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SYNOVIORTHESIS WITH RADIOACTIVE GOLD IN HEMOPHILIACS

Clinical and Radiological Follow-up

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Twenty-seven patients with hemophilia treated with intra-articular injection of radioactive gold were followed up clinically and radiologically for 3 to 9 years after treatment. To assess the radiological changes, a new classification was designed, with a score describing the severity of the changes in a more accurate manner than the methods previously used.

The treatment decreased the bleeding frequency and stopped the progress of the arthropathy if applied at an early stage when the arthropathy was still reversible. If the treatment was begun at a later stage, the arthropathy seemed to progress independently of the effect on the bleeding frequency. No negative effect of the radioactive gold was observed on the joint or the growing zone.

Key words: hemophilia; joint bleeding; radio-isotopes; synoviorthesis

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In patients with hemophilia repeated intra-articular hemorrhages or chronic synovitis may result in an arthropathy with typical radiological changes of various degrees. One method of treating synovitis and preventing recurrences of bleeding is synoviorthesis with chemical or radiological preparations (Ahlberg 1971, Menkes et al. 1975). Radioactive gold (^{198}Au) has been used at the International Hemophilia Treatment Centre in Malmö since 1968. The effect on synovitis and joint bleeding has been good (Ahlberg 1977) but the long-term effect on the arthropathy is still unknown. The present investigation was carried out in order to study the influence of intra-articular injection of ^{198}Au on the development of radiological changes in hemophilic arthropathy.

PATIENTS

During the period 1968–1978, 65 hemophiliacs aged 2–46 years were treated by intra-articular injection of ^{198}Au in 97 joints (46 knees, 25 elbows, 20 ankle joints, 6 shoulder joints) because of chronic effusion and/or repeated intra-articular bleeding, which had not responded to conservative treatment (immobilization, substitution therapy). Depending on the size of the joint, 2–5 mCi ^{198}Au in a colloidal solution with a particle size of 20 mμ was injected into the joint, and the patient was immobilized for 1–2 days. Before the injection, the level of A- or B-factor was raised to 20 per cent (Ahlberg 1977). Out of this group, all patients with a follow-up of 3 years or more, in whom a radiological examination of the joint had been performed less than 3 months prior to the gold injection, were included in this investigation. The material consisted of 14 children (16 joints) aged 2–15 years at the time of

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Table 1. Distribution of joints included in the study

	Children	Adults
Shoulder	0	2
Elbow	2	4
Knee	9	5
Ankle	5	3
Total	16	14

treatment and 13 adults (14 joints) aged 17–46 years (Table 1). Children were, by definition, those in whom epiphyseal fusion had not occurred at the time of treatment. Twenty-two patients had hemophilia A (17 severe and 5 moderate) four had hemophilia B (severe) and one von Willebrand's disease (severe). In three patients the administration of radioactive gold was repeated after 1–3 years and in two of these surgical synovectomy was performed 1 and 2 years after the first gold injection, owing to the detrimental effect of the injections.

METHODS

The patients were recalled for clinical investigation and radiological examination of the treated and contralateral joints. The clinical effect of the administration of radioactive gold was assessed according to the frequency and severity of joint hemorrhages before and after the treatment.

All available radiograms of the treated and the contralateral joints were reviewed, covering a period of 1–15 (mean 5.2) years before and 3–9 (mean 5.6) years after the treatment. To record radiological changes from one examination to the next, a classification was devised in which the changes were estimated as described in Table 2. At each examination the joint was given a total sum of points of 0–13 according to Table 2. This score expressed the severity of the radiological changes. The radiographs were also examined for the time and mode of epiphyseal fusion, and skeletal growth. A detailed description of the evaluation of the radiological findings will be published separately (Pettersson, in preparation).

The course of development of the radiological changes before and after the treatment with radioactive gold was compared and correlated with the frequency of hemorrhages.

Table 2. Radiological classification of hemophilic arthropathy

Radiological finding	Points
Effusion	0
Soft tissue changes	0
Enlarged epiphysis	1
Osteoporosis	1
Irregular subchondral surface	1–2
Erosions at joint margins	1
Subchondral cyst formation	1–2
Narrowing of joint space	1–2
Incongruence of articular surfaces	1–2
Deformity (valgus, varus, rotation)	1–2
Possible score	0–13

RESULTS

The effect of the radioactive gold on the synovitis and joint bleedings in this group of patients agreed well with that described for the total material (Ahlberg 1977). In 12 joints, no bleeding occurred after treatment, in eight the frequency decreased markedly, in five the frequency decreased temporarily, and in two there was no clinical improvement. These two patients were later synovectomized.

Figure 1 illustrates the development of the joint score before and after injection of ^{198}Au in all the joints studied. Irrespective of the clinical effect of the treatment, the progression of the radiological changes was unaffected if the joint had a score of three points or more at the time of administration of the radioactive gold (Figure 2). In three out of four joints with a score of two points or less at the time of treatment no further bleeding occurred and in the fourth, the frequency markedly diminished. In all these joints there was no progression of the radiological changes during the follow-up after treatment. No difference between children and adults was noted in these respects.

Acceleration or retardation of epiphyseal fusion or dysplastic skeletal growth was not noted in any case.

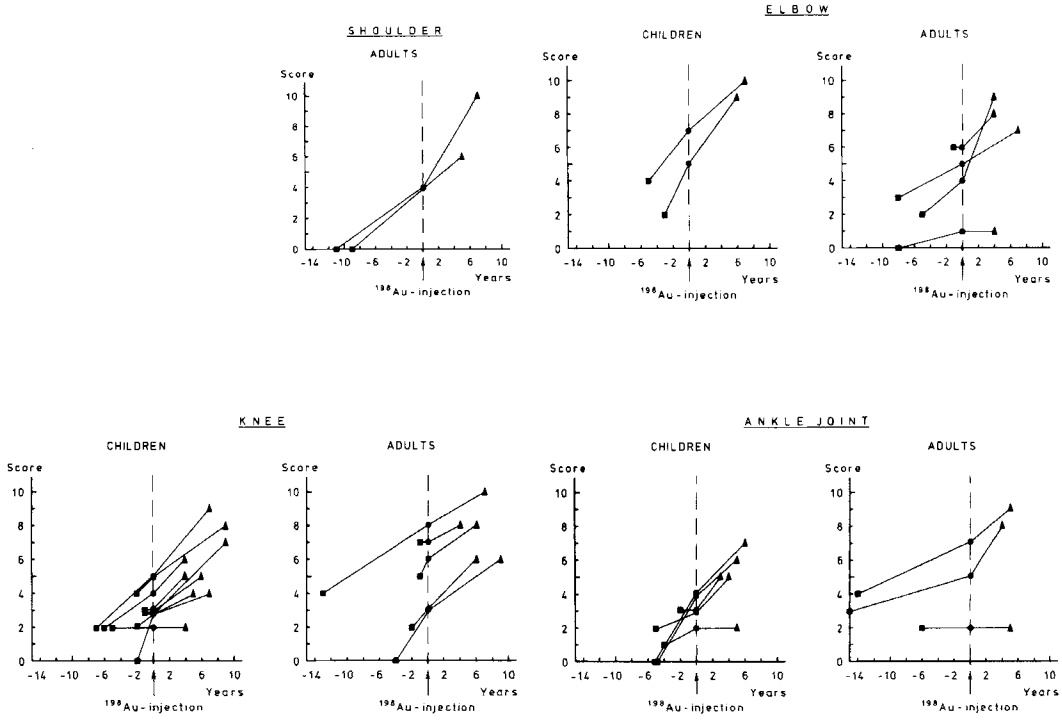

Figure 1. Development of joint score before and after injection of ^{198}Au.

DISCUSSION

In modern prophylaxis and treatment of hemophilia, radiology may be one objective method to assess the efficacy of the treatment on the arthropathy. In this assessment, small changes occurring between two examinations of the same joint may be important. Various methods for classification of the arthropathy have been described (De Palma & Cotler 1956, Jordan 1958, Ahlberg 1967, Wood et al. 1969, Arnold & Hilgartner 1977). In several patients in the present study, however, these methods proved to be insufficient to record the progression of the radiologically revealed arthropathy, and for that reason a new classification was designed (Table 2).

All the changes used in this classification, which are well known in the literature of hemophilic arthropathy, were given 0–2 points. The changes are listed in the order they occur chronologically. Effusion in the joint was given 0 points, since it may reflect only an acute stage of hemorrhage and not the more chronic consequences of the bleeding. Soft tissue changes were also given 0 points for the same reason and also owing to the varying technical quality of the radiograms which do not always allow an assessment of the soft tissues. The rest of the findings gave a maximal score of 13 points per joint, making it possible to register even small changes from one examination to another.

(a)

(b)

(c)

Figure 2. Progress of radiological changes despite good effect on joint bleedings.
a. Five years before treatment, age 3. Normal. Score: 0.
b. Immediately before treatment, age 8. Enlarged epiphysis (compared with contralateral side): 1 point; Osteoporosis (compared with contralateral side): 1 point; Irregular subchondral surface: 1 point; Narrowing of joint space: 1 point; Score: 4 points.
c. Six years after treatment, age 14. Enlarged epiphysis: 1 point; Osteoporosis: 1 point; Irregular subchondral surface: 2 points; Narrowing of joint space: 2 points; Subchondral cyst formation: 1 point; Score: 7 points.

In the patients with a score of two or less at treatment the effect was good not only on synovitis and bleeding but also on the radiologically revealed changes, which did not progress. In all patients with a score of three or more at treatment there was progression of the radiological changes in spite of the often good effect on the bleeding frequency. This is in agreement with the findings by Nilsson et al. (1976) who studied a group of children who had been given prophylactic treatment with AHF infusions. In their series the majority of children with unaffected joints at the onset of treatment also had intact joints after 2–13 years of prophylaxis. In another group of children with partly destroyed joints at the onset of the prophylaxis, the joint destruction continued despite the prophylaxis.

Although the pathophysiology underlying hemophilic arthropathy is not fully known, it seems that there exists an early stage with reversible changes, characterized by synovial reaction, and a late irreversible stage of cartilage degeneration as well as joint destruction resembling both rheumatoid arthritis and osteoarthritis (van Creveld et al. 1971, Arnold & Hilgartner 1977). From the present study it seems that the late stage is not only irreversible but also progressive and that this progression occurs irrespective of further bleeding into the joints.

Thus, synoviorthesis with radioactive gold, and probably also other methods used to minimize the frequency of hemarthroses, should be performed as early as possible in the course of the arthropathy in order to prevent the development of irreversible changes.

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