FACTORS IN GOLD DOSAGE AND TOXICITY IN RHEUMATOID ARTHRITIS

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Since the discovery of cortisone, the gold treatment of rheumatoid arthritis has been overshadowed by the dramatic action of this new remedy. As both cortisone and ACTH have been shown to be capable of maintaining their effect in a proportion of cases with appropriate maintenance dosage, and particularly as cortisone can be given by mouth, it would appear at first sight that there can no longer be a place for chrysotherapy in the treatment of this group of disorders. Though this may come to be the position in the future it certainly is not so at present, and until supplies of these newer agents are adequate to serve the needs of all rheumatoid sufferers, gold will continue to be used. It is essential, therefore, that it be used to the greatest advantage and any means by which toxicity can be reduced without impairment of therapeutic benefit must be carefully investigated.

The ability of gold to induce remissions in rheumatoid arthritis has been shown by controlled therapeutic trials (Ellman and Lawrence, 1938a, b; Ellman and others, 1940; Fraser, 1945; Kling and others, 1949), but the high relapse rates (Egelius and others, 1952) show that the effect at least with present therapeutic dosage is not curative, relapse being particularly frequent when low dosage has been used (Short and others, 1948; Browning and others, 1947). Owing to the very slow excretion rate of gold, however, relapses may not occur for some considerable time, and even after an observation period of 9 years patients treated with gold have been found to fare better than those receiving other methods of treatment (Kling and others, 1949). That the effect of gold is proportional to dosage has been shown in animals by Sabin and Warren (1940), and in man by Ellman and others (1940). Some workers have suggested that dosage of the order of 50 mg. weekly may be as effective as a larger dose (Freyberg and others, 1941 ; Comroe, 1945), but they have produced no statistical evidence in support of their claim. The indications from animal experiments are that the optimum total dosage is of the order of 100 mg./kg. (6 g./60 kg.) given over the shortest possible time.

It would appear, therefore, that successful gold treatment depends on administering a maximum dosage of gold whilst at the same time avoiding its more dangerous side-effects. Before discussing how this may best be achieved, it is necessary to consider certain pharmacological properties of gold.

Gold compounds injected intramuscularly are slowly absorbed from the site of injection, attaining, with normal therapeutic dosage, a maximum blood level of up to 2 mg./100 ml. of plasma by the 4th weekly injection. After stopping treatment the blood level slowly falls; reaches half its final level by the 9th week, but still continues to show detectable amounts at the end of the 4th month. Gold can be detected in the urine up to 10 months after stopping treatment (Freyberg and others, 1941; Hartung and others, 1941), and has been discovered in the tissues after periods of up to 3 years. In the blood, gold is combined with the plasma proteins (Freyberg and others, 1944). This gold-protein complex is a chemical compound and does not release gold ions in solution (Libenson, 1945). As colloids and other substances of high molecular weight present in the plasma can pass out of the circulation only through damaged capillaries, they tend to become concentrated at a site of induced inflammation (Menkin, 1936). It follows that gold in its combination with protein will not readily pass into the tissues except at a focus of inflammation. In a patient with active rheumatoid arthritis the gold will thus pass largely into the inflamed synovial tissues, and the concentration in such tissue has, in fact, been found to be some 18 times as great as in, for example, the skin (Bertrand and others, 1948). Thus, so long as there is active exudation into the diseased tissues, the danger of toxic effects in the skin, mucous

membrane, or haemopoietic tissue is likely to be reduced. As the disease process subsides, however, this shunting effect will diminish and the danger of gold deposition in healthy tissues will be liable to increase, which explains the tendency for toxic effects to be greater in those patients who derive the greatest benefit and greater in rheumatoid arthritis than in a resistant disease such as tuberculosis. It would also explain the inverse relationship between the erythrocyte sedimentation rate and gold toxicity noted by Ellman and others (1940), a relationship which is not absolute since toxic effects may arise when the erythrocyte sedimentation rate is still raised (Goldie, 1939; Price and Leichtentritt, 1943). The most serious and persistent manifestations nearly always arise when quiescence has been reached. In Goldie's series, for example, the erythrocyte sedimentation rate was below 10 mm. during the 2 weeks before the onset in eight out of eleven examples of desquamating erythema. In my own experience, though stomatitis and drug rashes frequently arise in patients in whom the erythrocyte sedimentation rate is still high, they are invariably transient. The persistent forms of stomatitis and dermatitis which were at one time such a distressing feature of chrysotherapy do not occur till the disease is almost or wholly quiescent.

Present Experiments

On the basis of these impressions and in view of the importance of giving the maximum tolerated dose, it was decided to treat a series of patients on a new schedule. In this the maximum dose was given from the start and was based on a scale related to the extent and activity of the disease process as measured by the erythrocyte sedimentation rate or preferably to the actual plasma fibrinogen concentration of which the erythrocyte sedimentation rate is an indirect measure. A fractional viscosity method (Lawrence, 1949, 1950) may conveniently be used for estimating the plasma fibrinogen. The corresponding viscosity differences are therefore given in Table I, which also shows the dosage.

Dosage.—The erythrocyte sedimentation rate or plasma fibrinogen is taken at 4-weekly intervals and the subsequent dosage regulated according to the same scale. Thus a female patient with an erythrocyte sedimentation rate of 50 mm. would start with a weekly dose of 200 mg., and this would be continued till the erythrocyte sedimentation rate fell below 25 mm. If, for example, it fell to 20 mm. the dose was reduced to 100 mg. weekly, if to under 15 mm. the dose fell to 50 mg. weekly. If the erythrocyte sedimentation rate rose, the dosage was increased again in accordance with the scale. No fixed limit was placed on total dosage unless this was necessitated by the appearance of toxic symptoms, but treatment was discontinued when the erythrocyte sedimentation rate had remained within normal limits for 2 months. When plasma fibrinogen values were substituted for the erythrocyte sedimentation rate it was found possible to include in the higher dosage group many cases in which the erythrocyte sedimentation rate was proving a fallacious guide to the activity of the disease process and to prolong treatment till recovery was more complete. If the erythrocyte sedimentation rate alone was used, the danger of an increased value due to anaemia had to be borne in mind. In such cases estimation of the plasma fibrinogen is essential.

Toxic Side-Effects.—Table II (opposite) shows the toxic symptoms in ninety patients. Thirty of these were treated on the old schedule and received two courses each of 2·5 g. gold at a weekly dosage of 200 mg., following the customary initial dose of 10, 20, 50, and 100 mg. at weekly intervals. These patients showed frequent toxic effects, and in many the symptoms were severe, stomatitis and extensive dermatitis causing great distress persisting for many months. One patient in this group developed agranulocytosis and purpura and died (Ellman and Lawrence, 1935).

Thirty others received 100 mg. weekly up to a total of 1·5 g. for each of two courses. Toxic effects were less frequent, stomatitis being comparatively rare and dermatitis less frequent. Blood and liver disorders were not encountered in this group. Nevertheless, the stomatitis and dermatitis of patients treated with such dosage may be severe and prolonged and fatal agranulocytosis is not unknown.

In the remaining thirty, the graded dosage-schedule described above was used. The majority of these patients received a dosage of 200 mg. weekly at some part of the treatment, and for some who proved resistant, doses of 300 mg. were used for a time. Nevertheless, there was significantly less stomatitis in this group than in those receiving set courses of gold at a similar weekly dosage. The difference between this group and those receiving the smaller doses is not significant as regards stomatitis, nor are there any significant differences between any of the groups in any other respect, though it should be noted that Group I shows most dermatitis and is the only

TABLE I
GOLD DOSAGE USED IN THIS INVESTIGATION

Fibrinogen		Erythrocyte Sedimentation Rate (mm./hr, Westergren)		Weekly Dosage of Gold Compound (mg.)
Mg. per cent.	Viscosity Difference	Female	Male	
Over 550	Over 25	Over 25	Over 20	200
450-550	20-24	15-24	10-19	100
Under 450	Under 20	15 and under	9 and under	50

TABLE II

RELATIONSHIP OF DOSAGE SCHEDULES TO TOXICITY IN RHEUMATOID ARTHRITIS TREATED WITH SOLGANAL B OLEOSUM

Group	Dosage	Toxic Side-Effects					Total Patients
		Stomatitis	Dermatitis	Agranulocytosis	Jaundice	Grippe aurique	
I	200 mg. weekly for two courses of 2·5 g.	8	8	1	1	1	30
II	100 mg. weekly for two courses of 1·5 g.	1	5	0	0	0	30
III	200-300 mg. weekly till E.S.R. normal: then 50 mg. weekly for 8 weeks ..	4	6	0	0	2	30
III A	Those in III who had an initial dose of 300 mg.	2	1	0	0	2	13
III B	Those in III who had a dose of 100 mg. for the first two injections	2	5	0	0	0	17

group to show agranulocytosis or jaundice. A feature noted in Group III in two instances and in Group I once was a febrile reaction associated with generalized urticaria, erythema, and aggravation of the joint symptoms occurring about the 12th day of treatment. This reaction closely resembles serum sickness and may well be of the nature of an acquired sensitivity to the gold-plasma-protein complex to which reference has already been made. In Group III it occurred only in those receiving a high loading dose and was then of such severity that a lower initial dosage was substituted. Since the initial two doses have been reduced to 100 mg. weekly it has not been encountered.

The data given in Table II can give only a very inadequate indication of the difference between these methods of treatment. The stomatitis and dermatitis encountered in Group III were very different in character from those in Groups I and II. In the latter they were frequently severe and associated with extensive ulceration of the mouth and gums and an eruption involving the face and limbs and sometimes also the trunk, the pain and itching sometimes causing serious loss of sleep. Moreover, both the stomatitis and dermatitis sometimes proved very intractable, the former sometimes lasting for a month or more, the latter for over a year in some instances. In Group III, on the other hand, the lesions of both mouth and skin were mild and transient and when they had subsided the gold treatment could, if necessary, be resumed with a modified dosage. Occasionally in this group a small scaly patch might persist on the arm or leg, but this did not cause discomfort.

Type of Preparation.—A number of preparations of gold have been used for the treatment of rheumatoid arthritis (Table III), but surprisingly little information is available on their relative toxicity. In acute toxicity experiments in animals (Sabin and Warren, 1941) toleration has proved high and has been found to depend less on the proportion of gold in a compound than on the nature of the radical to which the gold is attached and on its solubility. Thus the insoluble gold compounds such as calcium aurothiomalate were found least toxic, a dose of 5 g./kg. being tolerated, whereas only 0·2 g./kg. sodium aurothiomalate could be given. These doses, however, far exceed normal therapeutic doses in man which are of the order of 2 mg./kg. Chronic toxicity experiments in animals which would be much more informative do not appear to have been made.

TABLE III

ORGANIC GOLD COMPOUNDS USED IN TREATMENT

Chemical Name	Proprietary Name
Sodium aurothiosulphate	Sanocrysin, Crisalbine
Sodium aurothiopropanol sulphonate	Allochrysine
Sodium aurothioglucose	Solganal B
Sodium aurothiomalate	Myocrisin
Calcium aurothiomalate	Aurocalcium
Sodium aurothiosinamine benzoic acid	Lopion
Gold-keratin compound	Aurodetoxin

Gold toxicity in patients under treatment with gold was studied by Hartfall and others (1937), who used a number of gold preparations and did not find them all equally toxic. Toxic reactions were more frequent with Myocrisin and Crisalbine, containing 50 and 37 per cent. of gold respectively, than with Solganal and Lopion containing 40 and 50 per cent. respectively, so that toxicity was unrelated to gold content. Severe reactions occurred most frequently with Myocrisin (6 per cent. of 67 cases) and least commonly with Solganal (1·6 per cent. of 301 cases). With all preparations, skin manifestations were more frequent than any other toxic reaction and generally took the form of an erythematous eruption with pruritus. Peripheral neuritis was encountered in two patients, both of whom had been treated with Myocrisin. Stomatitis and jaundice were also relatively more frequent in those having Myocrisin. Purpura occurred in nine of the total of 1,415 patients and agranulocytosis in one, the purpura being equally distributed amongst patients receiving different preparations of gold.

Snorrason (1952) treated patients with Sanocrysin, and serious toxic effects occurred in 6 per cent. Sundelin (1941) administered calcium gluconate at the same time as the gold in a proportion of his

TABLE IV

TOXIC SYMPTOMS ARISING DURING TREATMENT WITH DIFFERENT PREPARATIONS OF GOLD

Preparation	Total Treated	Toxic Side-Effects									
		Stomatitis		Skin Eruption		Albuminuria		Polyneuritis	Purpura	Pruritus	
		No.	%	No.	%	No.	%			No.	%
Sodium aurothiomalate (aqueous)	33	19	63	11	37	5	20	2	0	2	7
Sodium aurothioglucose (oily) ..	25	8	30	8	30	5	20	0	1	2	8
Sodium aurothiomalate (oily) ..	2	0		0		0		0	0	0	
Sodium aurothioglucose (aqueous)	5	3		1		2		0	0	0	
Calcium aurothiomalate	4	3		1		0		0	0	1	

cases, but did not find the incidence of complications reduced.

The writer has, during the past 10 years, administered aurothiomalate (Myocrysin or Aurocalcium) to alternate patients with rheumatoid arthritis, and Solganal B to the remainder. In this way a group of 66 patients has been studied for a sufficient time to assess toxicity. The toxic symptoms are shown in Table IV; these patients were treated according to the schedule already described, in which the dose was greatly reduced when the erythrocyte sedimentation rate or plasma fibrinogen had reached a normal level. With this schedule, as already noted, there were no blood or liver disorders. Myocrisin was administered chiefly in aqueous solution, and Solganal B in a suspension in oil which was, until recently, the only form in which it was available. Since an aqueous solution of Solganal B has come available it has been studied alternately with the oily preparation in the Solganal group, and for comparison an oily suspension of Myocrisin is also now being used in alternate Myocrysin patients. The numbers treated with aqueous Solganal and oily Myocrisin on which data are available are as yet small and will be the subject of a later report, but they are included in the Table. Four patients treated with calcium aurothiomalate (Aurocalcium) are also included.

Results.—The most striking feature of this study is the high incidence of stomatitis in the Myocrisin treated series. Over half the patients had stomatitis at some time during the treatment, compared with only one out of eight receiving Solganal B. Despite the small numbers, this difference is highly significant. Dermatitis also tended to be more frequent in the Myocrisin group, but both in this group and in those receiving Solganal, it rapidly subsided when treatment was stopped, and it was found possible to resume treatment with a modified dosage where such a resumption was required. In a few instances, a small dry, scaly patch remained, generally in the region of the knee or elbow, but by then the disease had generally been controlled and only a low maintenance dosage was thereafter required. Albuminuria was found with similar frequency in those treated with Myocrisin and Solganal B. It was not associated with symptomatology or with laboratory evidence of renal impairment in either group, and, though dosage was modified when this complication arose, it was not found necessary to discontinue treatment. Polyneuritis supervened in two patients treated with Myocrisin. In one of these, who has already been reported (Leiper, 1946), it subsided in the course of the next 3½ months when it was found that the rheumatoid process had been completely suppressed. In the second patient it arose at a time when the value of monthly maintenance doses was being studied. As a monthly dose of 50 mg. had been found inadequate in earlier cases, 100 mg. monthly was used for this patient. The first six of these monthly maintenance doses were given without ill effect, but the seventh was followed by a severe histamine-like reaction, characterized by flushing and loss of consciousness, the pulse becoming imperceptible for about a minute. This was followed a day or two later by weakness of the right leg and both arms which is still present 19 months later. It should be pointed out that in this case a dose of 100 mg. was used at a time when both the erythrocyte sedimentation rate and plasma fibrinogen were within normal limits, so that dosage was excessive according to the schedule already outlined. Histamine-like reactions characterized by flushing, headache, and sometimes unconsciousness with imperceptible pulse, occurred in several patients treated with this batch of Myocrisin, but no others developed polyneuritis or other ill-effects. The samples had turned a dark-brown colour due to exposure to light and showed increased toxicity to chicks, and it was concluded that some highly toxic decomposition-product had been formed from the gold salt. Similar histamine-like reactions have been noted by others with certain batches of Myocrisin (Barber, 1952), and the author had a similar experience with another batch, which had, however, been kept in a hospital dispensary for 6 years.

The purpura which appeared in one patient on

TABLE V

RELATIVE EFFICIENCY OF AUROTHIOGLUCOSE AND AUROTHIOMALATE IN PATIENTS IN WHOM TREATMENT WAS STARTED BEFORE AUGUST, 1951*

Preparation	Weekly Dose	Total Patients	Results					Refused treatment or ceased to attend	Erythrocyte sedimentation rate finally normal in three consecutive monthly tests	
			Quiescent		Improved	No change	Worse			
			No.	%					No.	%
Sodium Aurothioglucose (Solganal B)	200-300 mg. 100 mg.	56 30	22 8	39 27	30 20	2 1	0 1	2	38 11	68 37
Sodium Aurothiomalate (Myocrisin)	200-300 mg.	27	10	37	16	0	0	1	15	55
Control	Sterile almond oil	30	1	3	22	6	1	0	4	13

* This table includes data from an earlier investigation (Ellman and others, 1940).

Solganal B was unassociated with thrombocytopenia and proved transient. Pruritus was complained of by two patients treated with Myocrisin and by two receiving Solganal. In the former it was limited to the anal region, in the latter it was more generalized. In all it was very transient and caused little inconvenience.

The number of patients treated with oily Myocrisin and aqueous Solganal is small, but it would appear that aqueous Solganal shows the same tendency to produce stomatitis as the aqueous preparation of Myocrisin. The use of Aurocalcium (calcium aurothiomalate) was discontinued after it had been used in four patients, all of whom developed toxic manifestations, three of them stomatitis. This stomatitis differed from that resulting from treatment with other gold preparations in being more widespread and always associated with an eruption on the inside of the cheeks.

Comparative Efficacy.—Diminished toxicity is of practical importance only if associated with undiminished therapeutic efficiency. Data on therapeutic effect are accordingly shown in Table V. In this table all patients on high dosage of Solganal B have been included, whether on the original two-course scheme or on the later schedule, the results by these two methods being closely similar. A group of patients on a lower dosage of Solganal B has also been included. Myocrisin was not studied in the lower dosage or by the two-course scheme. The control group received injections of sterile almond oil once weekly as described in a previous paper (Ellman and others, 1940). Assessment of results was made on completion of treatment or at the end of 9 months.

The term "quiescent" is used to indicate the absence of pain, either spontaneous or on movement of the affected joints, associated with a normal erythrocyte sedimentation rate and plasma fibrinogen. The erythrocyte sedimentation rate, estimated by the Westergren method, was considered normal when below 10 mm. in the male and 16 mm. in the female. A number of patients still complained of slight residual pain after the blood findings had become normal. Some of these showed evidence of osteo-arthritis in the painful joints, but were not labelled as quiescent.

It is clear from the data in Table V that Myocrisin has no greater therapeutic effect than Solganal B. The indications are rather that its effect may be less, fewer attaining a normal erythrocyte sedimentation rate amongst those treated with it, but the differences are not significant and may well be due to more frequent interruption of treatment because of toxicity in this group. Nor is there any significant difference between the Myocrisin group and those receiving small doses of Solganal. There are, of course, highly significant differences between both the Myocrisin and large-dose Solganal group and the controls, and the differences between high-dose Solganal and low-dose Solganal, and between low-dose Solganal and the controls are significant as regards the erythrocyte sedimentation rate.

Data are unfortunately not now available regarding return to work amongst the earlier cases studied, including those in the small-dose Solganal and control groups, but of the later high-dose Solganal and Myocrisin groups, all those below the age of 65 have returned to work, apart from one patient who also had severe disk degeneration.

Discussion

Preparation.—It is clear from all data so far considered that toxicity does not depend on the proportion of gold in the compound used, and some feature in the organic part of the molecule must

therefore be held responsible. On the other hand, the toxic symptoms are those which commonly arise in heavy metal poisoning and are presumably due to the gold ion. This may be explained if it is assumed that the organic fraction determines the distribution in the tissues and eventual disposal. As the excretion of gold is extremely slow, it is unlikely that relative excretion rates play an important part in toxicity, and it seems more probable that distribution in the body is the main factor. The importance of molecular size in determining the relative concentration in diseased tissues has already been noted in this connection, and it is therefore of interest that, whereas Myocrisin, which is more toxic, has a molecular weight of 390, the molecular weight of Solganal B is, by virtue of a certain degree of polymerization, of the order of 1,000. The fact that the Solganal used for the greater part of these trials was in an oily suspension and the Myocrisin was in aqueous solution may have played a part. If, for example, a higher peak blood level were attained after injection of an aqueous solution, the combining-power of the plasma proteins for gold might be exceeded and permit of greater diffusion of the gold through undamaged capillaries into tissues other than those of the diseased joints.

An important point which arises from this study is that total dosage of gold is not important. One patient in this series had as much as 9 g. without a pause, and apart from a transient pruritus and gingivitis, suffered no ill-effect. Though gold must undoubtedly accumulate in the tissues, it would appear to become fixed and to be no longer capable of producing toxic effects, though rarely a toxic effect on the blood-forming organs has been known to arise some time after treatment, possibly due to reactivation of gold fixed in the tissues.

Duration of Treatment.—A decision as to the duration of treatment must depend on whether gold therapy is regarded as curative or suppressive. It is well recognized that relapses are frequent in patients treated with gold, though they may not occur for some considerable time after the cessation of treatment, particularly if high dosage has been used. As, however, the excretion of gold is very slow and may not be complete after 3 years, a suppressive action is not ruled out. It is indeed supported in some measure by the differential agglutination test, whose titre is not at once reduced by successful aurotherapy, and may be higher when the disease has reached the quiescent stage than before starting treatment. In this respect gold resembles cortisone, which is also without effect on the differential agglutination test. Moreover, in arthritis of known aetiology, as, for example, the infective arthritis of rats, which histologically shows a close resemblance to rheumatoid arthritis, the causative virus has not been found susceptible, though the disease process can be completely suppressed by aurotherapy (Sabin and Warren, 1940).

If aurotherapy is merely suppressive, it would seem reasonable to provide some sort of maintenance treatment once the quiescent stage has been reached. This poses a difficult problem, and two alternative solutions are at present being studied:

(*i*) To give maintenance doses of, say, 50 mg. every 4th week for a prolonged period, until, for example, all signs of activity have been absent for 3 years. A longer period may, of course, prove to be necessary, and the differential agglutination test, if it is indeed an index of the continued presence of the aetiological agent, may assist in this respect. Even on such a maintenance dosage, the condition may recur, as happened in one patient in the present series. If this should happen the dosage should not be increased unless the plasma fibrinogen content rises, but the injections may be given more frequently.

(*ii*) To keep the patient under observation without maintenance dosage of gold, the erythrocyte sedimentation rate and plasma fibrinogen being taken at intervals of 3 to 6 months. If evidence of relapse appears the treatment may then be resumed.

It is too soon at present to say which of these alternatives should be preferred. The danger of relapse is probably greater when treatment is interrupted, as patients on this routine are more likely to stop attending, and may not reappear till the relapse is in an advanced stage. This must be placed against the possibility of toxic effects arising from maintenance dosage, if the former alternative is adopted.

Summary

Alternate patients on gold therapy for rheumatoid arthritis received aurothioglucose (Solganal B oleosum) and aurothiomalate (Myocrisin or Aurocalcium).

The aurothioglucose proved significantly less toxic, the incidence of stomatitis being halved. Polyneuritis occurred in two patients receiving aurothiomalate, but in none of those treated with aurothioglucose. The possible factors responsible for this difference in toxicity are discussed.

No significant difference in therapeutic efficiency was found between these two compounds.

A method is described whereby the greater therapeutic efficiency of a high dosage (up to 200 mg. weekly) of gold in rheumatoid arthritis may be attained without the greater incidence of side-effects

normally present with such a dose. The method depends on an adjustment of gold dosage in relation to the activity of the disease process as determined by the fibrinogen content of the plasma.

In a series of 66 patients treated in this way, no blood dyscrasias or chronic skin eruptions were encountered, and all those under the age of 65 were able to return to work. The blood sedimentation rate was maintained at a normal level in 57 per cent. of patients treated on this schedule as compared with 37 per cent. of patients receiving a standard dosage of 100 mg. weekly. Only two (4 per cent.) failed to improve.

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Facteurs posologiques et toxiques de la chrysothérapie de l'arthrite rhumatismale

RÉSUMÉ

Au cours de la chrysothérapie de l'arthrite rhumatismale les malades alternatifs ont reçu de l'aurothioglucose (Solganal B oleosum) et les autres de l'aurothiomalate (Myocrisine ou Aurocalcium).

L'aurothioglucose s'est montrée clairement moins toxique, réduisant de moitié la fréquence de la stomatite. La polynévrite survint chez deux malades traités par l'aurothiomalate, sans apparaître chez ceux traités par l'aurothioglucose. On discute les facteurs pouvant expliquer cette différence de toxicité.

On n'a pas trouvé de nette différence entre ces deux produits en ce qui concerne leur efficacité thérapeutique.

On décrit une méthode qui dans l'arthrite rhumatismale augmente l'efficacité thérapeutique grâce à l'emploi de fortes doses (jusqu'à 200 mg. par semaine) sans augmenter la fréquence des incidents secondaires que de telles doses entrainent généralement. D'après cette méthode on ajuste les doses des sels d'or en fonction de l'activité morbide indiquée par le taux sanguin du fibrinogène.

Dans un groupe de 66 malades ainsi traités on n'a pas observé de dyscrasie sanguine ou d'exanthème et tous les maldes âgés de moins de 65 ans ont pu reprendre leur travail. La vitesse de la sédimentation globulaire s'est maintenu normale chez 57% des malades traités par cette méthode et chez 37% seulement de ceux traités par des doses habituelles de 100 mg. par semaine. Deux malades seulement (4%) n'accusèrent pas d'amélioration.

Factores posológicos y tóxicos en la auroterapia de la artritis reumatoide

SUMARIO

En el curso de la crisoterapia de la artritis reumatoide los enfermos alternativos fueron tratados con aurotioglucosa (Solganal B oleosum) y los demás con aurotiomalato (Myocrisin o Aurocalcium).

La aurotioglucosa resultó ser netamente menos tóxica, reduciendo de la mitad la incidencia de estomatitis. La polineuritis sobrevino en dos enfermos tratados con el aurotiomalato sin aparecer en los tratados con aurotioglucosa. Se discute los factores probables que motivan esta diferencia de toxicidad.

No se encontró diferencia significante en la eficacia terapéutica de los dos productos.

Se describe un método de tratamiento de la artritis reumatoide que permite aumentar su eficacia con altas dosis (hasta 200 mg. semanales) de oro sin aumentar la incidencia de efectos secundarios, habituales con tales dosis. Este método consiste en un ajuste de las dosis de sales de oro en relación a la actividad morbosa reflejada en la tasa de fibrinógeno en el plasma.

En un grupo de 66 enfermos así tratados no hubo discrasia sanguinea ni exantema y todos los enfermos de menos de 65 años de edad pudieron volver a su trabajo. La velocidad de sedimentación globular mantúvose normal en el 57% de los enfermos tratados con este método y tan sólo en el 37% de los tratados con dosis habituales de 100 mg. por semana. Dos enfermos solamente (4%) no acusaron mejoría alguna.