

Three-Phase Bone Studies in Hemiplegia with Reflex Sympathetic Dystrophy and the Effect of Disuse

N. D. Greyson and P. S. Tepperman

St. Michael's Hospital and University of Toronto, Ontario, Canada

Eighty-five patients with cerebral vascular accidents were assessed with three-phase bone scintigraphy of the hands and with whole-body delayed bone imaging. Nine patients (10%) had normal three-phase bone images. Fifty-five patients (65%) showed decreased blood flow and blood-pool images of the hands and wrists with normal delayed bone scintigrams, indicating the effect of paralysis or disuse. Twenty-one patients (25%) had diffuse increased uptake with periarticular accentuation, felt to be bone-scintigraphic evidence of reflex sympathetic dystrophy of the hands and wrists; in two patients this occurred before its clinical appearance. Thirteen of the 21 reflex sympathetic dystrophy syndromes (RDS)-involved limbs (62%) had increased blood flow, whereas 8 (38%) had decreased flow. Gross limb blood flow appears to be related to the degree of muscle activity, but flow may be altered by the presence of sympathetic changes. A possible dissociation between whole-limb flow and bone blood flow in paralyzed limbs involved with RDS is discussed. The elbow was involved in only one case, and a true "shoulder-hand" distribution was seen in only 11 of 21 cases (52%). Five patients (6%) had leg involvement on whole-body imaging. Traumatic synovitis of the wrist, and trauma to subluxed shoulders, could be recognized on the delayed study.

J Nucl Med 25: 423-429, 1984

Although cerebrovascular accident (CVA) is not, per se, an indication to perform bone scintigraphy, bone and joint symptoms and clinical complications that may affect this condition sometimes necessitate radionuclide bone imaging. These patients frequently develop reflex sympathetic dystrophy syndromes (RSD) and the paralyzed extremity may be subjected to injury.

Radionuclide imaging of the extremities has been applied to a variety of arthritic problems (1-3), using [Tc-99m]pertechnetate "joint images" to show the periarticular soft-tissue blood pool, and Tc-99m-labeled bone-seeking phosphate derivatives (MDP), or both. Some publications have looked specifically at RSD (4-7), the effect of paralysis on bone uptake (8), and the

postsympathectomy effect (9). The purpose of this study was to look systematically at a large group of patients and to determine the radionuclide bone-image patterns occurring in them. In addition, the bone studies in this group of hospitalized CVA patients might help to explain some of the mechanisms of radionuclide uptake by bone, and to demonstrate the effect of limb disuse on a bone image.

PATIENT POPULATION

We reviewed 85 patients, 48 males and 37 females, all coincidentally right-handed, aged 29 to 91 yr, presenting with documented CVA (thrombosis, embolism, or hypertensive cerebral hemorrhage). Diagnosis was made through clinical assessment, history, radionuclide brain images, and/or TCT scans.

All patients were admitted to the hospital 2 to 20 wk

Received Feb. 17, 1983; revision accepted Oct. 11, 1983.

For reprints contact: N. D. Greyson, MD, FRCP(C); St. Michael's Hospital, 30 Bond St., Toronto, Ontario M5B 1W8.

following onset of CVA. The population is thus slightly biased in that this group of patients had severe symptoms and required hospitalization for rehabilitation.

Three-phase bone studies were performed within 48 to 72 hr of admission.

All patients were given a thorough admission history and physical examination, and were repeatedly reevaluated during their hospital treatment. We noted carefully whether articular disease and signs and symptoms of RSD existed at the initial presentation. These included pain and swelling, limitation of motion, edema, trophic skin changes, and vasomotor changes in the hands (10). All upper-extremity joints were assessed to detect subluxation or synovitis. Patients with known preexisting arthritis were excluded.

IMAGING TECHNIQUE

On the a priori assumption that most changes would be demonstrable in the upper extremities, comparative flow studies of the hands were performed. On the day of the bone study, physiotherapy was delayed until after the study to remove any possible exercise effect. Each patient included in the series had one or more three-phase bone images utilizing 15–20 mCi (550 to 740 MBq) of Tc-99m MDP.

The three-phase images consisted of a series of 5-sec sequential images immediately after the i.v. injection, blood-pool images 1–5 min after injection, and 2-hr-delayed spot views of the hands. When possible, both

No. of patients	Delayed	Blood flow	Diagnosis
3	N	N	normal
6	N	decreased (artifact)	normal
55	N	decreased	disuse
8	increased	decreased	RSD with disuse
13	increased	increased	RSD

hands were included on the same image. Otherwise, individual views of each hand were taken for the same time to provide a comparison of the relative blood pool or uptake in each hand. Spot films of both hands were followed by a whole-body image using a moving-bed apparatus.

RESULTS

Normal three-phase images of hands. (Table 1). Three patients showed the normal bone-image findings of the hand and wrist, as already described (2,3,11). In these three there was marked variation in the general quality of the images. Due to the age of most patients, overall poor bone metabolism could result in poor definition of the bones. Peripheral osteoarthritis, not related to the CVA, was a common finding. When there was no hyperemia, and the delayed image showed focal peri-



FIG. 1. Pattern of paralysis (right side). (A) Decreased flow to right hand (arrow), compared with normal left hand. (B) Blood-pool image of hand, showing decreased blood pool particularly in muscle bulk of thenar and hypothenar eminences, due to decreased metabolic demands of disused muscles. (C) Delayed bone study showing normal distribution of activity, with symmetrical uptake.

articular uptake in one or more peripheral joints of the hand or fingers or base of the thumb, this was thought to represent degenerative osteoarthritis and was not considered significant.

Normal delayed bone study with decreased flow and pool (Fig. 1). The most common finding (55 patients) was asymmetric decreased blood flow and reduced activity on the blood-pool image correlating with the side of the paralyzed limb. In addition to the quantitative difference in intensity on both flow and pool images, there was a qualitative difference in the appearance of activity in the early phases. There was a more homogeneous appearance of the hands with a less pronounced "palmar arcade" pattern of flow, and the blood-pool image showed less difference between the cool wrist activity and the blood-pool in the thenar and hypothenar eminences. There was occasional accentuation of the fingertips, possibly due to soft-tissue congestion.

In only a few patients with profound paralysis, the delayed image showed slight decreased uptake on the affected side, perhaps reflecting a loss of bone mass in association with atrophy of disuse.

In six patients with nearly normal delayed studies, the blood-flow and blood-pool images demonstrated less activity on the affected side, where the pattern of flow and pool differed from normal only in relative intensity. This asymmetric flow appeared to be due to relative increase on the unaffected side and may be an artifact of injection, possibly due to reactive hyperemia following removal of the tourniquet. Assuming this, we include these six patients with a normal three-phase pattern, but asymmetric intensity, with the other three patients with normal images, yielding nine normal images in 85 patients.

Increased delayed image. Twenty-one patients showed conspicuous, generalized increased uptake on the delayed image of the affected hand and wrist. There was accentuation of uptake in the carpal region and all small joints, particularly along the metacarpal-phalangeal joint. This was easily recognized by comparison with the unaffected side, which was uniformly normal except for possible osteoarthritic changes. The appearance was rather like a "super image" but localized to the affected limb. All patients with this finding eventually had clinical evidence of RSD, but in two patients the RSD pattern was noted on the bone image before the onset of other signs or symptoms.

RSD pattern with increased flow and hyperemia (Fig. 2). In 13 of 21 patients there was increased blood flow and hyperemia of the affected limb, particularly in the periarticular regions. All of these patients eventually showed clinical evidence of reflex sympathetic dystrophy, and the image appearance represented the manifestations of RSD with increased vascularity (2,4-6).

RSD pattern with decreased flow and absent hyperemia (Fig. 3). In eight of 21 patients, the early images showed

decreased flow and decreased blood pool that were indistinguishable from the common appearance in paralyzed limbs. These patients had clinical evidence of RSD, and the delayed images were similar to the typical RSD pattern.

Thus, in 13 of 21 patients with RSD there was increased flow and blood pool, while in eight of 21 there was a disparity between gross limb flow and bone blood flow, as demonstrated by the bone image. This subset of patients with RSD was felt to show the competing effects

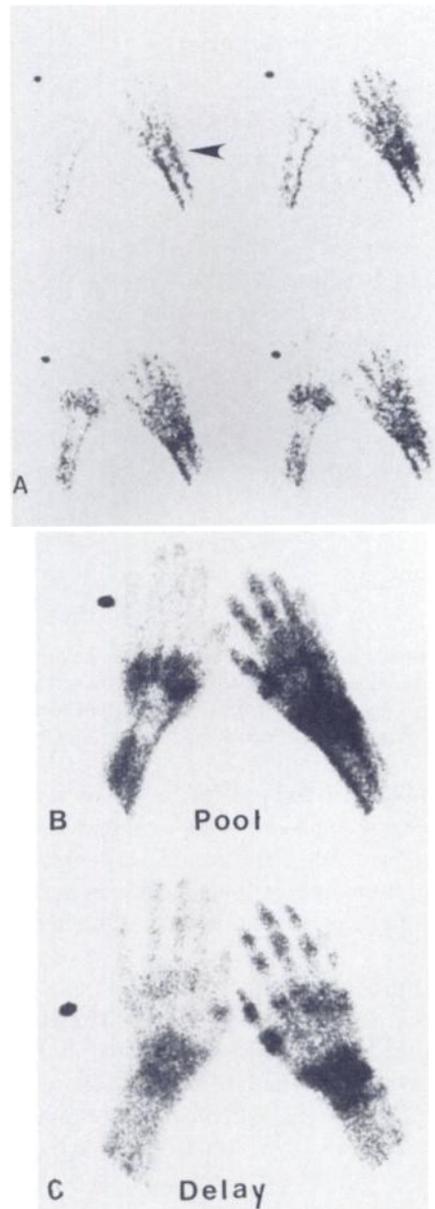


FIG. 2. Reflex sympathetic dystrophy with increased flow (left side). (A) Increased flow to left hand (arrow) relative to right. (B) Blood-pool image showing generalized hyperemia of left hand and fingers. Marked hyperemia of wrist indicates synovitis, which was common feature in association with RSD. (C) Delayed images showing generalized increased uptake of left hand, with periarticular accentuation.



FIG. 3. Reflex sympathetic dystrophy with immobilization effect (right side). (A) Decreased flow to right hand (arrow). (B) Blood-pool image showing diffuse hyperemia of right hand, despite overall decreased blood flow. Note uniform blood-pool pattern with loss of thenar and hypothenar accentuation (similar to Fig. 1), indicating muscle disuse. (C) Delayed image showing generalized increased uptake in right hand, with periarticular accentuation, typical of RSD, despite decreased flow.

of RSD and decreased flow due to immobilization.

Carpal-region hyperemia and local increased uptake (Fig. 4). In 32 patients, the normally cool carpal complex showed equal or greater flow and blood-pool. On the delayed study there was increased uptake in the carpal complex.

This pattern of hyperemia and increased uptake suggested synovitis of the wrist (1,2). The picture was a common feature in the 21 patients with RSD, but it also occurred as an isolated finding in the hemiplegic extremity of 11 patients without RSD or history of arthritis. In these patients it was considered to represent traumatic synovitis of the wrist.

Patterns seen on whole-body images. Distribution Of RSD. Although hemiparesis or hemiplegia also involve the lower limbs, in only five of the 21 patients with RSD was there increased uptake in the ipsilateral lower limb on the delayed image. No patient had the RSD bone-image pattern in an isolated leg.

In the upper limbs, ten patients showed increased

uptake only in the hands and wrists, and ten in the shoulder, hand, and wrist (sparing the elbow); in only one patient was there generalized increase in the entire upper extremity.

Abnormal shoulder uptake. Forty of the 85 patients had clinical evidence of shoulder subluxation on the paralyzed side. Twenty-two of the 40 had increased uptake in the affected shoulder. Excluding those patients with RSD, eight patients had increased uptake in the affected subluxated shoulder. All patients in this series were right-handed, but six of the eight had increased uptake in the left shoulder, and only two had right shoulder findings.

Asymmetric increased uptake in the shoulder is frequently associated with the dominant hand side (12), but in these patients without RSD, it correlated with the side of subluxation, and/or complaints of shoulder pain. Thus, as an isolated finding it was considered to be a traumatic change, perhaps associated with subluxation.

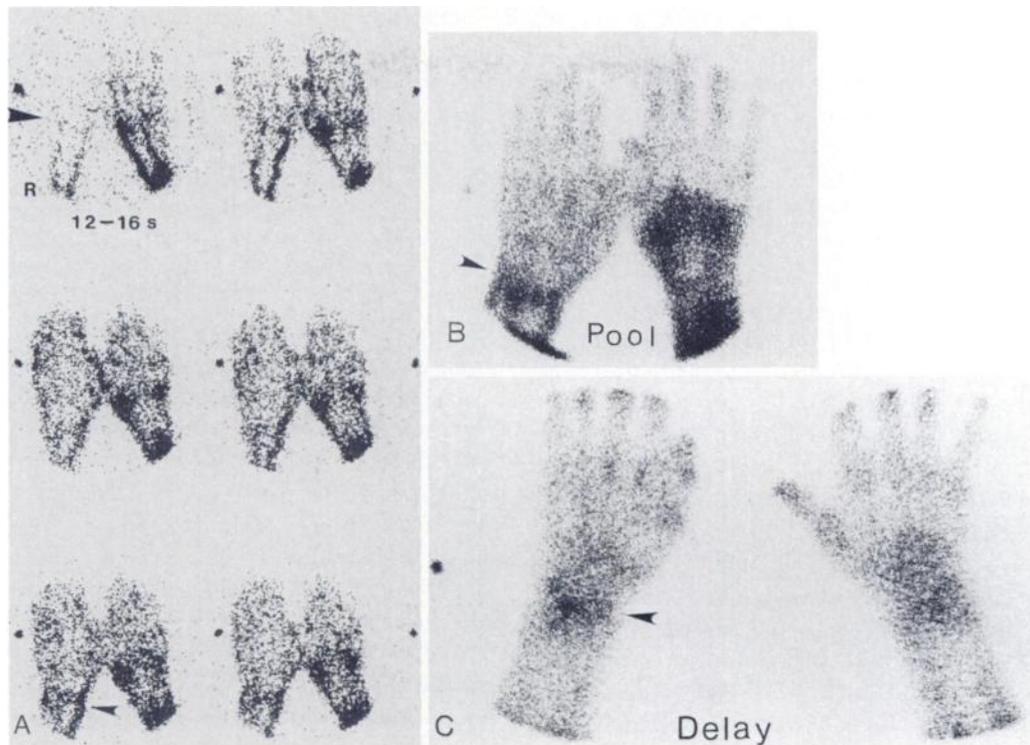


FIG. 4. Wrist synovitis with disuse pattern (right side). (A) Decreased blood flow to right hand, but hyperemia appears in band-like pattern across right wrist (arrow). (B) Disuse blood-pool pattern, with loss of thenar and hypothenar eminences but hyperemia in carpal region (arrow). (C) Delayed study showing increased uptake in right carpal region, likely due to traumatic synovitis. Remainder of bone image appears normal.

DISCUSSION

Unlike radiographs, which show the fine anatomic patterns in bone, radionuclide bone images demonstrate metabolic activity. Functional alterations of bone metabolism generally precede gross structural changes. A 30% to 50% alteration of calcium content is required to be demonstrable on a conventional bone radiograph. Demineralization may result from disuse atrophy associated with muscle paralysis (13), but it is also a feature of RSD. Thus, radiographs in poststroke patients are not generally helpful in differentiating atrophy of disuse from RSD (5-7,14,15).

The factors influencing the degree of uptake on a bone study include bone blood flow, osteoblastic activity, gross calcium turnover, and mechanical stress on bone (16-19). Bone blood is a dominant factor. Of itself, increased local blood flow will cause increased tracer uptake by bone (20). The uptake of radiotracers in bone has been used as a measure of bone blood flow (16,19-27).

Bone blood vessels are richly supplied with sympathetic nerves, which control vasomotor tone. Increased sympathetic stimulation reduces bone blood flow by constricting the arteriolar lumen. Decreased sympathetic stimulation due to loss of central sympathetic tone or following sympathectomy, opens the vascular bed and increases bone blood flow (16,26,28). Increased bone blood flow may be a significant mechanism for increased

uptake in reflex sympathetic dystrophy. Synovitis, with its attendant hyperemia, is a histological feature of RSD (29), and this might add to the periarticular accentuation.

Decreased blood flow on the paralyzed side was likely due to decreased metabolic demands of inactive muscles (21), also suggested by decreased blood-pool activity in the thenar and hypothenar regions.

Unlike flow in skeletal muscle, bone blood flow is relatively unaffected by exercise or immobilization (30), and except in cases of severe disuse atrophy, the delayed bone image is expected to be normal. In fact, Semb has shown increased bone blood flow through limbs of immobilized animals (21). This may be due to the opening of shunts in the marrow to compensate for the loss of the "muscle pump." This mechanism might prevent the acidosis that would otherwise be expected with decreased venous return.

Thus, in a paralyzed or immobilized limb, one might expect overall decreased blood flow and blood pool, due to decreased nutrient requirements of soft tissue, whereas blood flow to bone itself may actually be increased after a transient fall (21).

In an extremity with RSD, vasomotor instability may result in generalized increased blood flow to the soft tissues and bone, producing the characteristic soft-tissue hyperemia and decreased bone uptake. We may speculate, however, that in patients with coexisting paralysis

or pain-induced immobilization and RSD, these two mechanisms may act independently to decrease flow to muscle while increasing flow to bone. Kozin showed that in 15 patients with RSD there was overall increased blood flow, but he also had three patients with decreased flow (7). In our series, eight of 21 patients with the delayed bone-image appearance of RSD had overall decreased limb blood flow.

When pertechnetate blood-pool images and delayed bone images were compared, MDP had better specificity in diagnosis of RSD (1,2,5,6). Kozin et al. found that with pertechnetate only 49% of affected patients could be diagnosed, whereas with MDP there was 92% diagnosis of RSD (6). This again reflects a disparity between the soft-tissue blood pool and bone extraction in these patients, and the sensitivity of the bone image in the diagnosis of RSD.

Although increased flow is a feature of altered sympathetic tone, the blood-flow and blood-pool images of the wrists and hands were not highly sensitive in the diagnosis of RSD. Gross limb vascularity correlated with the degree of voluntary activity. Similarly, decreased blood flow was not useful in excluding RSD. Increased uptake on the delayed image, however, was the most characteristic finding.

The early diagnosis of RSD is important (10,14), but radiographs are frequently not helpful, as they show the loss of mineralization only as a late finding (5,6,14,15). It is frequently difficult to differentiate RSD from atrophy of disuse on a radiograph, since the radiographs show the gross mineralization of the bone, which is decreased in both situations. Increased uptake on the delayed image, however, is present in RSD but not in atrophy. Since this and other studies (2,6) have noted the bone-image appearance of RSD before the definitive clinical findings, it is likely that the radionuclide image is the most valuable early indicator of this process. Because of the selection of patients for this study, however, we made no attempt to determine whether the early diagnosis and subsequent treatment aborts or modifies the course of RSD.

The distribution on the whole-body image is assumed to show the distribution of altered sympathetic tone. We have found RSD to be confined to the upper limb in 16 of 21 patients, despite neurological involvement of the lower limb. We found no cases of bilateral involvement, although such symmetry has been found in other studies in which CVA patients were only a small component (29).

Localized hyperemia and delayed bone uptake of the wrist was found in association with RSD, but as an isolated finding it suggested synovitis, which may be the result of trauma to unprotected flaccid limbs. Similar findings were noted in patients with subluxed shoulders. These findings may have relevance to the management of paralyzed limbs.

Bone and soft-tissue blood flow appeared to act independently. When there was relatively decreased gross limb perfusion due to muscle disuse, there was still sufficient bone blood flow to produce normal bone-image appearances. The effect of altered sympathetic tone could also be noted in bone, despite decreased gross limb perfusion due to muscle disuse.

CONCLUSIONS

1. The delayed bone-image appearance of diffuse increased uptake of the limb, with periarticular accentuation, was a characteristic finding in RSD, occasionally preceding clinical symptoms and occurring in 25% of the hospitalized stroke population.
2. The mechanism of uptake is likely due to increased blood flow through bone due to loss of sympathetic vasoconstriction.
3. The blood flow to bone and muscle appeared to be independently controlled. RSD bone-image changes were noted in patients with overall increased or decreased limb blood flow.
4. In these paralyzed limbs, overall blood flow appeared to be related to muscle tone, flaccid limbs having less metabolic demand and thus less blood flow to the soft tissues.
5. Observations from this group of patients may have applications in the non-CVA population, for the understanding of changes in the bone image, blood flow, blood pool in patients with relatively immobilized painful limbs, with or without either focal bony lesions or RSD.

ACKNOWLEDGMENTS

The authors thank Dr. Jose Jiminez and Dr. Ludmila Hilbert for permission to include their patients in analysis. Thanks to Dr. J. Kirsh for critical review of the manuscript, to Mercedes Castiel for statistical review of patients' charts, and to Miss Corinne Kelbert for manuscript preparation. Illustrations were prepared by the St. Michael's Hospital Department of Medical Art and Photography.

REFERENCES

1. DESAULNIERS M, FUKS A, HAWKINS D, et al: Radiotechnetium polyphosphate joint imaging. *J Nucl Med* 15: 417-423, 1974
2. HOFFER PB, GENANT HK: Radionuclide joint imaging. *Semin Nucl Med* 6:121-137, 1976
3. SY WM, BAY R, CAMERA A: Hand images: normal and abnormal. *J Nucl Med* 18:419-424, 1977
4. CARLSON DH, SIMON H, WEGNER W: Bone scanning and diagnosis of reflex sympathetic dystrophy secondary to herniated lumbar disks. *Neurology* 27:791-793, 1977
5. GENANT HK, KOZIN F, BEKERMAN C, et al: The reflex sympathetic dystrophy syndrome. A comprehensive analysis using fine-detail radiography, photon absorptiometry, and bone and joint scintigraphy. *Radiology* 117:21-32, 1975
6. KOZIN F, GENANT HK, BEKERMAN C, et al: The reflex

- sympathetic dystrophy syndrome: II. Roentgenographic and scintigraphic evidence of bilaterality and of periarticular accentuation. *Am J Med* 60:332-338, 1976
7. KOZIN F, SOIN JS, RYAN LM, et al: Bone scintigraphy in the reflex sympathetic dystrophy syndrome. *Radiology* 138:437-443, 1981
 8. PRAKASH V, KAMEL NJ, LIN MS, et al: Increased skeletal localization of ^{99m}Tc-diphosphonate in paralyzed limbs. *Clin Nucl Med* 1:48-50, 1976
 9. LENTLE BC, GLAZEBROOK GA, PERCY JS, et al: Sympathetic denervation and the bone scan. *Clin Nucl Med* 2: 276-278, 1977
 10. KOZIN F: *Painful Shoulder and the Reflex Sympathetic Dystrophy Syndrome. Arthritis and Allied Conditions: A Textbook of Rheumatology*. 9th Ed, McCarthy DJ, ed. Philadelphia, Lea & Febiger, 1979, pp 1091-1120
 11. MAURER AH, HOLDER LE, ESPINOLA DA, et al: Three-phase radionuclide scintigraphy of the hand. *Radiology* 146:761-775, 1983
 12. SEBES JI, VASINRAPEE P, FRIEDMAN B: The relationship between radiographic findings and asymmetrical radioactivity in the shoulder. *Radiology* 120:139-142, 1976
 13. PANIN N, GORDAY WJ, PAUL BJ: Osteoporosis in hemiplegia. *Stroke* 2:41-47, 1971
 14. CHU DS, PETRILLO C, DAVIS SW, et al: Shoulder-hand syndrome: Importance of early diagnosis and treatment. *J Am Geriat Soc* 29:58-60, 1981
 15. DAVIS SW, PETRILLO CR, EICHBERG RD, et al: Shoulder-hand syndrome in a hemiplegic population: A 5-year retrospective study. *Arch Phys Med Rehab* 58:353-356, 1977
 16. CHARKES ND: Skeletal blood flow: Implications for bone scan interpretation. *J Nucl Med* 21:91-98, 1980
 17. JONES AG, FRANCIS MD, DAVIS MA: Bone scanning: radionuclide reaction mechanisms. *Semin Nucl Med* 6:3-18, 1976
 18. KIRCHNER PT, SIMON MA: Radioisotopic evaluation of skeletal disease. *J Bone and Joint Surg* 63-A:673-681, 1981
 19. SAGAR VV, PICCONE JM, CHARKES ND: Studies of skeletal tracer kinetics. III. Tc-99m(Sn) methylenediphosphonate uptake in the canine tibia as a function of blood flow. *J Nucl Med* 20:1257-1261, 1979
 20. SIEGEL BA, DONOVAN RL, ALDERSON PO, et al: Skeletal uptake of ^{99m}Tc-diphosphonate in relation to local bone blood flow. *Radiology* 120:121-123, 1976
 21. SEMB H: Experimental limb disuse and bone blood flow. *Acta Orthop Scand* 40:552-562, 1969
 22. SHIM SS, COPP DH, PATTERSON FP: An indirect method of bone-blood flow measurement based on the bone clearance of a circulating bone-seeking radioisotope. *J Bone and Joint Surg* 49-A:693-702, 1967
 23. CHARKES ND, MAKLER PT JR, PHILLIPS C: Studies of skeletal tracer kinetics. I. Digital-computer solution of a five-compartment model of [¹⁸F] fluoride kinetics in humans. *J Nucl Med* 19:1301-1309, 1978
 24. CHARKES ND, BROOKES M, MAKLER PT JR: Studies of skeletal tracer kinetics: II. Evaluation of a five-compartment model of [¹⁸F] fluoride kinetics in rats. *J Nucl Med* 20: 1150-1157, 1979
 25. LAVENDER JP, KHAN RAA, HUGHES SPF: Blood flow and tracer uptake in normal and abnormal canine bone: Comparisons with Sr-85 microspheres, Kr-81m and Tc-99m MDP. *J Nucl Med* 20:413-418, 1979
 26. VAN DYKE D, ANGER HO, YANS T, et al: Bone blood flow shown with F¹⁸ and the position camera. *Am J Physiol* 209: 65-70, 1965
 27. SHIM SS, PATTERSON FP: A direct method of qualitative study of bone blood circulation. *Surg Gyn Obst* 125:261-268, 1967
 28. DUNCAN CP, SHIM S-S: The autonomic nerve supply of bone: An experimental study of the intra-osseous adrenergic nervi vasorum in the rabbit. *J Bone Joint Surg* 59-B:323-330, 1977
 29. KOZIN F, MCCARTY DJ, SIMMS J, et al: The reflex sympathetic dystrophy syndrome. I. Clinical and histologic studies: Evidence for bilaterality, response to corticosteroids and articular involvement. *Am J Med* 60:321-331, 1976

**Sierra Valley Nuclear Medicine Association
SNM Northern California Chapter
16th Annual Spring Symposium**

May 4-5, 1984

Caesars Tahoe Hotel

Stateline, Nevada

The Sierra Valley Nuclear Medicine Association and SNM Northern California Chapter will hold the 16th Annual Spring Symposium May 4-5, 1984 at Caesars Tahoe Hotel, Stateline, Nevada.

The speakers and topics will include:

Daniel Berman, M.D.
Robert Carretta, M.D.
Sally DeNardo, M.D.
Edwin Glass, M.D.
Kenneth Krohn, Ph.D.
Ross McDougall, M.D.
Richard Peterson, M.D.

Correlative Nuclear Cardiology
Radioactive Waste Management
Clinical Potential of Radiolabelled Monoclonal Antibodies
New Applications of First Pass Radionuclide Angiography
Techniques for the Preparation of Monoclonal Antibodies
Clinical Applications of Indium Radiolabelled White Cells
Radioactive Waste Management

For additional information contact:

Craig Weiner, M.D.
Program Chairman
P.O. Box 161684
Sacramento, California 95816

This program will be approved for VOICE and 6 hr CME credit.