Controlled Evaluation of Gold Therapy In Rheumatoid Arthritis*

HANS WAINE, M.D., FRANCES BAKER, M.D., AND STACY R. METTIER, M.D., *San Francisco*

GOLD compounds have been used extensively during the last ten years in the treatment of rheumatoid arthritis. The results obtained in several thousands of patients have been interpreted to indicate that gold salts are beneficial. The validity of such conclusions is not always apparent from the evidence presented since the criteria for selection of patients and for evaluation of therapeutic results often are indefinitely stated and vary considerably with individual reports. Moreover, adequate time of observation, a prerequisite to the study of a chronic remitting disease, is frequently wanting and follow-up periods cover months rather than years. Of equal or greater importance are satisfactory controls which have generally been lacking in reports on chrysotherapy.

In the present study, we have tried to meet these requirements. We have observed 120 patients with active rheumatoid disease. All of them showed the characteristic general features of this chronic constitutional ailment as well as peripheral symmetrical polyarthritis and elevation of the sedimention rate. All were treated as ambulatory patients although two in each of the series to be described were also hospitalized briefly. All patients were seen by the members of the Arthritis Committee regularly from one to four times each month during the period of critical observation.

Sixty-two such patients, consecutively admitted to the clinic, were given general supportive treatment. This included limitation of activity, dietary regulation, supplemental vitamins, salicylates and intensive physical therapy, the latter under the direction of one of us (F.B.) in the Department of Physical Medicine. These patients had previously had a variety of treatments which we considered non-specific and which did not include gold compounds. The average duration of the illness in these patients prior to admission was 4.36 years, the average duration of treatment and observation in the clinic was 3.02 years. The group of 58 remaining cases was constituted in part (10) by patients unsatisfactorily controlled through supportive therapy, in part (48) by new patients. All were admitted consecutively to chrysotherapy and given general care very similar to that of the first group. The average length of the illness antedating therapy was 5.5 years in this group and the average duration of treatment and observation 2.9 years.

Two soluble gold compounds were used, Gold Sodium Thiosulphate and Gold Sodium Thiomalate. Only those patients were included who received at least 0.5 grams, calculated as gold. The mode of administration was similar to that generally used, but instead of giving one or more courses of injections, we employed continuous treatment. The average maintenance dose was 50 milligrams of the salt given as indicated by the activity of the disease at weekly, bi-weekly or monthly intervals. The average total dose amounted to 1.6 grams in terms of the metal.

According to the results of therapy, we grouped all 120 patients under four headings: arrested, markedly improved, improved, and unimproved. Patients with the first designation lost all evidence of active arthritis, by history, physical examination and laboratory tests. In some, there remained residual deformities and articular damage such as an ankylosed hip joint or a roughened articular surface, previously the sites of active arthritis; but all continued to be free of constitutional and local symptoms of rheumatoid disease. The second group consisted of patients who were restored to good health with the same qualification as to irreversible joint changes in some. However, in these patients we could not with certainty exclude a measure of active disease. In some instances the sedimentation rate failed to become entirely normal, and in some cases with marked articular injury there remained symptoms which might have been caused by continued mild activity of rheumatoid arthritis. The third category comprised patients who were subjectively improved with therapy and showed a reduction in the sedimentation rate. In these patients there was definite evidence of persistent, though less active arthritis. The last group experienced either no improvement or further progression of the disease.

The distribution of patients according to these definitions in the series treated with gold salts and in the control series is given in the following table:

Result	Chrysotherapy Number	Chrysotherapy Per Cent	Controls Number	Controls Per Cent
Arrested	12	20.7	6	9.7
Markedly improved	21	36.2	12	19.4
Improved	14	24.1	17	27.4
Unimproved	11	19	27	43.5
Total	58	100.0	62	100.0

DISCUSSION

We consider that the patients in the first two groups of each series, those who were arrested and markedly improved, showed noteworthy beneficial change under therapy. The combined figures for the two groups are 33, or 56.9 per cent, in the series treated with gold compared with 18, or 29.1 per cent, in the controls. This difference in com-

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From the Departments of Medicine and Physical Medicine of the University of California Medical School.

parable series is statistically significant and indicates that gold salts are an adjuvant to the treatment of rheumatoid arthritis.

The fate of ten patients who fared poorly on supportive therapy alone and were given gold subsequently seems especially interesting. One of these remained unimproved. Of eight patients who had not been benefited in an average period of 2.75 years, three were improved and five markedly improved after chrysotherapy had been used. In one patient who had experienced some improvement and suffered a recurrence, the disease became arrested. Mild to moderate toxic reactions calling for temporary omission of gold therapy occurred in 29 patients, or 50 per cent. Four more patients were unable to tolerate what we considered an adequate amount of gold, showing signs of severe toxicity, and were therefore eliminated from this series. Of these, one exhibited marked, two some, and one no improvement in their arthritis.

CONCLUSION

Our data show that soluble gold salts are therapeutically effective in peripheral rheumatoid arthritis, since the rate of significant improvement is approximately twice as high in the gold treated series as in the controls. The results closely approximate those obtained by Frazer in a well controlled study.[1] It is also quite evident that chrysotherapy in the form commonly used in rheumatoid arthritis is far from satisfactory, in that it is not applicable to all patients because of severe toxic reactions in some and minor disturbances in about half of those treated, and in that it does not significantly benefit approximately 43 per cent of the subjects. Perhaps of greater importance than the effective therapeutic rate is the establishment of an agent which can influence the course of rheumatoid arthritis, since further studies on its mode of action may increase our understanding of the pathogenesis of this disease.

REFERENCE

1. Fraser, T. N.: Gold Treatment in Rheumatoid Arthritis, Ann. Rheumat. Dis., 4:71-75 (June), 1945.