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Corneal chrysiasis and clinical improvement with chrysotherapy in rheumatoid arthritis

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SUMMARY The deposition of gold in the cornea—ocular chrysiasis—is a normal event during chrysotherapy. It may reflect tissue deposition of gold and be of value in predicting clinical improvement or toxic reactions. We studied 21 patients with rheumatoid arthritis on chrysotherapy but could find no relationship between the appearance of ocular chrysiasis, clinical improvement, and toxicity.

Gold salts have been used in rheumatoid arthritis since 1927,[1] although their efficacy was not conclusively demonstrated until 1961.[2] Since 1961 there has been continuous change in the regimens used for chrysotherapy and in the selection of patients. Careful monitoring of therapy has reduced the risk of serious toxicity, and gold tends to be given more frequently and much earlier in the course of the disease. In the days of the 1000 mg course of gold given as 50 mg weekly cutaneous and mucocutaneous toxicity was relatively common after 600 mg had been given.[3–5] With a higher proportion of 'early' patients being treated with gold, toxicity as a dose-related problem is likely to increase, as 'early' patients seem to require a smaller total dose to induce a remission.[5]

Attempts to predict impending toxicity by measuring gold levels in plasma, skin, hair, and nails have been disappointing, and eosinophilia or raised serum IgE levels are relatively nonspecific.[6–8] A simple noninvasive method of assessing tissue deposition of gold might offer the clinician useful support in deciding the right time to change from weekly injections and in predicting toxicity.

Ocular chrysiasis is a well-recognised phenomenon of gold therapy. Deposition of gold in the cornea has usually been noted after a total dose of 1500 mg. It is thought to increase with the total dose and diminish after cessation of gold therapy, and to be of no clinical significance. We have looked at ocular chrysiasis from a different point of view. If ocular chrysiasis is an index of tissue deposition of gold, would its appearance in the cornea coincide with clinical improvement and allow us to use corneal chrysiasis as an index of the best dose of gold at which to change the frequency of injections? Alternatively would it reflect impending tissue saturation and give warning of cutaneous or mucocutaneous reactions?

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Materials and methods

Twenty-one patients with rheumatoid arthritis undergoing chrysotherapy were examined on one or more occasions by an ophthalmologist. All were receiving sodium aurothiomalate (Myocrisin), the total doses ranging from 562·5 mg to 2050 mg. The usual chrysotherapy regime used was a 10 mg test dose, followed by 50 mg weekly until major improvement occurred, then fortnightly with gradual increase in the intervals. In the event of toxicity gold was withdrawn until the side effect cleared, and treatment was reintroduced with a greater interval between injections or with smaller doses. If no improvement occurs, 100 mg injections are given, usually after a total dose of 800–1000 mg have already been given.

Slit-lamp examination was performed without knowledge of the total dose of gold, and the presence or absence of corneal chrysiasis was recorded. An assessment of each patient's disease activity was made at the same visit by an independent observer, not involved in the patient's management. Evidence of clinical improvement and changes in haemoglobin levels and the erythrocyte sedimentation rate (ESR) during gold therapy were determined from the patient and from the case notes. Subjective improvement was assessed by a reduction in the number of symptomatic joints and duration of morning and immobility stiffness. Any possible side effect of gold was sought from the patient and from the outpatient records.

Results

Corneal chrysiasis was visualised as numerous tiny yellowish-brown glistening deposits, irregularly placed throughout the cornea.[9] Of the 21 patients examined 13 (62%) had corneal chrysiasis. Of these 13 patients 11 had received a total dose of less than 1500 mg (Table 1) and 3 had not yet improved. The dosage schedules, duration of treatment, and total doses of gold were comparable in those with and without corneal chrysiasis (Table 1). Of the latter, 7 had improved. In 1 patient who had no corneal chrysiasis at a total dose of 710 mg slit-lamp examination was repeated and corneal chrysiasis found at 860 mg.

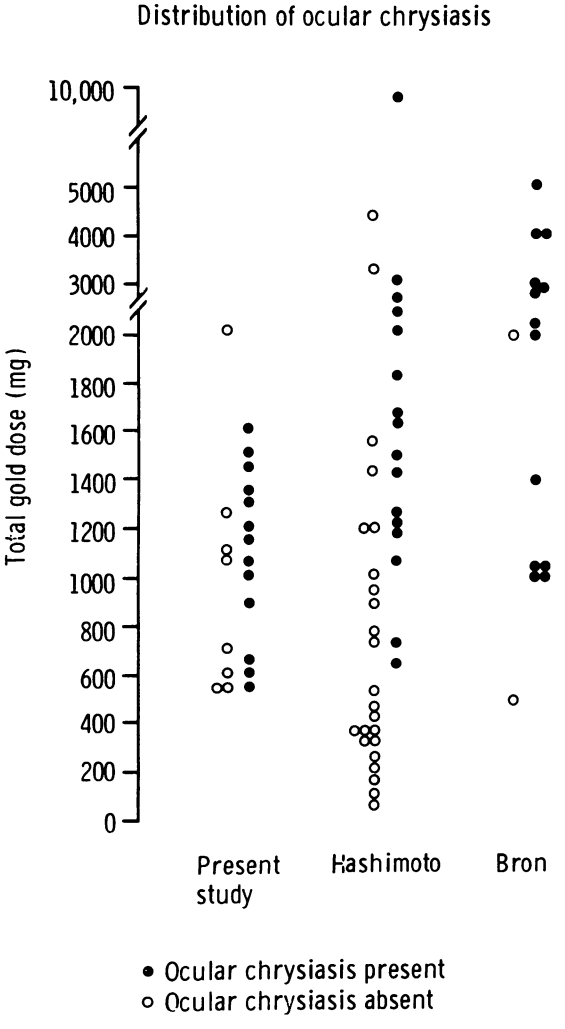

Fig. 1 *Presence or absence* ● *of ocular chrysiasis* ○ *according to total gold dosage (mg) in our patients, compared with those of Hashimoto and Bron* et al. [11]

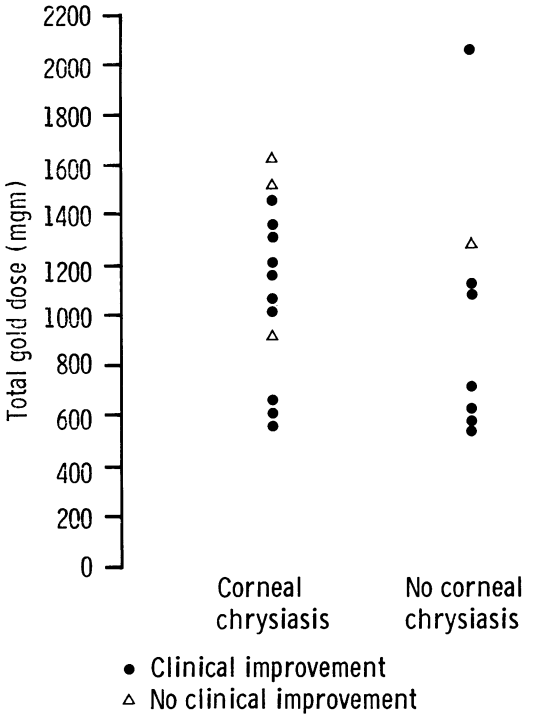

Fig. 2 *Response to chrysotherapy* (● *improvement* △ *no improvement*) *in patients with and without ocular chrysiasis according to total gold dosage.*

Seven patients (33%) had developed reactions possibly attributable to gold therapy—oral ulceration (4), skin rash (1), pruritus (1), and proteinuria (1). Of the 6 patients with mucocutaneous complications 3 had corneal deposits. In the 1 patient who developed proteinuria corneal deposits were also present; he had received 50 mg injections weekly till 960 mg, then 100 mg weekly injections till 1160 mg, but had ceased therapy 2 months prior to slit-lamp examination. No amyloid deposits were seen on rectal biopsy.

Discussion

This study explored a possible relationship between corneal chrysiasis and the best total dose of gold at which to alter the injection interval, or the possible onset of toxic symptoms, on the premise that the appearance of corneal chrysiasis reflects tissue gold levels. Our results show that major clinical improvement or toxic symptoms occur independently of corneal chrysiasis. Thus corneal chrysiasis would appear not to be related to the 'best' dose to have predictive value for possible complications of gold therapy (Fig. 1).

Corneal deposition of gold during chrysotherapy

Table *Corneal chrysiasis and clinical data in 21 patients with rheumatoid arthritis.*

Patients	*Age*	*Sex*	*Duration of RA (yr)*	*Duration of chrysotherapy (months)*	*Total dose (mg)*	*Injection dose (mg)*	*Frequency*	*Improvement*	*Complication dose (mg)*
1	59	M	5	9	562·5	20	Weekly	Yes	Mouth ulcers 482·5 mg
2	76	F	8	4	610	50	Weekly	Yes	
3	43	F	21	5	660	50	Weekly	Yes	Mouth ulcers 210 mg
4	66	F	1·3	6	900	50	Weekly	No	
5	51	M	9	10	1010	50	2 Weekly	Yes	Pruritus 1010 mg
6	58	F	5	5	1060	50	3 Weekly	Yes	
7	48	M	6	9	1160	100	Stopped 2/12	Yes	Proteinuria 1160 mg
8	74	M	1·5	6	1210	50	2 Weekly	Yes	
9	50	M	10	8	1310	50	2 Weekly	Yes	
10	63	F	4	11	1360	50	3 Weekly	Yes	
11	65	M	5	10	1460	50	4 Weekly	Yes	
12	73	M	4	11	1510	50	Weekly	No	
13	59	F	5	11	1610	50	Weekly	No	
No Corneal Chrysiasis									
14	59	M	20	4	550	50	Weekly	Yes	
15	61	M	8	3	560	50	Weekly	Yes	
16	39	F	5	3	610	50	Weekly	Yes	
17	59	M	2	8	710	50	4 Weekly	Yes	Skin rash 460 mg
18	71	F	6	13	1090	50	Weekly	Yes	Mouth ulcers 780 mg
19	66	M	4	8	1110	50	2 Weekly	Yes	
20	72	M	7	15	1270	50	4 Weekly	No	
21	46	F	13	36	2050	20	4 Weekly	Yes	Mouth ulcers 510 mg

Ocular chrysiasis was noted in patient 16 at dose 860 mg.

has been recognised for many years. Roberts and Walter in 1956 described a case in detail, considering it a rare occurrence.[10] In several series of patients examined for ocular chrysiasis, usually after 1 g had been given, corneal gold deposition has been found in percentages varying from 8% (Dippy) to 87% (Bron) [11–14] (and J. Dippy, 1979, personal communication). This difference cannot be explained just by variation in the total dose range of gold among the groups studied, as the range of total gold dosage and distribution within the dose ranges were comparable (Fig. 2) In these studies corneal chrysiasis was found mainly in the group who had received 1500 mg or more total dose. Our interest was in patients who had received smaller total gold doses, between 500 and 1500 mg total dose of gold. Hashimoto suggested in his study that corneal chrysiasis may be related to the individual dose and frequency of gold injections. He found corneal chrysiasis in 47% of his patients who had received between 500 and 1500 mg total dose, compared with 61% in our group over the same total dose range. Within the limits of our study group we did not find that the presence of corneal chrysiasis appeared to relate to the size or frequency of the gold injections (Table 1).

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