SKELETAL SARCOMATA AND GIANT-CELL TUMOUR

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There is no universal agreement on a classification of bone tumours. Many of the existing methods are based on varying criteria and consequently the nomenclature is confused. Numerous descriptive terms are employed to denote only minor and irrelevant differences in essentially similar tumours.

If a classification is to be more than an academic exercise, the diagnosis of a particular type of tumour, after adequate biopsy, should convey an impression of its probable behaviour and likely response to treatment. The importance of these principles has been stressed by Scarff (1947).

The most widely used classification of bone tumours was that adopted by the American College of Surgeons in 1928. This regarded all primary malignant tumours as osteogenic (arising from bone) sarcoma. The subdivisions of this group were: medullary and subperiosteal, telangiectatic, sclerosing, periosteal and fibrosarcoma, and parosteal. These appear to be purely arbitrary divisions based on descriptive terms assessed by varying methods including clinical, anatomical, radiological and naked-eye appearance, with little regard to the cellular pattern of the tumour. The chondrosarcomata were later separated from this large group (Ewing 1939) and other minor modifications instituted.

Geschickter and Copeland (1949) recognised chondrosarcoma and osteogenic (arising from bone) sarcoma. The latter group is apparently subdivided, mainly on radiological appearances, into osteosclerotic and osteolytic types. To quote these authorities: "If facilities for frozen sections are not available and consultation is required in the diagnosis the roentgenograms and not the sections should be sent, as a diagnosis can usually be obtained roentgenologically without the necessity of a preceding exploration if the proper authorities are consulted" (p. 206). This subdivision of the osteolytic and sclerotic types is an artificial separation depending entirely upon whether a tumour produces sufficient bone to be recognisable in a radiograph; in practice this has little prognostic value as their five-year survival figures were 16 and 21 per cent respectively.

In Great Britain a classification based on cellular appearances has been in use for many years (Scarff 1937). The terms chondrosarcoma, fibrosarcoma and spindle-cell sarcoma have proved valuable largely because they are self-descriptive and histologically accurate.

Much confusion still exists on the meaning of the term osteogenic sarcoma—whether it implies "bone-forming" or "arising from bone." Ewing used the term to denote a tumour arising from bone, but subsequent authors have altered the implications of the word to suit their own conceptions. At present most histologists in this country use the term to indicate bone formation within a tumour.

It is, however, fundamentally important to appreciate that the osteogenic (bone-forming) sarcoma is not itself a pure histological entity. Most types of bone tumour can undergo ossification, but, as will be shown in subsequent sections of this paper, it is not the mere presence of bone that is prognostically significant: it is the method of its formation. Bone formed by tumour cells—tumour bone formation or osteoblast sarcoma—carries a grave prognosis; bone that is merely laid down on the preformed cartilaginous or collagenous matrix of a tumour affects neither the diagnosis nor the general prognosis of that tumour.

If, therefore, in a histological classification, bone formation *per se* is emphasised, it may cause a relatively benign ossifying cartilaginous tumour to be regarded as highly malignant.

The "osteogenic" (bone-forming) sarcomata can readily be subdivided into three histologically recognisable entities: osteosarcoma (osteoblast sarcoma), ossifying chondrosarcoma, and ossifying fibrosarcoma. In our classification the word "osteogenic" in all its diverse meanings has been purposely omitted. The term osteosarcoma (osteoblast sarcoma) is used to denote an easily recognisable and specific tumour entity which is in no way synonymous with osteogenic (bone-forming) sarcoma.

MATERIAL

In order to reassess the value of the histological subdivision of bone tumours we have collected all cases of primary skeletal sarcoma and giant-cell tumour seen at the Middlesex Hospital since 1925. Only those cases with adequate clinical data and histological material have been used. Tumours arising from non-skeletal tissue in bone, such as haemangio-endothelioma, Ewing's tumour and the malignant reticulosos, have been excluded. One hundred and seventy-nine cases remained for analysis. The available pathological material of every patient was re-examined and the tumours have been classified as follows:

PRIMARY MALIGNANT SKELETAL TUMOURS :

- Osteosarcoma (osteoblast sarcoma).
- Chondrosarcoma.
- Fibrosarcoma.
- Spindle-cell sarcoma.
- Giant-cell tumour.

This is a purely histological classification and relies solely on the cellular pattern of the tumour. It is founded on the method proposed by Scarff (1937) and used in the Bland-Sutton Institute of Pathology since then. Macdonald and Budd (1943) and Lichtenstein (1952) have adopted classifications based on similar principles.

OSTEOSARCOMA

(Osteoblast sarcoma)

This is the most highly malignant group of the primary skeletal sarcomata. Histologically it forms a readily recognisable and specific tumour in which osteoid tissue is produced directly by malignant osteoblastic tumour cells with no intermediate matrix. A histologically accurate term is osteoblast sarcoma and, as previously stressed, it is not synonymous with "osteogenic" (bone-forming) sarcoma.

FIG. 1

Age incidence of osteoblast sarcoma. P denotes Paget's disease.

There are thirty-two examples of this tumour in the present series, five of which were associated with Paget's disease.

Age—More than a third of the tumours were observed between the ages of fifteen to twenty-five, and nearly two-thirds between ten and thirty (Fig. 1). Of the seven tumours occurring in patients over fifty, five were known to be associated with Paget's disease.

FIG. 2

FIG. 3

Osteoblast sarcoma of humerus. Radiograph of the specimen (Fig. 3) shows sclerosis of the primary tumour in the mid-shaft of the humerus. There are two sclerotic secondary deposits in the head of the humerus.

FIG. 4

FIG. 5

Osteoblast sarcoma of humerus. Radiograph of the specimen (Fig. 5) shows a relatively osteolytic example of this type of tumour.

Sex—Twenty-one of the thirty-two patients were male and eleven female. Four of the five cases associated with Paget's disease were in men.

Sites—The sites of origin of the tumours are shown in Table I. About two-thirds of the tumours arose in long bones, and half of these were in the region of the knee.

TABLE I
SITES OF OSTEOSARCOMA (THIRTY-TWO CASES)

Femur		Humerus	
Upper end .	3	Upper end .	5
Middle .	2	Middle .	3
Lower end .	8	Lower end .	---
		Ilium . . .	4
Tibia		Skull . . .	1
Upper end .	3	Jaw . . .	1
Middle .	---	Spine . . .	1
Lower end .	---	Foot . . .	1
Fibula . . .	---		

Length of history—The commonest presenting symptoms were aching pain and swelling. Except in the cases complicating Paget's disease, in which the onset of the tumour symptoms was difficult to assess owing to other skeletal symptoms, the average length of history before attending hospital was three months, and the longest nine months.

Macroscopic appearance—The affected bone is expanded by a solid tumour, the cut surface of which shows visible or palpable bony areas. The bone cortex is eroded, and there is early penetration of the periosteum with involvement of the adjacent soft tissues. Variations in the macroscopic appearance of individual tumours are immaterial to the general behaviour and prognosis of an osteoblast sarcoma.

The macroscopic and radiographic appearance of both the osteolytic and osteosclerotic forms of this tumour may be closely mimicked by other primary bone tumours, and even by secondary deposits of carcinoma (Fig. 14). Although most examples of osteoblast sarcoma have a characteristic appearance, the final diagnosis must always rest with the histology.

Microscopic appearance—The tumour is composed of malignant osteoblastic cells. Microscopically the diagnostic feature is the presence of irregular spicules of osteoid tissue formed and surrounded by malignant osteoblastic tumour cells which often show marked cellular variation and pleomorphism.

The spicules of osteoid tissue are sharply outlined and appear partly refractile; they stain a homogeneous pink with haematoxylin and eosin. In areas these spicules may fuse to form bony trabeculae, but the amount of definitive bone formed varies; the radiographic appearance of the osteosarcoma may, therefore, be either osteosclerotic or osteolytic.

There is usually no cartilage in this tumour, but its presence does not exclude the diagnosis. The specific diagnostic feature of the osteoblast sarcoma is that osteoid tissue is formed directly by the malignant osteoblasts with no intermediate matrix of cartilage or fibrous tissue. This process appears, therefore, to be the malignant counterpart of normal subperiosteal new bone formation, and of simple repair callus.

In spite of the apparent differentiation of the malignant osteoblastic cells in that they produce osteoid tissue, and the histological similarity between this tumour and repair callus (Figs. 11 to 13), the osteoblast sarcoma is, nevertheless, the most highly malignant tumour of bone.

Treatment—Thirteen of the thirty-two patients were treated by radical surgery alone,

including two in whom the tumour was associated with Paget's disease. Eleven patients received radiotherapy alone, including three with Paget's disease. Eight patients were treated by a combination of irradiation and radical surgery.

FIG. 6

A low power view of an osteoblast sarcoma with irregular bone formation.
($\times 100$.)

FIG. 7

A secondary deposit of osteoblast sarcoma in the lung. ($\times 100$.)

Prognosis—Three-quarters of the patients with osteoblast sarcoma in this series died within a year of treatment (Fig. 10). Only four patients were alive three years after diagnosis; two have lived for three years (one has pulmonary secondary deposits), the others have survived seven and ten years respectively.

The two patients who have survived three years were both treated by radiotherapy alone; one recently had a hindquarter amputation and histological examination at the site of the irradiated tumour revealed no recognisable tumour cells; this patient remains well.

FIG. 8

A high power view of an osteoblast sarcoma with malignant osteoblasts surrounding osteoid spicules. ($\times 400$.)

FIG. 9

A high power view of an osteoblast sarcoma in the lung. ($\times 400$.)

The other has had no subsequent surgery but has developed a local recurrence and pulmonary metastases.

The patient surviving seven years had an osteoblast sarcoma at the upper end of the humerus treated by pre-operative irradiation followed by a forequarter amputation. This

patient remains free from recurrence as does the ten-year survivor who was treated by hind-quarter amputation, during pregnancy, for an osteoblast sarcoma at the upper end of the femur. **Metastases**—In at least twenty of the twenty-eight fatal cases the patient is known to have had secondary deposits in the lung at the time of death. Three further patients had evidence of metastases in other bones. Many of the patients died outside hospital and, since post-

mortem examinations were not performed, the details of the metastatic spread of many of the tumours are unknown. All the secondary deposits in lung, bone and kidney that we examined histologically showed an appearance identical to that of the primary tumour. There is no available specimen showing a deposit of this type of tumour in a lymph node in the present series.

FIG. 11
A low power view of simple repair callus with its marked cellularity. ($\times 100$.)

Only one tumour treated by amputation recurred in the stump. A tumour in the mandible treated by local excision and radium implantation recurred rapidly.

DISCUSSION

The sole criterion for the diagnosis of the osteoblast sarcoma is the histological picture. This tumour has usually been diagnosed in the past as an osteogenic (bone-forming) sarcoma.

Its malignancy has frequently been underestimated because less malignant bone-forming tumours have been included with it. The commonest of these is the ossifying chondrosarcoma. Whereas most histologists agree that ossification may occur in a chondrosarcoma, many still classify the extensively ossifying cartilaginous tumours with the osteoblast sarcomata and

FIG. 12

An area of benign osteoblastic activity in simple repair callus. ($\times 400$.)

FIG. 13

The somewhat malignant appearance of the osteoblastic activity that may occur in simple callus. ($\times 400$.)

the ossifying fibrosarcomata, retaining the single heading osteogenic (bone-forming) sarcoma.

The presence of extensive areas of cartilage in a bone-forming tumour should raise the suspicion that the tumour is primarily a chondrosarcoma. Ossification in the matrix of some of these tumours can be very active, and the benign osteoblastic activity surrounding areas

of cartilage may give rise to diagnostic error; indeed if these osteoblastic areas are cut tangentially the cartilage in a given section may not even be a prominent feature.

This benign osteoblastic activity is particularly evident in ossifying chondrosarcomata that have been treated by irradiation. This is a pathological, but not a malignant, reaction to irradiation: the phenomenon is well known to the radiologist, who often sees a striking increase in the sclerosis of a treated tumour. In addition, the histological appearances of these tumours may be further complicated because the irradiation produces bizarre appearances in the benign osteoblasts. A tumour should not, therefore, be classified within this scheme from a post-irradiation biopsy or specimen.

FIG. 14

FIG. 15

Figure 14—The so-called " sun-ray spicules " in a tumour of the rib. This is the site of a secondary deposit of carcinoma from a primary in the colon.

Figure 15—Radiograph of the specimen.

The osteoblast sarcoma is considered to be the malignant counterpart of subperiosteal ossification and, as has already been mentioned, it is not always easy to differentiate from simple repair callus. This again may cause difficulty in histological diagnosis, for many tumours of bone, both primary and secondary, are surrounded by simple, benign subperiosteal bone formation (" sun-ray spicules " and Codman's triangle). Inadequate biopsy of a tumour may sample only this area of reactive new bone and lead to a false diagnosis of osteoblast sarcoma (Fig. 36).

The osteosarcoma is the most highly malignant of bone tumours, and only four patients in this series survived three years. This is a sinister outlook but, despite the small numbers,

we believe that this is a fair index of the behaviour of the tumour. Many published accounts of "osteogenic" (bone-forming) sarcoma with a five-year survival figure of 20 or 30 per cent must surely contain examples of the more benign bone-forming tumours (Fig. 64). If a critical analysis is made of this tumour, with histological examination as the only proof of identity, the prognosis of the osteoblast sarcoma will probably prove to be in the region of 10 per cent five-year survival.

In this series the histological grading of the tumour in relation to the degree of differentiation of the osteoblastic tumour cells, and the extent of bone formation, has proved of no value in assessing the prognosis.

FIG. 16

FIG. 17

Figure 16—Paget's disease of the skull with associated osteoblast sarcoma.
Figure 17—Radiograph of the specimen.

CHONDROSARCOMA

The diagnostic criterion of the chondrosarcoma is the presence of atypical cartilage which forms the predominant tissue. Many chondrosarcomata undergo ossification; when this is extensive the tumour is frequently classified under the heading of osteogenic (bone-forming) sarcoma.

There are sixty-eight examples of chondrosarcoma in this series; six were associated with Paget's disease.

Age—Chondrosarcoma occurs at all ages from ten to eighty, and is only slightly less common in the older age groups (Fig. 18). Of the seven tumours occurring over the age of sixty-five, six were associated with Paget's disease.

Sex—More than two-thirds of the cases occurred in male patients; there were forty-eight males and twenty females.

Sites—Table II shows the sites of origin of the sixty-eight tumours. The high incidence of pelvic primary sites may be in part accounted for by the number of patients referred to Sir Gordon Gordon-Taylor at this hospital with a view to hindquarter amputation.

FIG. 18

Age incidence of chondrosarcoma. P = Tumour associated with Paget's disease.

Length of history—The average length of history before examination was thirteen months: the patient with the shortest history had a pathological fracture, and the one with the longest had had a palpable tumour for ten years.

Macroscopic appearance—The glistening, translucent and lobulated appearance of the cut surface of a chondrosarcoma is familiar and most can be readily diagnosed at a glance. There is great variation in size, and although a few may remain intramedullary at the time of operation, most tumours have eroded the cortex, with considerable bulging of the tumour mass into the soft tissues, the bulk of the tumour appearing outside the normal contour of the bone.

TABLE II
SITES OF CHONDROSARCOMA (SIXTY-EIGHT CASES)

Humerus		Tibia or fibula	
Upper end .	6	Upper end .	6
Middle .	—	Middle .	1
Lower end .	—	Lower end .	1
Pelvis . . .		26	
Femur		Skull . . .	
Upper end .	10		3
Middle .	2	Jaw . . .	
Lower end .	6		2
		Chest wall .	
			3
		Finger . . .	
			1
		Scapula .	
			1

Many tumours show areas of calcification or ossification recognisable macroscopically. Some are so extensively ossified that the cartilaginous matrix is not visible to the naked eye. Others, especially the larger ones, show areas of degenerative softening of the cartilage with cyst formation.

FIG. 19

FIG. 20

Chondrosarcoma. Radiograph of the specimen (Fig. 20) shows extensive ossification of the tumour.

FIG. 21

FIG. 22

Chondrosarcoma. Radiograph of the specimen (Fig. 22) shows patchy areas of calcification in the tumour.

Microscopic appearance—The diagnostic feature of the chondrosarcoma is the presence of atypical cartilage. These tumours fall into three histological grades which correspond to low, average and high degrees of malignancy.

The low-grade, well differentiated chondrosarcoma is similar in appearance to its benign counterpart, the chondroma, and, as stressed by Lichtenstein and Jaffe (1943), it can sometimes be differentiated only by careful histological scrutiny of the pathological material. The bulk of the tumour is composed of a cartilaginous matrix which is relatively acellular; the cells in these areas are regular and do not give the impression of malignancy. In other areas, especially at the periphery, there is an increased cellularity with a diminution in the proportion of the matrix. The cells in these regions are atypical, with variation in their size, and although mitotic figures are rare, many double nuclear forms may be visible in one

FIG. 23

FIG. 24

Chondrosarcoma. Showing a chondrosarcoma of the shaft of the fibula with little calcification or ossification visible in the radiograph of the specimen (Fig. 24).

microscopical field. In addition, at the growing edge, evidence of local infiltration can be seen. These are the histological appearances of the low-grade chondrosarcoma.

The cartilage in the average-grade tumour, although still readily recognisable, is more atypical in appearance. The matrix is reduced, with a proportionate increase in the cellularity; the cells vary both in size and shape, and show many abnormal nuclear forms.

The high-grade chondrosarcoma is comparatively rare. The appearances are those of a highly malignant sarcoma, with a poorly differentiated cartilaginous pattern. The greater part of the tumour is composed of pleomorphic anaplastic cells with grossly abnormal nuclear configuration and mitotic activity. In the less undifferentiated areas highly atypical, but recognisable, islands of cartilage are seen.

Tumours of all grades of malignancy may show additional features. As in benign chondromata, there may be areas of myxomatous degeneration or calcification of the stroma.

FIG. 25

The cellular appearance of a grade I chondrosarcoma. This section was taken from a secondary deposit in the lung. This patient was alive, but with multiple metastases, twelve years after initial treatment. ($\times 400$.)

FIG. 26

FIG. 27

Figure 26—The cellular appearance of a grade II chondrosarcoma. There is an area of calcification. The patient died with metastases four years after initial treatment. ($\times 400$.) Figure 27—The cellular appearance of a chondrosarcoma of grade III malignancy. This patient died with metastases within a year of treatment. ($\times 400$.)

These have no prognostic significance. Ossification of the matrix frequently occurs. Solid bony trabeculae replace areas of cartilage, and in the zones of active ossification a margin of normal osteoblastic activity may be found. Similar changes are seen in a benign osteochondroma, and are analogous to the physiological process of ossification of the epiphysial cartilage during normal bone growth.

Prognosis—It has become more widely recognised that the chondrosarcoma has a better prognosis than the other bone sarcomata. Figure 28 shows the survival figures in this series. It will be seen that there is approximately a 50 per cent five-year survival and a 40 per cent

fifteen-year survival. These figures are clearly better than those for osteosarcoma and fibrosarcoma.

In this series there were twenty-seven cases of low-grade, thirty-one of average grade, and ten of high-grade malignancy as judged histologically. The survival figures have been analysed according to the different grades of malignancy (Fig. 29). It can be seen that tumours in these three grades behave differently. Nearly three-quarters of the patients with a low-grade tumour were alive ten years after treatment and more than a half at fifteen years. Of the average-grade cases less than half were alive at five years and only one-third at ten years. The high-grade chondrosarcoma behaves like the osteoblast sarcoma; only one of the ten patients survived three years.

Treatment. *Radical surgery*—Twenty-five patients were treated by radical surgery and of these, ten have died, eight with pulmonary metastases and two with local recurrences after amputation through the bone of origin (pelvis). Of these twenty-five tumours, nine were of low grade (one fatal), eleven were of average grade (five fatal), and five were of high grade

FIG. 30
Showing the double nuclear pattern visible in the cartilage cells of a grade II chondrosarcoma. ($\times 400$.)

FIG. 31
An extensively ossifying chondrosarcoma. ($\times 100$.)

(four fatal). Fifteen patients are alive at the present time, but three of these were treated less than four years ago.

Local surgery—Of the eighteen patients (fifteen low-grade tumours, three average) treated initially by local excision, five are alive and well (four low-grade tumours, one average).

Thirteen tumours recurred locally (eleven low-grade, two average), but five of the patients are alive and well six years after additional surgery (three low-grade tumours, two average). The remaining eight patients (all with low-grade tumours) with local recurrences all died despite additional treatment (radiotherapy in two cases, radical surgery in three, local surgery in three).

FIG. 32

Areas of calcification and active ossification in a chondrosarcoma. ($\times 400$.)

FIG. 33

A chondrosarcoma with spindle-cell areas. ($\times 400$.)

Thus of the eighteen patients originally treated by local excision ten are alive and well (seven low-grade tumours, three average).

Radiotherapy—Eleven patients were treated by radiotherapy alone (one low-grade tumour, seven average, three high). Seven patients died within a year of treatment, two in the third year and one in the sixth year; the patient with the low-grade tumour died in the tenth year.

Surgery and radiotherapy—Ten patients received combined irradiation and surgery as initial

treatment (three low-grade tumours, four average, three high). Four patients remain alive and well (two low-grade tumours, two average).

Four patients (all with tumours of average grade) died untreated.

Metastases—Of the thirty-eight patients who died at least seventeen are known to have had secondary deposits in the lungs, but, as many patients died outside hospital and did not have a post-mortem examination, this figure is almost certainly an underestimate. Other

FIG. 34

A chondrosarcoma in lung (see Fig. 25). ($\times 100$.)

FIG. 35

A secondary deposit of chondrosarcoma in kidney. ($\times 100$.)

secondary deposits have been found in distant bones, liver, kidney, pancreas and spinal dura. There is no available histological material in this series showing lymph node involvement. All the metastases that have been examined microscopically are similar in all respects to the primary tumour, indicating that a chondrosarcoma remains and metastasises as a chondrosarcoma.

DISCUSSION

As with the benign chondromata, the matrix of the chondrosarcoma often shows areas of myxomatous degeneration, calcification or ossification. These pathological changes are of

no prognostic significance, for the tumour appears to behave according to the histological grade of the chondrosarcomatous element.

The commonly used terms myxo-chondro-sarcoma, osteo-chondro-sarcoma and osteogenic (bone-forming) sarcoma are merely descriptions of irrelevant pathological appearances which neither aid the histological diagnosis nor serve as a guide to behaviour or prognosis.

The microscopic appearances of bone formation in cartilaginous tumours vary. In some areas calcification and bone formation are seen within the matrix of a cartilaginous island with no visible surrounding osteoblasts. In others active ossification is proceeding by simple, benign osteoblastic activity on the margin of the cartilaginous areas. This type of tumour is apt to be confused with the osteoblast sarcoma, especially in post-irradiation biopsies. In some particularly sclerosed examples of the ossifying chondrosarcoma areas of cartilage are largely replaced by bone, the structure of which tends to retain the basic cartilaginous pattern, thus indicating the true diagnosis.

FIG. 36

A chondrosarcoma with reactive subperiosteal new bone formation. ($\times 100$.)

The myxomatous appearance often visible in other types of chondrosarcoma is due entirely to a mucoid degeneration of the cartilaginous matrix which results in softening of the tumour substance and cyst formation. This appearance is not to be confused with the recently described chondromyxoid fibroma (Jaffe and Lichtenstein 1948), of which there are no examples in the present series.

The grading of the cartilaginous tumours according to their degree of histological differentiation appears to be of practical value. The low-grade tumours have no particular age incidence and behave less aggressively than those of other grades. Eleven of the twenty-seven patients died, six from local recurrence in surgically irremovable sites such as the sacrum and chest wall. Four patients died from pulmonary metastases, and one from sepsis soon after the operation.

Pulmonary metastases from low-grade tumours may not become apparent for many years after the initial treatment. In one patient a pulmonary deposit was found eight years after a forequarter amputation for the primary tumour in the humerus. The secondary deposit was removed from the left upper lobe of the lung by segmental excision, and the patient is still alive three years later, in spite of metastatic deposits elsewhere.

Although it was the low-grade chondrosarcoma that first drew attention to the better prognosis of the cartilaginous tumours, the average-grade examples also have a much less aggressive behaviour than the osteoblast sarcoma or the fibrosarcoma.

Of the thirty-one patients with average-grade tumours nineteen have died; at least eight of these had proven pulmonary metastases at the time of death, although in the absence of a terminal examination this figure is almost certainly too low.

At the malignant end of the scale the high-grade type of chondrosarcoma approximates in its behaviour to the osteoblast sarcoma.

FIBROSARCOMA

Fibrosarcoma of bone is a malignant tumour with one diagnostic feature, the formation of collagen by the tumour cells. Histologically it is identical with the more widely recognised fibrosarcoma of soft tissue.

FIG. 37

Age incidence of fibrosarcoma. P—Tumour associated with Paget's disease.

There are thirty-four examples of this tumour in the series, four of which were associated with Paget's disease.

Age—The tumours of this series occurred at all ages, with peaks in the third and sixth decades (Fig. 37). Of the five cases occurring over the age of sixty, three were associated with Paget's disease.

Sex—Eighteen patients were male and sixteen female.

Sites—Two-thirds of the tumours occurred in long bones and half of these arose in the region of the knee joint (Table III). The two tumours arising in the skull were associated with Paget's disease. The tumours in the other cases of Paget's disease arose in the mid-shaft of the tibia and in the calcaneum.

Length of history—The average length of history before the patient attended hospital was seven months; the longest was thirty months. The patient with the shortest history had no symptoms until a pathological fracture occurred through the site of the tumour.

Macroscopic appearance—These tumours have been described as periosteal and medullary, according to their supposed site of origin. The distinction between a soft-tissue, a periosteal and a medullary fibrosarcoma is, however, a matter of anatomical site and extent, for microscopically they are indistinguishable. Most of the tumours in this series are of the medullary type. Soft-tissue tumours have been excluded and the remainder are examples of fibrosarcomata which have arisen in the periosteal region, but which show evidence of invasion

FIG. 38

FIG. 39

Fibrosarcoma. A central tumour in bone with no invasion of the soft tissues. Figure 39 is a radiograph of the specimen.

FIG. 40

FIG. 41

Fibrosarcoma. Showing a fibrosarcoma of bone with invasion of the adjacent soft tissues. The radiograph (Fig. 41) shows reactive periosteal new bone formation.

and characteristic destruction of the medullary cancellous bone at an early stage of the disease. Fibrosarcomata arising in the periosteal region, but not invading bone, have been excluded because they are more rationally considered among the soft-tissue growths.

Many examples of this tumour remain wholly intramedullary at the time of amputation. They show characteristic lengthwise spread in the cancellous bone with erosion and expansion, but not complete penetration, of the cortex. Other examples, although still showing this

TABLE III
SITES OF FIBROSARCOMA (THIRTY-FOUR CASES)

Femur		Radius or Ulna	
Upper end .	1	Upper end .	—
Middle .	1	Middle .	1
Lower end .	8	Lower end .	1
Tibia or Fibula		Ilium . . .	2
Upper end .	6	Mandible . . .	2
Middle .	1	Skull . . .	2
Lower end .	2	Foot . . .	2
Humerus		Rib . . .	2
Upper end .	2	Scapula . . .	1
Middle .	—		
Lower end .	—		

intramedullary type of extension, have penetrated the cortex to involve soft tissues, forming a tumour mass outside the bone.

The cut surface of a fibrosarcoma of bone differs in no essential from its counterpart in the soft tissues, except that, in the early stages of intramedullary invasion, fragments of cancellous bone may be palpable in the fibrous tumour.

Microscopic appearance—Microscopically the relatively well differentiated examples show fibroblastic tumour cells with extensive collagen formation. The more cellular varieties exhibit greater pleomorphism, often with multinucleate forms and less collagen. The matrix of any fibrosarcoma may undergo mucoid degeneration and small areas of calcification may also occur. These changes are comparable to those seen in the stroma of a chondrosarcoma.

Since the tumour spreads by infiltration of cancellous bone, surviving bony trabeculae are visible, particularly at the margin of the tumour. In addition small areas of new bone formation are occasionally seen in which the collagen is replaced by osteoid tissue as a result of simple osteoblastic activity. This ossification is regular and appears comparable to the physiological process of "ossification in membrane." It is merely another example of bone formation in a tumour matrix; neither the cellular pattern nor the prognosis resembles that of the osteoblast sarcoma.

Treatment. Radical surgery—Fifteen patients were treated by radical surgery: eight died within three years of diagnosis and six are alive. Two of the survivors have lived for two years, two for three years, one for four years and one for fourteen years after treatment. One patient died of natural causes in the seventh year with no evidence of recurrent tumour.

Local surgery—The one patient treated by local excision has survived two years.

Radiotherapy—Ten patients were treated by radiotherapy alone (palliative in at least two instances); all died within three years.

Surgery and radiotherapy—Three tumours were treated by local surgery and irradiation as a combined treatment; all three patients remain alive and well, eight, ten and fourteen years later.

Three tumours were treated by radical surgery and irradiation as an initial treatment.

One patient died at one year, another was killed in an accident during the second year, and the remaining patient is alive at three years.

Two further patients died untreated.

FIG. 42

A fibrosarcoma of low-grade malignancy. ($\times 400$.)

FIG. 43

A fibrosarcoma of average-grade malignancy. ($\times 400$.)

FIG. 44

A fibrosarcoma of high-grade malignancy. ($\times 400$.)

Prognosis—The survival figures for fibrosarcoma are summarised in Figure 46. Half of the patients died within two years of diagnosis, and three-quarters within five years. Of the five patients who have so far survived five years, two were treated by radical surgery, and the remaining three tumours were locally excised and irradiated. One tumour, treated in

this manner, recurred locally six years after treatment, and amputation was performed; histology showed active fibrosarcoma in the bone, but the patient remains well two years later. **Metastases**—At least eleven of the twenty-one patients who died are known to have had secondary deposits in the lung, and in four cases there was histological evidence of lymph

FIG. 45

A secondary fibrosarcoma of bone in the lung. ($\times 100$.)

node metastases. Three patients died from bony secondaries in the spine. Five tumours recurred locally, three after irradiation, and two in the stump after subtrochanteric amputation for tumours at the lower end of the femur.

All secondary deposits that we have examined histologically have been identical in appearance to the primary tumour.

FIG. 46

Survival figures of fibrosarcoma.

DISCUSSION

Some authorities doubt the existence of the fibrosarcoma of bone as a separate entity. Thus Geschickter (1932) regarded all these tumours found in bone as arising in adjacent soft tissues, with subsequent bony invasion. He regarded fibroblastic tumours in the medullary cavity but with no extension into soft tissues as undifferentiated examples of "osteogenic" or chondrosarcoma with no characteristic matrix production.

Scarff (1937) included fibrosarcoma of the bone in his classification of bone tumours, and many subsequent authors have agreed (Macdonald and Budd 1943, Phemister 1948, Coley 1949, and Lichtenstein 1952). Macdonald and Budd (1943) recognised fibrosarcoma as a specific entity occurring in bone, and found that 31 per cent of the five-year survivors of "osteogenic" (arising from bone) sarcoma registered with the Bone Tumour Registry were in fact examples of this type.

The fibrosarcomata have a diagnostic microscopic appearance and the general prognosis, as judged from this present series, lies between that of the highly malignant osteoblast sarcoma and the chondrosarcoma group. This is not in agreement with the findings of Macdonald and Budd (1943), but they included the spindle-cell sarcoma in their series.

An attempt was made to grade the fibrosarcomata according to their degree of collagenous differentiation and cellular appearance. Of the thirty-four tumours only two were well differentiated (grade I), twenty were of average malignancy (grade II) and twelve of high-grade malignancy (grade III).

The histological distinction between fibrosarcomata of grades II and III was less readily definable than in the chondrosarcoma and giant-cell series because of the diversity of the histological pictures encountered.

The tumours of grades II and III in this series all behaved poorly, so the distinction between them has little practical value. The uncommon grade I tumours appear less aggressive, for both patients are among the survivors at the present time.

SPINDLE-CELL SARCOMA

The tumours of this group are highly cellular neoplasms composed of undifferentiated spindle cells. The relative absence of intercellular tissue is the striking feature. There are only eleven examples in the series.

Age—The ages were thirteen, fourteen, eighteen, eighteen, nineteen, twenty, twenty-one, twenty-five, thirty-two and fifty-two (age unknown in one case).

Sex—There were six males and five females.

Sites—The tumours arose in the foot, radius, clavicle, upper and lower femur and the upper end of the fibula; five arose from the pelvic bones.

Macroscopic appearance—The tumours are soft and haemorrhagic, with expansion and destruction of the bone of origin and in some cases invasion through the periosteum to involve the adjacent soft tissues.

Microscopic appearance—Histologically the tumour is composed of masses of spindle cells of uniform appearance: pleomorphic areas, mitotic activity and giant-cell forms are unusual. Most of the tumour is composed of these spindle cells with a negligible intercellular tissue. The absence of matrix is a striking feature of this tumour, and it indicates a complete absence of histological differentiation.

Treatment—Four patients had radical surgery alone; three died within six months from pulmonary metastases and one remains alive and well four years later.

Three patients were treated by radiotherapy alone; two died within six months, and one remains alive and well six years later.

Four patients had a local resection of the tumour as the initial treatment; the tumour recurred in all and was then treated by irradiation. One patient died with pulmonary secondaries five years later; the other three, treated by additional radical surgery, remain alive five, seven and fifteen years later.

Prognosis—Five of the patients died within the first six months after treatment and one after five years. Five remain alive four, five, six, seven, and fifteen years later.

Metastases—Four patients were known to have pulmonary metastases at the time of death, and a further patient had multiple bone secondaries.

DISCUSSION

This small group of tumours has an interesting histological picture and clinical course.

The spindle-cell sarcoma of bone, like the similar tumour of soft tissue, is a histologically descriptive title which does not imply a specific histogenetic entity. It is merely a group of tumours showing a characteristic cellular appearance with a marked absence of matrix. It may be that they are an undifferentiated form of fibrosarcoma with no collagen formation;

FIG. 47

FIG. 48

Figure 47—Spindle-cell sarcoma. A tumour involving the bones of the foot.
Figure 48 is a radiograph of the specimen.

they are often regarded as such. They present, however, quite a different appearance from the poorly differentiated fibrosarcoma; for the latter, in addition to areas of collagenous intercellular matrix, also shows a marked degree of pleomorphism with bizarre nuclear pattern and tumour giant cells. Compared with these, the uniform pattern of the spindle-cell sarcoma does not convey the same impression of malignancy, for both the cells and the nuclei are almost invariably regular, and mitotic activity is not a prominent feature.

For these reasons it seems logical to compare and contrast the behaviour of the spindle-cell sarcoma and the fibrosarcoma critically before accepting their coalition. Since there are only eleven cases in this series the details of behaviour must be accepted with reserve. In four of the five fatal cases the patient died within six months of treatment; those that survived this period have lived for five years or more, with the exception of one who is still alive and

FIG. 49
Showing the cellularity of a spindle-cell sarcoma. ($\times 100$.)

FIG. 50
Spindle-cell sarcoma of bone. Patient alive seven years after initial treatment.
($\times 400$.)

well at four years. One of these patients subsequently died at five and a half years, and another, although still alive, has pulmonary metastases in the seventh year after treatment.

There is a tendency for the spindle-cell sarcoma to occur at a younger age than the fibrosarcoma. Nine of the eleven tumours arose in patients between the ages of thirteen and twenty-five. There is also some evidence that the spindle-cell sarcoma is more radiosensitive.

It may be that a larger number of cases of this tumour type will show that there is little to be gained by their separation and that a single histological diagnosis of fibro-spindle-cell sarcoma will convey all that is of practical value. In the meantime, however, we prefer to retain the individual diagnoses of fibrosarcoma and spindle-cell sarcoma until the clinical value of this histological distinction can be accurately assessed.

GIANT-CELL TUMOURS

The histological feature of this group of tumours is the cellular stroma in which there are many giant cells of the osteoclast type. In the past these tumours have often been regarded as benign. This is far from the truth, for in this series of thirty-four tumours half recurred locally after treatment and a quarter of the patients died with metastases.

Age—The age incidence is shown in Figure 51. Most of the cases fall in the twenty to forty age group. Two tumours occurred in patients of sixteen but none below the age of fifteen. Three patients were over the age of sixty, two of whom were known to have Paget's disease.

Sex—There was an equal sex distribution with seventeen males and seventeen females.

FIG. 51

Age incidence of giant-cell tumours. P—tumour associated with Paget's disease.

Sites—More than three-quarters arose at the ends of long bones and three-quarters of these occurred in the region of the knee (Table IV). There are no examples of this tumour arising from the middle third of a long bone.

Length of history—The average duration of symptoms was seven months, varying from one month to three years, with the exception of two cases in which the patient presented with a pathological fracture.

Macroscopic appearance—As with the chondrosarcoma, the macroscopic appearance of the giant-cell tumour is well recognised and can frequently, but not infallibly, be diagnosed from the cut surface of the specimen or from the radiograph.

The bone is expanded by a red, fleshy, haemorrhagic tumour which replaces the medulla and markedly thins the expanding cortical bone. It commonly extends up to the articular cartilage, but the joint is spared, and the periosteum remains intact except in the more aggressive examples.

Microscopic appearance—The histological features of this tumour are a vascular cellular stroma in which there are many giant cells of the osteoclast type. The stromal cells are of two varieties: spindle cells are found which have elongated darkly staining nuclei and little cytoplasm, but the predominant cell has a plump pink-staining cytoplasm containing an oval or round vesicular nucleus. The giant cells, which form so prominent a feature, are uniform with an abundance of sharply defined pink-staining cytoplasm containing upwards

FIG. 52

FIG. 53

Giant-cell tumour. The appearance of a histologically grade I giant-cell tumour. Figure 53 is a radiograph of the specimen.

FIG. 54

FIG. 55

Giant-cell tumour. The appearance of a histologically grade II giant-cell tumour. Figure 55 is a radiograph of the specimen.

of fifty nuclei with a central aggregation. These nuclei are vesicular and closely resemble the predominant stromal cells in appearance; it seems likely that the giant cells have their origin from these.

The arresting feature of this tumour is the presence of the many giant cells, from which it derives its non-committal name. Some prefer the title of osteoclastoma because of the close

TABLE IV
SITES OF GIANT-CELL TUMOURS (THIRTY-FOUR CASES)

Humerus		Patella	1
Upper end .	3		
Middle .			
Lower end .	1	Vertebra	1
Femur		Pelvis	2
Upper end .	2		
Middle .			
Lower end .	10	Scapula	1
Tibia and Fibula		Jaw	1
Upper end .	10		
Middle .			
Lower end .	2		

similarity of these giant cells to the osteoclast (Willis 1949). Unfortunately from the prognostic aspect it is not the giant cells that form the important element, but rather the stromal cells (Jaffe *et al.* 1940). These authors suggest that the subsequent behaviour of any giant-cell

FIG. 56

FIG. 57

Giant-cell tumour. The appearance of a histologically grade III giant-cell tumour. Figure 57 is a radiograph of the specimen.

tumour can be assessed by the cytological features exhibited by the stromal cells. They divide these tumours into three grades, I, II, and III. The grade I tumours display a stromal pattern of uniform cells and giant cells of regular appearance. There is little mitotic activity and the whole picture is that of a slowly growing tumour. This grade forms about a third (eleven cases) of this series and has a low recurrence rate after local treatment.

FIG. 58

Showing the regularity of both the stromal and giant cells of a grade I giant-cell tumour. ($\times 400$.)

FIG. 59

Figure 59—Some irregularity of the stromal cells of a grade II giant-cell tumour. ($\times 400$.)

FIG. 60

Figure 60—Showing the irregularity of the stromal cells and the giant cells of a grade III giant-cell tumour. ($\times 400$.)

The grade II tumours show distinct cytological differences from those of grade I. There is increased cellularity of the stroma and the cells are irregular in shape, size and staining; mitotic activity is readily visible and the picture is one of a much more active tumour. The sixteen grade II tumours (nearly half the total) displayed more aggressive characteristics with a high incidence of recurrence.

The grade III tumours are those with a sarcomatous stroma. The cellular stroma is more pleomorphic, frankly mitotic activity becomes a prominent feature, and the diagnostic giant cells are irregular both in size and shape due to clumping of the stromal cells. These tumours are sarcomatous in behaviour; the seven in this series all invaded the soft tissues and four patients died with blood-borne metastases.

These three grades are very similar to the second, third and fourth grades suggested by the American College of Surgeons (Ewing 1939); their grade I tumours will be referred to here as giant-cell variants, for they are not true giant-cell tumours.

FIG. 61

A giant-cell tumour metastasis in lung. ($\times 100$.)

Prognosis—In the past the giant-cell tumours have usually been regarded as benign lesions, a small proportion of which gave rise to local recurrence, and rarely metastasised. In this series of thirty-four giant-cell tumours, eighteen recurred after local surgical and radio-therapeutic treatment, and eight patients died from distant metastases. In the course of treatment, sixteen patients have had amputations after the failure of more conservative treatment.

The survival figures are shown in Figure 62. This shows a five-year survival rate of approximately two-thirds. Figure 63 shows the mortality in the three histological grades of the tumour. To summarise briefly: five of the eleven patients with a grade I tumour developed local recurrences; all these responded to further treatment, although one patient died from natural causes. Of sixteen grade II tumours eleven recurred, and four patients died with metastases. Two further patients died, one from extension of the tumour in the sacral region, and the other from pulmonary embolism after an amputation for recurrence. Of the seven grade III tumours, two were associated with Paget's disease. Four died with pulmonary metastases and three remain alive and well three, six and twenty-six years after pre-operative irradiation and amputation.

It will be noted that all the fatal cases died before the end of the fifth year after treatment,

and no patient died during the first year. The only death among the patients with a grade I tumour was due to natural causes.

Treatment. *Radical surgery*—Four patients were treated by radical surgery alone. One had a resection of the patella (grade II tumour), another had an amputation of the leg (grade I tumour); both these patients remain alive and well. Two further patients died with pulmonary metastases after amputations (grade II and grade III tumours).

FIG. 62

Survival figures of giant-cell tumours.

FIG. 63

Survival figures of the three histological grades of giant-cell tumour.

Local surgery—One tumour was treated by local resection of a tumour in the fibula. This recurred in the tibia and further extension after irradiation necessitated amputation; the patient is well seven years after the initial treatment (grade II tumour).

Curettage—Eleven tumours (three of grade I, seven of grade II, and one of grade III) were treated initially by curettage; only one curettage was successful and this was combined with local carbolic acid cauterisation at the time of operation (grade II tumour). Ten tumours recurred locally and were treated by radiotherapy; five of these were successfully controlled (three grade II tumours and two of grade I). Four patients died from pulmonary metastases

after further radical surgery (three grade II tumours and one of grade III), and only one patient (with grade I tumour) remains alive after amputation.

Thus of the eleven patients originally treated by curettage, only seven are alive in spite of energetic treatment of the recurrences.

Radiotherapy—Fifteen patients were treated by irradiation, with no previous surgery other than the initial biopsy. Of these, six are alive and free from recurrence (five grade I tumours and one of grade II).

Nine tumours were not controlled by irradiation (six of grade II and three of grade III). Four were later removed by amputation and the patients remain alive two to five years after diagnosis (three grade II tumours and one of grade III). The remaining five patients with recurrent tumours died, three from pulmonary metastases (one grade II tumour, two grade III tumours), and two died at the age of forty with active tumour. One (grade II) was extending into the sacrum; the other (grade I) was in the femur and the certified cause of death was chronic bronchitis and emphysema.

Of the fifteen patients originally treated by radiotherapy, ten remain alive and well but four of these required subsequent amputation for recurrence. Five of the six tumours that were controlled by irradiation were histologically in grade I.

Surgery and radiotherapy—Three tumours were treated initially by a combination of surgery and radiotherapy. One patient (grade II tumour) had irradiation immediately after local excision, and two (grade II tumours) had pre-operative irradiation; these three patients are alive three, twelve and eighteen years after treatment.

In short, twenty of the thirty-four tumours in this series recurred after treatment—eighteen locally, eight after curettage, nine after irradiation and one after local excision. Two showed pulmonary recurrence only, after radical excision of the primary.

Metastases—Eight tumours showed evidence of blood-borne metastases at the time of death (four of grade II, four of grade III), seven of which were in the lung. All the secondary deposits that we have examined histologically resembled the primary tumour.

DISCUSSION

The giant-cell tumour, because of its histological picture, has many imitators. As stressed by Jaffe *et al.* (1940) these include simple bone cysts, fibromata, fibrous dysplasia, lipoid dystrophy, fibro-xanthomata, and giant-cell epulis, all of which may contain many giant cells of the osteoclast type in a cellular stroma. Moreover, areas of osteoclastic bone absorption are frequently seen at the periphery of any bone lesion. Inadequate biopsy, sampling only this area, is an insufficiently appreciated cause of error in histological diagnosis.

Originally this series contained many more cases, but on closer scrutiny of the histological material, many were found to be examples of the above mentioned "giant-cell variants." Most of these occurred in the first and second decades, and in the present series there are only three examples of the giant-cell tumour occurring under the age of twenty.

After the exclusion of these histological imitators, nearly all of which have an excellent prognosis, a group of specific giant-cell tumours remains. These form a formidable series with a high recurrence rate after local treatment.

The diagnosis can be made only after careful histological study, and the prevalent tendency to apply this histological label to a clinical or radiological impression of a lesion is both unscientific and inaccurate. The aggressive character of the true giant-cell tumour has been underestimated in many of the reported surveys owing to uncritical or even absent histological examination.

Once the diagnosis has been confirmed histologically, and the tumour graded, its treatment should not be undertaken lightly. In this series of thirty-four tumours no less than eighteen recurred locally, and eight patients died from distant metastases. It seems,

therefore, more realistic and logical to regard the giant-cell tumour as a locally malignant neoplasm, a significant proportion of which may cause fatal metastases.

It seems from the relatively small number of cases in this series that grading does give some guide to the prognosis of a given tumour. The grade I tumours may recur locally, but have not metastasised. The grade II tumours are likely to recur locally and may metastasise: the metastasising examples of this grade cannot be differentiated histologically and the microscopic appearance of the secondary deposits is identical to those of the primary tumour. The grade III tumours behave as frank sarcomata and, unless early and radical treatment is instituted, metastases inevitably occur.

DISCUSSION

The main purpose of this work is to subdivide malignant tumours of bone into histological groups and to reassess the prognostic value obtainable from this method of classification. The subdivisions are based solely on specific cellular appearances without recourse to the naked eye, radiological or clinical appearances of the tumour. This seems to be the most logical and valuable method of classification. It differs from most of its predecessors in the interpretation of the significance of bone formation within the tumour. In our view the formation of osteoid tissue directly by malignant osteoblastic tumour cells is the only type of bone formation of prognostic significance. Simple ossification of the stroma of a tumour neither alters the basic diagnosis nor materially affects the prognosis.

Most of the 180 tumours in this series can readily be placed in one of the four main groups, as the tumour cells produce a diagnostic amount of osteoid tissue, cartilage, collagen or giant cells of the osteoclast type. There are, however, eleven tumours in this series which lack this diagnostic differentiation in the stroma. These form the fifth group, the spindle-cell sarcoma.

The main difficulty with a histological method of classification is the occasional tumour which shows a mixture of malignant tissues. The few examples of this in the present series have all been predominantly cartilaginous tumours with additional areas of spindle-cell, fibrosarcomatous or osteoblastic tissue. These appearances are exceptional and, although they may represent examples of a mixed type of tumour, for practical purposes this cellular picture is taken to indicate a higher grade of malignancy than the pure cartilaginous areas would suggest, approximating to the prognosis of the additional tumour type.

Furthermore, as previously described, a narrow margin of simple osteoblastic activity is commonly seen surrounding an ossifying chondrosarcomatous matrix. Very occasionally this osteoid tissue may form a prominent feature and assume the malignant cellular pattern of the osteoblast sarcoma, with extensive areas of malignant tumour bone formation and no intermediate matrix of cartilage. These tumours are considered to have the prognosis of an osteoblast sarcoma since in areas they are histologically indistinguishable.

The occurrence of these relatively infrequent mixed tumours containing more than one type of malignant tissue is no valid reason for grouping all osteoblastic, cartilaginous, collagenous and spindle-cell sarcomata together, for the great majority can readily be segregated, and their distinction appears to be reflected in the behaviour of the individual groups.

A bone tumour metastasises true to its cellular type; thus a chondrosarcoma metastasises as a chondrosarcoma. In the mixed type of tumour the histological appearance of the metastases, and the prognosis, are usually that of the most malignant type present.

The only accurate method of establishing the exact diagnosis of a bone tumour is by histological examination of the tumour tissue. Although this tissue may be obtained from an amputated specimen it is essential to examine biopsy specimens before a tumour receives radiotherapy, for the histological picture may be radically altered by irradiation and the precise nature of the original tumour may ever remain in doubt.

Apart from the disputed risks of dissemination of the tumour cells by biopsy, there are certain diagnostic hazards associated with it. It is desirable that the tissues submitted should be adequate and representative of the tumour, and for these reasons an open biopsy is preferred to a drill biopsy. An inadequate biopsy specimen may be most misleading. If it samples only the edge of a tumour surrounded by reactive periosteal new bone, a false diagnosis of osteoblast sarcoma may result; conversely, an area of eroded bone with prominent osteoclastic activity may simulate a giant-cell tumour. Adequate biopsy with sufficient tissue from a representative area will permit accurate diagnosis in most cases and will form a reliable basis for the assessment of further treatment.

Injury has often been regarded as a predisposing factor in the causation of "osteogenic" (bone-forming) sarcoma. This seems to have its foundation on two points: firstly, aching pain and local swelling, both common presenting symptoms of bone tumours, are frequently ascribed by the patient to previous and often trivial injury in that region; secondly, the exuberant callus that accompanies some examples of bone repair may be histologically difficult to differentiate from an osteoblast sarcoma. A history of injury was recorded in about half the cases in this series.

It is extremely doubtful whether injury does more than draw attention to an already existing bone lesion and there seems little real evidence to substantiate it as an etiological factor. Many thousands of fractures have been treated at this hospital since 1925 but so far as is known not one has subsequently developed a primary bone sarcoma at the site of injury. Since major trauma of bone does not seem to cause neoplasia it seems unreasonable to suppose that minor trauma, often involving soft tissues only, can be responsible.

In this series seventeen bone tumours were associated with Paget's disease. These included examples of each of the four main types of tumour—five osteosarcomata, six chondrosarcomata, four fibrosarcomata, and two giant-cell tumours. With the exception of the giant-cell tumours, the prognosis of the tumours associated with Paget's disease is uniformly poor, irrespective of the type of sarcoma present, for all the patients died within nine months of diagnosis. One of the patients with a giant-cell tumour died three years after diagnosis, but the other is alive five years later.

FIG. 64

Comparison of the survival figures of the histological types of malignant bone tumours.

The application of a rational histological classification, based solely on cellular appearances, to the present series of bone tumours is strikingly reflected in the behaviour of the individual tumour groups. As will be seen from Figure 64, if all the bone sarcomata are considered together much information of prognostic importance is lost; thus it takes fifteen years for

three-quarters of the "osteogenic" (arising from bone) sarcomata to cause death, but the osteoblast sarcoma achieves this dismal figure in a year. The further histological subdivision of the chondrosarcomata and giant-cell tumours according to their histological grade of malignancy gives an additional guide to the behaviour of these tumours.

We feel that the details of the bone tumours in this series will endorse the practical value of a histological classification of bone sarcomata and that the amalgamation of all types under the collective heading of "osteogenic" sarcoma is ambiguous, pathologically inaccurate, and prognostically valueless.

SUMMARY

1. One hundred and seventy-nine cases of primary malignant bone tumour and giant-cell tumour seen at the Middlesex Hospital since 1925 are reviewed. Tumours arising from non-skeletal tissues in bone have been excluded.
2. The following histological classification is used. *Osteosarcoma* (osteoblast sarcoma): This tumour is not synonymous with osteogenic (bone-forming) sarcoma. The essential feature is the formation of osteoid tissue by malignant osteoblasts, with no intermediate matrix of cartilage or fibrous tissue. It is the most malignant bone tumour and only four of the thirty-two patients survived three years. *Chondrosarcoma*: These tumours are composed of cartilage, and some show secondary ossification. The behaviour of this group is related to the degree of cartilaginous differentiation. In general, compared with the osteosarcoma, it is of low-grade malignancy. More than half of the sixty-eight patients survived four years. *Fibrosarcoma*: The essential feature of this tumour is the production of collagen by malignant fibroblastic tumour cells. Tumours of this type invading the medullary cavity have an average prognosis between that of an osteosarcoma and a chondrosarcoma. Nine of the thirty-four patients survived three years. *Spindle-cell sarcoma*: These tumours are composed of spindle cells which produce no diagnostic matrix. In spite of the lack of differentiation the outlook is not hopeless. Six of the eleven patients survived for five years or more. *Giant-cell tumour*: This tumour is composed of a cellular stroma with diagnostic giant cells resembling osteoclasts. It is by no means a benign lesion, for half the tumours recurred after treatment and a quarter of the patients died with metastases.
3. The subdivision of primary malignant skeletal tumours into groups according to the histological pattern appears to be reflected in the behaviour of the individual tumours after treatment. The prognosis of each group has been stated in the appropriate sections.

We wish to thank Professor R. W. Scarff for advice and helpful criticism and Dr A. C. Thackray for some of the photomicrographs. We are indebted to members of the surgical staff of the Middlesex Hospital and to Professor B. W. Windeyer for permission to include clinical details of the patients under their care, and to Mr L. Atkinson for abstracting some of the case histories. We gratefully acknowledge the invaluable help received from Dr P. S. Andrews with the many specimens of bone tumours; also the photographs by Mr M. Tierney, and advice on the radiographic appearances of the specimens from Dr C. G. Whiteside and Dr J. N. Pattinson. We would like to thank Mr T. E. Cowan for his unfailing assistance with the case records and the follow-up details. The expenses of this investigation were defrayed by the British Empire Cancer Campaign.

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