

RADIOTECHNETIUM POLYPHOSPHATE JOINT IMAGING

M. Desaulniers, A. Fuks, D. Hawkins, Y. Lacourciere, and L. Rosenthal

The Montreal General Hospital, Montreal, Quebec, Canada

An assessment of the efficacy of ^{99m}Tc -polyphosphate ($^{99m}\text{TcPP}$) in the disclosure of synovitis in 27 patients is presented. A comparison was made between $^{99m}\text{TcPP}$, clinical evaluation, $^{99m}\text{TcO}_4$, and radiography. In general $^{99m}\text{TcPP}$ was found to be more sensitive in the detection of inflammatory synovitis in peripheral joints than the other three methods, but it is also non-specific as increased periarticular accretions were found in degenerative osteoarthritis, metabolic bone disease, and trauma. Although $^{99m}\text{TcPP}$ joint imaging qualifies as a screening procedure, regions of increased uptake should be radiographed to determine whether other causative factors exist.

Joint imaging employing a variety of radiopharmaceutical agents has been used as an adjunctive tool for the detection of inflammatory joint disease. Radioiodinated albumin was used originally (1) but the introduction of the radionuclide ^{99m}Tc resulted in the application of radiopertechetate ($^{99m}\text{TcO}_4$) and ^{99m}Tc -labeled human serum albumin (2) as the test agents of choice. The physical properties of these latter agents render a relatively low radiation absorbed dose for a high photon flux and thus considerably improve the quality of the joint images compared with ^{131}I -albumin. The radiopharmaceutical ^{99m}Tc -polyphosphate ($^{99m}\text{TcPP}$) has been used for the detection of osseous lesions in a variety of conditions. Because of the frequent involvement of periarticular and subchondral bone in the inflammatory arthritides, a preliminary study was designed to assess the utility of $^{99m}\text{TcPP}$ in the detection of joint disease and to compare its sensitivity with that of $^{99m}\text{TcO}_4$.

METHODS AND MATERIALS

Patients. Twenty-seven patients were selected at random from the outpatient population attending the

Rheumatology Clinic and from patients referred to the Rheumatology Service at the Montreal General Hospital. They varied in age from 21 to 66 years and their diagnoses are listed in Table 1. Initial studies were restricted to patients with evidence of inflammatory joint disease. A joint was considered clinically involved if swelling, warmth, tenderness, effusion, or pain on motion were present. This evaluation was made by the staff of the Rheumatology Service prior to radiographic and radionuclide studies.

Radiographic evaluation. A full radiographic survey consisting of examination of hands, wrists, feet, ankles, os calces, and sacroiliac joints was done in 22 of the 27 patients. Radiographic criteria of joint involvement were cartilage space narrowing, erosive bone changes, soft-tissue swelling, and deformity. Interpretation of the roentgenograms was made independently of the clinical information and without knowledge of the nucleographic results.

Radionuclide imaging. Fifteen millicuries of either $^{99m}\text{TcPP}$ or $^{99m}\text{TcO}_4$ were injected intravenously and imaging was performed with the scintillation camera. Nucleography was started 30 min after the administration of $^{99m}\text{TcO}_4$ and 2 hr after $^{99m}\text{TcPP}$. A total of 200,000 counts was accumulated for one shoulder and the time to reach this number was preset for the opposite shoulder, the elbows, hands, wrists, knees, ankles, and feet. The entire examination took approximately 1 hr. The radionuclide criterion for a positive image was a higher concentration of activity in the joint region relative to adjacent nonarticular bone. In effect, each patient served as his own control.

The independently accumulated clinical, radio-

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For reprints contact: Leonard Rosenthal, Div. of Nuclear Medicine, The Montreal General Hospital, 1650 Cedar Avenue, Montreal 109, Quebec, Canada.

TABLE 1. DIAGNOSES AND NUMBER OF PATIENTS

Diagnosis	Number of patients
Rheumatoid arthritis	13
Seronegative polyarthritis	4
Psoriatic arthritis	5
Reiter's syndrome	1
Behcet's syndrome	1
Gout	1
Infectious arthritis	1
Pulmonary osteoarthropathy	1
Total:	27

TABLE 2. COMPARISON OF CLINICAL ASSESSMENT AND $^{99m}\text{TcPP}$ IMAGING

		Clin +ve	Scan +ve	Scan +ve Clin -ve	Clin +ve Scan -ve
Shoulder	Right	8	4	0	4
	Left	10	3	0	7
Elbow	Right	7	5	1	3
	Left	7	5	1	3
Wrist	Right	16	22	6	0
	Left	14	22	8	1
Hand	Right	20	24	4	0
	Left	19	24	5	0
Hip	Right	1	1	0	0
	Left	0	0	0	0
Knee	Right	11	6	0	5
	Left	14	7	0	7
Ankle	Right	12	18	7	1
	Left	12	17	6	1
Foot	Right	7	17	11	1
	Left	6	16	10	0
Total:		164	191	59	33

graphic, and radionuclide data for each patient were collated at the completion of the investigation.

Of the 27 patients who had $^{99m}\text{TcPP}$ joint nucleography prior to therapy, 16 had repeat studies between 2 and 4 months after the initiation of active therapy.

A comparison of $^{99m}\text{TcO}_4$ and $^{99m}\text{TcPP}$ was possible in 16 patients. The radiopharmaceuticals were administered within 5 days of each other and before active treatment of the joint disease was initiated.

RESULTS

Clinical assessment versus $^{99m}\text{TcPP}$ imaging. All 27 patients studied had clinical and $^{99m}\text{TcPP}$ evaluations. The results are shown in Table 2. Nucleographic examination disclosed a total of 189 affected joints compared with 162 noted clinically. Positive scans were obtained in a total of 58 joint regions which were judged to be normal clinically. Of these, 33 were in the feet and ankles. On the other hand, a clinically affected joint region was not disclosed by radionuclide imaging in 33 instances.

As noted in Table 3, of 27 patients examined, 19 had more lesions by $^{99m}\text{TcPP}$ imaging than by clinical examination. Seven had the same number and location of "positive" joints and in only one case were more joints judged to be affected by clinical examination than by $^{99m}\text{TcPP}$ imaging.

$^{99m}\text{TcPP}$ imaging versus radiographic assessment.

The results are shown in Table 4. Positive scans were obtained in 73 joint regions in which the radiographic features of arthritis were lacking. There were eight joint regions judged to be abnormal radiologically that were normal by $^{99m}\text{TcPP}$.

Comparison of $^{99m}\text{TcO}_4$ and $^{99m}\text{TcPP}$ imaging.

Sixteen patients were examined by both $^{99m}\text{TcO}_4$ and $^{99m}\text{TcPP}$ modalities (Table 5). The $^{99m}\text{TcO}_4$ imaging in 12 patients yielded fewer positive joint regions than were involved clinically. In two patients the $^{99m}\text{TcO}_4$ scan revealed more affected joints than were recognized clinically. The results in the same 16 patients when examined with $^{99m}\text{TcPP}$ were strikingly different. No patient had fewer positive areas with $^{99m}\text{TcPP}$

TABLE 3. COMPARISON OF CLINICAL ASSESSMENT AND ^{99m}Tc -POLYPHOSPHATE RESULTS

	Number of patients
Same number and location of lesions by scan and clinical examination	7
More lesions on scan than clinical examination	19
More lesions on clinical examination than scan	1
Total:	27

TABLE 4. COMPARISON OF $^{99m}\text{TcPP}$ IMAGING AND RADIOGRAPHIC ASSESSMENT

		X-ray +ve	Scan +ve	X-ray +ve Scan -ve	Scan +ve X-ray -ve
Shoulder	Right	1	3	0	2
	Left	1	2	1	2
Elbow	Right	0	5	0	5
	Left	0	5	0	5
Wrist	Right	9	19	0	9
	Left	10	18	0	9
Hand	Right	12	19	0	7
	Left	12	18	0	5
Hip	Right	1	1	0	0
	Left	0	0	0	0
Knee	Right	3	4	1	2
	Left	3	5	1	3
Ankle	Right	9	16	1	8
	Left	11	15	2	6
Foot	Right	10	14	1	5
	Left	10	14	1	5
Total:		92	158	8	73

TABLE 5. COMPARISON OF CLINICAL ASSESSMENT AND RESULTS OF $^{99m}\text{TcO}_4$ AND $^{99m}\text{Tc-PP}$ IN 16 PATIENTS WITH ARTHRITIS

Radiopharmaceutical	Number of patients showing same number of affected joints as with clinical assessment	Number of patients showing more affected joints than by clinical assessment	Number of patients showing fewer affected joints than by clinical assessment
$^{99m}\text{TcO}_4$	2	2	12
$^{99m}\text{Tc-poly-phosphate}$	1	15	0

TABLE 6. COMPARISON OF CLINICAL ASSESSMENT AND $^{99m}\text{Tc-PP}$ RESULTS FOLLOWING TREATMENT

	Number of patients
Clinically improved* and scan improved	6
Clinically improved and scan unchanged	3
Clinically improved and scan worse†	1
Clinically unchanged and scan improved	0
Clinically unchanged and scan unchanged	1
Clinically unchanged and scan worse	4
Clinically worse and scan improved	0
Clinically worse and scan unchanged	0
Clinically worse and scan worse	1
Total:	16

* Improved denotes fewer lesions recorded relative to pretreatment assessment.

† Worse denotes more lesions recorded relative to pretreatment assessment.

compared with clinical assessment, and, in fact, 15 patients had more positive areas by imaging.

Pre- and post-treatment $^{99m}\text{TcPP}$ joint studies. Sixteen patients were scanned both before and 2–4 months after initiation of full and active therapy. The results are shown in Table 6. Clinical and nucleographic evaluations of change of joint status were concordant in 8 of the 16 patients. The scans in four patients were unchanged or worse despite definite clinical improvement. In four other patients who were clinically unchanged, the scan was worse. No patient whose clinical status was unchanged or showed extension of disease had improvement in the $^{99m}\text{TcPP}$ joint study.

CASE REPORTS

Case 1. This patient had infectious arthritis of the left knee. Radiography showed moderate demineralization about the left knee joint and an effusion. All other joints were normal by x-ray and clinical examination. The $^{99m}\text{TcPP}$ joint survey (Fig.

1) demonstrates a much higher concentration in the periarticular bones of the inflamed left knee joint relative to the right. Note the normal periarticular uptake of $^{99m}\text{TcPP}$ of the shoulders, elbows, hands, wrists, and ankles.

Case 2. The clinical examination of this patient with rheumatoid arthritis in March 1973 disclosed joint inflammation of the shoulders, wrists, hands, knees, and right first metatarsal-phalangeal joint but the ankles were normal. Radiography only showed involvement of both wrists and the third and fourth metacarpal-phalangeal joints of both hands. The $^{99m}\text{TcPP}$ joint survey of March 22, 1973 exhibited

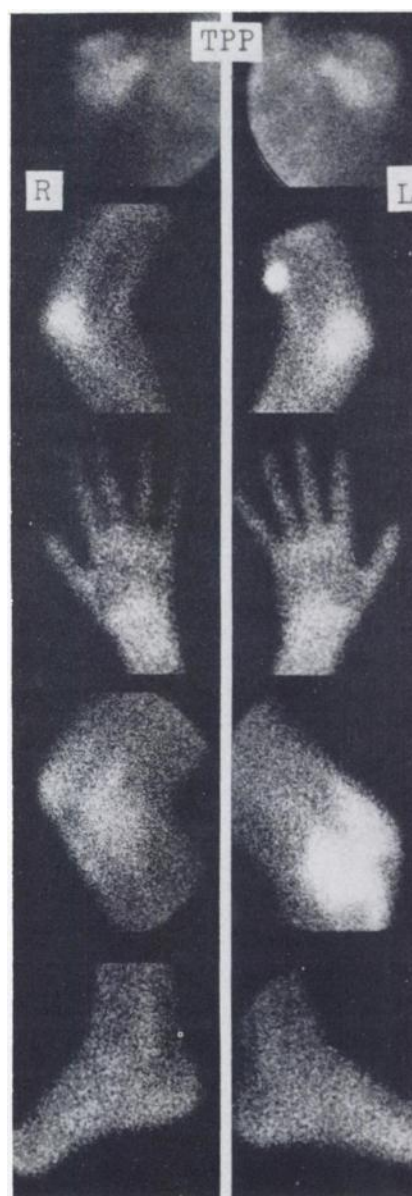


FIG. 1. Case 1. Infectious arthritis of left knee. From above down: shoulders, elbows, hands and wrists, knees and ankles. Increased uptake in periarticular bones of left knee. All other joints illustrated are normal.

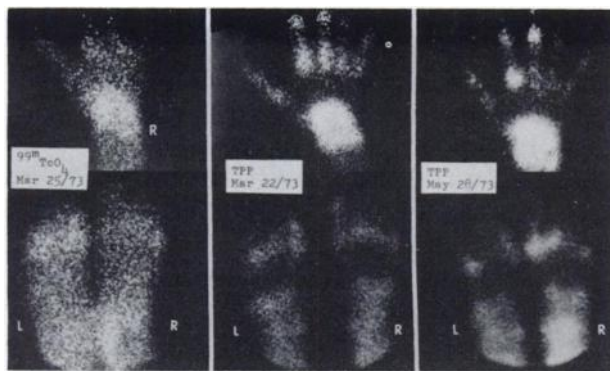


FIG. 2. Case 2. Rheumatoid arthritis. Right hand and both feet and ankles are illustrated. Comparative study of $^{99m}\text{TcPP}$ and $^{99m}\text{TcO}_4$ on 3/22/73 and 3/25/73, respectively, before active therapy of rheumatoid arthritis. Examination using $^{99m}\text{TcPP}$ on 5/28/73 during course of therapy showed regression of uptake in some joints and further accretion in others.

the same regional involvement as manifested clinically but, in addition, abnormal uptakes were registered in the ankles, tarsal joints, and the 1–4 metatarsal-phalangeal joints of the left foot and 1–5 metatarsal-phalangeal joints of the right foot (Fig. 2). When the patient returned on May 28, 1973 the hitherto normal ankles were hot and stiff on examination. The $^{99m}\text{TcPP}$ scans on that day showed regression of uptake in some of the joints of the hands and feet and an increase in others. A higher accretion was also present in the right ankle.

The $^{99m}\text{TcPP}$ scans of the right hand and feet (Fig. 2 illustrated) show more lesions than $^{99m}\text{TcO}_4$, and the lesions stand out with greater clarity.

Of interest in this case is that the $^{99m}\text{TcPP}$ study of March 22, 1973 anticipated the clinical manifestations of inflammatory disease of the ankles.

Case 3. A radiographic survey on December 12, 1972 was normal in this patient with psoriatic arthritis. Clinically there was inflammation of the left elbow, left wrist, and left ankle. The $^{99m}\text{TcPP}$ images

(Fig. 3) showed an abnormal accretion in the left ankle, left tarsals, and possibly the left elbow but the left wrist was normal. The absence of uptake in the left wrist represents an instance where the radionuclide image was not concordant with the clinical findings. The patient was placed on active therapy and the followup study on January 30, 1973 exhibited further accretion of $^{99m}\text{TcPP}$ in the left elbow, left ankle, and left tarsals. In addition, there were abnormal concentrations in the hitherto normal right ankle and tarsals, right wrist, and the distal interphalangeal joint of the left thumb. At this time clinical assessment revealed joint involvement of both ankles, right foot, and left elbow. The hands and wrists were normal in spite of the abnormal uptake of $^{99m}\text{TcPP}$ in the right wrist and DIP joint of the left thumb. Periosteal reactions were seen for the first time by x-ray at both ankles.

Case 4. A diagnosis of Reiter's syndrome was made in this 23-year-old male. There was clinical inflammatory disease of both ankles and about the distal phalanges of the big toes. Roentgenograms showed soft-tissue swelling and erosive bone changes of both these phalanges, more prominent on the right (Fig. 4A). Soft-tissue thickening was also noted in the right second toe and marked bone erosion was present at the site of the Achilles tendon attachment to the os calcis. Comparative $^{99m}\text{TcO}_4$ and $^{99m}\text{TcPP}$ studies (Fig. 4B) showed a much higher concentration of the latter in those joints visualized by both radiopharmaceuticals. In addition, the $^{99m}\text{TcPP}$ demonstrated more extensive involvement of the tarsal bones and a slight accretion in the left wrist and both metatarsal-phalangeal joints of the fifth toes. Note the normal $^{99m}\text{TcO}_4$ knee scan but the rather high equal uptake of $^{99m}\text{TcPP}$ which can be a source of difficulty in interpretation. The knees were normal clinically.

Case 5. A radiographic arthritic survey in this pa-

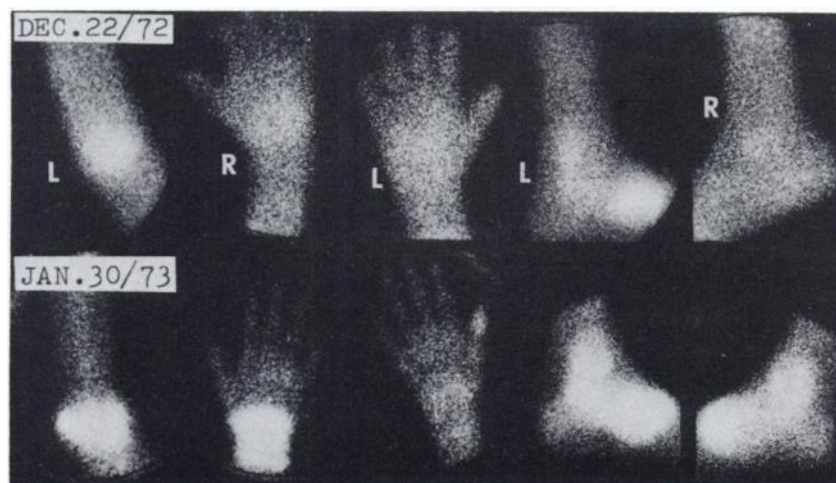


FIG. 3. Case 3. Psoriatic arthritis. Joint images with $^{99m}\text{TcPP}$ from left to right, of left elbow, right hand and wrist, left hand and wrist, left ankle and right ankle on 12/22/72 and 1/30/73. Patient was placed under full and active treatment after 12/22/72 and during 1/30/73 radionuclide study.

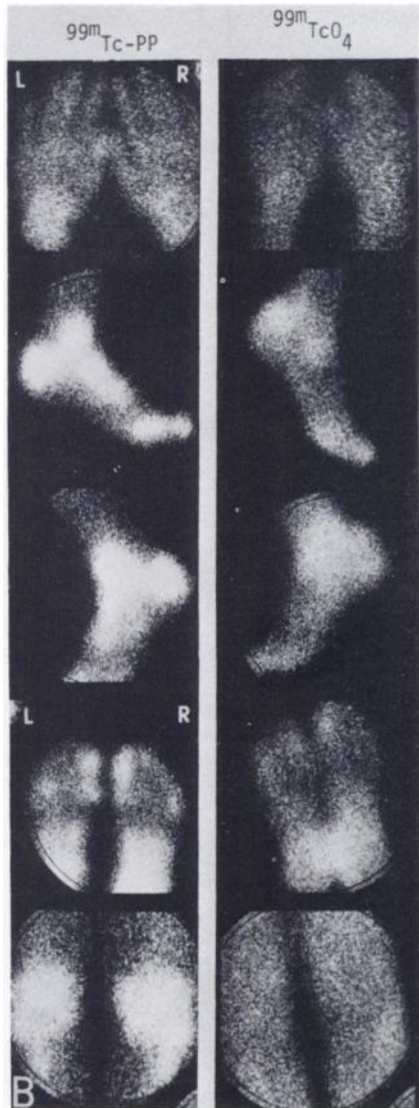
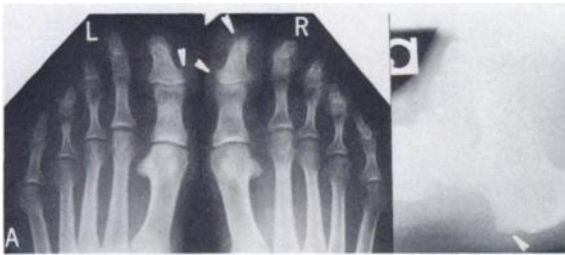


FIG. 4. Case 4. Reiter's syndrome. (A) Erosions are present at base of distal phalanx of left big toe (arrow), base and tuft of the distal phalanx of right big toe (arrows), and of os calcis at site of Achilles tendon attachment. (B) Comparative study of $^{99m}\text{TcPP}$ and $^{99m}\text{TcO}_4$ before initiation of medical treatment. Illustrated, from above downward, are hands, right ankle and foot, left ankle and foot, feet and knees.

tient with rheumatoid arthritis was negative save for degenerative osteoarthritis of the distal interphalangeal joints of the hands. Clinically, there was inflammatory involvement of the wrists and metacarpal-phalangeal joints bilaterally. The illustrated

right hand and wrist (Fig. 5) exhibit increased concentration in the inflamed joints with both $^{99m}\text{TcO}_4$ and $^{99m}\text{TcPP}$. The $^{99m}\text{TcPP}$ images also show an abnormal concentration in the third and fourth proximal interphalangeal joints which were not seen well with $^{99m}\text{TcO}_4$. Degenerative osteoarthritis of the distal interphalangeal joints of the first, third, fourth, and fifth digits are also portrayed with $^{99m}\text{TcPP}$ and not $^{99m}\text{TcO}_4$.

Case 6. A comparative radionuclide study in a patient with bilateral degenerative osteoarthritis of the hips is shown in Fig. 6B. The $^{99m}\text{TcPP}$ shows increased uptake at the affected joints whereas the $^{99m}\text{TcO}_4$ image is normal. A normal hip image with $^{99m}\text{TcPP}$ is illustrated in Fig. 6A for comparison.

Case 7. This 25-year-old female had a Billroth II subtotal gastrectomy 1 year ago. She presented with weight loss and aching pain in the legs. No clinical

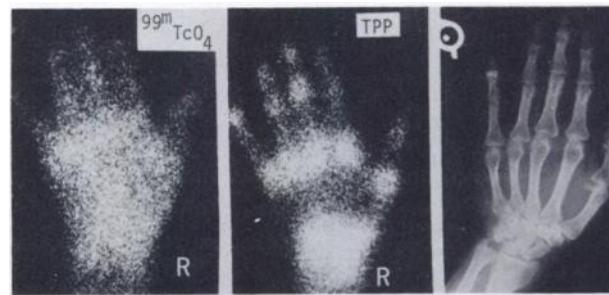


FIG. 5. Case 5. Rheumatoid arthritis. Comparison of $^{99m}\text{TcO}_4$, $^{99m}\text{TcPP}$, and x-ray of right hand and wrist. DIP joint changes in roentgenogram are secondary to osteoarthritis.

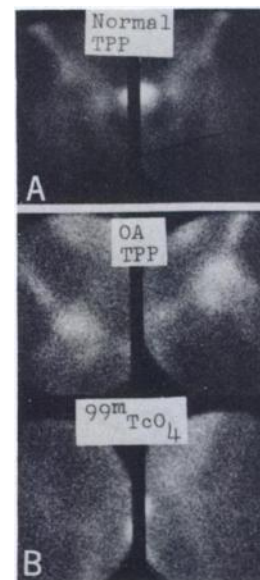


FIG. 6. Degenerative osteoarthritis of hips. (A) $^{99m}\text{TcPP}$ images of normal right and left hip. No abnormal uptake is registered. (B) Comparison images obtained with $^{99m}\text{TcPP}$ and $^{99m}\text{TcO}_4$ in patient with bilateral degenerative osteoarthritis of hips. Increased uptakes are present with $^{99m}\text{TcPP}$ but images are normal with $^{99m}\text{TcO}_4$.

evidence of synovitis was present except at the site of the fractured right ankle which was plated after several operations for nonunion. Serum calcium, phosphate, and alkaline phosphatase were normal. All joints demonstrated a high accretion of $^{99m}\text{TcPP}$ but were normal with $^{99m}\text{TcO}_4$, except for the synovitis near the fracture site (Fig. 7). An iliac crest biopsy specimen showed frank osteomalacia.

COMMENT

Cases 5, 6, and 7 demonstrate the lack of specificity of $^{99m}\text{TcPP}$. Its uptake in periarticular bone and cartilage is not limited to hyperemia secondary to inflammatory synovitis. Unlike $^{99m}\text{TcO}_4$, which visualizes for the most part only the inflamed synovium, the bone accretion of $^{99m}\text{TcPP}$ is increased in degenerative osteoarthritis, trauma, metabolic bone disease, infarction, etc. The sensitivity of $^{99m}\text{TcPP}$ qualifies it as a screening procedure for synovitis but all sites

of increased uptake should be radiographed to determine whether causes other than synovitis are present which may produce a positive image.

DISCUSSION

The present studies suggest that $^{99m}\text{TcPP}$ imaging is a much more sensitive method for the detection of inflammatory joint disease than radiography. It appears to be more sensitive than clinical evaluation in the disclosure of joint inflammation of the wrists, hands, ankles, and feet. In a number of instances, joint abnormalities visualized by $^{99m}\text{TcPP}$ preceded clinically evident exacerbations of these joints by several days to a week or two. This finding supported our initial hypothesis that increased uptake of $^{99m}\text{TcPP}$ did indeed reflect an inflammatory process. On the other hand, $^{99m}\text{TcPP}$ imaging was less sensitive than clinical assessment in the detection of shoulder, elbow, and knee involvement. Normally

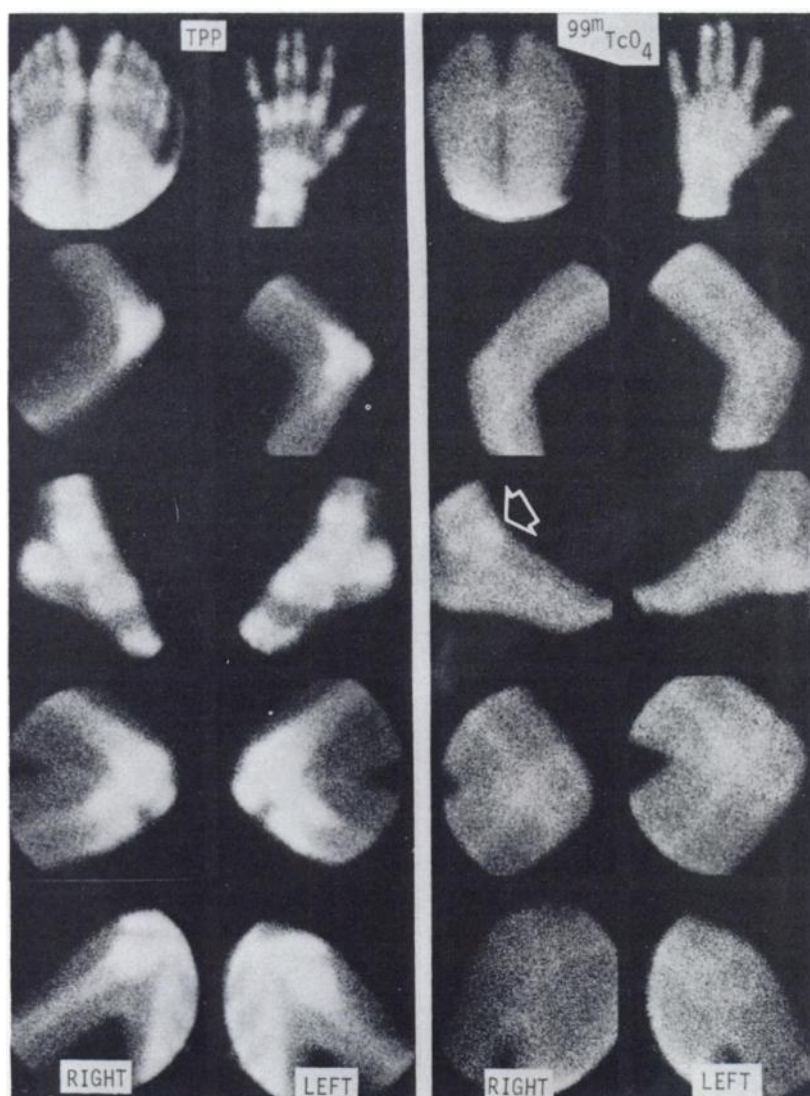


FIG. 7. Case 7. Comparative $^{99m}\text{TcPP}$ and $^{99m}\text{TcO}_4$ joint images of patient with osteomalacia. Arrow points to synovitis associated with fractured ankle.

there is some slightly increased uptake of $^{99m}\text{TcPP}$ in the region of large joints such as shoulders, elbows, and knees which is variable in degree from patient to patient and therefore analysis by ordinary visual means is difficult. When uptake of $^{99m}\text{TcPP}$ is unequal in paired joints, the diagnosis of unilateral involvement causes no difficulty. However, an abnormally high but equal concentration is more difficult to interpret.

Joint imaging with $^{99m}\text{TcPP}$ yielded more easily interpretable scans than with $^{99m}\text{TcO}_4$ because of the higher target-to-background ratios obtained. As noted in Table 5, $^{99m}\text{TcPP}$ imaging almost uniformly revealed more lesions than clinical examination and did not miss any lesions in this particular subgroup of patients. The $^{99m}\text{TcO}_4$ imaging, on the other hand, failed to reveal some clinically affected joints in 75% of the patients assessed.

Technetium-99m-polyphosphate is also useful in followup studies. Eight of 16 patients imaged before and during therapy showed concordant progression of scan and clinical course. In the other eight patients the scans continued to reveal disease despite clinical improvement or were worse without change of clinical status.

The reasons for these findings and for the discrepancies between $^{99m}\text{TcO}_4$ and $^{99m}\text{TcPP}$ imaging are probably related to the mechanism of accumulation of these radiopharmaceuticals at the sites of joint inflammation. The increased concentration of $^{99m}\text{TcO}_4$ at the site of joint inflammation is largely due to an increased vascular pool and extravascular accumulation in the thickened and inflamed synovium (3-5). Synovial fluid content of $^{99m}\text{TcO}_4$ is generally not sufficient to enhance appreciably the overall concentration and thus plays only a minor role (4). The increased uptake of $^{99m}\text{TcPP}$ at the joint site is most likely related to increased blood flow to bone secondary to the inflammatory syno-

vit. Juxta-epiphyseal and epiphyseal vessels arise from the synovial network to supply the epiphysis and metaphysis. Thus hyperemia surrounding an inflamed joint includes the periarticular bone. This hyperemia to bone, with or without pannus erosion of subchondral bone, leads to increased bone turnover with concomitant increased uptake of $^{99m}\text{TcPP}$ in the periarticular bone and renders a positive radionuclide image. There is very little contribution to the image from the inflamed soft tissues of the joint 2 hr after $^{99m}\text{TcPP}$ administration in the presence of normal renal function. The continued enhanced uptake of this radiopharmaceutical in clinically quiescent joints may be related to continued bone turnover secondary to pannus erosion, subclinical hyperemia, and inflammation or healing of the articular bone.

Surveys with $^{99m}\text{TcPP}$ are useful and recommended as the radiopharmaceutical of choice in: (A) screening patients with arthralgias for the presence of inflammatory disease, (B) documenting the sites and extent of inflammatory articular disease, (C) disclosing affected joints which are not clinically suspected and (D) in detecting extension of disease during followup.

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