CHAPTER 38 Malignant Bone Tumors

Osteosarcoma

INTRODUCTION

Osteosarcoma (osteogenic sarcoma) is the most common malignant bone tumor in children and adolescents. The neoplasm is composed of a sarcomatous stroma and malignant osteoblasts that directly form tumor osteoid or bone, although fibrous and cartilaginous elements may coexist or even predominate. The classic osteosarcoma develops in the medullary cavity of a bone, usually in the metaphysis of a long bone. There are several variants of the classic high-grade osteosarcoma. Osteosarcomas may also arise from the surface of bones in relation to the periosteum and immediate periosteal connective tissue. These are termed juxtacortical osteosarcomas and are less common than the central lesions. They may be low-grade, fibroblastic osteosarcomas, termed parosteal osteosarcomas,[60,403,483] or intermediate-grade, chondroblastic osteosarcomas, termed periosteal osteosarcomas.[169,403,510] Rarely, a low-grade endosteal osteosarcoma variant that arises within bone from the endosteum has been encountered.[42] These lesions grow slowly and metastasize later in the course of the disease and less frequently than high-grade osteosarcoma. Thus, the names of the lesions vary with their location in relation to the bone, but the key feature to remember is that the histologic grade of the sarcoma determines its biologic aggressiveness. Telangiectatic osteosarcoma is a high-grade malignant lesion that shows little evidence of ossification but undergoes cystic and necrotic changes owing to its rapid growth. Because the bone is weakened by the rapid destructive osteolytic process, pathologic fracture is common.* Paget's sarcoma is not encountered in children.[134] In this chapter classic osteosarcoma is discussed.

CLASSIC OSTEOSARCOMA

Generally, the tumor occurs between the ages of 10 and 25 years, although it has been found in children as young as 5 years and in the elderly. When osteosarcoma develops in an older person, the possibility of malignant transformation of a preexisting benign bone disease such as Paget's disease of bone or fibrous dysplasia should be considered.† Osteosarcomas may also arise in bones that have been irradiated for other reasons.* The incidence in boys is almost equal to that in girls.

The tumor is usually situated near the metaphyseal region of a long bone, but on occasion it may be diaphyseal in location. The most common sites, accounting for over 50 percent of cases, are the lower end of the femur and the upper end of the tibia.[58,310,500] The upper ends of the humerus and the femur are next in frequency. Less commonly, a classic osteosarcoma is encountered in the fibula,[278] pelvic bones,[120,122,157,230] or the vertebral column.[127,350,426] Occurrence in the distal part of a limb (hand or foot) is rare.[331,336] However, the tumor has been described in every bone in the body. There are also numerous reports of multiple or multicentric osteosarcomas.†

Pathologic Findings. The tumor ordinarily begins developing in the medullary cavity of a long bone near the metaphysis, but by the time it is recognized it has already penetrated and extended through the cortex, raising the periosteum (Fig. 38–1).‡ In more advanced cases the periosteal barrier may be broken and a soft tissue tumor mass may be seen invading the contiguous muscle tissue. In general, the central portions of the neoplasm are more heavily ossified than the peripheral areas. The ossified portions are of a gritty consistency and have a yellowish appearance; the more cellular areas are softer and tan to whitish in color. In a sagittal section of an amputated specimen, the boundaries of the epiphyseal end of the tumor are not clearly distinguishable. The physis is less readily violated than the cortical wall and remains unpenetrated until later in the course of the disease. The articular hyaline cartilage serves to block the extension of the neoplasm into the joint. Transepiphyseal extension has been reported,[117,143,337,433] but extension across the articular cartilage does not occur unless there has been a fracture. The tumor may enter the joint, however, by extending along ligament and capsular structures (such as the cruciate ligaments).[406,435] Toward the diaphyseal end, the advancing tumor presents as a conical plug that marks the limit of growth of the lesion lengthwise along the shaft. Skip metastases (isolated foci of tumor in the same bone separated from the main tumor mass by normal marrow) may occasionally occur, a fact that must be borne in mind in determining the optimum level for resection.[59,116] This is

*See references 124, 294, 295, 308, 359, 384.
†See references 167, 168, 200–202, 209, 316, 404, 461, 513.

*See references 18, 54, 122, 134, 206, 265, 363, 429, 478.
†See references 53, 79, 165, 190, 222, 255, 279, 281, 332, 344, 423, 460.
‡See references 56, 66, 81, 212, 301, 402, 480, 481.

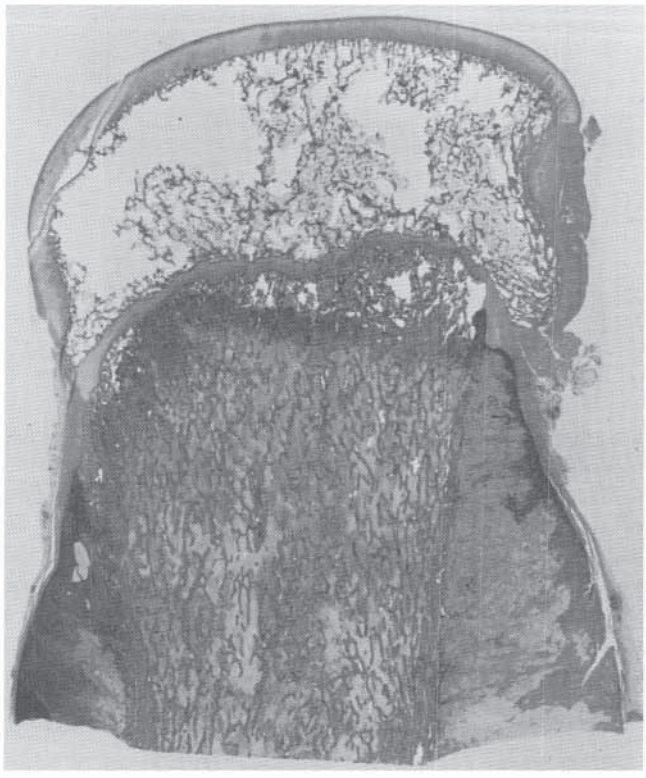


FIGURE 38–1 Osteogenic sarcoma of the proximal humerus. Photomicrograph of sagittal section of amputated specimen. The neoplasm is metaphyseal in location; it has perforated the cortex and raised the periosteum. The physis is unbroken; it does not become violated until later in the course of the disease (×10).

usually detectable by bone scans and magnetic resonance imaging (MRI)[328] and portends a poorer prognosis, similar to that of a patient with lung metastases.[511]

The histologic findings of osteosarcoma usually show a frankly sarcomatous stroma and direct formation of neoplastic osteoid and bone (Fig. 38–2).* In some pathologic specimens, however, tumor osteoid bone cannot be demonstrated, only collagen strands interwoven with the tumor cells. In anaplastic areas the neoplasm will consist of pleomorphic cells with little intercellular substance. In other tumors neoplastic cartilage and atypical spindle-shaped cells may be the predominant feature. Aegerter and Kirkpatrick have divided the microscopic picture of osteosarcoma into four types.[5] In the first form, osteoid production is the predominant finding; in the second type, both osteoid and cartilage are formed. In the third type, neither osteoid nor cartilage is produced, but collagen is formed. In the fourth type, there is little or no indication of the presence of these intercellular substances. Attempts to correlate the four histologic types with the clinical manifestations of osteosarcoma have been futile. On the basis of histologic findings alone, one cannot predict the rate of growth, the advent of metastasis, or the duration of survival.[58,82,148,361,463,500] The important point to remember is that osteosarcoma may have large areas with little or no bone formation, but if any neoplastic bone is present it is called osteosarcoma and treated as such.

*See references 49, 56, 82, 83, 163, 289, 402, 480, 482, 500.

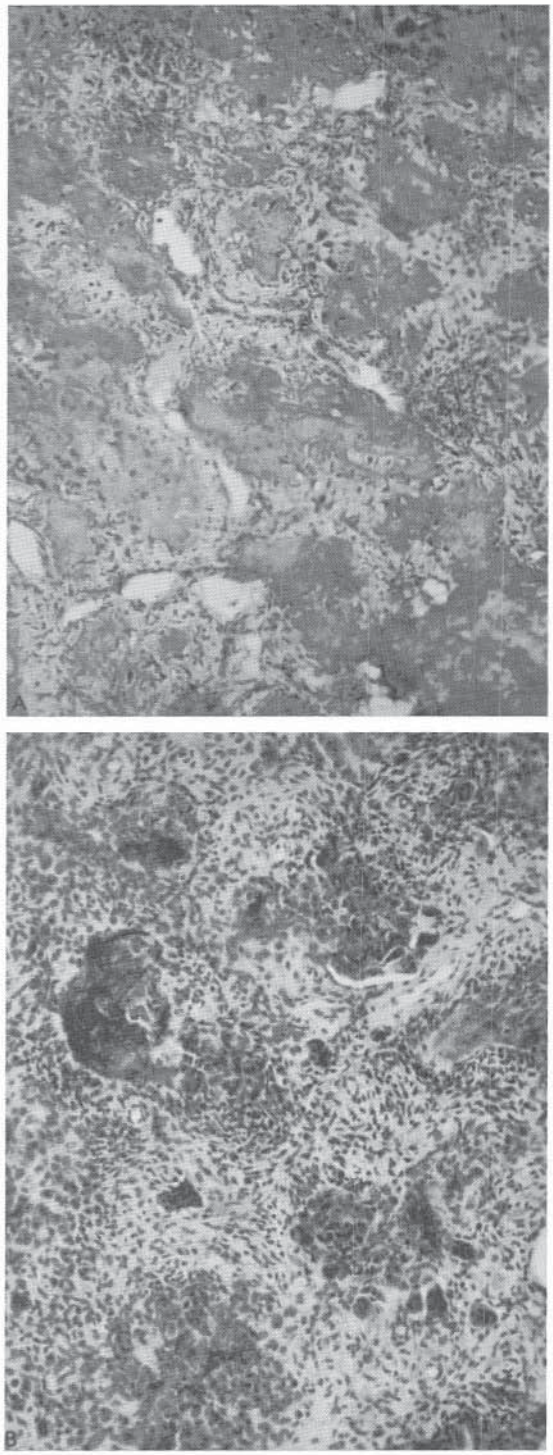


FIGURE 38–2 Histologic findings in Osteogenic sarcoma. **A,** Photomicrograph showing the sarcomatous stroma and the direct formation of neoplastic osteoid and bone (×100). **B,** Greater magnification (×250).

In an adolescent, the diagnosis of chondrosarcoma should be viewed with suspicion, despite demonstration of only high-grade chondrosarcoma in a biopsy specimen. It is highly likely that examination of the entire specimen of a "chondrosarcoma" in an adolescent will reveal neoplastic bone formation.

The pathologist determines the histologic grade of the

tumor based on cellularity, atypia, pleomorphism, degree of tumor necrosis, and number of mitoses. A three- or four-grade system is used, depending on the pathologist. The prognostic significance of the number of mitotic figures is uncertain; at best, it is an index of the rate of growth.[305] The histologic grade of the tumor is important in that a low-grade surface or central osteosarcoma[42,60,245,361] has a much better prognosis than a high-grade (grade 2 or 3) osteosarcoma.[82,308,330,463,500,510]

Clinical Findings. Local pain in the affected part is the presenting complaint. Initially the pain is intermittent, but within a matter of weeks it becomes severe and constant. There may be a history of trauma that has precipitated discomfort from the tumor. It is often presumed that the trauma caused the tumor, but it is more likely that the injury called attention to the affected site. When a lower limb is affected, an antalgic limp may develop. As the condition progresses, a local mass that is hard and fixed to the underlying bone may be palpated (Figs. 38–3A and B). There may also be increased local heat and sensitivity to pressure. The firmness of the tumor varies, depending on the extent of ossification. The tumor may become visible as it increases in size. Limitation of joint motion and disuse atrophy of the muscles are other findings. It is important to recognize that patients with osteosarcoma are not "sick." They do not have fever, weight loss, or cachexia, and except for disease at the primary site, they appear to be healthy. This is one reason why the diagnosis may be delayed. On rare occasions, however, in an instance of rapidly growing neoplasm with pulmonary metastases occurring in the early stages, the patient's general condition may be very poor. A pathologic fracture through the lesion may be the presenting condition.[2,216,361,417]

Imaging Findings. Osteogenic sarcoma has a typical radiographic picture characterized by destructive and osteoblastic changes (Figs. 38–3D and E to 38–6).[4,65,132,198,393,418] It may be purely radiodense or purely radiolucent, but commonly it is a mixture of both. The neoplasm usually begins eccentrically in the metaphyseal region of a long bone. Bone destruction is evident as loss of the normal trabecular pattern and the appearance of irregular, ill-defined, poorly marginated, ragged radiolucent defects. New bone formation may be neoplastic or reactive and appears as areas of increased radiopacity. The cortex is invaded by the growing tumor, as evidenced by destruction of the cortical wall and raising of the periosteum. The tumor is large and poorly marginated. There is an incomplete attempt of the host to contain the tumor by periosteum (the so-called Codman's triangle). Codman's triangle has its base perpendicular to the shaft and is created by the subperiosteal reactive new bone; it is not diagnostic of osteosarcoma, as it is also seen in osteomyelitis and Ewing's sarcoma. The "sunburst" appearance is produced by the formation of spicules of new bone laid down perpendicular to the shaft along the vessels passing from the periosteum to the cortex. A soft tissue mass will be discernible on the radiographs as the tumor advances and transgresses the cortex. Pathologic fracture may occur.

Osteosarcomas do not always exhibit the classic radiographic pattern. They may be subtle in the early stages. They may be radiolucent and diaphyseal, leading one to assume it is Ewing's sarcoma. I have seen one case detected by serendipity on a comparison radiograph obtained for a suspected fracture. Pathologic fracture may make the diagnosis very difficult and it is not uncommon to see patients treated for long bone fractures, only to have an underlying neoplasm discovered weeks later. Aneurysmal bone cysts can mimic osteosarcomas, and the latter may have fluid-fluid levels on MRI, adding to the confusion. Clinical suspicion should be raised if a teenager presents with unexplained pain about the knee or shoulder, especially if the pain does not resolve quickly or is present at rest or at night. Radiographs in such cases should be critically analyzed, and if any doubt exists, the patient should be further evaluated by radionuclide scintigraphy or MRI.

Once the diagnosis of osteosarcoma has been made, the disease should be staged. Staging involves determining the local extent of the tumor and searching for metastatic spread. The questions to be answered are (1) Is the tumor limited to the bone (intracompartmental) or has it spread to the adjacent soft tissues (extracompartmental)? and (2) Is there evidence of metastatic spread to the lungs or other bones? Once these questions are answered, a biopsy is done to determine the diagnosis and the grade of the lesion.

MRI and computed tomography (CT) are of great value in depicting the details of bone destruction and tumor bone production within the lesion. MRI has largely replaced CT as the optimal modality for imaging the primary tumor, and CT is used to evaluate the chest for pulmonary metastases.[197,217,456,485,514] On CT the neoplastic bone appears amorphous and not stress oriented (Fig. 38–7). The areas of cortical erosion by the tumor tissue are well delineated. MRI optimally demonstrates the degree of soft tissue extension and the relationship of the extracompartmental tumor to fascial planes and neurovascular structures. Perhaps the best feature of MRI is the ability to precisely evaluate the medullary cavity. This is very useful when planning limb-sparing resections. The radiologist can measure the extent of the tumor from fixed palpable bony landmarks to help the surgeon plan bone osteotomies. Occult skip metastases of 2 mm or more in long bones are also well seen on MRI. MRI is also useful in evaluating the adjacent joint for tumor spread.

Pulmonary metastases 3 to 7 mm or more in diameter are identified with CT.[349] Conventional radiographs of the chest (dual inspiration and expiration views) will show metastatic nodules 10 mm or greater in diameter. The importance of pulmonary CT in the staging of osteosarcoma cannot be overemphasized.[71,72,94,349,488] Approximately 10 to 20 percent of patients with osteosarcoma will present with radiographically detectable metastases at diagnosis. Most of these are in the lungs. Chest CT is superior to plane radiography in demonstrating these metastases, and spiral CT is superior to conventional CT for this purpose.[72,73,186,349,488]

Bone scan with technetium 99m will show a marked increase in the uptake of the radionuclide in the primary tumor. The increased uptake is due to active formation of new tumor and host bone as well as the vascularity of the lesion (Fig. 38–8). Radionuclide bone scintigraphy is used to look for bony metastases in the involved bone (skip

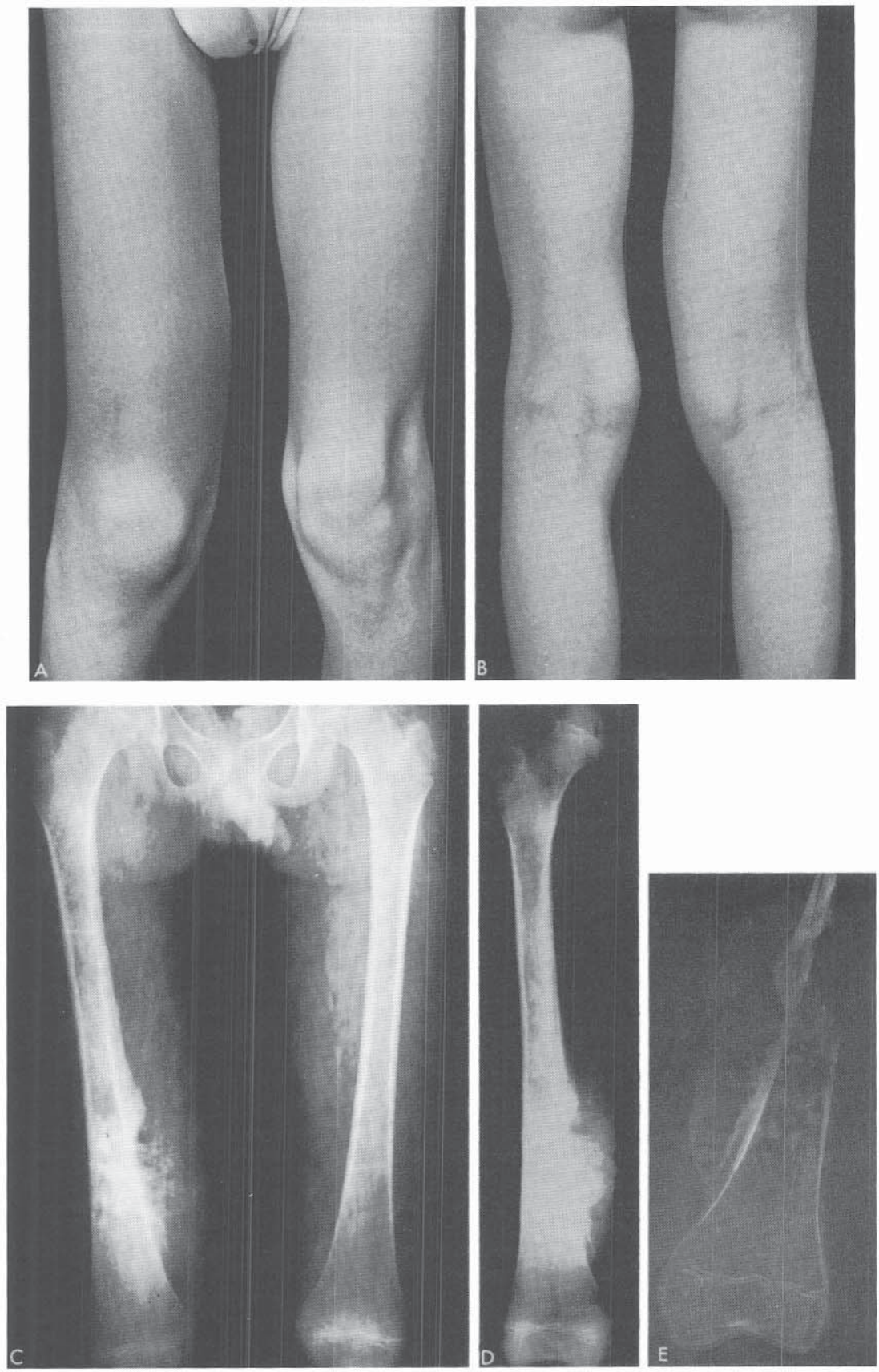


FIGURE 38–3 Osteogenic sarcoma of the right distal femur. **A** and **B,** Clinical appearance, showing swelling of the patient's right lower thigh. **C** and **D,** Radiographs of the femora. Note both the "sunburst" appearance and the areas of increased radiopacity (neoplastic bone) and radiolucency (bone destruction). **E,** Radiograph of sectional segment.

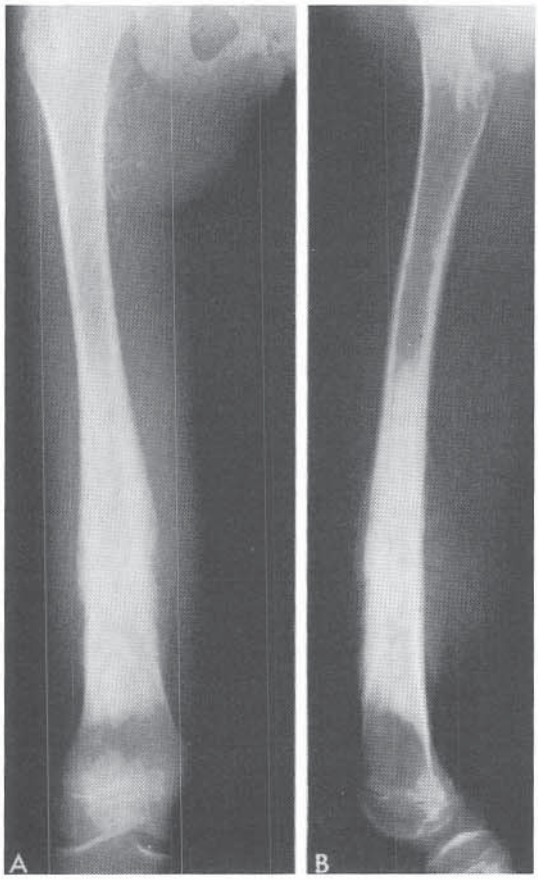


FIGURE 38–4 Osteogenic sarcoma of the distal femur in a 12-year-old girl. **A** and **B,** Radiographs of the femur. The normal trabecular pattern is lost as the neoplastic bone has invaded the cortex and has raised the periosteum. Note the "sunburst" appearance and Codman's triangle. The conical plug of the tumor in the midshaft (best seen on the lateral view) marks the proximal limit of the lesion lengthwise along the shaft.

metastases)[59,69,116,418,511] and at other skeletal sites.* The intensity of the uptake increases with the vascularity of the lesion. Ordinarily the margins of the increased isotope activity mark the extent of the osteosarcoma; this is not absolute, however, as the tumor may extend beyond the margin of increased radioisotope uptake.

Angiography is of great value in delineating the extent of soft tissue extension and its relationship to adjacent neurovascular structures but is seldom used anymore since MRI can display this information more easily and less invasively. Angiography has been useful in demonstrating response to preoperative chemotherapy, but dynamic MRI also has replaced this imaging modality.[65,196,198,418]

Laboratory Findings. There are no specific laboratory tests for osteosarcoma. The complete blood cell (CBC) count is usually normal and, although the erythrocyte sedimentation rate (ESR) may be elevated, it is not specific. The serum alkaline phosphatase (ALP) level is usually elevated in osteosarcoma, reflecting osteogenesis in the neoplastic tissue.[23,123,361] The degree of elevation of this enzyme is commensurate with the activity of the neoplastic osteoblasts within the lesion and the size of the tumor. In some studies, an elevated ALP level has been associated with a worse prognosis. The course of osteosarcoma can be monitored by serial determination of serum ALP levels. Following ablation of the tumor, the enzyme level falls to near normal; it rises with the development of metastases and with recurrence. Clinically sequential determinations of serum ALP levels are utilized to assess response to chemotherapy. The lactate dehydrogenase (LDH) level has been shown in some studies to be of prognostic importance. An elevated LDH level is associated with a worse prognosis.[269]

Differential Diagnosis. Osteosarcoma is treated by wide or radical resection or amputation and adjuvant chemotherapy. The clinical and radiographic diagnosis should always be confirmed by histologic examination of adequate tissue obtained by open or needle biopsy prior to definitive treatment.

The primary entity from which osteosarcoma must be differentiated is Ewing's sarcoma, but benign conditions may also mimic osteosarcoma. Exuberant callus of a fatigue fracture, subacute osteomyelitis, active myositis ossificans, aneurysmal bone cyst, and Langerhans cell histiocytosis (eosinophilic granuloma) are some of the benign conditions that may be mistaken for osteogenic sarcoma. Ewing's sarcoma, fibrosarcoma, lymphoma, and metastatic carcinoma are some of the malignant lesions that must be excluded. Age is a major factor in sorting out the various diagnostic possibilities. In a child less than 5 years old, histiocytosis, metastatic Wilms' tumor, or neuroblastoma should be considered. In the adolescent, osteosarcoma and Ewing's sarcoma are the most common bone malignancies. Chondrosarcoma is very uncommon in children and adolescents, and most lesions considered to be "chondrosarcoma" by biopsy are really chondroblastic osteosarcomas. Leukemias and lymphomas should also be considered in an adolescent with an aggressive bone neoplasm.

Staging. Carefully planned imaging of the lesion should precede open biopsy. Once the histologic grade of the lesion has been determined, a stage can be assigned. The objectives of the staging workup are to establish the final tissue diagnosis, to delineate the local extent of the tumor, and to discover any distant metastases. Both radiologic staging and open biopsy should be done by the surgeon who will perform the definitive operation.[38,285,286,354,432,434] If a needle biopsy is chosen, the surgeon should direct the placement of the needle. Determining the local extent of disease after biopsy performed elsewhere is difficult and inaccurate because of the disruption of tissue planes, hematoma formation, edema, and wound healing. In choosing the proper surgical procedure it is vital to know whether there are natural barriers to tumor extension.[115,118,434] Is the lesion intracompartmental (bounded by natural barriers to tumor extension) or extracompartmental (with no proximal, distal, or peripheral barriers to tumor extension)? During staging the surgeon should meticulously assess the muscle compartment and tumor proximity to neurovascular structure to determine whether limb salvage is feasible.

In the preoperative staging of osteosarcoma the following diagnostic tests are performed: (1) a complete history and physical examination; (2) CBC count with differential, ESR, and determination of serum levels of calcium, phosphorus,

*See references 28, 79, 190, 222, 255, 281, 367, 423, 460.

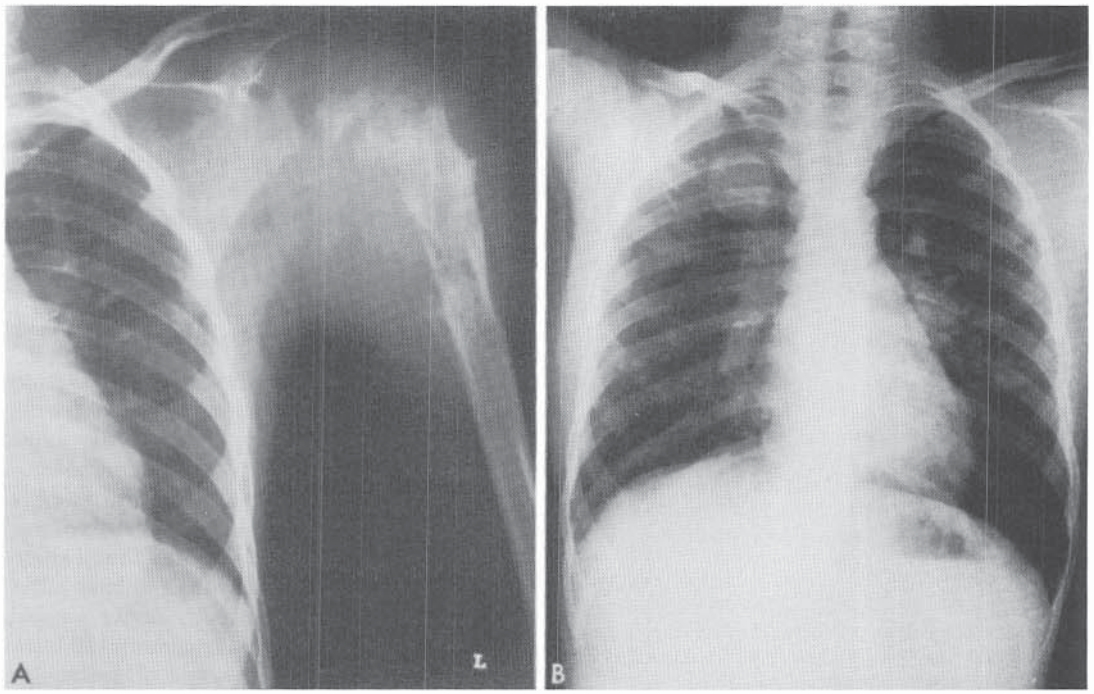


FIGURE 38–5 Osteogenic sarcoma of the left proximal humerus in a 12-year-old boy. The patient complained of pain in the left arm and shoulder of 1 month's duration. **A,** Radiograph of the left humerus showing the malignant lesion. **B,** Chest radiograph showing metastasis in the right upper lobe.

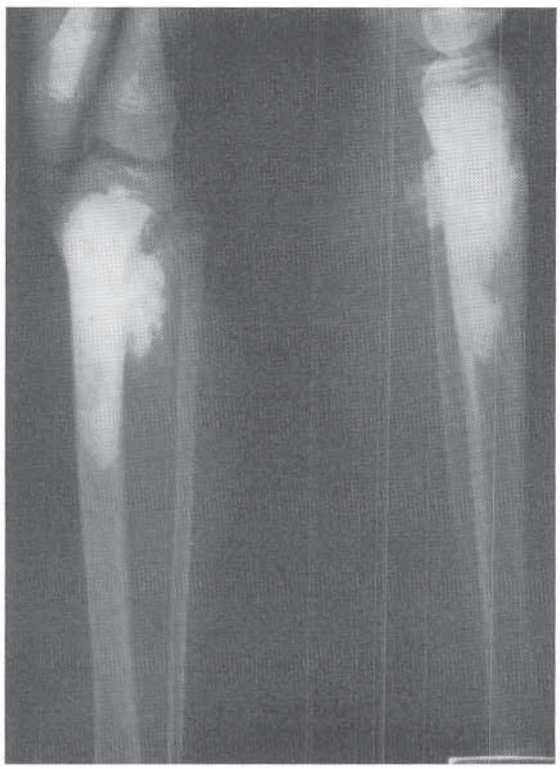


FIGURE 38–6 Osteogenic sarcoma of the proximal tibia: initial radiograph.

ALP, and LDH; (3) conventional radiographs of the part and the chest; (4) scintigraphy with technetium 99m; (5) MRI to assess intraosseous extent, joint involvement, and the relationship of the soft tissue mass to adjacent neurovascular structures; and (6) CT of the chest to rule out metastases.[434]

A pediatric oncologist, radiologist, and pathologist should be part of the treatment team from the beginning; they should be involved in the staging and decision-making process. The management of osteosarcoma requires a multidisciplinary approach. The patients should be treated in medical centers specializing in pediatric oncology.

Biopsy. Before performing an open biopsy the surgeon should be knowledgeable in the differential diagnosis and local extent of the lesion; before placing the incision, he or she should be cognizant of the principles of limb salvage surgery and amputation flaps. The surgeon who will perform the definitive operation should perform the biopsy. The technical details of performing a biopsy are presented elsewhere (see Chapter 36, General Principles of Tumor Management). It is crucial to verify the biopsy site with radiography in the operating room. Frozen sections should be used to ensure that diagnostic tissue has been obtained, and cultures of the tissue specimen should be performed. The pathologist should have the radiographic studies for review prior to or at the time of biopsy. Special stains, cytology, electron microscopy, and immunocytochemistry may be important in establishing the correct diagnosis.

There is always danger of the tumor spreading locally as a result of open biopsy. Adequate hemostasis must be obtained. The use of a tourniquet is up to the discretion of the surgeon. If a drain is used, it should be placed near and

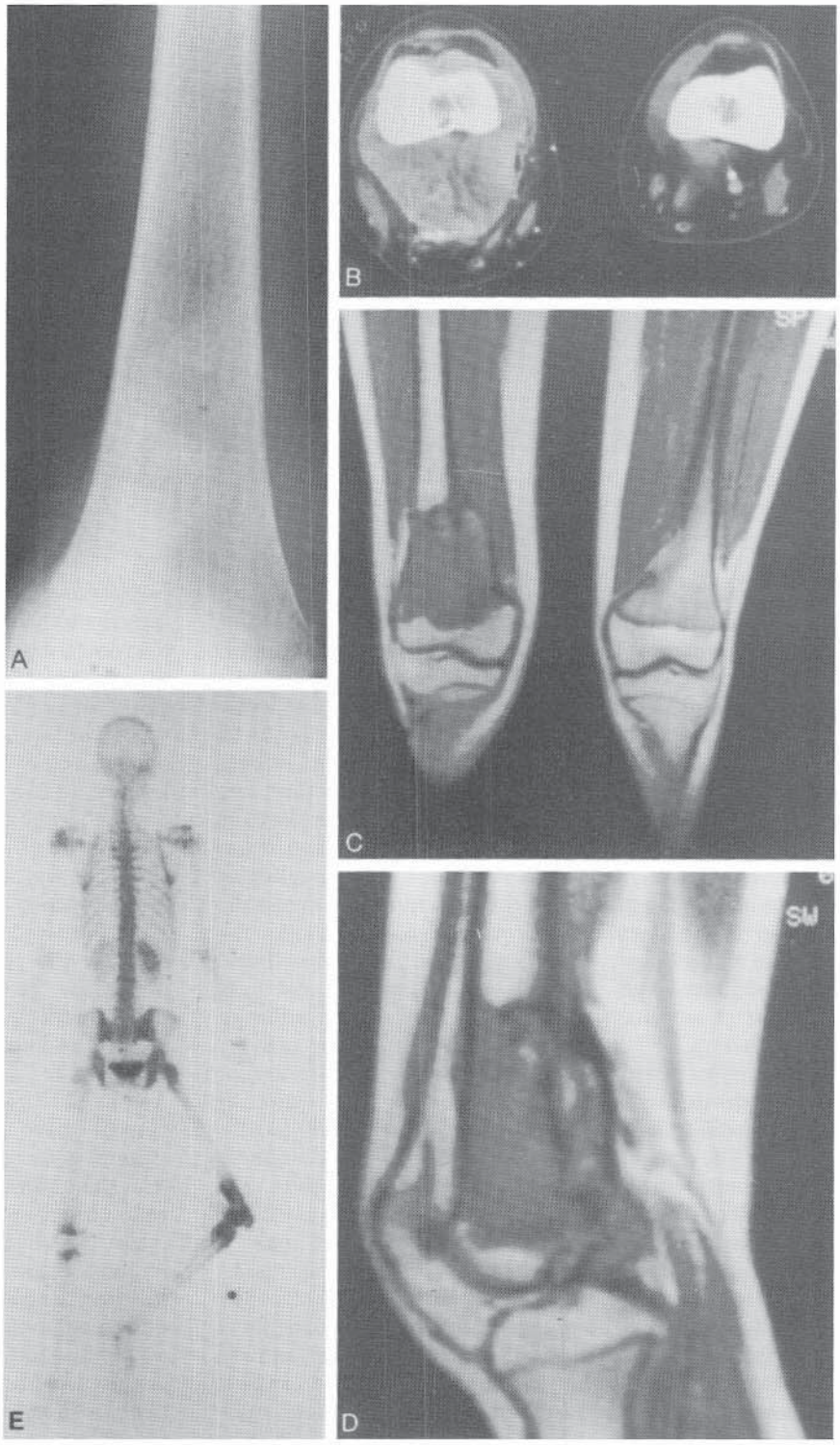


FIGURE 38–7 Osteogenic sarcoma of the left distal femur. **A,** Plain AP radiograph. Note the distal metaphyseal and lower diaphyseal sclerotic lesion. **B,** CT scan showing bone-forming tumor. **C** and **D,** MR images showing the extent of the tumor and its relationship to the popliteal soft tissue. **E,** Bone scan with technetium 99m showing increased uptake in the distal femoral metaphyseal region.

along the direction of the biopsy tract, because it will be excised at the time of primary resection. Core needle biopsies or fine needle aspirations are employed at institutions with experience in these techniques, but not all pathologists are comfortable in making the diagnosis from limited tissue.[239,354,432,451,501] Immediate definitive wide excision of osteogenic sarcoma requires a thorough clinical, radiologic, and pathologic correlation, but is seldom performed. An experienced pathologist might make a correct diagnosis on the basis of a frozen section, but definitive surgical therapy is not performed at the time of biopsy because most patients will receive preoperative (neoadjuvant) chemotherapy. It is always best to rely on permanent sections for the final diagnosis. If there is uncertainty about the diagnosis, an experienced bone pathologist should be asked to review the slides.

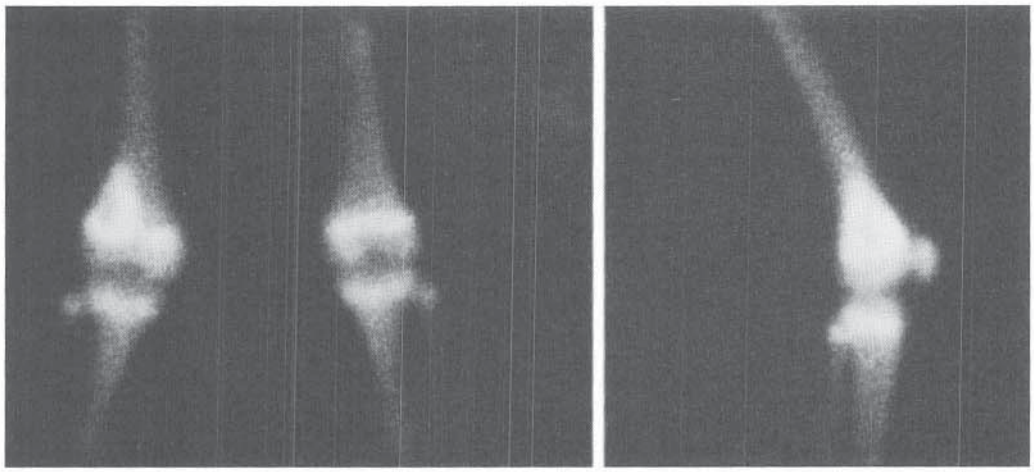


FIGURE 38–8 Osteogenic sarcoma of the right distal femoral metaphysis: bone scan findings with technetium 99m. Note the increased uptake in the lesional area.

Treatment. The treatment of high-grade osteosarcoma can be thought of in two phases: (1) the administration of adjuvant chemotherapy, and (2) surgical resection of the tumor. It is important to recognize that osteosarcoma is a systemic disease in most cases. Following amputation alone, metastatic disease, usually in the lungs, will occur in 80 to 90 percent of patients within the first 2 years.* This implies that micrometastatic disease is present from the time that osteosarcoma is clinically detected. Because micrometastatic disease is often controlled by adjuvant chemotherapy, it was hypothesized in the 1960s and 1970s that administration of chemotherapy might prevent the appearance of metastatic disease.[213,458] This hypothesis proved to be true, although the premise was challenged initially.[462] Both randomized and nonrandomized studies have shown a disease-free and overall survival advantage in patients who received adjuvant chemotherapy.[113,269,462] Prior to the chemotherapy era, the probability of remaining disease free after amputation for osteosarcoma was less than 20 percent.[82,151,153,154,289] Currently this probability is between 65 and 80 percent, or perhaps higher.† The dramatic improvements made in the ability to cure patients with osteosarcoma have come at a price. The toxicity of the drugs used is high, and the toxic effects include infections from neutropenia, cardiotoxicity, renal toxicity, and hearing loss, to name a few.‡ The standard agents include high-dose methotrexate, Adriamycin, and cisplatin. These agents have been tested in large series of patients in national trials of the Pediatric Oncology Group and the Children's Cancer Group, which provide a good example of how cooperative groups can carry out trials to study outcomes following therapy of a rare disease. Initially there was doubt about the effectiveness of chemotherapy. A randomized study definitively addressed this issue and conclusively demonstrated that adjuvant chemotherapy improves the disease-free and overall survival rate of osteosarcoma patients.[269,270] The next advance in treatment was the use of preoperative, or neoadjuvant, chemotherapy. By administering chemotherapy prior to resection, one could treat the micrometastatic disease earlier, perhaps shrink the tumor to make resection easier and study the histologic response to the drugs.[25,30,383,506] There was concern, however, that if the patient's tumor did not respond, it might progress during the preoperative period. This also was studied in a randomized trial, and it appears that outcome is similar irrespective of whether the chemotherapy is administered both pre- and postoperatively or postoperatively only. This study, not yet reported, was difficult to complete, because by the time it was opened, surgeons had a bias toward preoperative chemotherapy. Because of poor patient accrual, the power to detect a 15 percent difference in the two groups was only 80 percent. Nevertheless, preoperative chemotherapy is now the standard. One of the main advantages is that it provides prognostic information. The pathologist can examine the specimen for the percent of histologic necrosis following resection.* Patients with a higher degree of necrosis (>95 percent) have a better outcome than those with a lesser amount of necrosis. It would seem logical that giving alternative chemotherapy to patients with less tumor necrosis would improve outcome, but this has not been found to be the case in studies that have addressed this issue. The most recent cooperative trial in the United States is focused on studying the results of the addition of a newer agent, ifosfamide, and an immunostimulant (MTP-PE) to determine in a randomized trial whether the addition of either or both of these agents would further improve the survival of patients with osteosarcoma. Data from this trial are not yet available.

Many advances have been made in the treatment of osteosarcoma, yet 20 to 40 percent of patients do not respond to treatment despite similar histology, staging, and other patient characteristics. Just as there are some patients who could benefit from more aggressive chemotherapy, there are others who might need very little or no chemotherapy. It is hoped that more information about the molecular makeup

*See references 58, 80, 151, 154, 269, 301, 500.

†See references 27, 31, 135, 213, 269, 270, 311, 372, 386, 389, 458, 508, 509.

‡See references 34, 44, 110, 135, 155, 214, 224, 232, 238, 271, 419.

*See references 205, 223, 383, 387, 397, 507.

of these tumors will provide insight in this regard and perhaps allow us to target therapy more precisely. This has led to research efforts in drug resistance mechanisms, genetic alterations in these sarcomas, and novel radiographic approaches to detect nonresponders at diagnosis. Multidrug resistance has been demonstrated in osteosarcoma and is a powerful prognostic indicator.[33,68] The P-glycoprotein membrane pump actively exports agents such as Adriamycin out of the cell and can be detected by a variety of immunohistochemical methods. The exciting aspect of these findings is that this resistance pump can be blocked by other agents, offering a potential avenue of overcoming resistance in these patients. Genetic alterations in tumor suppressor genes have also been demonstrated in osteosarcomas, and there is some indication that in addition to providing clues to the etiology of the tumor, they will be of prognostic and possibly therapeutic import.* Finally, more aggressive or intensified administration of chemotherapy and novel agents may further improve outcome. Some of these avenues are currently being investigated in cooperative trials.

LOCAL CONTROL. In addition to advances in the medical management of osteosarcoma, the surgical treatment has advanced in the past 20 years. Amputation was once the standard of care and remains an important part of the armamentarium of the tumor surgeon, especially in children, but most patients who present with osteosarcoma are now treated with a limb-sparing procedure. There was initial concern about the effect of limb salvage on survival rates, and no randomized studies have been carried out that compare limb salvage and amputation.† The nonrandomized studies, however, do not show a survival advantage for patients treated by amputation, and the local recurrence rate after limb salvage procedures is similar to that after cross-bone amputation.[26,144,392,437] One large retrospective study of distal femoral osteosarcomas showed a higher local recurrence rate after limb salvage procedures and cross-bone amputation than after hip disarticulation, but the three groups did not differ in overall or disease-free survival.[392,431] It is apparent that achieving a wide margin is important, and that, coupled with a good response to chemotherapy, is associated with a low incidence of local recurrence. A less than wide margin or a less than good histologic response dramatically increased the recurrence rate in one study.[26]

AMPUTATION. Irrespective of the method chosen to optimally treat osteosarcoma, the local tumor must be completely excised with negative margins. Although amputation is used less frequently now than in the past, it remains the gold standard of local control and in the lower extremity may be the most functional "reconstruction" in young athletic patients. The primary indications are very young age where limb length inequality would be a major problem (lower extremity), displaced pathologic fractures, large soft tissue masses involving neurovascular structures, disease progression during chemotherapy, and local recurrence following limb salvage procedures. In the upper extremity, one usually tries very hard to preserve at least hand function, because prosthetic replacements are not nearly as good as a functional hand, but in the lower extremity, modern prosthetics are very functional (Fig. 38–9).[228]

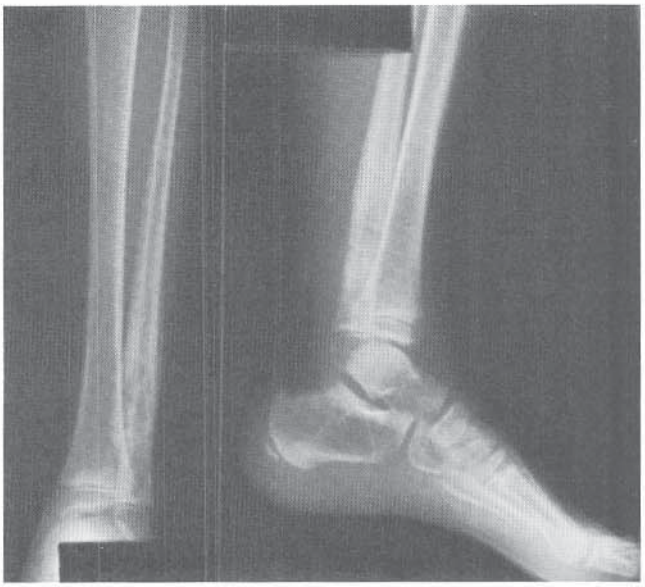


FIGURE 38–9 Osteogenic sarcoma of the distal left fibula in a 5½-year-old Caucasian girl. Initial radiographs of the left leg showed a destructive lesion of the distal metaphysis of the fibula with periosteal new bone formation and soft tissue swelling. Chest CT and bone scan showed no other lesions. Histologic examination of a biopsy specimen disclosed the tumor to be osteosarcoma. Because of the location of the tumor and the age of the patient, she was treated with a below-knee amputation in addition to adjuvant chemotherapy.

The level of amputation is determined by close scrutiny of conventional radiographs, bone scans, and MR images. These surgical staging studies should be performed immediately before definitive surgery is undertaken and after completion of preoperative chemotherapy. The entire involved bone should be carefully be evaluated by MRI for skip metastases. Most frequently a wide cross-bone amputation is performed rather than a radical (whole bone) amputation. Exceptions might be a young child with a tibial osteosarcoma, in whom knee disarticulation or above-knee amputation is performed, or a hindfoot osteosarcoma requiring a below-knee amputation. For distal femoral lesions, a hip disarticulation is seldom performed and is not routinely necessary, as shown by a study from the Musculoskeletal Tumor Society.[392,431] The operative techniques of amputation and disarticulation at various levels in the upper and lower limbs are described and illustrated in Plates 38–1 through 38–9. In very young children, stump overgrowth may be a problem. For below-knee amputations this may be addressed by placing a metacarpal plug in the distal tibial canal if the ipsilateral foot is uninvolved by tumor.[333] Furthermore, in very young children, the predicted length of the stump at maturity may be very short if a growth plate is resected. For foot tumors, this can be addressed with a Syme's type amputation rather than a below-knee amputation,[11] and for proximal tibial lesions, a knee disarticulation may be preferable to an above-knee amputation.[37,274,319] These can be revised at maturity if necessary for prosthetic fitting.

Text continued on page 2026

*See references 13, 99, 137, 164, 174, 248, 275, 300, 334, 439, 471, 472, 479.

†See references 59, 144, 268, 378, 430, 437, 446, 508.

Hemipelvectomy (Banks and Coleman)

The patient lies on the unaffected side and is maintained in position with sandbags and kidney rests, which are placed well above the iliac crests. The underneath normal limb is flexed at the hip and knee and fastened to the table by wide adhesive straps. The uppermost arm is supported on a rest. The perineal area and, in the male, the scrotum and penis are shielded and held out of the operative field with sterile self-adhering skin drapes. The operative area is prepared and draped so that the proximal thigh, the inguinal and gluteal regions, and the abdomen are sterile. It should be possible to turn the patient onto his or her back and side without contaminating the surgical field.

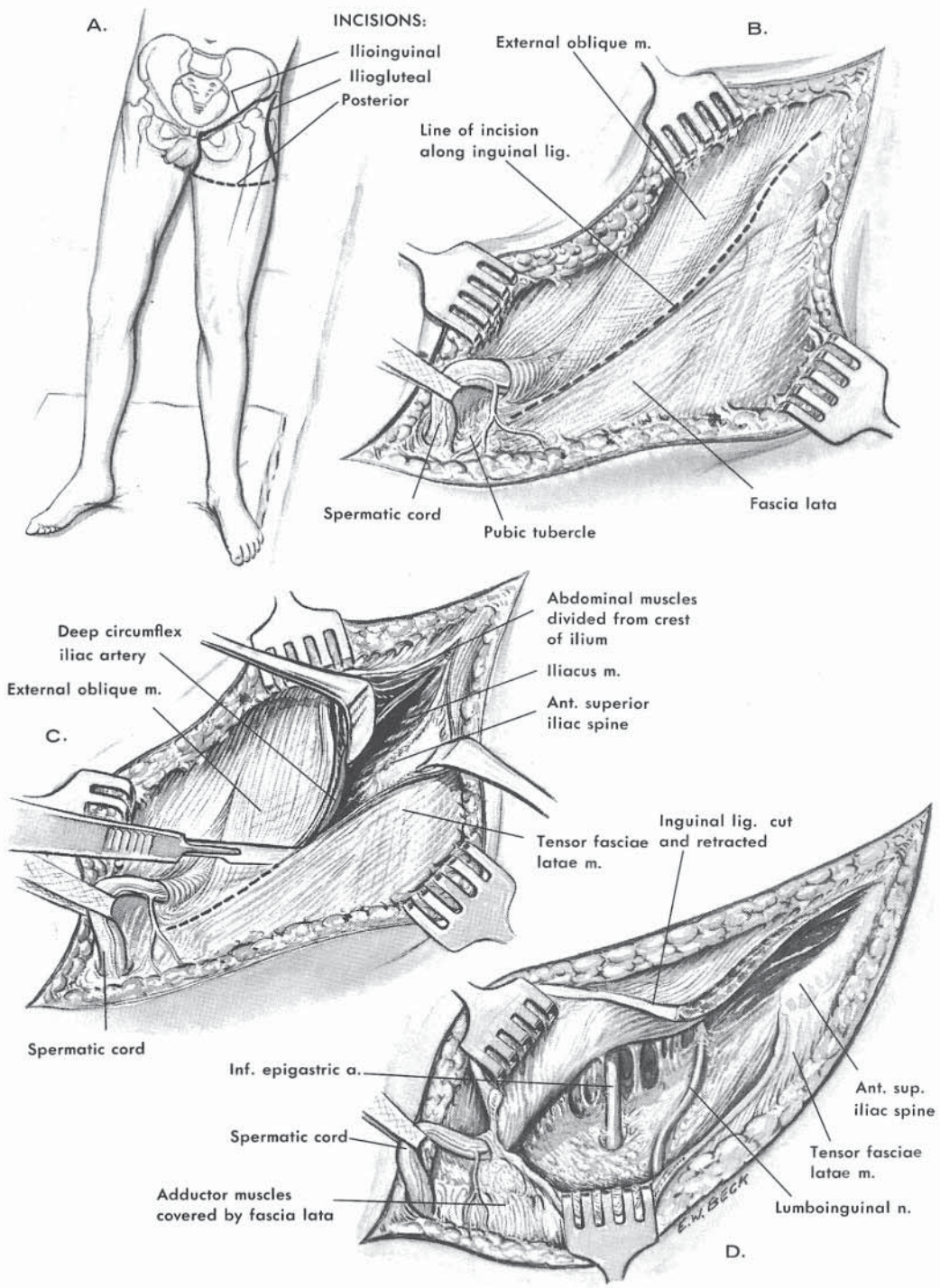
A, The outlines of the skin flaps, consisting of ilioinguinal, iliogluteal, and posterior incisions, are marked with methylene blue. With the patient placed on his or her back, the ilioinguinal incision is made first. It begins at the pubic tubercle and passes upward and backward parallel to Poupart's ligament to the anterior superior iliac spine and then posteriorly on the iliac crest. Its posterior limit depends on the desired level of section of the innominate bone.

B, The subcutaneous tissue and fascia are divided along the line of the skin incision. The periosteum over the iliac crest is incised between the attachments of the abdominal muscles superiorly and the tensor fasciae and the gluteus medius inferiorly.

C, The abdominal muscles are detached from the iliac crest and medial wall of the ilium. The tributaries of the deep circumflex vessels are ligated.

D, Next, the inguinal ligament is divided and retracted superiorly, along with the spermatic cord and abdominal muscles. The lower skin flap is retracted inferiorly, and by blunt dissection the inner pelvis is freed. The inferior epigastric artery and lumboinguinal nerve are exposed, ligated, and divided.

PLATE 38–1. Hemipelvectomy (Banks and Coleman)

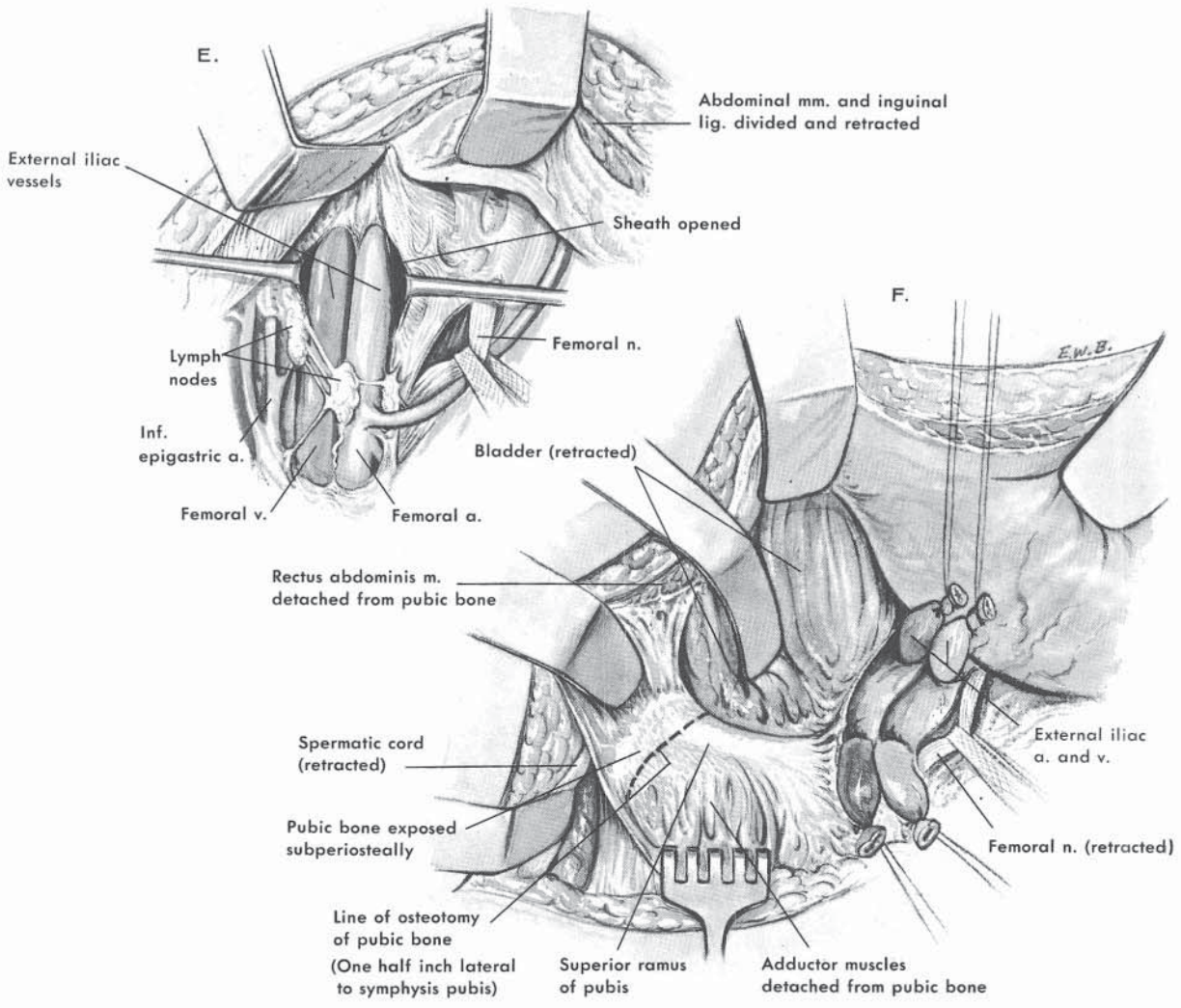


Hemipelvectomy (Banks and Coleman) *Continued*

E, In the loose areolar tissue the external iliac vessels and femoral nerve are gently dissected out. The external iliac artery and vein are individually clamped, severed, and doubly ligated with needle suture 0 silk.

F, The rectus abdominis and adductor muscles are detached from the pubic bone, which is subperiosteally exposed. The bladder is retracted superiorly. The pubic bone is osteotomized 1.5 cm lateral to the symphysis. Depending on the proximity of the tumor, the osteotomy may have to be made at the symphysis pubis. Injury to the bladder or urethra should be avoided. Any bleeding from the retropubic venous plexus is controlled by coagulation and packing with warm laparotomy pads.

PLATE 38–1. Hemipelvectomy (Banks and Coleman)



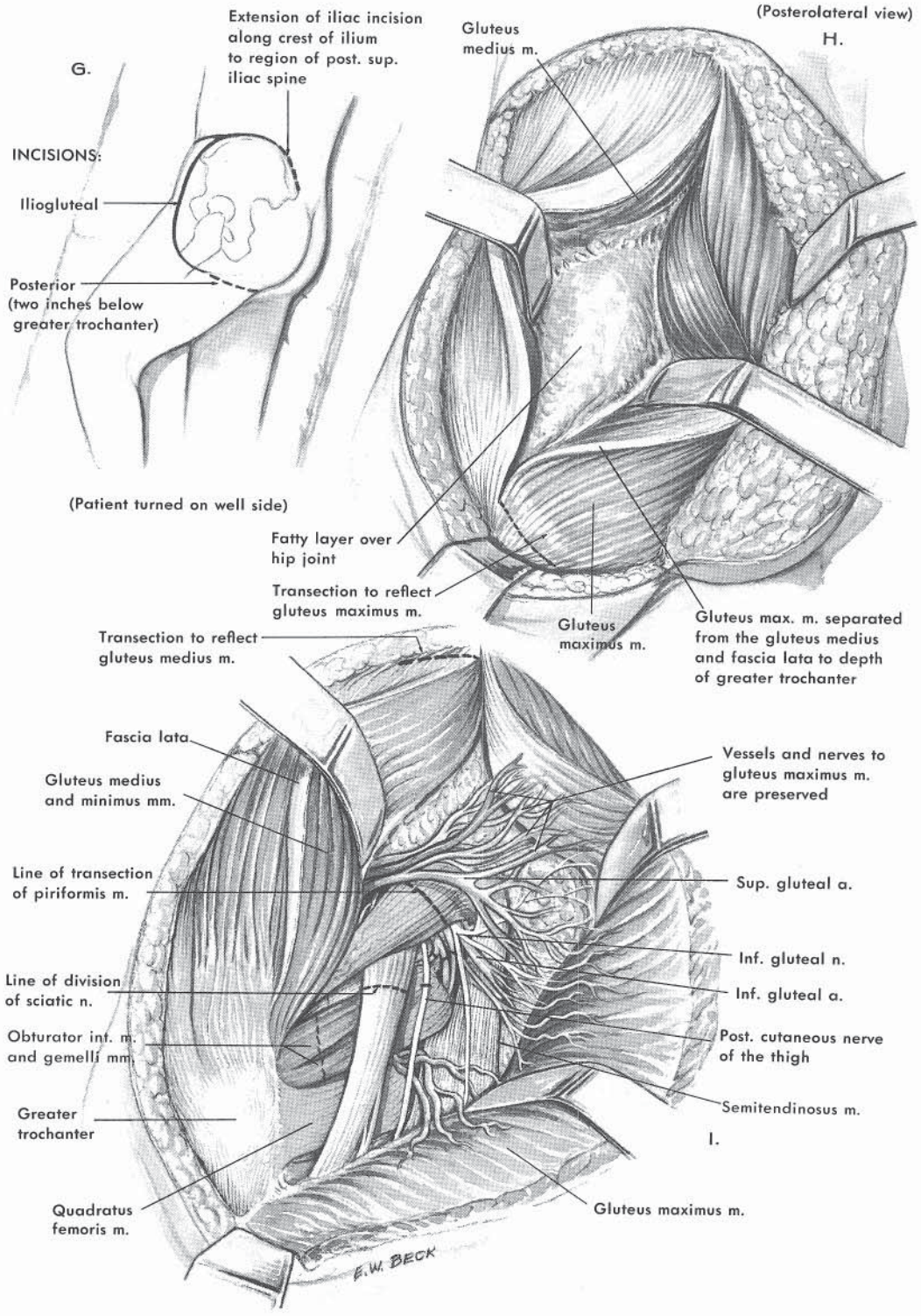
Hemipelvectomy (Banks and Coleman) *Continued*

G, The patient is then turned onto his or her side. The drapes are adjusted and reinforced to ensure sterility of the operative field. First the anterior incision is extended posteriorly to the posterior superior iliac spine. From the upper end of the anterior incision, the second or iliogluteal incision is started. It extends to the thigh, curving forward to an area about 5 cm distal to the greater trochanter. It then passes backward around the posterior aspect of the thigh to meet the anterior incision. The subcutaneous tissue and fascia are divided in line with the skin incision.

H, By blunt and sharp dissection the gluteus maximus is separated from the gluteus medius and tensor fasciae latae to the depth of the greater trochanter. The gluteus maximus is transected at its insertion, mobilized by blunt dissection, and retracted posteriorly. Vessels and nerves to the gluteus maximus muscle are preserved. (The inferior gluteal nerve and artery emerge distal to the piriformis muscle, and the superior gluteal artery emerges proximal to it.)

I, The sciatic nerve is clamped, ligated, and sharply divided distal to the origin of the inferior gluteal nerve. The piriformis, gemelli, and obturator internus muscles are transected near their insertion.

PLATE 38–1. Hemipelvectomy (Banks and Coleman)



Hemipelvectomy (Banks and Coleman) *Continued*

J, The ilium is exposed subperiosteally by elevation and detachment of the latissimus dorsi and sacrospinalis muscles, the posterior portion of the gluteus medius, and the anterior fibers of the gluteus maximus. The inner wall of the ilium is also subperiosteally exposed anteriorly to the sacroiliac joint. Chandler retractors are placed in the sciatic notch, and with a Gigli saw the ilium is osteotomized about 5 cm anterior to the posterior gluteal line. The site of osteotomy of the ilium depends on the location of the tumor; it is placed further posteriorly if the neoplasm is adjacent to the gluteal line.

K, Next, the patient is repositioned on his or her back, and the hip is maximally flexed in some abduction. The posterior incision is completed.

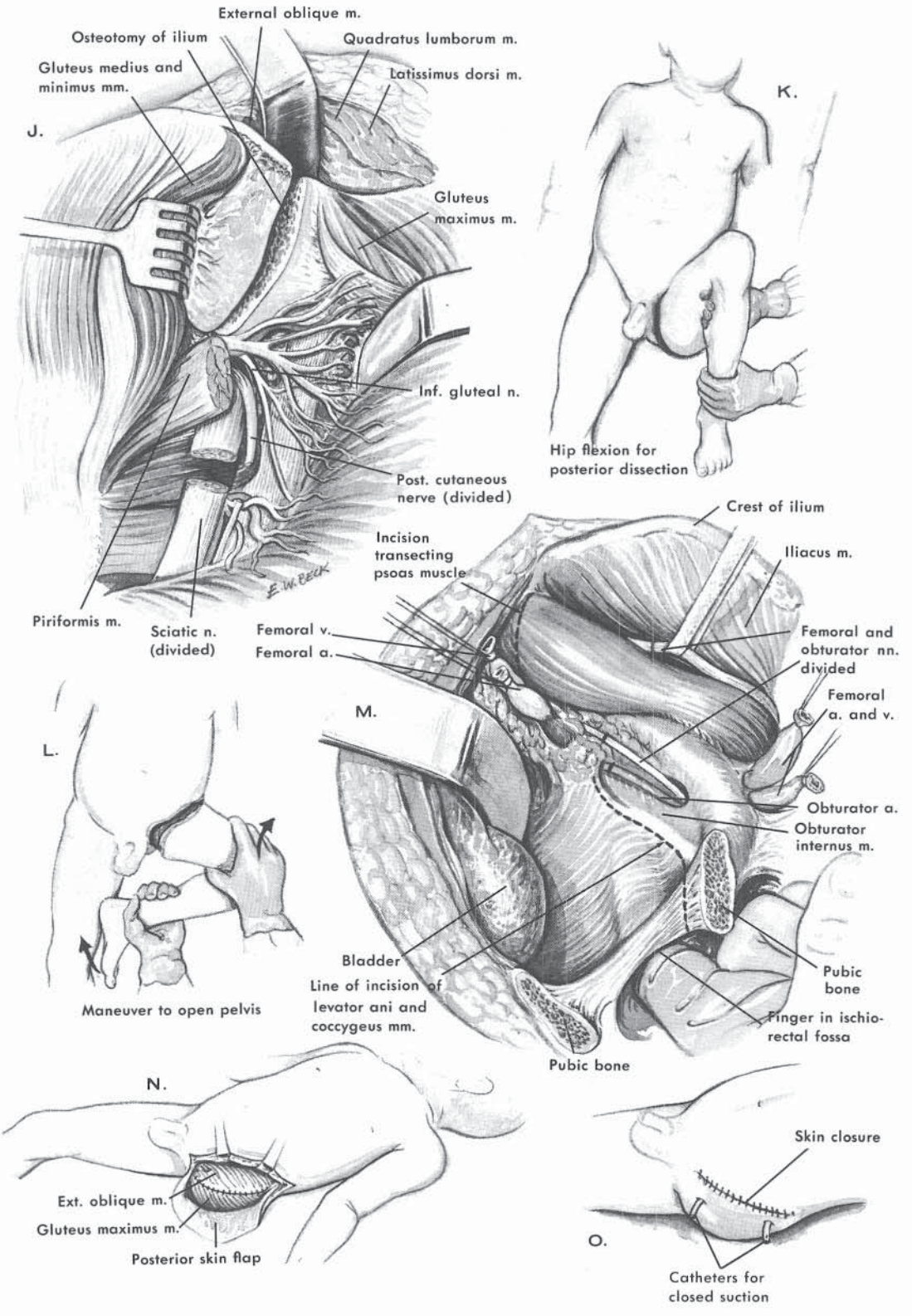
L, The hip is manipulated into maximal abduction and external rotation, laying open the pelvic area and widely exposing the remaining intrapelvic structures to be severed.

M, From above downward, the femoral nerve, iliopsoas muscle, obturator vessels, obturator nerve, levator ani, and coccygeus muscles are sectioned. The vessels are doubly ligated prior to division to prevent troublesome bleeding.

N, The gluteus maximus muscle is sutured to the divided margin of the external oblique muscle and lateral abdominal wall. A couple of perforated silicone catheters are inserted and connected to Hemovac suction.

O, Fascia, subcutaneous tissue, and skin are closed in layers in the usual manner. A pressure dressing is applied.

PLATE 38–1. Hemipelvectomy (Banks and Coleman)



Hip Disarticulation

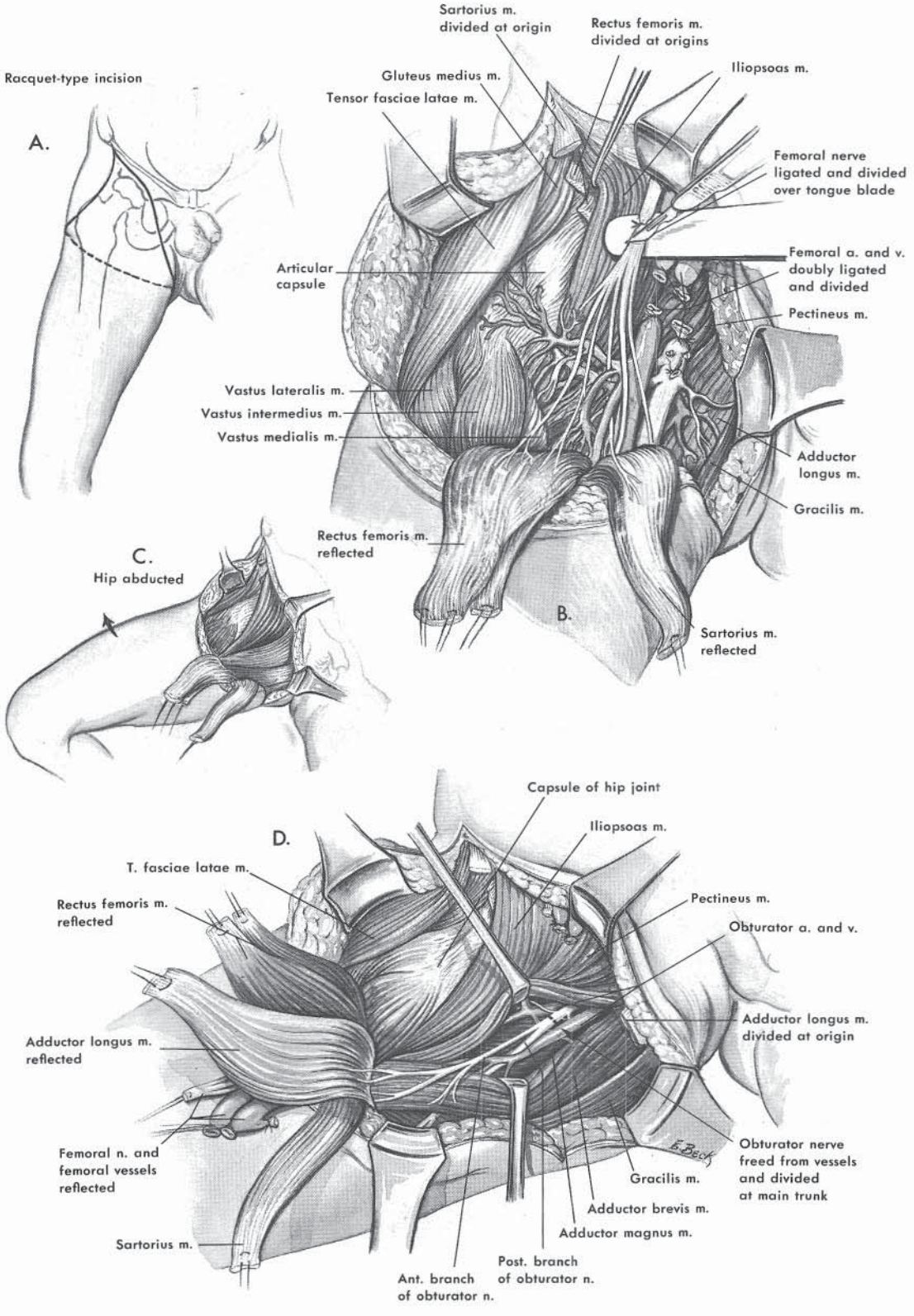
A, An anterior racquet type of incision is made starting at the anterosuperior iliac spine and extending medially and distally, parallel to Poupart's ligament, to the middle of the inner aspect of the thigh about 2 inches distal to the origin of the adductor muscles; then it is continued around the back of the thigh at a level about 2 inches distal to the ischial tuberosity. Next, the incision is carried along the lateral aspect of the thigh about 3 inches distal to the base of the greater trochanter and is curved proximally and medially to join the first incision at the anterosuperior iliac spine.

B, The subcutaneous tissue and the fascia are divided in line with the skin incision. The long saphenous vein is exposed and ligated, after the operator traces it to its junction with the femoral vein. If lymph node dissection is indicated, it can be performed at this stage. The sartorius muscle is divided at its origin from the anterosuperior iliac spine and is reflected distally. The origins of the two heads of the rectus femoris, one from the anteroinferior iliac spine and the other from the superior margin of the acetabulum, are detached and reflected distally. The femoral nerve is isolated, ligated with 0-0 silk sutures, and divided on a tongue blade with a sharp scalpel or razor blade just distal to the ligature. The femoral artery and vein are isolated, doubly ligated with 0-0 silk sutures proximally and distally, and severed in between the sutures.

C, Next, the hip is abducted to expose its medial aspect, and the adductor longus is detached at its origin from the pubis and reflected distally. The anterior branch of the obturator nerve is exposed deep to the adductor longus and is traced proximally.

D, The adductor brevis is retracted posteriorly. The posterior branch of the obturator nerve is isolated and dissected proximally to the main trunk of the obturator nerve, which is sharply divided. Next, the obturator vessels are isolated and ligated. One should be careful not to sever the obturator artery inadvertently, as it will retract into the pelvis and cause bleeding that is difficult to control.

PLATE 38–2. Hip Disarticulation

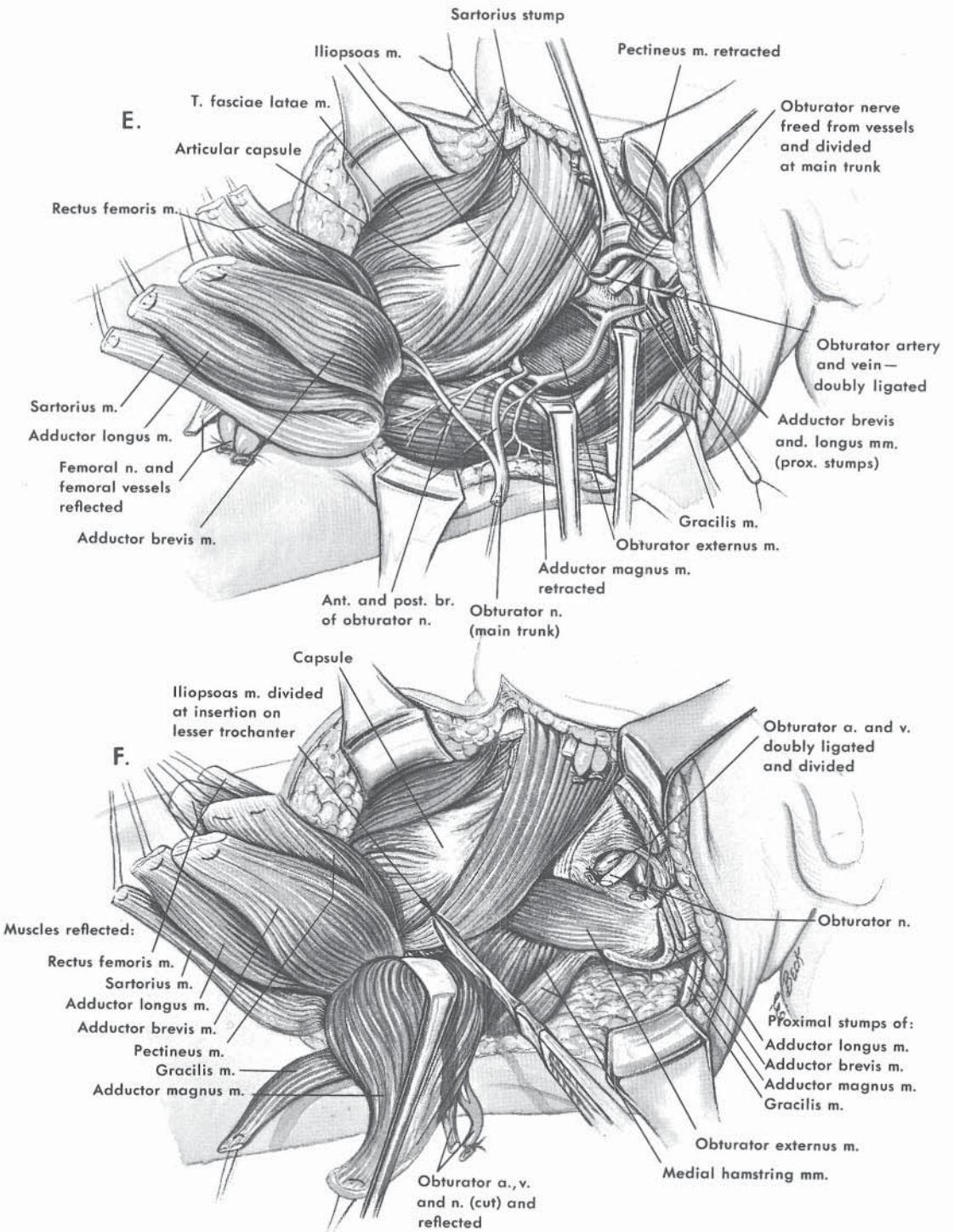


Hip Disarticulation *Continued*

E, The pectineus, adductor brevis, gracilis, and adductor magnus are severed near their origin. It is best to use a coagulation knife.

F, The hip is then flexed, externally rotated, and abducted, bringing into view the lesser trochanter. The iliopsoas tendon is exposed, isolated, and divided at its insertion and reflected proximally.

PLATE 38–2. Hip Disarticulation



Hip Disarticulation *Continued*

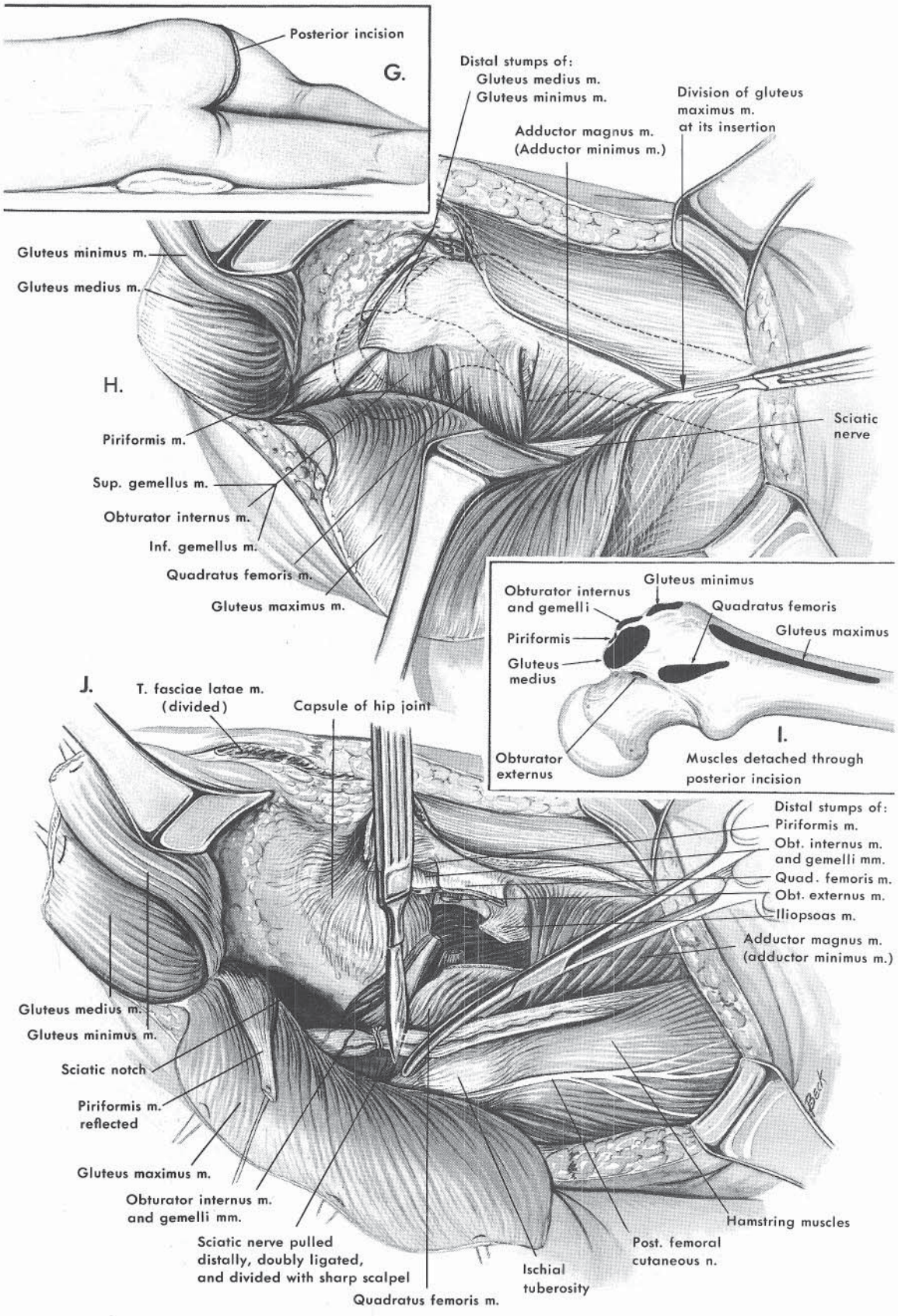
G, Next, to facilitate surgical exposure, a sterile sandbag is placed under the pelvis and the patient is turned onto the side away from the site of operation. The hip is internally rotated.

H, The gluteus medius and gluteus minimus muscles are divided at their insertion into the greater trochanter and, together with the tensor fasciae latae muscle, are reflected proximally. The gluteus maximus muscle is detached at its insertion and retracted upward. The free ends of the gluteus maximus, medius, and minimus muscles and the tensor fasciae latae muscle are marked with 0 silk suture for reattachment.

I, The muscles to be detached at their insertion through the posterior incision are shown. The short rotators of the hip—that is, the quadratus femoris, obturator externus, gemelli, and obturator internus—are detached from their insertion into the femur.

J, Next, the sciatic nerve is identified, dissected free, pulled distally, and crushed with a Kocher hemostat at a level 2 inches proximal to the ischial tuberosity, and is ligated with 0-0 silk suture to prevent hemorrhage from its accompanying vessels. Then it is sharply divided just distal to the ligature.

PLATE 38–2. Hip Disarticulation

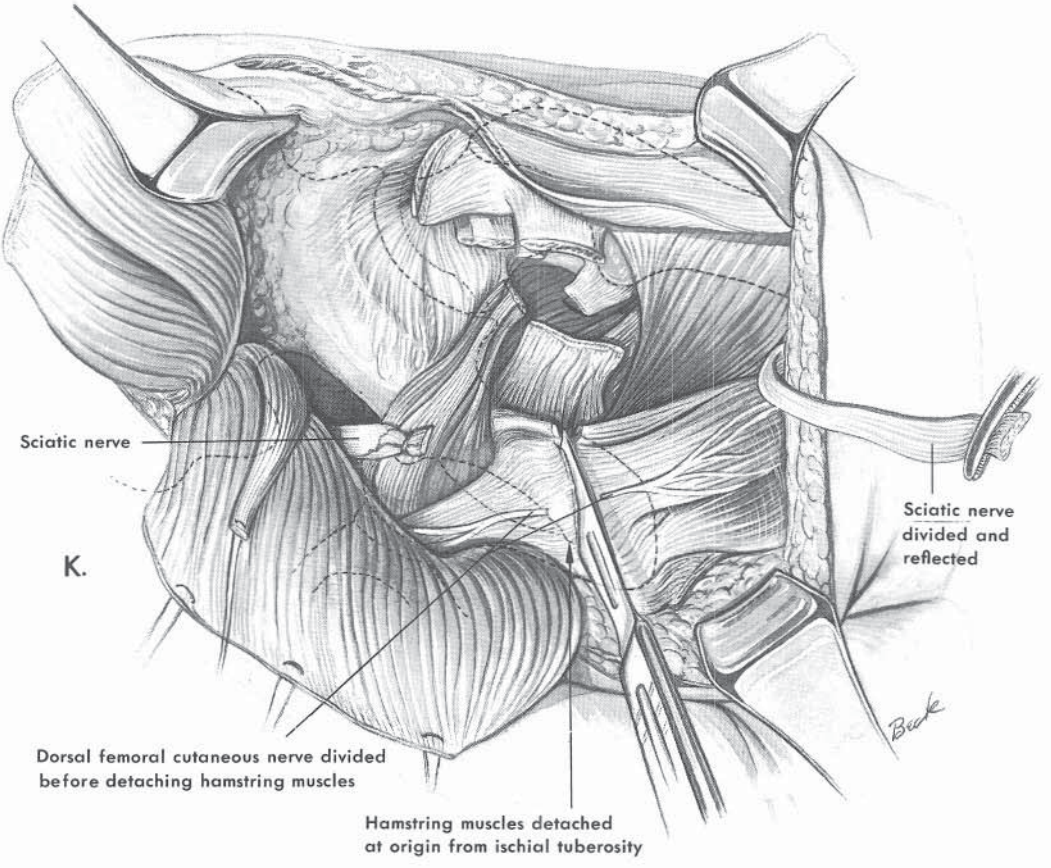


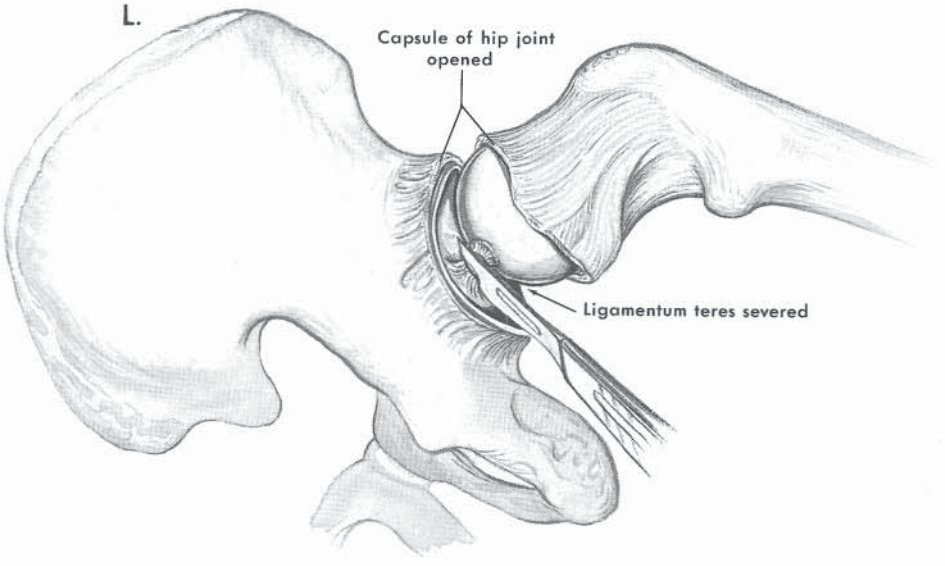
Hip Disarticulation *Continued*

K, The hamstring muscles are detached at their origin from the ischial tuberosity.

L, The capsule of the hip joint is divided near the acetabulum and the ligamentum teres is severed, completing the disarticulation.

PLATE 38–2. Hip Disarticulation



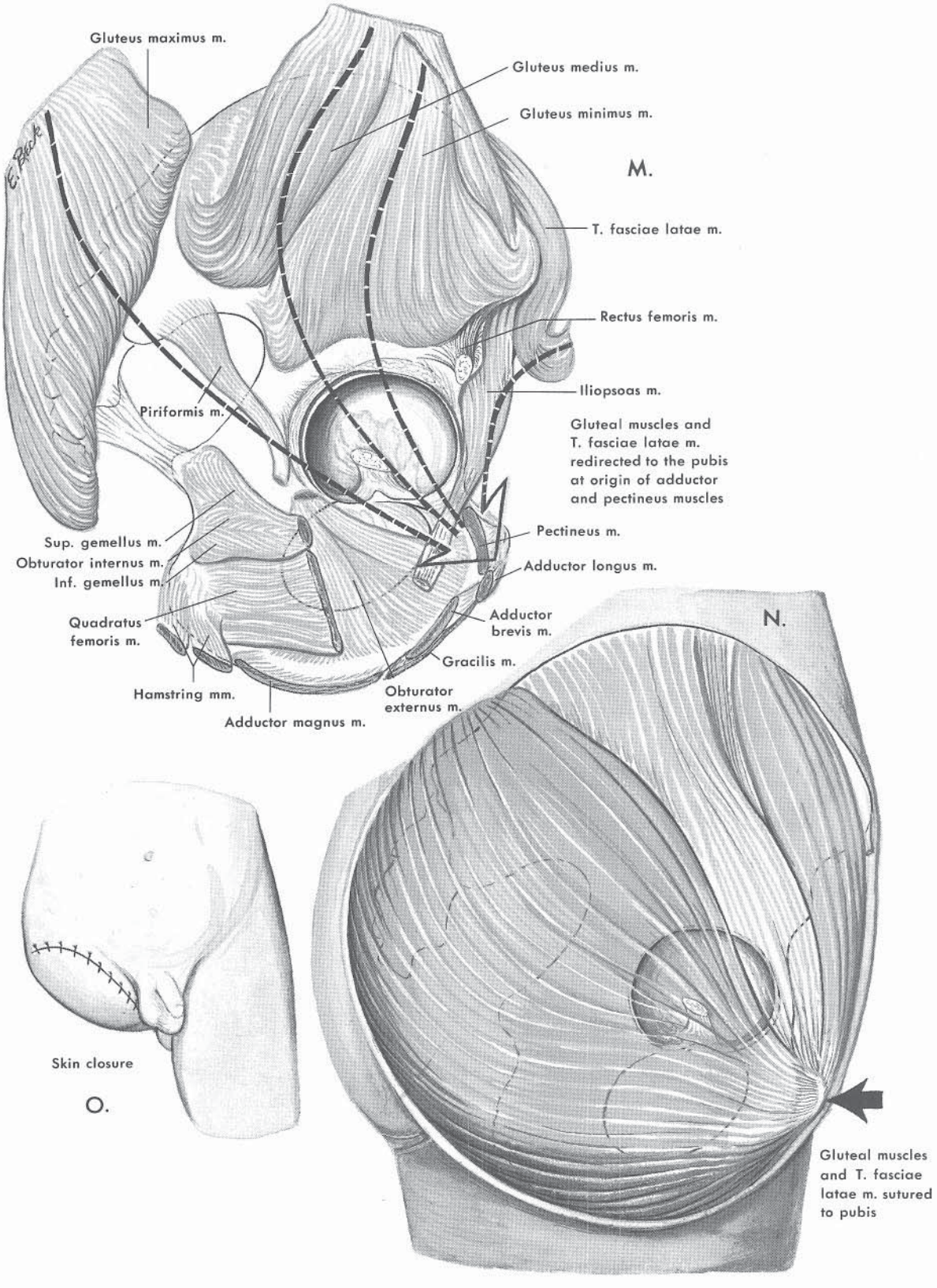


Hip Disarticulation *Continued*

M and N, The gluteal flap is mobilized and brought forward, and the free distal ends are sutured to the pubis at the origin of the adductor and pectineus muscles.

O, The wound is closed in routine fashion. A Hemovac closed suction drain is placed in the inferior portion of the wound. It is removed in 1 to 2 days.

PLATE 38–2. Hip Disarticulation



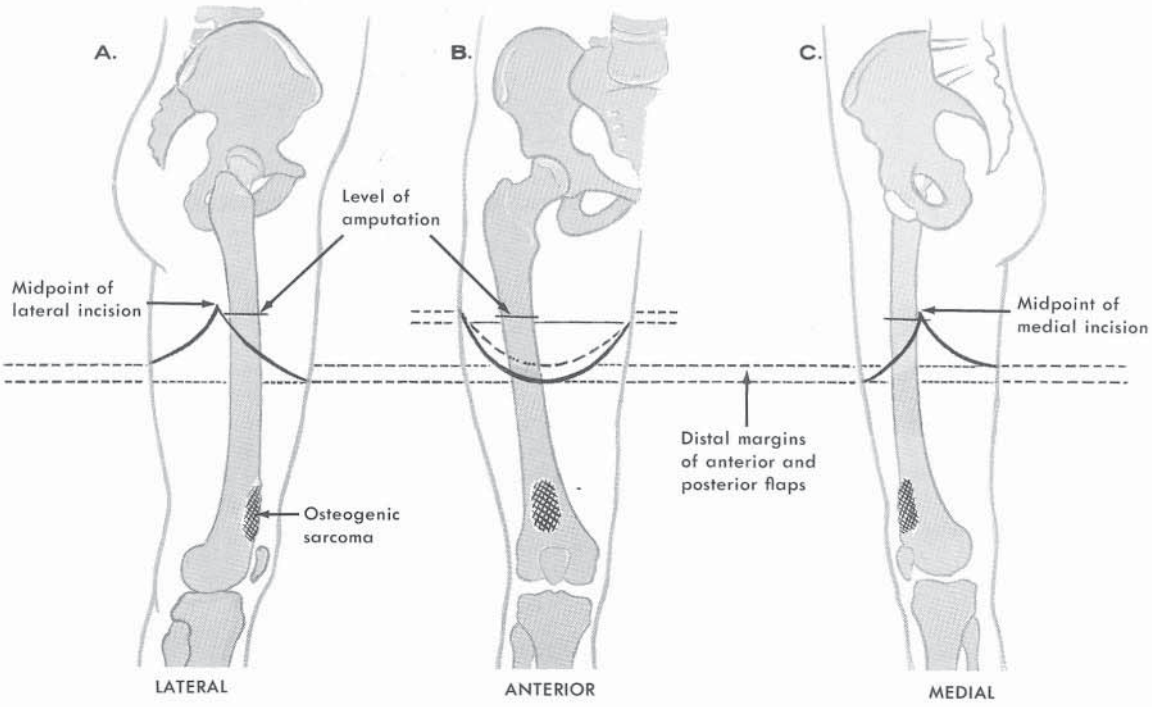
Ischial-Bearing Above-Knee Amputation (Midthigh Amputation)

The level of amputation is determined by measurements made with a Bell Thompson ruler on the preoperative radiographs. Measurements are made from the top of the greater trochanter and from the knee joint line. If the level of amputation permits, a pneumatic tourniquet or an Esmarch bandage is employed for hemostasis. A sandbag is placed under the ipsilateral buttock.

The following areas are marked with methylene blue: (1) the intended bone level of amputation, (2) the midpoints of the medial and lateral aspects of the thigh 1 cm above the bony level, and (3) the distal border of the anterior and posterior incisions. The latter is determined by a rule of thumb: the combined length of the anterior and posterior flaps is slightly longer than the diameter of the thigh at the intended bone level, and the length of the anterior flap is 2.5 cm longer than the posterior flap.

A to **C,** The skin incision begins at the midpoint of the medial aspect of the thigh, gently curves anteriorly and inferiorly to the distal border of the anterior incision, and passes convexly to the midpoint on the lateral aspect of the thigh. The posterior incision starts at the same medial point, extends to the distal margin of the posterior flap, and swings proximally to end at the midpoint on the lateral thigh.

PLATE 38–3. Ischial-Bearing Above-Knee Amputation (Midthigh Amputation)

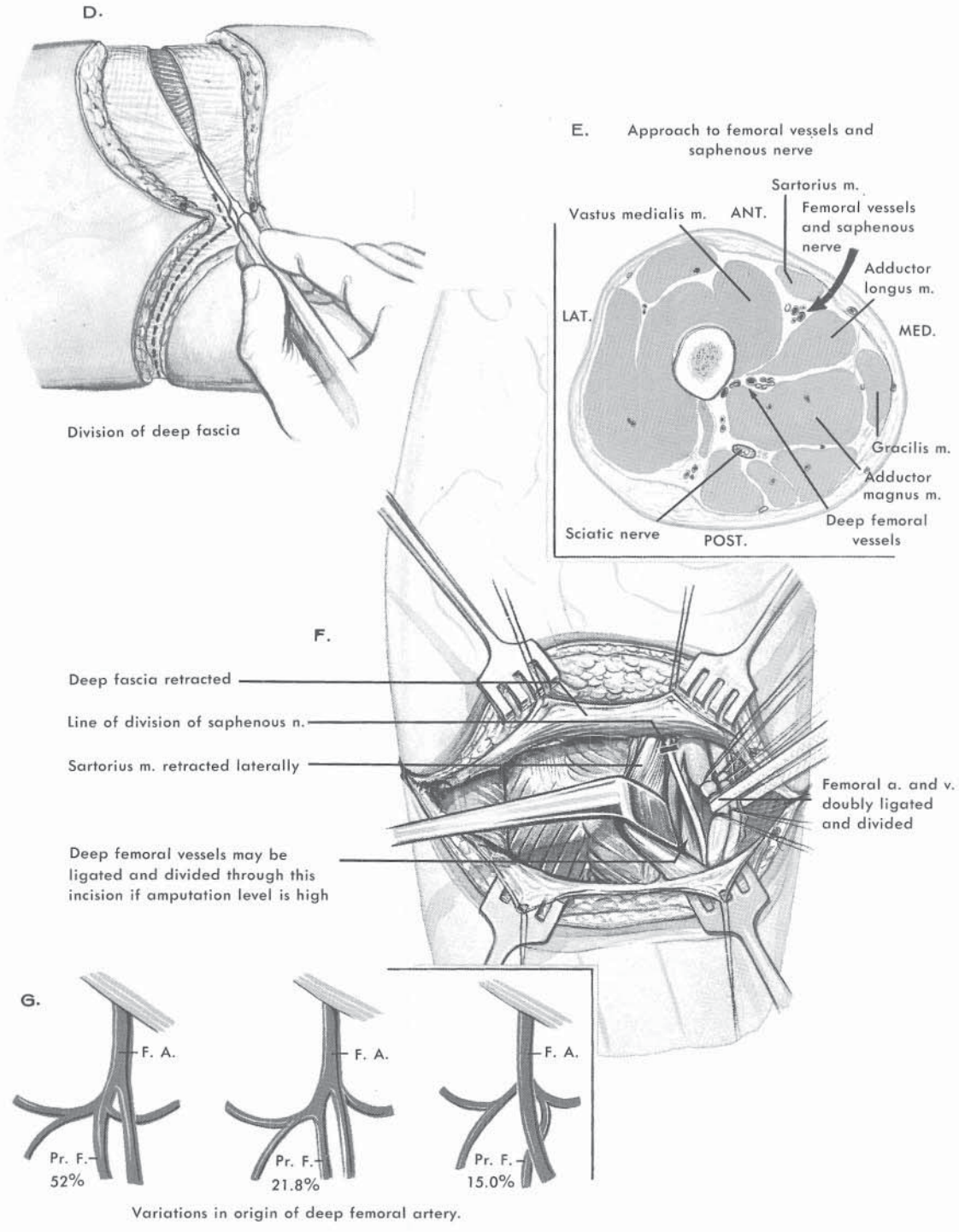


Ischial-Bearing Above-Knee Amputation (Midthigh Amputation)
Continued

D, The subcutaneous tissue and deep fascia are divided in line with the skin incision, and the anterior and posterior flaps are reflected proximally to the amputation level.

E to **G,** Next, the femoral vessels and saphenous nerve are identified. They are located deep to the sartorius muscle, between the adductor longus and the vastus medialis muscles. The deep femoral vessels are found adjacent to the femur in the interval between the adductor magnus, adductor longus, and the vastus medialis muscles. There are variations in the origin of the deep femoral artery, as shown in G. The femoral artery and vein are isolated, doubly ligated with heavy silk sutures, and divided. The saphenous nerve is pulled distally and divided with a sharp scalpel. If the amputation level is high, the deep femoral vessels may be ligated and divided through this anteromedial approach.

PLATE 38–3. Ischial-Bearing Above-Knee Amputation (Midthigh Amputation)



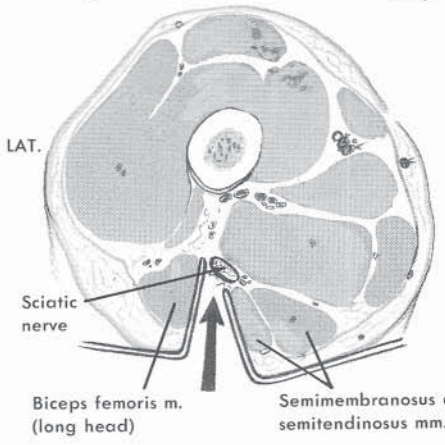
Variations in origin of deep femoral artery.

Ischial-Bearing Above-Knee Amputation (Midthigh Amputation)
Continued

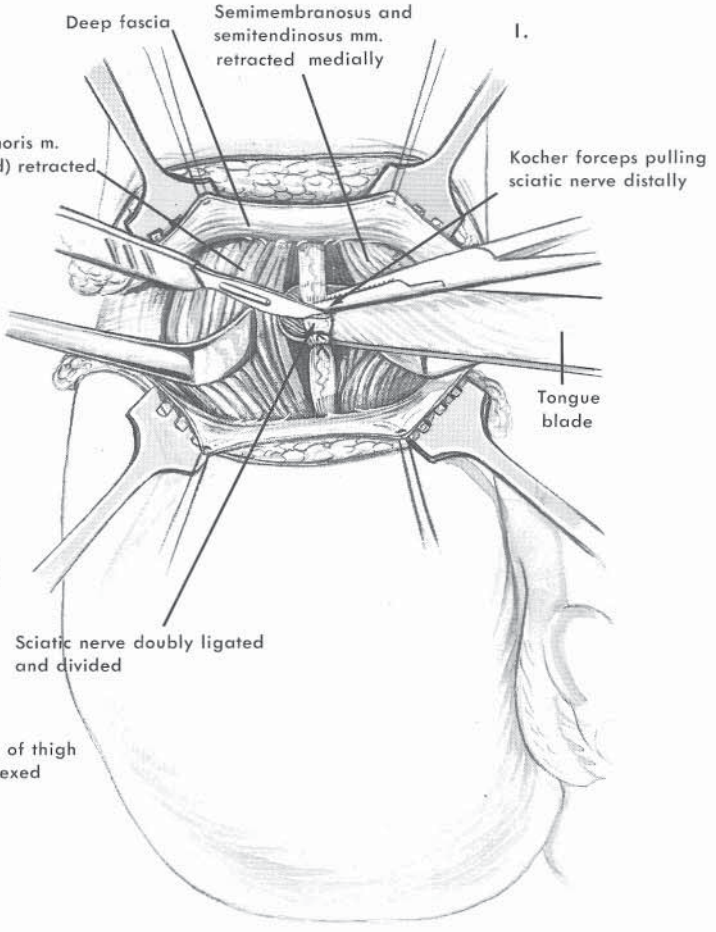
H and **I,** Next, the hip is acutely flexed to approach the posterior structures. The sciatic nerve is exposed in the interval between the medial hamstrings medially and the long head of the biceps femoris laterally. With a Kocher forceps, it is pulled distally, doubly ligated, and sharply divided over a tongue blade.

J and **K,** The posterior approach to the deep femoral vessels when the level of amputation is distal.

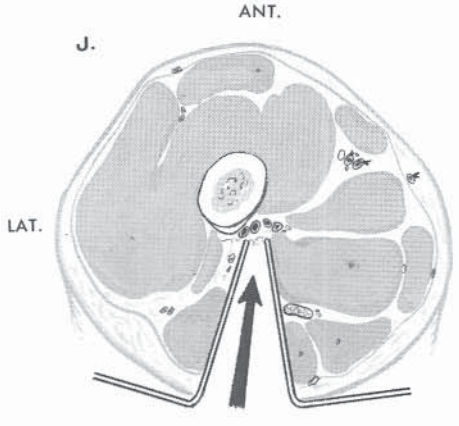
PLATE 38–3. Ischial-Bearing Above-Knee Amputation (Midthigh Amputation)



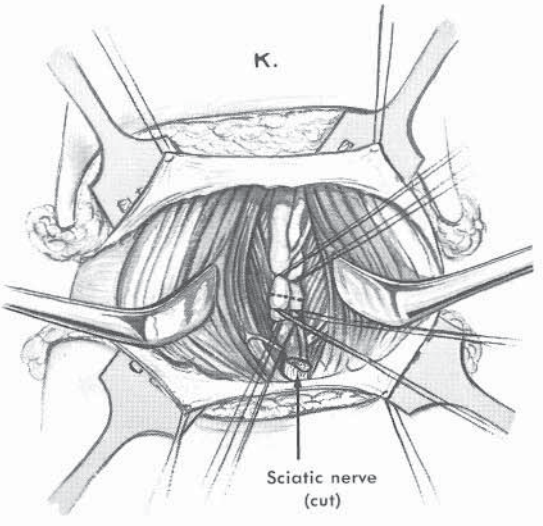
Approach for exposure of sciatic nerve



Posterior view of thigh
Hip acutely flexed



Alternate approach to deep femoral vessels



Deep femoral vessels doubly ligated and lines of division

Ischial-Bearing Above-Knee Amputation (Midthigh Amputation)
Continued

L, With an amputation knife, the quadriceps and adductor muscles are sectioned and beveled upward to the site of bone division so that the anterior myofascial flap is approximately 1.5 cm thick. The posterior muscles are divided transversely. Muscular branches of the femoral vessels are clamped and ligated as necessary.

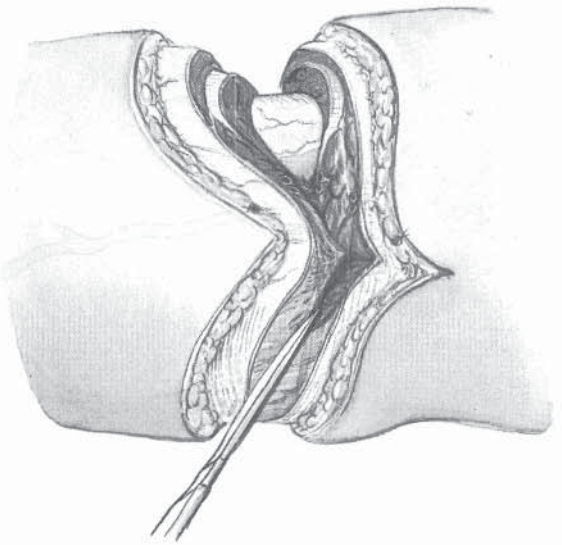
M, The proximal muscles are retracted upward with an amputation shield, and the periosteum is incised circumferentially.

N, Next, the femur is sectioned with a saw immediately distal to the periosteal incision.

O, With a rongeur, the prominence of the linea aspera is excised and the bone end is smoothed with a file. The wound is irrigated with normal saline solution to wash away all loose fragments of bone.

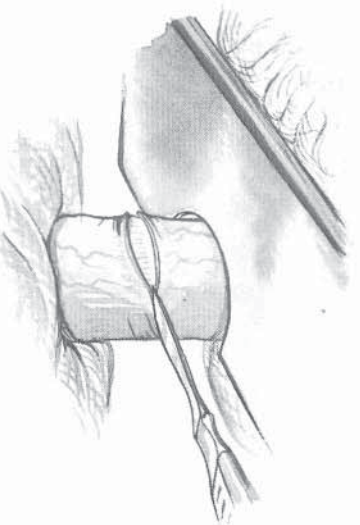
PLATE 38–3. Ischial-Bearing Above-Knee Amputation (Midthigh Amputation)

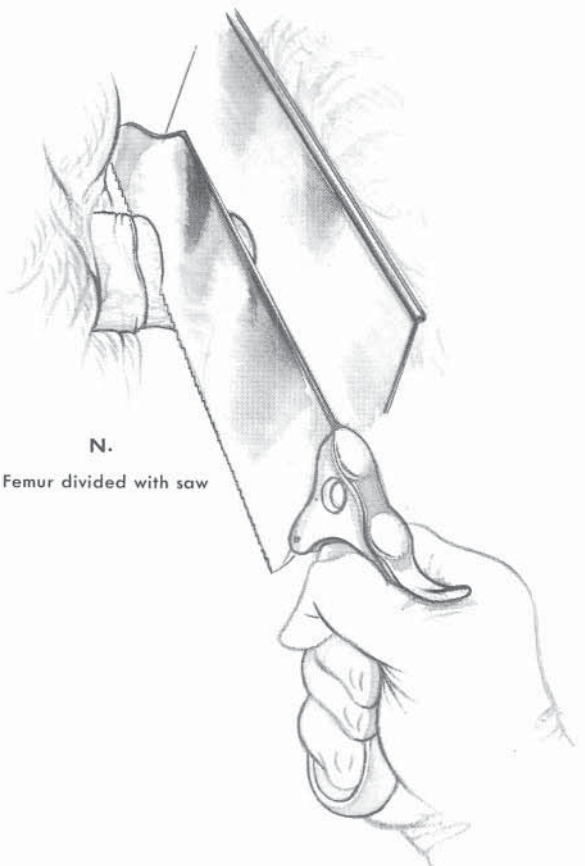
L. Division of muscles



M.

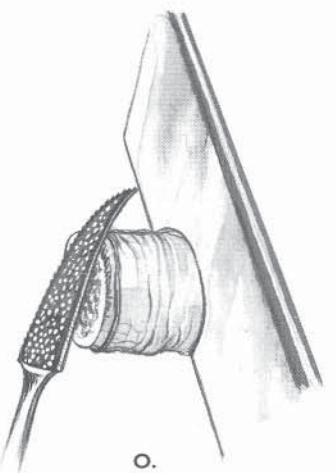
Circular incision of periosteum of femur





N.

Femur divided with saw



O.

Irregular bone ends smoothed with rasp

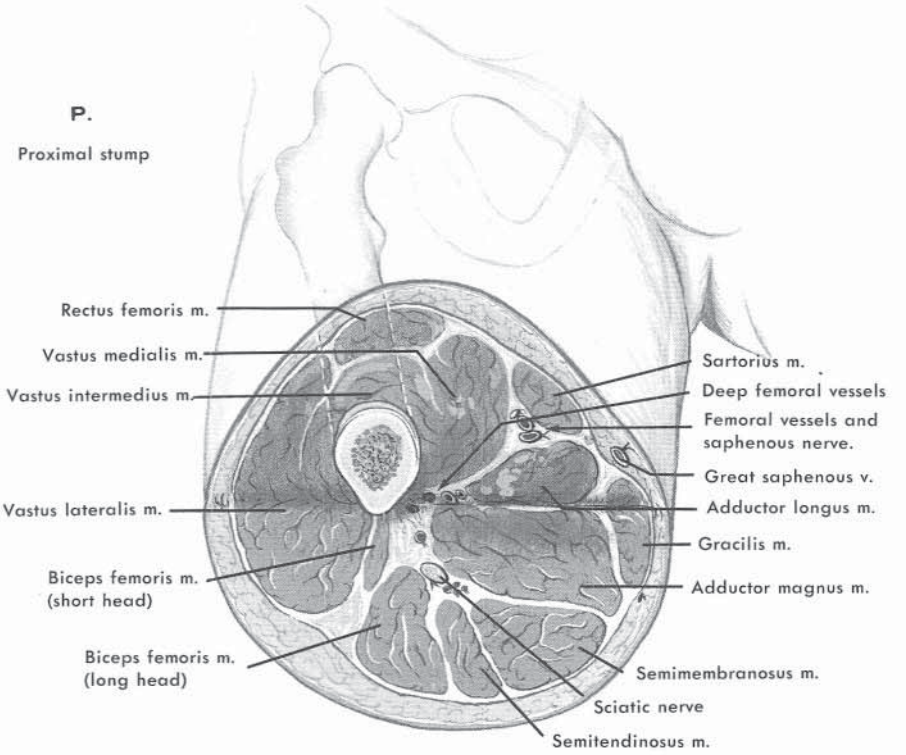
Ischial-Bearing Above-Knee Amputation (Midthigh Amputation)
Continued

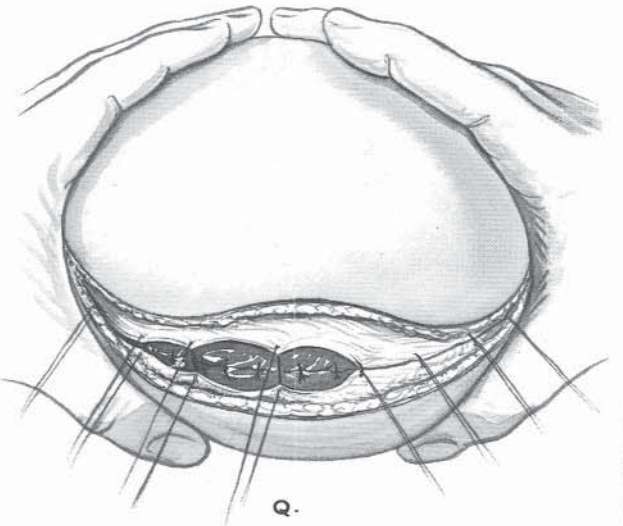
P, Hot packs are applied over the wound and the tourniquet is released. After 5 minutes the stump is inspected for any bleeders.

Q, The anterior and posterior myofascial flaps are pulled distally and approximated with interrupted sutures through their fascial layer. Suction catheters are placed in the wound and connected to a Hemovac evacuator.

R, The subcutaneous tissue and skin are closed in the usual manner. I perform immediate prosthetic fitting in the operating room. The patient is allowed to be ambulatory on the first postoperative day.

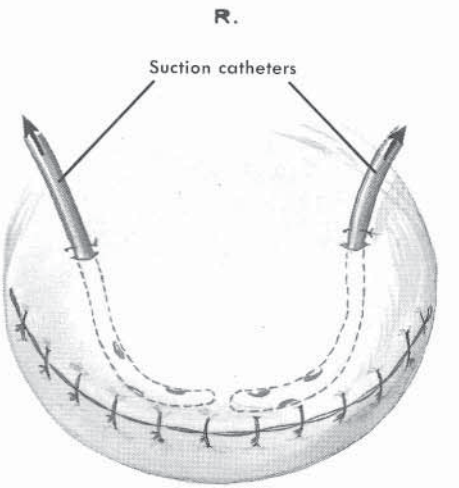
PLATE 38–3. Ischial-Bearing Above-Knee Amputation (Midthigh Amputation)





Q.

Closure of deep fascia



Skin edges approximated and closed

Disarticulation of the Knee Joint

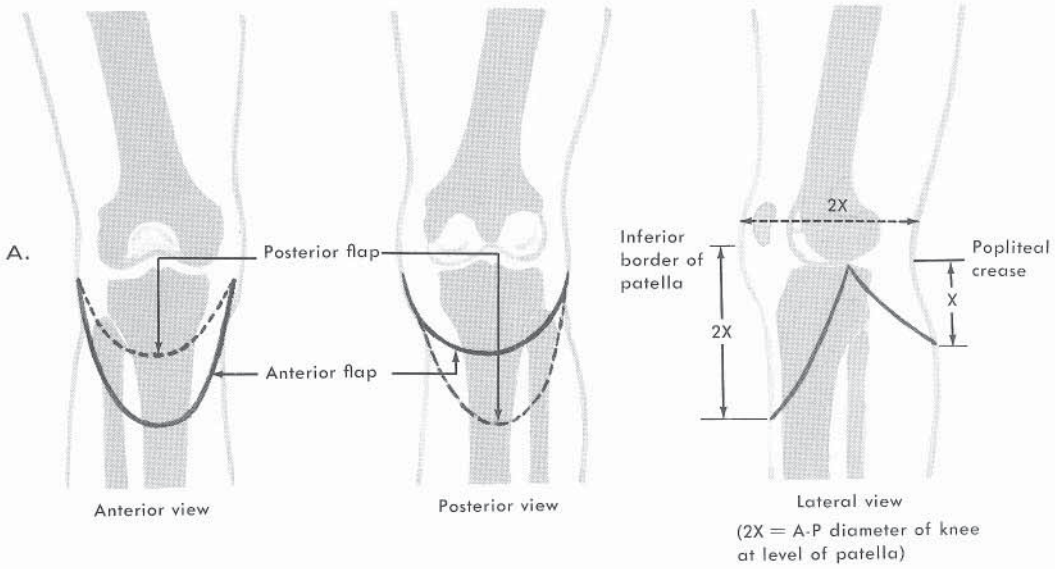
The patient is placed in lateral position so that he or she can easily be turned to a supine, prone, or semilateral position. The operation is performed using pneumatic tourniquet ischemia.

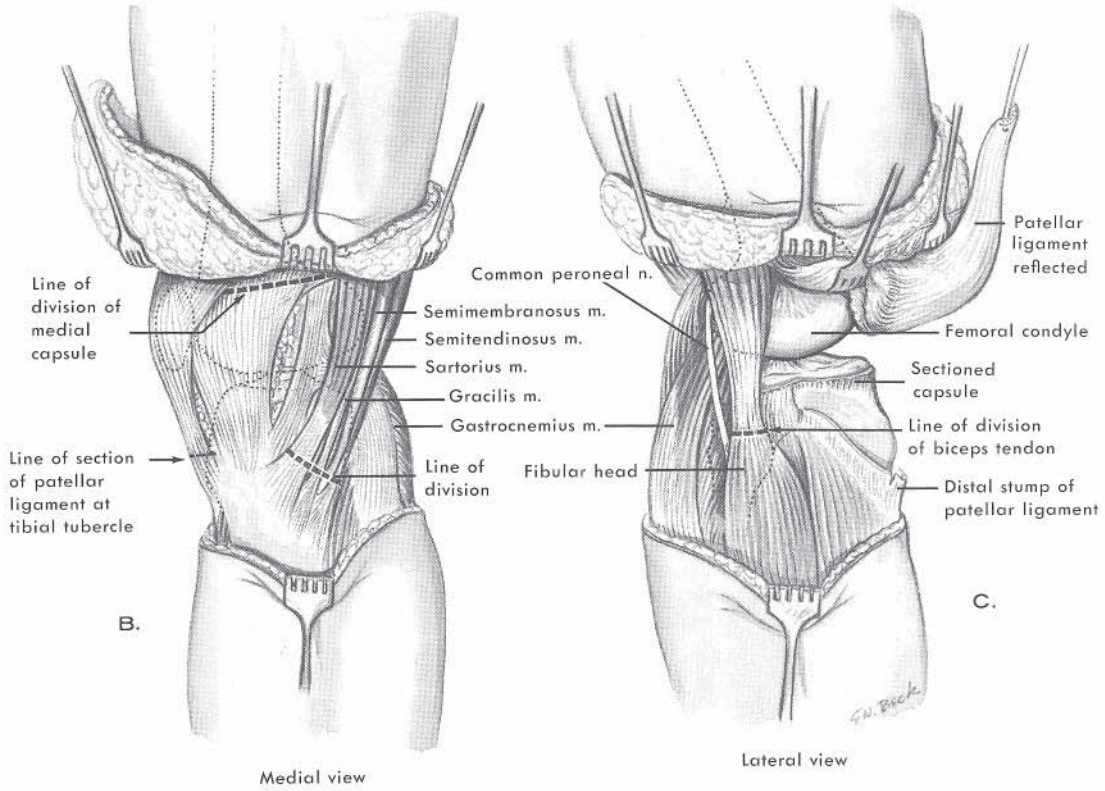
A, The skin incisions are placed in such a manner that a long anterior and a short posterior flap are provided; thus, the operative scar is posterior and away from the weightbearing skin. Measuring from the distal pole of the patella to the distal border, the length of the anterior flap is equal to the anteroposterior diameter of the knee, whereas the posterior flap is half the length of the anterior flap. The medial and lateral proximal points of the incisions are at the joint line at the junction of the anterior two-thirds and posterior one-third of the diameter of the knee. The anterior and posterior wound flaps are raised, including the subcutaneous tissue and the deep fascia.

B, The medial aspects of the knee joint and the proximal tibia are exposed. Tendons of the sartorius, gracilis, semimembranosus, and semitendinosus muscles are identified and marked with 0-0 silk whip sutures, then sectioned near their insertions on the tibia. The ligamentum patellae is detached at the proximal tibial tubercle. The anterior and medial joint capsule and synovial membrane are divided proximally near the femoral condyles.

C, Next, the lateral aspect of the knee joint is exposed. The iliotibial tract is divided and the biceps femoris tendon is sectioned from its attachment to the head of the fibula. The lateral part of the joint capsule and synovial membrane is divided above the joint line.

PLATE 38–4. Disarticulation of the Knee Joint





Disarticulation of the Knee Joint *Continued*

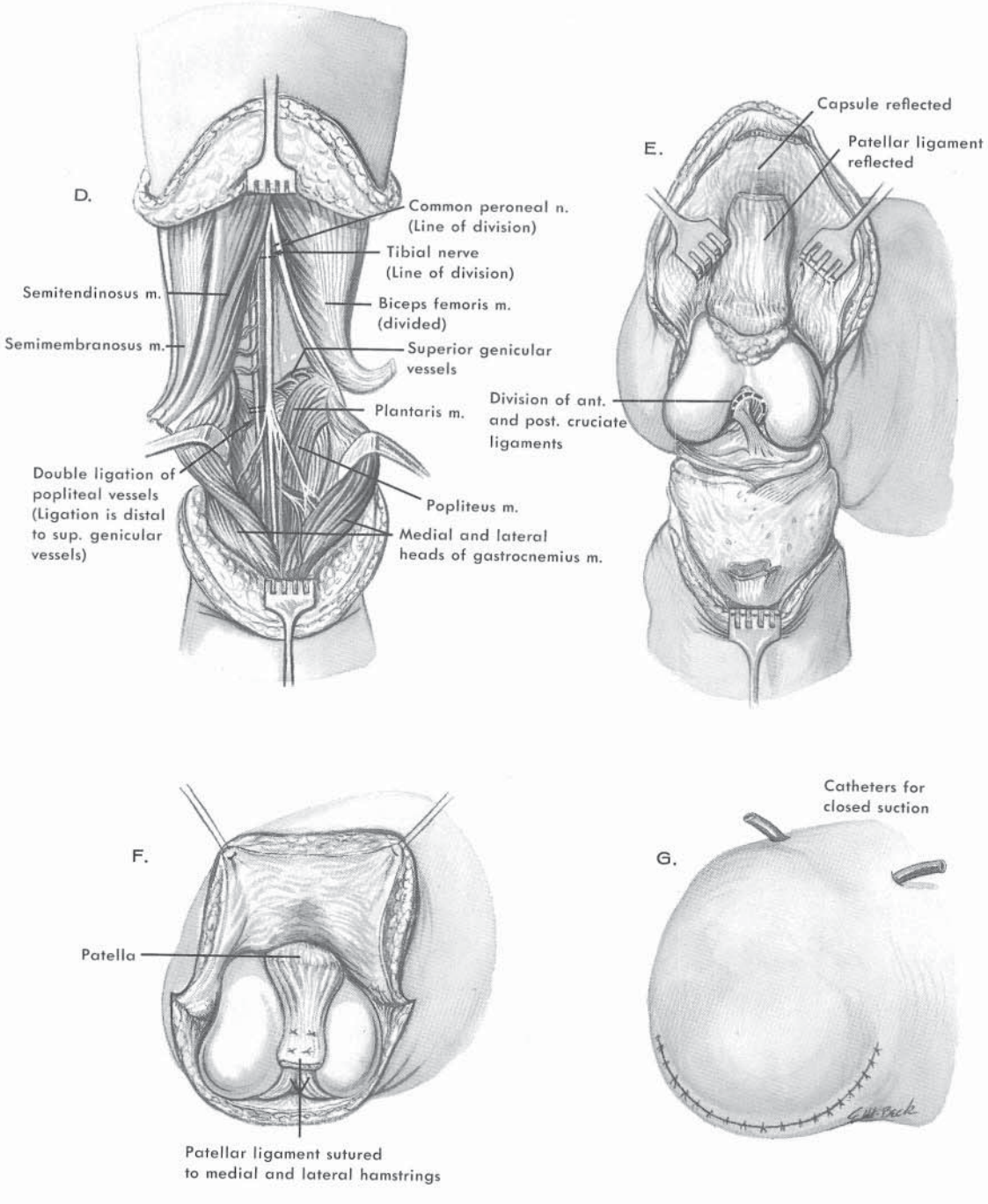
D, Now the patient is turned into the semiprone position and the popliteal fossa is exposed. By blunt dissection the popliteal vessels are identified; the popliteal artery and vein are separately doubly ligated distal to the origin of the superior genicular branches and divided. The tibial nerve and common peroneal nerve are pulled distally, sharply divided with a scalpel, and allowed to retract proximally. The medial and lateral heads of the gastrocnemius are extraperiosteally elevated and stripped from the posterior aspect of the femoral condyles. The distal femoral epiphyseal plate should not be damaged. The plantaris and popliteus muscles, the oblique popliteal ligament, the posterior part of the capsule of the knee joint, and the meniscofemoral ligaments are completely divided.

E, Next, the patient is placed in a semisupine position and the knee is acutely flexed. The cruciate ligaments are identified and sectioned, completing the amputation. The pneumatic tourniquet is released and complete hemostasis is secured.

F, The patellar ligament is sutured to the medial and lateral hamstrings in the intercondylar notch. In children, the patella usually is not removed and reshaping of the femoral condyles should not be performed because of the danger of damage to the growth plate. Synovectomy is not indicated.

G, Two catheters are placed in the wound for closed suction. The deep fascia and subcutaneous tissue of the anterior and posterior flaps are approximated with interrupted sutures, and the skin is closed in routine fashion.

PLATE 38–4. Disarticulation of the Knee Joint



Below-Knee Amputation

The level of amputation is determined preoperatively. With the patient supine, a pneumatic tourniquet is applied on the proximal thigh.

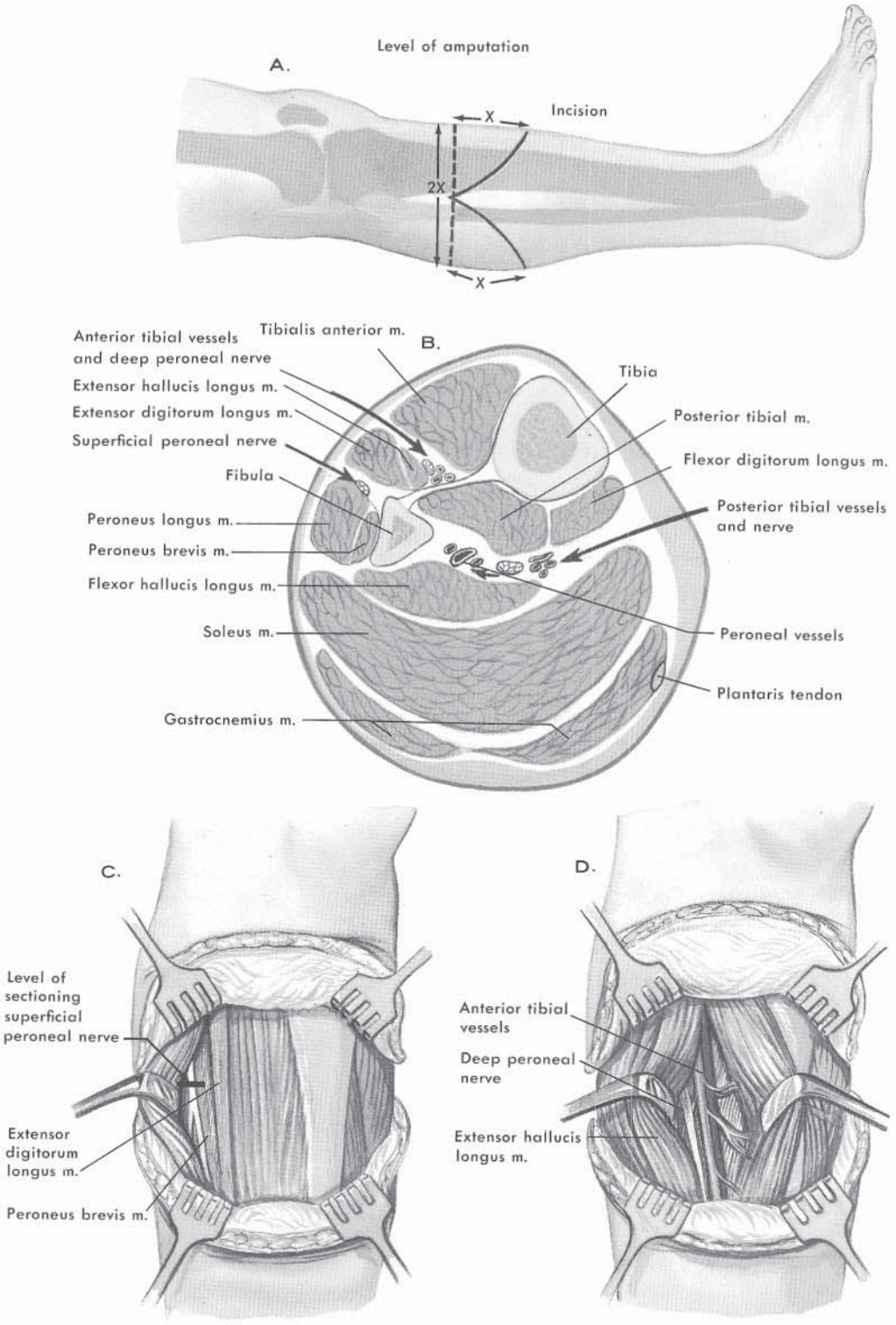
A and **B,** The line of incision for the anterior and posterior flaps is marked on the skin, and the AP diameter of the leg at the level of bone section is measured. The anterior flap can be fashioned slightly longer than the posterior flap, or they may be made of equal length, as the position of the scar is not especially important in prosthetic fitting. The length of each flap is half the AP diameter of the leg.

C and **D,** The incisions are deepened to the deep fascia, which is divided in line with the skin incision. The anterior and posterior flaps are raised proximally in one layer, including skin, subcutaneous tissue, and deep fascia. Over the anteromedial surface of the tibia, the periosteum is incised with the deep fascia, and both are elevated as a continuous layer to the intended level of amputation.

In the interval between the extensor digitorum longus and peroneus brevis muscles, the superficial peroneal nerve is identified; the nerve is pulled distally, sharply divided, and allowed to retract proximally well above the end of the stump.

The anterior tibial vessels and deep peroneal nerve are identified, doubly ligated, and divided.

PLATE 38–5. Below-Knee Amputation



Below-Knee Amputation *Continued*

E and **F,** The muscles in the anterior tibial compartment are sectioned about 0.75 cm distal to the level of bone section. The tibial crest is beveled as follows. Beginning 2 cm proximal to the level of amputation, a 45-degree distal oblique cut is made, ending 0.5 cm anterior to the medullary cavity.

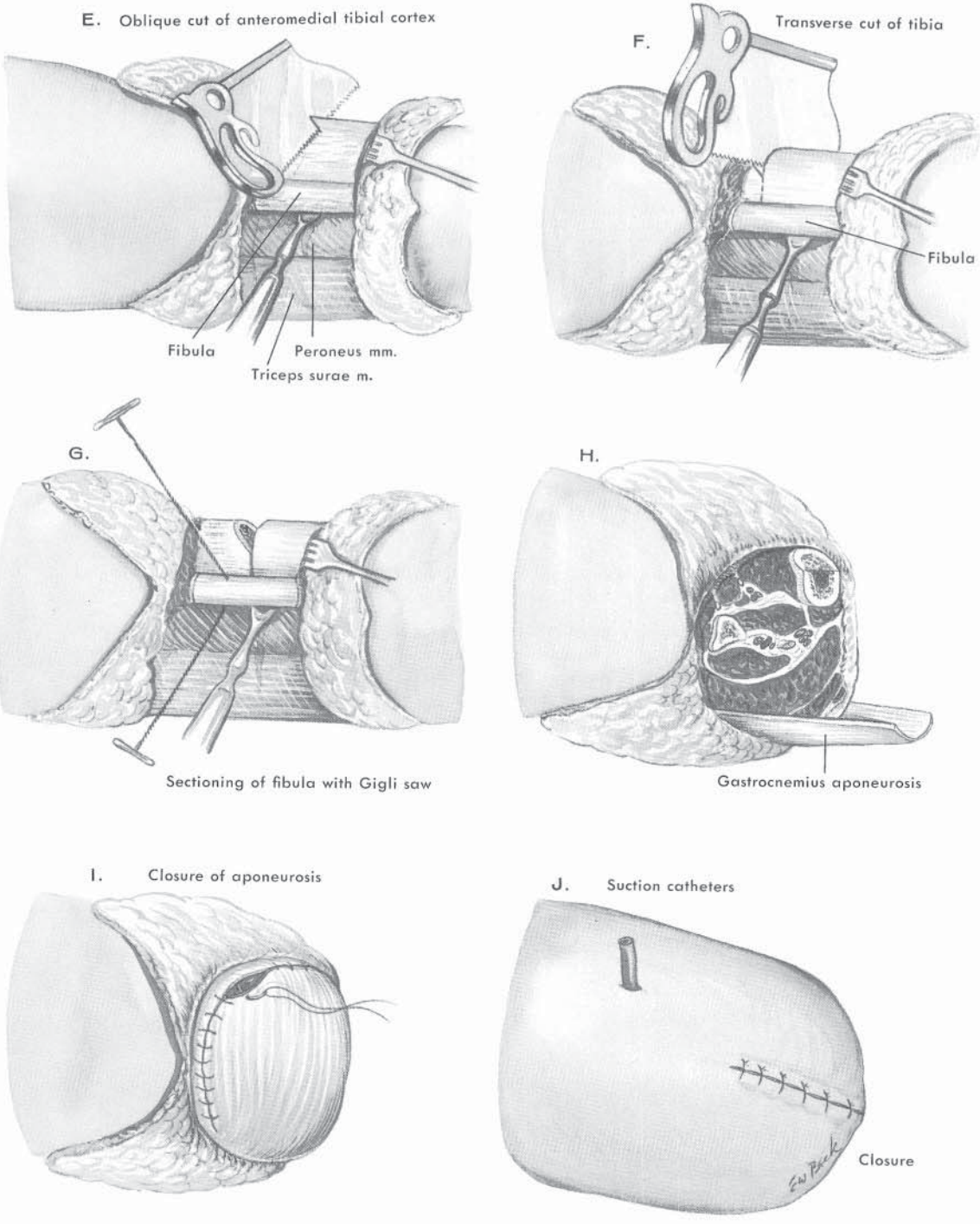
G, Then the tibia is transversely sectioned. The angle of division should be at a right angle to the axis of the bone.

H, The fibula is cleared of surrounding muscle and, with a Gigli saw, it is sectioned 2 to 3 cm proximal to the distal end of the tibia. The bone ends are smoothed and rounded with a rasp. All periosteal fringes are excised, and the wound is irrigated with normal saline solution to remove bone dust.

Next, the posterior muscles in the leg are sectioned. The posterior tibial and peroneal vessels are carefully identified, doubly ligated, and then divided. The tibial nerve is pulled distally and divided with a sharp knife. A fascial flap is developed from the gastrocnemius aponeurosis so that it can be brought forward to cover the end of the stump.

I and **J,** The tourniquet is released following application of hot laparotomy pads and pressure over the cut surfaces of the muscles and bones. After 5 minutes the pads are removed and complete hemostasis is secured. The wound should be completely dry. The fascia of the gastrocnemius muscle is brought anteriorly and sutured to the fascia of the anterior compartment muscles. The muscles may be partially excised if they are bulky at the side of the stump. Hemovac suction drainage catheters are placed deep to the gastrocnemius fascia. The subcutaneous tissue and skin are closed with interrupted sutures. A nonadherent dressing and a plaster of Paris cylinder are applied for immediate prosthetic fitting.

PLATE 38–5. Below-Knee Amputation



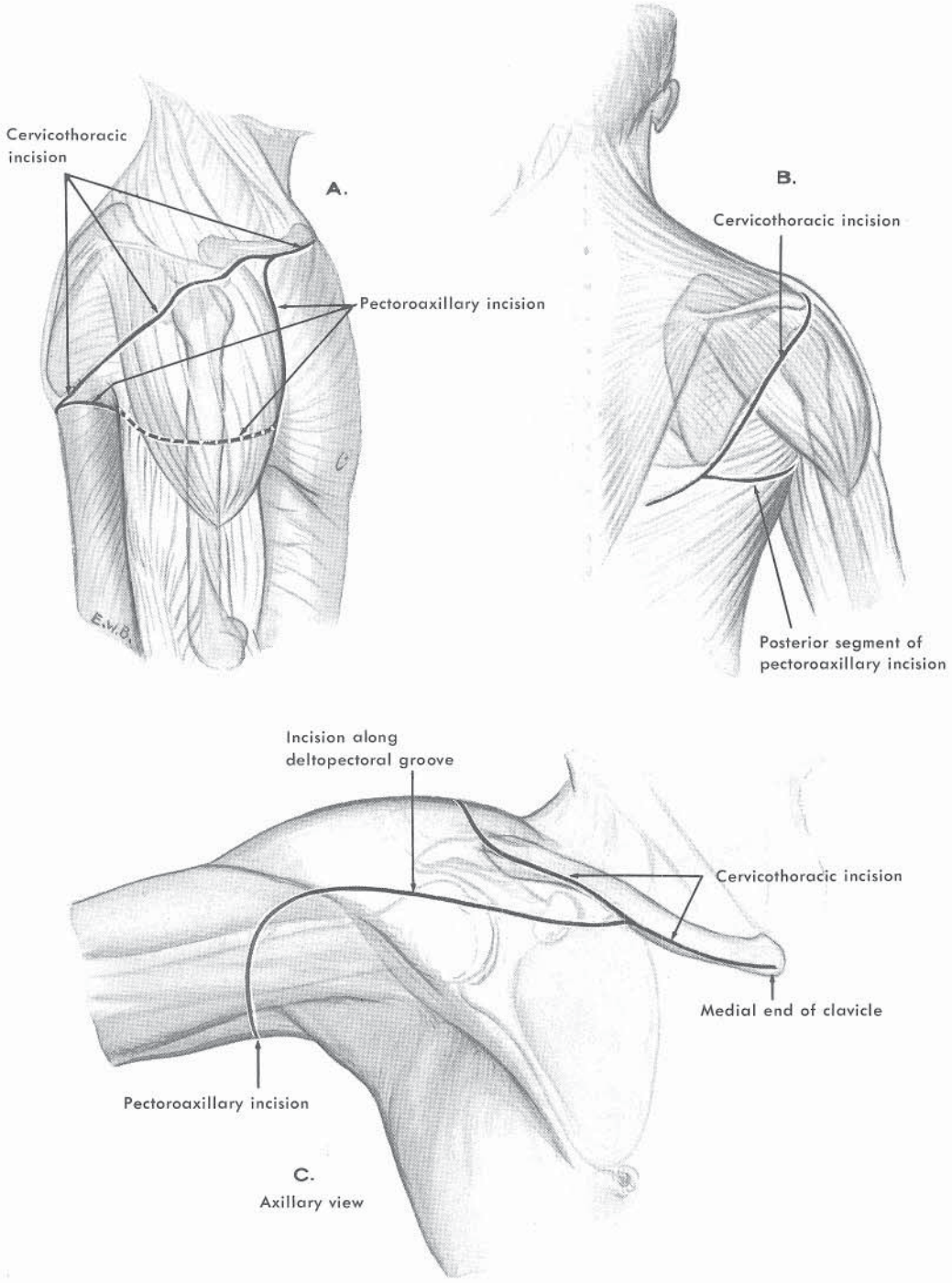
Forequarter Amputation: Posterior Approach (Littlewood Technique)

The patient is placed in the lateral position and neck, chest, and whole upper limb are prepared and draped. Blood loss is minimal, but adequate whole blood should be available for transfusion if necessary.

A to **C,** The cervicothoracic incision begins at the medial end of the clavicle and extends laterally along the anteroinferior border of the clavicle to the lateral protuberance of the acromion, where it curves posteriorly; then it is continued along the lateral border of the scapula to its inferior angle, where it curves medially to terminate 3 to 4 cm lateral to the midline of the spine.

The pectoroaxillary incision begins at the center of the clavicle and extends inferolaterally along the deltopectoral groove; it then crosses the anterior axillary fold and joins the posterior incision at the lower third of the lateral border of the scapula. The subcutaneous tissue and fascia are divided in line with the skin incision and the wound flaps are mobilized to expose the underlying muscles.

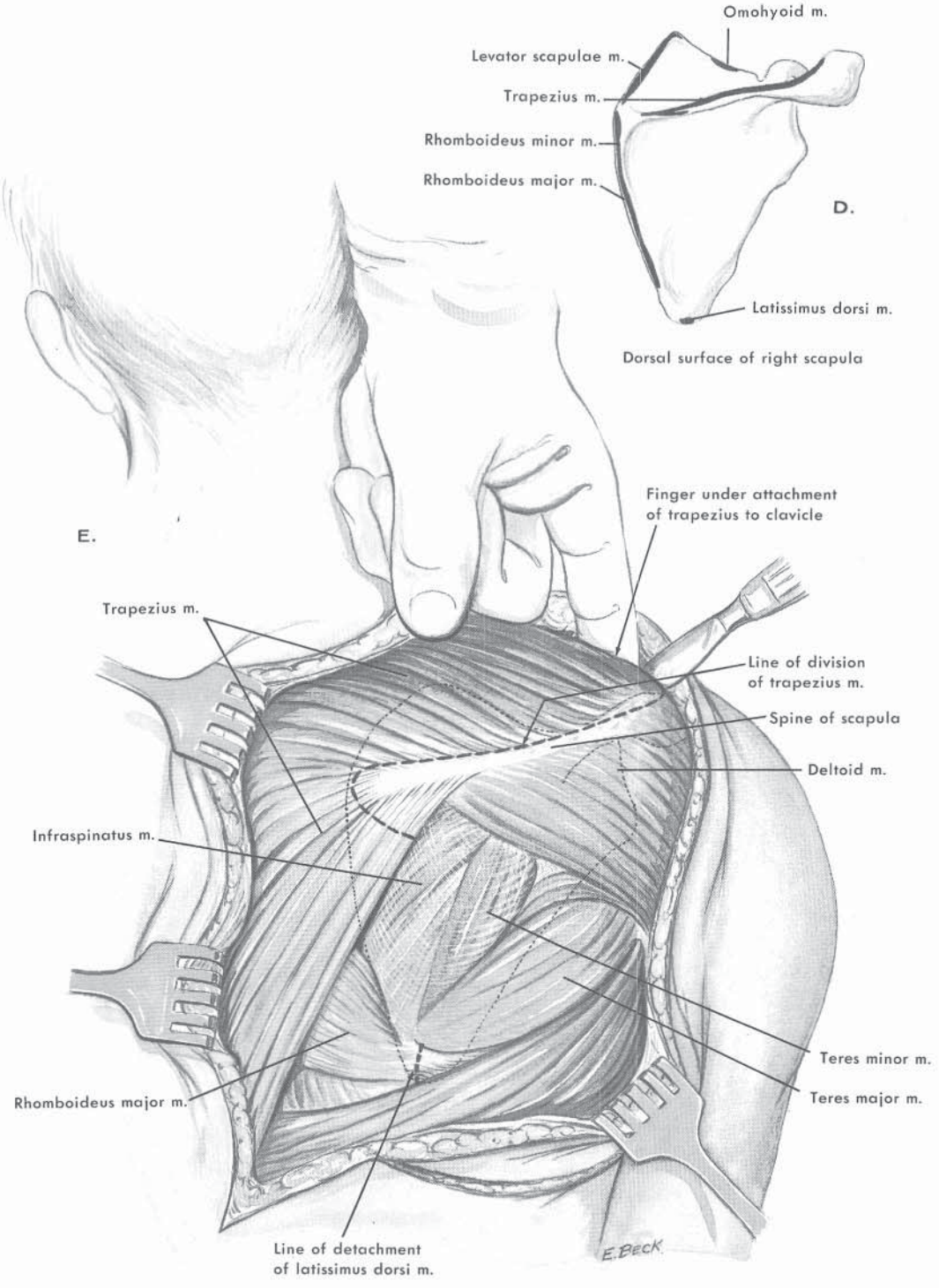
PLATE 38–6. Forequarter Amputation: Posterior Approach (Littlewood Technique)



Forequarter Amputation: Posterior Approach (Littlewood Technique) *Continued*

D and **E,** Then the muscles connecting the scapula to the trunk are detached from the scapula in layers and marked with silk whip sutures. First the trapezius and latissimus dorsi are divided.

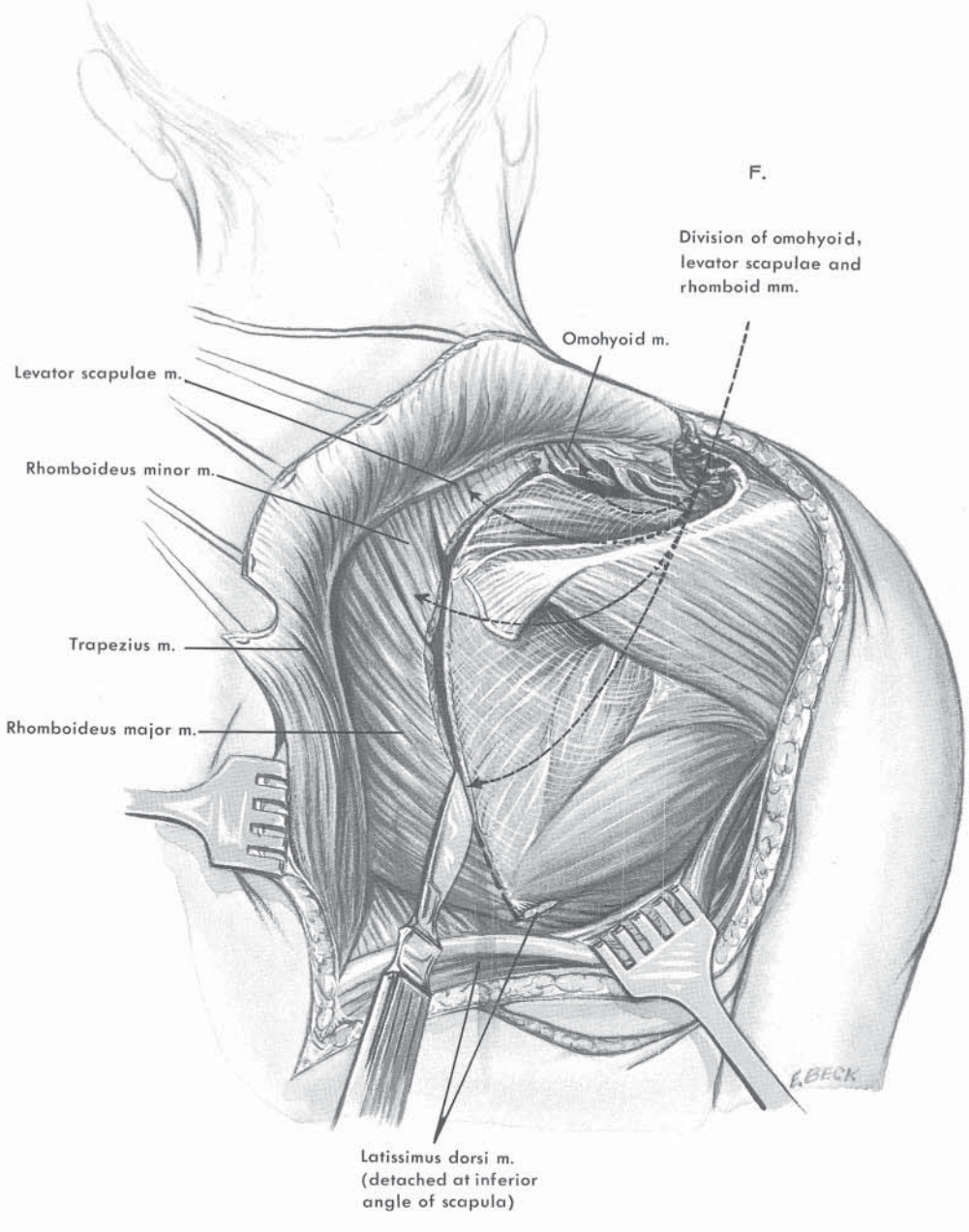
PLATE 38–6. Forequarter Amputation: Posterior Approach (Littlewood Technique)



Forequarter Amputation: Posterior Approach (Littlewood Technique) *Continued*

F, Next, the omohyoid, levator scapulae, and rhomboid muscles are detached. Transverse cervical and transverse scapular vessels are ligated and divided as dissection proceeds. The cords of the brachial plexus are sectioned with a very sharp scalpel near their origin.

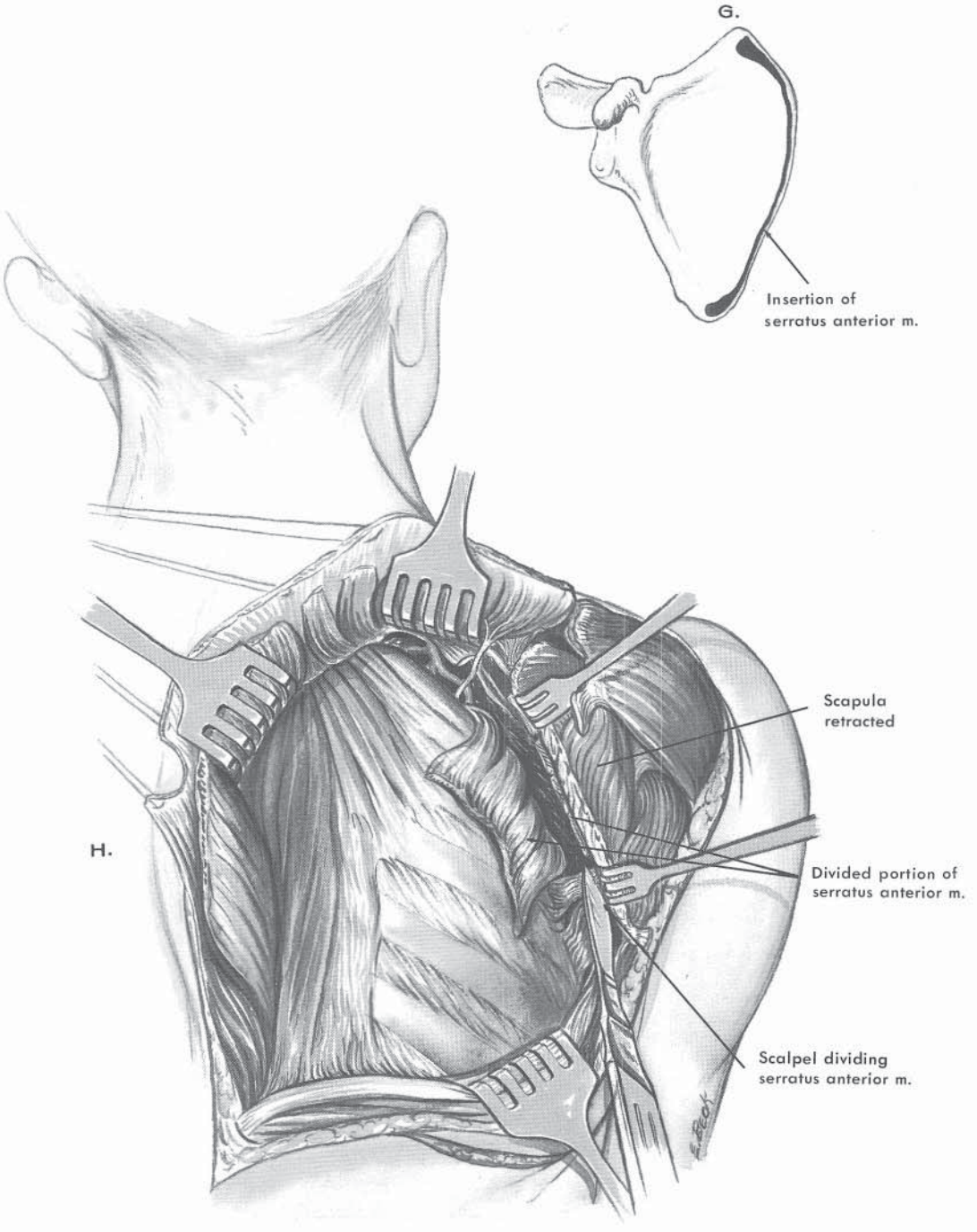
PLATE 38–6. Forequarter Amputation: Posterior Approach (Littlewood Technique)



Forequarter Amputation: Posterior Approach (Littlewood Technique) *Continued*

G and **H,** The scapula is retracted forward and the serratus anterior muscle is sectioned and detached from the scapula.

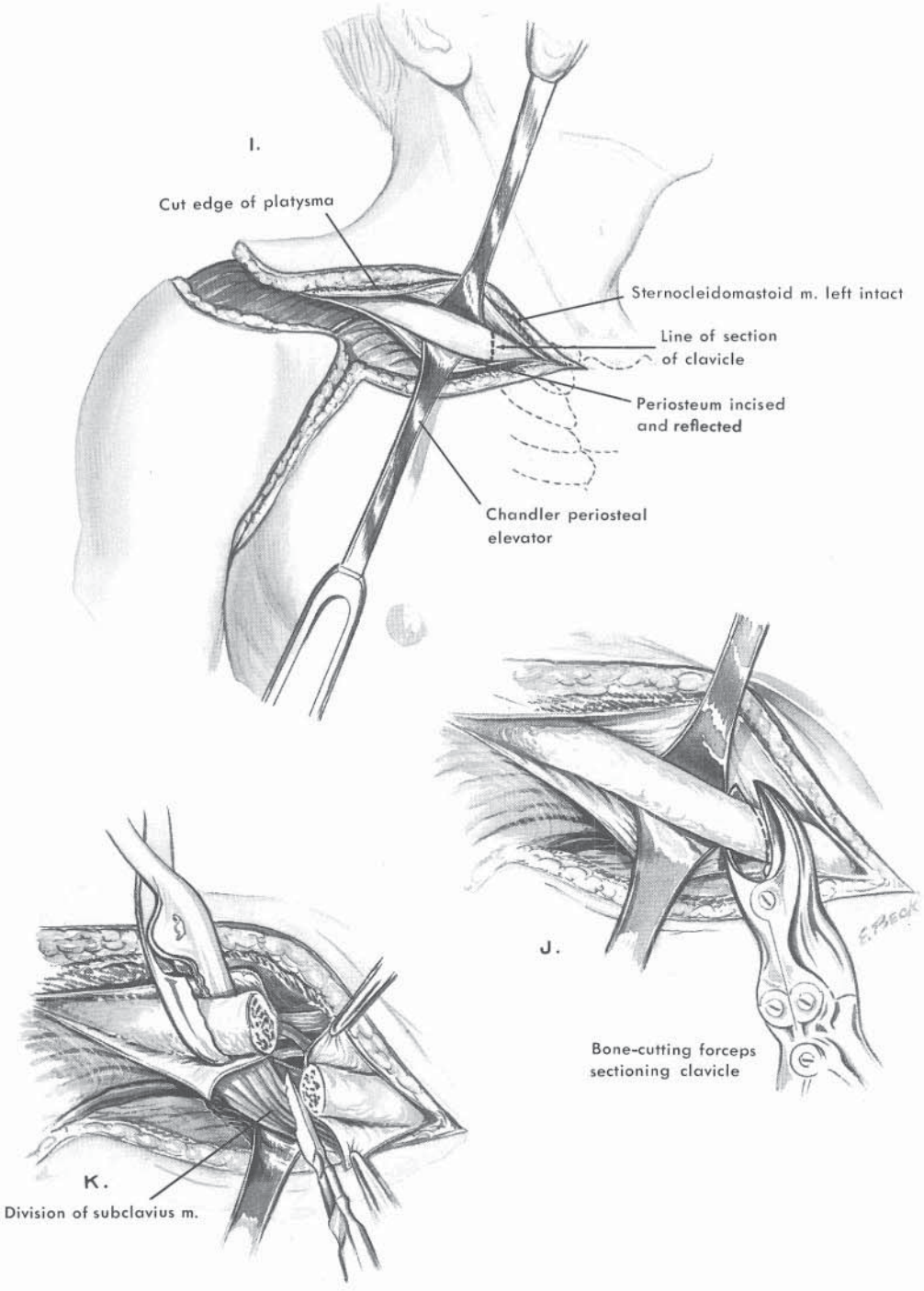
PLATE 38–6. Forequarter Amputation: Posterior Approach (Littlewood Technique)



Forequarter Amputation: Posterior Approach (Littlewood Technique) *Continued*

I to K, Next, the patient is turned onto his or her back and the medial end of the clavicle is subperiosteally exposed. Chandler periosteal elevators are placed deep to the clavicle to protect the underlying neurovascular structures. With bone-cutting forceps or a Gigli saw, the clavicle is sectioned near its sternal attachment. The subclavius muscle is divided next.

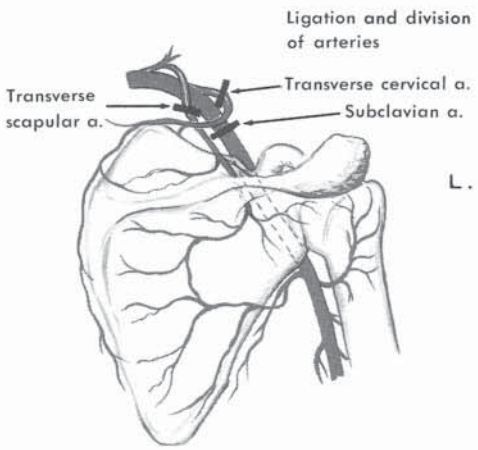
PLATE 38–6. Forequarter Amputation: Posterior Approach (Littlewood Technique)



Forequarter Amputation: Posterior Approach (Littlewood Technique) *Continued*

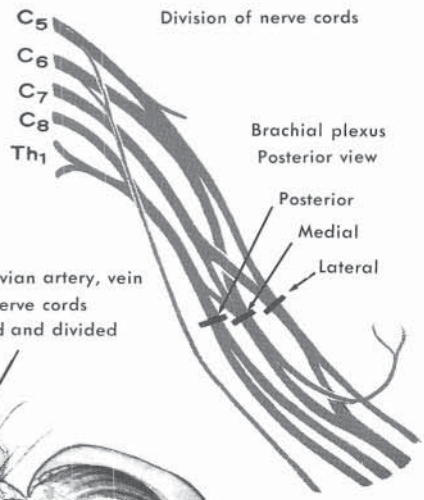
L to N, The subclavian vessels and brachial plexus are exposed by allowing the upper limb to fall anteriorly. The subclavian artery and vein are isolated, individually clamped, doubly ligated with sutures, and divided.

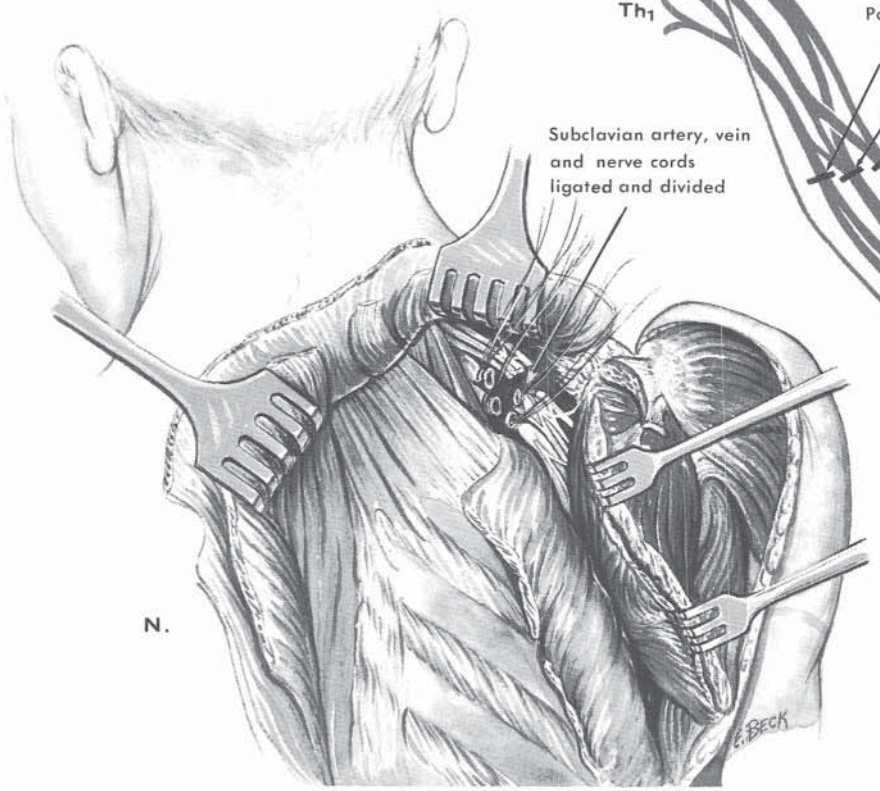
PLATE 38–6. Forequarter Amputation: Posterior Approach (Littlewood Technique)



L.

M.





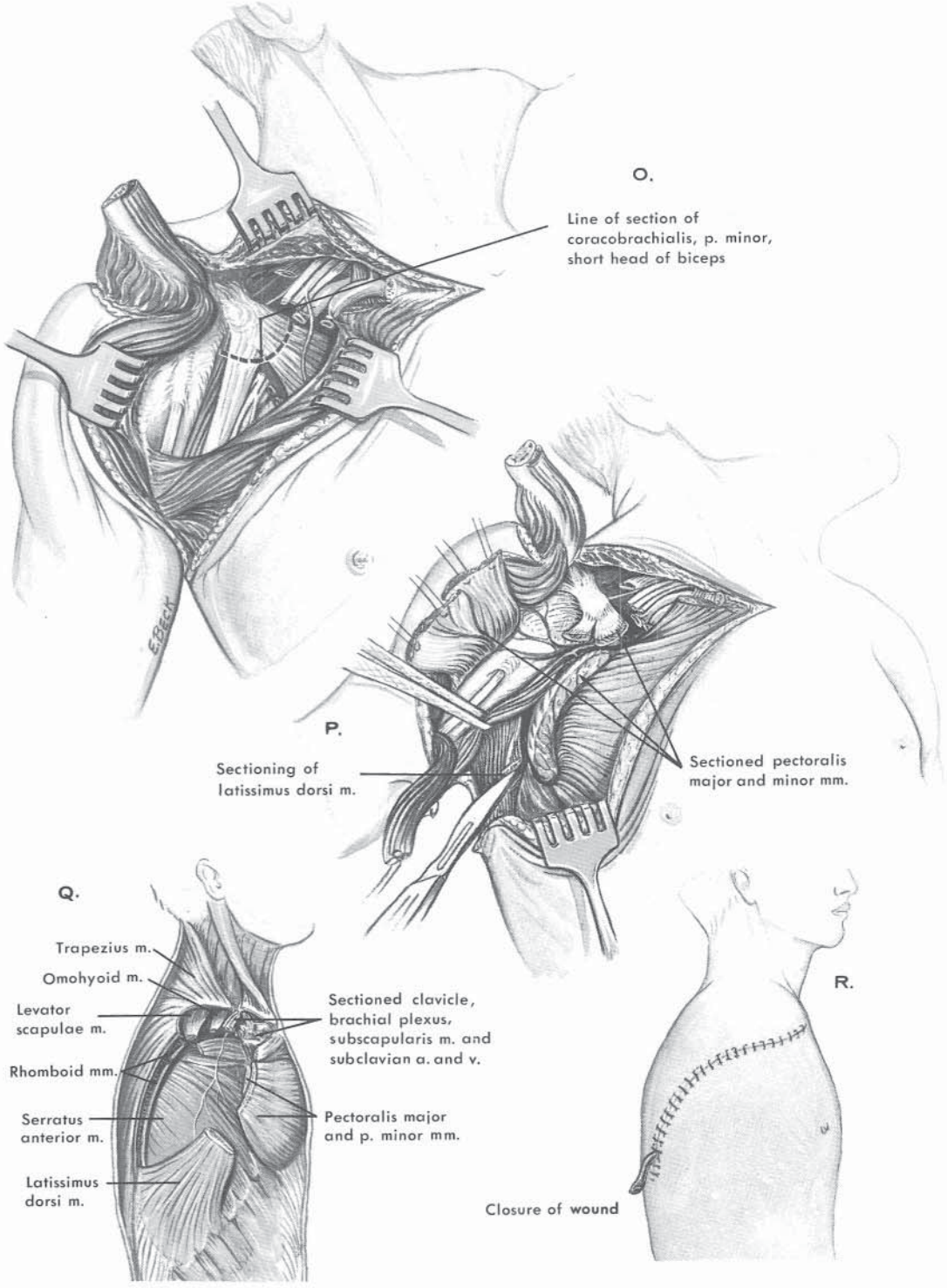
N.

Forequarter Amputation: Posterior Approach (Littlewood Technique) *Continued*

O to **Q,** Then the pectoralis major and minor, the short head of the biceps, coracobrachialis and latissimus dorsi are sectioned, completing ablation of the limb.

R, The wound flaps are approximated and sutured together. Closed suction catheters are inserted and connected to the Hemovac evacuator. A firm compression dressing is applied.

PLATE 38–6. Forequarter Amputation: Posterior Approach (Littlewood Technique)



Disarticulation of the Shoulder

The patient is placed in a semilateral position so that the posterior aspect of the affected shoulder, scapula, axilla, and the entire upper limb can be prepared and draped sterilely.

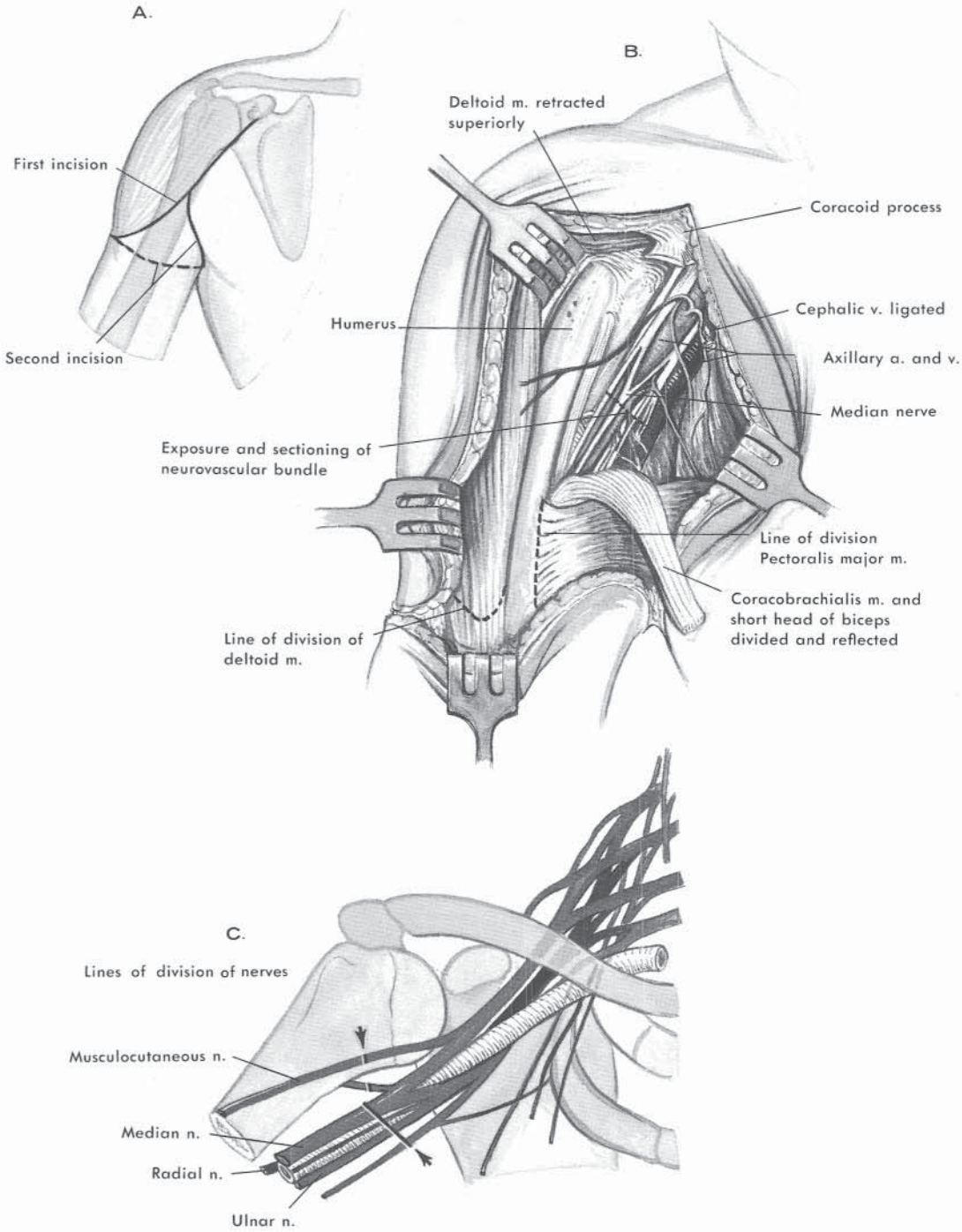
A, The skin incision begins at the coracoid process and extends distally in the deltopectoral groove to the insertion of the deltoid muscle, and then is continued proximally along the posterior border of the deltoid muscle to terminate at the posterior axillary fold. A second incision in the axilla connects the anterior and posterior borders of the first incision.

B, In the deltopectoral groove, the cephalic vein is identified, ligated, and excised. The deltoid muscle is retracted laterally to expose the humeral attachment of the pectoralis major muscle, which is divided at its insertion and reflected medially. The coracobrachialis and short head of the biceps are divided at their origins from the coracoid process and are reflected distally.

Next, the deltoid muscle is detached from its insertion on the humerus and retracted proximally.

C, The axillary artery and vein and the thoracoacromial vessels are identified, isolated, doubly ligated with 0 silk suture, and divided. The thoracoacromial artery is a short trunk branching from the anterior surface of the axillary artery. Its origin is usually covered by the pectoralis minor muscle. The median, ulnar, musculocutaneous, and radial nerves are identified, isolated, pulled distally, and divided with a sharp knife, then allowed to retract beneath the pectoralis minor muscle.

PLATE 38–7. Disarticulation of the Shoulder



Disarticulation of the Shoulder *Continued*

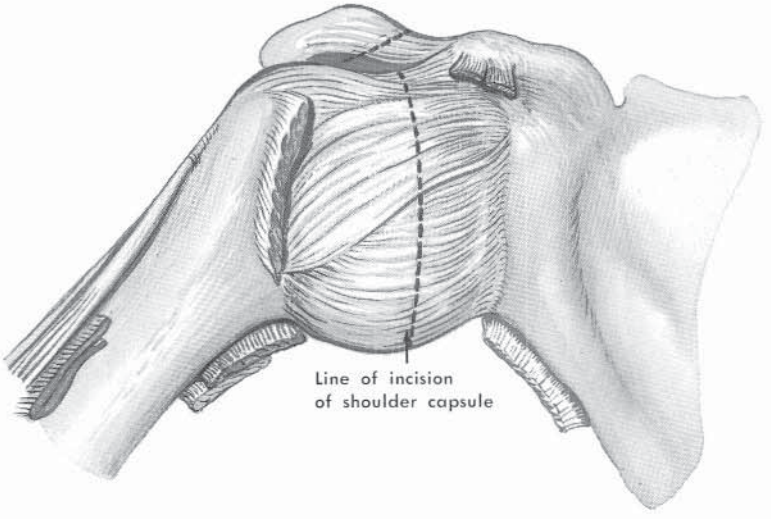
D, The capsule of the shoulder joint is exposed by retracting the deltoid muscle superiorly. Next, the arm is placed in marked external rotation. The subscapularis muscle, the long head of the biceps at its origin, and the anterior capsule of the shoulder joint are divided. The teres major and latissimus dorsi muscles are sectioned near their insertion to the intertubercular groove of the humerus. The acromion process is exposed extraperiosteally by elevating the origin of the deltoid muscle from its lateral border and superior surface. The acromion process is partially excised with an osteotome to give the shoulder a rounded smooth contour.

The arm is placed across the chest with the shoulder in marked internal rotation. The supraspinatus, infraspinatus, and teres minor muscles are divided at their insertion. The capsule of the shoulder joint is divided superiorly and posteriorly. The long head of the triceps brachii is sectioned near its origin from the infraglenoid tuberosity of the scapula. The inferior capsule of the joint is divided, completing disarticulation of the shoulder. The hyaline articular cartilage of the glenoid cavity is curetted, exposing cancellous raw bleeding bone. The cut ends of the muscles are sutured to the glenoid fossa.

E, The deltoid muscle is sutured to the inferior aspect of the neck of the scapula. Suction catheters are placed deep to the deltoid muscle and connected to a Hemovac evacuator. The subcutaneous tissue and skin are closed in layers with interrupted sutures.

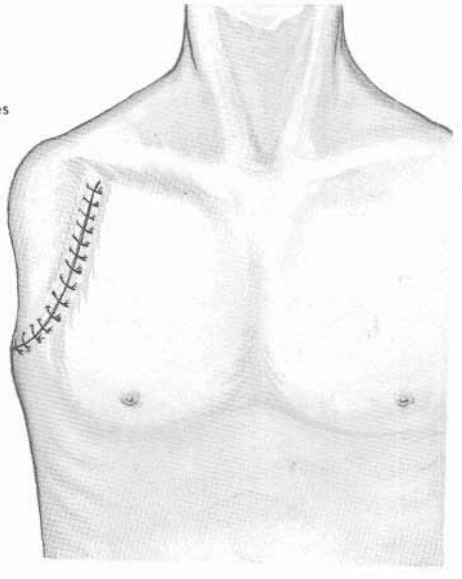
PLATE 38–7. Disarticulation of the Shoulder

D.



E.

Skin closure with
interrupted sutures



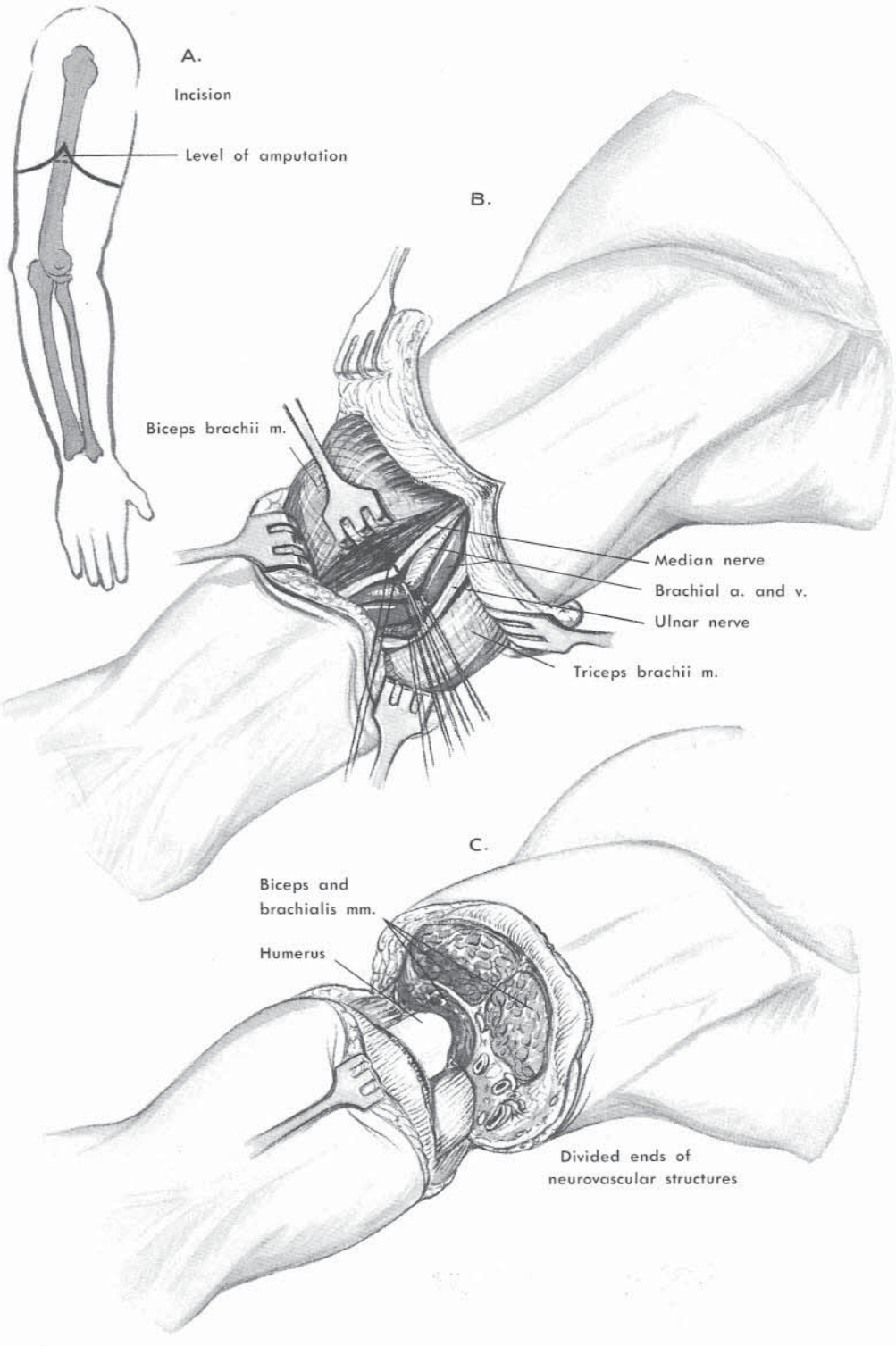
Amputation Through the Arm

The patient is placed in a supine position with a sandbag under the shoulder that is to be operated on. A sterile Esmarch tourniquet is applied in the axillary region for hemostasis.

A, Anterior and posterior skin flaps are fashioned so that they are equal in length and 1 cm longer than half the diameter of the arm at the intended level of amputation. The subcutaneous tissue and deep fascia are divided in line with the skin incision and the wound flaps are retracted.

B and **C,** The brachial artery and vein are identified, doubly ligated, and divided. The median and ulnar nerves are isolated, pulled distally, sectioned with a sharp knife, and allowed to retract proximally. The muscles in the anterior compartment of the arm are divided 1.5 cm distal to the site of bone division, and the muscle mass is beveled distally.

PLATE 38–8. Amputation Through the Arm



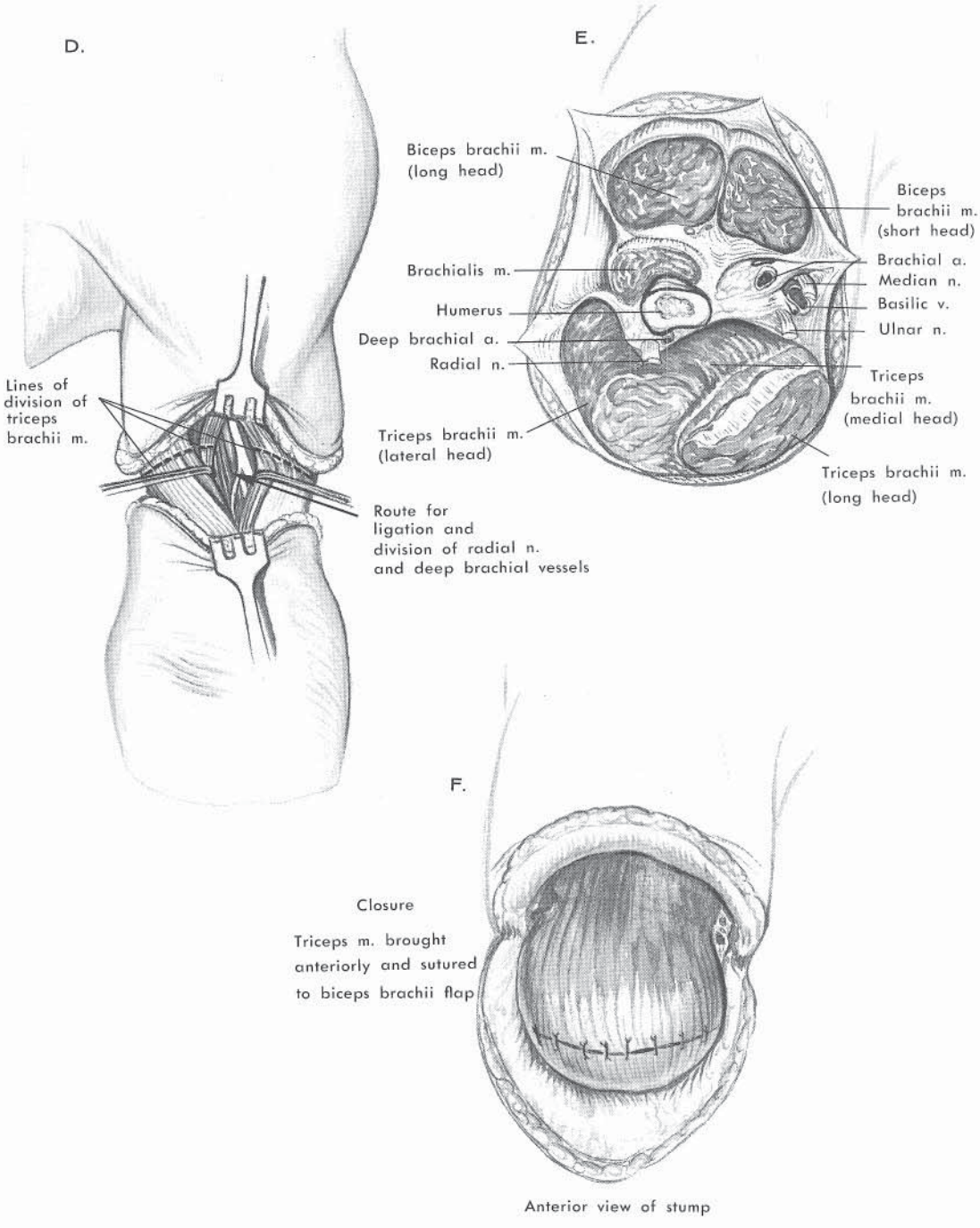
Amputation Through the Arm *Continued*

D, The radial nerve is isolated, pulled distally, and sectioned with a sharp knife. The deep brachial vessels are doubly ligated and divided. The triceps brachii muscle is sectioned 3 to 4 cm distal to the level of the bone section and beveled to form a skin flap.

E, The humerus is divided and the bone end is smoothed with a rasp.

F, The distal end of the triceps muscle is brought anteriorly and sutured to the deep fascia of the anterior compartment muscles. Catheters are inserted for closed suction and the wound is closed with interrupted sutures.

PLATE 38–8. Amputation Through the Arm



Disarticulation of the Elbow

The operation is performed with a pneumatic tourniquet on the proximal arm.

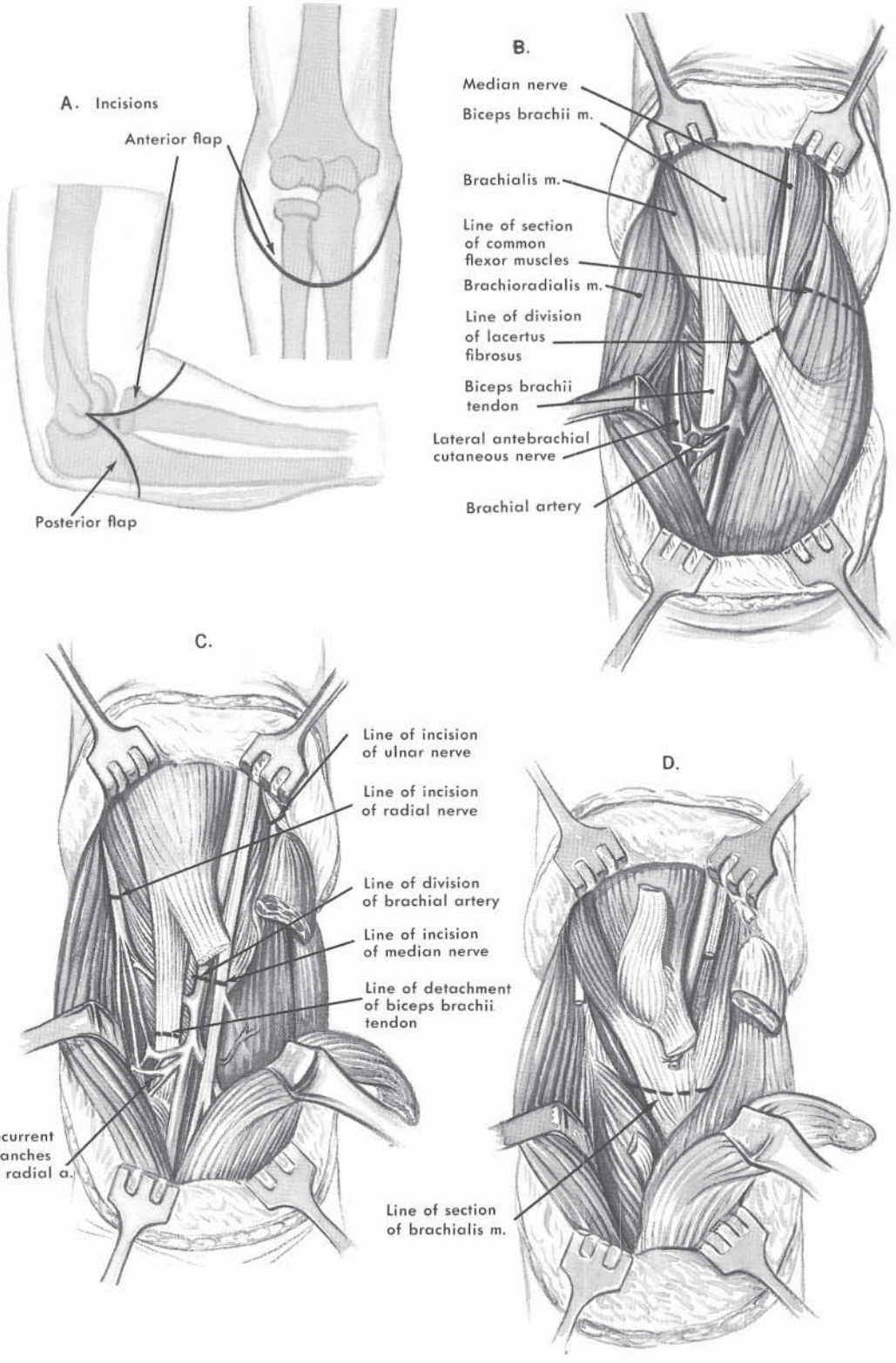
A, The anterior and posterior skin flaps are fashioned to be equal in length to the medial and lateral epicondyles of the humerus, which serve as the medial and lateral proximal points. The lower margin of the posterior flap is 2.5 cm distal to the tip of the olecranon; the distal margin of the anterior flap is immediately inferior to the insertion of the biceps tendon on the tuberosity of the radius.

B, The wound flaps are undermined and reflected 3 cm proximal to the level of the epicondyles of the humerus. The lacertus fibrosus is sectioned. The common flexor muscles of the forearm are divided at their origin from the medial epicondyle of the humerus, elevated extraperiosteally, and reflected distally.

C and **D,** The brachial vessels and the median nerve on the medial aspect of the biceps tendon are exposed. The brachial vessels are doubly ligated and divided proximal to the joint level. The median nerve is pulled distally, divided with a sharp knife, and allowed to retract proximally. The ulnar nerve is dissected free in its groove behind the medial epicondyle, drawn distally, and sharply sectioned. The biceps tendon is detached from its insertion on the radial tuberosity.

The radial nerve is isolated in the interval between the brachioradialis and brachialis muscles. The nerve is pulled distally and divided with a sharp knife. The brachialis muscle is divided at its insertion to the coronoid process.

PLATE 38–9. Disarticulation of the Elbow



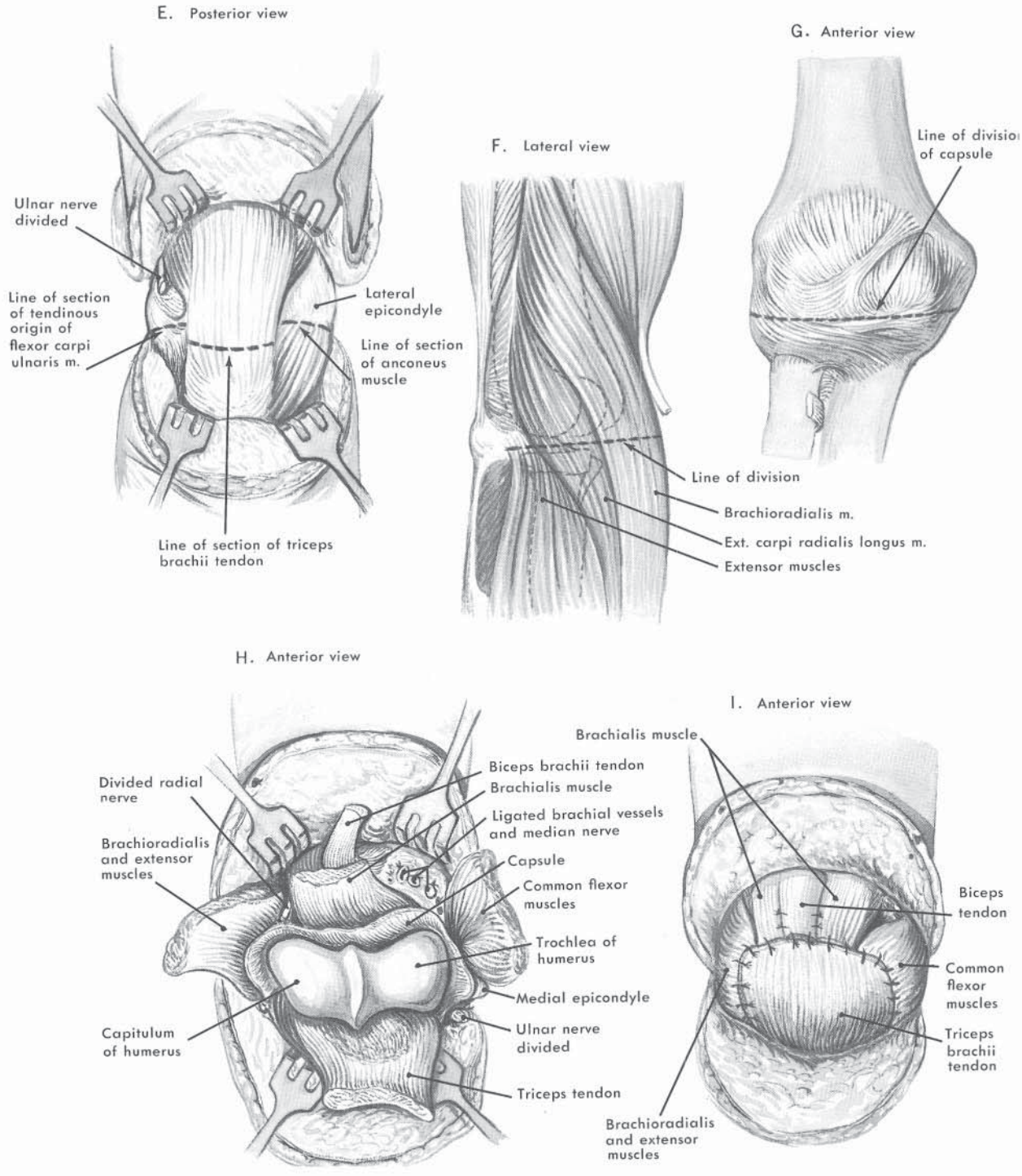
Disarticulation of the Elbow *Continued*

E and **F,** The brachioradialis and common extensor muscles are sectioned transversely about 4 to 5 cm distal to the joint line. Following detachment of the triceps tendon at its insertion near the tip of the olecranon process, division of the common extensor muscles of the forearm is completed.

G and **H,** The capsule and ligaments of the elbow joint are divided and the forearm is removed. The tourniquet is released and complete hemostasis is obtained.

I, The triceps tendon is sutured to the brachialis and biceps tendons. The proximal segment of the extensor muscles of the forearm is brought laterally and sutured to the triceps tendon. The wound flaps are approximated with interrupted sutures. Catheters are placed in the wound for closed suction.

PLATE 38–9. Disarticulation of the Elbow



An alternative to amputation for distal femoral osteosarcomas is the rotationplasty (Fig. 38–10). Young children with high-grade sarcomas of the knee area have limited options for reconstruction following resection of the sarcoma. An above-knee amputation for a distal femoral osteosarcoma in a very young patient leaves the child with a very short lever arm to power a prosthesis, and it becomes relatively shorter as the child grows. The operation described by Borggreve and adapted for congenital defects (such as proximal femoral focal deficiency) by Van Nes has been applied to the tumor setting and provides a reconstruction option for certain situations.* It can be thought of as an intercalary amputation of the distal femur (or proximal tibia). The reconstruction employs the distal leg, which is rotated 160 to 180 degrees, providing the advantage of a longer lever arm, and an active "knee" joint provided by the ankle and foot.

The indications for rotationplasty include a distal femoral or proximal tibial osteosarcoma in a skeletally immature patient or a patient who wants to continue sporting activities, a failed distal femoral reconstruction, or a pathologic fracture. It must be possible to preserve the sciatic nerve and its branches, although the vessels may be divided and anastomosed to increase the margin if necessary. The advantages of a rotationplasty are the wide margin (which includes the skin, adjacent knee joint, and all thigh muscles), the avoidance of phantom pain, rapid healing of the osteosynthesis site, and a relatively low complication rate. The obvious drawback is the appearance, which is repulsive to some. Interestingly, a young child usually does not view the procedure as an amputation because the foot remains, and with a good prosthesis he or she is able to function better than and appear similar to standard amputees. Follow-up studies have not demonstrated any adverse psychological outcomes,[55,187,229,240,303] and in my experience, the selected patients who have undergone the procedure are quite happy with it.[307] Preoperative discussions must be honest and complete so that the child and the family are aware of the nature of the procedure and the expected outcome. It is helpful for them to meet with a physical therapist who is familiar with this procedure, view videotapes of patients who have undergone the procedure, and ideally meet a patient with a rotationplasty. I employ all of these modalities, and I spend considerable time explaining the rationale and the relative advantages and disadvantages of this and the other options, such as amputation and limb-sparing procedures. Recently the number of patients willing to undergo this procedure has diminished: many prefer to try a limb-sparing procedure and reserve rotationplasty until or unless it fails.

The procedure itself is well described in the literature.† It is important to plan the skin flaps carefully, and modifications of the rhomboid incision described by Kotz are quite satisfactory.[241,412] In my experience, there is a tendency to make the thigh long, so that the rotated "knee" appears to be distal to the contralateral knee. It is difficult to accurately predict growth remaining because the distal tibial physis and the tarsals become analogous to the contralateral distal femoral growth plate. One can attempt to plot the growth remaining using standard tables, but in general, a boy older than 14 and a girl older than 12 years of age should probably have the rotationplasty "knee" placed opposite the contralateral knee. For younger patients placing it 2 to 4 cm more caudal is appropriate. I prefer to resect the vessels with the specimen to increase the amount of normal tissue margin. An anastomosis of the vein and artery can be completed after achieving osteosynthesis. An alternative is to dissect the vessels free from the tumor and loop them carefully back on themselves with the nerves.[241,307]

This procedure has also been described for tumors of the proximal tibia, with successful results.[88,171,187,242] Modifications of this procedure have also been described for lesions about the hip or involving a large portion of the proximal femur.[268,504,505] The ilium and distal femur must be preserved for this procedure to provide a "hip" and a "knee." I have had no personal experience with rotationplasty at these sites.

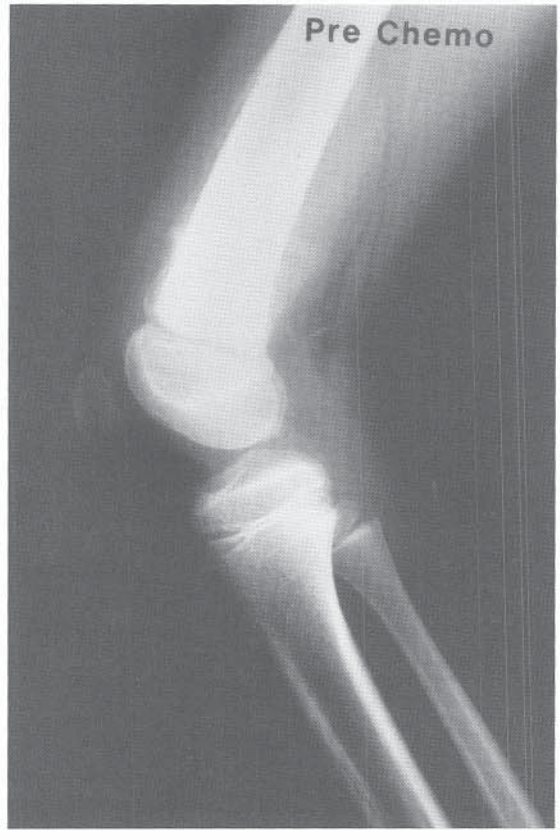
Rotationplasty for a distal femoral osteosarcoma offers a durable and functional if cosmetically displeasing reconstruction option for selected patients with a sarcoma. For very young patients with a distal femoral lesion, it avoids the repeated surgical procedures necessary to achieve limb length equality and allows the child to run and play exceedingly well. The other useful indication is for a failed limb salvage procedure when amputation would be the only alternative.

The child and parents may need psychological support when considering both amputation and rotationplasty. Initially there will be tremendous emotional resistance to ablation of a limb. It is helpful for these patients to see other children with amputations and prostheses prior to the operation. A physical therapy consult and a visit to the prosthetist are also valuable. Treatment of these children and adolescents in a children's hospital with a specialized multidisciplinary oncology team is of great value. Fitting with a temporary prosthesis may also be of psychological benefit, although they seldom function well. Usually a permanent prosthesis can be made 6 to 8 weeks following the procedure.

LIMB SALVAGE. After a complete staging workup, biopsy, and (usually) preoperative chemotherapy, the primary tumor is reassessed for response. MRI will often show a reduction in the amount of edema surrounding the tumor, but seldom does the mass decrease in size because of the matrix within the tumor. There are as yet no proven ways to accurately judge or predict the histologic response of the tumor preoperatively, but thallium scans, dynamic MRI, and position emission tomography (PET) may prove to be of use in this regard.[208,329,374,385,400,490] Limb salvage is considered if there has been no progression of disease locally or distantly and if the nerves and blood vessels are free of the tumor. The most important issue is the ability to completely resect the tumor with wide margins. The adjacent joint and growth plates are assessed for tumor involvement, and the amount of muscle that is involved is assessed. There is no agreement regarding the "safe" amount of normal tissue that must surround the resected specimen, but in general, at least a 3 to 5 cm bone marrow margin and a 5 to 10 mm soft tissue margin is desirable. The thickness of the soft tissue margin depends on the type of tissue. A fascial margin is considered to be a more substantial barrier to tumor spread than a

*See references 32, 55, 67, 88, 156, 171, 187, 237, 240, 241, 307, 317, 447, 505.

†See references 32, 55, 63, 141, 156, 171, 183, 187, 211, 229, 237, 240, 241, 307, 412, 505.



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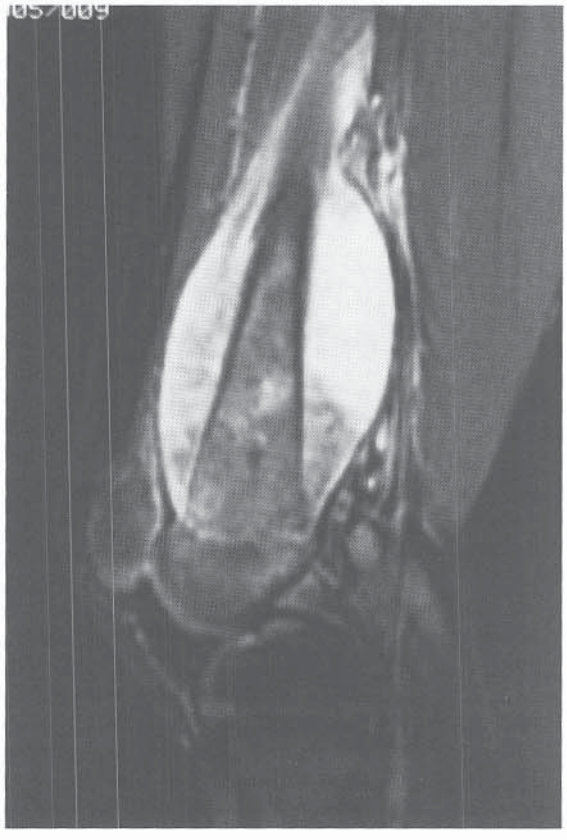

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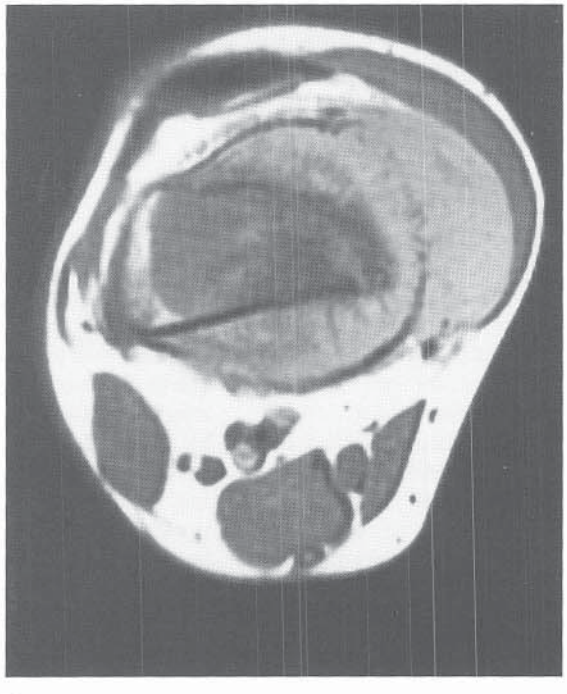

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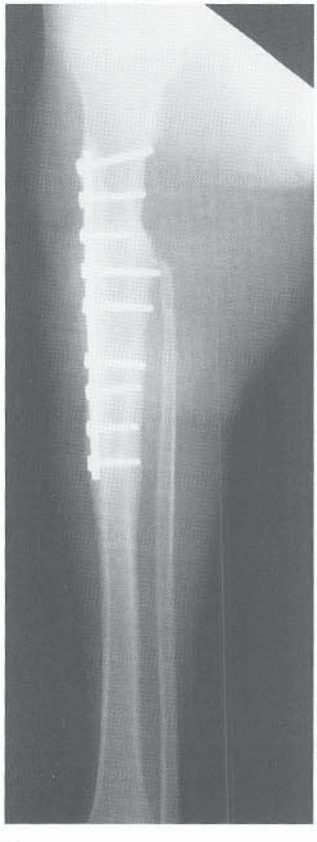


D

FIGURE 38–10 Osteosarcoma in a 10-year-old boy. **A,** Lateral radiograph of the femur showing a radiodense lesion of the distal femur with a large soft tissue mass. There is a "starburst" type of periosteal reaction of the soft tissue mass. Codman's triangle is seen along the anterior cortex. A biopsy confirmed the diagnosis of osteosarcoma. **B,** Sagittal MR image showing the extent of the soft tissue mass and extension into the marrow. Anteriorly the tumor approaches but does not invade the joint. Posteriorly the femoral vessels are close to the mass but do not appear to be encased, and the posterior knee capsule is uninvolved. **C,** Axial MR image showing that the vessels and nerves are uninvolved, and the extent of the soft tissue mass. The patient elected to have a rotationplasty because of his age and his desire to play sports. **D,** Radiograph of the lower extremity obtained 1 year later. The boy remains free of disease and fully active 5 years later.

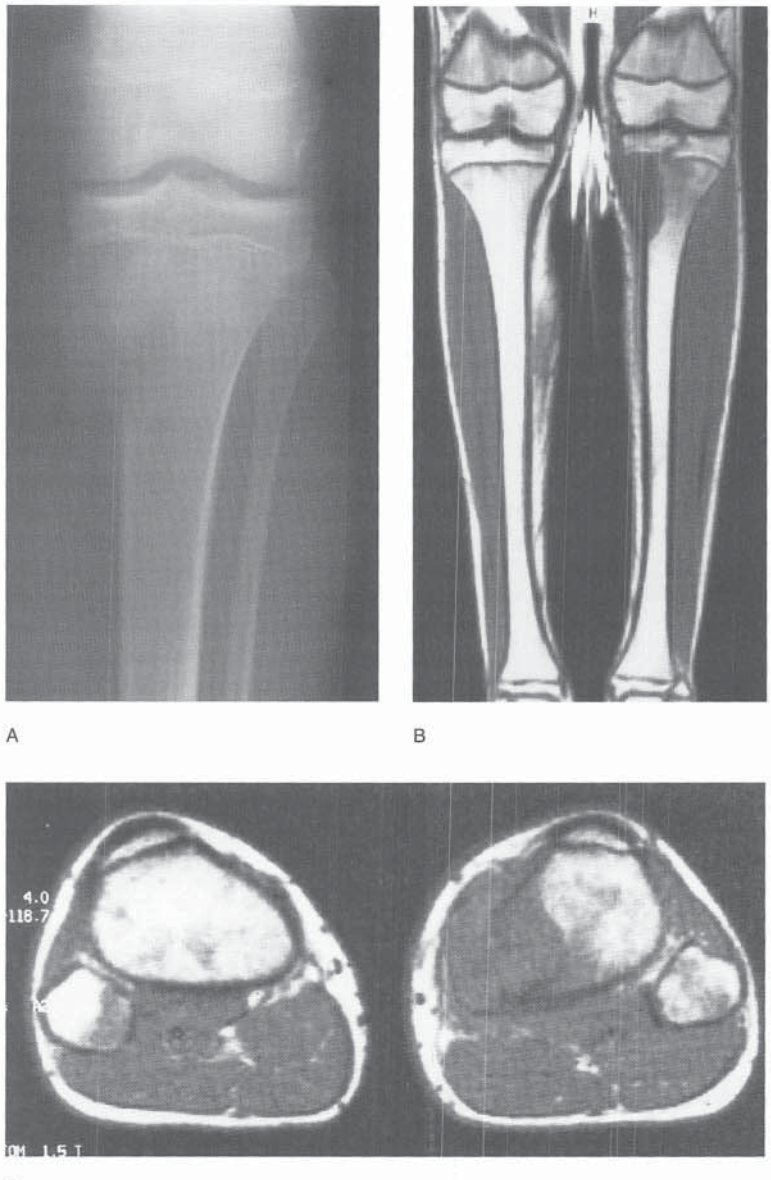
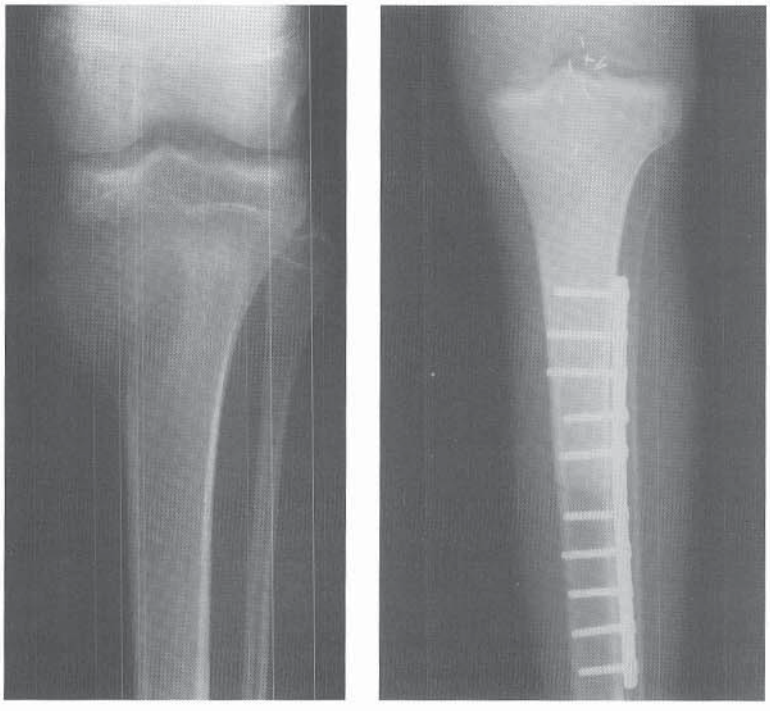


FIGURE 38–11 High-grade osteosarcoma in a 16-year-old boy. **A,** AP radiograph of the tibia. There is a destructive lesion of the proximal metaphysis with internal mineralization. It is poorly marginated and has destroyed the cortex. It appears to stop at the growth plate. At this age, an osteosarcoma would be the most likely diagnosis. **B,** T1-weighted MR image showing the medullary extent of this tumor and the soft tissue mass. The epiphysis appears to be uninvolved except for a linear signal abnormality that may represent a fracture. The adjacent joint appears to be uninvolved. **C,** Axial MR image showing the extent of the soft tissue mass and the relationship of the lesion to the popliteal vessels. The vessels are uninvolved. An incisional biopsy showed that the tumor was a high-grade osteosarcoma.

similar thickness of fat. The resection should be planned with regard to achieving local control, and reconstruction options should be a secondary consideration.

In "expendable" bones such as the clavicle, fibula, scapula, and rib, a resection without reconstruction can be considered. Lesions of the radius and ulna are rare and can usually be resected with minimal reconstruction or with fibular autografts or allografts employed for reconstruction. Lesions of the hands and feet usually require amputation, although at times ray amputation and partial amputations that preserve some hand or foot function can be performed. For lesions of the extremities that are deemed resectable the reconstruction can become quite complex and depends on the age of the patient and the location in reference to joints and growth plates. For most distal femoral and proximal tibial osteosarcomas, an intracompartmental, intra-articular resection can be carried out. The same is usually possible for lesions of the proximal humerus. Reconstruction is achieved either with an osteoarticular allograft or with a metallic prosthesis. There are no proven advantages of one over the other, and the decision of which to use is usually based on surgeon and patient preference. In boys younger than 12 to 14 years and girls younger than 10 to 12 years with lesions about the knee, growth considerations come into play. Limb length is usually not a major concern, and can be addressed by standard limb equalization techniques after the chemotherapy is completed (such as epiphysiodesis, limb lengthening, limb shortening, and so on). Alternatively, a metallic prosthesis that can be expanded as the child grows can be used.* For older patients with growth remaining, it is usually possible to make the reconstruction 1 to 2 cm longer than the amount resected, resulting in nearly equal limb lengths at maturity. Fortunately, most osteosarcomas occur in this age group. The choice of metallic prosthesis versus allograft

*See references 75, 109, 128, 231, 405, 407, 484, 495.



D E

FIGURE 38–11 *Continued.* **D,** AP radiograph obtained following preoperative chemotherapy. There is mineralization of the tumor, and a more complete periosteal shell of bone around the periphery of the lesion. This is considered to be a sign of response to chemotherapy. After preoperative chemotherapy, the patient underwent an intra-articular wide resection of the osteosarcoma and reconstruction with an osteoarticular allograft. **E,** AP radiograph showing the reconstruction with early healing of the osteosynthesis site 9 months after reconstruction.

is debatable. The prosthesis is more stable initially and returns the patient to function earlier than an allograft, but there is concern about the longevity of the implant over time in this young age group. Loosening, particle disease, and metal and polyethylene failure are unsolved problems. I prefer to use allograft reconstructions in skeletally immature children (Fig. 38–11). Allografts offer the advantage of restoring bone stock but require a longer recuperation period and are associated with relatively high fracture, infection, and nonunion rates.[8,41,138,139,276,284] The longevity of the articular cartilage is also of concern, and some will require conversion to a more standard joint replacement over time. One advantage to using osteoarticular allografts in children is the ability to preserve the adjacent growth plate. In the proximal tibia, the ability to reattach the patellar tendon to the allograft tendon is another advantage.[70,191] Similarly, the ability to reconstruct the rotator cuff in the shoulder is an advantage of an allograft in that location.[140]

For diaphyseal osteosarcomas, intercalary resections are frequently possible. These resections allow preservation of the adjacent joints and sometimes the growth plates. The defects can be reconstructed with allografts, vascularized fibulae, or metallic spacers, and because the joints are preserved, the function is usually superior to function following osteoarticular resections (Fig. 38–12).[8,335] It is critical to accurately assess the MR image to plan tumor-free marrow margins. If the growth plate must be sacrificed, standard limb equalization procedures can be used later.

Pelvic osteosarcomas are an extremely difficult challenge. Tumors of the ilium that spare the acetabulum can be resected with little functional loss, but if the acetabulum is involved, there is no adequate reconstruction option, and it is frequently difficult to achieve tumor-free margins. The adjacent sacrum is frequently involved, making it necessary to sacrifice nerve roots at times. Nevertheless, resections of the ilium and acetabulum, even with little or no reconstruction, can result in decent ambulatory function. Options for reconstruction include osteoarticular allografts, allograft arthrodeses, pseudarthroses of the femur to the remaining pubis, or metallic prostheses.[1,39,57,120,157] The complication rate is quite high, and careful attention to soft tissue coverage should be made. Adjuvant radiotherapy may be necessary if it is not possible to achieve microscopically negative margins.

METASTATIC OSTEOSARCOMA

Patients who present with osteosarcoma are carefully scrutinized for the presence of gross metastatic disease. The most common site is the lungs, followed by bone.[175,312] The prognosis for patients with metastases at diagnosis is much poorer than that of patients with no demonstrable metastatic disease. However, efforts to develop newer drugs to treat these patients are ongoing. Recent studies have shown that if aggressive chemotherapy plus resection of all gross disease can be accomplished, it is possible to achieve long-term survival in about 30 to 40 percent of patients with metastatic disease at diagnosis.[175,312] Patients whose disease cannot be completely resected and those with bony metastases are usually not salvageable. In general, patients with lung metastases are more likely to survive than patients with metastases to other sites. Patients presenting with bony metastases have a dismal prognosis, with few reported survivors, but they may survive functionally and pain-free for long periods, so aggressive treatment is employed. It is difficult to distinguish a patient with multifocal osteosarcoma from one with metastatic osteosarcoma, and the definitions are somewhat arbitrary. Multifocal osteosarcoma may be synchronous (multi-

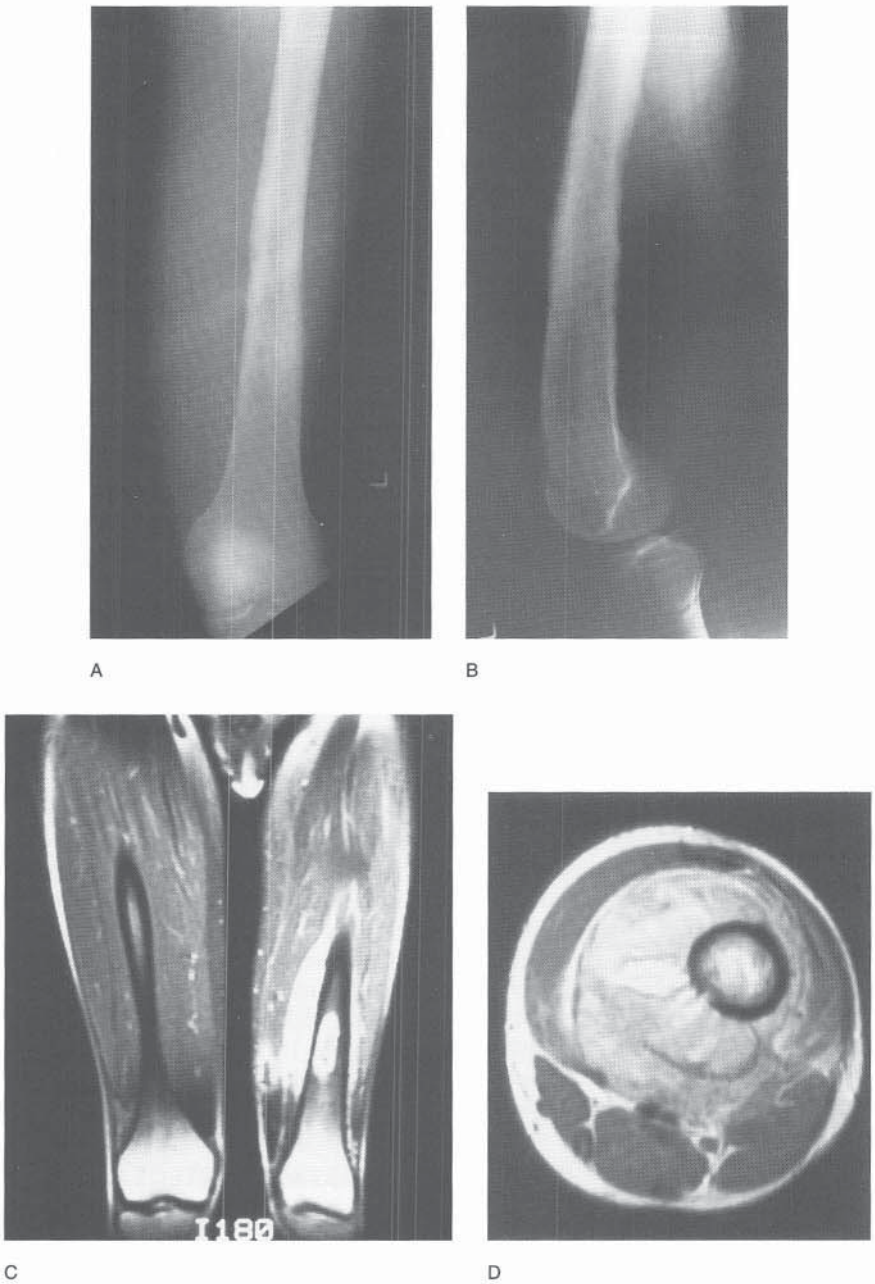


FIGURE 38–12 Ewing's sarcoma/PNET in a 15-year-old boy. **A,** AP radiograph showing a permeative, destructive lesion of the femoral diaphysis. There is a suggestion of a soft tissue mass. **B,** Lateral radiograph. The mass is better seen, and there is erosion of the posterior cortex. **C,** Coronal MR image showing the medullary extent of the tumor. **D,** Axial MR image showing that huge soft tissue mass almost completely surrounding the femur. This appearance is typical of Ewing's sarcoma PNET. Because the tumor does not make tumorous bone or cartilage, there is no mineralization as is seen in osteosarcoma. A biopsy confirmed the diagnosis of Ewing's sarcoma/PNET.

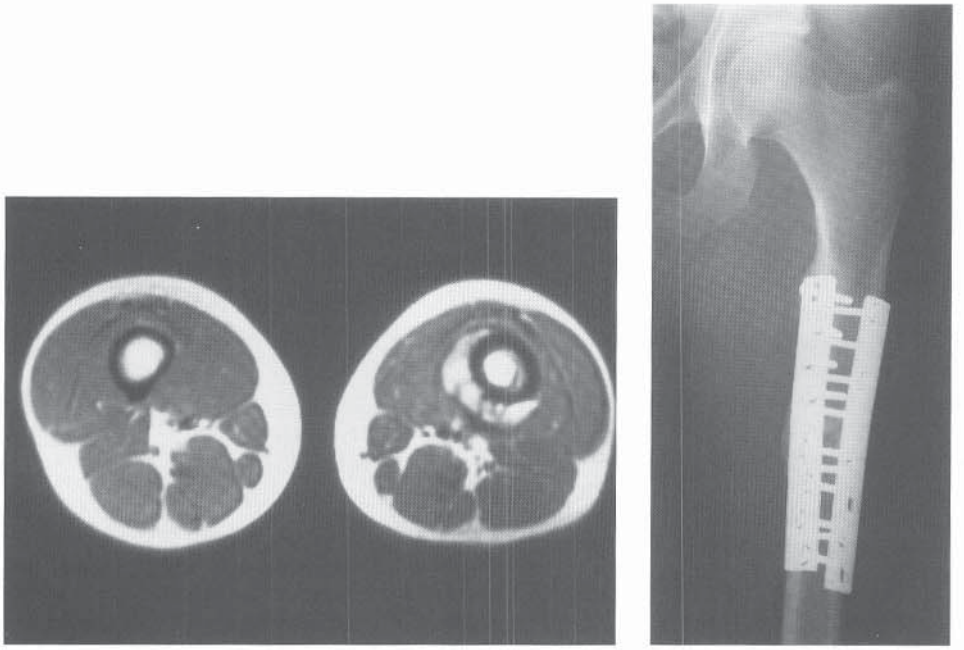
ple bony lesions at the time of diagnosis) or metachronous (secondary bone lesions occurring years later).*

Metastatic disease that develops following the completion of chemotherapy usually occurs in the lung. Approximately 30 to 40 percent of these patients can be salvaged by thoracotomy and resection of the metastases with or without further chemotherapy.† Sometimes multiple thoracotomies are employed with success. More recently, thoracoscopic resections have been employed.[145]

EWING'S SARCOMA AND PNET

A second primary malignant bone neoplasm in children, composed of primitive, malignant round cells, was named after James Ewing, who first described it as a distinct entity in 1921.[199] He originally named it "diffuse endothelioma" or "endothelial myeloma," in accordance with his

*See references 28, 165, 279, 281, 344, 367, 423, 460.
†See references 52, 114, 152, 288, 436, 465, 494, 509.



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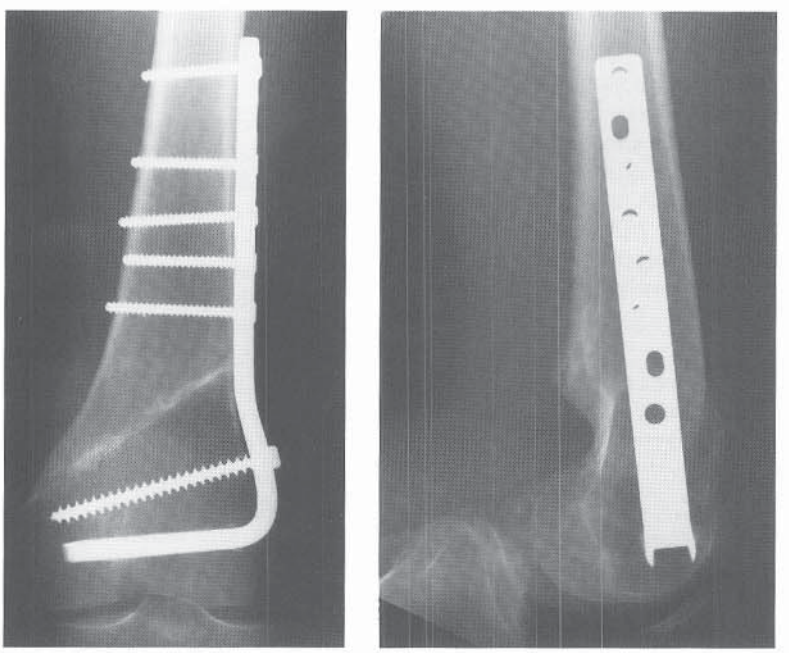


G H

FIGURE 38–12 *Continued.* **E,** Axial MR image obtained following induction chemotherapy. There has been considerable reduction in the extent and size of the soft tissue mass. After discussing the alternatives of radiation therapy and surgery for local control, the patient elected to undergo surgical resection. **F** to **H,** Radiographs showing the reconstruction. An intercalary resection with wide margins was performed and an allograft reconstruction was carried out. Both the hip and the knee joints were preserved. Both osteosyntheses healed, with very good function.

belief that it was derived from vasoformative tissue. There has been much debate, however, concerning its pathogenesis. Currently it is thought that Ewing's sarcoma is part of a family of peripheral primitive neuroectodermal tumors (PNET) that share a common cytogenetic translocation of chromosomes 11 and 22, t(11:22). There are subtle histologic differences between Ewing's sarcoma and PNET, and both may involve either soft tissue or bone, but the treatment approaches are currently the same for both entities. Ewing's sarcoma is poorly differentiated, whereas PNET exhibits definite neural differentiation. There is currently debate relative to whether one or the other has a better prognosis.[91,166,427] This discussion will consider these tumors to be the same entities, while occasion-

ally pointing out some of the observed differences between them.

Ewing's sarcoma is the second most common primary malignant tumor of bone in children.[159,192,348] It has characteristic predilection for an age group between 10 and 20 years. It is very rarely found in individuals less than 5 years old or more than 30 years old. If similar findings are encountered in a child less than 5 years, neuroblastoma or Wilms' tumor should be considered, whereas if similar findings are encountered in a patient over the typical age range, lymphoma should be considered. In patients more than 50 years old, metastatic carcinoma or myeloma should be considered. Ewing's sarcoma is slightly more common in boys than in girls. It is very rare in black populations of America or Africa and in children of Asian origin.[159,192,348]

The location of Ewing's sarcoma/PNET is most often in the pelvis and lower extremity.[236] The sites of disease from a large Intergroup Ewing's Sarcoma Study trial are shown in Table 38–1. The ilium, femur, and fibula are common sites, the humerus and tibia less so. In the long tubular limb bones, the lesion is more often situated in the diaphysis than in the metaphysis. Ribs are another common site, where the lesion frequently manifests with pneumonia or pleural effusion. Other infrequent sites include the scapula or vertebra. Rarely, the bones of the hands or feet are affected.[74,105,272,424]

Pathologic Findings. On gross inspection the neoplasm appears as a whitish gray soft tissue mass that arises in the marrow spaces of the interior of the affected bone.[133] Necrotic and hemorrhagic areas in the tumor are frequent. Anatomic involvement of bone is much more extensive than is apparent on radiographs, although MRI reliably demonstrates the extent of bone marrow involvement. The neoplastic tissue destroys and replaces the involved bone. The periosteum is elevated and often is perforated. Nearly always there is a large soft tissue mass extending well beyond the bony boundaries. The tumor is not encapsulated and invades the surrounding muscle. When an innominate bone is involved, the soft tissue mass will protrude into the iliacus, often displacing the pelvic organs toward the midline, and laterally the mass will invade the abductor muscles. Not infrequently the soft tissue mass crosses the sacroiliac joint and invades the adjacent sacrum.

TABLE 38–1 **Sites of Ewing's Sarcoma in the Intergroup Ewing's Sarcoma Study**

Primary Site		Percent
Pelvis	*Percent*	20
Ilium	12.5	
Sacrum	3.3	
Ischium	3.3	
Pubis	1.7	
Lower Extremity		45.6
Femur	20.8	
Fibula	12.2	
Tibia	10.6	
Feet	2.0	
Upper Extremity		12.9
Humerus	10.6	
Forearm	2.0	
Hand	0.3	
Axial Skeleton/Ribs		12.9
Face		2.3

From Kissane JM, Askin FB, Foulkes M, et al: Ewing's sarcoma of bone: clinicopathologic aspects of 303 cases from the Intergroup Ewing's Sarcoma Study. Hum Pathol 1983;14:773.

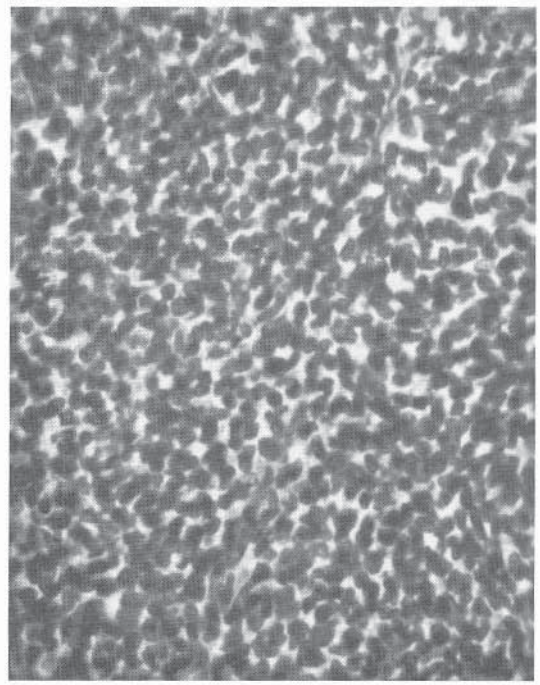


FIGURE 38–13 Ewing's sarcoma: histologic findings. Photomicrograph shows the round cells, which are polyhedral with pale cytoplasm and small hyperchromatic nuclei (×400).

Histologic examination discloses compact sheets of small polyhedral cells with pale cytoplasm and ill-defined boundaries.[91,111,381,425] It is one of a group of tumors referred to as small round cell tumors. Ewing's sarcoma/PNET must be distinguished from neuroblastoma, non-Hodgkin's lymphoma, and rhabdomyosarcoma.[476] The nuclei are uniform, round or oval in shape, and contain scattered areas of chromatin (Fig. 38–13). The cytoplasm is scant. There are multiple thin-walled vascular channels among a scant stroma. Reticulin fibers are not a consistent feature of Ewing's sarcoma/PNET. Another distinguishing histochemical finding is the presence of glycogen in the cells of Ewing's sarcoma; in lymphoma, the cells do not contain glycogen. The cytoplasmic material is PAS positive and diastase digestible, but this finding is not specific for Ewing's sarcoma/PNET. Occasional rosette or pseudorosette formations may be present, and some pathologists view this finding as evidence of a PNET.[381] On light microscopic examination, the cytologic findings may be difficult to differentiate from neuroblastoma, lymphoma, or other round cell lesions.[476] Special immunohistochemical stains, electron microscopy, and at times cytogenetic studies are necessary to establish the correct diagnosis.* It is important to remember that Ewing's

*See references 89, 91, 95, 170, 304, 346, 381, 425, 469, 493.

sarcoma is a very primitive tumor and lacks differentiation along any specific mesenchymal lineage, whereas PNET has signs of neural differentiation (S-100, neuron-specific enolase staining, rosettes, and neural elements by electron microscopy).[90] Extensive necrosis and degenerative changes may also confuse the picture. Hemorrhage may provoke a reparative inflammatory reaction to the tumor, a finding that may be misinterpreted as a mere infection.[108]

Ultrastructural studies have shown small to medium-sized cells, round or polyhedral in shape, with round nuclei, scant membranous organelles, abundant glycogen, absence of filaments, and primitive intercellular junctions.[97,192,195,273,280,366]

Recently, monoclonal antibodies (HBA-71 and 12E7) to p30/32MIC2, a cell surface glycoprotein that is encoded by the *MIC2* gene, have been found useful in the diagnosis of Ewing's sarcoma/PNET.[125] The *MIC2* gene is a pseudoautosomal gene located on the short arms of human chromosomes X and Y. Glycoprotein expression is not specific for these tumors (it is expressed on T cells), but both Ewing's sarcoma and PNET cells express the *MIC2* gene in very high amounts, which helps to distinguish them from other round cell tumors.[10] Mesenchymal chondrosarcomas, small cell osteosarcomas, and malignant lymphomas do not routinely express this product. *MIC2* staining should not be relied on as the sole criterion for the diagnosis of Ewing's sarcoma and related tumors because false negatives in these tumors and positive results in tumors other than PNET occur.[95,373] In recent studies of Ewing's sarcoma/PNET, 91 to 97 percent showed a diffuse strong membranous pattern, suggesting that *MIC2* expression is highly reliable when the results are interpreted in the context of clinical and pathologic parameters.[259,355] Hence, *MIC2* is a useful screen for Ewing's sarcoma and is used routinely in most pathology laboratories.

The most definitive test for Ewing's sarcoma/PNET is demonstration of the chromosomal translocation by karyotyping or reverse transcriptase-polymerase chain reaction (RT-PCR) detection of t(11;22).* Approximately 80 to 95 percent of patients with Ewing's sarcoma have a translocation either of chromosomes 11 and 22 or of chromosomes 21 and 22.[19,159] The resultant fusion gene is composed of part of the *EWS* gene from chromosome 22 and the *FLY1* gene of chromosome 11 or the *ERG* gene from chromosome 21. The fusion gene is a chimeric transcription factor that retains DNA-binding regions of *FLY1* and allows it to bind to DNA. The resultant gene can transform NIH 3T3 cells in culture, demonstrating that it acts as a dominant oncogene which promotes tumors growth and suggests that this is mechanism of carcinogenesis in this tumor.[93,298] The t(11;22) is the most common translocation and the t(21;22) is the next most common.[441] Rarely a third translocation, t(7;22), is encountered.[219] Currently these findings are being employed in the diagnosis and staging of patients with Ewing's sarcoma and PNET. Rather than performing difficult and time-consuming karyotype analysis, RT-PCR is employed to establish the presence of a translocation.[36,130] Correlation with the clinical presentation and routine histologic and immunohistochemistry studies is necessary, as other tumors may rarely exhibit similar translocations.[442,470]

*See references 19, 92, 104, 130, 159, 244, 259, 470.

Of perhaps more interest is that variability in the presence of these transcripts among patients with Ewing's sarcoma/PNET may be of prognostic significance.[469,496] It is also hoped that in the future, vaccines to elicit T-cell immunity with specificity for the tumor-specific fusion peptides in Ewing's sarcoma and PNET can be employed as therapy for these tumors and others, such as rhabdomyosarcoma.[19,159,192]

Clinical Findings. Local pain and swelling are the presenting complaints.[159,192] The pain may be present for months or years before the patient seeks medical attention;[24,440] in one study, 50 percent of patients had symptoms for 6 months or more.[371] The delay was less in those with constant symptoms and the presence of a mass, and did not adversely affect outcome.[440] In the extremities, a tender, local mass is invariably present. Some degree of stiffness of the adjacent joint is common in cases of long bone involvement, and a limp is usually present. Other symptoms depend on the site of the lesion. When a rib is involved, a pleural effusion may be noted. When the lesion is in the lumbar spine, the nerve roots may be involved, producing symptoms resembling those of disk herniation, such as sciatic pain, tingling sensations, or motor weakness. Rectal and urinary complaints may result when the neoplasm is located in an innominate bone and impinges on pelvic organs or involves the sacral nerve roots. On occasion the presenting feature is a pathologic fracture of a femur or tibia involved by Ewing's sarcoma/PNET.

On physical examination, one can usually palpate a tumor mass (61 percent of the cases in a Mayo Clinic series)[503] that is tender on pressure. It is larger than the bony lesion seen on the radiograph, indicating that the neoplasm has violated the cortex and has spread extraosseously into the surrounding soft tissues. In about 20 percent of cases, the presenting lesion is in some part of the innominate bone.[236] If the pubis or ischium is involved, an irregular globular mass may be palpated on rectal examination; or if the ilium is the site of the lesion, a tumor mass may be present in the lower quadrant of the abdomen or in the gluteal region. Pathologic fracture may also be a presenting finding (16 percent in the Mayo Clinic series).[503]

It is important to appreciate that in both osteosarcoma and Ewing's sarcoma/PNET, the patients are not systemically ill at presentation and seldom become so until late in the disease. Fever, weight loss, secondary anemia, leukocytosis, and an increase in the sedimentation rate are not frequently seen unless the case is quite advanced. When present, these findings may lead to confusion with osteomyelitis and lymphoma. These findings are hallmarks of a fulminating course and are more likely to be present if there are metastases at diagnosis.[362] LDH may be elevated; an elevated level has been shown to correlate with a worse prognosis in several recent studies.[149,277]

Radiographic Findings. The radiographic appearance is fairly characteristic but not pathognomonic (Figs. 38–12A and B, 38–14, and 38–15). Mottled rarefaction of the spongiosa with permeation of the overlying cortex is the principal finding, reflecting rapid bone destruction. The bone at the site of the lesion may show some enlargement. Periosteal new bone formation, often of the laminated "onion-peel" form, is common but is not specific for Ewing's sarcoma.[5,159,192,212] A soft tissue mass overlying the area of bone

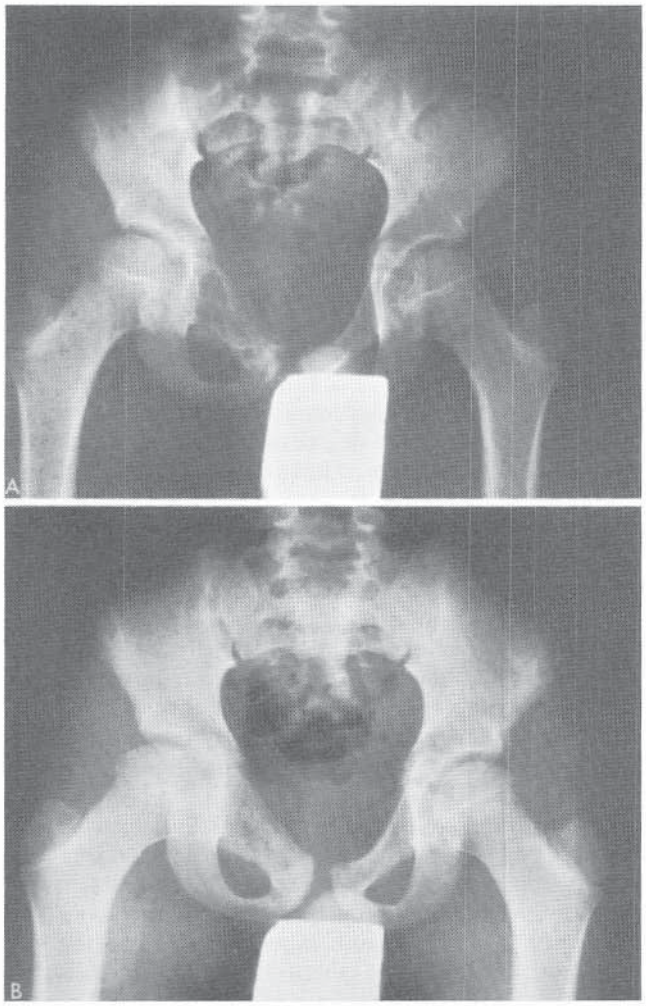


FIGURE 38–14 Ewing's sarcoma of the right pubis. **A,** Initial radiographs. Treatment consisted of irradiation and chemotherapy. **B,** Nine months later, some healing is apparent. However, the disease metastasized, and the patient died a year later.

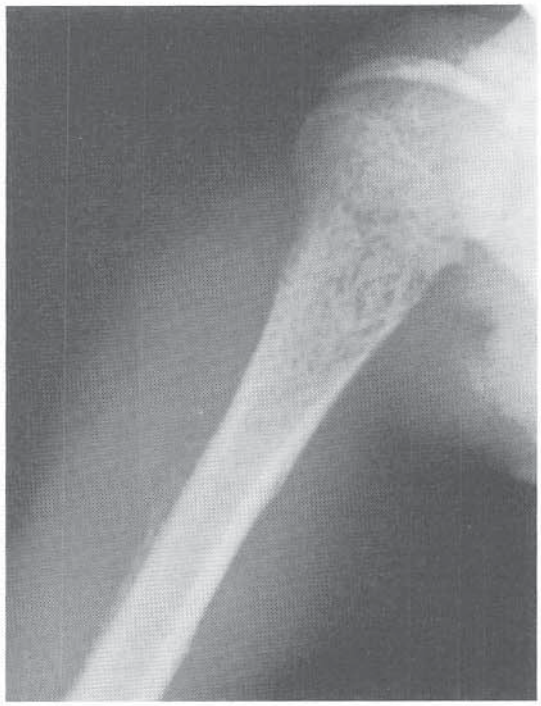


FIGURE 38–15 Ewing's sarcoma of the humerus. Note the mottled areas of rarefaction and subperiosteal reaction.

destruction is frequently seen on the radiograph, indicating that the neoplasm has perforated the cortex and has spread to the adjacent soft tissues. In the long bones, the lesion is frequently diaphyseal in location and involvement is extensive. Pathologic fractures are uncommon.[503]

The radiographic findings resemble those of histiocytosis, lymphoma, "osteolytic osteosarcoma," metastatic neuroblastoma or Wilms' tumor, leukemia, and osteomyelitis.[194,212] MRI may add to the confusion, as the inflammatory reaction around the bone and the medullary extent of histiocytosis may be quite extensive and mimic the findings of Ewing's sarcoma, although usually it is possible to make the distinction.[172]

Staging. The staging of Ewing's sarcoma/PNET is similar to that for osteosarcoma, although there are no specific staging systems for Ewing's sarcoma/PNET.[115,118,159,194,434] MRI is useful to determine the extent of the lesion within the bone and adjacent soft tissue (Figs. 38–12C to E).[47,172,197,207] In general, tumor involvement of the bone marrow is best assessed on T1-weighted sequences and tumor involvement of the soft tissue is best seen on T2- weighted sequences. Although it may be inferior to CT for assessing cortical destruction, MRI is very helpful in assessing the extent of bone marrow involvement, soft tissue tumor extent, and the relationship of tumor to neurovascular structures.[47,217] Because Ewing's sarcoma/PNET may extend throughout the entire medullary cavity and skip metastases may rarely be present, the whole bone should be imaged by MRI.[217,457] Subtraction techniques and dynamic MRI have made it possible to use this modality to assess the response to chemotherapy.[173,189,264]

Metastatic disease is present at diagnosis in approximately 25 percent of patients.[159,192] Approximately half of patients who present with metastases will have pulmonary involvement, approximately 25 percent will have bony metastases, and bone marrow involvement is seen in about 20 percent.[61,360] Liver and lymph node metastases are rare. CT is performed to search for metastatic disease in the chest. A bone scan is obtained to search for other areas of bone involvement or skip metastases. A bone marrow biopsy specimen is obtained to look for detectable disease in the marrow. Most of the time this can be accomplished by light microscopy,[258] but recently RT-PCR techniques have been used to look for bone marrow and peripheral blood cells which amplify EWS/HumFLI1.[104,496]

Biopsy. The definitive diagnosis is made from histologic study of tissue sections obtained at open or needle biopsy.[354,432,434] In children an open biopsy is usually done that observes the usual precautions of avoiding neurovascular structures and creating a longitudinal incision that can be included with the resected specimen. In Ewing's sarcoma it is best to avoid making a cortical defect in a long bone, because if radiation is chosen for local control, the chances of pathologic fracture are greater.[445] It is crucial that the surgeon obtain a frozen section and review it with the pathol-

ogist to ensure that adequate tissue is obtained for histology, immunohistochemistry, and sometimes cytogenetic studies. The histologic differential diagnosis of these small round cell tumors includes neuroblastoma, rhabdomyosarcoma, malignant lymphoma, small-cell osteogenic sarcoma, Wilms' tumor, and desmoplastic small-cell tumor,[428] histiocytosis, and osteomyelitis. Needle biopsy may be performed in surgically difficult accessible sites (such as vertebral bodies), but adequate amounts of tissue must be obtained for special stains and culture. Radiographic guidance should be used (unless there is a large palpable mass) to ensure that the specimen is taken from the correct site. Frozen sections are also advisable to ensure that representative tissue has been obtained. Tumor necrosis may make the tissue appear to be a purulent exudate and lead one to confuse Ewing's sarcoma/PNET with osteomyelitis.

Prognosis. In the past, the outlook for patients with Ewing's sarcoma/PNET was uniformly poor, with an overall 10 percent 5-year survival rate.[29,159,192,371] With the advent of adjuvant chemotherapy and proper local control, the outlook is considerably better, with recent studies showing 5-year and event-free survival rates of approximately 50 to 60 percent.[159,192] Patients with large central lesions, especially in the pelvis, have a worse outcome than those with distal tumors.* Obviously, patients who present with metastases at diagnosis, especially bony metastases, have a poorer outcome.† In one large study the event-free survival rate for patients who presented with metastases 4 years after diagnosis was 27 percent overall. The site of metastasis affected outcome in that the event-free survival rate was 34 percent for patients with isolated lung metastases, 28 percent for those with bone or bone marrow metastases, and 14 percent for those with combined lung and bone/bone marrow metastases ($P = 0.005$).[61]

Other factors that portend a poorer prognosis are large tumor volume,[6,188,225,401] size greater than 8 cm,[177] an elevated LDH level,[14,149,235,518] and age greater than 17 years.[159,168] Controversy exists regarding whether the designation of Ewing's sarcoma or PNET is related to prognosis. In some studies, PNET has a worse prognosis, whereas in others it portends the same or a better prognosis.[176,409,467]

Treatment. The treatment of patients with nonmetastatic Ewing's sarcoma consists of the administration of multiagent chemotherapy and efforts to achieve local control. Ewing's sarcoma/PNET tumors are systemic diseases with a very poor prognosis when treated by local measures alone.[29,159,192,371] Beginning in the 1960s, it was shown that adjuvant chemotherapy offered a survival benefit in these patients.[215,235,362,388] The standard chemotherapy regimens have included vincristine, actinomycin D, Cytoxan and Adriamycin.[51,322] More recently, the addition of ifosfamide and etoposide has been shown to offer additional benefit in some but not all studies.[159,192,226,326] To test this observation, the Pediatric Oncology Group and the Children's Cancer Group carried out a randomized study comparing the standard Adriamycin/VAC regimen to the standard regimen plus ifosphamide and etoposide. At 5 years the event-free survival rate for patients with nonmetastatic disease was 52 percent in the standard treatment arm, compared to 68 percent in patients treated with ifosphamide and etoposide. These results were highly statistically significant.[159] It is a very toxic regimen, and the treatment course lasts nearly a year, but it has offered significant survival benefit to these patients. Recent focus has been on intensifying therapy early in the course of treatment, either by using higher doses of standard drugs or by decreasing the interval between cycles of chemotherapy.

LOCAL CONTROL. Radiation therapy has traditionally been used to treat local disease. This treatment became established in part because the tumor responds to radiotherapy, in part because before chemotherapy was available, physicians were reluctant to perform amputation in these patients with such a dismal prognosis. Radiation therapy effectively controls local disease, especially when combined with chemotherapy. The usual dose is 5,500 to 6,600 cGy to the affected tissues.[293,454,464,466] Attempts to lower the radiation dose when this modality is used in combination with chemotherapy have not proved successful.[177] Initially it was felt that the entire bone should be irradiated because of the difficulty in judging the medullary extent, but since MRI accurately demonstrates the extent of disease, this is no longer felt to be the case. A recent study by the Pediatric Oncology Group showed no difference in local control when the initial tumor volume plus a 2-cm margin was treated compared to whole bone irradiation.[103] The local recurrence rate in patients with small, distal tumors is reported to be 10 percent or less, but in those with large bulky tumors (such as pelvic tumors) it may be 30 percent or more.[17,48,177,380,466] In young children with lower extremity primaries, growth is a consideration.[218,266] Irradiation of one or more growth plates in the lower extremity can lead to significant limb length inequality in young children (Fig. 38-16). In patients in whom the biopsy created a hole in the cortex, pathologic fracture may be a significant problem (Fig. 38–17).[86,218,445] Despite internal fixation and bone grafting, union of these fractures in irradiated bones is difficult to obtain. Vascularized fibular grafts may be necessary.

Perhaps the most concerning adverse effect of radiation therapy (combined with alkylating agents) is the late occurrence of a secondary malignancy in the involved bone. This phenomenon was not observed until relatively recently, because most patients succumbed to their disease, but now that patients are surviving long term, secondary malignancies have become a significant concern. The exact incidence is unknown, but secondary malignancies are believed to occur in 5 to 30 percent of survivors treated with alkylating agents and radiation therapy.[15,158,246,438,452,478]

SURGICAL TREATMENT. Concern over secondary neoplasms and the observation in some studies that surgically treated patients have a better prognosis have led treating physicians to reconsider surgical ablation of the primary tumor. Techniques of limb salvage learned from treating osteosarcoma have been successfully applied to patients with Ewing's sarcoma. With adequate chemotherapy, the soft tissue mass usually shrinks considerably (unlike osteosarcoma), making it possible to resect less tissue than might be anticipated at initial presentation. The obvious advantage is the avoidance of second neoplasms. Local control rates appear to be equal to or better than those obtained with radiation therapy.

*See references 64, 85, 133, 188, 267, 416, 515.
†See references 14, 61, 351, 352, 398, 468, 491.

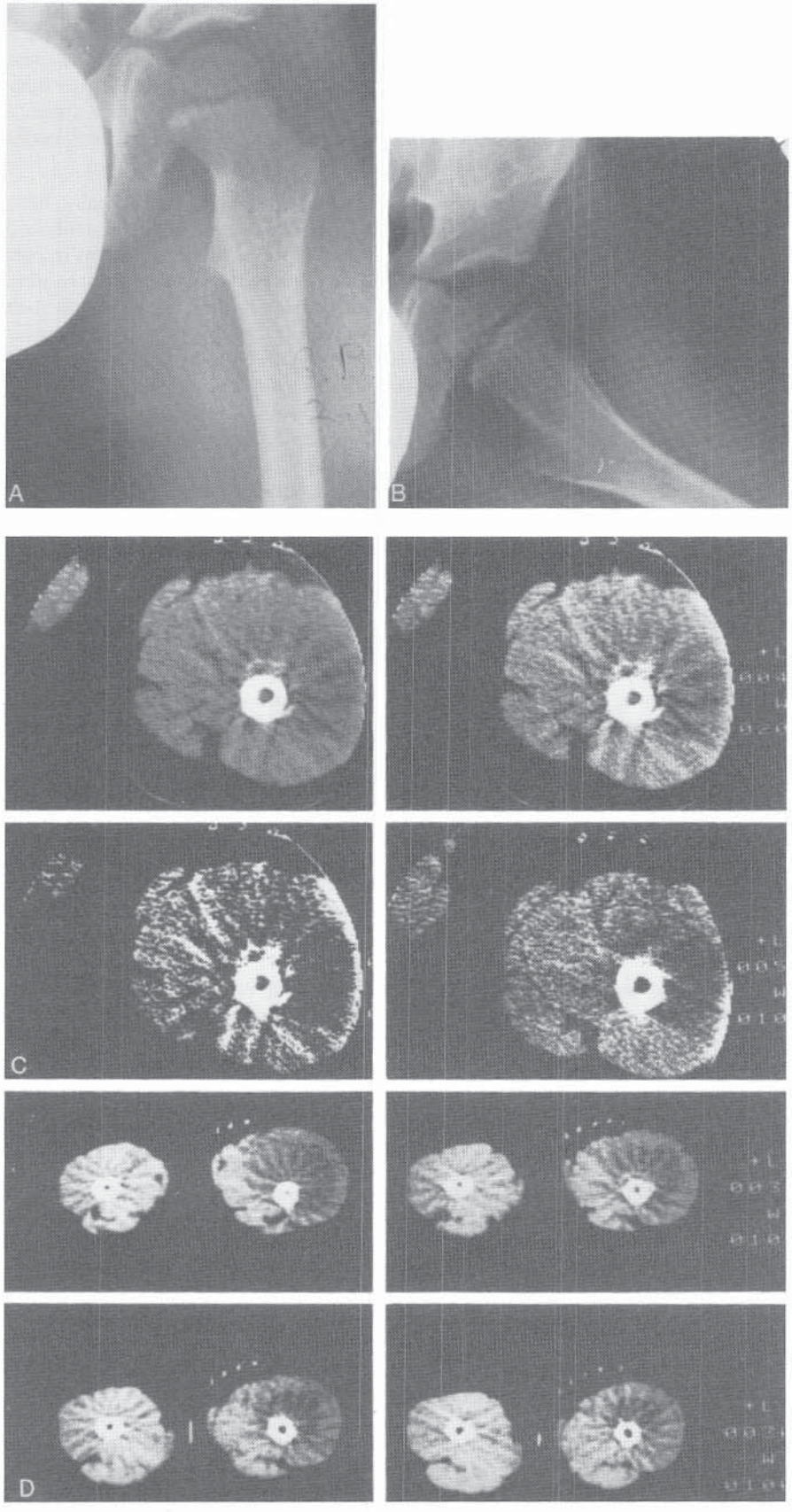


FIGURE 38–16 Ewing's sarcoma of the proximal femur in a 5-year-old boy. **A** and **B,** AP and lateral radiographs of the proximal femur showing subperiosteal reaction and mottling of the outer cortex. **C** and **D,** CT scan showing cross sections of the bony and soft tissue changes in the proximal femur. Treatment was by irradiation and chemotherapy.

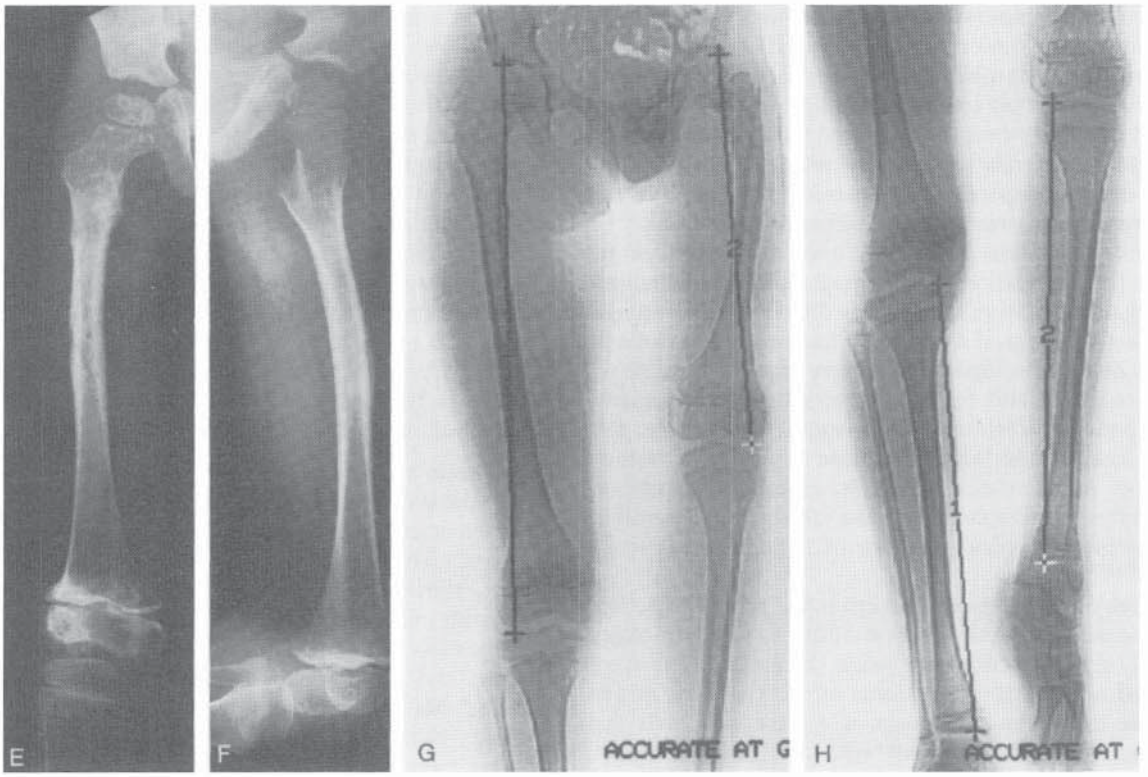


FIGURE 38–16 *Continued.* **E** and **F,** Immediate postoperative radiographs. **G** and **H,** CT scan measurements show the marked lower limb length disparity due to postirradiation growth arrest of the proximal and distal femoral physes.

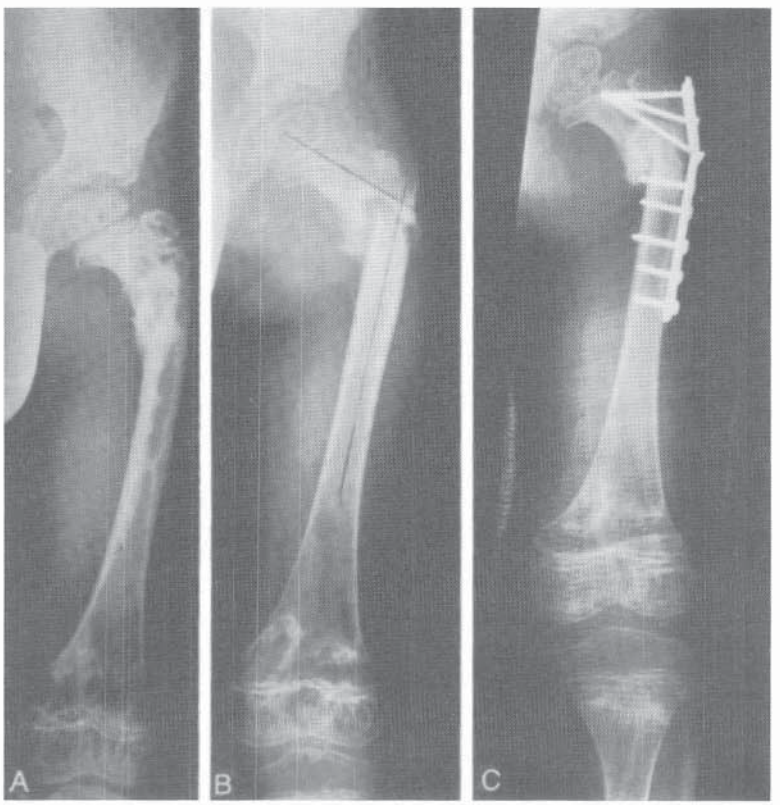


FIGURE 38–17 Subtrochanteric pathologic fracture in Ewing's sarcoma of the proximal femur treated by internal fixation with plate and screws. **A,** Prefracture radiograph showing the sclerosis and radiolucent changes in bone. **B,** AP radiograph of the femur showing the subtrochanteric pathologic fracture. **C,** Postoperative AP radiograph. Internal fixation with plate and screws was used.

Many studies have shown that the disease outcome is superior in patients whose primary tumors are resected, but it should be noted that none of these studies were randomized, and patients whose tumors become resectable after preoperative chemotherapy probably have other favorable prognostic factors in addition to the resection.* In other studies, patients who underwent surgical resection did not have a survival advantage relative to those who did not undergo surgery when retrospectively compared to patients whose primary tumor was treated by radiation therapy alone.[107,416] The relative functional results are even more difficult to compare. Each modality has advantages and disadvantages in that regard. Radiation therapy has the obvious advantage of obviating the surgical resection of major bones and muscles, but advances in limb salvage have made it possible to perform resection and functional reconstruction in many of these patients. Resection offers another advantage: the ability to assess the histologic response to preoperative chemotherapy. As in osteosarcoma, it appears from several recent studies that histologic necrosis following preoperative chemotherapy is a good measure of response and prognosis.[7,14,357,358,486,512]

One area of considerable concern is the pelvis. Resection of the iliac wing with preservation of the acetabulum offers reasonably good function, but when the acetabulum must be resected, a satisfactory functional reconstruction is nearly impossible to obtain. Obviously, if it were clear that the disease outcome were superior with resection than with irradiation, one would sacrifice function, but the results are not clear. There are no randomized studies of surgery versus radiation therapy in the pelvis or elsewhere. Some studies have shown an improvement with resection of pelvic Ewing's sarcoma/PNET,[85,133,515] others have shown no benefit.[64,416] Suffice it to say that the decision of which modality or combinations of modalities to employ for local control for pelvic Ewing's sarcoma/PNET is difficult to make and requires careful consideration by the treatment team as well as discussions with the patient and family.

The approach employed at my institution is to completely re-stage the patient following the induction phase of chemotherapy. If there has been a good response, and if a resection can be carried out with a reasonable expectation of negative margins and good functional result, a surgical resection is advised. Both radiation therapy and surgery are discussed with all patients and they are offered the choice. Our belief is that the main advantage of resection is the avoidance of secondary malignancies. Margins and histologic necrosis in the resected specimen are examined, and if the margins are widely negative, or negative with a good histologic response, no further local control measure is advised. If the margin is positive, postoperative radiation therapy is advised, but the dose used is less than if the patient were treated with radiation therapy alone. Patients with tumors in "expendable" bones, such as the fibula, clavicle, and ribs, do not undergo reconstruction. Patients with primary tumors in major long bones undergo reconstructions similar to those employed in osteosarcoma patients.

Patients with a poor histologic response, especially those with very close or positive margins, are advised to receive radiation therapy postoperatively. Patients with large bulky tumors after induction chemotherapy, especially pelvic tumors, are usually advised to receive radiation therapy and then are reassessed for the possibility of resection. Those patients with tumors in sites where resection would be functionally devastating or impossible (e.g., the sacrum and spine) or those with widespread metastatic disease are usually treated by irradiation for control of the bony disease. Those with periacetabular lesions are often treated by radiation therapy because of the lack of a good reconstruction option for this site and the absence of demonstrable disease outcome benefit to resection.[416]

Amputation is considered in very young patients with lower extremity primaries, especially about the knee, where irradiation would result in growth arrest and limb length discrepancy. Other indications for amputation include pathologic fractures and bulky tumors that do not respond to chemotherapy and irradiation.[96,262,453]

Metastatic Ewing's Sarcoma/PNET. Patients who present with metastatic disease have a significantly worse prognosis, with expected survival rates of approximately 25 percent at 5 years.[61] Those with metastases isolated to the lung fare better; those with bony metastases have a much worse prognosis. Current treatment strategies involve dose intensification of known active drugs, stem cell transplantation, and trials that involve novel chemotherapeutic agents,* but the results of these strategies are mixed. The primary tumor is usually treated by irradiation, but when there are pulmonary metastases only and a good response to chemotherapy (i.e., the pulmonary metastases disappear), it is not unreasonable to consider resection of the primary if a functional reconstruction is possible. The role of thoracotomy is unclear in these patients.[22,251,184]

CHONDROSARCOMA

Chondrosarcoma occurs primarily in adults; it is rarely encountered in adolescents and almost never in children.[16,203,254,516] The diagnosis of a high-grade chondrosarcoma on frozen section in an adolescent should raise the suspicion of a chondroblastic osteosarcoma. There are four types of chondrosarcoma: primary, secondary, mesenchymal, and dedifferentiated.[444] The great majority of cases are primary or secondary chondrosarcoma. The mesenchymal and dedifferentiated types are extremely rare.[78,185] The concern of the pediatric orthopaedist is to distinguish a benign enchondroma or osteochondroma from a secondary chondrosarcoma.[16,136,306] Chondrosarcoma arising from a solitary osteochondroma or enchondroma in childhood virtually never occurs, in my experience. Similarly, chondrosarcoma arising in a patient with Ollier's or Maffucci's syndrome is seldom if ever a concern in the pediatric age group and is even more rare in patients with hereditary multiple exostoses.[516] The literature is confusing on this subject, and the conclusions from pediatric centers are different from those of adult cancer centers in this regard. The reported 25 percent incidence of malignant degeneration is probably a gross overestimation. Malignant transformation is extremely unusual in multiple hereditary exostosis, and several large series in the pediatric age group fail to show evidence of this

*See references 14, 150, 290, 327, 369, 370, 371, 396, 473, 474, 503.

*See references 20, 50, 77, 360, 448, 491, 497.

occurrence.[263,408,502] Chondrosarcomas do occur with increased frequency in patients with Ollier's and Maffucci's syndromes but are rare in the pediatric age group.[62,413,455] These patients are also subject to malignancies in other organ systems. It may be challenging to differentiate benign from malignant cartilage tumors, and there are no failsafe guidelines, but in general, the clinician should be more concerned about large central lesions and those that enlarge after skeletal maturity. Pelvic osteochondromas, although rare in childhood, are the most likely to be malignant, whereas in enchondroma, a metaphyseal lesion about the knee is the most likely to be malignant. In such cases the presenting complaint is a dull aching pain in the centrally located chondrosarcoma; the clinical picture of a peripheral chondrosarcoma is a mass or deformity of the limb.

Imaging Findings. Radiographic features of a secondary chondrosarcoma show evidence of the preexisting benign cartilaginous lesion—exostosis or enchondroma. These entities are described elsewhere (see Chapter 37, Benign Musculoskeletal Tumors). In exostotic lesions, sarcomatous proliferation of the cartilage cells occurs from the cartilaginous cap that extends and protrudes into the surrounding soft tissues.[136,325] Calcifications of the cartilaginous cap may be present. Septal enhancement on MRI after intravenous administration of gadopentetate dimeglumine aids in the characterization of cartilaginous tumors and may assist in distinguishing low-grade chondrosarcoma from osteochondromas.[142] The process is indolent in nature, and the sarcomas are usually low-grade. It is important to understand that benign osteochondromas can become quite large and grow during the years of skeletal maturity without having malignant features. I do not advise removal of a solitary osteochondroma to "prevent" a malignancy; rather, they are removed when symptoms occur. An exception may be a pelvic osteochondroma. Enchondromas are much less commonly encountered in children (probably because they are completely asymptomatic) and therefore are not of much concern in this age group.

In the rare exostotic chondrosarcoma, radiographs show an irregular cartilaginous mass with calcification of varying density around the periphery of the exostosis and minimal or no permeative reaction of the underlying cortex. Some authors use the thickness of the cartilaginous cap as a guide to malignancy,[294,325] but it is the histology of the cap, not the thickness, that dictates whether or not this is a chondrosarcoma. It may be difficult to distinguish a sessile osteochondroma or a periosteal chondroma from a periosteal osteosarcoma or chondrosarcoma. Perhaps the best guideline is to realize that a sessile chondrosarcoma would be very rare in childhood and that a key feature of a sessile osteochondroma is that is shares a cortex with the underlying bone and the medullary cavities communicate. A periosteal osteosarcoma will not have these features; the underlying cortex is present, indicating that this is a juxtacortical neoplasm. Similarly, a periosteal osteosarcoma has an underlying cortex and is a surface lesion. It can be difficult at times to distinguish a periosteal chondroma from a periosteal osteosarcoma.

A central chondrosarcoma, which may at times arise in an area of a preexisting enchondroma, has radiographic features indicative of its malignant character.[147,444] These features include medullary radiolucency, poorly marginated bone destruction, and the presence of a soft tissue mass, which may be variably mineralized. Endosteal scalloping with gradual erosion of the cortex occurs. The preexisting enchondroma is usually mineralized, whereas the malignant area is radiolucent. The cortex may respond with endosteal and periosteal thickening, which may mask the malignant nature of the lesion.

MRI and CT are very useful in assessing the cartilaginous nature of these lesions and their soft tissue and medullary extent.[390] Osteochondromas with large bursae can mimic chondrosarcoma; MRI is particularly useful in making this distinction.[368,492] A radionuclide bone scan[302] will show increased uptake and is not helpful for the primary lesion, but will demonstrate other lesions in patients suspected of having Ollier's syndrome or multiple exostoses. Radionuclide scintigraphy is not helpful in distinguishing benign from malignant cartilage neoplasms, but if a patient is followed by sequential bone scans, a increase in uptake may be a worrisome sign.[119] A lesion that does not exhibit marked uptake is also a reassuring sign. Chest CT is needed to search for pulmonary metastases from high-grade cartilage tumors, but it should be remembered that that these lesions will most likely be chondroblastic osteosarcomas.

Pathologic Findings. On gross inspection chondrosarcoma has a lobulated appearance and seems to consist of gray unmineralized cartilage intermixed with chalky white cartilage. It feels firm on palpation. There may be areas of necrosis and degeneration.

The histologic appearance varies with the grade of the lesion and requires the expertise of an experienced bone pathologist.* In low-grade lesions, the cell-matrix ratio is low (i.e., relatively more matrix than cells), with the malignant chondrocytes grouped in small clusters among wide areas of chondroid matrix.[283] Malignant chondrocytes with double nuclei are a feature of chondrosarcoma. In high-grade lesions the cell-matrix ratio is high, with no clustering pattern; the hyperchromatic chondrocytes are multinuclear and show numerous mitoses. When a biopsy shows such an area in an enostotic lesion, more tissue should be obtained to look for the presence of neoplastic bone. In the vast majority of cases, a high-grade chondrosarcoma in a child is really a chondroblastic osteosarcoma; this becomes evident when the entire specimen is available for review. In my opinion these patients should be treated with adjuvant chemotherapy as for any osteosarcoma.

Treatment. Chondrosarcomas are treated by surgical resection.[119,260,444] For low-grade lesions this should be sufficient, and there is a high probability of cure. In a high-grade lesion, it is probably best to treat these lesions like high-grade osteosarcomas. Limb salvage resections or amputation following neoadjuvant chemotherapy is the proper management. In the very rare instance of a true high-grade chondrosarcoma, surgical ablation with wide margins is the most reasonable treatment. The role of chemotherapy in these cases is not well established, but chemotherapy is employed in the patient with an "unresectable" primary lesion or metastatic disease.[16,106,119,233,260]

*See references 119, 146, 203, 314, 444, 516.

Soft Tissue Sarcomas

Soft tissue sarcomas in children are much less common than benign soft tissue lesions but can be difficult to distinguish from them. The most common soft tissue sarcoma in childhood is rhabdomyosarcoma;[19,347,459,498] unlike in adults, the other soft tissue sarcomas are much less common. They account for 4 percent of malignant tumors in children 15 years of age or younger. The incidence is between 4 to 7 per 1 million children, and approximately 250 new cases are diagnosed annually in the United States.[243,498] Rhabdomyosarcomas occur in both the first and second decades of life. Boys are affected slightly more often than girls. Black and Asian children have a lower incidence than white children.[449,450] Rhabdomyosarcomas can occur in all parts of the body, including the head and neck (26 percent), orbit (9 percent), mediastinum and abdomen (22 percent), genitourinary system (24 percent), and the extremities (19 percent).[343,498] This review will focus on extremity rhabdomyosarcoma.

RHABDOMYOSARCOMA

Clinical Findings. Rhabdomyosarcomas present as painful or painless deep masses in the extremity. Because they are usually deep masses, redness, warmth, and increased local vascularity are not evident.[178] Symptoms may be present for several months prior to diagnosis. There are usually no generalized or systemic signs. The parents frequently note a preceding traumatic event that calls attention to the lesion. The mass may be mistaken for a hematoma or a benign neoplasm. Regional lymph nodes may be involved, especially in the alveolar form.[180,282]

Pathologic Findings. Rhabdomyosarcomas are histologically classified into embryonal, alveolar, botryoid, and pleomorphic types.[101,323,477] Although embryonal rhabdomyosarcoma is the predominant form overall in children, it accounts for only about half of the extremity lesions.[323] The other histologic types in the extremity and trunk are alveolar and undifferentiated types. In general, embryonal rhabdomyosarcomas have a much more favorable prognosis than alveolar rhabdomyosarcomas, and the latter are more likely to have lymph node metastases.[179] These lesions on histologic analysis are round cell tumors with few distinguishing characteristics. Histologically large cells with eosinophilic cytoplasm, some of which may contain muscle striations, are seen. Immunohistochemistry stains reveal the expression of muscle-specific actin and myosin, desmin, myoglobin, Z-band protein, Myo-D, and vimentin to distinguish the muscle phenotype.[101,345,477] Unlike in Ewing's sarcoma/PNET, *MIC2* expression is not seen.[159,338,477] The distinction between alveolar and embryonal rhabdomyosarcoma is difficult to make and may not be as important as other prognostic factors in extremity lesions.[253]

Embryonal rhabdomyosarcoma is a spindle cell sarcoma with an abundant myxoid stroma that separates the tumor cells. This histotype has a loss of heterozygosity on chromosome 11 at the 11p15 locus.[19,414,415] The exact significance of this deletion is unclear, but it involves loss of maternal chromosomal information, possibly leading to overexpression of *IGFII* or loss of a tumor suppressor gene.[19,498] DNA ploidy has been shown to have prognostic significance in this histologic type and in nonmetastatic, unresectable tumors, with DNA diploid tumors having a worse prognosis than hyperdiploid tumors.[421] The alveolar variety is distinguished by its obvious alveolar pattern, similar to alveoli in the lung, but they are lined by large, high-grade tumor cells. The cells are round and densely packed rather than spindled and loosely dispersed in a matrix, as in the embryonal variety.[498]

Alveolar rhabdomyosarcoma has been demonstrated to have a translocation of chromosomes 2 and 13, t(2:13)(q35:q14), and less commonly t(1;13)(p36:q14), which can be helpful in the diagnosis.[19,87,342,422] The novel gene products of these translocations are being explored as possible antigens for specific immunotherapy for rhabdomyosarcoma. Other mutations in oncogenes or tumor suppressor genes such as *p53* and overproduction of *IGFII* have been identified and may be of importance in the pathogenesis of rhabdomyosarcoma.[19,498]

Imaging Findings. Patients who present with a deep soft tissue mass should be evaluated for a possible sarcoma. A complete history and physical examination should be performed. Laboratory studies should include a CBC count and differential, liver function tests, and determination of electrolyte, calcium, and phosphorus levels. Plane radiographs should be obtained for extremity and trunk lesions. The differential diagnosis includes nontumorous conditions such as hematoma and myositis ossificans and benign neoplasms such as schwannomas and lipomas. Growth of a painless mass in the absence of trauma should be viewed with suspicion.[498]

A bone scan is obtained to exclude bony metastases, but MRI is more accurate in demonstration adjacent bone involvement.[420] MRI is very useful in determining the extent of the soft tissue mass and its relationship to surrounding neurovascular structures and bone.[299] Chest CT should be performed to assess for the presence of lung metastases. Unlike in bone sarcomas, regional lymph nodes are involved with tumor in approximately 15 percent of the cases,[257] and this worsens the prognosis.[253,282] One recent study of extremity sarcomas achieved histologic documentation of lymph node status in 70 percent of patients; histologically positive nodes were found in 40 percent.[253] The regional lymph nodes should be carefully assessed clinically and by MRI. If lymph node involvement is suspected, lymph node sampling should be done. Some authors recommend regional lymph node biopsies in all extremity rhabdomyosarcomas.[12] Although controversial, most investigators do not recommend routine lymph node dissection as a therapeutic maneuver.[220] The oncologist will usually perform a bone marrow aspiration and biopsy to search for bone marrow involvement.

Treatment. The treatment of rhabdomyosarcoma of the extremity is multidisciplinary and involves pediatric oncologists, radiation therapists, and surgical oncologists. In the patient with nonmetastatic disease, the primary tumor is completely excised and adjuvant chemotherapy is employed.[19,180,181,220,252] The international Intergroup Rhabdomyosarcoma Study (IRS) has documented the value of adjuvant chemotherapy in several large multimodality, sequen-

TABLE 38–2 **Clinical Grouping System Based on Residual Tumor After Resection: Intergroup Rhabdomyosarcoma Study III**

Clinical Group	Description
I	Completely resected tumor
IIa	Microscopic residual tumor, negative nodes
IIb	Positive regional nodes, resected
IIc	Positive regional nodes with microscopic residual margins and/or nodes
III	Gross residual disease
IV	Distant metastatic disease

From Andrassy RJ, Corpron CA, Hays D, et al: Extremity sarcomas: an analysis of prognostic factors from the Intergroup Rhabdo-myosarcoma Study III. J Pediatr Surg 1996;31:191.

TABLE 38–3 **Estimated 5-Year Survival Rates in Patients with Extremity-Site Tumors versus All Patients: Intergroup Rhabdomyosarcoma Study III**

	Survival (%)	
Clinical Group	Extremity Site	Overall
I	95	93
II	67	81
III	58	73
IV	33	30

From Andrassy RJ, Corpron CA, Hays D, et al: Extremity sarcomas: an analysis of prognostic factors from the Intergroup Rhabdo-myosarcoma Study III. J Pediatr Surg 1996;31:191.

tial trials beginning in the 1970s.* Standard chemotherapy regimens include vincristine, cyclophosphamide, and actinomycin D (VAC).[178,498] The details of the sequential trials are beyond this discussion but are summarized elsewhere.[178,498] The sequential trials have increased the intensity of the chemotherapy and defined prognostic groups and local treatment measures. Outcomes have improved from a less than 20 percent survival rate with surgical treatment alone to a survival rate of about 60 percent today.[178,459] Unfortunately, although the survival rate improved with each successive IRS study, children with nonmetastatic, extremity rhabdomyosarcoma have an estimated 5-year survival rate of 74 percent, which is worse than survival from disease at other sites, such as orbital or genitourinary sites.[12]

The prognosis varies with the stage of the disease, and there are a variety of staging systems, including the one used by the Musculoskeletal Tumor Society,[115,118] that could be applied to rhabdomyosarcoma. However, the IRS has traditionally used a clinical grouping of patients based on residual tumor after initial resection (Table 38–2)[12] for reporting most of their studies. It is important to have some familiarity with this system because it differs from many in that the initial surgical procedure affects the grouping. One drawback to using this system for extremity lesions is that a lesion of the hand or foot could be classified in group I, II or III, depending on the surgical procedure, and an extremity tumor of virtually any size could be placed in group I or II if an amputation was performed. Treatment obviously can vary in aggressiveness from center to center and from surgeon to surgeon. These groups were clearly predictive of outcome in extremity rhabdomyosarcomas and overall (Table 38–3), but assignment to group had the disadvantage of depending on the initial surgical procedure and did not take into account other prognostic factors that might be important based on staging prior to surgical intervention. This led to the creation of a prospective staging system that is being tested in the IRS IV protocol and is based on prognostic information identified by Lawrence and Gehan and others using IRS I data (Table 38–4).[256] It should be noted that because extremity and truncal sarcomas have a poorer prognosis, they are never included in stage 1 in the Lawrence-Gehan staging system.

A recent study of 35 extremity rhabdomyosarcomas from a single institution found that tumor invasion beyond the muscle of origin was a prognostic factor at diagnosis on multivariate analysis.[253] Other prognostic factors found to be of importance in extremity rhabdomyosarcoma on univariate analysis in that study were regional node involvement, alveolar subtype, size of the primary, and complete resection. Amputation and location of the primary were not significant factors.

The local treatment is of rhabdomyosarcoma is controversial. Some surgeons prefer to attempt a wide excision at diagnosis. Others prefer to treat patients with preoperative chemotherapy with the hope that the lesion will decrease in size and become more amenable to resection without sacrifice of as much normal tissue. Neither approach has been shown to be superior to the other.[12,253] In most cases, radiation therapy is employed either before or after surgical resection.[299,499] Novel techniques such as brachytherapy and hyperfractionation may be employed to maximize local control and minimize damage to adjacent growth plates.[102,318] Careful review of the staging studies with the radiologist and the treatment team is necessary. If resection would involve loss of major neurovascular structures, radiation therapy alone is indicated. In very young children with lower extremity lesions, an amputation may be the optimal method of local control.[162,180] These decisions can be quite difficult to make and require detailed discussions among the treatment team and with the parents and child.

The overall survival rate for extremity rhabdomyosarcoma has improved from 47 percent in IRS I to 74 percent

TABLE 38–4 **Lawrence-Gehan Staging System**

Stage	Description
1	Favorable site, M0 (orbit, head and neck, genitourinary, *not extremity*)
2	Other site, any T, a, N0, M0 (extremity)
3	Other site, any T, b, or N1, M0, or any T, a, N1, M0 (extremity)
4	M1

Abbreviations: M0, no distant metastases; M1, distant metastases; T0, no tissue invasion past muscle of origin; T1, tissue invasion past muscle of origin; N0, no regional nodal metastases; N1, regional nodal metastases; a size $\leq$ 5 cm; b, size $>$ 5 cm.

From Andrassy RJ, Corpron CA, Hays D, et al: Extremity sarcomas: an analysis of prognostic factors from the Intergoup Rhabdo-myosarcoma Study III. J Pediatr Surg 1996;31:191.

*See references 76, 98, 180, 296, 297, 376, 338, 377, 499.

in IRS III for patients without distant metastases at diagnosis. The outcome varies by clinical group in IRS III (Table 38–3).[12]

About 20 percent of patients with rhabdomyosarcoma have metastatic disease at diagnosis, and their prognosis is much poorer. Five-year survival rates are about 20 to 30 percent overall.[12,19] These patients are treated with more intensive chemotherapy and radiation therapy delivered to the primary tumor. Patients with local relapse should be restaged, and if the recurrence is localized, surgical resection is used if possible. This is often combined with chemotherapy and radiation therapy. Resection of pulmonary metastases may be appropriate. Patients with local relapse and distant metastases or with distant metastases alone are most often treated with chemotherapy and palliative radiation therapy.[498]

NONRHABDOMYOSARCOMA SOFT TISSUE SARCOMA

Soft tissue sarcomas other than rhabdomyosarcoma are quite rare, collectively accounting for less than half of soft tissue sarcomas in children.[517] For the most part these lesions appear and behave similar to adult soft tissue sarcomas except in the very young. In very young children (less than 5 years old) the histopathology of the soft tissue sarcomas is somewhat different and the biologic behavior is more benign than the adult counterparts.

Congenital Fibrosarcoma. Congenital fibrosarcoma is encountered in neonates.[35,84,365] Fibrosarcoma is one of the more common nonrhabdomyosarcomas in childhood and is the most common soft tissue sarcoma in children less than 1 year old.[443,450] There is a second peak in incidence between ages 10 and 15 years. In general, congenital fibrosarcoma has a more benign clinical course than fibrosarcoma in older children, which behaves more like the adult counterpart.[121,443]

CLINICAL FINDINGS. Congenital fibrosarcoma presents as a rapidly growing mass at birth or shortly thereafter (Fig. 38–18). It occurs most commonly in the extremities, usually in the distal extremity.[45,443] As is the case for all soft tissue sarcomas, there is nothing in the history or physical examination to alert the physician that this is a malignant process, and congenital fibrosarcomas are frequently mistaken for hemangiomas, lymphangiomas, or lipomas initially.[365] Metastases at diagnosis occur less than 20 percent of the time and are more frequent for truncal lesions.[320]

PATHOLOGIC FINDINGS. The histology is that of a high-grade spindle cell sarcoma arranged in a herringbone pattern intermixed with collagen fibers.[315] It is a very cellular lesion with many mitoses, but despite this appearance, surgical treatment alone is curative in more than 90 percent of cases.[365] It may be difficult to distinguish congenital fibrosarcoma from congenital fibromatosis, but recently chromosomal alterations have been identified in congenital fibrosarcoma but not in other fibrosarcomas. The most common alteration is a nonrandom gain of chromosome 11, yielding a trisomy 11.[3,40,84,399] Chromosal alterations can be demonstrated with fluorescent in situ hybridization techniques on paraffin-embedded tissue and can be helpful in confirming the diagnosis.[129,411]

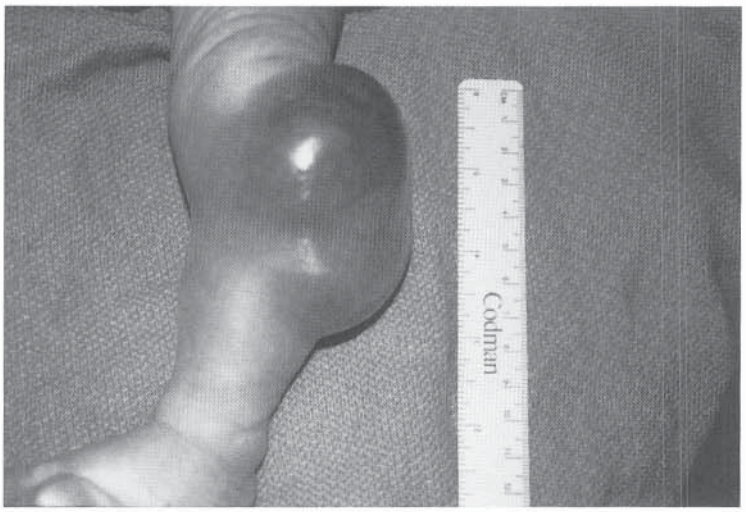
TREATMENT. Treatment is surgical excision whenever feasible. In the extremity this is frequently possible, although it may be difficult to achieve wide margins in these young children. Local recurrence does not appear to worsen the prognosis, so that limb-sparing procedures that preserve function and avoid amputation are preferred.[315,365] Radiation therapy is not generally used for extremity lesions because of the late effects of irradiating growth plates, although occasionally it is employed using techniques such as brachytherapy that avoid growth plates. For unresectable lesions, treatment with adjuvant chemotherapy often results in a dramatic response.[160,247,324] If a complete resection is possible, chemotherapy is not needed as an adjuvant, and it is best to avoid the side effects. However, when used preoperatively, dramatic responses may be seen, making subsequent surgical resection possible. The preferred agents are vincristine and dactinomycin[315] because of their relative lack of long-term side effects, but other agents have been employed. Chemotherapy can be followed by resection if possible, but chemotherapy alone may be curative when used in "unresectable" situations. Rare instances of spontaneous regression have been noted, so ablative surgery should be considered as a last resort. Fibrosarcomas in older children behave like those in adults and will be considered with the other nonrhabdomyosarcomas below.

NONRHABDOMYOSARCOMA SOFT TISSUE SARCOMA IN OLDER CHILDREN

Nonrhabdomyosarcomas are rare in the older child and adolescent.[100] They vary widely in their histology and perhaps in their biologic behavior, but in general they are collectively treated similarly following concepts developed in the adult. Certain histologic types such as fibrosarcoma and synovial sarcoma may respond to chemotherapy, but in general this group of lesions is considered to be a surgical disease. They have the same histologic features and behavior as adult soft tissue sarcomas, but the relative frequency of the histologic subtypes differs. In children, liposarcoma is virtually never encountered, whereas in adults it is quite common. In children, synovial sarcoma, fibrosarcoma, malignant schwannoma, and undifferentiated sarcomas are the most common histologic subtypes.* Other subtypes, such as malignant fibrous histiocytoma are much less frequent but do occur.[375,475] It is beyond the scope of this chapter to discuss each entity in specific, but they are nicely reviewed elsewhere.[315]

Clinical Findings. The clinical presentation is that of a painless or tender mass of varying size in the extremity or trunk. The mass may compress or arise in association with peripheral nerves, yielding nerve pain, weakness, or sensory findings. Systemic symptoms are absent unless there are widespread metastases.[476] Although benign masses far outnumber malignant ones, they may be difficult to distinguish. In general, a lesion that is enlarging, is deep to the fascia, and is greater than 5 cm in diameter should be suspected as being malignant until proved otherwise. Unfortunately, vascular malformations, hemangiomas, lymphangiomas, fibromatosis, and nontumorous entities such as myositis

*See references 43, 100, 126, 249, 261, 291, 315, 339, 379, 410.



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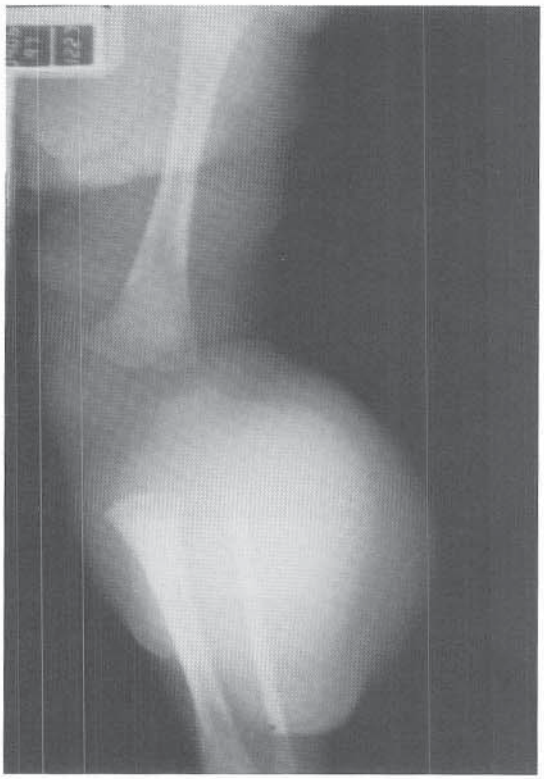

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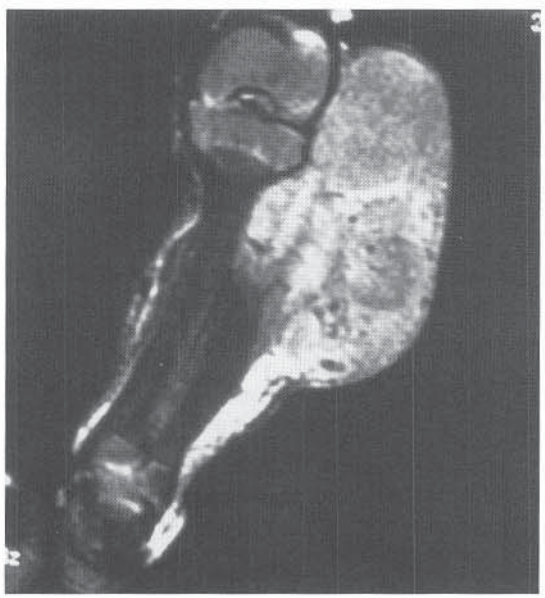

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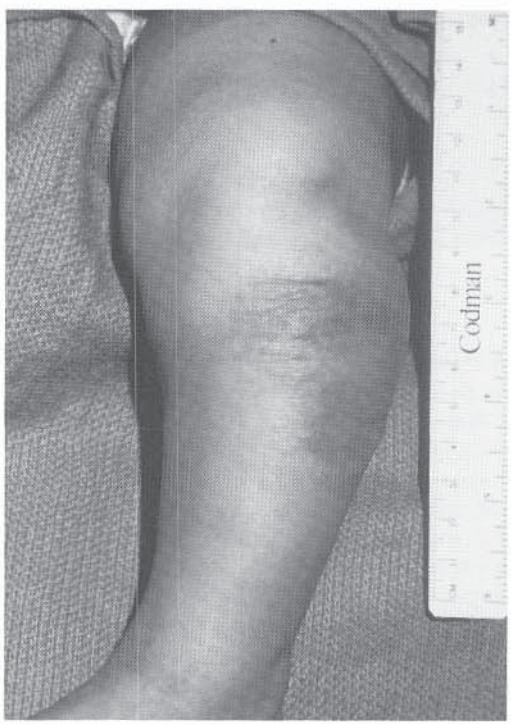
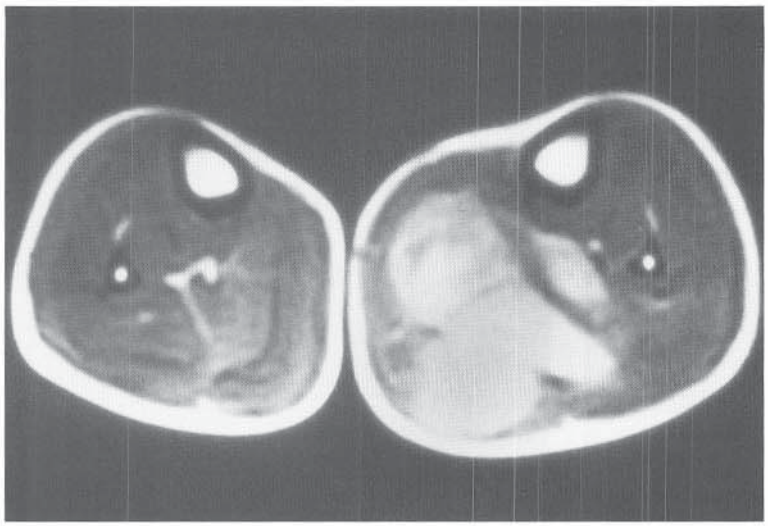


D

FIGURE 38–18 Congenital fibrosarcoma in a newborn baby. **A,** Clinical appearance at birth. The mass in the left leg increased significantly in the first hours of life. A needle biopsy showed congenital fibrosarcoma. The options of immediate amputation versus adjuvant chemotherapy were discussed, and chemotherapy was begun. **B,** AP radiograph of the child's lower extremity showing the soft tissue mass and no definitive evidence of bone involvement. **C,** MR image showing a large soft tissue mass adjacent to the bone and knee joint with no evidence of bony infiltration. **D,** Appearance of the leg after neoadjuvant chemotherapy. The lesion shrank considerably. Excision of the tumor bed revealed no evidence of recurrent tumor. The child is now 1½ years from diagnosis and free of disease, with a normally functioning lower extremity.



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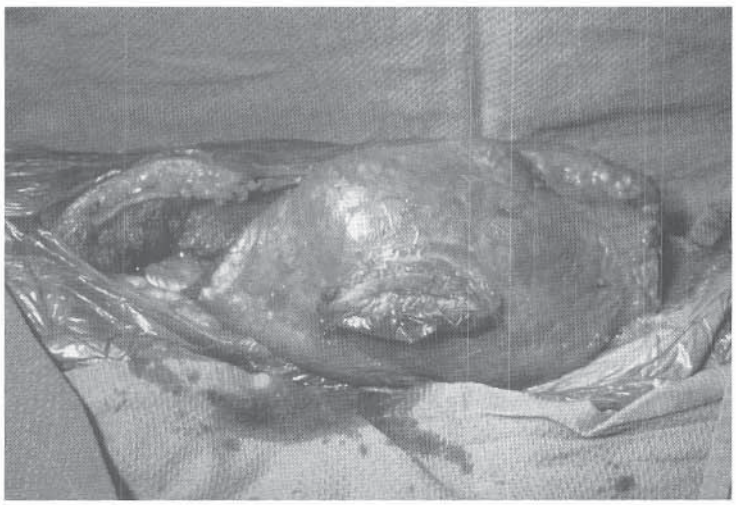


B

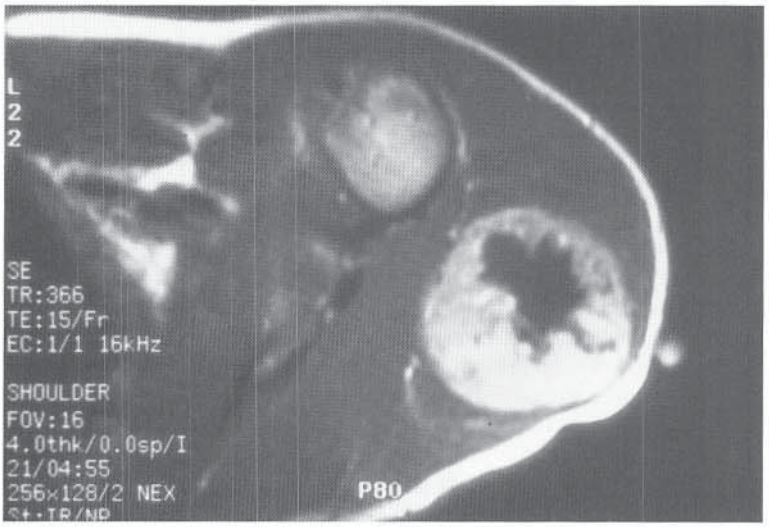
FIGURE 38–19 Synovial sarcoma in a 17-year-old boy. The calcified lesion in the leg was initially mistaken for myositis ossificans over a 6-month period. **A,** MRI showed extensive involvement of the superficial posterior compartment of the leg. The lesion is close to the deep posterior compartments and neurovascular bundle but does not involve these structures. An incisional biopsy showed that the lesion was a synovial sarcoma. Unfortunately, the patient had multiple pulmonary metastases. Preoperative chemotherapy and radiation therapy resulted in an initial response in the pulmonary metastases. **B,** The patient underwent wide resection of the tumor that included the superficial compartment (the biopsy tract is also visible). After extensive chemotherapy the patient did well for several years, but he ultimately died of metastatic disease 3 years after the diagnosis.

ossificans can make the distinction difficult.[46,182] Large lipomas and nerve sheath tumors mimic sarcomas. It should be remembered that small superficial lesions might at times be subcutaneous sarcomas (malignant fibrous histiocytoma and synovial sarcoma). A patient with type I neurofibromatosis and an enlarging, painful mass should be carefully evaluated for a malignant peripheral nerve sheath tumor. Up to 15 percent of patients with neurofibromatosis type I will develop a peripheral nerve sheath tumor.[315] Likewise, a patient with a malignant schwannoma should be carefully evaluated for the possibility of unrecognized neurofibromatosis.

Staging and Imaging Studies. A careful physical examination with particular attention to regional lymph nodes is important. Chest CT is included in the staging workup because the lung is the most frequent site of distant metastases. A bone scan is usually performed in children, because bony metastases are occasionally encountered. MRI is the most useful diagnostic tool to assess the primary lesion, but except for lipomas, benign vascular lesions, and perhaps nerve sheath tumors, it will not allow the distinction between the various types of neoplasms (Fig. 38–19). It may allow the distinction between benign and malignant soft tissue masses.* It is very useful in planning surgical and radiotherapeutic treatment.

Treatment. Treatment of these soft tissue sarcomas in children is similar to treatment in adults. An open or needle biopsy is essential, following the principles of biopsy discussed earlier.[286,354,432] Because these neoplasms are difficult to classify, special immunohistochemical stains and cytogenetic studies may be necessary to establish the correct diagnosis. Most important, a pathologist knowledgeable in pediatric soft tissue neoplasms should examine the pathology slides. For small, superficial lesions, an excisional biopsy may be considered, but if there is a suspicion of malignancy, wide margins should be achieved, or the excision should be carried out in such a manner that a wide excision of the tumor bed could subsequently be carried out. Incisions should be longitudinal and not transverse for extremity masses. When in doubt, it is best to perform an incisional biopsy.

*See references 112, 250, 287, 309, 353, 487, 489.



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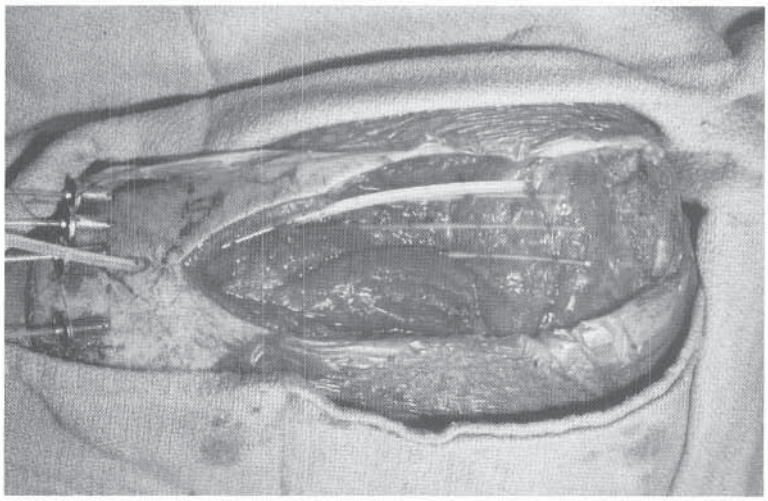

B

FIGURE 38–20 Malignant schwannoma of the left deltoid in a 10-year-old boy. **A,** MRI appearance. Because of the child's age, it was desirable to limit external beam irradiation to the proximal humerus. He was treated with a modified field preoperatively to avoid the growth plate. **B,** Operative appearance. A wide resection was performed with a negative but narrow margin and preservation of part of the axillary nerve. Brachytherapy catheters were placed, to deliver focused radiation to the closest margin. The boy remains free of disease 5 years after the diagnosis.

Complete surgical resection is the optimal treatment, often in combination with radiation therapy (Fig. 38–19B).* A multidisciplinary approach involving pediatric oncologists, radiation oncologists, and surgeons is necessary to arrive at the appropriate treatment regimen. The staging studies should be carefully reviewed to ascertain the relationship of the mass to surrounding osseous or neurovascular structures. Most of the time a complete excision with wide margins of normal tissue surrounding the tumor is possible. For some lesions it is not possible to achieve an excision of this degree without sacrificing normal structures. In those cases, preoperative treatment with chemotherapy and/or radiation therapy may be indicated. It is not necessary to remove entire muscle groups from origin to insertion (radical excision) unless the muscle is totally involved. If there has been a prior unplanned excision of the tumor, the tumor bed should be re-excised to ensure that complete gross and microscopic tumor eradication has been achieved. In the hand or the foot, ray amputations that resect part of the hand or foot and preserve some meaningful function are usually possible.[21,161,162,221,234,336]

Lymph node involvement at diagnosis is not as frequent as in rhabdomyosarcoma (possibly up to 15 percent in high-grade sarcomas), and, although controversial, routine lymph node dissection is not performed.[379] Lymph node dissection may be indicated if lymph node involvement is suspected on clinical grounds. As in patients with bone sarcomas, thoracotomy to resect pulmonary metastases may be indicated if local control has been achieved.[184,210,364,391]

Radiation is useful in cases where microscopically residual tumor remains that cannot be excised[77,131,234,249,291,292] or that extends to the margin of resection. If radiation therapy is planned, measures should be taken to avoid growth plates, depending on the location of the lesion and the age of the child. Novel techniques such as brachytherapy or special fields are sometimes employed to minimize the amount of surrounding normal tissue that is exposed (Fig. 38–20). The decision regarding preoperative versus postoperative radiation is controversial; each has advantages and disadvantages.

*See references 43, 161, 162, 315, 341, 356, 379.

The role of adjuvant chemotherapy is less well established.[315] No study has definitively documented its value as an adjuvant to prevent systemic relapse,[315,339] but chemotherapy is being evaluated in the treatment of high-risk patients (those with high-grade metastatic or unresectable soft tissue sarcomas) on a protocol of the Pediatric Oncology Group. Recent studies of patients with synovial sarcoma suggest a benefit to adjuvant chemotherapy, but this has not been documented in randomized trials.[126,227,249,339,395] On occasion responses will be noted that make subsequent resection and radiation therapy more feasible. Tumor regression in patients with metastatic or unresectable disease has also been documented with various chemotherapy regimens.[227,315,395]

The outcome for patients with nonrhabdomyosarcomas who present without metastases is generally good. One study showed an 82 percent 5-year survival rate, with local and systemic recurrence rates of 21 percent.[315] At my institution, 75 percent of patients survived 10 years or more following a treatment regimen that included an attempt at resection and, in most cases, radiation therapy.[291] Histologic grade was important in that freedom from local recurrence or systemic relapse was the rule in low- to intermediate-grade tumors (92 percent), whereas 73 percent of patients with high-grade neoplasms remained relapse free ($P = 0.09$). The ability to eradicate the local disease is also important. Despite radiation therapy, the local relapse rate was 50 percent in patients with gross residual tumor remaining, whereas only one patient relapsed locally after complete excision. In another study 84 percent of patients remained free of disease after complete removal of the tumor, whereas one of 26 survived when incomplete excision occurred.[193] Prognostic variables include size, grade, location, surgical margin, and the presence or absence of metastases.[9,321,340,379,382]

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