Bone Imaging in Infants and Children: A Review

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Radionuclide imaging of the growing skeleton is virtually in its infancy. It was not until the discovery of the technetium-99m phosphate compounds in 1971 (*1*) that radionuclide bone imaging became a practical diagnostic tool in infants and children. In the past, the tracers that were available for bone imaging (Sr-85, Sr-87m, and F-18) delivered too great a radiation dose to the patient to be considered for routine use in children (*2,3*). Now that low-radiation-dose pharmaceuticals are available, it appears that the potential uses of gamma imaging of the normal and abnormal growing skeleton are just beginning to be realized. The purpose of this paper is to review the status of radionuclide bone imaging in a variety of disorders affecting the skeleton of infants and children.

METHODS

Although the basic principles of gamma imaging apply to both children and adults, the approach in children differs considerably. The techniques that are unique to the practice of pediatric nuclear medicine have been well described (*4*). A few helpful hints in the approach to pediatric radionuclide bone imaging, and some of the pitfalls in the interpretation of the resulting bone images, are worthy of mention.

To obtain a satisfactory gamma image, it is essential that the child remain still during the examination. Because infants and young children are not always able to cooperate, sedation may be necessary. As a rule, sedation is not necessary in the older child; however, even a cooperative child may have difficulty remaining still for the long periods of time required when a rectilinear body scanner is used. With a gamma camera, on the other hand, there is less need to sedate the child, since the complete study is divided into several images. The time for each image is relatively short and the child is able to relax briefly between imaging periods.

A primary consideration in pediatric nuclear medicine is to minimize the absorbed radiation dose. Thus, the oral administration of potassium perchlorate to minimize uptake of free technetium by the thyroid must not be forgotten. Whereas the dose of tracer used in adults is generally the same for each patient, the dose to be used in children must be determined for each child. The doses recommended on the basis of body weight may be reduced when a limited area of the body is to be imaged (*5*). This increases the time required to obtain an adequate image but decreases the absorbed radiation dose.

The interpretation of the bone images of children is challenging, since the normal growing skeleton will appear different from one age group to another. In the region of the growth plate there is an increase in radionuclide uptake, and this will gradually decrease until maturation at that site is complete. The increased activity at the growth plate may be difficult to evaluate unless it is compared with the activity of the contralateral growth plate. However, meticulous attention must be given to the positioning of the patient, since minor differences in positioning may simulate a unilateral increased activity. The small size of the bones of infants and young children necessitates the frequent use of pinhole and converging collimators. This is of particular importance in imaging the hips of children (*6,7*).

Selection of one Tc-99m phosphate compound over another remains an open issue. All of the available compounds appear to provide satisfactory images. There have been no differences reported between children and adults in the physiologic and imaging properties of the approved bone agents (*8,9*).

Infection. Osteomyelitis continues to be a common disease of childhood. The early diagnosis and prompt institution of therapy are critical factors for the cure

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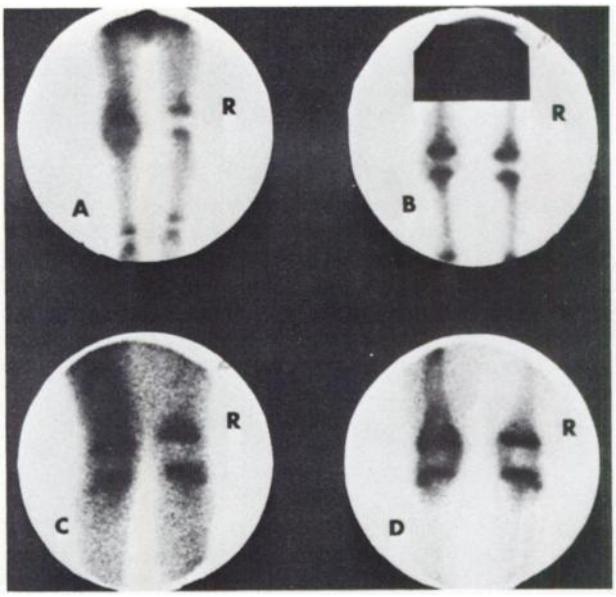

FIG. 1. Blood pool and delayed bone images of a 2-year-old boy with septic arthritis (A, B), and of a 12-year-old girl with osteomyelitis (C, D). Increased blood-pool activity surrounds joint in septic arthritis (A), whereas in osteomyelitis it is most marked in region of involved bone (C). Delayed images in osteomyelitis (D), reveal increased activity in distal femur. In septic arthritis (B), note residual soft-tissue hyperemia without focal bone accumulation on delayed images.

of osteomyelitis and the prevention of its crippling complications. The early radiographic changes of osteomyelitis, however, are subtle and often nonspecific. In addition, its clinical differentiation from cellulitis and septic arthritis is often difficult. On the other hand, radionuclide bone imaging may permit differential diagnosis early in the course of the disease (*5,10–14*).

On a bone image, osteomyelitis is characterized by an intense focal uptake of tracer at the site of bone involvement. Localized hyperemia accompanies the infection in the bone and, as a result, blood-pool images obtained early will reveal increased bone and soft-tissue activity in and about the site of the infection. Focal accumulation of the tracer in the bone becomes more apparent on the delayed images as the soft-tissue activity wanes (Fig. 1, C and D).

Very early in the course of the illness there is a temporary occlusion of local small blood vessels, but subsequently the affected area becomes hyperemic. Therefore, a bone image obtained during the early phase of transient ischemia may reveal either normal or decreased activity (*15–17*).

At the 1977 annual meeting of the Society of Nuclear Medicine, Ash reported the frequent occurrence of false-negative images in neonates with osteomyelitis (*18*). Even though radiographic changes of osteomyelitis were present in her infants, the bone images did not reveal increased activity. The reason for this seeming paradox is unknown. One possible explanation may be that the resolving power of the camera is such that the increased activity of the growth plate cannot be separated from that of the infection in the small-bone metaphyses of the neonate. Another factor to consider is that the pathophysiology of osteomyelitis in the neonate differs from that of the older infant and child.

The role of gallium-67 in the diagnosis of inflammatory bone and joint disease has yet to be fully explored. Lisbona and Rosenthall evaluated the sequential use of Tc-99m phosphate and Ga-67. Their study showed that gallium imaging revealed bilateral focal osteomyelitis adjacent to tibial growth plates—lesions that were difficult to detect on technetium phosphate images (*19*).

Whereas antibiotic treatment may mask the x-ray changes of osteomyelitis, such treatment does not appear to affect the gamma image (*5*).

In cellulitis and septic arthritis, the increased activity at the affected site, as demonstrated by the blood-pool images, reflects the degree and extent of the reactive hyperemia present. Although it is to be expected that the delayed bone images will be normal, it is not uncommon to find a mild increase in bone uptake and some persistence of soft-tissue activity. When this occurs, the pattern of increased activity in the bone is diffuse (*11,14,20*) and lacks the focal tracer localization characteristic of osteomyelitis (Fig. 1, A and B).

Since any process causing hyperemia in and around a joint will appear the same on blood-pool and bone images, it is not possible to differentiate septic arthritis from other arthritides or trauma (*21*). The role of imaging lies in the early identification of osteomyelitis, or its exclusion when nonspecific or confusing symptoms exist. In sites difficult to assess radiographically, such as the spine and sacroiliac region, bone imaging has been particularly helpful in detecting inflammatory disease (*22*).

Vascular disorders. Bone infarctions in children are usually related to the sickle-cell hemoglobinopathies, steroid therapy, or a storage dysfunction such as in Gaucher's disease. It is often difficult to differentiate a bone infarction from early osteomyelitis clinically or radiographically. A vascular compromise is expected to result in an area of decreased bone uptake on technetium phosphate imaging, in contrast to a bone infection, which results in a focal area of increased activity (*5,14*). Unfortunately, a clear distinction between osteomyelitis and bone infarction may not be possible on the basis of bone imaging alone. As previously mentioned, a photon-deficient area may be seen on delayed bone images in early osteomyelitis and may simulate the pattern of a bone

infarct. Just as confusing may be the increased uptake noted in instances of a healing bone infarct as a result of reactive perfusion. Interpretation of bone images therefore may be difficult, and it is important to take into consideration all available clinical information before arriving at a definitive diagnosis. The typical appearance of early healing of a bone infarct is that of an area of circumferential increased activity about an area of decreased activity (Fig. 2, A and B). This patern may be difficult to visualize on routine images, but magnification views can be helpful (*20*).

Bone-marrow imaging with Tc-99m sulfur colloid can be very helpful in the diagnosis of bone infarcts if the phosphate imaging is nondiagnostic (Fig. 2, C and D). Lutzker and Alavi have shown marrow infarction to be associated with bone infarction, but not with osteomyelitis (*23*). Some areas of infarcted marrow never repopulate and may remain as photon-deficient areas on subsequent bone-marrow scans.

By means of bone imaging it is possible to diagnose aseptic necrosis of an epiphysis, as in Legg-Perthe's disease, before the appearance of x-ray changes (*7,24*). The region of bone that has lost its blood supply will appear as a photon-deficient area (Fig. 3). Imaging must be performed using the pinhole collimator in order to obtain adequate resolution. Both hips must be examined, with careful attention to symmetric positioning and equal imaging time.

Considerable data are available regarding bone imaging of the hips of children at the time when characteristic radiographic changes of Legg-Perthe's disease are present (*25,26*). The initial decreased uptake is followed by an increase in uptake as healing ensues. Serial imaging following the diagnosis is advocated as a way of assessing the healing process, as well as to reveal any recurrence of avascular necrosis.

The efficacy of bone imaging in the early diagnosis of aseptic necrosis has led to the institution of screening programs in children who are at risk for the development of aseptic necrosis, such as in children following renal transplantation (*24*).

Trauma. Within hours following a fracture, the bone scan will be abnormal (*27,28*). Because bone imaging is extremely sensitive for the diagnosis of trauma, it has proven of particular help when fractures are not demonstrated radiographically, as may often be the case in battered children (*29*) (Fig. 4). The bone scan is also particularly suited to the detection of fractures in areas that are difficult to evaluate on routine radiographs, such as the spine and ribs. Some difficulty in the bone-scan diagnosis of a fracture may be expected when the site of the truma

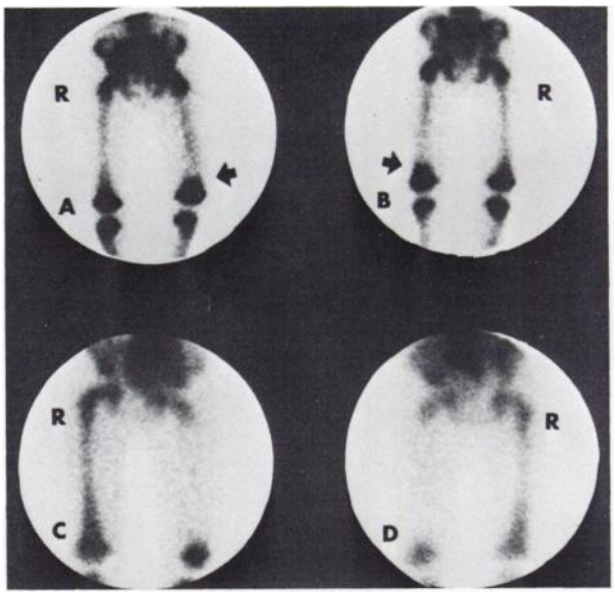

FIG. 2. Sickle-cell disease in 19-month-old boy. (A, B) Typical infarction pattern of decreased activity (arrow) on 2-hr images with Tc-99m pyrophosphate. (C, D) Bone-marrow imaging with Tc-99m sulfur colloid, 48 hr after pyrophosphate study, shows absent marrow uptake in entire shaft.

is near the growth plate, since the normal increased activity of the growth plate may mask the increased uptake associated with the fracture. It must also be remembered that injury of the periosteum alone will also result in increased uptake (*30*).

Neoplastic disease. The earliest application of bone imaging in the pediatric age group was in children with bone tumors. Samuels made the general observation, based on strontium-87m scans in children, that malignant bone tumors generally exhibit a greater uptake than do benign tumors. He cautioned, however, that osteomyelitis, osteochondroma, and a traumatized benign bone cyst also exhibit an intense uptake, as also do osteosarcoma, reticulum-cell sarcoma, and Ewing's sarcoma (*31*) (Fig. 5). Conversely, a lesion with decreased or normal uptake may be malignant, as has been reported for

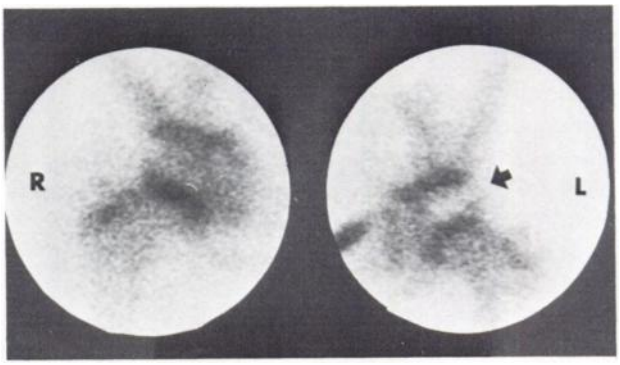

FIG. 3. Ten-year-old boy with traumatic avascular necrosis of left capital femoral epiphysis (arrow).

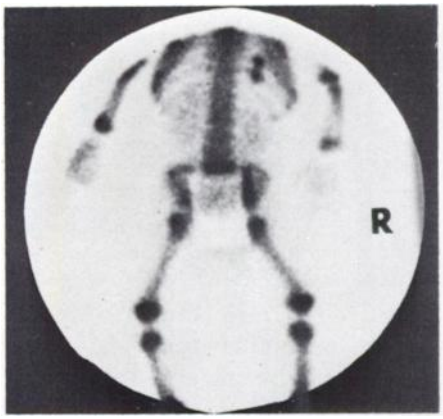

FIG. 4. Two-month-old battered child. Note two right rib fractures.

cases of metastatic neuroblastoma (*15,34*). Others who have incorporated blood-pool imaging as a part of the evaluation of bone tumors have noted that hyperemia is most often associated with malignant tumors, whereas this is less likely in benign tumors (*32*).

Perhaps the greatest contribution of bone imaging is its superiority over conventional radiography in the detection of metastatic bone tumors (*33*). In a recent series, Gilday et al. reported that skeletal metastases were detected only by gamma imaging in 30 of 44 children (*34*). Bone imaging has been particularly successful in evaluating patients for bone involvement with neuroblastoma and lymphoma. Results to date support the current policy of many institutions regarding the use of bone imaging as the primary examination of the skeleton in staging and following patients with malignant neoplasms.

There is some experience in the use of Ga-67 in children with metastatic bone disease, although here gallium is not as efficient as the technetium phosphates. (*35,36*).

In addition to the focal uptake in the bone lesion, there is often increased uptake in the normal adjacent bones. This extended pattern of increased uptake should not be misinterpreted as an extension of the neoplasm (*37,38*). The bone image may also be difficult to interpret if radiation therapy and/or chemotherapy has been used in the treatment of the lesion. Such therapy alters bone function and consequently the skeleton is susceptible to occult trauma and infection. As already noted, both trauma and infection result in increased activity, which may simulate neoplastic uptake (*39*).

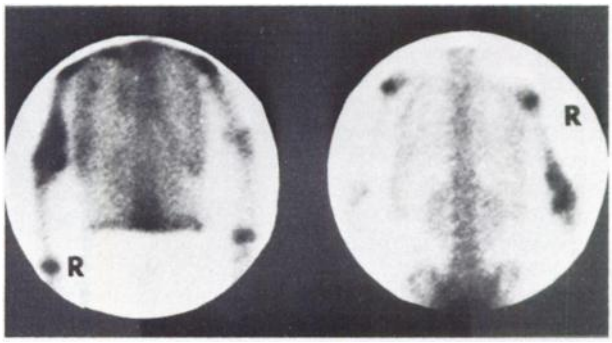

FIG. 5. Eight-year-old girl with Ewing's tumor in distal right humerus. Osteomyelitis or trauma could give similar appearance.

Benign bone neoplasms display variable activity patterns but in general do not exhibit increased uptake. This is a reflection of their slow growth and nondestructive nature. The osteoid osteoma is one of the exceptions, and is characterized by a focal area of increased activity (*32,40*). The osteoid osteoma (particularly one in the spine or hip) may be difficult to visualize radiographically, whereas no such difficulty in detection occurs on bone images. It is for this reason that a bone scan should be performed if osteoid osteoma is considered in the differential diagnosis in a child with local bone pain and no identifiable lesion on x-ray examination.

Although eosinophilic granuloma may exhibit increased activity on a bone image, the increased uptake is not always marked. A variety of patterns of uptake has been reported in osteochondroma, enchondroma, aneurysmal bone cyst, and simple cyst, but usually a slightly increased uptake is observed at the margins of these lesions. In the presence of a benign cortical defect the bone scan will be normal. Injury to a benign lesion has led to confusion in the interpretation of the bone scan, since trauma will cause the lesion to exhibit an increase in uptake. Therefore, if the lesion is benign radiographically but shows increased radionuclide activity, trauma must be considered as an associated factor (*15,32*).

Whereas the efficacy of bone imaging in the search for metastatic disease and osteoid osteoma cannot be disputed, its use in the evaluation of lesions demonstrated radiographically is tenuous. Radionuclide imaging cannot differentiate the benign lesion from the malignant (*41*).

Systemic diseases. Radionuclide bone imaging provides a functional as well as an anatomic study. New roles appear to be ahead in areas of systemic, metabolic, and congenital bone diseases where little pediatric work has been done to date.

Collagen vascular diseases occur in children and, as in the adult, joint symptoms are frequently found. The sensitivity of the technetium phosphates in demonstrating joint involvement in the adult has been shown (*42,43*), and similar application to childhood disorders is appropriate. Detection of abnormal joints by gamma imaging (Fig. 6) is possible before the

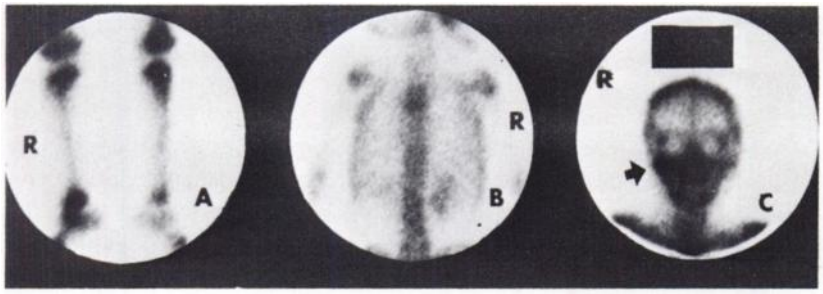

FIG. 6. Four-year-old boy with juvenile rheumatoid arthritis. Increased activity is present at symptomatic sites: right ankle (A) and collapsed thoracic vertebral body (B), as well as an asymptomatic site (C) at right temporomandibular joint (arrow). Note asymmetric renal activity (B) due to small, poorly functioning left kidney.

onset of clinical symptoms (*21*). In addition to early identification of manifestations of the collagen disorders, another attractive consideration is the use of gamma imaging in the assessment of the response to therapy.

Systemic bone disorders that alter metabolism are likely to produce symmetric alterations of bone images, making the detection of the abnormality difficult. As methods for the measurement of radionuclide activity within bone are developed, these disorders can be studied more extensively. Such quantitative techniques have been applied to patients with renal osteodystrophy, and an increased uptake throughout the skeleton has been observed (*44*).

Weigmann et al. have proposed that the increased uptake of technetium phosphates in metabolic bone disease is a reflection of abnormal collagen metabolism (*45*). The increased uptake that we observed in the growth plates of a teenager with untreated vitamin-D-resistant rickets may provide further support for this hypothesis. Following treatment, this patient's image pattern changed and a more balanced distribution of the tracer resulted (Fig. 7). As more is learned about the pharmacokinetics of bone-seeking radionuclides, and the effects of hormones upon them, bone imaging may prove to be more sensitive than the x-ray examination in assessing metabolic abnormalities of the skeleton.

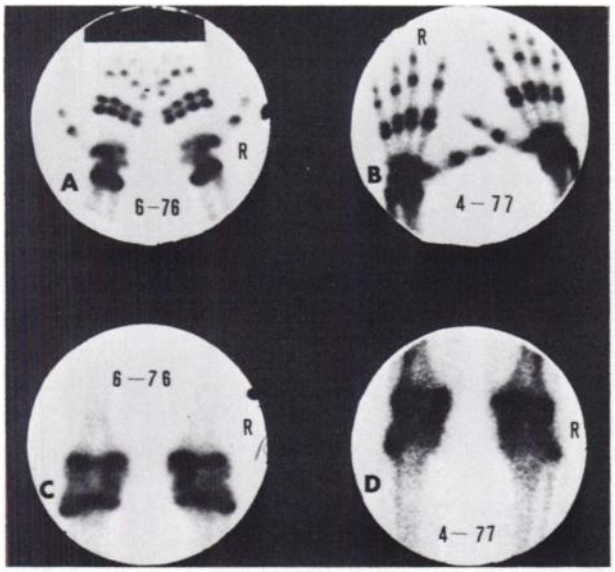

FIG. 7. Sixteen-year-old youth with hypophosphatemic vitamin-D-resistant rickets. (A, C) before treatment, marked uptake at growth plates masks activity in adjacent bones. (B, D) following treatment, activity throughout bones is visible because of relative decrease in activity at growth plates.

CONCLUSION

The technetium-99m phosphate compounds have enabled bone imaging to become a practical diagnostic tool for pediatric patients. The efficacy of tracers in differentiating inflammatory conditions, identifying vascular disorders, and managing neoplastic disease in the growing skeleton has been clearly established. This noninvasive technique, which provides both a functional and an anatomic evaluation of bone, has proven more sensitive than conventional radiography. Future applications of gamma imaging in systemic and metabolic bone disorders of childhood seem certain. The development of new bone-imaging agents will undoubtedly revolutionize the state of the art as we know it.

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