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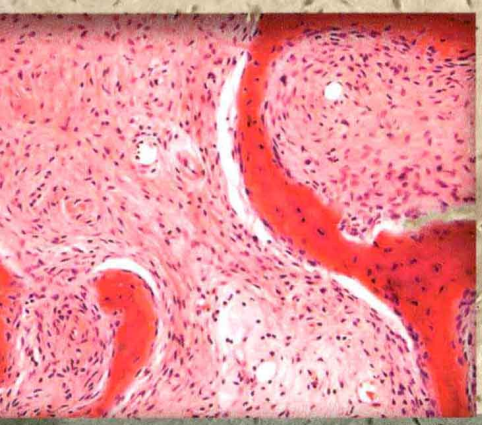
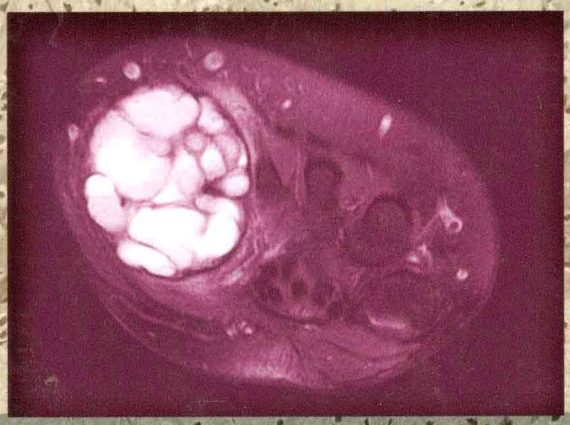
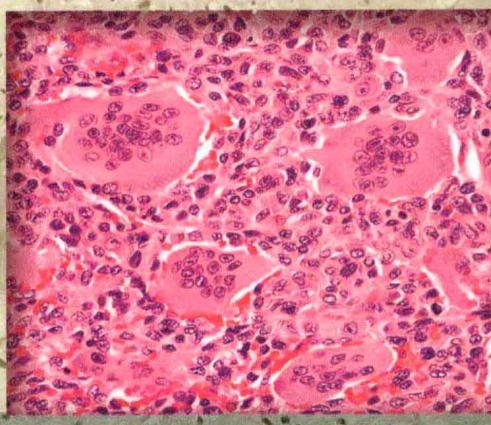
Dahlin's Bone Tumors

SIXTH EDITION

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General Aspects and Data on 10,165 Cases

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To Dave and Helen Dahlin
and our families,
Sheila, Akhil, Aditiya, and Adosh
David, Sarah, and Ryan

Preface

The Fifth Edition of *Bone Tumors* included statistics on bone tumors from the Mayo Clinic files until the end of 1993. This updated Sixth Edition contains information about cases recorded until the end of 2003. We have tried to remain true to the format first used by Dr. David C. Dahlin in the First Edition of this book. However, we have made some modifications. In the first chapter, more emphasis has been placed on the handling of bone specimens, both biopsy and larger specimens, and grading and staging of neoplasms. There is much confusion in the literature about grading of sarcomas. General concepts about grading schemes used at Mayo Clinic are provided. These schemes have been elaborated on in the appropriate sections concerning specific neoplasms. Staging of neoplasms is one of the more important advances in our understanding of bone tumors. The grade of the tumor is the cornerstone on which staging is based.

Most of the illustrations have been replaced. More attention has been paid to computed tomographic and magnetic resonance images. The emphasis is still on diagnoses based on histologic sections stained with hematoxylin and eosin. However, results of immunoperoxidase studies have been incorporated when considered important.

Several clinicopathologic studies incorporating large numbers of cases have been done since the Fifth Edition of this book. Such large numbers were possible because of the consultation cases. Although follow-up information may not be ideal in these cases, these large studies have provided important information about radiographic and histologic variations in different tumor types. Chondroblastoma, osteoblastoma, and parosteal osteosarcoma are examples in which this new information has been incorporated. The section on neoplasm simulators has been expanded to include some conditions, such as neuropathic joint, that may present as a neoplasm. The diagnosis should be made on radiographic grounds, and the pathologist should not have to look at the biopsy specimen. However, we see a number of cases every year in which this condition has been mistaken for a neoplasm.

We hope that pathologists, orthopedic surgeons, radiologists, and oncologists will find the information provided in this book to be useful to their practice.

K. K. Unni, M.B.B.S.
C. Y. Inwards, M.D.

Acknowledgments

Surgeons in the Department of Orthopedics at Mayo Clinic have had a long-standing interest in the management of patients with bone tumors. Drs. Ralph K. Ghormley, Henry W. Meyerding, and Mark B. Coventry, among others, contributed immensely in this area. However, it was Dr. Jack Ivins who established orthopedic oncology as a separate discipline at Mayo Clinic. In addition to being an expert surgeon, Dr. Ivins was a wonderful human being, and we learned a great deal from him. The work that these men started is continued by Drs. Franklin Sim, Douglas Pritchard, Thomas Shives, and Michael Rock. To these men, we are very grateful for the collaborative studies over the years, and without them, of course, there would be no Mayo Clinic series.

Orthopedic oncology is probably the finest example of a multidisciplinary approach to caring for patients. Radiology plays a vital role in this management. Dr. David Pugh was a giant in the field of orthopedic radiology. Drs. John Beabout, Richard McLeod, and, more recently, Doris Wenger, Ronald Swee, Kay Cooper, Mark Adkins, and Mark Collins, continued this great tradition. Without the help of these radiologists, the practice of orthopedic pathology would be much more difficult and much less fun. Dr. Doris Wenger has been particularly helpful in improving the illustrations pertaining to imaging in this edition.

It was the work of Dr. David C. Dahlin, however, that put Mayo Clinic on the map in the field of bone tumors. Without question, Dr. Dahlin was one of the great surgical pathologists of our time and certainly the greatest bone tumor pathologist. As he himself said, he taught us everything we know but not everything he knew. He was generous to a fault toward us. This book is his brainchild and it will always remain associated with him.

Debbie M. Balzum typed and retyped the manuscript, working long hours. We are grateful for her patience. Several members of the Section of Media Support Services helped in obtaining negatives and developing prints. The Section of Scientific Publications was extremely helpful, especially O. Eugene Millhouse, PhD, who performed the laborious task of editing the manuscript, and Roberta Schwartz, Kristin M. Nett, and Kenna Atherton.

We have been very lucky in being associated with some of the foremost surgical pathologists in the world. More than anything, they have taught us a philosophy of surgical pathology that we think is invaluable. Drs. Malcolm Dockerty, Lewis Woolner, Edward Soule, J. Aidan Carney, George Farrow, Ed Harrison, and Louis Weiland have all been responsible for our training. We are grateful that Dr. Lester Wold was an integral part of our orthopedic pathology team. We continue to benefit by the work done by our younger colleagues.

Contents

CHAPTER

1

Introduction and Scope of Study

Tumors of bone are among the most uncommon of all types of neoplasms. For instance, it is estimated that 2,900 new sarcomas of bone are recorded in the United States per year. In comparison, 169,500 new cases of carcinoma of the lung and 193,700 new cases of breast carcinoma are diagnosed. On a numeric basis, obviously, bone tumors are relatively unimportant. However, many of the bone tumors affect young children and are managed by radical surgery, with or without radiotherapy and chemotherapy, which may have significant side effects. Most centers do not acquire extensive experience in handling bone tumors. Hence, surgical pathologists in most institutions are not familiar with neoplasms of bone; consequently, a reasonably straightforward diagnosis may be a difficult one.

A team approach is necessary in the management of a patient with a bone tumor. Good communication among radiologists, orthopedic surgeons, and pathologists is important for accurate diagnosis of most of these neoplasms. A pathologist who tries to make a diagnosis on a difficult bone lesion without the advantage of information about the clinical and radiographic features is at a distinct disadvantage. Close cooperation of the different specialties with one another ensures that mistakes are kept to a minimum.

The importance of radiographs in the interpretation of bone tumors cannot be overemphasized. Radiographs, after all, are the gross representation of the neoplasm. Although it is important for surgical pathologists dealing with neoplasms of bone to have a rudimentary understanding of the interpretation of radiographs, it is even more important to have a radiologist available who is interested and has enough experience to be helpful. Pathologists with a special interest in bone tumors may refuse to make a diagnosis on a bone biopsy specimen if the radiographs are not available for review. This approach is too extreme. If the biopsy shows an osteosarcoma, the diagnosis is an osteosarcoma regardless of what the radiographs show. Knowing that the radiographic features support the diagnosis of osteosarcoma will be comforting, but it is not strictly necessary to review the radiographs personally. On the other hand, in some instances, it is foolhardy to render a diagnosis without having the radiographs available for review. Most cartilaginous tumors belong in this category.

For most bone tumors, the patient's local symptoms and the results of physical examination are relatively nonspecific. The usual symptoms—pain or swelling or both—serve mainly as a guide to the correct site for the radiographic studies and for biopsies. Accordingly, clinical features of bone tumors have been relegated to a relatively minor place in the discussion to follow. Clinical judgment is always important; an osteoid osteoma, in which referred pain may be at a site distant from the lesion, may deceive an unwary clinician.

Laboratory studies are of little aid in the diagnosis of the average bone tumor. Myeloma, with its sometimes practically pathognomonic alteration of proteins in the serum or urine, is a notable exception. Alkaline phosphatase levels may be increased with an osteoid-producing neoplasm, either primary or metastatic. Increased levels of acid phosphatase suggest metastatic prostatic carcinoma. The ominous nature of a rapidly growing sarcoma, such as Ewing tumor, may be indicated by systemic evidence, including fever, anemia, and a rapid erythrocyte sedimentation rate.

Neoplasms of bone are being studied with several new modalities, including immunohistochemical stains, flow cytometry, and cytogenetics. These methods may prove very important in the future. When such studies are of practical importance, they have been so indicated in the text. As of now, however, a diagnosis on which therapy must be predicated and prognosis estimated depends on the correct interpretation of material removed by biopsy and stained by techniques that

have been known for decades, augmented significantly by gross pathologic alterations, including those seen on the radiograph. Electron microscopy is of very limited value in the diagnostic interpretation of bone tumors. Immunoperoxidase stains also have contributed very little to improving our diagnostic skills in bone tumors, with the notable exception of small cell malignancies.

In the chapters that follow, the information provided is based mainly on the personal experience of the authors and not an exhaustive review of the literature. Hence, the bibliography is short, and as in earlier editions, specific references are not cited in the text.

IMAGING MODALITIES

The following section provides some basic information about the different imaging modalities commonly used in the work-up of a patient with a bone tumor.

BONE SCAN

Radioisotope bone scans are used to localize a bone lesion and are especially useful to detect multicentric disease. A positive bone scan merely suggests bone formation, which may be reactive, and hence provides no information about the type of pathologic process.

PLAIN RADIOGRAPH

Plain radiographs provide the most useful information about the type of lesion being studied.

LOCATION

The type of bone involved is very important information; one should hardly consider the diagnosis of adamantinoma if the radiograph does not show involvement of the tibia. The site of involvement within the bone also is of critical importance. We see even experienced orthopedic surgeons list "tumor of the hip." Does this mean the joint, the proximal femur, or the acetabulum? Most tumors and tumor-like conditions arise in the metaphysis of long bones, but a few are typically epiphyseal. Cortical involvement is characteristic of adamantinoma.

The type of defect produced in the bone provides diagnostic clues. An area of lytic destruction is described as being *geographic*. If the lesion is well demarcated, a benign process is suggested. If, in addition, the lesion is circumscribed with sclerosis, a benign lesion is highly likely. If the lesion is poorly demarcated or "marginated," an aggressive lesion is likely. However, it is not necessarily malignant.

A rapidly evolving lesion produces small defects in bone with interspersed normal tissue. This pattern is referred to as *moth-eaten*. Osteomyelitis and malignant tumors (especially small cell tumors) frequently produce this pattern.

If the lesion is extremely fast growing, it produces minute defects that may be difficult to detect on plain radiographs. This feature is suggestive of small cell malignancies such as Ewing tumor.

The pattern of involvement of the cortex also provides clues to the nature of the lesion. A thickened cortex means that the bone has responded to the lesion present, and hence it is likely to be indolent. If the cortex is breached and the periosteum lifted, periosteal new bone is usually formed. The Codman triangle is composed of reactive new bone formation at the site where the periosteum is lifted off and has no diagnostic significance. Slow-growing lesions are generally associated with thick continuous layers of periosteal new bone, whereas aggressive lesions are associated with thin discontinuous layers of new bone.

PRACTICAL APPROACH TO RAPID HISTOLOGIC DIAGNOSIS

Successful therapy for malignant disease requires that treatment be accomplished before systemic dissemination has occurred. It is axiomatic, therefore, that when the treatment of choice is ablative surgery, the procedure should be done at the earliest practical moment in an attempt to remove the tumor before neoplastic embolization leads to death of the patient.

At least 90% of bone tumors have soft portions that can be sectioned and examined for immediate diagnosis. In most cases, these soft portions afford the best material for diagnosis. For example, a sclerosing osteosarcoma almost invariably has noncalcified zones at its periphery. Study of the radiograph guides the surgeon to these zones, from which biopsy specimens can be obtained for early diagnosis. Protracted decalcification of densely sclerotic portions of the tumor or adjacent cortical bone only delays therapy.

Fresh frozen sections allow an immediate, accurate, definitive diagnosis of more than 90% of bone tumors. The rare lesion that is too difficult or too ossified for rapid interpretation can also be easily recognized. As with fixed sections of various types, good histologic preparations and sound basic understanding of the pathologic features are requisites for successful interpretation of frozen sections. Deficiency in either requisite tends to make one deprecate this diagnostic medium.

At Mayo Clinic, the frozen-section laboratory is adjacent to the surgical suites. The surgeon frequently comes to the frozen-section laboratory carrying the biopsy specimen and the corresponding radiograph. It is important to examine the biopsy specimen grossly to separate fragments of bone from the soft, fleshy

material that almost all bone tumors have. This step is important even if frozen sections are not obtained. Some neoplasms, such as lymphoma, may be associated with a sclerotic reaction. It may be necessary to tease out small fragments of fleshy tumor with the tip of a scalpel blade. This material can be processed separately and does not require decalcification.

At our institution, a freezing microtome, rather than a cryostat, is used for making frozen sections. The biopsy material is placed on the stage, which is then cooled. The tissue freezes from the bottom toward the top. When about half of the material is frozen, the unfrozen material from the top is cut off with a microtome; this material usually does not have many frozen-section artifacts and can be used for permanent sections. A section is obtained from the frozen tissue, and the section is rolled off the blade with a glass rod. The tissue is stained with methylene blue, and excess stain is washed off. The stained section is mounted with water. The whole process should take no more than 30 to 45 seconds.

This method has several advantages. First and most important perhaps is the identification of viable and diagnostic material. Even if a specific diagnosis is not made on the frozen section, the surgeon can be reassured that diagnostic material has been obtained and it is not necessary to obtain better material. Second, if the lesion under consideration is deemed to be infectious, cultures can be done. Third, a definite diagnosis can be made with assurance in most tumors. Many malignant neoplasms are no longer treated surgically immediately after diagnosis is made. However, many of the benign and low-grade malignant tumors can be treated immediately. This has the advantages of not subjecting the patient to a second anesthetic procedure and reducing hospital stay. Fresh frozen sections can also be used for checking the adequacy of margins. Obviously, it is impossible to check all margins on a large sarcoma of bone or soft tissue. However, at least margins deemed "close" by the surgeon can be checked microscopically. A margin that is free only microscopically may be too close.

If a diagnosis cannot be made immediately, it should still be possible to make one within 24 hours. As mentioned above, almost all bone tumors have soft portions. It is very important to separate the material from the bony fragments with which it may be admixed. This material should be processed without decalcification. However, decalcification may be necessary in some rare instances, even for diagnostic material. Decalcification is certainly necessary for larger specimens, such as resections for osteosarcoma after chemotherapy. Several different decalcification methods are available. At Mayo Clinic, 20% formic acid and 10% formalin are routinely used. The solution is made by mixing 400 mL of formic acid in 1,600 mL of 10% formalin. It is important to make thin slices of tissue so that decalcification is rapid. Examining the specimen periodically to make sure that overdecalcification does not occur is important.

Core needle biopsy and fine-needle aspiration are also popular methods for diagnosing bone lesions; the latter has more or less replaced the former. At our institution, we use a method that combines the two. The biopsy is performed by a radiologist under computed tomographic guidance with a 14- to 16-gauge needle. Smears are made and stained with a Papanicolaou technique. If they yield diagnostic material, the radiologist is so informed, and the small core of tissue that is always obtained is used to make permanent sections. We occasionally make a frozen section from the core if the smears are negative. The biopsy may be repeated if both are negative.

We reviewed our experience with fine-needle aspirations for the period from April 1993 to April 2003. The number of procedures performed each year has changed little (about 84 per year). It was disappointing that the number of nondiagnostic biopsies has not diminished with increasing experience. Part of the explanation may be that aspirations are done in lesions, such as cysts, with little hope of obtaining diagnostic material. As with any "new" technique, there is a temptation to overutilize it. Next to "nondiagnostic" (39%), metastatic carcinoma was the most common diagnosis made. Myeloma, lymphoma, and osteosarcoma were the most common "primary" neoplasms diagnosed.

Performing fine-needle aspirations clearly has advantages. The most obvious is the avoidance of using an operating room. The chance for contamination of the biopsy site is also reduced. Fine-needle aspiration is often said to be cost-effective; however, a negative biopsy adds to the cost. Increasingly, oncologists are demanding special studies, such as cytogenetics and molecular studies, before a patient is admitted to a protocol. Radiologists are responding by taking multiple cores for this purpose. It must be remembered that we do not examine the tissue that is used for special studies; hence, we cannot be sure that the material being studied is representative.

A special laboratory for handling specimens of bone is not necessary. The gross dissection is similar whether the specimen is a major resection or an amputation. Comparing the gross specimen with the radiograph is important to determine the exact location of the neoplasm. The soft tissue surrounding the bone and the attached neoplasm are dissected away, so that only the bone and the attached neoplasm are left behind. The specimen is cut in half with a band saw or a butcher's meat saw. The specimen is washed gently with running water and bone dust is removed with a brush. Cleaning the specimen avoids artifacts in the

microscopic sections caused by bone dust. An alternate method is to freeze the entire specimen and bisect it. Although this method has the advantage of preserving the gross anatomy, it has the disadvantages of delay and freezing and thawing artifacts.

GRADING AND STAGING OF BONE TUMORS

The grading system used at Mayo Clinic essentially follows the grading system that Dr. A. C. Broders proposed for epithelial malignant tumors. The grade of the neoplasm depends on the cellularity of the lesion and the cytologic features of the neoplastic cells. Low-grade neoplasms simulate the appearance of the putative cell of origin of the neoplasm. High-grade malignant lesions have such undifferentiated malignant cells that their cell of origin is, at best, conjectural. Although more common in higher grade neoplasms, necrosis is not used as a criterion for grading. Similarly, mitotic figures are more common in higher grade malignant lesions, but mitotic count is not used for grading tumors. Most bone tumors are graded 1 to 4, with the exception of cartilage tumors and vascular neoplasms, which have only three grades. Grading of a neoplasm demands a morphologic variation within a given entity. For example, because Ewing sarcoma has little variation from tumor to tumor, there is no practical way to grade Ewing sarcoma. This is true also of some low-grade neoplasms, such as adamantinoma. In some neoplasms, such as chordomas, experience has shown that variation in cytologic features is not correlated with clinical prognosis. Hence, there is no point in grading chordomas.

This grading system is admittedly subjective, but no more so than other grading systems. Orthopedic oncologists demand that tumors be graded because the grade of the neoplasm is an important part of staging. Fortunately, it is only necessary to say whether the neoplasm is low grade or high grade.

The staging system used by the Musculoskeletal Tumor Society is a distinct advance in the management of patients with bone tumors. Tumors are staged primarily on the grade of the neoplasm and the extent of involvement. When no distant metastases are present, all low-grade tumors are stage I and all high-grade tumors are stage II. If the neoplasm is confined to the bone, it is considered stage A, and if the tumor has also involved the soft tissues, it is considered stage B. Hence low-grade tumors can be divided into stages IA and IB, depending on the anatomic extent of the neoplasm. Similarly, high-grade tumors, that is, stage II, can also be divided into A and B on the basis of the anatomic extent of the tumor. All tumors with distant metastasis are considered stage III regardless of other considerations. This staging system promotes the use of uniform criteria for comparison of results of treatment from different institutions around the world. It also affords prognostic information.

It is useful to know the terminology orthopedic oncologists use in referring to surgical margins. When the entire compartment in which the neoplasm is situated is removed completely, *radical margin* is the term used. In a tumor involving the distal femur, a radical margin requires that the entire femur be removed. When the tumor is removed completely with surrounding normal tissue, *wide margin* is the term used. This surrounding tissue should also include the so-called reactive zone around the neoplasm. The reactive zone is an area composed of capillary proliferation apparently surrounding a tumor as it grows. When the tumor is removed completely but the resection margin does not remove the entire reactive zone, the term *marginal margin* is used. The resection is considered to be intralesional when the tumor is removed but no attempt is made to obtain normal tissues around it.

CLASSIFICATION

The classification in this book (Table 1.1) is similar to that advocated by Lichtenstein. One significant difference is that little attempt is made to draw a relationship between benign and malignant tumors, because so few of the latter take origin from the former. The classification is based on the cytologic features or the recognizable products of the proliferating cells. In most instances, the tumors are considered to arise from the type of tissue they produce, but such an assumption cannot be proven. For example, most chondrosarcomas begin in portions of bone that normally contain no obviously benign cartilaginous zones. In any event, basing classification on what is actually seen histologically allows reduplication of results on subsequent analysis. Some of the lesions in the general classification are probably not neoplasms in the strict sense.

The tabulated statistics in this book are of an unselected series of bone tumors, except for the following factors. A case is included when a complete surgical specimen or adequate biopsy material was obtained and excluded when histologic verification of the diagnosis according to modern pathologic concepts was impossible. The pathologic features have been reviewed in most of these cases as part of clinicopathologic studies. All patients were seen at Mayo Clinic for care, a circumstance that could have introduced a possible selection factor of questionable significance. The material collected in the consultation files is not used in the tabulations. However, material from this source is used for better understanding of the radiographic and histologic features of many of these neoplasms.

TABLE 1.1. Distribution of Bone Tumors by Histologic Type and by Age of Patients

Histologic Type	*Age Distribution by Decades*										*Total no of Patients*
	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	
					Benign						
Hematopoietic											0
Chondrogenic											
Osteochondroma	115	502	184	111	55	33	14	10			1,024
Chondroma	40	88	76	86	88	54	28	14	4		478
Chondroblastoma	4	89	24	13	5	11	1				147
Chondromyxoid fibroma	5	11	18	6	4	5		1			50
Osteogenic											
Osteoid osteoma	53	200	89	37	8	3	4	2			396
Osteoblastoma	6	49	33	10	3	5	1	1			108
Unknown origin											
Giant cell tumor	4	98	236	166	94	49	18	5	1		671
Histiocytic											
(Fibrous) Histiocytoma		1	3	1	3	1	1				10
Notochordal											0
Vascular											
Hemangioma	5	16	18	23	36	26	18	6	1		149
Lipogenic											
Lipoma			1	1	3	2	3	1			11
Neurogenic											
Neurilemmoma		5	6	3	3	1	3	2			23
Total benign	232	1,059	688	457	302	190	91	42	6		3,067
					Malignant						
Hematopoietic											
Myeloma		1	10	66	165	288	311	184	40	4	1,069
Malignant lymphoma	23	70	89	86	123	171	184	119	36	4	905
Chondrogenic											
Primary chondrosarcoma	7	56	128	209	222	217	154	68	11	1	1,073
Secondary chondrosarcoma		10	42	39	34	20	8	2			155
Dedifferentiated chondrosarcoma		2	3	10	26	46	27	23	7	1	145
Clear cell		3	3	7	8	3	2				26
Mesenchymal		8	14	17	5	1		1			46
Osteogenic											
Osteosarcoma	94	874	329	170	164	129	134	47	11		1,952
Parosteal osteosarcoma		13	29	21	8	4					75
Unknown origin											
Ewing tumor	101	356	98	37	14	5					611
Malignant giant cell tumor			8	11	11	6	3				39
Adamantinoma	2	12	17	3	2	2		2			40
Malignant fibrous histiocytoma	1	13	8	16	21	11	20	6	2		98
Fibrogenic											
Desmoplastic fibroma	2	5	3	1	1	3			1		16
Fibrosarcoma	6	32	35	55	39	51	38	23	6		285
Notochordal											
Chordoma	8	18	28	53	80	108	92	41	8	1	437
Vascular											
Angiosarcoma	3	17	17	17	15	17	14	8	1		109
Hemangiopericytoma		2		3	4	3	2	1			15
Lipogenic											
Liposarcoma				1		1					2
Neurogenic											0
Total malignant	247	1,492	861	822	942	1,086	989	525	123	11	7,098

HEMATOPOIETIC TUMORS

Hematopoietic tumors, 1,974 in number, were the third most prevalent tumors of bone in the files at Mayo Clinic. Included were 1,069 myelomas and 905 lymphomas. In the previous editions of this book, hematopoietic tumors were the most prevalent tumors. However, in this edition, we have included only those cases of myeloma diagnosed with a closed or open biopsy of a bone tumor and not those diagnosed with a bone marrow biopsy.

CHONDROGENIC TUMORS

The largest group consisted of 3,118 chondrogenic tumors. These tumors were placed in this group because their histologic appearance proved or suggested a relationship to hyaline cartilage. This group formed more than 30% of the total series, and the osteochondromas (osteocartilaginous exostosis) constituted 32.8% of the chondrogenic group. The osteochondroma results from the growth of its cartilage cap, which makes the lesion basically chondrogenic. Chondroma, whether centrally or subperiosteally located, is a tumor of hyaline cartilage that may contain variable amounts of calcification and ossification within its substance. Benign chondroblastoma has been differentiated from the "wastebasket" of giant cell tumor of bone because its proliferating cells produce foci of a matrix substance similar to that of hyaline cartilage. Although chondromyxoid fibroma has a variegated histologic appearance, large or small zones ordinarily bear a striking resemblance to hyaline cartilage. Both primary and secondary chondrosarcomas occur. Approximately 10% of either type dedifferentiate into highly malignant neoplasms. Mesenchymal chondrosarcoma is recognized as a distinctive lesion.

OSTEOGENIC TUMORS

Of the 2,531 osteogenic tumors, 1,952 were osteosarcomas. For a tumor to qualify for this group, the malignant neoplastic cells of the tumor must, in at least some portions, produce recognizable osteoid substance. With this basic qualification, the osteosarcomas logically fall into three classes, namely, osteoblastic, chondroblastic, and fibroblastic, depending on the dominant histologic structure. The basic biologic behavior of these tumor subtypes, however, is similar, as shown in the chapter on osteosarcoma.

Periosteal osteosarcoma is now recognizable as a separate entity, and its features will be illustrated. The 67 telangiectatic osteosarcomas are described in Chapter 11.

The clinically indolent and pathologically slowly progressing low-grade tumors that have become generally known as parosteal, or juxtacortical, osteosarcomas have been placed in a separate subdivision. In addition, there are 21 examples of low-grade intraosseous osteosarcomas.

The Mayo Clinic files contained 396 osteoid osteomas. They have arbitrarily been classified as bone tumors, notwithstanding the controversy about whether this lesion is a true neoplasm or some peculiar reaction in bone. The 108 tumors that may be called *giant osteoid osteoma*, or *osteoblastoma*, still generate controversy.

TUMORS OF UNKNOWN ORIGIN

The most frequent tumor of unknown origin recorded in the Mayo Clinic files was benign giant cell tumor (671 examples). Almost as prevalent was Ewing tumor (611 cases). The giant cells of the benign giant cell tumor appear to arise from stromal cells, the exact origin of which is unknown. It has been suggested that the mononuclear cells arise from undifferentiated mesenchymal cells of bone. The diagnosis of malignant giant cell tumor cannot be substantiated unless typical zones of benign giant cell tumor can be demonstrated in the current or previous tissue from the same case. Only 39 examples of malignant giant cell tumor are recorded in the Mayo Clinic files. Adamantinoma of long bones, still considered of unknown origin, accounted for only 44 tumors (in 40 patients) in the series.

FIBROGENIC TUMORS

In the fourth edition of this book, fibroma of bone, or metaphyseal fibrous defect, was included as a benign counterpart of a fibrogenic tumor. This lesion is now categorized as a neoplasm simulator because it is not considered to be a true neoplasm. Only one example of the rare and controversial fibrocartilaginous mesenchymoma was found in the series. There were 16 examples of desmoplastic fibroma; although classed among the malignant tumors, they probably occupy a gray zone between benign and malignant neoplasms. Hence, fibrosarcoma becomes the dominant tumor in this group.

HISTIOCYTIC TUMORS

Neoplasms of apparent histiocytic origin are still uncommon in bone. Benign and atypical fibrous histiocytoma is a nebulous diagnosis at best. The term *malignant fibrous histiocytoma* is used when the tumor is pleomorphic and shows no matrix production. Only 98 tumors were classified as malignant fibrous histiocytoma in the Mayo Clinic files.

TABLE 1.2. Skeletal Distribution of Bone Tumors

	Femur	*Tibia*	*Fibula*	*Tarsals*	*Foot*	*Patella*	*Humerus*	*Radius*	*Ulna*	*Carpals*	*Hand*	*Scapula*	*Clavicle*	*Ribs*	*Sternum*	*Vertebrae*	*Sacrum*	*Innominate*	*Skull*	*Mandible*	*Maxilla and Nasal Cavity*	*Total*
Benign																						
Osteochondroma	320	153	40	8	3	0	147	21	10	0	15	43	4	24	0	22	4	70	0	0	0	884
Chondroma	81	22	13	1	17	1	72	6	5	2	180	11	0	0	2	5	1	7	0	0	0	426
Chondroblastoma	42	26	1	12	0	4	29	1	1	0	0	6	0	3	0	1	0	13	7	1	0	147
Chondromyxoid fibroma	6	16	1	0	7	0	1	2	2	1	1	1	1	0	0	1	0	8	2	0	0	50
Osteoid osteoma	147	72	6	19	4	0	34	7	12	6	27	6	0	0	0	36	8	9	2	2	0	397
Osteoblastoma	11	9	2	5	0	1	5	0	1	1	1	1	1	2	0	34	10	9	2	11	2	108
Giant cell tumor	203	166	16	7	2	1	35	75	15	5	11	1	0	5	2	42	56	34	6	0	0	682
Fibrous histiocytoma	2	1	0	0	1	0	1	0	0	0	0	0	0	0	0	5	0	0	0	0	0	10
Hemangioma	9	4	2	2	0	1	3	1	1	0	1	4	1	5	0	37	3	5	55	6	9	149
Lipoma	3	1	1	1	0	0	1	0	1	0	0	0	0	1	0	0	0	0	2	0	0	11
Neurilemmoma	2	1	0	0	0	0	0	0	0	0	0	1	0	1	0	0	9	0	3	6	0	23
Total benign	826	471	82	55	34	8	328	113	48	15	236	74	7	41	4	183	91	155	79	26	11	2,887
Malignant																						
Myeloma	157	11	1	0	0	0	86	5	4	0	0	27	37	157	32	296	52	138	41	6	7	1,057
Malignant lymphoma	200	60	4	5	1	3	83	6	13	1	2	35	18	61	22	125	47	130	39	36	14	905
Primary chondrosarcoma	224	65	31	12	9	0	133	9	3	1	14	55	6	120	28	61	24	237	9	2	29	1,072
Secondary chondrosarcoma	27	12	7	2	1	0	11	0	0	1	0	8	2	7	0	9	5	62	0	0	1	155
Dedifferentiated chondrosarcoma	57	6	1	0	0	0	20	0	0	0	0	5	0	5	0	3	0	48	0	0	0	145
Clear cell chondrosarcoma*	11	0	0	0	0	0	5	0	1	0	0	0	0	2	1	3	0	2	0	0	1	26
Mesenchymal chondrosarcoma	6	1	1	0	1	0	1	1	0	0	0	1	0	4	0	4	2	4	1	5	4	36
Osteosarcoma	771	357	62	16	3	1	185	25	10	0	5	36	14	40	11	47	40	178	46	63	74	1,984
Parosteal osteosarcoma	53	9	3	0	0	0	8	0	2	0	0	0	0	0	0	0	0	0	0	0	0	75
Ewing tumor	131	50	41	13	16	0	56	13	13	1	4	27	11	48	2	25	36	115	6	6	0	614
Malignant giant cell tumor	16	6	0	0	0	0	5	0	0	0	0	0	0	0	0	2	5	5	0	0	0	39
Adamantinoma	2	34	4	0	0	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0	43
(Fibrous) histiocytoma	35	14	1	0	0	0	8	1	3	0	0	2	0	0	1	2	6	12	6	1	6	98
Desmoplastic fibroma	2	2	0	1	0	0	1	2	1	0	0	2	0	0	0	0	0	2	0	3	0	16
Fibrosarcoma	75	42	5	4	0	0	23	1	1	0	3	7	1	9	1	14	18	44	7	19	12	286
Chordoma	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	70	197	0	170	0	0	437
Angiosarcoma	13	11	2	2	6	2	11	1	2	0	7	1	2	5	0	15	2	20	5	0	2	109
Hemangiopericytoma	2	1	0	0	0	0	1	0	0	0	0	0	0	1	1	2	1	4	1	1	0	15
Total malignant	1,771	682	162	55	37	6	632	65	54	4	35	206	91	457	98	675	434	999	332	142	149	7,086
Total series	2,597	1,153	244	110	71	14	960	178	102	19	271	280	98	498	102	858	525	1,154	411	168	160	9,973

*These tumors are included in the primary chondrosarcoma group.

NOTOCHORDAL TUMORS

The series included 437 chordomas. Metastasis of notochordal tumors is somewhat unusual, and because death usually results from local recurrence and extension, the lesion has been placed in the category of malignant tumors.

TUMORS OF VASCULAR ORIGIN

Although angiomas are commonly seen on radiographs, only 149 hemangiomas were recorded in the Mayo Clinic files. The terms *hemangioendothelioma*, *hemangioendothelial sarcoma*, and *angiosarcoma* have all been used for malignant tumors of endothelial origin, and 109 such examples were located in the Mayo Clinic files. Primary hemangiopericytoma in bone, extremely rare, accounted for only 15 tumors noted in the Mayo Clinic files.

LIPOGENIC TUMORS

The present series included 11 lipomas of bone and only 2 primary liposarcomas. Most tumors with multinucleated giant cells possessing foamy cytoplasm that suggests origin from adipose connective tissue were classified with the osteosarcomas or with the malignant fibrous histiocytomas. This decision was based on the observation that other tumors containing zones of obvious osteosarcoma or qualifying as fibrous histiocytomas had similar histologic appearances.

NEUROGENIC TUMORS

Primary neurilemmoma of bone is uncommon. There were 23 examples in the Mayo Clinic files. Six involved the mandible and nine the sacrum. When the tumor involves the presacral region, it is frequently difficult to know whether it should be considered a primary bone neoplasm or a soft-tissue lesion invading bone secondarily. There were no malignant neurogenic tumors originating in bone.

UNCLASSIFIED TUMORS

A few tumors had to be excluded from the total series because there was insufficient tissue for accurate classification. Another group, constituting approximately 1% of the total, did not fit into a niche in the classification. These neoplasms form a heterogeneous group that, for the time being, must be called *unclassified.*

SKELETAL AND AGE DISTRIBUTION

The skeletal distribution of the various types of bone tumors in Table 1.2 affords the reader a convenient guide for comparative incidence, whether interest is in a specific neoplasm or in an affected bone. The knowledge that some tumors almost never occur in a certain bone and that other tumors have a predilection for certain bones often is of assistance in arriving at the correct diagnosis. It is noteworthy, for instance, that only 5 of the 1,984 osteosarcomas affected bones of the hands and wrist and that all but 4 of the 103 lesions of the sternum were malignant.

Some tumors have a decided predilection for patients of certain age groups. This knowledge is often useful in arriving at a preoperative diagnosis. In the succeeding chapters, the age distribution for each neoplasm is shown by a bar graph. Tables 1.1 and 1.2 show the specific data for each neoplasm.

BIBLIOGRAPHY

1951 Lichtenstein, L.: Classification of Primary Tumors of Bone. Cancer, 4:335–341.

1951 Pugh, D. G.: Roentgenologic Diagnosis of Diseases of Bones. New York, Thomas Nelson & Sons, 316 pp.

1953 Dockerty, M. B.: Rapid Frozen Sections—Technique of Their Preparation and Staining. Surg Gynecol Obstet, 97:113–120.

1955 Schajowicz, F.: Aspiration Biopsy in Bone Lesions: Cytological and Histological Techniques. J Bone Joint Surg, 37A:465–471.

1958 Jaffe, H. L.: Tumors and Tumorous Conditions of the Bones and Joints. Philadelphia, Lea & Febiger, 629 pp.

1971 Murray, R. O. and Jacobson, H. G.: The Radiology of Skeletal Disorders: Exercises in Diagnosis. Baltimore, Williams & Wilkins Company, 1,320 pp.

1972 Lichtenstein, L.: Bone Tumors, ed. 4. St. Louis, C.V. Mosby Company, 441 pp.

1973 Edeiken, J. and Hodes, P. J.: Roentgen Diagnosis of Diseases of Bone, ed. 2, vols. 1 and 2. Baltimore, Williams & Wilkins Company, 1,156 pp.

1973 The Netherlands Committee on Bone Tumours: Radiologic Atlas of Bone Tumours, vols. 1 and 2. Baltimore, Williams & Wilkins Company, 600 pp.

1981 Madewell, J. E., Ragsdale, B. D., and Sweet, D. E.: Radiologic and Pathologic Analysis of Solitary Bone Lesions. Part I: Internal Margins. Radiol Clin North Am, 19:715–748.

1981 Ragsdale, B. D., Madewell, J. E., and Sweet, D. E.: Radiologic and Pathologic Analysis of Solitary Bone Lesions. Part II: Periosteal Reactions. Radiol Clin North Am, 19:749–783.

1981 Sweet, D. E., Madewell, J. E., and Ragsdale, B. D.: Radiologic and Pathologic Analysis of Solitary Bone Lesions. Part III: Matrix Patterns. Radiol Clin North Am, 19:785–814.

1989 Mirra, J. M.: Bone Tumors: Clinical, Radiologic, and Pathologic Correlations. Philadelphia, Lea & Febiger, 1,831 pp.

1990 Campanacci, M.: Bone and Soft Tissue Tumors. New York, Springer-Verlag, 1,131 pp.

1991 Huvos, A. G.: Bone Tumors: Diagnosis, Treatment, and Prognosis, ed. 2. Philadelphia, W.B. Saunders Company, 784 pp.

1994 Schajowicz, F.: Tumors and Tumorlike Lesions of Bone: Pathology, Radiology, and Treatment, ed. 2. New York, Springer-Verlag, 649 pp.

1998 Dorfman, H. D. and Czerniak, B.: Bone Tumors. St. Louis, Mosby, 1,261 pp.

CHAPTER

2

Osteochondroma (Osteocartilaginous Exostosis)

Osteochondromas arise on the surface of bone and are composed of a cartilage-capped osseous stalk that is continuous with the underlying bone. The majority of osteochondromas occur as solitary lesions. However, approximately 15% of osteochondromas occur in the setting of *multiple osteochondromas* or *hereditary multiple exostoses*, an autosomal dominant disorder characterized by multiple osteochondromas. In almost 90% of patients with hereditary multiple exostoses, germline mutations in the tumor-suppressor genes *EXT1* or *EXT2* are found. In addition, *EXT1* has been found to act as a tumor suppressor gene in the cartilage cap of solitary nonhereditary osteochondromas. Growth of osteochondromas usually parallels that of the patient, and the lesion often becomes quiescent when the epiphyses have closed. Spontaneous regression has been described.

Bony spurs that result from trauma or degenerative joint disease may simulate the appearance of osteochondromas but do not belong in the same group.

Some patients with multiple hereditary exostoses also have other developmental abnormalities of bone such as shortening of the ulna and displacement of the radius outward. The fibula also may be shortened. In addition, there is lack of tubulation of the long bones, which may be especially prominent in the femoral neck region. Each tumor in patients with multiple hereditary exostoses has a characteristic that will be described for the solitary form. The exact risk of chondrosarcomatous change in patients with multiple exostoses is unknown because of selection factors related to the indication for surgery in individual patients with benign or suspected malignant tumors and the lack of follow-up from birth to death in a large group of selected patients with multiple osteochondromas (the same drawbacks apply to the calculation of the risk for patients with other benign conditions, such as multiple chondromas). Peterson, after follow-up studies in a number of patients with multiple hereditary exostoses, thought that malignant change occurs in fewer than 1% of patients.

In a study of 75 patients with chondrosarcoma secondary to osteochondroma, Garrison and coauthors found that 27.3% of patients with multiple osteochondromas who underwent surgery had secondary chondrosarcomas, whereas only 3.2% of patients with the solitary form had malignant change. A later study by Ahmed and coauthors found the incidence to be 36.3% and 7.6%, respectively. However, these figures are probably an exaggeration because of selection factors. Patients with secondary malignant lesions are much more likely to seek medical attention. Most patients with multiple exostoses have many, sometimes innumerable, lesions that may be grossly deforming, although an occasional patient has only two or three lesions. One patient in the Mayo Clinic series had polyposis of the colon.

Subungual exostoses are peculiar projections from the distal portion of the terminal phalanx, usually the first toe. They are almost certainly a form of heterotopic ossification. These exostoses are not included in the data on osteochondromas, although they possess some of the radiographic and pathologic features of osteochondroma.

INCIDENCE

Osteochondromas accounted for 33.4% of the benign bone tumors and 10.1% of all tumors in the Mayo Clinic series. Of all tumors in the chondrogenic series, 32.8% were osteochondromas. Most osteochondromas are asymptomatic and are never found, and many of those that are discovered are never excised, so that the actual incidence is much greater than these figures for surgical cases indicate. Approximately 86% of the patients (884) had solitary lesions. One patient with a lesion of the proximal fibula had received radiation treatment for a desmoid tumor previously (Fig. 2.1).