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Bone Scan Update

Helen R. Nadel, MD, FRCPC (Diag Rad) (Nuc Med), ABR (Diag Rad) (Ped Rad), ABNM

The radionuclide bone scan is one of the most commonly performed pediatric nuclear medicine procedures. Bone scintigraphy is used as the diagnostic procedure of choice for diagnosis of bone and soft-tissue infection and can aid in the diagnosis of occult trauma without radiographic findings. There is a complimentary role for bone scintigraphy in the assessment of a child with suspected nonaccidental injury. The use of bone scan in a child with unexplained bone pain or limp may provide a diagnosis that could be related to trauma, tumor, or inflammation. A negative bone scan can help relieve concern for significant pathology. Bone scans in children require careful attention to technique to obtain high-quality diagnostic images. Routine whole-body imaging, magnification, additional views, and the use of single-photon emission computed tomography also are a routine part of this examination in children. Correlation with conventional radiographs is mandatory, and the judicious use of hybrid imaging with the addition of computed tomography may further improve diagnostic acumen, confidence and accuracy. New radiopharmaceuticals such as fluorine-18 may also play a role in changing techniques for pediatric bone scintigraphy.
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As bone scintigraphy is among the commonest of pediatric nuclear medicine exams, this update will focus on some of the major differences encountered when performing and interpreting bone scintigraphy in children. The clinical discussion will focus on specific diagnoses observed on traditional ^{99m}Tc bone scans that may have different patterns in children than in adults. New directions will be discussed for the use of single-photon emission computed tomography/computed tomography (SPECT/CT) in pediatric bone scintigraphy. Although most of the comments in this update are in relation to ^{99m}Tc bone scintigraphy, the use of ^{18}F bone scintigraphy for pediatric bone scans will be introduced as a possible future direction.

Technical Points

After the injection of the ^{99m}Tc bone scan agent, such as methylene diphosphonate (MDP), 3-phase imaging is routine to assess for infection/inflammation and trauma. Immediate imaging could be obtained for flow and blood pool imaging if the clinical indication is for focal disease. Whole-body blood pool imaging is a sensitive screening tool for a systemic inflammatory process. It is mandatory to screen the whole body in a child younger than 2 years of age for the hematogenous spread of osteomyelitis, and this should include whole-body blood pool imaging. There has been some discussion recently among pediatric nuclear medicine physicians as to the requirement for blood flow immediate imaging. I find this imaging helpful to evaluate for reflex sympathetic dystrophy (RSD) and also to distinguish between cellulitis and osteomyelitis. Early and sustained hyperemia may be more in keeping with bone involvement. In RSD, the abnormality may be more evident on immediate phase imaging.

In children, after tracer is injected whole-body delayed imaging is the routine. We do not perform regional bone scans. Focal symptoms may be masking a systemic process such as neoplasm (Fig. 1). However, whole-body imaging does not replace the additional acquisition of joint to joint spot views when abnormality is detected on the whole-body pass. SPECT is mandatory when back pain is the presenting complaint but can be helpful to clarify focal abnormal uptake found on planar imaging. It is particularly helpful to localize for lesions in smaller bones such as feet and hands. The addition of judicious use of hybrid imaging with the addition of CT for localization and/or diagnostic evaluation or fusion to anatomic imaging by software techniques may also improve the specificity of bone scintigraphy. The acquisition of 24-hour delayed images may be useful in certain cases, for example, where the distinction between cellulitis and osteo-

Division of Nuclear Medicine, Department of Radiology, British Columbia Children's Hospital, University of British Columbia, Vancouver, BC, Canada.

Address reprint requests to Helen R. Nadel, MD, Department of Nuclear Medicine, British Columbia Children's Hospital, 4480 Oak Street, Vancouver, BC V6H 3V4, Canada. E-mail: hnadel@cw.bc.ca

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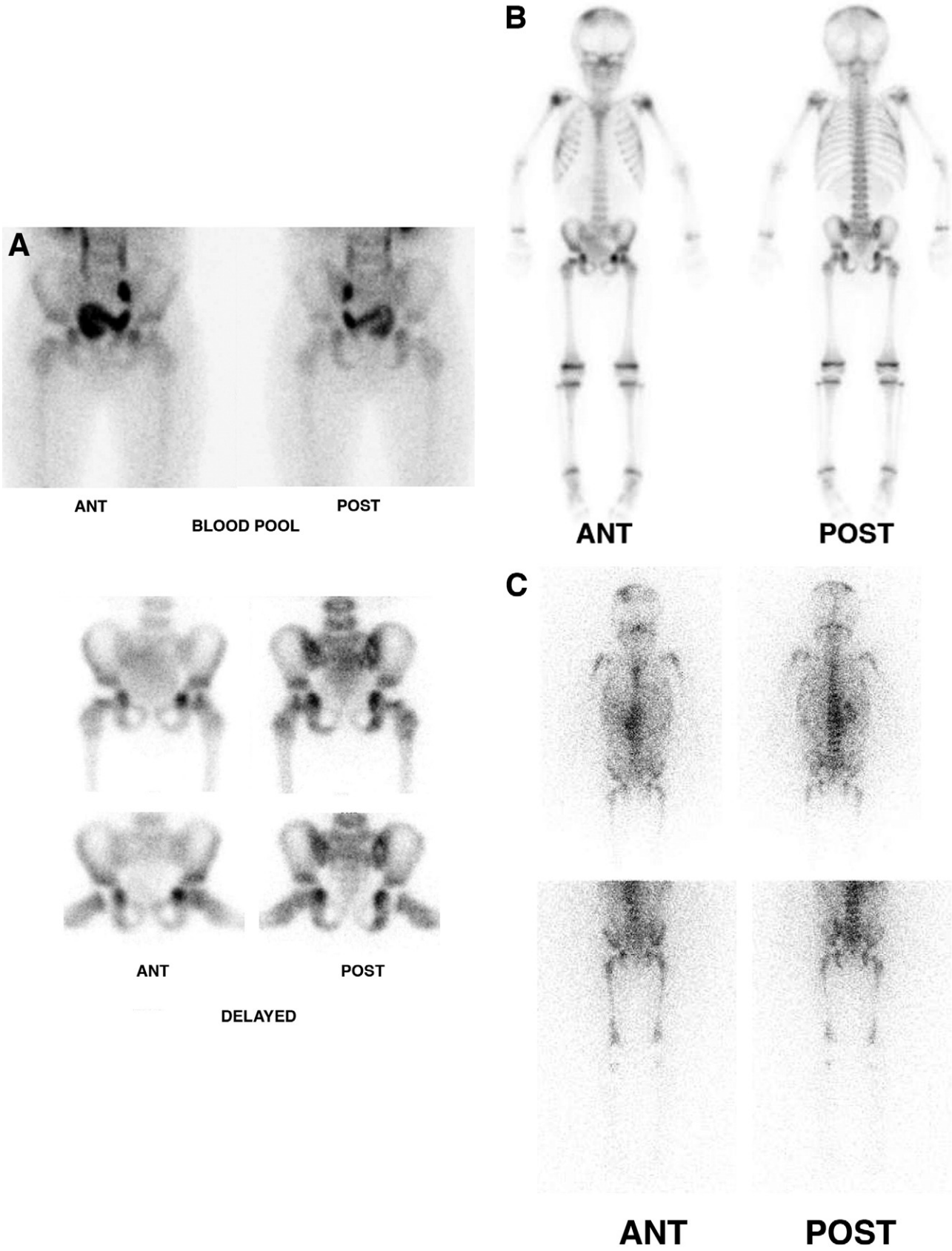

Figure 1 Child presenting with hip pain. (A) 3-phase bone image of the pelvis and hips show abnormality diffusely in the pelvis and lumbar spine. (B) Whole-body imaging shows diffuse skeletal abnormality in skull, ribs, pelvis, and hips that suggests systemic disease such as malignancy. The differential diagnosis for this appearance would include neuroblastoma, leukemia, lymphoma, or possibly Langerhans cell histiocytosis. The final diagnosis was stage 4 neuroblastoma. (C) Correlative ^{123}I MIBG scan shows the multifocal disease and abdominal mass that did not show MDP uptake. Whole-body bone scan images are the routine in pediatrics as systemic disease such as widespread neoplasm can present with symptoms of focal bone pain.

myelitis cannot be confidently made on the basis of the standard imaging protocol.

Bone scintigraphy does not need special preparation, but imaging too early in suspected osteomyelitis can produce a false-negative result. Symptoms should be present a minimum of 24 hours before performing bone scan. A false-positive scan result can occur if bone biopsy or joint aspiration is performed before bone scintigraphy. It is therefore important to have all pertinent history as to onset of symptoms and prior treatment/procedures before undertaking a bone scan in a child.

As to prior preparation for the bone scan, we do not find the need to routinely sedate children for bone scintigraphic procedures, even if SPECT is to be performed. Gaining the cooperation of a child can be achieved by having dedicated pediatric nuclear medicine technologists who reassure the child and provide an age appropriate explanation of the procedure. Liberal use of topical anesthetics for injection site preparation is helpful. Distraction techniques (videos, books, music) provided for the children can go a long way to gaining their cooperation during the scan.

Clinical Considerations

Infection

To correctly diagnose an inflammatory process as being caused by osteomyelitis, septic arthritis, or cellulitis, a 3-phase MDP bone scan with blood flow, blood pool, and delayed imaging is recommended. The aforementioned 3 inflammatory processes all demonstrate hyperemia, and all 3 can coexist. Twenty four-hour delayed images in the presence of cellulitis without osteomyelitis will show clearing of mainly the soft tissue activity without focal abnormal bony localization that would be observed with osteomyelitis. This can also help to improve the specificity of the study. Occasionally, the 3-phase bone scan can help to identify subtle soft tissue abnormalities without bony involvement with careful attention to all 3 phases of the scan and correlation with appropriate clinical findings and other imaging studies.

Classically osteomyelitis shows focal hyperemia on the blood flow and blood pool images with focal delayed increased uptake in bone on the delayed images. Some children presenting with acute virulent onset of disease, including high fever, rapid onset of symptoms, and severe bone pain, may have "cold" bone lesions with decreased uptake in bone on the initial imaging study delayed views.[1-3] Delayed "cold" bone scans usually however, show evidence of increased hyperemia in the blood flow and blood pool phase of the study at the margins of the inflammatory process. Regardless, all bone scans are positive by the end of the first week, which is considerably earlier than radiographic change would be seen.

It is ideal to obtain the bone scan before a joint aspiration because the aspiration procedure itself may cause some bone reaction and increased activity on the scan images. There may be less reactive change on the scintigraphic examination if the scan is performed within a few hours of aspiration. A transient photopenic joint on the scan caused by the inability of the radiopharmaceutical to reach the site of infection can be seen if there is increased joint pressure such as in the presence of a joint effusion.[4]

Because the bone scan may not become positive until 48 to 72 hours after the onset of infection, an early scan may be equivocal. Imaging with ^{111}In oxine-labeled white blood cells is not recommended in children because of its high radiation burden.[5] The addition of other specific inflammatory radiopharmaceutical imaging will increase the sensitivity in those patients in whom there is a convincing clinical suspicion of osteomyelitis, but this option provides a greater radiation burden. Sometimes a repeat bone scan in 48 to 72 hours after the first scan may confirm the diagnosis and provide less of a radiation burden to the child.

Age or size of the patient is no longer a deterrent to performing skeletal scintigraphy. Neonatal osteomyelitis, once thought to be poorly assessed with bone scintigraphy, now can be diagnosed with careful attention to technique with appropriate magnification spot views to detect focal skeletal involvement in a majority of cases.[6] In children younger than 2 years of age, a multifocal pattern may be detected on blood pool and delayed imaging, and this is again a reason to perform whole-body body scans in children.

Chronic recurrent multifocal osteomyelitis or chronic nonbacterial osteomyelitis is a distinct variant of osteomyelitis that occurs in children and adolescents. Its peak incidence is at age 14 years and is more common in girls. Although an infectious agent is suspected, no specific pathogen has been found and its etiology remains unknown. These children present with symptoms from weeks to months of recurrent attacks of infection at multiple sites in the skeleton that are self limited and eventually resolve after a few years of an unpredictable clinical course. Variable radiographic appearances of mixed lytic and sclerotic lesions in common sites of involvement at the metaphyseal portions of the long bones, medial ends of the clavicles, face, spine, pelvis, and upper extremities are present. Sequestra and sinus formation are not commonly present.

Bone scintigraphy can identify both symptomatic and asymptomatic foci and the multifocal pattern of disease. The findings on scintigraphy at typical sites are similar to that for conventional osteomyelitis. A 3-phase abnormality is found at active sites, but nonactive sites may not express abnormal activity. However, the differential diagnosis is nonspecific based on the scintigraphic findings alone and can include primary musculoskeletal neoplasm and Langerhan's cell histiocytosis.[7]

Trauma

Bone scintigraphy can be helpful in detecting occult trauma in children (Fig. 2). Toddler's fractures are occult injuries that occur when children are just beginning to bear weight. Repetitive stress on normal bone can affect most commonly the tibia, but any lower-extremity bone may be involved. The diagnosis is usually made on radiographs, but when radiographs are equivocal or the fibula or small bones of the feet

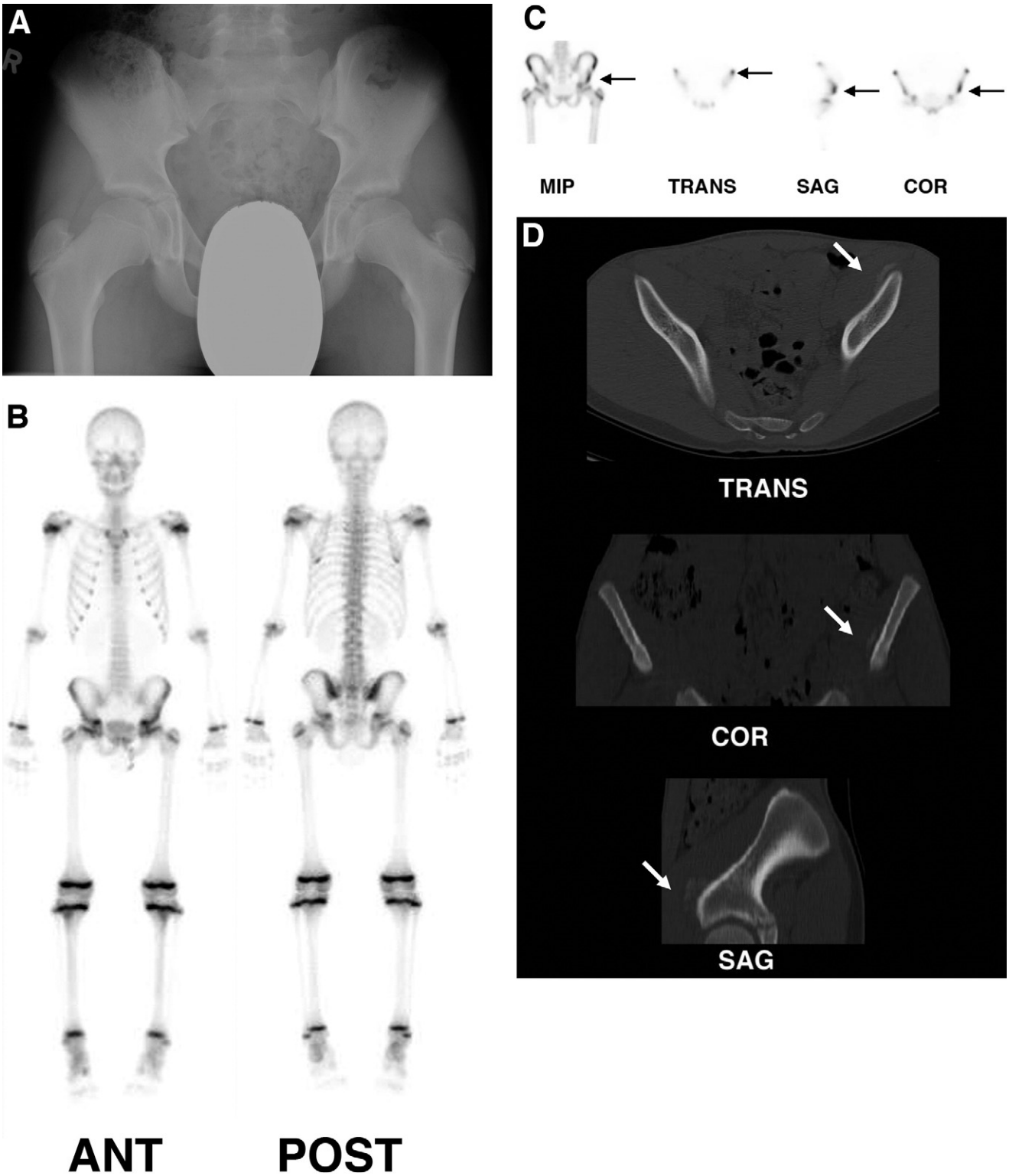

Figure 2 Athletic child who presents with pain in the left hip. (A) Radiographs of the pelvis are normal. (B) Bone scan planar imaging is essentially negative. (C) Because of the symptoms, SPECT of the pelvis was performed and identifies focal increased activity in the left anterior inferior iliac spine. (D) Subsequently, multiplanar reformatted CT images identify the healing avulsion.

are involved, scintigraphy will be positive. The bone scan will show a 3-phase abnormality.

Bone scan plays a complementary role in the evaluation of children with suspected nonaccidental injury.[8,9] The bone scan can provide a quick assessment to characterize the extent of trauma but must be correlated with radiographs.[10] A negative bone scan is not confirmatory that trauma has not occurred, but a positive scan may be caused by both soft-

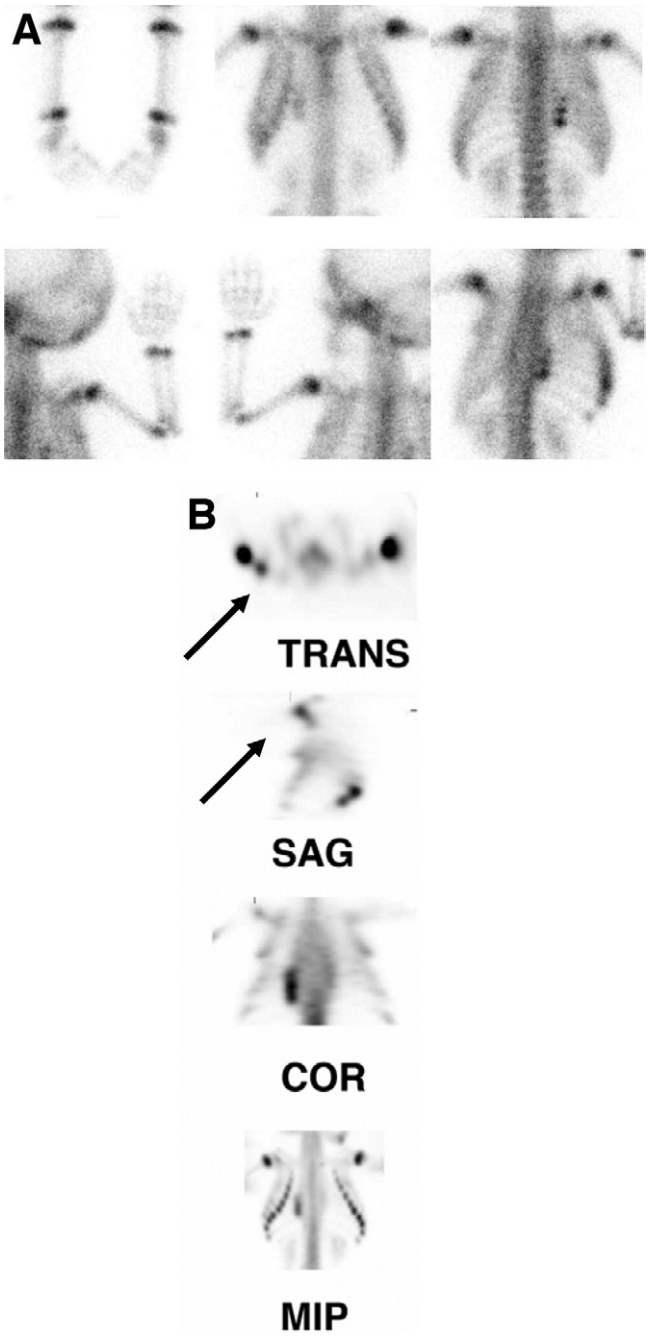

Figure 3 Infant presenting with suspected nonaccidental injury. (A) Selected delayed bone scan spot images show characteristic linear appearance of uptake in contiguous posterior ribs. (B) SPECT clearly identifies the focal abnormality in the ribs as well as identifying abnormal increased activity in the spine of the right scapula (arrow). The scapula is a difficult bone to image with conventional radiographs but the finding of abnormality in this bone is highly specific for nonaccidental injury.

tissue and bone trauma. Characteristic sites of trauma in nonaccidental injury such as in ribs and diaphyses of the extremities may be more easily identified on the more sensitive bone scan (Fig. 3). Scintigraphy can be particularly helpful in young infants when subtle areas of bony injury may either be too early to detect on radiographs or completely healed areas may be radiographically normal. In both of these instances, the bone scan may show areas of increased activity.

Reflex sympathetic dystrophy or chronic regional pain syndrome has various clinical forms, precipitating factors, localizations, physiological, physiopathological hypotheses, and diagnostic criteria and is now used to encompass all variants of the syndrome, which include pain, hyperesthesia, vasomotor disturbances, and dystrophic changes that usually improve with sympathetic denervation. Acute or even months-old remote trauma is the most common precipitating factor. However, children may not have a defined antecedent event and the pain can be misdiagnosed as having a psychiatric cause causing a delay in diagnosis. Treatment is usually supportive and includes physiotherapy to begin using the affected limb rather than immobilization.

Few radiographic imaging techniques will show an abnormality with this suspected diagnosis. Whereas the 3-phase bone scan is often abnormal and can lead to the diagnosis of this condition, in adults, the classic RSD scintigraphic appearance includes intense periarticular activity in an involved extremity on the delayed phase of the scan preceded by hyperemia in a similar distribution on the immediate post injection blood flow and blood pool phases of the scan. A cold scintigraphic variant is the more common form found in children.[11,12] Scan findings in the cold variant of RSD include photopenic abnormalities on the delayed scan and hypoemia on the immediate blood flow and blood pool phase. The abnormality can be recognized in children who have open epiphyses by the incongruence of the involved epiphyseal activity compared with remote ipsilateral and contralateral epiphyseal plate activity (Fig. 4).

Back pain is an uncommon symptom in childhood, and vertebral scintigraphy with SPECT is an essential and sensitive means of assessing this area. After localizing the area of abnormality on scintigraphy, cross-sectional anatomic imaging with CT as either hybrid or stand- alone studies and/or magnetic resonance imaging can define the abnormality. Diskitis, or infection of the intervertebral disk space, is a specific inflammatory process that occurs in children. The usual pattern is delayed bone scan uptake in the vertebrae on either side of the affected disk space; however, in adolescents, the increase in uptake may affect only a single end plate. The differential diagnosis of acute back pain may be spondylolysis, with focal involvement of the pars interarticularis area best seen on the tomographic images.

Tumor

Although functional molecular imaging may replace bone scintigraphy in the future, bone scan still has a major role in the evaluation of a child with diagnosed malignancy that can potentially have bone involvement. This includes mainly musculoskeletal tumors such as Ewing sarcoma and osteosarcoma, rhabdomyosarcoma, lymphoma, and neuroblastoma. At the time of diagnosis, evaluation is for staging evaluation for metastatic or skip lesions. Bone scintigraphy is a good screening tool for metastatic disease before major treatment decision points and or local control. Subsequently, it

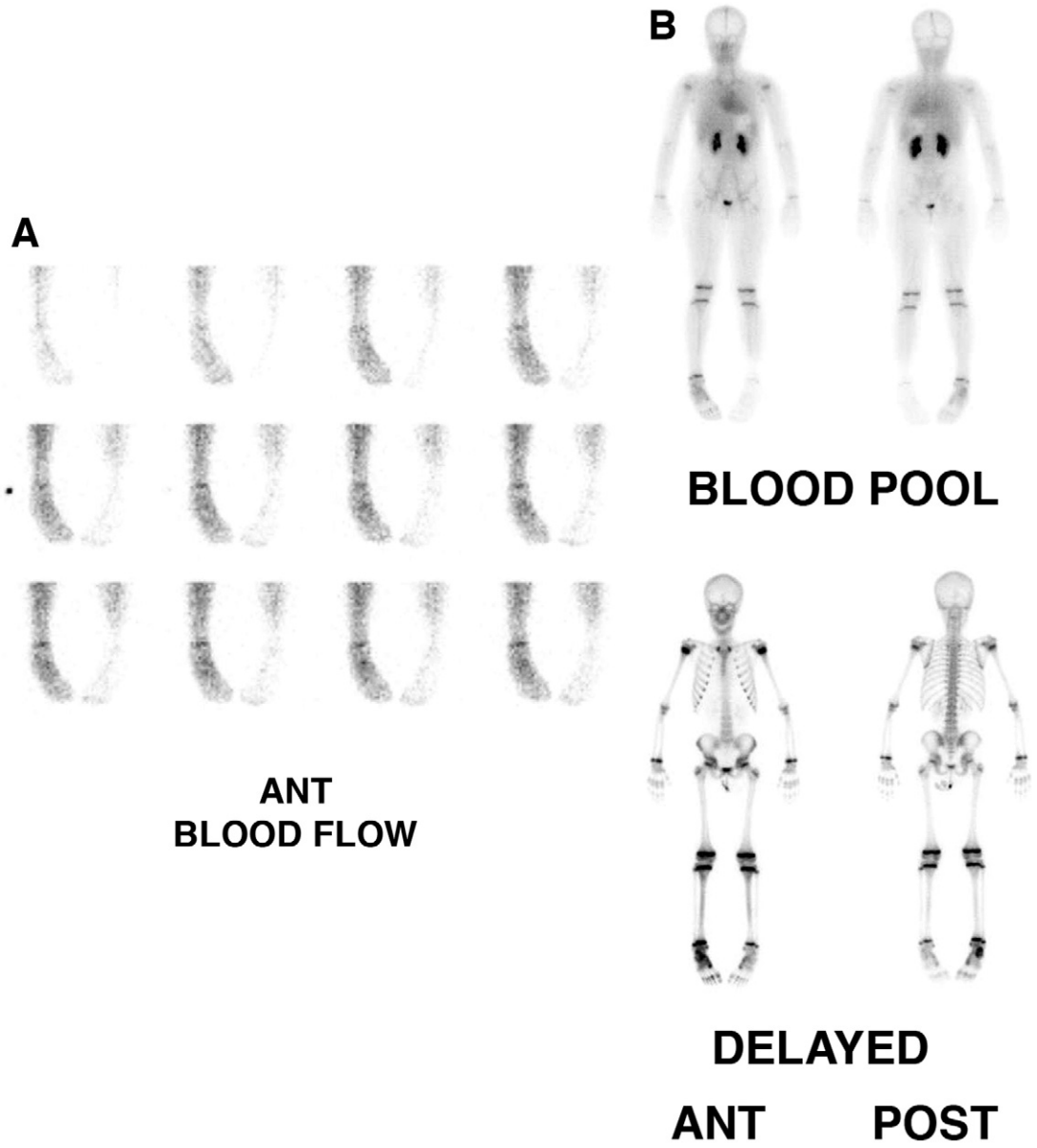

Figure 4 Girl who had remote history of trauma presents with left leg pain. Bone scan includes blood flow images of the feet and ankles (A). (B) Whole-body blood pools and delayed imaging identify 3-phase cold abnormality of the left leg consistent with cold form of reflex sympathetic dystrophy.

should be performed as a baseline after completing therapy. For routine surveillance in high-risk patients who have completed treatment, a bone scan should be performed when directed by new symptoms or abnormal findings on other imaging studies. Children's Oncology Group is working to standardize minimum imaging requirements for all common pediatric tumors. Such guidelines will soon be available for children with Osteosarcoma and Ewing Sarcoma.

New Directions

SPECT/CT

SPECT/CT techniques are emerging as beneficial in the field of musculoskeletal imaging. The addition of SPECT routinely on bone scans that have equivocal planar findings has already improved sensitivity of bone scintigraphy. What first started as hybrid techniques with low-dose CT systems has now progressed to hybrid machines that are capable of high-resolution diagnostic spiral CT image sets that directly match SPECT findings. This may further increase the diagnostic accuracy of this already highly sensitive but less-specific study. Adult applications include the ability to detect and/or exclude osteomyelitis and to define sites of inflammation and confirm anatomic correlate of focal findings in both benign and malignant disease.[13-15] Pediatric applications have lagged behind adults because of the slower introduction of these hybrid machines in dedicated pediatric hospitals but, more importantly, perhaps the result of the more cautious use of this tool that could increase the absorbed radiation dose to the child.

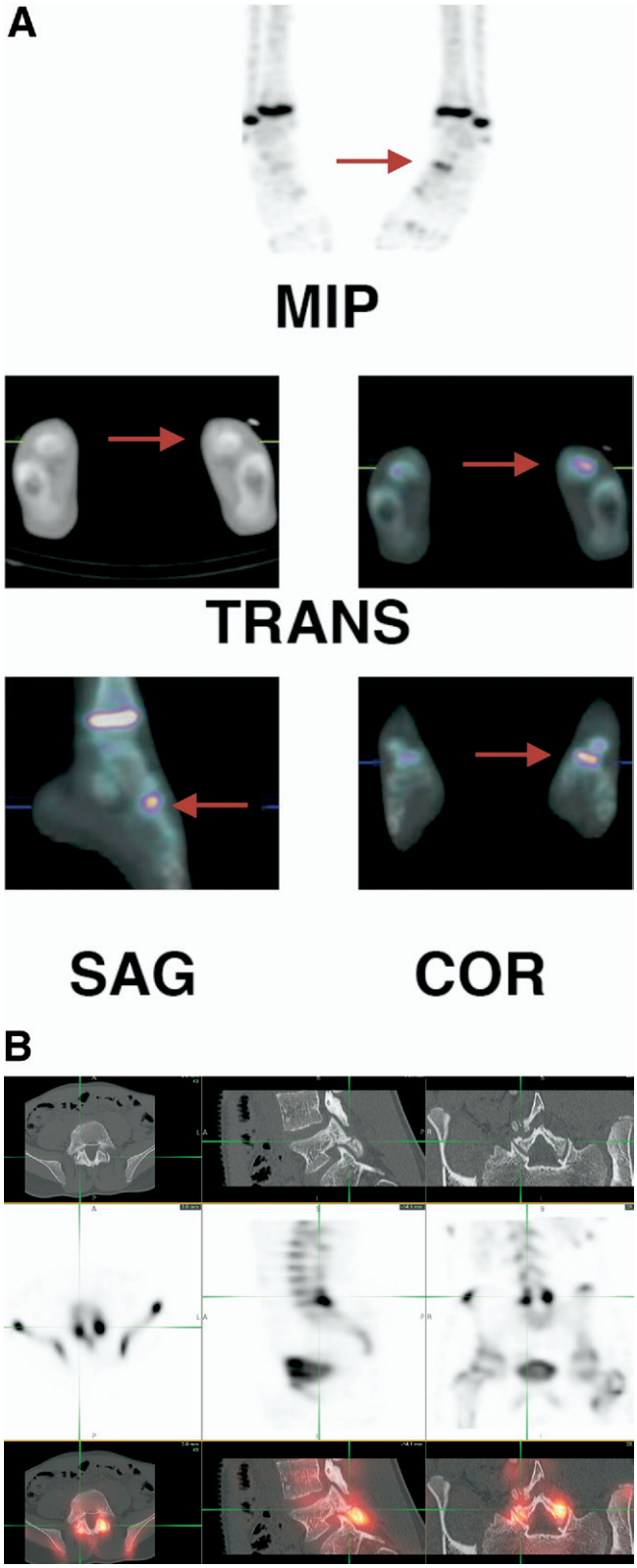

Figure 5 SPECT/CT imaging in two different adolescents. (A) Fused images clearly localize abnormal increased MDP activity to the navicular bone. (B) SPECT/CT confirms bilateral spondylolysis at L5.

Potential applications in pediatrics could include the combined imaging in children with back pain who would likely have further anatomic correlative imaging with CT for their specific symptoms. This might shorten the diagnostic evaluation time as the patient would not have to return for a second examination at a later date. It should be noted that in pediatrics, no "routine" standard SPECT/CT acquisition should be performed with each scan for a certain indication. Each examination should be tailored to the individual child to ensure appropriate adherence to ALARA concept for radiation protection.

Attentuation correction is not the issue in pediatrics, but anatomic and diagnostic localizaton are the important indication for performing such a hybrid examination in a child. The individualized tailoring of the examination should include a low kVP/mAs technique with or without the use of intravenous contrast enhancement for CT where indicated. Physician imaging specialists trained in both CT and nuclear medicine techniques should be determining the indication for such techniques and then issuing a report that incorporates the findings of both modalities to maximize the diagnostic potential of such an imaging study.

Technical issues as to who performs the studies, that is, a nuclear medicine technologist with CT training or both nuclear medicine technologist and dedicated CT technologist has not been standardized as yet. As well, the reporting structure for both a diagnostic CT scan and nuclear medicine bone scan may not be as simple as reporting of a standard bone scan. Further evaluation of this technique with careful attention to appropriate use may clarify some of these issues (Fig. 5).

Another potential future change in bone imaging may relate to the use of alternate radiopharmaceuticals. ^{18}F positron emission tomography is being used as a alternative to ^{99m}Tc MDP bone scintigraphy. In those centers that have positron emission tomography imaging readily available for pediatric use, this radiopharmaceutical could potentially reduce the time for bone scan imaging. The imaging with this agent occurs 30 minutes after the injection of ^{18}F. Lim and coworkers[16] reported on their early experience for imaging for symptoms of back pain and their series did include adolescents. They found similar radiation dosimetry to MDP in a 55-kg patient size. Cost considerations may be a factor in the use of this agent for routinely imaging children.

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