenogram which Dr. Garland showed on the other screen, I think it may be possible to make some interesting comparisons).

You can see this area of marked condensation which corresponds quite accurately with this zone of ebornated bone. However, in this region here, which appears a bit "lytic" in the film, we found an undifferentiated type of osteogenic sarcoma in the sections. Elsewhere it is a sclerosing osteogenic sarcoma. The hemorrhage is due to the biopsy.

I am sure that you will recall many fields of varied histologic composition. In some areas there was abundant imperfectly formed osteoid between tumor cells, many large multi-nucleated giant tumor cells and a high degree of vascularity.
This is a large celloidin section through a similar tumor. It helps, I think, to explain the way an osteogenic sarcoma of this sort makes its way through the cancellous spaces. At the periphery it is apt to be very highly cellular as we see it here, with the nucleii giving the dark stain. The formation of new bone is a little slower in development. Here is subperiosteal elevation where the tumor has broken through the cortex. The epiphyseal cartilage plate may be invaded and in time the epiphysis is involved.

In this photograph of higher power one sees the cellular parts extending through the marrow spaces. We could go on with a group of a half dozen or more slides showing the varying histologic features of different types of osteogenic sarcoma but I think, to save time, we should pass those.

DR. RUSSELL: This case is open for general discussion. (NONE) Let's have the roentgenological diagnoses which were submitted.

Radiologists' Diagnoses Tabulation

Osteogenic sarcoma 34
Ewing's tumor 3
Calcified hematoma 1
Synovitis 1
Fibrosarcoma 1

DR. GARLAND: Well most agreed with osteosarcoma. Why some diagnosed Ewing's I don't know, with quite so much bone production and such an extensive lesion. The calcified hematoma perplexes one. Synovitis is totally unexplainable; and fibrosarcoma I wouldn't understand that with bone production. But on the whole the batting average, I think, was pretty good.

Pathologists' Diagnoses Tabulation

Osteogenic sarcoma 54
Chondroblastic sarcoma 2
Ewing's sarcoma 1
Osteomyelitis 1
Synovioma 1
DR. BENNETT: The pathologists have a good batting average on this case; 54 having called it an osteogenic sarcoma; 2 a chondroblastic sarcoma. Actually in most examples one can find a certain amount of tumor tissue differentiating a bit more like cartilage than like bone, but I don't think that is any reason for pronouncing it a chondrosarcoma. Ewing's sarcoma (1 vote) is difficult to understand because in all parts of the tumor which I examined there was evidence of the formation of intercellular substance; the cells were not uniform or closely packed as they are in Ewing's. I cannot understand the diagnosis of osteomyelitis (1 vote) and certainly I cannot understand the diagnosis of synovioma. My own diagnosis on this case is sclerosing osteogenic sarcoma.

In recent years, in our own hospital, we have had 19 cases of osteogenic sarcoma. Thirteen of these have been in male patients and 6 in female patients. Three patients, all over 50 years of age, had Paget's disease. Of these 19 verified cases, 14 have died of the neoplasm, one is living and well after 11 years following the amputation; one is living and seemed well for seven years. Recently, however, I was informed that multiple densities in the lung fields had been discovered in this patient. Three patients are living and well for periods from one to three years after treatment.

Some writers have listed five year survivals running as high as 20 or 25%. Others have given figures of five year survivals below 10%.

DR. GARLAND: Your figure is agreed with by McDonald in his analysis of the cases from the Bone Sarcoma Registry. They had a 12% survival in a fair number of cases.

DR. RUSSELL: Could you give us anything of a follow-up on this case, Dr. Bennett, since you submitted it?

DR. BENNETT: Amputation was performed and death from metastases occurred after an interval of six months. This was eight months after the onset of the symptoms.

DR. HALPERT (Houston, Tex.): I should like to ask Dr. Bennett how many of his cases occurred, or how many cases he knows of in which osteogenic sarcoma occurred, in the first decade of life; and whether all of his cases were unicentric
in origin. Dr. Hatfield Brucer and I published a case of a child where there was multicentric origin of osteogenic sarcoma in a child in the first decade of life.

DR. BENNETT: In the group on which I commented, only one case fell within the first decade, this was in the last year of the first decade. With respect to the multicentric foci of development, I have not seen an instance of this. I think it must be exceedingly rare.

DIAGNOSIS: Osteogenic sarcoma.
CASE 106

A white man 36 years of age experienced gradual, painless swelling in the right knee following an accident sixteen years previously. Arthrotomy was performed and numerous fibrous bodies were found which were removed together with the synovia, patella and the medial and lateral cartilages.

DR. GARLAND: The appearance is one of synovial effusion or synovial thickening. There is displacement of the retropatellar triangular pad of fat.

Lo and behold, nine years later he's alive and well enough to have an x-ray; he has enormous synovial distension this time; posteriorly you see displacement of the retrocapsular fat shadow by a large mass. Now what could a patient have that goes for nine years? Chronic tuberculous synovitis with such tremendous soft tissue changes and no more bone changes than the slight osteoporosis he had would be phenomenal. A benign synovioma would hardly have escaped the surgeon all this time. What might this curious synovial disease be? We believe it to be so-called "villonodular synovitis".

A pneumo-arthrogram was made but does not add anything in particular. It does perhaps rule out any periosteal reaction along the cortex here where we might have missed it in the previous film, but I don't think the air study in this particular case is of great diagnostic benefit.

DR. BENNETT: Well, as you see from this Kodachrome, Dr. Garland's interpretation is correct. This is a lesion which usually is called pigmented villonodular synovitis. Here we see the articular surface of the patella, quite well preserved but surrounded by this tremendous overgrowth of synovial tissue with large villous projections. Some parts of the synovia are nodular. It is stained brown because of siderotic pigment.

Another photograph to show some of the extension of these polypoid-like masses which account for the tremendous widening of the articular space.
And here is a single photomicrograph.

In this case I made only one because it is quite similar to many others which we have studied. I thought we might use this case as a point of departure for a brief discussion of reactive and neoplastic lesions of synovia.

(At this point Dr. Bennett showed some examples of synovitis, giant cell tumors of tendon sheath and synovial sarcomas.)

DR. RUSSELL: Can we go directly to the diagnoses now, as submitted by the radiologists.

Radiologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
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</thead>
<tbody>
<tr>
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<tr>
<td>Synovioma</td>
<td>13</td>
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<tr>
<td>Osteochondromatosis</td>
<td>4</td>
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<tr>
<td>Giant cell tumor</td>
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<tr>
<td>Chronic post-traumatic arthritis</td>
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<tr>
<td>Tuberculosis</td>
<td>1</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Infec. with cartilaginous changes</td>
<td>1</td>
</tr>
</tbody>
</table>

DR. GARLAND: Well the radiologists, I think, were batting pretty high on this one. Both villonodular synovitis and synovioma, I think, are acceptable terms. Osteochondromatosis, I think, was ruled on by the final description. Giant cell tumor - no; chronic post-traumatic arthritis; T.B.; sarcoma; and infection - no. I don't see why they include that. I think that 28 out of the 39 diagnoses submitted were pretty close to the true entity. Thank you Mr. Chairman.

Pathologists' Diagnoses Tabulation

<table>
<thead>
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<th>Diagnosis</th>
<th>Count</th>
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<tbody>
<tr>
<td>Villonodular synovitis:</td>
<td>51</td>
</tr>
<tr>
<td>(Synovitis, etc.)</td>
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<tr>
<td>Xanthoma type synovioma</td>
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</tr>
<tr>
<td>Synovial sarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Chronic bursitis of Jaffee</td>
<td>1</td>
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</tbody>
</table>
DR. BENNETT: Well I notice that almost all pathologists gave a correct diagnosis, with 51 calling it villonodular synovitis. I would like to know, specifically, what was in the minds of those who called this lesion a synovioma. The five who made this diagnosis should at least have designated the lesion benign. Xanthoma type of synovioma, recorded twice, is a descriptive differentiation that probably is of no great consequence. Synovial sarcoma - I'm unhappy to see this diagnosis listed here because the process is not a malignant tumor.

DR. BRINDLEY (Galveston, Tex.): I would like to ask Dr. Bennett to clarify the relationship of the so-called giant cell tumors with benign giant cell tumors of tendon sheath in this series.

DR. BENNETT: It is my belief that there is a group of productive lesions within the synovial membrane of the large joints which are benign neoplasms. These should be called benign synoviomas. One can match this lesion with giant cell tumors, so-called benign giant cell tumors of tendon sheath origin. I think the only significant difference is brought about through the compression of the tendon sheath tumor against rather resistant structures, either against the tendon itself or perhaps between the tendon and the bone which molds it into a more compact and more sharply circumscribed tumor nodule. From our experience we believe that the benign giant cell tumor of tendon sheath is a neoplasm. This tumor needs to be removed completely because they have a tendency to recur and, like quite a number of tumors including the giant cell tumors of bone, recurrent lesions are frequently more aggressive than the first lesion. I have seen instances in which it was no longer possible, with a purely local operation, to remove the lesions. The same thing happens with the large tumors inside the joints, even though they are more diffuse or bulky. It is my feeling that, histologically, they are basically the same as the giant cell tumors of tendon sheath. They do have the capacity of recurring when incompletely removed and indeed in some instances they may actually invade bone and invade beneath the perichondrial border to produce a lesion which is difficult to remove in its entirety.

DIAGNOSIS: Pigmented villonodular synovitis.
CASE 107

A white boy 7 years of age developed pain in the left knee which disappeared and recurred three years later, with swelling and drainage of apparently purulent material. Following biopsy, the left leg was disarticulated at the hip.

DR. GARLAND: It was my impression that here was an extensive destructive lesion in the middle two thirds of the shaft of the femur. Periosteal changes are gross. There is a larger soft tissue mass than is ordinarily seen with osteomyelitis. Therefore, we think of tumor, bone, malignant. The most common tumor, bone, malignant that would do this in a person of this age and with this history is Ewing's tumor. The next might be a bizarre metastatic neuroblastoma and the last would be a bizarre lymphoma. Occasionally, a severe Hodgkin's disease or localized leukemia in bone can do this, but that's exceptional. My own diagnosis is Ewing's tumor. I won't be a bit astonished if it turns out to be a metastatic neuroblastoma, but I think that's unlikely from the history.

DR. BENNETT: We will go directly to the photographs. This is the appearance of the extremity. There is a good deal of atrophy in the muscles of the leg and a considerable degree of swelling over the lower aspect of the thigh.

As the record pointed out, a disarticulation amputation was performed. My first contact with this patient came in the operating room where I was asked to look at some of this soft greyish tissue which we see here, which had been exposed. I was asked to do a frozen section. This obviously was a neoplasm, obviously it was malignant. We see the destructive changes in the lesion. These correlate very well with the film reproduction before you. Actually there was a pathologic fracture with a great deal of hemorrhage into the deep lying portion of the tumor adjacent to bone. Down here we see some areas of condensation of bone and here we see areas of reactive bone proliferation which is not, as it turns out in this case, the production of bone by tumor cells. This formative reaction represents the periosteal overgrowth.
Here is an enlarged photograph. The marked destructive changes in the bone shaft and the fusiform swelling produced by the tumor mass beneath the periosteum is well shown. This tumor tissue is soft, friable, almost gelatinous in quality and it is easily pulled apart in the preparation of histologic sections.

At this time I would like to apologize to you for the preparation of the slides on this case. We have the habit in our place, after having taken what we think are suitable samples of tissue for histologic study, of freezing the specimens and sawing them in the frozen state. Those of you who attended the recent meetings in New York may have seen excellent preparations made by sawing the unfrozen tissue and that is accomplished by getting the saw to run at the right speed. But, in freezing a certain specimen and then taking that frozen tissue for histologic examination, you find a tremendous distortion of the structural features. Unfortunately the first block of tissue which was sent to Dr. Russell was from frozen material. Later, when we discovered the error, we sent on a paraffin block and those of you who limited your examination to the paraffin section were better off.

Histologically this is a highly cellular tumor mass. It has a uniform cytologic pattern. The cells are made up mainly of nuclei having prominent nucleoli. There is very little cytoplasm. Next slide please -

There is a small amount of connective tissue partioning the tumor mass.

We classified this tumor, as did Dr. Garland, as an example of Ewing's sarcoma.

DR. RUSSELL: Discussion on the case that was presented. Would the radiologists like to comment?

DR. KOENIG (Ft. Smith, Ark.): I wonder if Dr. Bennett would care to discuss the relationship of a Ewing's sarcoma and metastatic neuroblastoma. I believe you are aware of Willis' statement that there is no such thing as Ewing's sarcoma.
DR. BENNETT: Yes, I have heard Dr. Willis comment on this problem. I am sure that all of us have the greatest respect for Dr. Willis and for most of his opinions. In this particular instance, however, I simply cannot agree with the idea that Ewing's sarcoma is a metastatic neuroblastoma. We have had several instances in which we have had complete post-mortem studies. Careful examination of the peripheral osseous lesion and examination of the adrenal glands and of all other tissues failed to reveal neuroblastoma.

DR. RUSSELL: Would you care to give the pathologists some of the criteria you use in a histologic differentiation of neuroblastoma and the Ewing's myeloma?

DR. BENNETT: The neuroblastoma, if it is a well differentiated tumor, presents the rosette structure and often there are tufts of fibrilli within these rosettes. In the less well differentiated tumors, of course, one sees a cellular neoplasm that histologically may be quite indistinguishable from the Ewing's sarcoma. I think that every one of these cases deserves a most careful examination to prove it is or is not a neuroblastoma with osseous metastasis. The subsequent developments in Ewing's sarcoma following radical operative procedures or x-ray treatment procedures has been uniformly bad in our experience. I checked over the cases which we have seen in the last few years. There were eleven cases of Ewing's sarcoma. Six of these were in male children and five were in females. The ages ranged from 7 1/2 to 19 years of age. Most of these cases were treated by radical operative procedures but a few of them were treated by local resections. In all instances the tumor led to a fatal outcome. Death occurred in from 3 to 24 months after the tumor was recognized and in periods ranging from a few weeks to thirteen months after therapy.

DR. GARLAND: Dr. Bennett, I think it is advantageous for the clinician to know whether a given lesion is Ewing's or metastatic neurocytoma. There are a small number of cases of authenticated Ewing's in the literature which were salvaged for five years or more by radical radiotherapy; we have two (one for 11 years, one for 5). But no neurocytomas, in our experience. Radical radiotherapy has a moderate place in Ewing's if the lesion isn't too extensive. One ought to treat the whole bone, and try to put about 4,500 roentgens into it in a period
of four weeks. Now if it's a metastatic neuroblastoma I doubt if more than 2,000 roentgens is warranted. First of all, that dose will give pain relief and shrinkage of the tumor and secondly, if the child lives a few years, and gets a recurrence, you can retreat after such dosage. So that I would urge you to try and distinguish them and to treat selected cases of Ewing's by radical whole bone radiotherapy, and metastatic lesions by moderate palliative dosage.

DR. RUSSELL: I would like to ask Dr. Bennett if he agrees that this is a generalized disease, like you would consider a disease of multi-centric origin. I believe that was your idea was it not, Dr. Garland?

DR. GARLAND: Well, Ewing's is almost like myelomatosis at times. You see cases in a phase of one bone involvement; later many show multiple bone lesions in a certain period of time, but most with or without visceral lesions.

DR. BENNETT: In our experience we have seen a number of instances in which the process was generalized in the skeleton. It is my impression, however, that Ewing's sarcoma begins as a solitary lesion in bone. The most common site of metastases, in our experience, has been the lungs.

UNIDENTIFIED PARTICIPANT: I'd like to ask if anyone feels that the history of this patient for three years previously had anything to do with the present lesion.

DR. BENNETT: We went into that with a good deal of care at the time the patient was first seen. It is my impression that we concluded, despite the rather striking history of draining sinus and something that pointed to an infectious process, that the initial lesion was separate and apart from the tumor and that this was a coincidence rather than an example of one lesion leading to another type of lesion.

DR. HALPERT (Houston, Tex.): Isn't it true, Dr. Bennett, that the neuroblastoma as it metastasizes is more apt to involve the cranial bone and the Ewing's sarcoma would arise more in the peripheral extremities rather than involve the cranial parts? That might be an eventual feature sometimes.
DR. BENNETT: I think that is true as a general rule. Also I think that lymph node metastases are much more prevalent in cases of neuroblastoma than in Ewing's sarcoma.

Radiologists' Diagnoses Tabulation

- Ewing's tumor: 29
- Osteogenic sarcoma: 8
- Neuroblastoma: 2
- Myeloma: 1
- Tubercular osteomyelitis: 1
- Fibrosarcoma: 1
- Osteomyelitis: 1

DR. GARLAND: Well this one shows a good batting average. It is acceptable for the radiologist to diagnose the lesion as osteogenic as long as he diagnoses it a malignant bone lesion. Two neuroblastomas, that's interesting; one myeloma, I don't understand that; and the other three ought to be turned in to the F. B. I.

DR. BENNETT: The third from the last diagnosis (tubercular osteomyelitis) might well have been forthcoming because of the history suggesting an infectious lesion.

DR. GARLAND: Granted, but I think that the good pathologist and radiologist ought to be just as discriminating in analyzing histories as he is other pieces of information. We all know how misleading the history can be. Here we have obvious findings of a wide-spread destructive process with much soft tissue swelling.

Pathologists' Diagnoses Tabulation

- Slide 2: Ewing's sarcoma 42
- Slide 1: Metastatic neuroblastoma 20
- Reticulum cell sarcoma: 1
- Chondrosarcoma: 1

(NOTE: Not all pathologists made diagnoses)
DR. BENNETT: I'm afraid a good many of the pathologists were upset by the poor slide which I referred to before. That is a wretched slide from that block of tissue which had been frozen. Therefore, in having this slide (diagnoses tabulation) made up this morning, I asked that Slide No. 2 be listed first. This list refers to the paraffin section and we see that 42 of the 61 who replied called that a Ewing's sarcoma. However, in Slide No. 1, which is the section of bone, 20 thought that that might be a metastatic neuroblastoma; 1 reticulum cell sarcoma; 1 chondrosarcoma. I didn't think the slide was that bad but it is obvious that, since not everyone replied, there was some degree of confusion over this specimen.

DIAGNOSIS: Ewing's sarcoma.
CASE 108

A white woman 66 years of age noted a small mass over the left scapula which gradually enlarged over a period of two years without becoming painful. A large segment of the left scapula was excised and during the next 18 months two recurrent tumors from this region were removed. The tumor tissue was composed of peripherally firm and centrally necrotic substance.

DR. GARLAND: This was really a tough case - a large tumor in a large lady.

On the left you can see what we could salvage out of the A.P. material sent us via Dr. Russell. There is questionable destruction of the caudal end of the scapula. In a sagittal view of the scapula, there is obvious decalcification; it looks somewhat like a chondromatous change, but the soft tissue mass doesn't have any of the earmarks of a chondroma or an osteochondroma. Therefore one reaches the possibility of a large soft tissue tumor invading the scapula rather than arising in it. A tumor of such proportions makes you think of a liposarcoma and I think you would be wise to stop there. Lipoma or liposarcoma. I have not seen lipomas produce quite as much bone destruction as this and therefore I would think of liposarcoma. Now if you want to throw in adjectives like fibro, myxo, hemangio and what not (which pathologists like to do) you may do so, but I think the essential entity is liposarcoma.

DR. BENNETT: I took only a single photomicrograph of this lesion because it was all pretty much alike. It is a tumor made up of cartilage cells arranged in groups and clusters with a considerable amount of a rather dense, well-formed connective tissue stroma, supporting the lobules by cartilagenous tissue. This neoplasm was described in the information which came to me as being a very large tumor mass. From this and the interpretation which was given to the radiologic findings I envisioned, possibly erroneously from what I have just seen of the films, a tumor which had arisen in a cartilagenous exostosis or osteochondroma. I believe that was the impression which was held by the contributor.
(At this point Dr. Bennett presented a classification of benign and malignant tumors of cartilage. This was illustrated with x-rays, gross photographs, and photomicrographs.)

DR. BENNETT: The case under discussion, Case 108, is, in my estimation, a chondrosarcoma. It is possible, indeed probable, that it arose in a pre-existing osteochondroma.

DR. RUSSELL: Dr. Lyons is present. I'd like to ask if there is any further follow-up on this case.

DR. LYONS (Wichita Falls, Tex.): Nothing more, Dr. Russell, than that which I had submitted to Dr. Garland. The patient had two recurrences, both of which were quite large.

Radiologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Diagnosis</th>
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</tr>
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<tbody>
<tr>
<td>Chondrosarcoma</td>
<td>15</td>
</tr>
<tr>
<td>Fibrosarcoma</td>
<td>12</td>
</tr>
<tr>
<td>Liposarcoma</td>
<td>4</td>
</tr>
<tr>
<td>Recurring giant cell</td>
<td>2</td>
</tr>
<tr>
<td>Myeloma</td>
<td>2</td>
</tr>
<tr>
<td>Myxochondroma</td>
<td>1</td>
</tr>
<tr>
<td>Angiosarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Neurosarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Metastases to scapula</td>
<td>1</td>
</tr>
</tbody>
</table>

DR. GARLAND: Well I see that my colleagues did a better job and labelled it, rightly, chondrosarcoma in the majority of cases; fibrosarcoma next, liposarcoma next. Recurring giant cell I don't understand. The incidence of chondrosarcoma is, in our experience, greater than that of liposarcoma; the large size of the tumor is equivocal.

Pathologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Diagnosis</th>
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</thead>
<tbody>
<tr>
<td>Chondrosarcoma</td>
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</tr>
<tr>
<td>Chondroma</td>
<td>5</td>
</tr>
<tr>
<td>Chondromyxosarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Osteochondroma</td>
<td>2</td>
</tr>
<tr>
<td>Ewing's</td>
<td>1</td>
</tr>
</tbody>
</table>
DR. BENNETT: The pathologists have agreed quite well on this specimen, with 53 votes for chondrosarcoma. I am unable to explain the proposal of Ewing's sarcoma - perhaps the slides became mixed.

DR. HALPERT (Houston, Tex.): I wonder whether Dr. Bennett really meant it or thought that this arose in a cartilagenous exostosis or osteochondroma of the scapula and then became a malignant growth, the chondrosarcoma. Cartilagenous exostosis of the scapula is very rare. Some twenty years ago I reviewed the literature and added two cases to the less than twenty which had been reported to that date and not many have been reported since. Wouldn't it be simpler just to assume that this was a chondrosarcoma. In the description, Dr. Bennett frequently referred to those chondrosarcomas which seem to be undifferentiated, as he described them, and which, in fact, perhaps resemble more embryonal cartilage. I just wonder whether the term "embryonal cartilage" would be better than "undifferentiated cartilage". Would the two, perhaps, be the same thing?

DR. BENNETT: As I explained, I was in Chicago and the films and other material were elsewhere. All I had to go on was the information which Dr. Lyons was good enough to send me. It seemed reasonable to believe that this sarcoma may have originated in an osteochondroma. This was the reason that I selected the case for the seminar. Actually, now that I have seen the material presented here, I do not know just how this tumor developed, but I feel certain that it is a chondrosarcoma. With respect to terminology, I am a little bit more in the habit of speaking of degrees of differentiation or undifferentiation rather than using such terms as "embryological". I don't think it makes a great deal of difference, as you pointed out, which way you say it.

DIAGNOSIS: Chondrosarcoma, probably arising in pre-existing osteochondroma.
CASE 109

A white woman 61 years of age experienced progressive stiffness in the fingers and toes with subsequent stiffness and pain in the hips, back and shoulders. The patient was hypertensive and endured episodes of auricular fibrillation. The radiological findings were consistent with hypertrophic arthritis and presented only faint circumscribed radiolucencies in the calvarium suggestive of a diffuse metastatic process. The woman expired suddenly four months after first being seen.

DR. GARLAND: We have a plurality of films in this case. Most of the bones show a slight degree of osteoporosis such as would be physiological for a 61 year old person living in California. The extremities showed signs of degenerative arthritis. In the skull there are some areas of decalcification which are not just vascular depressions; they are probably pathologic areas. With her history and with the findings of Bence-Jones proteinuria (and no other general systemic disorders to explain it), I think that this should be a case of multiple myeloma without bone changes, except in the skull. About 10% of cases of multiple myeloma come to necropsy without x-ray evidence of bone tumors, although microscopically they have myelomatous infiltration of the marrow. So my diagnosis, therefore, is multiple myeloma.

She developed a right hydrothorax from a failing heart; whether she had myelomatosis of her myocardium or not, I don't know.

DR. BENNETT: I was rather intrigued by the sections from this case when they first arrived. The first section which came to my attention was a section of the tongue. It showed a marked deposition of a hyaline substance in the muscle and in the submucosal parts of the tongue. Another section showed marked osteoporosis. This, as Dr. Garland pointed out, is compatible with atrophy of old age. However, the marrow within this bone showed a fairly diffuse replacement with uniform cells of the plasma cell type. Next slide -

In this photograph we have a selected field which shows an abundance of cells from this particu-
lar type; cells which have a good deal of cytoplasm, and small round or oval shaped eccentrically placed nuclei. These are the typical cells of the plasma cell myeloma type. However, in this instance there were no solid masses of tumor cells. Our diagnosis is plasma cell myeloma with marked amyloid deposit.

DR. RUSSELL: Would the radiologists like to comment here? I'd like to raise one question and that is the matter of the congo red test. This was reported, as I recall, as of questionable value and there obviously was an extensive amyloidosis at the time of death, at least judging from the section of the tongue that we had. I'd also like to ask Dr. Bennett if, in his experience, he has seen amyloidosis restricted to the tongue in cases of this type.

DR. BENNETT: No, I have not seen it restricted to the tongue in these cases. We have seen instances in which the amyloid deposit in the tongue, thyroid and neck region was very prominent early in the course of the disease. However, when these people come to autopsy there is found, as in this case, widespread amyloid deposition. I have been informed by the contributor of this case that there was widespread deposition of amyloid throughout the body. The anatomic diagnoses which were set forth at autopsy included a) myeloma kidney, b) amyloid deposit in the tongue with macroglossia, c) amyloid deposits in endocardium, myocardium, synovial tissues, subcutaneous tissues, urinary bladder and adrenals.

Radiologists' Diagnoses Tabulation

<table>
<thead>
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<th>Diagnosis</th>
<th>Count</th>
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<tbody>
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<td>Cardiovascular nephropathy</td>
<td>5</td>
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<tr>
<td>Metastatic malignancy</td>
<td>3</td>
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<tr>
<td>Ca. of thyroid with met.</td>
<td>1</td>
</tr>
<tr>
<td>Meig's syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Parathyroid tumor</td>
<td>1</td>
</tr>
<tr>
<td>Carcinoma of ovary</td>
<td>1</td>
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</tbody>
</table>

DR. GARLAND: Well, I'm glad to see that quite a group of them paid good attention to the history in this case. Cardiovascular nephropathy is - well - questionable at least. Metastatic malignancy was not too unreasonable. We unfor-
Unfortunately see some cases of gastric and mammary carcinoma with diffuse osseous metastases but few x-ray changes. Meig's syndrome - well there's no reason for throwing that one in; parathyroid tumor, I don't understand that, nor the carcinoma of the ovary.

Pathologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Slide A</th>
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<tbody>
<tr>
<td>Multiple myeloma</td>
<td>49</td>
</tr>
<tr>
<td>Myeloma</td>
<td>7</td>
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<tr>
<td>Hyperparathyroidism</td>
<td>1</td>
</tr>
<tr>
<td>Focal necrosis related to</td>
<td></td>
</tr>
<tr>
<td>Collagen disease</td>
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</table>

DR. BENNETT: If we combine the first two diagnoses we have 56 with the correct interpretation. Hyperparathyroidism, one vote. I would like to go along with Dr. Garland and forget that anyone named this disorder. I do not understand what is meant by focal necrosis related to Collagen disease. Anyway, it is entirely wrong.

Pathologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Slide B</th>
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</thead>
<tbody>
<tr>
<td>Amyloidosis, tongue</td>
<td>47</td>
</tr>
<tr>
<td>Diffuse scleroderma</td>
<td>2</td>
</tr>
<tr>
<td>Colloid degen. of skin</td>
<td>2</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>1</td>
</tr>
<tr>
<td>Pseudoepitheliomatous hyperplasia</td>
<td>1</td>
</tr>
<tr>
<td>Venous tumor thrombosis</td>
<td>1</td>
</tr>
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</table>

DR. BENNETT: Amyloidosis of the tongue 47; diffuse scleroderma 2; colloid degeneration of skin 2. The last two groups are looking at the same material but interpreting it differently; multiple myeloma (1 vote) must have been carried down from Slide A and not based on the tongue. Someone seems to have been impressed with the epithelial layer overlying the amyloid deposit. I don't recall seeing anything unusual about the epithelium of the tongue, and I don't recall seeing anything unusual about the venous structures. The diagnosis which I recorded on Slide A was plasma cell myeloma; on Slide B it was amyloid deposit and, based on the story given, macroglossia.

DIAGNOSIS: See directly above.
CASE 110

A negro man 26 years of age complained of a progressively enlarging tumor mass in the mid part of the left arm, associated with sharp radiating pain for one year. Radiologic examination showed soft tissue density with irregular calcification in the mid part of the left arm. A forequarter amputation was performed for tumor located within the biceps muscle which measured 8 cm. in maximum dimension.

DR. GARLAND: On this particular case, when the material was sent out to you, there weren't any films available. But, there were films available to me and there was a soft tissue tumor. This looks a little like the ruptured biceps that the beer drinker got in the text-books when you were a student. However, clinically there was a soft tissue mass. The diagnosis lies between benign and malignant process in the soft tissue; fibrosarcoma would be my first thought, then myosarcoma. The location, of course, would be good for myosarcoma, but again that's a refinement we radiologists cannot make. So, therefore, the diagnosis is sarcoma, soft tissue.

DR. BENNETT: I was furnished, by the contributor, with this one Kodachrome showing the location of the tumor and its general configuration. It was described as being a firm, cellular and friable tumor. The sectioned surface was glistening and had a mucinous quality in many parts. Areas of degeneration were noted within the tumor. It was close to the periosteal layer but, as I understand it, was considered not to involve the periosteum or the bone. Actually it is stated to have been located within the biceps muscle. Next please -

I am sure you will all recall this interesting tumor, that is, interesting from the standpoint of the histologic detail. Out near the periphery where the tumor is invading between the muscle fibers, it looks like an ordinary fibrosarcoma. However, in its interior part, particularly, the tumor has an organoid structure with many accumulations of cells around open spaces. Some of these clefts actually are lined with vascular endothelium. Next please -
In some parts the tumor shows the presence of large tumor giant cells which are close to, if not actually lining, these vascular spaces. Then here and there there is a suggestion of a hyalin inter-cellular substance in between the tumor cells.

Finally, if we go to a high enough magnification, we find - under one's own microscope this is more convincing than it is here - homogenous hyalin material. This is interpreted to be osteoid matrix which has been formed by the adjacent tumor cells. The diagnosis which I have recorded is malignant mesenchymal tumor showing prosoplasia and organoid quality; essentially an extra-osseous osteogenic sarcoma.

We have some follow-up information. The operation, I understand, was performed at the end of July, 1951; the patient appeared to be free of metastases and well until mid-September, 1951. In February of this year, seven months after operation, the patient developed a productive cough, pleuritic pain and dyspnea. Films of the chest revealed round areas of solidification in several regions of the lung fields.

DR. GARLAND: Dr. Bennett, please! We are reasonably confused about bone tumors as it is, but to start telling the radiologists who are present about extra-osseous osteogenic sarcoma is going to compound confusion. Would it not be more permissible to refer to it as a soft tissue sarcoma with metaplasia and production of bone, and leave the term "osteogenic" to the malignant sarcomas arising in bone?

DR. BENNETT: Well, I agree with you on the point you are trying to make. You will notice that the diagnosis I gave was malignant mesenchymal tumor. We can stop there if you wish. But I think pathologists should push themselves to make a little more refined histologic diagnosis. Then too, I think one should try to ascertain what are the most differential qualities of the tumor. I think we will all agree that bone forming tumors can and do occur in non-osseous tissues. From the standpoint of significance of the lesion, I don't think it makes a great deal of difference whether we call it a malignant mesenchymal tumor or whether we try and work out a refinement and call it an extra-skeletal osteogenic sarcoma.
DR. RUSSELL: Is there further discussion on terminology?

DR. HERTZOG (New Orleans, La.): I would like to ask Dr. Bennett to define osteogenic sarcoma.

DR. BENNETT: I would define osteogenic sarcoma very simply; a tumor, the cells of which have the potential capacity to form osseous matrix.

DR. RUSSELL: I would like to ask how many cases you have seen of truly extra-skeletal osteogenic sarcoma.

DR. BENNETT: I would have to guess on that. Perhaps a half a dozen in all.

Radiologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrosarcoma</td>
<td>36</td>
</tr>
<tr>
<td>Osteogenic sarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Hemangioendothelioma</td>
<td>1</td>
</tr>
</tbody>
</table>

DR. GARLAND: Well, you see that the majority of them thought of fibrosarcoma. Why 3 of them thought of osteogenic, I don't know. The original film showed no evidence of calcium anywhere in the mass, no evidence of bone or periosteal reaction. The hemangioendothelioma is inexplicable. I still entertain the diagnosis of fibrosarcoma with metaplasia, Mr. Chairman.

Pathologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteogenic sarcoma</td>
<td>13</td>
</tr>
<tr>
<td>Synovial sarcoma</td>
<td>11</td>
</tr>
<tr>
<td>Fibrosarcoma</td>
<td>10</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>6</td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td>4</td>
</tr>
<tr>
<td>Mesenchymoma</td>
<td>4</td>
</tr>
<tr>
<td>Myxosarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Periosteal fibrosarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Neurofibrosarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Misc. sarcomas (1 each)</td>
<td>6</td>
</tr>
</tbody>
</table>
DR. BENNETT: Perhaps some of the pathologists have worked out other refinements over and above what we have been talking about. We see, however, that the majority (13) agree with the diagnosis of osteogenic sarcoma. Synovial sarcoma (11 votes) is a bit difficult for me to understand. In all likelihood this diagnosis was based on the presence of the tissue spaces or clefts and the tufts of tissue projecting into them. Fibrosarcoma (10 votes) there are parts of the tumor in which one would certainly make that diagnosis. I think I indicated before that different pathologists had fastened their attention on different qualities of the neoplasm. This probably explains the remaining diagnoses. It all adds up, Dr. Garland, to this being a malignant tumor of mesenchymal origin.

DIAGNOSIS: Malignant mesenchymal tumor showing prosoplasia and organoid quality. Essentially an extraosseous osteogenic sarcoma.
CASE III

A white man 59 years of age presented a gradually increasing tumor mass in the muscles of the left thigh which was radically extirpated. A metastatic lesion appeared in the lower lobe of the right lung which was removed by lobectomy. One year later a pathologic fracture developed in the right femur and following biopsy the right leg was amputated by disarticulation at the hip. Subsequently a tumor mass appeared in the left deltoid region. The patient died two years after the onset of the first tumor in the thigh muscle with generalized metastases.

DR. GARLAND: The original roentgenograms showed a soft tissue tumor of the left leg. One would suppose from the history and the age that it was a sarcoma, perhaps a fibrosarcoma. I wouldn't exclude myosarcoma or a rhabdomyosarcoma. Then we had an x-ray of his pelvis, made in August, 1948 - slide please -

The pelvis shows the lamellar thickening of the cortex, of both innominate bones, with patchy areas of porosis and sclerosis characteristic of Paget's disease, also Paget's disease in the neck of each femur and the proximal shaft of the right femur. Probably a conventional case of Paget's disease in a patient with an independent fibrosarcoma of the middle third of the left thigh. Next please -

This is a film made in January, 1950. A little of the cortex on the mesial aspect of the proximal end of the shaft of the right femur and the lesser trochanter are missing. One therefore has a destructive process. One knows that in about 1% of patients with Paget's disease malignant changes occur, and one is worried, therefore, that this patient had either got a bone metastasis from the sarcoma in the opposite leg, or that an independent osteogenic sarcoma developed. The latter is the likely diagnosis. Next please -

Then he went ahead and fractured his right leg, in February, 1950, a pathologic fracture through the area of osteogenic sarcoma complicating Paget's (independent of the fibrosarcoma of the left thigh).
DR. BENNETT: I was furnished with the complete record of this case, and I would like to compliment the pathologists who prepared the protocol. It is one of the most complete and carefully written autopsy protocols which I have had the pleasure of reading in a long time. The interesting features this case brings up are: (1) the relationship of sarcoma of bone to Paget's disease or of Paget's disease to sarcoma of bone, and (2) the possible relation, in this instance, of the first tumor to the subsequent development of osteogenic sarcoma in other portions of the body. The high points of the case as they have been stated were: the discovery by x-ray examination in 1946 of Paget's disease; the development, one year later, of pulmonary metastasis, apparently with almost identical histological features; the fracture of the left femur in December of 1949; fracture of the right femur in February of 1950 due to a tumor; and finally widespread metastases. Now if we may see the slides -

This photograph, badly fractured in mailing, shows a part of the tumor which was first removed from the thigh. Next -

This photograph shows a sectioned surface of this tumor, which was described as being fleshy, highly cellular and friable. It contained areas of necrosis and hemorrhages which are clearly evident. It spread through the muscle but was not directly attached to bone. Next -

These are pulmonary metastases, late in the disease. They can be seen throughout the lung fields. One lung weighed approximately 900 grams and the other lung weighed approximately 1500 grams, mostly due to metastases. Some of these were described as fleshy in appearance, others had a gritty sensation, and on histologic examination some of them are highly anaplastic and some show distinct evidence of bone formation. Next -

This is a photograph of the left femur showing the point of fracture. There is some widening of the cortex of the femur, especially above the fracture. There is no evidence of healing and on microscopic examination a great deal of necrosis of bone was visible. Next -
This is one of the vertebral bodies showing a lesion which can be quite clearly made out. These lesions, when examined histologically, showed osteogenic sarcoma such as you have seen in your slides.

DR. RUSSELL: May I interrupt, Dr. Bennett? Dr. Garland would like to comment here regarding one point on his findings.

DR. GARLAND: In my summary, Dr. Bennett, I failed to mention that I had also sent in to Dr. Russell the diagnosis of radiation osteitis of the left femur from the very heavy radiotherapy, and of the pulmonary metastases which were easily seen in the films.

DR. BENNETT: I think that was in keeping with the histologic findings too. I did not have an opportunity to see the section labelled "A" in your slide sets until it arrived just a few days ago. As I understand it now, this is a section of the original tumor. Dr. Russell was kind enough to prepare hastily one or two photomicrographs of this one section, Section "A". You will recall that this is a highly undifferentiated sarcoma, that the background is formed chiefly of spindle or round oval cells with many bizarre cells, some with trailing cytoplasmic processes, some were multinucleated, others had large lobulated and distorted giant nuclei. This type of picture is frequently interpreted as rhabdomyosarcoma and indeed a number of the consultants who saw this slide were of that impression. Others thought that it was a mesenchymal tumor which might perhaps be classified as liposarcoma. I do not think, having looked at other sections from this case, that this lesion is incompatible with an undifferentiated, so-called lytic type of osteogenic sarcoma. I was unable, as apparently all other consultants were, to distinguish any cross striations in any of the cells or in the cell processes. Next-

This photograph represents the section you have from the bony part. We find that there is highly vascular and poorly differentiated tumor tissue with an imperfect "watery" type of osteoid material in the framework or the stroma of the tumor. Next slide-

In still other areas we see the original cancellous bone. In this we note a bizarre pattern of cement
lines and irregularities at the peripheral margins of the bone trabeculae. This is characteristic of Paget's disease. Then filling the medulary spaces throughout is a rather well differentiated tumor which is forming a great deal of bone matrix. So here we have an osteogenic sarcoma invading and replacing bone which was previously affected by Paget's disease.

DR. RUSSELL: This was from the right thigh, Dr. Bennett?

DR. BENNETT: That is correct.

DR. HALPERT (Houston, Tex.): I didn't quite get it clear, Dr. Bennett, whether your diagnosis on the soft tissue tumor was that of a rhabdomyosarcoma or whether you thought it was an undifferentiated branch of the growing fibrosarcoma.

DR. BENNETT: My diagnosis on Section 111-A is malignant mesenchymal tumor (sarcoma) undifferentiated osteogenic sarcoma?, rhabdomyosarcoma? I do not know how one can establish the diagnosis of rhabdomyosarcoma without finding striations. With respect to 111-B, my diagnosis is Paget's disease complicated by osteogenic sarcoma.

GENERAL DE COURSEY (Washington, D.C.): Do you think that the irregularities of large cells may have been secondary to the irradiation?

DR. BENNETT: It is my recollection from reviewing this case history that this tumor had not been irradiated at the time the original block of tissue was taken.

DR. RUSSELL: Dr. Fletcher could answer that question. Was the tumor irradiated before it was taken out?

DR. FLETCHER (Houston, Tex.): No.

DR. RUSSELL: It was not irradiated.

DR. GARLAND: Dr. Bennett in his opening remarks said that a good pathologist always looked at the roentgenograms, as well as the slides. Having looked at the roentgenograms of this man's left femur, would you still entertain as seriously the diagnosis of osteogenic sarcoma, in view of the enormous size of the soft tissue mass with the almost absent bone reaction?
DR. RUSSELL: Might it not be, if you believe that it is an osteogenic sarcoma, a metastasis from the other lesion that was not suspected at that time?

DR. BENNETT: In answer to both questions - I do not see any evidence in the gross specimen or in the roentgenogram of the left femur that this is a sarcoma involving bone or even adjacent to bone. I accept this lesion as being a tumor of soft tissue, away from bone. If it is an undifferentiated osteogenic sarcoma then I think one has to accept it as an extraskeletal osteogenic sarcoma or a metastasis. I would think that the latter possibility is rather unlikely in view of the sequence of events and the long period of time before other foci of osteogenic sarcomas appeared.

DR. RUSSELL: At the time of autopsy there was no residual tumor left in the left leg. Apparently this soft tissue sarcoma - ? osteogenic sarcoma - at least had been cured locally by roentgenotherapy. Is there further discussion?

DR. HALPERT (Houston, Tex.): I am still a little bit confused. Does Dr. Bennett think that this man had just one neoplasm or two? Also the metastases in the lung, were those from the skeleton or were they from the soft tissue, or was it just all one tumor?

DR. BENNETT: I think it probable that the patient had more than one primary tumor. With respect to the sections which I have had an opportunity to review, I think one can find undifferentiated sarcomatous tissue which is entirely compatible with the first tumor histologically. Also, can find tumor metastases which, histologically, are compatible with more highly differentiated tumors that were discovered in bone at the time of autopsy. Finally I would point out that the range of histologic patterns within the metastatic lesions are compatible with the range of variations in a single focus of osteogenic sarcoma, irrespective of its type. Next slide please -

(At this point, illustrations of other examples of Paget's disease and bone sarcomas were shown.)
DR. RUSSELL: Thank you, Dr. Bennett. If there are no further discussions from the floor, I'll ask Dr. Garland to discuss the radiological diagnoses which were submitted.

DR. GARLAND: One comment on the diagnosis of osteogenic sarcoma in Paget's. Dr. Bennett, we see a lot of Paget's disease of bone in ordinary general radiological practice. Between the San Francisco County Hospital, St. Joseph's Hospital and our office, I suppose we see about 40 cases a year. I personally recollect in the last twenty years only four cases of complicating osteogenic sarcoma. I therefore think the incidence is very low. Cushing, of course, had a high incidence of between 4 and 8% in skull lesions, but after all he received very selected material. What is your own guess as to the incidence of sarcoma in Paget's?

DR. BENNETT: Of course I see them for entirely different reasons and I am always impressed with the frequency of osteogenic sarcoma in Paget's disease. We see the cases who develop tumors or who die. The usual figures which are given indicate that from 5 to 15% of patients with clinically demonstrable Paget's disease develop osteogenic sarcoma.

DR. GARLAND: That's very interesting because in our experience we put it much closer to 1% and we have followed now a fair number of patients for as long as 20 years.

Early diagnosis of the change is difficult because there are all phases of bone change in Paget's disease, notably in the skull. When the diploic or medullary areas are grossly disorganized, and there are patchy areas of severe porosis in the cortex, it may resemble neoplasia. Yet we've followed some of these for many years and they have not developed sarcoma.
DR. GARLAND: Well, these are the diagnoses submitted by the radiologists on this case. There were 39 answers to the questionnaire: 18 of them reported Paget's and 6 sarcomatous degeneration in Paget's. Four mentioned rhabdomyosarcoma; 2 metastatic - I suppose they meant the lungs; one fracture result of x-ray therapy, that's correct (it was radiation osteitis of the left femur); one hyperparathyroidism - inexplicable.

Pathologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhabdomyosarcoma</td>
<td>35</td>
</tr>
<tr>
<td>Osteogenic sarcoma</td>
<td>21</td>
</tr>
<tr>
<td>Paget's disease with sarcomatous changes</td>
<td>2</td>
</tr>
<tr>
<td>Squamous cell Carcinoma, Grade IV</td>
<td>1</td>
</tr>
<tr>
<td>Liposarcoma</td>
<td>1</td>
</tr>
</tbody>
</table>

DR. BENNETT: In Slide A, rhabdomyosarcoma led the list with 35; that would agree, I think, with the preference expressed by consultants on the primary tumor. If I had been presented with that initial tumor only I would have been among the thirty-five. Osteogenic sarcoma in 21 instances; Paget's disease with sarcomatous change (2) - I don't know just how that diagnosis could be established with the one slide. I do not see how squamous cell carcinoma (1 vote), even a Grade IV, could have been very seriously entertained. Liposarcoma (1 vote), I notice one of the consultants suggested that possibility. The next slide is the one in which you had some bone to study.
## Pathologists' Diagnoses Tabulation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Votes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteogenic sarcoma in Paget's</td>
<td>29</td>
</tr>
<tr>
<td>Paget's disease</td>
<td>11</td>
</tr>
<tr>
<td>Osteogenic sarcoma</td>
<td>9</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Metastatic Ca. to bone</td>
<td>2</td>
</tr>
<tr>
<td>Squamous cell Ca., Grade IV with metastases</td>
<td>1</td>
</tr>
</tbody>
</table>

**DR. BENNETT:** Here the diagnosis of osteogenic sarcoma in Paget's - 29; Paget's disease without specifying osteogenic sarcoma seems a little surprising to me, 11 instances; and osteogenic sarcoma (9 votes) without specifying Paget's disease is also surprising. Rhabdomyosarcoma (3 votes). I have no way of accounting for this diagnosis. Metastatic carcinoma of bone, 2 votes. This is exceedingly difficult to explain. Squamous cell carcinoma (1 vote) is even more difficult to understand.

**DIAGNOSIS:** 111-A Malignant mesenchymal tumor, sarcoma. Possibilities are: 1) undifferentiated osteogenic sarcoma; 2) rhabdomyosarcoma.

111-B Paget's disease of bone (osteitis deformans) and osteogenic sarcoma.
DR. RUSSELL: I would like to turn the microphone over to Dr. Garland, who has some remarks regarding radiotherapy of bone tumors and lesions.

DR. GARLAND: Well, first of all I want to thank you again, Mr. Chairman, very much for the opportunity of taking part in this symposium. I've learned a lot, as I think have all the radiologists in the room.

A few words about therapy of primary bone tumors, directed to you pathologists who are in a unique position, because so often the family doctor says to you, "How shall I treat this patient?"

Some of you have had training in institutions where enthusiasm for radiotherapy is conspicuous by its absence. I would, therefore, like to give you my own impressions, based on 25 years in radiology in San Francisco and on observing the work of men like Dr. Newell, Dr. Chamberlain, Dr. Pendergrass and others who have careful follow-up on their cases and who realize how disheartening the radiotherapy of many primary bone lesions is. First let us consider the more common primary malignant bone tumors - the osteogenic sarcomas and chondrosarcomas. These are rarely significantly benefited by radiotherapy, except for palliation. However, there are three primary malignant bone tumors in which I think judicious radiotherapy has a useful place. (1) Apparently localized myeloma. I think a tumor dose of 2,500 r in four weeks time will arrest some localized myelomas. We have a few such cases that went three years, and one that went ten years with pain relief and recalcification. The latter then generalized and proved fatal. (2) Reticulum cell sarcomas. Many of these tumors are benefited by whole bone radiation. We would like to suggest a tumor dose of about 3,500 r in four weeks time. (3) Ewing's sarcoma. In suitable cases of Ewing's sarcoma we believe a tumor dose of 4,500 r in four weeks time to the entire bone will give long-term control. This dose is approaching the hazardous level. If the patient does survive five years, he may have a ten percent chance of developing late radiation osteitis, with or without spontaneous fracture. However, that's a chance which I think you must take.

Of the primary benign bone tumors, there are two that I think we can help. (1) Benign giant cell tumors. We have treated 27 patients. Fifteen have been treated over ten
years ago and we have followed them. Two are dead of malignancy. One, I think, was a chondrosarcoma from the start and we misdiagnosed it; the other apparently did become malignant. The rest are cured, to date. We think that small tumor doses such as 600 - 1,000 r into the lesion in a week's time, repeated if necessary once or twice, will control many benign giant cell tumors. (2) Benign hemangioma. We believe that 600 r into the tumor in a few days time, repeated monthly, twice, will arrest many of these tumors. We do not recommend heavy doses for benign lesions. One of my colleagues in the northwest reports using 4,000 r for benign giant cell tumor; this we regard as unwise. Please note that the above doses are approximations. One cannot standardize dosage and effect in such biologically variable entities as bone tumors. Thank you, Mr. Chairman.

DR. RUSSELL: We've finished right on time. I'm going to step down from the platform and ask that the audience join me in applause as an expression of appreciation for the splendid and most stimulating presentation by our two speakers this afternoon.