Skeletal Radiol. 5, 1–14 (1980)

Skeletal Radiology

Bone Scanning in the Child and Young Adult

Part I*

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Abstract. Radionuclide bone scanning will identify readily areas of the skeleton where vascularity or osteogenesis is disturbed. Frequently, this will be achieved with a greater sensitivity than orthodox radiology by reflecting altered local physiology of bone. This procedure is, therefore, valuable not only for identifying metastatic disease, but also in benign skeletal disorders characterised by altered blood flow or osteoblastic reaction. These changes occur in many diseases involving bone which are more common in children and young adults. Special attention to the performance of the study and to its interpretation is, however, required in these age groups. The bone scan is invaluable in detecting metastatic disease related to either primary bone tumours or other neoplasia, both in the initial investigation and in the evaluation of therapy. Extra-osseous uptake may also occur, providing useful information relevant to the care of these patients.

Key words: Technetium phosphates – Skeletal scintigraphy – Children – Bone tumours – Skeletal metastases – Neuroblastoma – Histiocytosis.

The development of ^{99m}Tc-phosphate bone-seeking complexes revolutionised skeletal scintigraphy. Following the introduction of polyphosphate in 1971 [40] and subsequently of other phosphate complexes, there was an outpouring of publications so that by 1976 it was possible to prepare a bibliography of almost 700 references [30]. The interest and use has continued unabated. Initially, the dominant application was in oncology, a field in which, as reviewed recently by Brady and Croll [2], bone scanning now has a firmly established role. Increasingly, skeletal scintigraphy with these agents has also been found to be of great value in the diagnosis and evaluation of therapy of many benign bone disorders. Many of the uses for which the technique has become established in the adult are equally applicable to the child. However, skeletal scintigraphy has a number of applications in infants, children, and young adults because of the skeletal disorders which are unique to or more common in these age groups, but which may be readily identified by the procedure. The potential value which appeared to be offered by skeletal scintigraphy in children on the basis of experience with earlier bone-seeking agents [34] has now been fully realised [2, 21].

Interpretation and Techniques

In general, the study of the bone scan in a child requires attention to the same aspects as in the adult: the bone-soft tissue ratio, the presence of any focal areas of increased or decreased accumulation in bone or any asymmetry of uptake, the renal image, and extra-osseous patterns. Awareness of the pitfalls, such as reviewed by Thrall et al. [45] is critical. In particular, it is important to remember that, in the child, intense uptake is to be expected in the metaphyseal-epiphyseal areas of the long bones. This uptake diminishes with increasing age until fusion. In children, the growth complex activity in the knee is usually 4–7 times that of the diaphysis. Such accumulation results in a greater radiation dose to the growth complex which Thomas et al. [43] have calculated to range from 0.8–4.7 rads, from an administered activity of 200 μCi/kg. Kaufman et al. [26] have emphasised that in pre-ambulatory children, the meta-epiphyseal complex demonstrates intensely increased uptake as com-

* Part II of this article will appear in the next number of Skeletal Radiology

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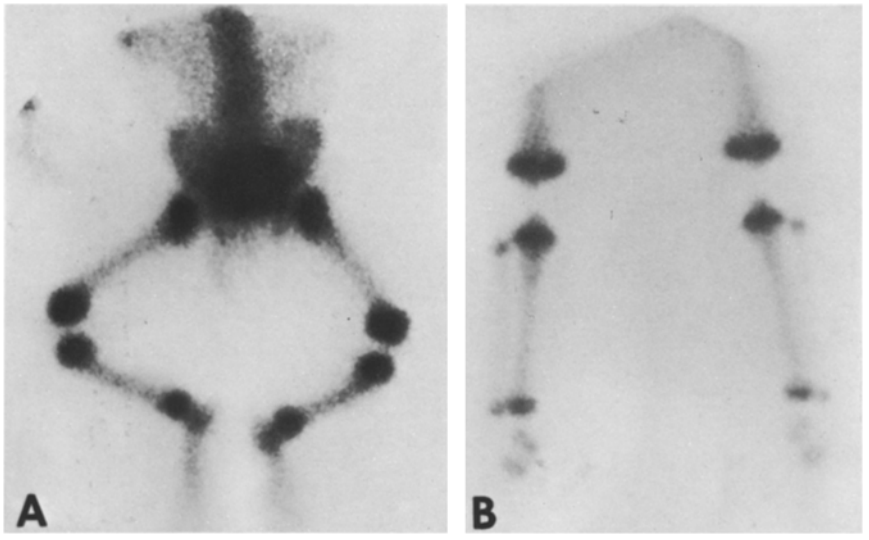


Fig. 1A and B. In infants, the growth complexes will, because of size, natural posture, and avidity of isotope uptake, be visualised by standard camera views as intense globular foci of radionuclide accumulation as in **A** a 3-month-old infant. Attention to positioning and density will improve the scan quality as in **B** a 2-week-old girl

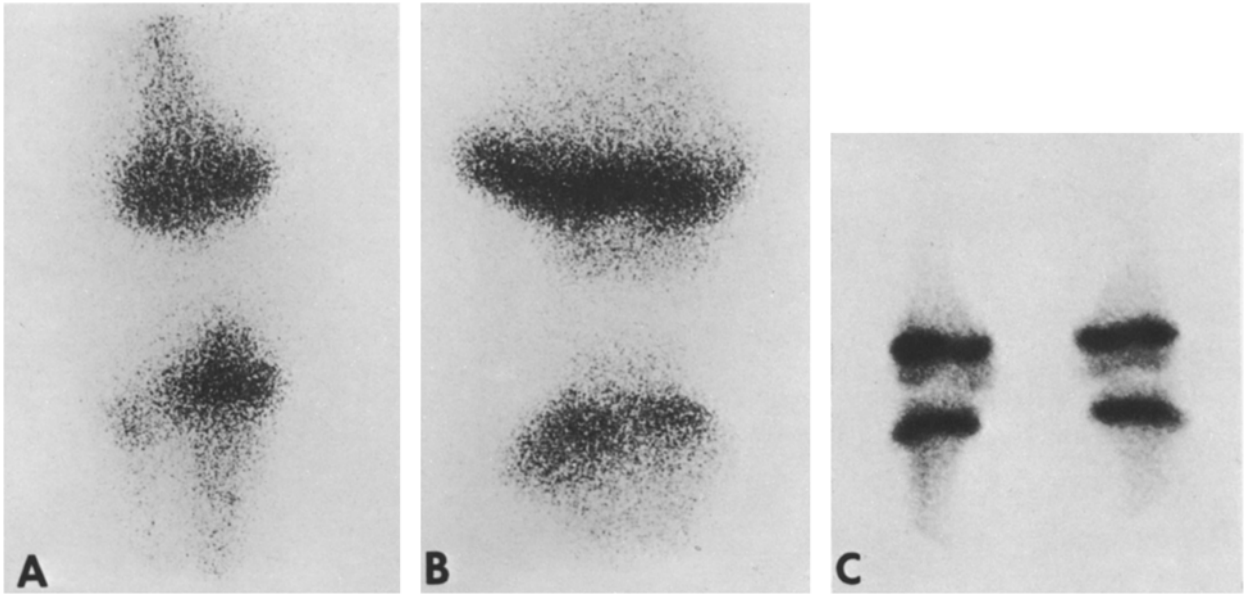


Fig. 2A–C. Even with magnification views with a pin-hole collimator, the globular appearance of the infantile growth complex persists. (**A** a 2-week-old infant). At later ages, with these views, the components of the growth complex can be delineated, as in **B** a 15-month-old boy in whom flattening of the elliptical growth plate is commencing. This still contrasts with the sharply demarcated linear pattern of the growth plate in the older child. (**C** an 8-year-old boy)

pared to the diaphysis and it is difficult to distinguish between the epiphysis and the epiphyseal growth plate. Thus, in these infants, the growth complexes are usually of a globular shape. Kaufman and his colleagues point out that poor positioning of the knee contributes to poor visualisation of the meta-epiphyseal complex; the common position in infants of slight knee flexion and external rotation of the lower extremity can result in superimposition of the growth plate on the epiphysis and metaphysis, so accentuating the globular appearance (Fig. 1).

After a child begins to walk, the epiphyseal plate becomes more readily identified as a linear transverse area of preferential uptake (Fig. 2). The activity of the metaphysis adjacent to the plate is approximately equal to the epiphyseal activity and, while there is a gradient between the plate and diaphysis through the zones of provisional calcification, and primary and secondary spicule formation, the edge of the plate should be well demarcated. Any blurring of the edge or right-left asymmetry should arouse suspicion. The importance of care in examining these areas lies in

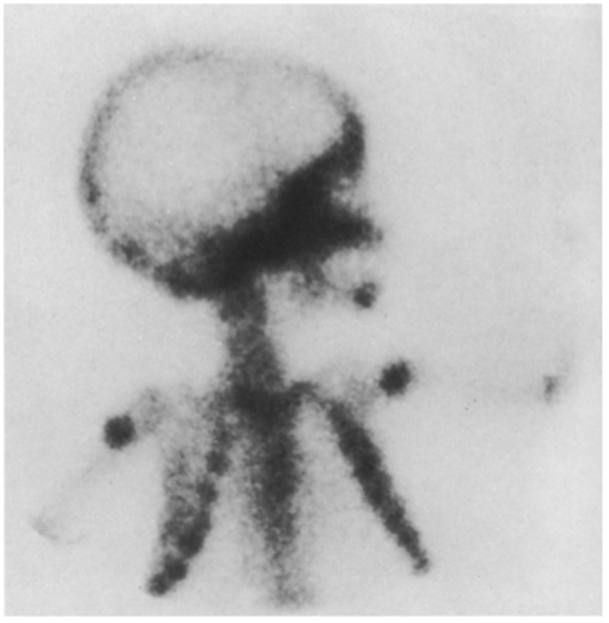


Fig. 3. Normal distribution of Tc-pyrophosphate in a 3-month-old infant, showing preferential uptake in the base of the skull, costo-chondral junctions, and epiphyses

the predilection for the metaphysis in children of disorders such as osteomyelitis or neuroblastoma metastases. The latter in particular can cause considerable difficulty since frequently the deposits may be symmetrical or present as photon deficient or 'cold' areas. Further, Conway et al. [7] have pointed out the value of obtaining a normal bone scan in children in whom normal developmental configuration of the distal femoral metaphysis may result in a radiological abnormality which may be considered pathological.

In order to ensure that lesions around the growth complex are not missed, Kaufman et al. [26] suggest that it is important to avoid over-exposure of the meta-epiphyseal complex which may occur if the information density is set for optimised appearance of the diaphysis. Comparison of each side is so important that it is desirable to visualise both sides in the same field with the gamma camera 'spot views' whenever peri-epiphyseal pathology is suspected, in preference to whole-body survey scans. If this is not possible, comparison is facilitated by performing the study on each side with the same pre-set time rather than pre-set counts. In this way, not only will meta-epiphyseal pathology be demonstrated but changes in the metabolic status of the epiphyseal plate may be noted; for example, the effect of radiation or chronic steroid therapy. Frequently, particularly in the investigation of the hips and small bones of the hands and feet, magnification views using a pin-hole collimator are desirable. Optimal delineation of the hip requires views in both external ("frog-leg") and maximum internal rotation, the latter considered by Paul et al. [33] to provide better definition of the femoral head and epiphyseal plate.

Other areas in which preferential uptake may be noted include the base of the skull in infants, the sutures of the skull, and the costo-chondral junctions (Fig. 3).

Almost any benign or malignant disorder in bone which causes alterations in bone blood flow or increased bone turnover can be associated with an abnormal scan. This sensitivity, however, does result in a lack of specificity and close correlation of the bone scan with both the clinical and radiological findings is essential. However, differentiation of the na-

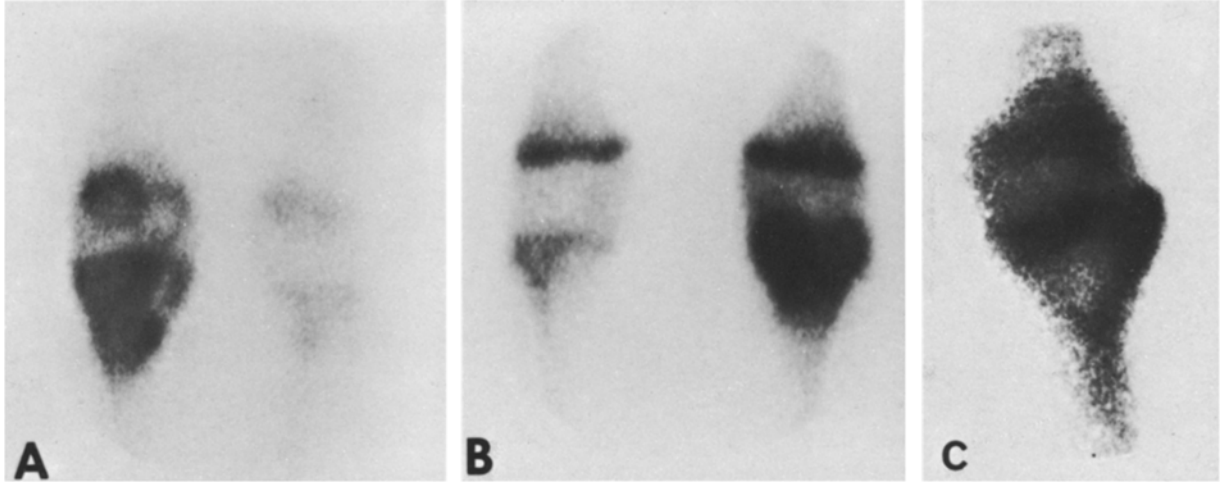


Fig. 4A–C. Primary bone tumours in the proximal tibia (**A** osteogenic sarcoma; **B** Ewing's tumour; **C** osteoclastoma) demonstrating the difficulty which may be encountered in differentiating the type of tumour by scintigraphy

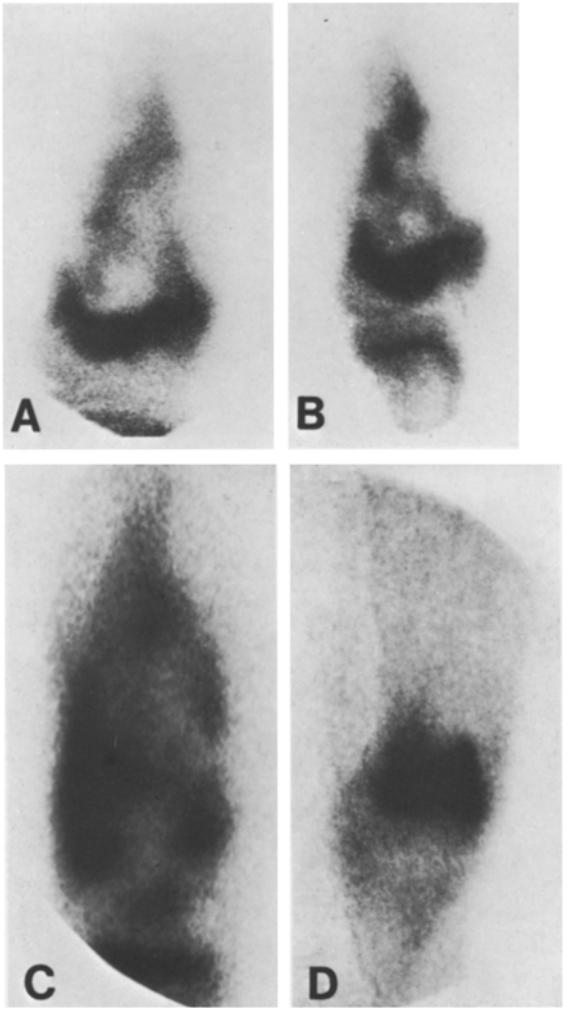


Fig. 5A–D. **A** and **B** Typical scan pattern (in anterior and lateral views) of the distortion of bone outline and growth plate and the patchy but intense uptake frequently observed in osteogenic sarcoma. This lesion arose in the distal femoral metaphysis of a 16-year-old boy. **C** Telangiectatic osteogenic sarcoma in the femur of a 13-year-old boy. **D** In contrast with **A** and **B**, the uptake in a parosteal osteogenic sarcoma in a 17-year-old girl is more uniform

ture of some lesions in children may be achieved by studying the vascularity. This can be accomplished by acquiring "blood pool" images of the area of clinical or radiological abnormality immediately after the administration of radiopharmaceutical. This procedure should indeed be routine in many problems such as the investigation of possible focal infection or for distinguishing between benign and malignant tumours.

Primary Bone Tumours

Malignant primary tumours are observed always as areas of increased bone uptake, frequently demonstrated as hyperaemic in blood pool studies. Rarely however, does the scan provide diagnostic information regarding the type of the lesions comparable to that obtained with the radiograph and may indeed be very similar in different tumours (Fig. 4). Nevertheless, apart from the characteristic location and age incidence of the different tumours, a general pattern of scan changes does emerge. An osteogenic sarcoma is usually associated with considerable distortion of the bony outline, often irregular and intense radionuclide uptake, more frequently with areas of absent and patchy accumulation within it (Fig. 5). Ewing's sarcoma rarely demonstrates this patchiness and presents a picture of very intense uptake within more smooth expansion of the bone outline (Fig. 6). Both are usually very hyperaemic in the blood pool study (Fig. 7). Osteoclastoma, while uncommon in children, does result in less bone distortion and, although the whole lesion may be the site of intense uptake, it is often seen as a rim of increased accumulation surrounding a photopenic area (Fig. 4). Similarly, differences in distribution may be observed in cartilaginous tumours; chondrosarcomata typically demonstrate

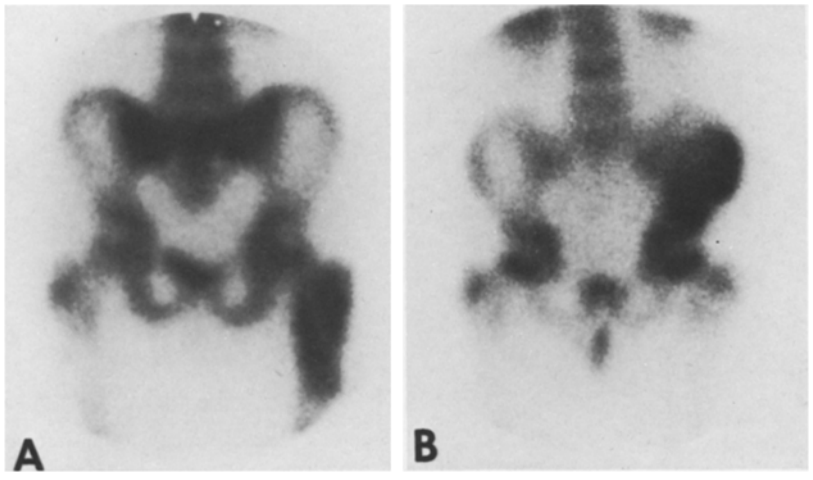


Fig. 6A and B. Scan pattern of mild expansion of bone outline but intense generalised uptake frequently found in Ewing's tumour
A In upper femur of an 11-year-old boy
B In ilium of a 9-year-old girl

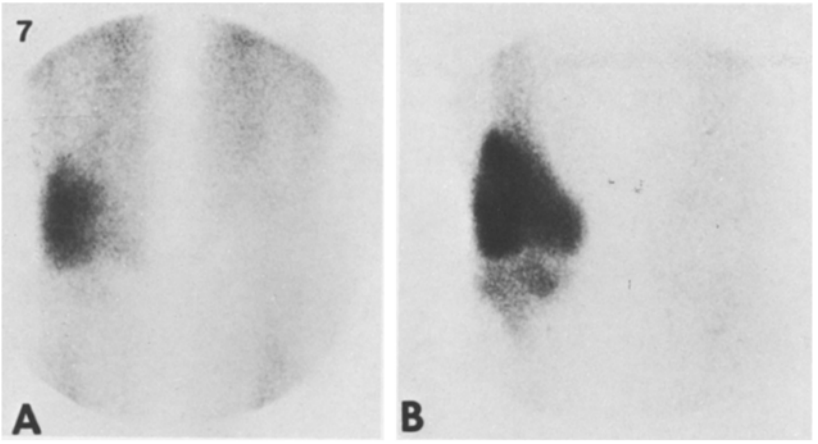


Fig. 7A and B. The "blood pool" image **A** demonstrates the vascularity of an osteogenic sarcoma. In the subsequent delayed view **B**, there is greater concentration of radionuclide in the tumour than in surrounding bone where diffuse accumulation results from hyperaemia

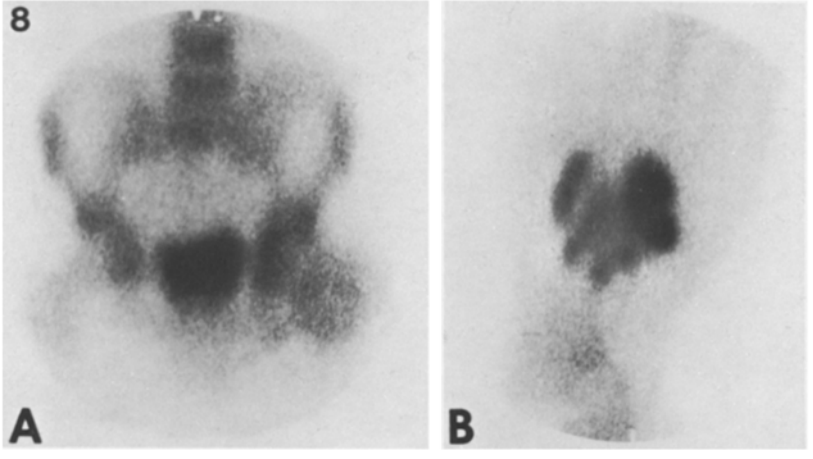
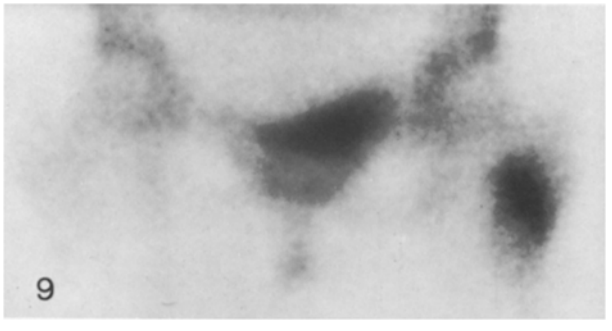
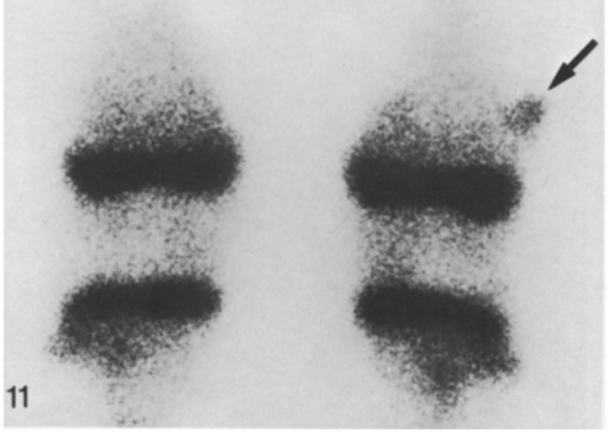


Fig. 8A and B
A Diffuse mild increase in expanding chondroma in upper femur in a 23-year-old male
B Intense focal areas of uptake in a chondrosarcoma producing gross distortion of the outline of the lower femur in an 18-year-old male

Fig. 9. Focal scan of pyrophosphate uptake, surrounded by hyperaemia in a fibrosarcoma in a 21-year-old female. Sequential scans three months following hind-quarter amputation, demonstrated multiple metastatic deposits throughout the skeleton





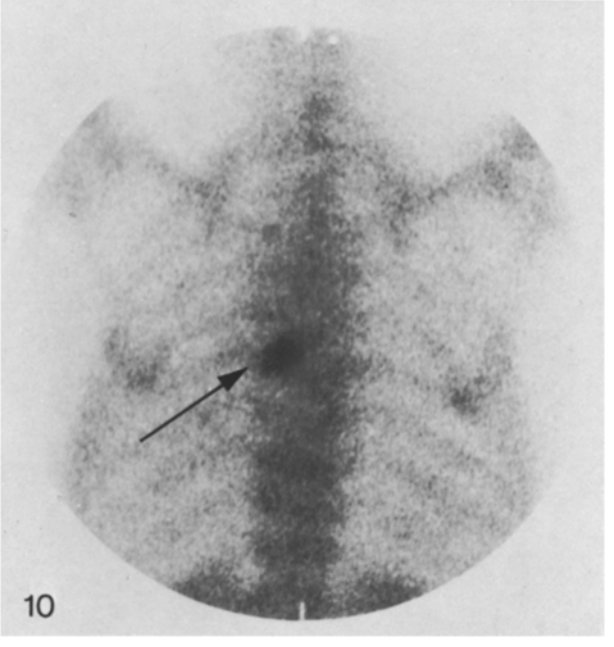


Fig. 10. Intense focal accumulation in a thoracic vertebra identifies an osteoid osteoma as cause of back pain

Fig. 11. Osteochondroma in lower femur in a 13-year-old girl

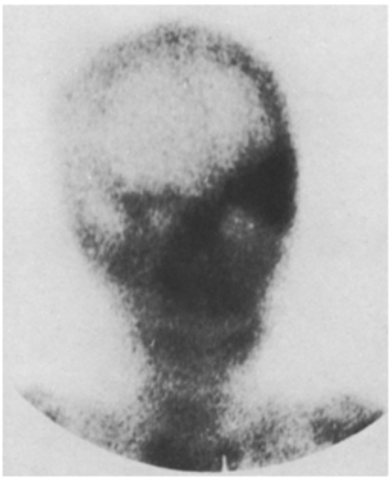


Fig. 12. Intense accumulation typical of cranio-facial fibrous dysplasia in a 4-year-old boy

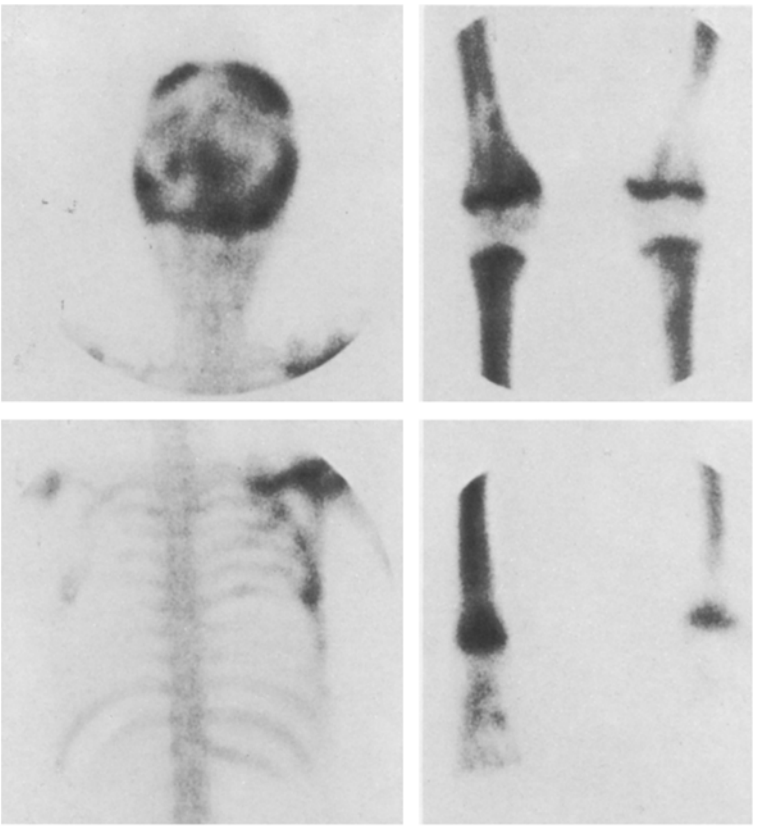


Fig. 13. Multiple extensive areas of increased uptake demonstrating extent of polyostotic fibrous dysplasia in a 6-year-old girl.

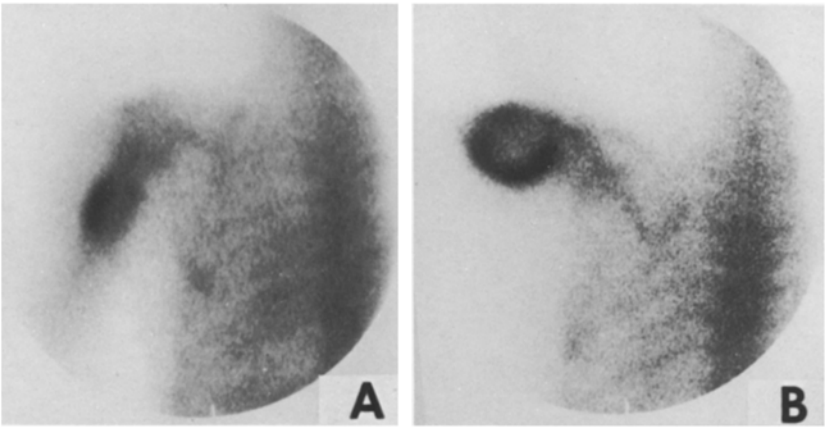


Fig. 14A and B. Scan appearances of an aneurysmal bone cyst in an 18-year-old girl demonstrating expansion of the lesion over an eight month period between study **A** and **B**

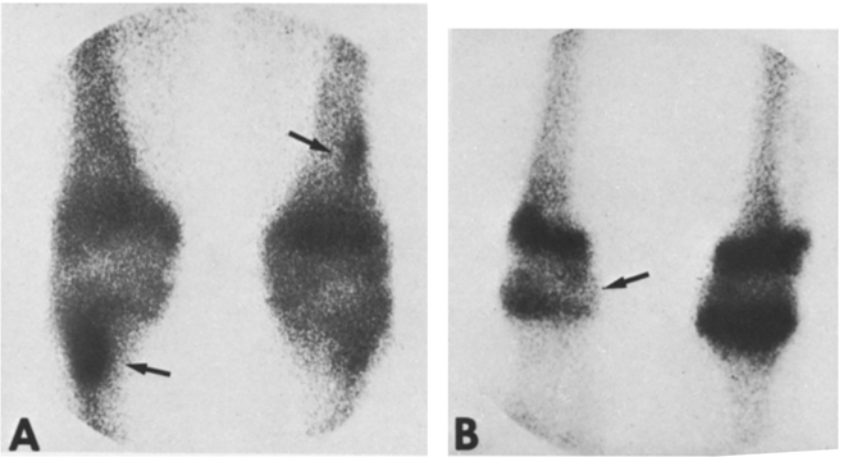


Fig. 15A and B
A Metastatic deposits of neuroblastoma in a 16-year-old male in typical sites in metaphysis and in shaft of femur
B "Cold area" in upper tibial growth complex of a $6^1/_2$-year-old boy with disseminated neuroblastoma

avidity which may be in focal patches throughout the tumour (Fig. 8), while chondroma and chondroblastoma demonstrate expanding lesions with a diffuse uptake of a degree comparable to normal bone or slightly increased. Fibrosarcoma have presented totally varied scan patterns; the most focal and smallest resulted in widespread skeletal metastases within three months (Fig. 9).

It has been considered that the scan might provide more information than the X-ray regarding the extent of a primary bone tumour. However, the extent or boundary of the tumour is frequently obscured by a non-specific uptake in adjacent bone, possibly related to regional hyperaemia [44]. Such hyperaemia may indeed be noted to extend throughout the affected limb in a variety of bone lesions, malignant and benign. Goldman and Braunstein [19] reported increased radionuclide uptake in either the affected or unaffected limb in 10 of 13 patients with osteogenic sarcoma. In five of these, histological examination of such abnormal areas failed to identify tumour cells. It was postulated that the abnormal uptake might reflect the increased vascularity of the tumour or be related to early disuse osteoporosis, similar to the increased activity in bone scans which may be observed in regional migrating osteoporosis.

Benign bone tumours rarely demonstrate hyperaemia in the blood pool study and special views are often required to demonstrate the abnormal uptake. The effort can, however, be rewarding, identifying lesions causing bone pain such as osteoid osteoma (Fig. 10) [20]. Gilday and Ash [16] reported that the bone scan revealed 19 examples of this lesion, only 14 of which could be detected radiologically, even with tomography. This was most frequently encountered with osteoid osteoma of the spine and has been reported also in osteoblastoma of the axial skeleton [28]. Osteochondromata generally are visualised only by the bone scan when at the site of bone growth (Fig. 11). Multiple endochondromatoses are identified readily as numerous focal areas of increased uptake [2], the scan usually serving to detect areas not appreciated radiologically. Since up to 27% of patients with cranio-facial fibrous dysplasia have at least one other site of skeletal involvement, scintigraphy can be useful to assess the extent of this disorder, visualised as being extremely hyperaemic and associated with avid uptake of the radiopharmaceutical (Fig. 12), [11, 47]. Similar but widespread abnormalities are demonstrable in polyostotic fibrous dysplasia (Fig. 13).

It is unusual for any significant abnormality to be demonstrated with bone cysts unless following trauma, such as fracture, which results in increased focal accumulation and may be identified with greater sensitivity by scanning than radiologically. We have observed an aneurysmal bone cyst which did induce sufficient bone reaction to permit visualisation and indeed, with the sequential study, demonstration of expansion of the lesion (Fig. 14).

Table 1. Bone scan demonstration of metastases in 1° bone tumour

	Gilday et al. [31]	Present series
Osteogenic sarcoma	7/19	8/35
Ewing's sarcoma	2/8	8/20
Chondrosarcoma	1/1	0/8
Fibrosarcoma	0/2	1/4
	10/30	17/67

Metastatic Disease

Bone scanning is unquestionably more sensitive in detecting early osseous disease than radiological skeletal survey. In most reviews, the scan has identified metastases not visualised by X-ray in over 30% of adults with malignant disease [5]. This sensitivity appears to be even greater in children since Gilday et al. [17] in a study of 159 children with a variety of malignant disorders, found that metastases were present in 44, 68% being detected by the scan only. Detection of metastatic disease is particularly important in children with primary bone tumours and a skeletal radionuclide survey should be mandatory in all such patients. Gilday et al. [17] identified metastases in 10 of 30 children with primary tumours while we have found distant disease in 17 of 67 patients (Table 1).

It is obvious that diagnosis of metastatic disease will affect therapy. This is particularly relevant in osteogenic sarcoma. McNeil [29] has commented on the experience of the Sidney Farber Cancer Institute. In a 10 year period, 2% of children presenting with osteogenic sarcoma had distant bone metastases, including those with multi-focal osteosarcoma. In our series, 3 of 35 had distant bone lesions at presentation and 5 of 18 in whom sequential scans were performed developed bone metastases. Pulmonary metastases were evident at presentation in two children but developed in another 15 of 24 cases in whom there has been follow-up for an adequate period in this hospital. In 3 of the 18 children who developed pulmonary or skeletal lesions and underwent serial scans, the bone metastases are detected prior to or in the absence of the lung metastases. This incidence (17%) is similar to the 15% encountered in the Boston study. McNeil emphasises that this reflects the increasing effectiveness of adjuvant therapy. Thus, prior to the current forms of treatment, 75% of their patients developed

lung metastases in the 1st year and 50% later developed bone metastases [25]. However, in the past five years, 50% developed lung metastases while 75% of these also developed bone metastases. Accordingly, McNeil suggested that all children presenting with osteogenic sarcoma should have a bone scan at presentation and if on adjuvant therapy, follow-up studies every six months for the first two years.

A similar regime should be employed with Ewing's sarcoma. In 20 cases studied by us, two had multiple bone lesions at presentation and six others subsequently developed bone metastases. Lung metastases were diagnosed in 11, including 2 at presentation, but in 5 of these, skeletal lesions were present either before or in the absence of pulmonary metastases. In the Sidney Farber Cancer Institute series [29], bone metastases were demonstrated in 3 of 26 patients at presentation and in the follow-up period, occurred in 1/3. In over 50%, these were detected in the absence of or before lung metastases.

The sensitivity of scintigraphy in detection of metastases has, in children, been of value in a variety of malignant disorders, for example, Wilm's tumour. Howman-Giles et al. [23] have reviewed the results in 49 patients with neuroblastoma Skeletal metastatic disease was detected in 29. In 20 children investigated by us, metastases in bone were detected in 10 and Sty et al. [38] reported bone metastases in 7 of 13 cases. The metastatic deposits in this disorder may be disseminated but, of course, typically involve the metaphysis of a long bone (Fig. 15). Accordingly, Howman-Giles and his colleagues [23] state that in children with neuroblastoma, whenever there is extension of uptake into the metaphyseal region with blurring of the growth plate, metastatic involvement should be considered. In their series a bone scan identified all but one of the lesions involving bone. Kaufman et al. [26] however, in an investigation of 12 children, found that in 6 of these a total of 18 lesions were present, 14 of which were only detected radiologically. These authors ascribe this to small lesion size, lytic radiological appearance, and the metaphyseal location. They emphasise the difficulties in imaging the knee and detecting small deposits close to the epiphyseal plate, particularly if photopenic and bilateral, as in 78% of the lesions in their series. Howman-Giles et al. however, found that metastases, when involving the metaphyses and epiphyses of long bones, were asymmetrical in 24 patients and symmetrical in 9. They did comment that in one case the lesions were photon deficient. We have on two occasions, noted this phenomenon in deposits in the sacroiliac region, associated with pelvic neuroblastoma. Spencer [37] has reported a case of neuroblastoma in whom not only was a lesion in the femoral head not seen, but the growth plate was associated with markedly diminished radiopharmaceutical accumulation suggesting that the lesion had compromised the blood supply or extended into the growth centres.

Generalised Paediatric Disease

Other disorders of children, in which the skeleton may be involved, also result in abnormal bone scans. In some instances, deposits in bone may provoke an osteoblastic reaction which will be demonstrated as areas of avid uptake while in others the infiltration may compromise the vascular supply and photopenic areas may result. The skeletal radionuclide survey can be useful to identify the extent of the disorder, which may alter the staging of the disease.

In the group of Histiocytosis X disorders, lesions may be well delineated (Fig. 16). Gilday et al. [17] found that in 19 children with Histiocytosis X, lesions in three were only detected by scanning. However, Antonmattei et al. [3] have drawn attention to the variability of scan changes in eosinophilic granuloma, reporting a case in whom the scan revealed areas of increased, normal, and decreased uptake. Some were seen with the scan and others by X-ray only. It seemed likely that the "cold" lesions and those with normal uptake were secondary either to bony destruction with very little residual viable bone or the result of inadequate osteoblastic reaction [18]. These factors may be responsible for the similar variability with which lesions are detected by bone scanning in leukaemia and lymphoma. However, intense uptake can be visualised in skeletal deposits in these disorders (Fig. 17). Gilday et al. [17] found that in three of nine children, the lesions due to leukaemia and lymphoma were identified by scan only and Schuechter et al. [35] reported that, in 26 patients, conventional radiology was normal in 35% of those with abnormal scans. Scanning did detect lesions in the absence of pain and serial studies reflected the response to chemotherapy.

Gaucher's disease also presents variable changes in bone scans. Gross focal abnormalities may result from pathological fractures but the infiltrative process may cause only a moderate increase. However, Cheng and Holman [6], in reporting one patient in whom there was decreased uptake in the femoral head, the site of recent pain, suggested that this reflected avascular necrosis, similar to the "bone crisis" of sickle-cell anaemia.

In contrast to such focal changes resulting from disseminated infiltrative paediatric disease, disorders of calcium metabolism result in bone scans with a generalised increase of the radiopharmaceutical

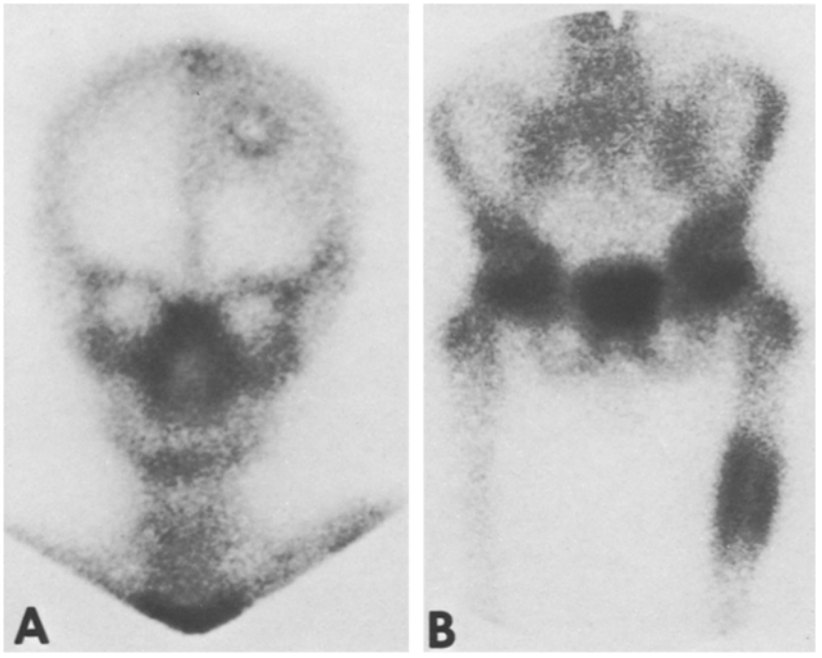


Fig. 16A and B. Scan appearances of Histiocytosis X. **A** Skull lesion in 5-year-old boy. **B** In femoral shaft of 7-year-old boy (compare with Ewing's tumour illustrated in Fig. 6A, with greater avidity and bone outline distortion)

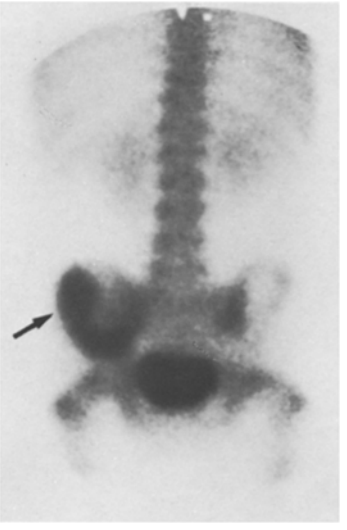


Fig. 17. Intense accumulation in ilium, indicating skeletal involvement by non-Hodgkin's lymphoma in a 4-year-old boy

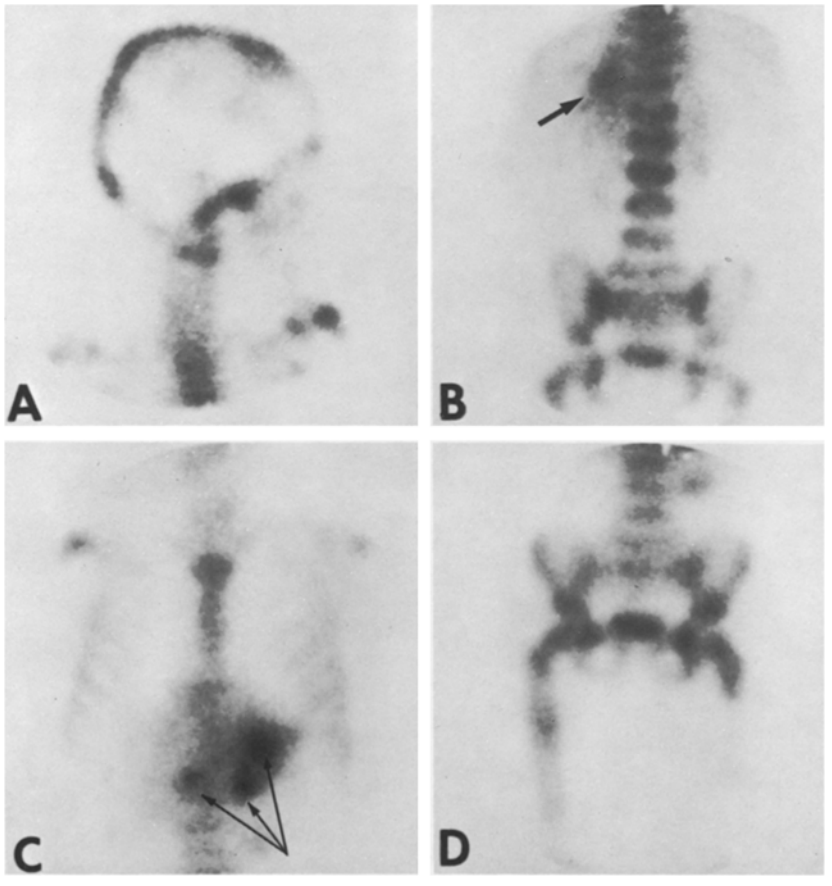


Fig. 18A–D. Scan findings in a $4^1/_2$-year-old boy with neuroblastoma. Multiple areas of focal accumulation throughout the skeleton (**A** and **D**) indicate metastatic deposits. Pyrophosphate uptake was present in the primary tumour in the left adrenal (**B**, *arrow*) and in multiple metastases in the liver (**C**, *arrowed*)

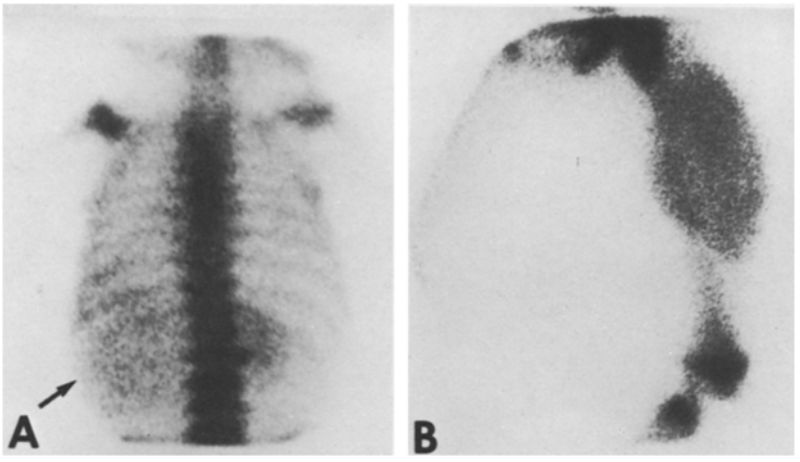


Fig. 19A and B. Accumulation of Tc-pyrophosphate in extra-osseous tumours **A** Rhabdomyosarcoma in a 3-year-old girl **B** Fibrosarcoma of the thigh in a 4-year-old boy

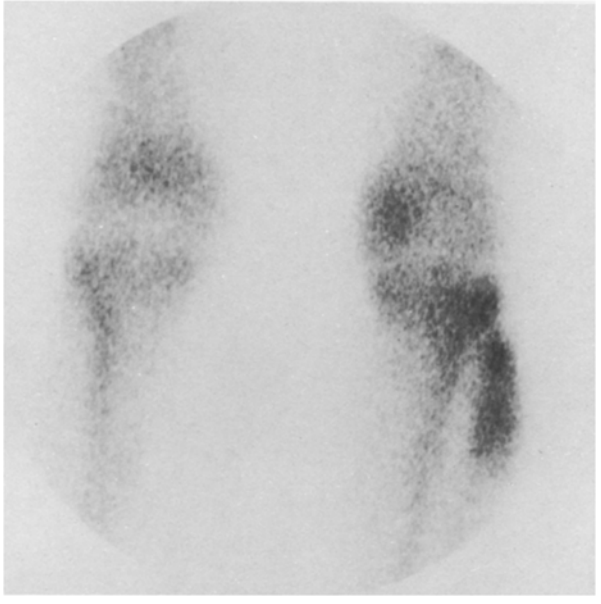
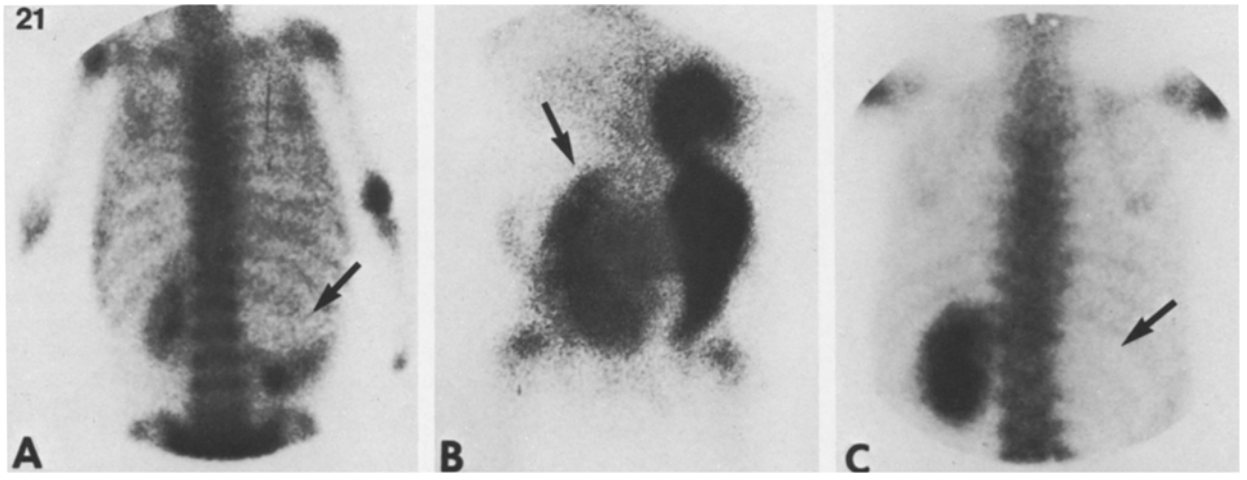


Fig. 20. Plexiform haemangioma; demonstrating some pyrophosphate uptake within the tumour, which was markedly hyperaemic in the blood pool study, but with more intense accumulation indicating involvement of the fibula

throughout the skeleton. Characteristic patterns of this avid accumulation may be noted in hyperparathyroidism [42] and osteomalacia [12]. In such disorders, increased diagnostic information can be obtained by quantification of the fate of the phosphate complexes [22]. In a youth with hypophosphataemic vitamin-D resistant rickets, Harcke [21] observed gross increase in uptake at growth centres with a return to a more balanced distribution of activity following therapy. Fogelman et al. [13] studied two children with this disorder, finding scintigraphic changes similar to those in renal osteodystrophy [8]. It is however, very difficult in children to assess the presence of increased uptake in the costo-chondral junctions, a typical find-

Fig. 21A–C. Urinary tract abnormalities noted on bone scanning. **A** Displacement of the right kidney downwards and lateral by neuroblastoma in which there is no pyrophosphate accumulation. **B** Retention of radioactive urine in mega-ureter resulting from obstruction by pelvic neuroblastoma in which there is pyrophosphate uptake (*arrow*). **C** Total absence of pyrophosphate accumulation in the right kidney in an 8-year-old girl, presenting with a loin mass which was subsequently demonstrated to be a Wilm's tumour



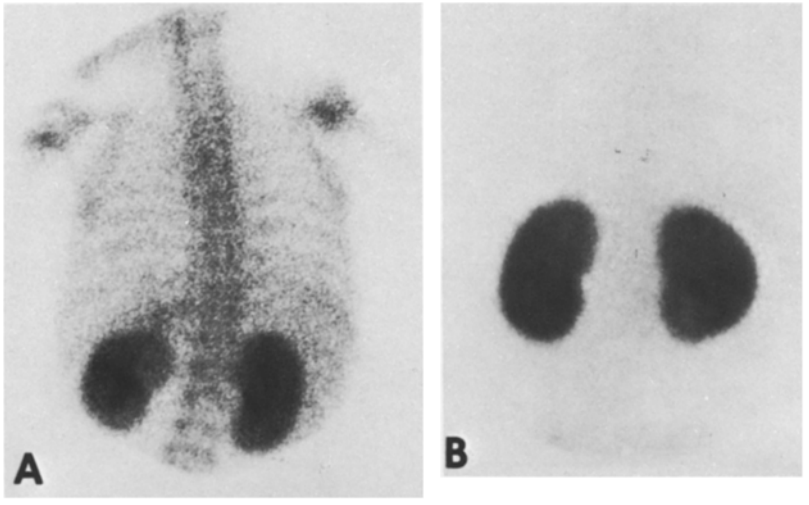


Fig. 22A and B
A Sequential scan in the child shown in Fig. 18 demonstrating "hot kidneys" following chemotherapy of neuroblastoma and regression of the multiple skeletal metastases
B Gross renal accumulation and markedly reduced bone uptake of pyrophosphate associated with iron overload, resulting from repeated transfusions, in a 14-year-old boy with thalassaemia major

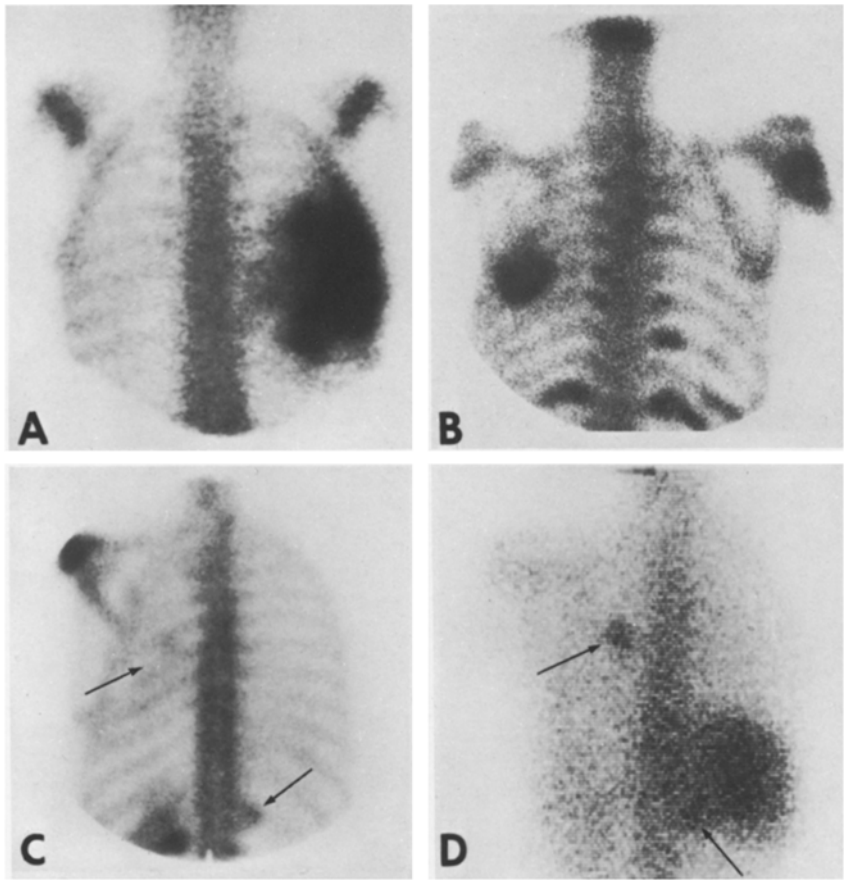


Fig. 23A–D
A Gross uptake in the chest associated with an unusual osteogenic sarcoma arising from the ribs in a 4-year-old girl
B In a 20-year-old male with an osteogenic sarcoma, evidence of avid pyrophosphate uptake in multiple skeletal lesions and in a large pulmonary metastasis
C Less avid but identifiable pyrophosphate uptake in the lungs of a 15-year-old boy who had previously undergone fore-quarter amputation for an osteogenic sarcoma in the right humerus
A second focal area of uptake is present in the right renal bed
D Uptake of gallium-67 in the metastases noted in C

ing in adults with primary or secondary hyperparathyroidism, since preferential uptake in these sites usually persists physiologically until at least 16 years of age.

Extra-Osseous Uptake

In the course of performing a radionuclide bone study, uptake of the bone-seeking radiopharmaceutical may be identified in extra-osseous sites. A large variety of lesions, malignant and benign, may be associated with such uptake [31]. In particular there may be uptake in non-osseous metastases, such as illustrated in Figure 18, a child with neuroblastoma in whom avid accumulation is visualised, not only in the widespread bone metastases, but also in hepatic metastatic deposits. It may also be noted that focal

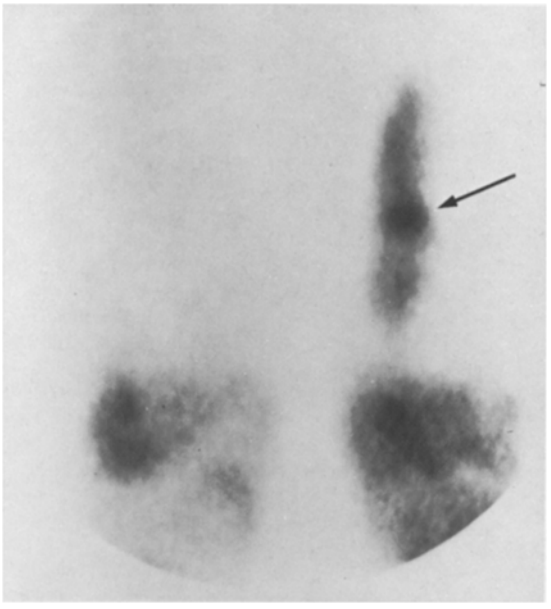


Fig. 24. Pyrophosphate uptake in myositis ossificans in the thigh, developing in an 18-year-old youth following prolonged immobilisation after multiple fractures. Note the focal area of uptake suggesting "fracture" of the ectopic calcified mass

uptake occurred in the primary lesion situated above the left kidney. Such uptake in the primary lesion has been observed in many children with neuroblastoma. Sty et al. [38] reported demonstration of the tumour in all of 13 children with neural crest tumours but Howman-Giles and co-workers [23] found uptake in the primary lesion in 17 (35%) of 49 cases of neuroblastoma. We have identified primary tumour accumulation in only 5 of 16 children studied preoperatively. Howman-Giles et al. [23] commented that since they had not seen such primary tumour uptake in any soft-tissue malignancies, they considered that primary tumour uptake in the paediatric age group was almost pathognomic of neural crest tumours. We have, however, noted it in other tumours, e.g. rhabdomyosarcoma and fibrosarcoma (Fig. 19). Abnormal scans in other soft-tissue tumours such as haemangiopericytoma and plexiform haemangioma (Fig. 20) have usually been the result of extension and involvement of bone.

Howman-Giles and co-workers [23] also drew attention to their findings that in 17 of their series in whom the primary tumour was in the abdomen, evidence of obstruction or displacement of the adjacent kidney was present and in three cases there was no visualisation of the left kidney. We found similar abnormalities in 8 of 14 children with abdominal neuroblastoma. An extreme example is shown in Figure 21, in which not only is uptake shown in the large pelvic neuroblastoma, but also gross accumulation in the megaureter produced by obstruction. Such abnormalities do, of course, reflect the renal excretion of the proportion of the technetium bone agents not bound to bone. Vieras and Boyd [46] have reported the variety of renal pathology which may be either incidentally found in the course of bone scanning or which provided additional information regarding the disorder under investigation. Sty et al. [39] have, in particular, reviewed the urinary tract abnormalities which may be observed in paediatric oncology noting that such changes were present in 26 of 177 children (15%). They described five distinct scintigraphic patterns; bilateral renal enlargement, bilateral increased renal accumulation ("hot kidney"), focal renal defects, renal size discrepancies, and obstructive uropathy. The "hot kidney" (Fig. 22) was first described by Lutrin et al. [27] who observed this phenomenon in 17 children in whom bone scans were performed within one week following chemotherapeutic drugs. We have also observed this phenomenon (Fig. 22) in a 14-year-old boy with thalassaemia major for which he had received blood transfusions. Similar gross renal uptake associated with iron overload has been described in adults by Parker et al. [32].

Bone imaging agents have also been noted to concentrate in the pulmonary metastases of osteogenic sarcoma [15]. Recently Siddiqui et al. [36] reported

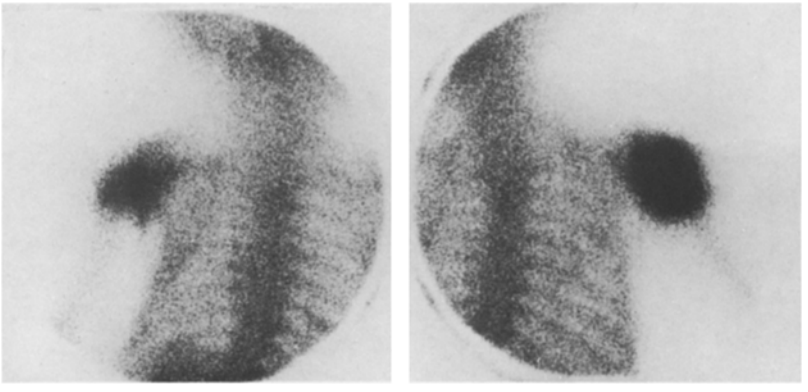


Fig. 25. Intense pyrophosphate accumulation in the ectopic calcification in a 3-year-old girl with tumoral calcinosis

this finding in five consecutive cases of osteogenic sarcoma, in two of whom radiographs were normal. Gilday et al. [17], however, commented that lung metastases have to be extremely large to be apparent on the bone images. We have only identified uptake in pulmonary lesions in 4 of 14 children with radiological evidence of lung metastases, similar to the experience of Hughes et al. [24] who noted such uptake in three of eight patients. These metastases may also be detected with gallium-67 citrate (Fig. 23) which has been found to be of value in the investigation of the other neoplastic disorders of childhood with the exception of neuroblastoma [4, 9] and as an adjunct to therapy [49].

Other causes of extra-osseous accumulation of the technetium phosphate complexes peculiar to children include neonatal fat necrosis [48] and McArdle syndrome [41] in which intense muscle uptake may be observed following exercise tests. Increased accumulation in early and late subperiosteal haematoma, reflecting the subperiosteal reaction, has been described in two children with scurvy [14].

Ectopic calcification, such as myositis ossificans (Fig. 24) will be associated similarly with uptake of the bone-seeking radiopharmaceuticals. Intense accumulation can be observed in tumoral calcinosis (Fig. 25) and Abbud et al. [1] have suggested that sequential studies may be useful in following the progression of the lesions in response to therapeutic measures.

Acknowledgements. The author wishes to thank Miss J.A. Tatham, Nuclear Medicine Technician, for her continued and enthusiastic assistance in all aspects of the preparation of this review. He also thanks Dr. W.L. Ashburn, University Hospital, San Diego, California, for permission to include Figure 13, and Dr. J.J. Burke, St. George Hospital, Kogarah for Figures 11 and 25; the Department of Medical Illustration, University of New South Wales and Teaching Hospitals, for assistance in preparation of the illustrations; and Mrs. Daphne Williams for her secretarial assistance.

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