THE NUCLIDE BONE-SCAN IN THE DIAGNOSIS AND MANAGEMENT OF PERTHES’ DISEASE

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The nuclide bone-scan will reliably diagnose Perthes’ disease with a sensitivity of 0.98 and a specificity of 0.95. The comparable figures for radiographic sensitivity and specificity are respectively 0.92 and 0.78. In addition, it is possible on the scan to recognise the onset of revascularisation of the femoral capital epiphysis some months before there are radiographic signs of new bone formation. Scintigraphy also suggests that in some cases of transient synovitis there may be a period of reversible ischaemia of the capital epiphysis, which may have relevance to the pathogenesis of Perthes’ disease.

Perthes’ disease is a self-limiting condition which, if untreated, progresses to a satisfactory result in many cases (Catterall 1971). Some cases, however, progress to deformity of the femoral head and eventual osteoarthritis. Catterall (1971) has suggested that treatment should be reserved for those patients whose prognosis is poor but who still have a spherical femoral head. At the present time the prognosis for individual patients must be judged from factors such as the radiological appearance, the age and sex of the child, and the degree of synovitis. Further information about the degree of involvement of the femoral head and the stage of revascularisation would be of value in the management of this condition.

Since 1974 a few sporadic reports (Ash, Gilday and Reilly 1975; Danigelis et al. 1975; Danigelis 1976; Harcke 1978) have appeared in the literature describing the appearances on the nuclide bone-scan in Perthes’ disease, but there has not been wide interest shown in this new investigation for this disease. Its precise place in diagnosis and prognosis has not yet been defined.

The nuclide scan would, in theory, hold out the hope of detecting the proportion of vascularised to devascularised bone and of observing revascularisation and reossification as they occur. One author (Danigelis 1976) claims to be able to recognise the signs of revascularisation of the femoral capital epiphysis earlier by scintigraphy than by radiological examination.

We undertook a review of our experience to delineate the role of the nuclide scan in the diagnosis of Perthes’ disease. In addition, we wished to confirm the presence of the additional features on the scan described by Danigelis et al. in 1975 and by Danigelis in 1976 and to investigate their significance.

Fig. 1
Fig. 2
Fig. 3

The classical scan appearance of Perthes' disease of the left hip shown in parallel-hole (Fig. 1) and pinhole views (Figs 2 and 3). Note the normal uptake in the right femoral capital epiphysis.

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MATERIAL AND METHODS
A retrospective survey was carried out of children referred to the Department of Nuclear Medicine for the exclusion of Perthes' disease during the period from March 1975 to December 1978. The 131 children reviewed were the total of consecutive referrals with suspected abnormality of the hip, except those with pyogenic infection or injury. The case records were reviewed and the length of history and the mode of presentation were noted. All the scans were re-read "blind", but in no case was a significant discrepancy found from the original reports.

Each child received methylene diphosphonate labelled with technetium-99m in an intravenous dose of approximately 215 microcuries per square metre of body surface area. One and a half hours after injection the hip was imaged with a gamma camera (Searle Pho Gamma 1V) in the anterior position with both parallel-hole and pinhole collimation, and with the hip in full medial rotation (Paul et al. 1974). Most children were studied by nuclide scan only once, but seven were studied sequentially; and all were studied radiographically at least once and those suffering from Perthes' disease were studied sequentially.

The diagnosis of Perthes' disease was made from the scan if there was a significant void in the activity of the femoral capital epiphysis (Figs 1 to 3). Additional features noted included a stripe of activity in the most lateral part of the femoral capital epiphysis, increased activity in the growth plate, and increased activity in the adjacent metaphysis (Figs 4 and 5). In order to determine whether these features represented signs separating total from partial epiphysial involvement or signs of revascularisation, as believed by Danigelis, we catalogued the signs and used them for two separate purposes. First, we used them to classify our cases into partial or total involvement of the head. Secondly, we separated the cases into those showing minimal revascularisation or none, and those showing established revascularisation.

RESULTS
Of the 131 children in the series, 48 were assigned a final diagnosis of Perthes' disease, 79 transient synovitis, two rheumatoid arthritis, one epiphysial dysplasia and one chondrolysis. The age range of those with Perthes' disease varied from 3 to 13 years with a mean of 6.3 years. The sex ratio was five boys to one girl.

The appearance of Perthes' disease on the scan was highly characteristic, with a marked void in activity in the position of the femoral capital epiphysis. This was easily distinguished from a normal capital epiphysis which could be seen clearly to accumulate the nuclide in a moderate degree between the activity in the growth plate and that in the acetabular rim (Fig. 2). The scan findings were never equivocal.

<table>
<thead>
<tr>
<th>Table 1. The diagnostic accuracy of the nuclide scan</th>
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<tbody>
<tr>
<td>True positives (TP)</td>
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<tr>
<td>False positives (FP)</td>
</tr>
<tr>
<td>True negatives (TN)</td>
</tr>
<tr>
<td>False negatives (FN)</td>
</tr>
<tr>
<td>Complete revascularisation</td>
</tr>
<tr>
<td>Sensitivity</td>
</tr>
<tr>
<td>Specificity</td>
</tr>
<tr>
<td>Accuracy</td>
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<td>Predictive value of a positive test</td>
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<td>Predictive value of a negative test</td>
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Two of the children with Perthes' disease had histories exceeding 18 months in duration and the scan showed complete revascularisation. Forty-five of the remaining 46 were correctly diagnosed from the scan. There was thus one false-negative scan. Of the 83 children subsequently shown not to be suffering from Perthes' disease, 79 were correctly categorised from the scan; four had scans which were positive for Perthes' disease. There were thus four false-positive scans (Table I).

The initial radiographic report correctly identified 41 children with Perthes' disease. For an additional 10 cases, the radiologist reported that the diagnosis was considered possible or probable. A total of 27 other cases were reported as negative. The results were based on the initial radiographs and did not include the subsequent scan. When this radiographic report was compared with the eventual diagnosis, it was found that the initial radiograph was correct in 16 cases and incorrect in 11 cases. In the remaining 10 cases, the diagnosis was considered possible or probable.

Of these 27 cases, 20 were reported as normal, but in 4 cases the presence of lytic signs was noted. Two of these cases were subsequently shown not to have Perthes' disease, but in the remaining 2 cases the diagnosis was considered possible or probable. These results indicate that the initial radiograph was correct in 16 cases and incorrect in 11 cases. In the remaining 10 cases, the diagnosis was considered possible or probable.

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Table II. The diagnostic accuracy of the radiograph

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<tbody>
<tr>
<td>True positives (TP)</td>
<td>44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>False positives (FP)</td>
<td>18*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>True negatives (TN)</td>
<td>65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>False negatives (FN)</td>
<td>4</td>
<td></td>
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</tbody>
</table>

* This classification does not imply a definite radiological diagnosis of Perthes' disease but represents those cases where the possibility was raised by the reporting radiologist.

Sensitivity

\[
\text{Sensitivity} = \frac{TP}{TP + FN} = 0.92
\]

Specificity

\[
\text{Specificity} = \frac{TN}{TN + FP} = 0.78
\]

Accuracy

\[
\text{Accuracy} = \frac{\text{Correct results}}{\text{All results}} = 0.83
\]

Predictive value of a positive test

\[
\text{Predictive value of a positive test} = \frac{TP}{TP + FP} = 0.71
\]

Predictive value of a negative test

\[
\text{Predictive value of a negative test} = \frac{TN}{TN + FN} = 0.94
\]

Table III. Comparison of radiographic and scan classification

<table>
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<tr>
<th>Catterall grade</th>
<th>Partial</th>
<th>Total</th>
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<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>17</td>
<td>7</td>
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* Partial or total involvement of the femoral head as shown by the presence or absence of the lateral stripe.

The means of these groups were significant (P<0.01) using the Wilcoxon sum-of-ranks test (Mann and Whitney 1947). For seven children sequential scans were available for study and for each a progression in revascularisation with time could be identified.

DISCUSSION

These results highlight the diagnostic accuracy of this investigation. The predictive value of a positive test is 0.92, which indicates that the probability of the disease being present, given a positive test, is 92 per cent (Vecchio 1966). Even greater diagnostic worth is indicated by the predictive value of a negative test, which is 99 per cent. The value of these results is shown when compared with the diagnostic precision of radiography. The radiograph is normal in a small but significant number of cases of Perthes' disease in its early stages (Figs 6 to 9). Of perhaps greater importance is the quite large number of children who did not suffer from Perthes' disease, but for whom the initial radiograph did not confidently exclude this diagnosis. The very high predictive value of a negative scan makes this examination preferable to some months of diagnostic uncertainty.

We were surprised at the occurrence of four false-positive results, considering the very typical appearance of the scan in Perthes' disease and its marked difference from a normal scan. We reviewed these cases carefully and there is no doubt that the scans
Figures 6 and 7—Scan showing Perthes' disease in the left hip. Figure 8—Normal radiograph at that time. Figure 9—Classical radiographic stigmata of Perthes' disease seven months later.
A false-positive study. Figures 10 and 11—A scan demonstrating avascularity of the right capital femoral epiphysis. Figures 12 and 13—The scan two weeks later was normal. Figure 14—Normal radiograph.
show a typical void in activity in the femoral capital epiphysis (Figs 10 and 11). Three of these patients presented with severe symptoms and a very short history—only 10 days compared with 13 weeks for the series—whereas only 23 per cent of the total series showed marked signs or symptoms. Two were scanned again a few weeks after the initial diagnosis and these scans were quite normal (Figs 12 and 13), as was the radiograph (Fig. 14). We believe that this is a real appearance and may represent a tense effusion in the joint so that the blood supply of the epiphysis is temporarily embarrassed. If this is so, it raises interesting speculations about the relationship between transient synovitis and Perthes' disease, and whether there may be a "forme fruste" of the disease. This finding may also provide some support for the contention that Perthes' disease in its classical form results from more than one ischaemic episode (Inoue et al. 1976).

The one false-negative scan—the only one to be reported in the literature—was from a child with limited involvement of the femoral head (Figs 15 to 18). However, this does not altogether explain the normal appearance on the scan since the other Catterall Group 1 hips all exhibited a complete void on the scan.

As a result of this series we agree with Danigelis that additional signs can be recognised on the scan which allow a classification of cases of Perthes' disease. There is no evidence from this series to support the idea that this classification is a grading, akin to the Catterall radiographic grading. This is disappointing as, on the present evidence, the degree of involvement of the femoral head seems to be one of the important prognostic indicators (Catterall 1971). The surprising finding that hips in the lowest Catterall grade invariably showed total head involvement on the scan leads us to speculate as to whether the degree of avascularity is
Sequential scans showing progression from the early appearances to complete revascularisation: Figure 19—October 1976; Figure 20—January 1977; Figure 21—March 1977; Figure 22—June 1977.

usually more complete than that suggested by the radiological appearance. This concept is supported by Inoue et al. (1976) who studied biopsy specimens from 57 hips with Perthes' disease and found that "every hip biopsied showed histological evidence of at least one infarct throughout its extent".

The hypothesis put forward by Danigelis that these variations in the scan are signs of revascularisation (Fig. 5) is supported by the correlation between the findings on the initial scan and the time that elapses before there is radiological evidence of revascularisation. The seven patients undergoing sequential scans also showed a progression of revascularisation with time (Figs 19 to 22). It is therefore possible on the scan to classify Perthes' disease into stages of revascularisation. There is no evidence at present that such a classification is of prognostic importance, but further study along these lines is warranted.

REFERENCES

Mann H, Whitney D. On a test of whether one of two random variables is stochastically larger than the other. Ann Math Stat 1947;18:50-60.