PREVENTION OF SEVERE REACTIONS IN THE GOLD TREATMENT OF RHEUMATOID ARTHRITIS

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In view of the widespread use of the injection of gold salts for the treatment of rheumatoid arthritis I thought that my own experiences in attempting to prevent the skin reactions which so frequently bring this valuable treatment to a premature end might prove interesting.

In 1934 C. Mayer¹ published a paper describing his technique for the administration of gold to tuberculous patients at the Laennec Hospital in Paris. His method, although varying according to the initial state of the patient and the early responses to this mode of treatment, is, broadly, as follows.

A first injection of 0.1 gram crisalbine in 5 c.cm. of distilled water is given, and a week later 0.15 gram is used; the dose is then increased to 0.25 gram, which is also given in 5 c.cm. of distilled water, and ordinarily this dose is continued for four months for a single course. If severe reactions of any type occur he uses, instead of distilled water, 10 c.cm. of a 10 per cent. solution of calcium gluconate. If the patient is febrile at the beginning of the treatment he employs the gluconate solution instead of distilled water from the outset. By this method it appears that he has been able to administer gold over very long periods without producing any untoward reactions, even in single doses of as much as 1 gram where this has been necessary.²

Encouraged by these results I have tried the method in the gold therapy of rheumatoid arthritis, and I think that it has entirely justified itself. Before adopting it I was unfortunate enough to get skin reactions of greater or lesser degree in as many as one-third of the patients under treatment. In one case a generalized exfoliative dermatitis ensued in a woman of 58 after only 0.15 gram of allochrysine given in three weekly doses of 0.05 gram each. She recovered after intensive sodium thiosulphate treatment, but was very ill for nine weeks. Another woman of 56, who had received a course of allochrysine, amounting in all to 1.95 grams and administered as 0.1 gram doses weekly, with the exception of the first three doses, which were each 0.05 gram, developed a hepatitis six days after receiving the first dose of 0.1 gram of her second course, there having been an interval of two months following the first course.

In neither of these cases was there any evidence of a renal inefficiency, which, if present, might have led one to regard the patients as bad subjects for treatment of this kind. The first case must be regarded as one with a very marked personal idiosyncrasy towards the metal, for so small a quantity as 0.15 gram to have produced such marked toxic manifestations. These were the most severe of the reactions that I encountered during my earlier series of cases, before I used calcium gluconate concurrently with gold salts. The absence of anything other than mild reactions has been very striking in the cases treated since.

Gold Preparation and Dosage Employed

The gold preparation I use is allochrysine, and it is given in doses of 0.1 gram weekly up to a total dosage (for one course) of 1.8 to 2.4 grams, the total dosage being decided on by the alteration in the red cell sedimentation rate, as well as by the clinical condition of the patient. Previous to using calcium gluconate with the gold my first doses were 0.05 gram, and this amount was continued for two or three injections before going on to 0.1 gram. Now, however, I begin with 0.1 gram, and this seems to be quite safe when calcium gluconate is administered as well.

The allochrysine solution is mixed directly with 10 c.cm. of 10 per cent. calcium gluconate, the ampoule of saline solution supplied in the packages of allochrysine being discarded; the injection is then given intramuscularly. Mayer used a preparation known as "gluconyl" for his supply of calcium gluconate, this being already made up as a 10 per cent. solution. A more easily obtainable preparation in this country is one put up by the firm of Sandoz; this is prepared as a 10 per cent. solution sterilized ready for use in 10 c.cm. ampoules. The contents of the allochrysine ampoule mix readily with this.

Results in Sixteen Cases

Since April of this year I have treated sixteen cases of rheumatoid arthritis and one case of polyarticular gonococcal arthritis by this modification of Forestier's method,³ and in no instance has it been necessary to stop or even to intermit the treatment because of severe reactions. Probably the most instructive case in this series is that of a girl aged 25, who had been suffering for eighteen months from a very active type of rheumatoid arthritis. Her treatment was commenced before I had started the concurrent administration of calcium gluconate, and after receiving 0.4 gram of allochrysine she developed a severe papulo-erythematous rash, most profuse on the limbs, but also marked on the trunk. She felt ill and had to go to bed, where she was treated with sodium thiosulphate. The rash was succeeded by considerable desquamation, and she received no more gold for a month. When her treatment was restarted she was given calcium gluconate as well, and a full course of allochrysine, totalling 2.4 grams, of which 2 grams were administered after the subsidence of the skin reaction, was successfully given without further interruption.

The only reactions I have seen during the administration of gold and calcium gluconate together have been the following: (1) The development of a few itchy papules on the hands and less commonly on the feet. These have occurred in three cases, but they have been ignored and nothing more has happened; the treatment has not been suspended in consequence of their occurrence. They have been followed by a little desquamation of the skin of the hands, and presumably represent an abortive attempt at a skin reaction. One of these cases was that of the girl referred to above, and the papules appeared when she had received 1.4 grams. It is probable that had she not been protected by the calcium gluconate she would have developed another severe skin reaction. (2) A mild stomatitis, not unlike that occurring very rarely as a secondary reaction to nirvanol, but not nearly so severe. These reactions were in subjects who were at the end of their first courses of allochrysine, and so the effect which the further continued administration of gold would have had on the condition can only be speculative. It will be of interest, however, to note whether or not the stomatitis recurs early during their second courses of allochrysine and calcium gluconate.

In conclusion, when I first adopted this method I thought that perhaps the administration of calcium gluconate would neutralize not only the toxic effects of the gold but also its therapeutic effects. This fear, however, does not seem to have been justified, for not only does the clinical condition of the patient improve as with unadulterated gold, but the blood sedimentation rates also return to normal, and this latter test, when used with an appreciation of its limitations, seems to be the most useful index we have of whether or not the disease process is becoming quiescent.

REFERENCES

- ¹ Mayer, C.: *Brit. Journ. Tuberc.*, 1934, xxxviii, 131.
- ² Burrell, L. S. T.: *Medical Annual*, 1935, p. 454.
- ³ Forestier, J.: *Lancet*, 1932, i, 442.