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PROGRESS IN THE USE OF RADIONUCLIDES IN ORTHOPAEDICS

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For more than two centuries the advancement of knowledge in the field of bone physiology has been intimately linked with progress in the use of tracer techniques applied to bone. For example, use of metal markers by Hales and Duhamel in the eighteenth century put an end to the theory of interstitial elongation and showed that growth occurred by apposition. Further refinement of this technique was made possible when roentgenograms were used for *in vivo* localization of metal markers or other landmarks, such as growth arrest lines, exostoses or striae caused by metal poisoning. Use of madder for vital staining of forming bone tissue permitted a detailed description of bone remodelling in experimental animals. This technique was of crucial importance to Kölliker in his attempt to link bone cells, as seen in the microscope, to specific functions in the metabolism of bone. Use of lead, beta-emitting radionuclides like ^{32}P or ^{45}Ca, and tetracycline increased the sensitivity of the intravital staining techniques; compared with madder these tracers provided much higher resolution.

Refinement of tracer techniques thus involves localization and quantitation of tracer. This can be done conveniently in man only if the tracer can be administered and detected safely *in vivo* without a biopsy. These requirements are met by gamma-emitting radionuclides. Use of radionuclides for the study of skeletal physiology and pathology in man thus constitutes an important link in a chain of events which has its origin in the eighteenth century.

In particular, the application of radionuclide tracer techniques has provided clinical orthopaedics with an insight into metabolic problems comparable to that which has so long been the prerogative of those studying the parenchymatous organs. For example, such important conditions in orthopaedics as arthrosis, necrosis of bone, tumour, septic conditions and rheumatoid arthritis can now be analysed on a clinical level with the aid of tracer techniques. In all these conditions, comparison of these metabolic data with information derived from conventional morphologic methods has yielded new insight immediately useful in diagnosis and therapy.

On the basis of previous reviews of the use of radionuclides in orthopaedics (Bauer et al. 1958, Bauer 1965, 1968, Dreyer & Georgi 1972) five subjects of particular interest will be discussed in this article: osteonecrosis, the infected endoprosthesis, functional studies of bone metabolism, choice of tracer, and detection techniques. Finally, the present indications for radionuclide scintimetry in clinical orthopaedics will be defined.

OSTEONECROSIS

Cameron (1969) first showed that radionuclide scintimetry may demonstrate an abnormality in non-traumatic necrosis of the head of femur long before morphologic changes are visible by radiography. Ahlbäck et al. (1968) showed that non-traumatic necrosis of bone is a relatively common condition also in the knee and that radionuclide scintimetry may be of distinct value in the early diagnosis of the condition. These findings have subsequently been confirmed by Julien (1974) and others. In an extensive study of 70 patients with non-traumatic osteonecrosis of the hip and the knee, Julien found agreement between scintimetry/graphy (see below) and the clinical and radiographic development of the disease in all but 3 of 95 involved joints.

By currect interpretation, high scintimetry values mean a high level of metabolic activity. One may then ask why the scintimetry values are high when the bone is dead. The resolution of this paradox is that the high metabolic activity is secondary to the primary process; bone death starts a pathophysiologic process characterized by removal of dead bone and formation of new bone. The scintimetry values thus reflect the strong tendency to repair, noted by D'Aubigné et al. (1965). Immediately at onset, necrosis of bone should thus yield low or normal rather than high scintimetry values. To my knowledge, only one patient has thus far been studied at such an early stage of osteonecrosis of the knee; ^{85}Sr scintimetry was indeed normal. One month later, the values were exceedingly high, whereas the typical radiographic lesion did not appear until much later.

Recently, similar techniques have been applied to the study of osteonecrosis secondary to intracapsular fracture of the neck of femur (Shoji et al. 1972, Asnis et al. 1975). Shoji et al. showed that the scintimetry values in nine cases of osteonecrosis of the head of femur were remarkably high compared to the values in uncomplicated fracture cases. Asnis et al. in the same laboratory refined the technique further. They demonstrated high accuracy in the prediction of necrosis and/or non-union by measurements made 2 months or later after fracture. On the basis of these data from the Hospital for Special Surgery in New York it now seems possible to define a new clinical strategy in cases of fracture of the neck of femur. Already during the first few months following injury a diagnosis of impending necrosis and/or non-union can be made and a hemi- or total arthroplasty performed. The dream of predicting these complications already at the time of the initial surgical procedure has not materialized, however. Methods based on clearance of tracer injected into the head of femur have proven imprecise, probably because of the difficulties encountered in definition of injection site. Methods based on accumulation of tracer have failed, very probably because such methods have now proven to depend on the repair reaction being under way.

THE INFECTED ENDOPROSTHESIS

On the basis of earlier work (Nöh 1972, Groher et al. 1972, Venohr et al. 1972, Bauer et al. 1973), Sjöstrand (1974) has made a thorough analysis of radionuclide scintimetry in total hip arthroplasty. The purpose of his investigation was to develop a method to be used in differential diagnosis of pain after total hip arthroplasties. A base material of 135 hips was divided into three series: (1) hips without pain, (2) hips with proven infection and (3) hips with pain but without proven infection. Scintimetry was performed 2 weeks after administration of ^{85}Sr. The patients were examined by rectilinear scanning over the hips. The data were analysed with regard to the acetabulum, the intraarticular space and the proximal femur, and mean values of activity were related to a total body activity index. The values thus obtained showed a regular pattern in the uncomplicated arthroplasties; a rapid increase after surgery and then a slow drop to a rather stable plateau some 8 months after surgery. Infected hips showed markedly elevated values of either both or one of the components of the endoprosthesis. Other causes of abnormally high activity were ectopic bone formation, femoral fracture, non-union of the great trochanter, perforation of the femoral shaft, Paget's disease and osteonecrosis caused by radiotherapy.

By dividing the material into subsets based on clinical and radiographic data, Sjöstrand analysed the scintimetry values with regard to causes of loosening of the femoral component. This analysis permitted a description of the varus migration of the femoral component, common and severe in infected cases but not infrequent even in otherwise normal canals. The cause of fracture of the femoral cement could thus be identified in all cases. In infected cases scintimetry permitted identification of the exact location of infections which did not always involve both components of the endoprosthesis. In one case the infected component has subsequently been replaced with the non-infected component left in situ; the outcome is still successful 1 year after the operation. Very probably the scintimetry method may considerably shorten the period of time needed for diagnosis of the so-called infected total hip.

FUNCTIONAL STUDIES OF BONE METABOLISM

The development of radionuclide scintimetry of the skeleton has progressed from (1) topologic identification of abnormality, for example cancer metastases or osteonecrosis of the knee, to (2) interpretation of abnormally high values in the face of a known skeletal abnormality, for example osteonecrosis in fracture of the neck of femur or the infected total hip endoprosthesis, to (3) distinction between different types of development of one and the same condition. It is the third type of application of tracer techniques that I have denoted as analysis of function. The best example of this third generation type of tracer studies of the skeleton has been furnished by Koshino & Ranawat (1970) who studied ^{85}Sr scintimetry patterns following high tibial osteotomy for osteonecrosis and/or arthrosis of the knee. The purpose of the osteotomy was to shift the body-weight from the diseased medial compartment of the knee to the less involved lateral compartment. They found that in those cases where the osteotomy had been mechanically successful, the preoperatively high focus of uptake had shifted laterally. However, in those cases that were under-corrected, i.e. where the osteotomy had not achieved its mechanical purpose, the highest scintimetry values were located medially even postoperatively. These observations are thus a practical example of Wolff's law which relates function, metabolism and form of the skeleton (Bauer 1968).

Further examples of analysis of the function of the skeleton by radionuclide scintimetry have been furnished by Segmüller (1971) and by Muheim (1973). Segmüller thus showed how different types of pseudarthrosis of the lower leg may differ in their scintimetric pattern and that these differences were correlated to the clinical course. Muheim found a striking difference in ^{87m}Sr uptake in fractures treated conservatively as compared to fractures treated by a compression plate. His data furthermore suggested that serial scintimetry may be useful for early detection of incipient non-union.

Finally, Muheim & Bohne (1970) have demonstrated that the prognosis in osteonecrosis of the knee as regards development of arthrosis is related to the scintimetry pattern observed during an early stage of the condition.

CHOICE OF RADIONUCLIDE TRACER

Until recently ^{85}Sr has been the tracer of choice for radionuclide scintimetry of the skeleton. This choice has been based on a thorough knowledge, both clinically and experimentally, of the similarities and differences between strontium and calcium metabolism, on the favourable radiation characteristics of ^{85}Sr and on the convenient half-life of ^{85}Sr which makes it readily available in the laboratory and permits measurements at the time when the soft tissues have been cleared from tracer. However, the long half-life of ^{85}Sr raises objections to its use in non-malignant conditions in children. Therefore a number of short-lived tracers have been tried and some are now well established for routine work. Thus, Muheim & Crutchlow (1971) and Asnis et al. (1974) have shown that for certain purposes a 1-hour scan with ^{18}F may be comparable to a 1- or 2-week scan with ^{85}Sr. Also ^{87m}Sr may be used in a similar fashion as discussed by Charkes (1969) for bone tumour assay and by Staheli et al. (1972) in studies of bone and joint infections in children. Finally, Subramanian et al. (1974), Julien (1974) and several others are at present investigating the possibility of using ^{99m}Tc labelled phosphate compounds for clinical bone scintimetry.

There is no doubt that the shorter-lived tracers may considerably widen the scope of bone scintimetry under clinical conditions. As compared to ^{85}Sr the shorter-lived tracers have the great advantage that they permit higher activity levels at comparable radiation dose. Even more important is the possibility of doing repeat measurements, due to the rapid disappearance of the tracer and the lower radiation dose. The possibility of making measurements immediately after administering the tracer is only an apparent advantage, however; this can be achieved also with ^{85}Sr.

Even though different tracers may have different advantages and disadvantages when applied to any particular clinical problem, it should be emphasized that each laboratory has to build up considerable experience with each of the tracers used in order to interpret the data properly. For example, the interpretation of the high scintimetry values in osteonecrosis or in the infected hip rests on a firm basis of values recorded in normal cases.

DETECTION TECHNIQUES

The body of knowledge in radionuclide tracer techniques for the study of bone is based on analysis of digital data. For certain clinical purposes it may be advantageous to display such data in non-digital forms, for example by the use of colour (Bauer et al. 1973) or other analogues (Asnis et al. 1973). However, these techniques permit ready translation of the data recorded into precise digital values because the detection devices used in the quoted references have high precisely defined resolution. I have used the term *scintimetry* for these techníques in contrast to *scintigraphy* which denotes measurements made with the aid of a gamma camera and displayed as shades of grey on a photographic film. Even though the gamma camera has reached an admirable level of sophistication when applied to the skeleton it cannot as yet compete with the rectilinear scan performed with a suitably collimated detector. Whereas the camera has been highly successful for the study of parenchymatous organs, the skeleton permits such precise topology, with the aid of radiography, that it pays to develop tracer data of similar precision. This, unfortunately, cannot as yet be made with the gamma camera. The clinician should be aware of this problem. Unless the radionuclide laboratory can furnish him with data performed in optimal fashion, he may well be misled in interpretating tracer data.

CONCLUSION

The general indications for radionuclide scintimetry in clinical orthopaedic problems are bone and/or joint pain without evidence of radiographic abnormality. When applied in this way, scintimetry may aid in the early detection of infection (Staheli 1972), tumour and osteonecrosis. When morphologic changes have already occurred, scintimetry may aid in the differential diagnosis of the primary condition, for example vertebral fracture (Defiore et al. 1970, Segmüller 1972), or in the early detection of complications, for example necrosis and/or non-union in fracture of the femoral neck (Asnis et al. 1975) or infection in total hip arthroplasty (Sjöstrand 1974). Finally, radionuclide scintimetry may permit a better understanding of the basic properties of bone, to wit the examples given above of the relation between function, metabolism and form of the skeleton. In this sense radionuclide scintimetry is forming a new bridge between clinical orthopaedics and basic science (Bauer 1968).

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