

AN INVESTIGATION INTO THE USE OF GOLD THERAPY IN
THE RHEUMATOID TYPE OF ARTHRITIS WITH CONTROLS.

BY

J. S. LAWRENCE.

Of recent years there has been an amount of literature indicating the favourable effects of certain gold compounds in the rheumatoid type of arthritis. Our perusal of this literature has, however failed to reveal any systematic investigation carried out with adequate controls, which owing to the variable course of the disease and the tendency to natural cure is, we feel, essential if any satisfactory conclusion is to be reached. We ourselves have, during recent years, utilised gold therapy in a very large number of cases but are concerned in this work with only a limited number of these where it has been possible to prolong our observations over a period of time and make comparisons with control cases.

The classification of arthritis is unfortunately confusing and chaotic. From the aetiological, pathological and clinical standpoints there are, as Garrod originally described, two distinct groups corresponding to

- (a) the so called rheumatoid type and
- (b) the osteo-arthritic type.

Basing ourselves on the works of Nichols and Richardson, on the pathological studies of chronic arthritis of Assman, of Allison and Ghormley and of Timbrell Fisher, we have adopted a classification which is comparatively simple and at the same time comprehensive. The two groups recognised are :- (a) the rheumatoid type of arthritis and (b) the osteo-arthritic type.

Each has as a rule its distinctive aetiology, pathology and symptoms and signs, although a mixed type due to osteo-arthritic changes supervening on a long standing rheumatoid arthritis, can and does exist.

Gold Therapy. History.

Up to the present time no drug therapy has been shown to have any appreciable effect on this condition so that if gold therapy proves successful it will undoubtedly revolutionise the prognosis of the disease.

The modern use of gold salts in disease dates back to 1912 when Bruck and Gluck used them in the treatment of lupus erythematosus. In 1916 the first organic preparation, gold-thio-salicylic acid, was introduced by Feldt. Since then numerous other organic and inorganic gold compounds have made their appearance. They all possess one feature in common, namely the sulph-hydryl linkage, which, in the opinion of pharmacologists, plays an important part in the therapeutic activity of the compound.



In 1924 Møllgaard and his associates carried out some important experiments on the action of Sanocrysin. This particular compound is a double thiosulphate of gold and sodium containing 37% of gold. It was found that it prevented the growth of tubercle bacilli in culture and that it had the same effect when injected into a lesion. It was furthermore then regarded by Møllgaard as of immense value in tuberculosis, particularly where the disease was detected while still in its early stages.

Feldt and others (1926) worked out the chemotherapeutic index of a number of organic gold compounds, using dogs infected with syphilis. This index gave a comparison between the minimum curative and the maximum tolerated dose. It was shown to vary from $1/2$ to $1/10$ in the case of sulphonylat and of salvarsan. Similar results were obtained with mice infected with spirochaeta recurrens fever. Schieman and Feldt (1926) tested the effect of gold on mice infected with streptococci, of raised virulence, from a case of puerperal fever. Of the cases treated by the subcutaneous administration of gold 58% recovered. Intravenous administration caused a recovery rate of 28%. every one of the controls died.

Feldt (1930 I) also introduced auro-thio-glucose or solganol B a compound containing 50% of gold. It was found, when tested on canine syphilis, to have a therapeutic index of $1/75$. A dog tolerates 2 gms. of this drug per kilogram of body weight. Streptococcal infections in mice were cured by a dose equal to $1/8$ of the tolerated dose.

These preparations were used in 1924 in tuberculosis, lupus erythematosus, disseminated sclerosis and syphilis. Five years later papers appeared by Umber (1929) and Forestier (1929) on their use in rheumatoid arthritis.

Effect of Gold in Rheumatoid Arthritis.

Forestier (1932 I) using Allochrysin in doses of 0.05, 0.05, 0.05, 0.1, 0.1, till 2.0 gms. in all had been given and after 6 weeks rest a further course or courses if necessary found that about 70% of his cases reacted favourably. The result appeared to depend on the duration of the disease. In cases of less than one year's duration there was improvement in 100% and cure in 56%-70%. In cases of 1-4 years duration there was improvement in 70% and cure in 25-30%, and in cases of 5 or more years duration there was improvement in 50%. The majority of his cases had a high sedimentation rate, the average figure being 42 mm. Under gold treatment the sedimentation rate became less eventually reaching normal figures (below 10 mm.). After completion of the treatment the patient reported at intervals for further estimations of the sedimentation rate, a rise being regarded as an indication for further treatment.

Feldt (1930 II) treated 24 cases of infective arthritis with Solganol. Of these 4 showed no improvement, 2 showed a slight change and the rest were definitely better. The majority lost pain and joint swellings though at first there was normally an aggravation of the pain. This proved to be a favourable sign as it was followed by a rapid improvement, starting after about 1 gm. of Solganol had been given.

Denier (1930) obtained his best results by giving gold together with local X-ray treatment.

Fehlow (1930 & 1933) gave large doses of Solganol, 0.1 to 0.5 gms. every second day. He considered that each dose should

be so regulated as to produce a rise of temperature and he believed that in this way he obtained the best and most lasting results. Israelski (1931) gave Solganol orally. Freund (1931 II) tried both oral and parenteral routes but obtained the most favourable results with the latter. The former however had the advantage of producing no complications. Maliwa(1932) gave Solganol orally. He decided that the physical treatment was thereby rendered more effective. Huhn(1932) treated 22 cases of infective arthritis with Solganol B. Of these 62% showed increased mobility though some pain remained. 9% showed slight improvement and 5% no change. He used doses of 0.01-0.24 gms. with a total of 3.5 gms. for the course. Secher(1932) gave Sanocrysin in doses of 0.25-0.75 gms. Severe joint reactions followed, especially at first and pyrexia invariably occurred. Of 23 cases of primary progressive chronic arthritis, 24% were cured, 70% improved and 6% remained unchanged. Faber(1933) who used doses of 0.1-0.6 gms. of Sahnocrysin also noted marked focal reactions. Slot et al(1934) gave injections of 0.01-0.5 gms. of Solganol B at four-day intervals with resulting improvement in all cases. Pemberton(1935) found that 17% of his cases were cured, 39% much improved, and 31% slightly improved. 13% were unchanged. The average duration of the disease in the cured cases was 1½ years, in the improved cases 5 years and in those which remained unaltered, 7 years. Allochrysin, Crisalbine, and Myocrysin were used, and all proved equally efficacious.

Crosby(1936) treated 27 cases of arthritis with Allochrysin and Solganol B oleosum. 33% were greatly improved, 41% moderately improved, 11% slightly improved and 15% unaltered.

Copeman and Tegner(1937) using small doses (up to 0.1 gms) in cases of rheumatoid arthritis, found that 58% were greatly improved, or cured, 36% were moderately improved and 6% showed no change. The effect on cases of spondylitis was found to be negligible. The sedimentation rate fell in 69%, was unaltered in 18%, and rose in 4%. A fall in sedimentation rate heralded improvement in the joint condition. A preliminary rise after the first few injections of gold occurred in 9% of cases.

Hartfall, Garland and Goldie(1937) treated 690 cases of rheumatoid arthritis. 9.9% were cured, 56.8% showed marked improvement, 13% moderate improvement, 6.2% slight improvement, 8.9% no improvement, 2.5% were worse after the treatment and 2.7% died during the course of treatment. They used four different preparations of gold - Crisalbine cured 23%, myocrysin 0%, Solganol 4.2% and Lopion 10.8%. If, however, all cases showing marked improvement or cure are taken, it is found that the results obtained do not differ appreciably.

Plan of Investigation

For the purposes of this investigation only the most typical cases of rheumatoid arthritis were used. Monarticular cases or any in which the clinical picture did not conform accurately to type

were not used. Reference to the case histories (see page 23) will illustrate this point.

The joints found to be most commonly affected were the carpal tarsal and proximal-interphalangeal joints of the fingers and toes. They showed peri-articular swelling and limitation of movements. Movements of the wrists were usually severely restricted and painful and ankle, knee and elbow joints and feet were also frequently involved in the arthritic process. The age of the patients ranged between 18 and 68.

Before beginning gold the patients were put on a preliminary course of physical treatment varying from 1-12 months. Some had already had physiotherapy for a year or more when this investigation was first started but only those who showed little or no response to physical treatment were selected. They were then divided into two equal groups, one for treatment with gold salts, the other for purposes of controls. Both groups included old-standing as well as recent cases and also cases with high and with low sedimentation rates. The patients of the control group were given injections of oleum amygdale dulcis in doses of 0.1, 0.2, 0.4 and 1.0 cc into the buttock once a week, the last dose being repeated till 15 injections had been given in each course. This oil is one frequently used for suspending gold preparations.

It is possible that the various preparations of gold have different degrees of activity when used in the treatment of rheumatoid arthritis and for this reason the more valuable conclusions are to be drawn from a series of cases treated with the same compound. This investigation is, accordingly, concerned purely with the effect of Solganol B.

Solganol B may be given intravenously in aqueous solution or intramuscularly as a suspension in oil, the latter having been the method utilised in the majority of the cases under consideration in this paper. We have preferred the intramuscular method of administration as we consider the slower absorption less likely to produce toxic reactions. Injections were begun with a very small dose containing 0.01 gms. of the preparation. If this dose caused no reaction the amount injected was gradually increased, viz., 0.05 gms., 0.1 gms., 0.2 gms. The last dose was continued until a total of 2.5 gms. had been given. After six weeks another course has been given in this series in precisely the same dosage. At further intervals of not less than six weeks further courses have been given if symptoms and signs have persisted and the sedimentation rate has remained high.

In a further series of cases, also recorded in this paper we have employed a smaller dosage as follows:- 0.01 0.02 0.04 0.075 0.1 gms. Solganol B oleosum at weekly intervals, the last dose being continued till the sedimentation rate has reached normal figures (below 10mm. in the 1st hour). Four doses of 0.05 gms. were then given at weekly intervals, and another estimation of the sedimentation rate was then carried out. If this remained within normal limits treatment was discontinued for six weeks. The first course in this

series was therefore frequently very long in some cases, lasting as much as 12 months. In the second course the dose of 0.05 gms. was not exceeded unless the sedimentation rate again rose above 10 mm. Our reasons for this method will be discussed later when the toxic effects of gold are considered. In certain cases a more gradual increase in dosage was necessitated by the severe reactions experienced by the patient. These reactions usually took the form of an aggravation of joint pain but were in some cases pyrexial.

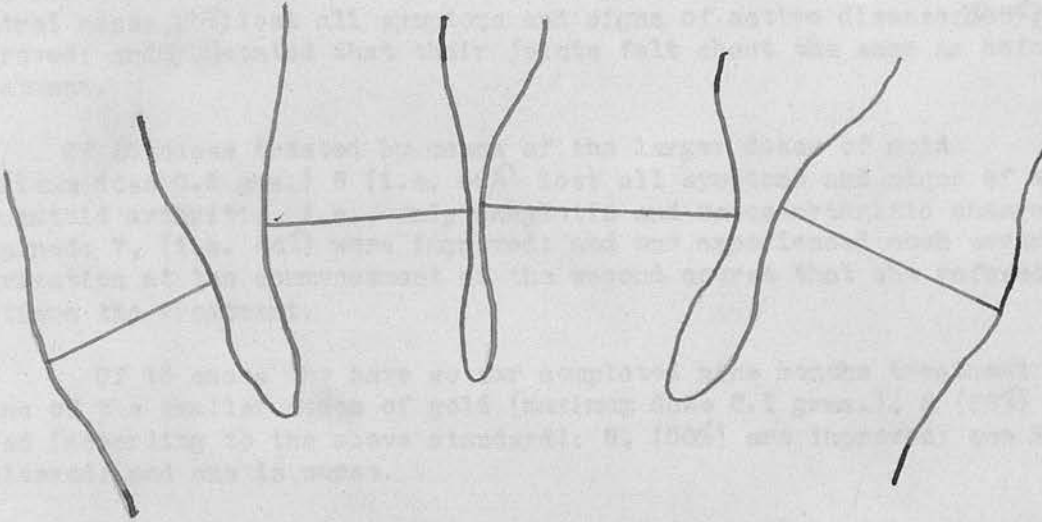
Before beginning treatment patients were interrogated with regard to a personal or family history of purpura or bleeding, owing to the likelihood of such cases developing purpura haemorrhagica when gold is administered (q.v.) The urine was examined for albumin and the specific gravity recorded. If the specific gravity was found to be below 1020 the patient was asked to abstain from fluids for 12 hours and to bring the first specimen passed subsequently. If the specific gravity was persistently below 1020 gold was not given. On one occasion we departed from this procedure. The patient developed an extensive stomatitis with pyrexia, pruritus and deafness after the third injection. She had hypertension in addition to advanced infective arthritis. The specific gravity of her urine varied between 1013 and 1015 on repeated examination. The chief danger, however, of giving gold to a patient with poor kidney function is that it may all too readily increase the kidney damage.

Routine Tests used in this Investigation

Throughout the duration of the treatment the following routine tests were carried out:

1. Haematological. Once a month 4 ccs. of blood were withdrawn from an antecubital vein with a minimum of stasis. The sedimentation rate was estimated by the Westergren method, using a 200 mm. tube. The reading for the sedimentation rate was taken after the first hour only. If any haemolysis had taken place the result was discarded. White blood and differential counts were carried out. When examining the blood film the presence of platelets was noted.
2. Urine. This was tested once a week for albumin.
3. Weight. All patients were weighed once a week. Dosage of gold was reduced if loss of weight became excessive.
4. Measurements. All swollen joints were measured once a month. In the case of interphalangeal joints this was done by placing the patient's hand on a piece of paper and drawing the outline. Measurements of these outlines were found to give a reasonably accurate indication of the progress of the joint swelling.

Below is an illustration indicating the practical value of tracing the outline of the hand.



In the case of the knees, wrists and metacarpo-phalangeal joints the circumference was measured with a tape measure, but it was not found practicable to make accurate measurements of any other joints.

An attempt was made to estimate the progress in the subjective symptoms e.g. pain and stiffness, by means of a questionnaire. The patient was asked each month whether the pain and stiffness of the joints was the same as on the previous occasion or if not, whether the change was an improvement or the reverse.

Radiographs.

These were taken of the hands before and after treatment with a standard exposure, penetration and distance.

Results in our own Cases.

Although we have followed carefully the course of the pain and stiffness in every case with which we are dealing, we have not attempted to tabulate this side of our investigations since we feel that too much depends on the mode of expression of the patient and his sensitivity to painful stimuli. Nevertheless, these results are of interest when compared with the joint swelling, sedimentation rate and dosage of gold and will be discussed with these other figures when the cases are considered individually.

The final results in the case of patients who have had, where necessary, nine months treatment, are, however, of special interest. Among twenty control cases, 1 (5%) lost all symptoms and signs of active disease; 12 (65%) were improved; and 6 (30%) stated that their joints felt about the same as before treatment.

Of 16 cases treated by means of the larger doses of gold (maximum dose 0.2 grms.) 8 (i.e. 50%) lost all symptoms and signs of active rheumatoid arthritis, i.e., only ankylotic and osteo-arthritic changes remained; 7, (i.e. 44%) were improved; and one experienced such severe aggravation at the commencement of the second course that she refused to continue the treatment.

Of 16 cases who have so far completed nine months treatment by means of the smaller doses of gold (maximum dose 0.1 grms.), 6 (38%) are cured (according to the above standard); 8, (50%) are improved; one is unaltered; and one is worse.

Although the number of cases recorded here is not large, we feel that the differences are so striking as to be significant. Only 5% of the control cases satisfied our standard of cure, but 50% of the cases treated by large doses of gold attained this standard. And, whereas none of the gold cases showed no change, 30% of the control cases stated that there had been no definite improvement in joint pain and were found on examination to show no definite change in the physical signs.

Unfortunately, most observers have not attempted to assess the percentage of cures obtained. Secher, using larger doses than ours, but over a shorter period, gives 24% of cures. Pemberton gives 17%; while Hartfall, Garland and Goldie, using a standard of cure similar to our own, give 9.9% as cured. They, however, used doses smaller than ours, and the courses were also smaller and more widely spaced. It must be remembered too that we have chosen only the most typical cases of rheumatoid arthritis, and that we have treated them at the same time by means of physio-therapy, which we considered to be an important adjunct to auro-therapy. Bach (1936) who also used physio-therapy in conjunction with large doses of gold, states that in half his cases the disease was arrested. This corresponds very closely with the figures in our series treated with the larger doses.

The Effect of Gold on Joint Swelling

Table I shows our measurements of the swollen interphalangeal joints. The figures represent diameters in thirtyseconds of an inch taken from the outline drawings already described. They are not actual diameters of the fingers, as the thickness of the pencil also comes into the figure; but as the same pencil was used on every occasion, they can be compared accurately with one another.

Table I
Effect of gold on swelling of interphalangeal joints.

		<u>Gold Cases. (Large doses)</u>													
Months---		1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	12th	13th	
CASE 6	Digit 5	30	31	31	32	29	29	27	29	29	27				
"	" 12	3	38	36	37	36	35	35							
"	" 13	3	30	30	29	30	28	28	27	26					
"	" 14	5	28	26	26	26	25								
"	" 18	3	32	30	32	30	29	30							
"	" 18	4	29	31	29	30	29	30							
"	" 18	5	27	26	25	25	26	26							
		<u>Control Cases.</u>													
"	" B	3	31	33	32	32	31	30	29						
"	" B	5	27	28	28	26	26	26	27						
"	" C	3	33	34	35	34	35	34	35	36	36				
"	" E	3	31	30	30	30	32	32	31	31	30	31	33	33	31
"	" E	4	31	30	30	31	33	31	32	30	31	31	32	30	30
"	" E	5	26	27	27	27	28	27	27	26	27	27	28	27	27
"	" F	2	31	31	31	31	31	32	31	31					
"	" F	3	33	34	33	33	33	33	34	33					
"	" F	4	36	37	36	35	36	37	36	36					
"	" F	5	29	30	29	29	30	29	29	29					
"	" G	3	30	31	30	30	30	29	29	30					
"	" L	2	33	31	31	30	31	32	32	32					
"	" L	3	36	35	35	33	34	35	35	34					
"	" L	4	36	35	34	35	35	34	34	34					
"	" L	5	28	28	28	29	29	29							
		<u>Gold Cases (Small doses)</u>													
"	" 25	2	32	33	32	31	31	30	29	30	30	30	30	30	
"	" 25	3	33	33	32	32	33	31	31	32	32	33	32		
"	" 25	4	38	36	34	34	35	34	34	36	36	35	34		
"	" 25	5	30	30	28	27	28	28	27	28	29	28	28		
"	" 31	4	35	34	31	31	32	33	32						
"	" 32	2	32	31	32	33	33	34							
"	" 32	3	33	34	30	31	33	32							
"	" 32	4	35	32	31	31	33	30							
"	" 32	5	28	27	27	27	27	27							
"	" 29	3	34	33	34	32	32	32	32						
"	" 39	2	31	31	32	30	30								
"	" 39	4	29	29	30	28	30								
"	" 40	3	31	31	30	30	28	30	30	31	29	30	29	29	
"	" 40	4rt.	31	29	28	28	28	28	27	28	27	28	26	27	
"	" 40	4lt.	27	27	27	25	25	25	26	26	26	26	25	24	

In order to discover the experimental error involved in this method of measurement, several drawings were made of the same hand and the measurements compared. The maximum error was found to be 1/32 inch.

Changes of this size should, therefore, be ignored in considering this table.

In the cases treated with large doses of gold, seven swollen interphalangeal joints have been measured throughout the treatment. Of these, 5 (71%) show a definite diminution in size; and 2 (29%) show no appreciable change. In the control cases 14 joints have been measured throughout the treatment; of these 2 (14%) show a diminution, 11 (79%) no change, and 1 (7%) an increase. Of the 16 joints measured in cases treated with small doses of gold, 9 (56%) are smaller after nine months treatment: 6 (38%) are unchanged; and 1 (6%) is increased. In those joints showing a diminution in size, the average reduction in swelling is 2 thirtyseconds of an inch in the controls; 2.9 in the cases having small doses of gold; and 3 in the cases having large doses.

We see, therefore, that whereas in the control cases 14% of the joint swellings are reduced, with small doses of gold 56% are reduced, and with large doses 71% are reduced. The figures obtained are therefore somewhat similar to those found from a calculation of the percentage of cures (i.e. 5%, 30%, and 50%). Figure I shows the above results in graphic form. In the controls (dotted line) the average joint swelling is not subject to any marked variation, whereas on the gold cases there is a rapid diminution, more continuous in the cases having large doses (continuous line) than in those having small doses (broken line).

Fig. I

Effect of gold on swollen interphalangeal joints.

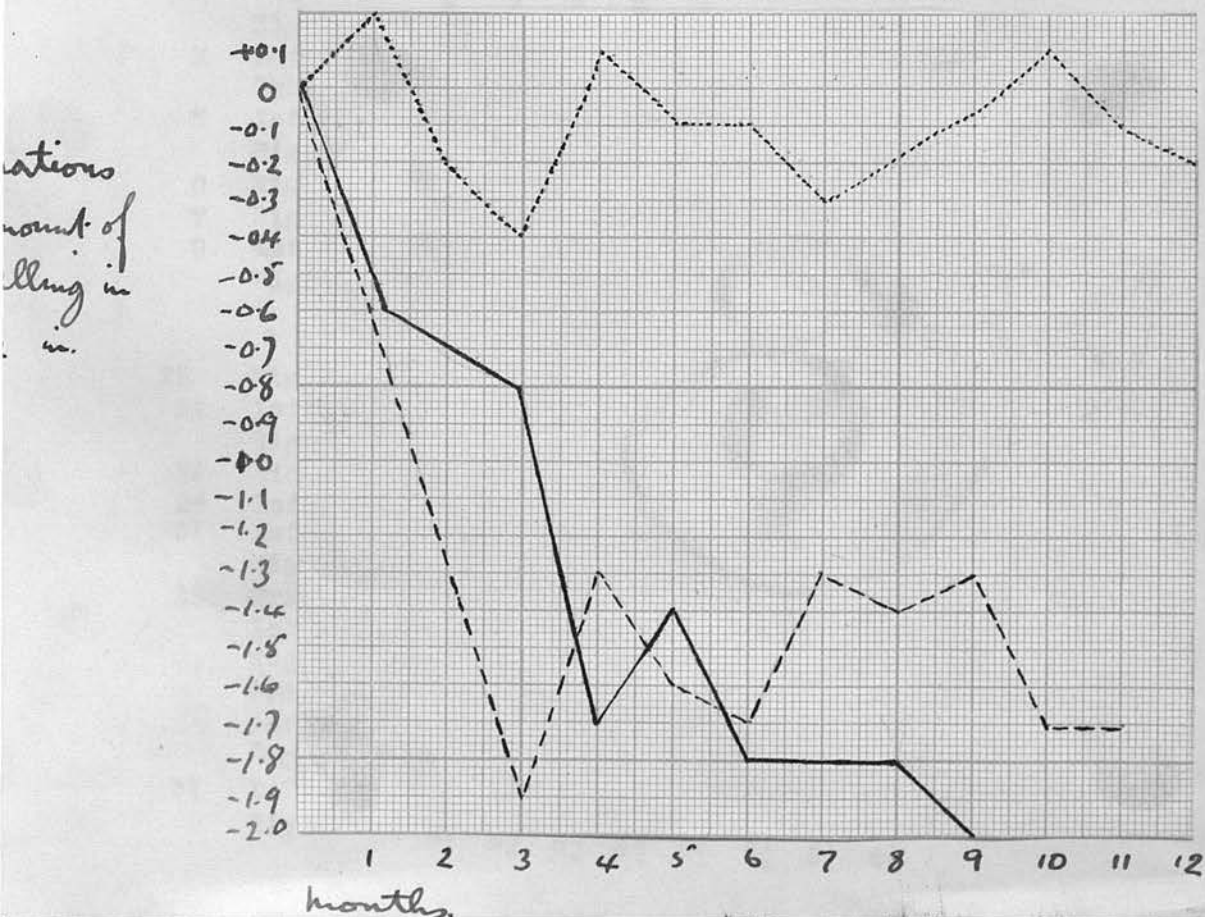


Table II (continued)

Case 38 Wrists

Left 6 6 $5\frac{3}{4}$ 6Right 6 $5\frac{3}{4}$ 6 6

Metacarpo-phalangeal

Left $6\frac{3}{4}$ $6\frac{1}{2}$ $6\frac{1}{2}$ $6\frac{3}{4}$

In the control cases, 2 (17%) are diminished; 7 (58%) are unaltered; and 3 (25%) show an increase. In the gold (small dosage) cases, 14 (82%) are diminished; 2 (12%) are unaltered; and 1 (6%) is increased. In the gold (large dosage) cases 8 (73%) are diminished; and 3 (27%) show no change. ~~So that~~, whereas 17% are diminished among the control cases; 82% are diminished among those having small doses of gold; and 73% among those having large doses of gold. This would make it appear as though the wrists had received greater benefit from the small doses, but actually this is not so as the diminution in size had been much greater in those receiving large doses. This is clearly seen in Fig. II, which shows how the control cases (dotted line) have on an average remained unaltered, while the small dose cases (broken line) have become reduced, and the large dose cases (continuous line) have become markedly reduced.

Fig. II

Effect of gold on swollen wrist joints.

Variations in the amount of swelling in $\frac{1}{4}$ inches.

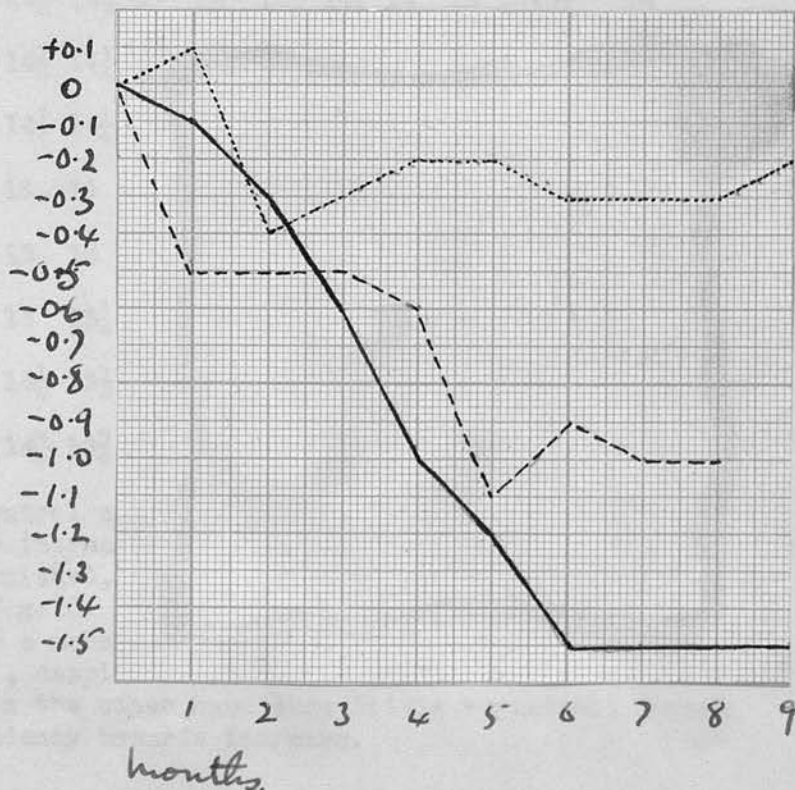


Table III shows the measurement of the swollen knee joints in inches.

Table III

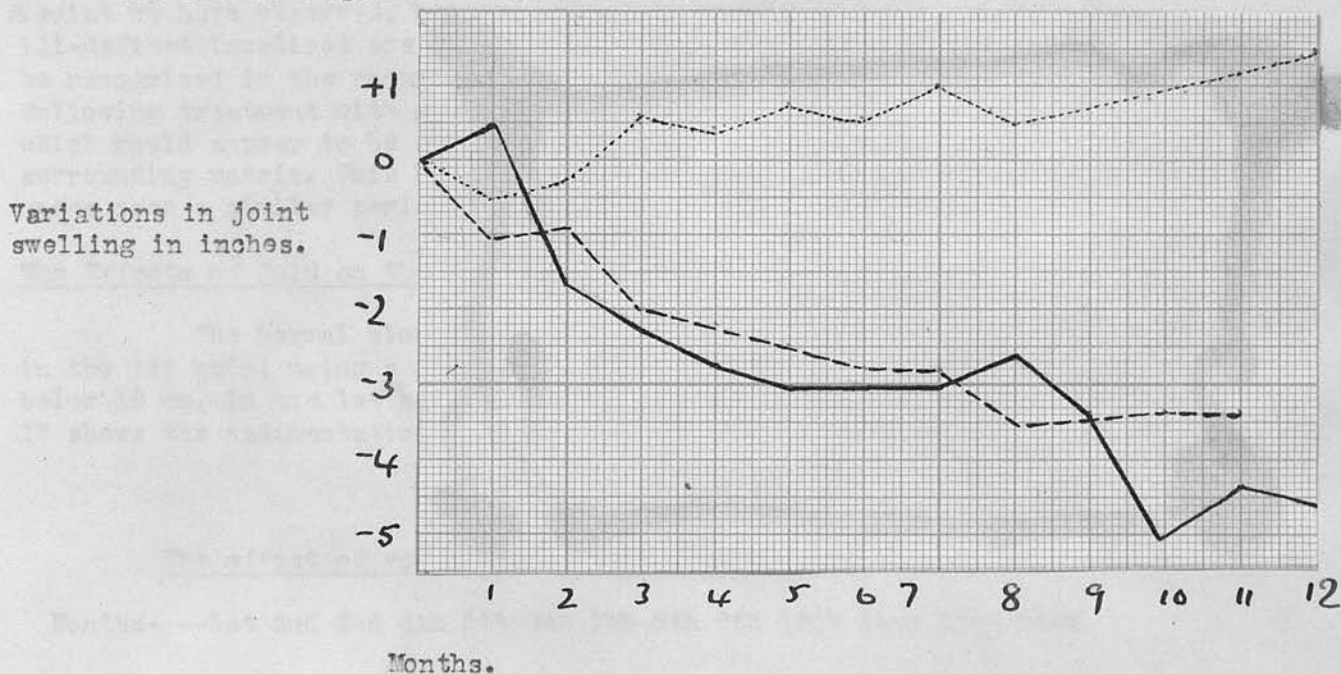
Effect of gold treatment on swelling of knee joints.

Months-----	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	12th	13th
<u>Gold cases (large doses).</u>													
Case 6 Left	13 $\frac{1}{4}$	13 $\frac{1}{2}$	13	13	12 $\frac{3}{4}$	13	12 $\frac{3}{4}$	12 $\frac{3}{4}$	13	12 $\frac{3}{4}$	12	12 $\frac{3}{4}$	12 $\frac{1}{2}$
Right	14	14	13 $\frac{1}{4}$	13 $\frac{1}{4}$	13 $\frac{1}{4}$	13	13	13 $\frac{1}{4}$	13 $\frac{1}{2}$	13	12 $\frac{1}{2}$	13	13
7 Right	13 $\frac{1}{4}$	13 $\frac{1}{2}$	13	12 $\frac{1}{2}$	12 $\frac{1}{2}$	12 $\frac{1}{4}$	12 $\frac{1}{2}$	12 $\frac{1}{4}$	12	12 $\frac{1}{4}$	12 $\frac{1}{4}$	11 $\frac{1}{2}$	
<u>Control cases.</u>													
F Right	16 $\frac{1}{2}$	-	-	-	16 $\frac{1}{4}$	-	16	16 $\frac{1}{2}$	16	-	-	-	16 $\frac{1}{2}$
G Right	14	14	14	-	-	14 $\frac{1}{2}$	-	14 $\frac{1}{2}$	-	-	-	-	15 $\frac{1}{4}$
T Left	13	12 $\frac{3}{4}$	12 $\frac{3}{4}$	15									
Right	13 $\frac{1}{4}$	12 $\frac{3}{4}$	12 $\frac{3}{4}$	13									
U Left	14 $\frac{1}{4}$	14 $\frac{1}{4}$	14 $\frac{1}{2}$	14 $\frac{3}{4}$	15								
Right	14 $\frac{1}{4}$	14 $\frac{1}{4}$	14 $\frac{1}{2}$	15 $\frac{1}{4}$	15								
<u>Gold cases (small doses).</u>													
20 Left	14 $\frac{1}{4}$	14	14 $\frac{1}{2}$	14 $\frac{1}{4}$	15	14 $\frac{3}{4}$	14 $\frac{1}{4}$	14 $\frac{1}{4}$	14	14	13 $\frac{3}{4}$	14	
Right	14 $\frac{1}{2}$	14 $\frac{1}{2}$	14 $\frac{1}{2}$	14 $\frac{1}{4}$	14 $\frac{1}{2}$	14	14 $\frac{1}{4}$	14	13 $\frac{3}{4}$	13 $\frac{3}{4}$	13 $\frac{1}{2}$	13 $\frac{1}{2}$	
25 Left	14 $\frac{1}{2}$	14 $\frac{1}{4}$	14 $\frac{1}{4}$	14 $\frac{1}{4}$	14	14	14	14	13 $\frac{1}{2}$	13 $\frac{3}{4}$	14	14	
Right	16 $\frac{1}{2}$	16	16	16	15 $\frac{3}{4}$	16	15 $\frac{3}{4}$	15 $\frac{1}{2}$	15 $\frac{1}{4}$	15 $\frac{1}{2}$	15 $\frac{1}{2}$	15 $\frac{1}{2}$	
30 Left	13 $\frac{1}{2}$	13	13	13	13								
Right	13 $\frac{1}{4}$	13	13	13 $\frac{1}{4}$	13								
30 Left	14 $\frac{1}{2}$	14 $\frac{3}{4}$	14 $\frac{1}{2}$	13 $\frac{1}{2}$	13 $\frac{1}{4}$	13 $\frac{1}{4}$	13	13 $\frac{1}{2}$	13				
Right	15 $\frac{1}{4}$	14 $\frac{3}{4}$	14 $\frac{3}{4}$	13 $\frac{3}{4}$	13 $\frac{1}{2}$	13 $\frac{1}{2}$	13 $\frac{1}{2}$	13 $\frac{1}{2}$	13 $\frac{1}{2}$	13 $\frac{1}{2}$			

In the control cases 1 (17%) is diminished; 2 (33%) are the same; and 3 (50%) are increased. Under small doses of gold, the 8 joints measured are all diminished, and similarly with the 3 joints in cases having large doses of gold. A study of figure III shows that the large dose cases show a more marked reduction on the average than the small dose cases, despite an initial increase in the first month. The controls on the other hand show little variation, though there is a slight tendency towards increase.

Fig. III

The effect of gold on swollen knee joints.



In Table IV the changes in the X-ray during gold treatment are represented, ~~some~~ classified as changes in decalcification, changes in periarticular swelling, and changes in joint space. The number of cases in which we have had X-rays before and after treatment are unfortunately few, but they serve to give some idea of the changes to be expected under treatment with gold.

Table IV

Effect of gold on the X-ray picture.

	Gold cases (large doses)		
	Decalcification	Periarticular swelling	Joint space.
Increased	2	0	0
Unaltered	3	1	4
Diminished	1	5	2
	Gold cases (small dosage)		
Increased	0	0	0
Unaltered	7	1	8
Diminished	2	7	1
	Controls.		
Increased	4	2	1
Unaltered	6	8	8
Diminished	0	0	1

Although the number of results in this table is small, it nevertheless serves to confirm the diminution of joint swelling in the gold cases, as already noted clinically. In contrast with this is the marked absence of change in the other X-ray features, viz.

de-calcification and joint space. In the control series there is a notable absence of change in all the X-ray features of the disease. A point we have observed, however, which is worthy of note, is that the ill-defined localised areas of decalcification which have come to be recognised in the rheumatoid type of arthritis have shown, following treatment with gold, a tendency to an increase in definition, which would appear to be due to a condensation of the immediate surrounding matrix. This has definitely not been observed in the control cases over a similar period of time.

The Effects of Gold on the Blood

The normal blood sedimentation rate lies between 2 and 6 mm. in the 1st hour, using a 200 mm. tube (Westergren), but any figure below 10 mm. in the 1st hour is now usually accepted as normal. Table IV shows the sedimentation rates in our own cases.

Table IV

The effect of gold on the sedimentation rate.

Months----	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	12th	13th
	<u>Controls.</u>												
Case A	47	43	40	26	20	32	21	37	40	53			
B	55	47	36	34	28	36	26	37	29	28	17		
C	15	11	10	12	23	33	16	19	23				
D	28	26	12	14	15	11	20	18	38	33			
E	17	14	10	13	19	22	16	13	13	13	14		
F	32	22	32	26	32	30	25	30	29				
G	24	30	26	14	24	29	23	29	28	47			
H	10	16	45	30	18	16	16	20	21	20	31		
I	9	10	9	13	13	10	10	16	10	14			
J	9	10	9	3	4	4	6	3	2				
K	34	9	11	12	6								
L	13	15	14	10	11	9	11	9	12	15			
M	22	18	20	21	17	19	10	13	21	30			
N	10	9	10	9	17	8	7	8	6				
O	41	37	35	34	19	29							
P	28	26	17	14	10	8	9	9	8				
Q	36	35	34	35	52	44							
R	15	10	11	7	10	12	13	13	8				
S	18	16	16	18	29	17	17	20					
	<u>Gold Cases. (large dosage).</u>												
1	11	8	6	6	4	5	4	4	5	5			
2	14	21	16	7	7	10	3	7	8	8	11	7	
3	24	17	18	8	10	9	16						
4	60	77	75	44	28	14	18	20	18	24			
6	27	23	16	12	12	6	12	9	10	8	9	7	
7	10	3	2	2	2	2	2	2	2	1	2	2	
8	12	11	4	5	-	-	-	-	-	16	12	7	
9	8	19	12	7	6	4	4	4	5	9	3	3	
10	27	20	3	2	2	1	1	2	1	1	2	2	
11	34	27	14	9	8	6	6	4	4	3	4	2	

Table IV (continued).

Months---	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	12th	13th		
Case 12	15	14	18	9	3	2	5								
13	14	14	22	9	6	4	16	4							
14	8	9	12	4	4	5	4	4							
15	36	39	24	16	8	7									
16	28	26	19	14											
17	12	27	26	17	9	7									
18	44	55	48	30	52	44	44	28	34	40	33	41			
19	42	44	21	17	15	12	6	5	4						
						<u>Gold cases (small dosage)</u>									
20	45	53	20	31	30	25	30	24	30	13	23	21	35	16	
21	23	16	19	11	5	7	19	8	7	5					
22	25	14	9	59	13	11	28	23	14						
23	36	44	42	28	18	20	17	12							
24	51	54	62	34	36	21	27	28	28	29	14				
25	39	26	20	25	22	21	13	15	18	13	12	210			
26	49	31	12	8	7	9	8	10	7	7	2				
27	18	16	16	6	8	5	6								
28	59	60	38	17	25	32	36								
29	11	8	8	8	7	7	9	6	8						
30	52	61	29	20	26										
31	16	19	6	6	8	11	8	12							
32	69	69	69	66	51	49	28								
33	47	48	14	9	8	4									
34	39	31	27	17	16										
35	11	9	17	18	16	10	6								
36	37	20	30	33	34	37	36	58	49						
37	12	10	9	5	6	5	4	4	-	-	5				
38	37	45	39	43	31										
39	27	20	4	3	4										
40	20	11	10	9	10	9	6	7	6	5	7	8	7		

A study of this table shows the marked variations which may occur in any one case. The common practice of having a single estimation of the sedimentation rate carried out to discover whether the disease is active or not is seen to be quite fallacious. In case K, for example, the initial estimation gave a figure of 34 mm. in the first hour, whereas the remainder of the readings were practically normal. In case H, on the other hand, a normal reading of 10 mm. was obtained on the first occasion and two months later the reading was 45 mm., although no marked change occurred in the clinical condition.

Among the 19 control cases, the sedimentation rate is seen to be higher at the end of treatment in 10 cases, (53%) and lower in 9 (47%); so that, on the average, physiotherapy alone, given over a period of nine months, produces no definite change in the sedimentation rate.

The natural progress of the disease towards the inactive stage has not had time to manifest itself.

In the 18 cases treated with large doses of gold, there is a fall in the sedimentation rate in every case. In all except 3 of

the cases the sedimentation rate was within normal limits at the end of treatment, and in one of these 3 cases (case 3) it had at one time fallen to normal, rising at the last estimation concurrently with the onset of a fatal agranulocytosis. It is worth noticing that in several cases the sedimentation rate rises at the second or third month. This rise is then followed by a rapid fall to normality. A similar rise was also noted in a case of gout; a disease not normally associated with a raised sedimentation rate. Our opinion on the point is that it is probably a specific effect of the gold. We consider it likely that a rise of sedimentation rate would probably be produced in normal, healthy individuals if gold were administered.

In the 21 cases treated with small doses of gold, 20 (95%) show a fall in the sedimentation rate, and 1 (5%) a rise, so that there is no marked difference between these and the figures obtained with large doses of gold. On the other hand, only 9 (43%) are found to have reached a normal level at the time of the last estimation. This forms a striking contrast with the number (83%) which reached normality after treatment with large doses of gold.

To summarise:- The sedimentation rate in cases treated with physiotherapy alone is not appreciably altered during a period of ten months observation; about half the figures are increased, and half diminished. With small doses of gold, the sedimentation rate is diminished in 95% of cases, but reaches normal limits in only 43%. With large doses of gold, the sedimentation rate is diminished in every case, and reaches normality in 83%.

Table V shows the leucocyte counts in the control group and in the group treated with large doses of gold.

Case No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
1	12000	11000	10000	9000	8000	7000	6000	5000	4000	3000	2000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
2	11000	10000	9000	8000	7000	6000	5000	4000	3000	2000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
3	10000	9000	8000	7000	6000	5000	4000	3000	2000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
4	9000	8000	7000	6000	5000	4000	3000	2000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
5	8000	7000	6000	5000	4000	3000	2000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
6	7000	6000	5000	4000	3000	2000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
7	6000	5000	4000	3000	2000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
8	5000	4000	3000	2000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
9	4000	3000	2000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
10	3000	2000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
11	2000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
12	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
13	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
14	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
15	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
16	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
17	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
18	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
19	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
20	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
21	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000

Table V shows the leucocyte counts in the control group and in the group treated with large doses of gold. The control group shows a steady decline in leucocyte counts over the ten months period, while the group treated with large doses of gold shows a marked increase in leucocyte counts, reaching normality in 83% of cases.

Table V

Effect of gold on the leucocyte count.

Months---	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th
<u>Controls.</u>											
Case A	6700	6900	8000	7500	6100	4700	---	5700			
B	6800	---	8300	4600	9200	6000	8600	7100	8100	7400	10300
C	7700	5600	8000	6600	4000	9000	8400	6600	5800	4700	
D	4900	6800	7000	7900	8400	7500	8500	5600	9200	7100	
E	12000	13500	11400	13100	14100	8300	---	10500	9600	9500	7900
F	6400	10800	13800	9300	11500	12000	10500	8200	18200		
G	14300	7700	13100	12200	6800	10800	7400	15400	14100		
H	10300	9800	6700	10100	14600	12300	9200	5300			
I	5900	4800	---	4300	5300	6300	4900	---	6400	6300	
J	7000	8600	5500	8700	14400	12400	6500	7000	14500		
K	9300	7900	7600	14700	9800						
L	8700	11800	14300	7400	7400	6400	---	12000	7000	6800	
M	8000	5100	4700	6000	7400	7200	8700	6500	7400	6400	
N	7000	5600	6200	5900	4200	5300	8500	7600	4300		
O	7900	7700	6700	6500	9800	5300					
P	5200	7600	4400	3800	4400	---	5100	---	2900		
R	7800	6100	7500	5100	5300	---	7300	11200	5000		
<u>Gold Cases.</u>											
1	7200	7400	8000	4500	4000	5700	3500	4000	5000	5500	3600
2	8600	6300	6300	4900	6800	6000	6900	4800	6500	6100	5300
3	7800	5900	6500	6500	8000	7300	3100	1100	800		
4	4000	8000	8100	4700	5100	4300	6100	---	7200	4200	4900
6	8100	6100	6300	4900	2200	6600	5800	8300	6200	5800	4300
7	5300	6700	6200	5000	6500	4900	6700	7300	7100	6300	6200
8	10000	5600	6100	11800	---	---	---	---	---	6900	8500
9	4100	4800	5100	4900	6600	5100	---	---	---		
10	8200	2600	8300	9400	9800	7200	7500	12700	6200	7700	7800
11	7300	6700	5600	9500	7300	6700	9900	5700	6500	6000	
12	9700	8600	14000	10200	7600	---	4500				
13	9100	8900	9100	8900	6200	12700	6000				
14	7700	9800	8400	16400	9400						
15	6800	12100	6800	11600	5600	4600					
16	9000	---	8500	---	---	---	7400	9100	5800		
17	8600	---	---	7800	---	4700					
18	5400	5600	5600	8000	---	6400	5800	3400	5100	8000	5900

Apart from case 3, which developed an agranulocytosis, there is no marked change to be seen as a result of gold treatment. 12 (71%) of the gold cases show a lower figure at the end of the treatment than at the beginning, and 5 (29%) a higher figure. In the control series, 11 (65%) show a lower figure and 6 (35%) a higher one. It is worth noting that there is a greater tendency for subnormal counts to occur in the gold series, counts lower than 5,000 per cu. mm. occurring in 11 (65%) of gold cases and in 6 (35%) of the control cases. This does not appear to have been due to an incipient agranulocytosis

as it was not associated with a decrease in the percentage of polymorphs, as will be seen from table VI.

Table VI

Effect of gold on the percentage of polymorphs in the blood.

Months---	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th
	<u>Controls.</u>										
Case A	73	63	--	68	--	65	59	65			
B	63	58	55	59	61	56	60	63	64	54	
C	71	67	67	57	60	56	72	73	68	71	
D	62	84	65	76	67	76	67	85	67	70	
E	72	80	61	66	73	59	76	77	71	59	58 70
F	72	73	62	65	63	62	70	67			
G	55	53	67	47	58	39	59	52	47		
H	68	73	55	77	--	61	70	68			
I	49	68	48	52	53	54	44	64	50	60	
J	67	54	57	65	71	71	71	67	74		
K	74	74	71	61	76						
L	65	66	65	75	63	70	71	70	66	67	
M	61	50	50	58	59	46	62	59	39		
O	66	48	69	62	45	61					
P	70	66	68	69	63	64	68	69	68		
R	68	69	72	72	72	72	75	70			
S	53	58	53	56	52	42	59	54			
	<u>Gold Cases.</u>										
1	65	68	67	52	53	51	55	61	65	63	56
2	48	66	58	60	59	59	56	64	62	49	56 59
3	70	68	78	77	64	77	27	10 0			
4	64	59	64	56	53	--	69	66	65	59	55 44
6	--	78	72	63	50	49	63	71	71	77	71 64
7	57	60	49	48	65	60	70	47	70	65	60 54
8	53	69	72	70	61	63	63	--			
9	58	68	67	56	58	--	65	58	61	--	78 64
10	77	68	78	73	68	77	65	62	73	65	54 67
11	71	68	78	67	61	69	76	74	68	71	69
12	63	59	84	79	72	79	59				
13	63	62	49	64	55	57	68				
14	64	56	72	77	64	75					
15	60	75	76	71	75						
16	53	--	62	--	--	60	59	62			
17	76	66	56								
18	47	45	56	64	46	47	54	58	53	64	
19	63	68	60	51	48	57	60	58	69		

We have not observed the high leucocyte and polymorphs counts in cases which have reached a point of saturation with gold, as described by Dumaret, Mollard and Pavie (1931). The Von Bonsdorff count, in our experience, is not abnormal in cases of rheumatoid arthritis. Nor is there any alteration in the ratio of polymorphs, monocytes and lymphocytes, as described in tubercle treated by gold by Houghton(1932).

Punctate basophilia was only observed on two occasions, although it was noted frequently by Griffiths and Race (1935) in cases treated with myocrysin.

Table VII gives the lymphocyte counts in the control and gold cases respectively. The figures for the lymphocyte percentages have not been given, as they vary so much with the percentage of polymorphs.

Table VII

Effect of gold on the lymphocyte count.

Months---	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	
	<u>Controls.</u>											
Case A	1550	2100	2200	----	1600	----	1700					
B	2200	3300	1900	----	3100	2300	2700	2500	1900	3800		
C	1800	1300	2200	1700	1100	2300	2000	2200	2000	1500		
D	1600	800	2000	1700	2600	1400	1900	600	2100	----	1300	
E	3200	2400	3600	3300	2100	2000	1500	1800	2300	2800	2500	
F	1700	2800	4400	3900	3200	3400	2000	4600				
G	4400	3000	3900	5700	2700	6300	2300	5900	6600			
H	2400	2200	2500	1600	3400	2700	1700	1500				
I	2800	1400	1400	1800	1800	3100	2000	2900	2100			
J	2100	3300	1700	2200	2600	2900	1100	2200	2800			
K	2200	1500	1600	4100	1400							
L	2800	2500	4400	1400	2400	1500	----	3000	1800	1400		
M	2300	1600	1300	1900	2900	2300	2800	2500	3500	1400		
N	2500	2400	2500	1900	1200	2500	2800	2800	2000	3900		
O	2100	2600	1800	1800	4500	1500	----					
P	1400	2300	1100	650	1400	1500	1400	1100	850			
R	2000	1300	1800	1100	1200	1300	1800	2400	1400			
	<u>Gold Cases.</u>											
1	2500	2100	2100	1000	2000	1700	1700	1000	1400	1500	1500	1400
2	4400	1800	2400	1800	2500	2300	2000	2200	2300	2200	1800	2300
3	1900	1600	1200	1300	1500	2100	1000					
4	1300	2400	2800	1600	1800	1600	----	2200	1300	1700	2600	
6	1100	1800	1600	2300	680	1500	1300	1400	1000	1400		
7	2000	2500	2300	1800	1500	1800	3200	1600	1500	1900	1700	2400
8	4200	1400	1500	2800	1900	2300	1500					
9	1400	1500	1600	1900	2500	1700	1000	1200	780	840	850	710
10	1100	650	1700	2000	1800	1300	2000	3800	1200	2200	2200	1600
11	1700	2400	950	2600	2000	1700	1600	1100	1600	1300		
12	2900	3000	1800	1600	1200	----	1400					
13	2100	3100	3000	2100	2400	4200	1600					
14	2200	3400	1600	3100	1600							
15	2000	2300	1000	2400	730							
18	2400	2400	1800	2300	----	2500	1700	1100	1500	2600	1500	

No constant change is to be found in the lymphocyte count under gold treatment. As the blood was taken 7 days after the injection, the figures would only reflect the final results and no immediate effect which the gold may have had on the lymphocyte count.

Table VIII shows that gold does not produce any definite effect on the percentage of large mononuclears in the blood.

Table VIII

Effect of gold on the percentage of large mononuclears in the blood.

Months----		1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	
		<u>Controls.</u>											
Case	A	2	6	3	-	0	5	4					
	B	4	5	3	3	6	2	-	1	3	6	8	
	C	3	6	2	3	5	2	0	5	5	7		
	D	2	5	2	1	2	7	4	9	9	2		
	E	1	2	1	3	1	1	6	1	4	4	4	
	F	2	1	3	1	7	2	4	8				
	G	1	7	2	5	1	2	8	5	6			
	H	5	3	3	2	2	12	6	4	7			
	I	3	0	3	3	9	4	3	4	4	6		
	J	6	4	7	8	8	4	9	2	7			
	K	1	10	6	8	7							
	L	3	8	4	5	3	6	5	5	9	12		
	M	5	10	9	2	9	8	3	6	4	7		
	O	7	15	4	10	9	9						
	P	3	4	5	13	3	5	5	3	4			
	R	4	7	1	3	2	3	1	3				
	S	3	3	7	1	8	1	3	8				
		<u>Gold Cases.</u>											
	1	0	3	2	5	2	6	2	8	7	8	5	8
	2	0	3	2	2	1	5	1	2	0	5	5	2
	3	5	3	4	3	6	4	2	3				
	4	2	2	0	2	3	3	1	2	4	6	6	
	6	-	3	2	4	2	2	6	4	3	6	4	7
	7	6	2	8	7	6	7	2	4	7	10	8	6
	8	3	3	1	4	8	6	7					
	9	4	1	2	4	2	-	3	13	8	6	8	10
	10	8	2	1	3	12	5	6	8	5	6	6	4
	11	3	3	1	2	6	6	6	6	5	6	4	
	12	4	4	2	2	7	7	9					
	14	8	8	9	4	6	10	12					
	16	1	-	4	-	-	2	5					
	18	3	3	7	7	11	4	10	9	11	10	8	8
	19	2	1	3	2	2	1	3	6	4			

Table IX shows the percentage of eosinophils. in the blood.

Table IX

Effect of gold on the percentage of eosinophils in the blood.

Months-----1st 2nd 3rd 4th 5th 6th 7th 8th 9th 10th 11th

Case	Controls.										
	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th
A	0	0	-	0	0	2	0				
B	0	0	1	1	0	1	1	3	4	1	
C	3	2	3	0	0	2	3	4	0	4	
D	3	1	2	1	0	2	4	0	1	0	0
E	0	0	5	3	1	3	10	9	0	1	2
F	0	0	2	0	2	4	1	0			
G	1	0	1	1	1	1	1	4	0		
H	4	2	5	4	4	5	6	0	4		
I	0	0	3	4	3	-	1	3	6	0	1
J	0	4	4	2	3	1	3	0	0		
K	1	1	1	2	2						
L	0	1	0	1	1	0	2	0	0	0	
M	2	1	2	3	3	1	1	0	1	1	
N	0	2	3	1	2	0	0	0	0	1	
O	1	2	0	1	0	1					
P	1	0	0	1	2	0	1	0	0		
R	3	0	2	1	1	0	2	0			
S	3	2	4	0	1	1	2	1			

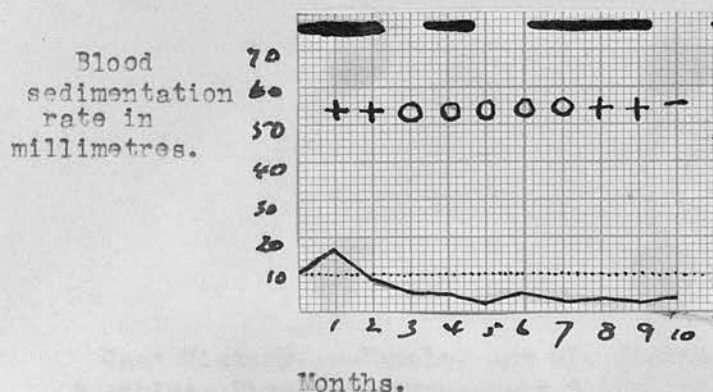
Gold Cases (large doses).												
1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	12th	
1	0	1	0	2	0	15	11	4	2	2	2	0
2	1	0	0	0	2	0	0	0	1	0	0	2
3	0	0	0	1	2	0	1	0				
4	0	1	0	1	9	-	0	0	2	6	1	2
6	-	0	0	1	0	2	0	2	1	0	1	4
7	0	0	7	0	1	2	1	2	1	0	2	1
8	1	3	1	2	-	-	1	3	6			
9	1	0	0	0	1	2	1	0	0	1	3	0
10	0	1	0	3	1	0	0	0	1	0	2	0
11	1	2	4	3	2	2	0	2	2	0		
12	3	2	1	1	4	1	2					
13	1	2	9	3	4	1	0					
14	0	1	0	0	2	0	0					
15	3	2	3	1	4							
16	2	-	3	-	-	3	0	-	-	4	0	3
18	2	1	4	0	0	1	3	0	2	0	2	3
19	1	0	1	16	18	10	9	4	1			

Gold Cases. (small doses).												
1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	12th	
20	0	2	0	0	1	0	3	3	2	2	0	1
21	0	2	2	5	2	2	0	1	1	2	1	
22	1	2	0	1	0	1	0	1	4	1		
23	1	0	1	6	1	9	5	4				
24	1	1	4	3	5	2	1	0	0	3	2	
25	0	2	1	3	3	2	2	1	0	2	1	2
26	1	2	7	1	4	2	2	5	3	2		
27	6	11	5	12	15	14	7	2	5	1		

Study of Individual Cases.

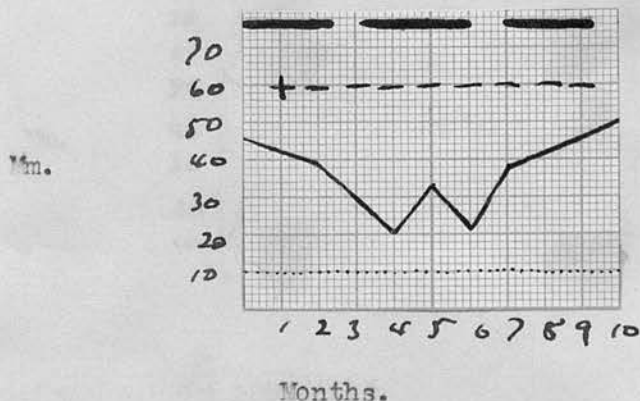
In order to discover the relationship of the blood sedimentation rate to the joint pain and swelling, and the effect of gold treatment on these, we append below graphs showing the course of these various factors in each individual case with a short explanation. The continuous lines on the graphs represent the course of the blood sedimentation rate and the broken lines the course of the joint swelling. Pain and stiffness are represented by plus and minus signs, indicating respectively aggravation and amelioration. The heavy horizontal lines along the top of each graph show the periods during which gold or sterile oil was being administered.

Case 1. Gold, large dose.



Case History.--Female, age 52. Joints affected--interphalangeal, metacarpo-phalangeal and wrists. Physical signs--periarticular swelling & limitation of movement. X-ray--diminished joint space. Duration 6 yrs. Progress--onset of bronchitis & stomatitis after a total of 1.01 gms. of solganal. Recurrence of stomatitis every time gold injections were resumed, even in doses as small as 0.02 gms. Blood sedimentation rate rose in 1st month & then fell gradually to 4 mm. afterwards remaining at about this figure.

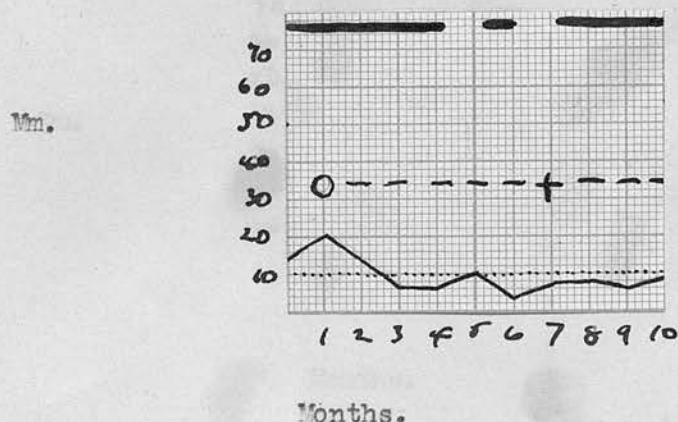
Case A. Control.



Case History.--Female, age 52. Joints affected--hands, shoulders

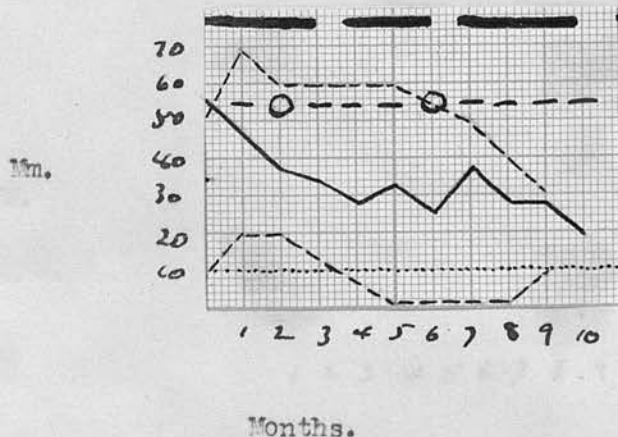
& knees. Physical signs--spindle swelling, pain & limitation of movement. X-ray---destruction of cartilage especially in carpus. Duration 8 yrs. Progress-- the sedimentation rate followed a very variable course but never reached normal limits. The patient stated that there was considerable improvement in the pain & stiffness during each course of injections but that she has become worse since stopping them. At the end of treatment the joint swelling was unaltered & there was no obvious change in the radiological appearances.

Case 2. Gold , large dose.



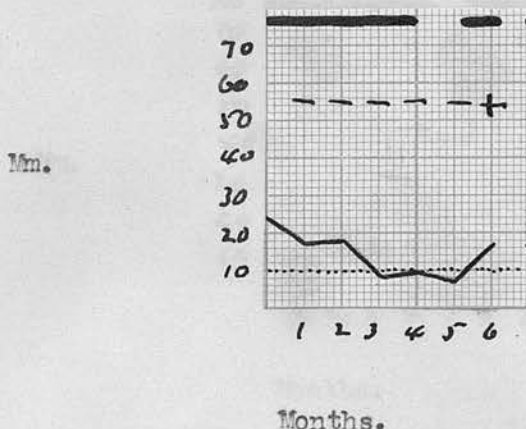
Case History.---Female, age 61. Joints affected--wrists, knees & ankles. Physical signs--pain & limitation of movement. X-ray--cartilage gone , bones eroded. Ankylosis of 3rd right terminal interphalangeal joint. Duration 8 yrs. Progress--dosage had to be considerably modified latterly owing to severe stomatitis. After an initial rise, the blood sedimentation rate fell to normal limits & remained there despite slight rises each time the injections were discontinued. Final result--pain & stiffness much better. Slight still in one wrist (almost ankylosed) & one knee which shows marked degenerative changes.

Case B. Control.



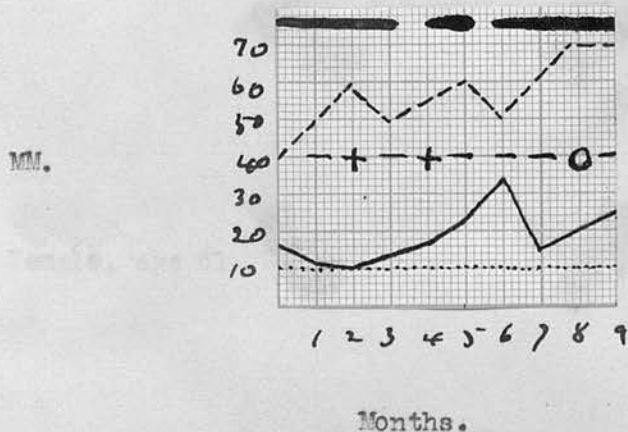
Female, age 36. Joints affected--fingers, shoulders & knees. Physical signs--swelling & limitation of movement. Crepitus--right knee. Duration 12 months. Progress-- the sedimentation rate shows a definite downward trend in this case but with fluctuations as noted in case A. It does not reach normal limits. There is no relationship between the changes in sedimentation rate, joint swelling & pain. Final result--pain & stiffness much better than before the injections.

Case 3. Gold, large doses.



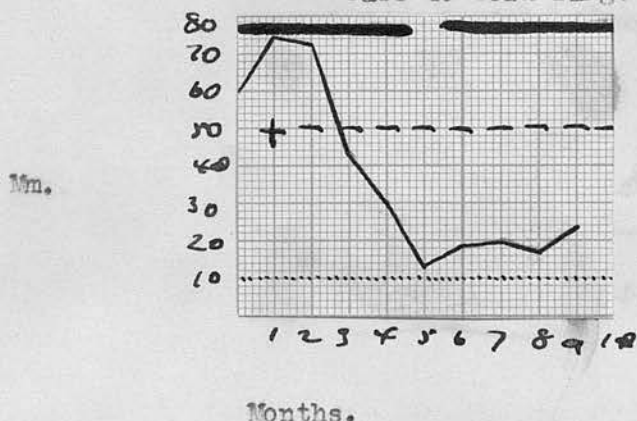
Female, age 61. Joints affected--fingers, elbows, mandibular & sterno-clavicular joints, knees & ankles. Physical signs--swelling & limitation of movement. X-ray--diminished joint space, lipping, decalcification. Duration 19 yrs. Progress--a gradual fall of the sedimentation rate to normal in the 1st course with lessening of pain & stiffness. Erythematous eruption after each injection in the second course with increase of pain & stiffness, rise of sedimentation rate & onset of rapidly fatal purpura with agranulocytosis. Conclusions--in this case the rise in sedimentation rate above normal during the second course was probably due to the agranulocytosis as this is a recognised association. Were it not for this it would probably have remained within normal limits.

Case C. Control.



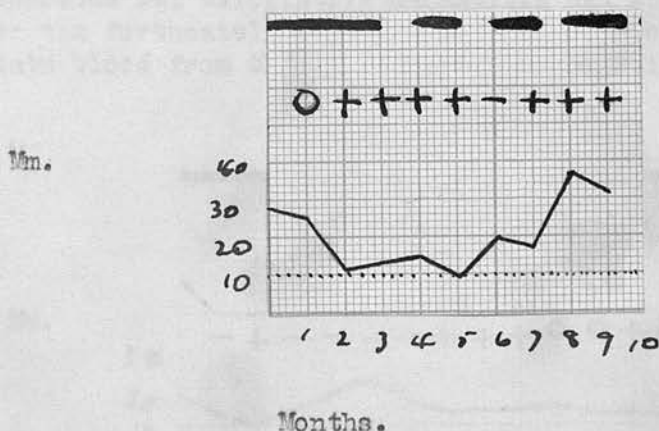
Female, age 45. Joints affected--wrists, neck, knees & feet. Physical signs--swelling & limitation of movement. Duration 2 months. Progress-- as in cases 1 & 2 the sedimentation rate starts at a low level, only slightly above normal, but unlike the two gold cases it does not show a rapid fall to within normal limits, but follows a variable course, reaching a height of 33 mm. on one occasion. Final result--pain & stiffness much better but joints still become stiff after rest. General health also improved.

Case 4. Gold large doses.



Female, age 49. Joints affected--fingers, wrists, ankles & feet. X-ray--diminished joint space, decalcification, peri-articular swelling. Duration 8 yrs. Progress--although in this case the sedimentation rate never reached normal limits, there was a very decided drop following the initial rise. All pain & stiffness disappeared & had not returned when she was seen 6 months later.

CASE D. Control.



Female, age 51. Joints affected--hands, elbows, knees & feet.

Physical signs--swelling & limitation of movement. X-ray--omitted in error. Duration 10 yrs. Progress--although the sedimentation rate fell rapidly during the first 2 months, it again rose to a high figure before the completion of treatment. This patient nearly always complained of increasing pain & stiffness during the injection periods but at the completion of treatment she stated that her joints felt better than they were before she started having injections.

Case 5. Gold (large doses).

Min.

no graph made.

Blood not obtained.

Months.

Female. Age 40. Joints affected--jaw, fingers & knees. Physical signs--spindle swelling of finger joints. pain on flexion of knee. X-ray--periarticular swelling. Duration 6 months. Progress--pain & stiffness improved slowly during the first course of Solganal injections & during the rest which followed it, all symptoms & signs disappeared completely. When seen 6 months later there had been no recurrence but exfoliative dermatitis had appeared which however was fortunately not extensive. It was only found possible to obtain blood from this patient on one occasion.

Case E. Control.

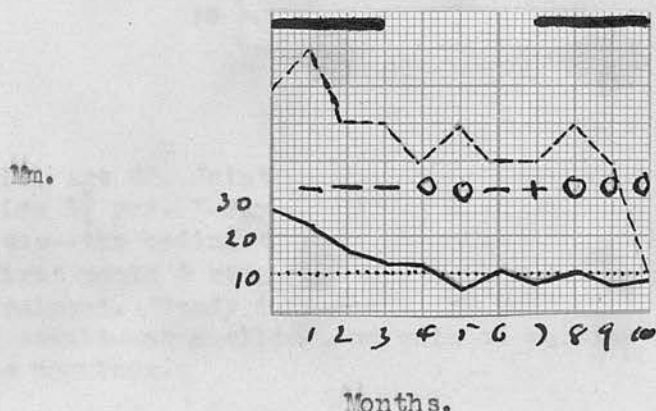
Min.



Months.

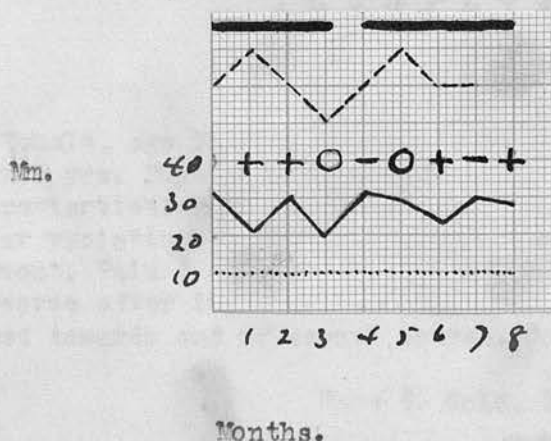
Female, age 34. Joints affected--fingers, wrists & ankles. Duration 9 yrs. Physical signs--periarticular swelling, pain & limitation of movement. X-ray--periarticular swelling. Progress--the sedimentation rate shows slight variations but no definite improvement. Swelling of one finger joint shows marked decrease with each course of injections, increasing again during each interval (an interesting example of coincidence).

Case 6. Gold, large doses.



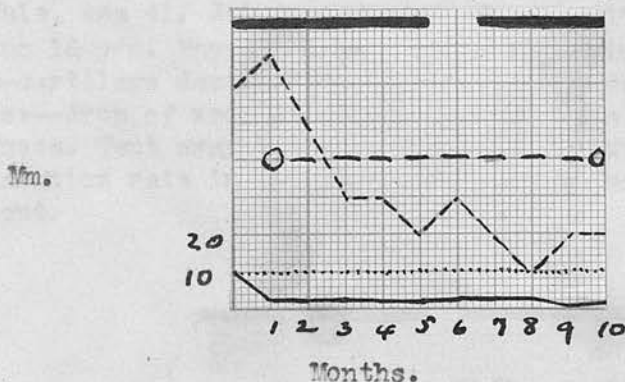
Female, age 47. Joints affected--hands, shoulders, knees & feet. Duration 17 yrs. Physical signs--swelling & limitation of movement. X-ray--decalcification & diminished joint space. Progress--In this case a long interval was allowed between the 1st & 2nd courses on account of a low leucocyte count. There was a gradual fall of the sedimentation rate to normal during the 1st course followed by a slight rise above normal during the interval. The joint ^{swelling} was affected in a similar manner. Final result--no pain or stiffness.

Case F. Control.



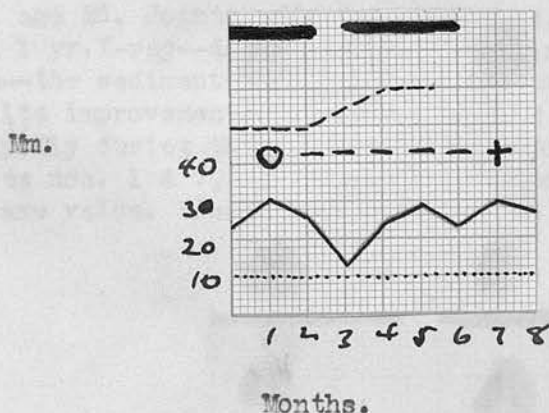
Female, age 32. Joints affected--fingers, wrists, knees & feet. Duration 12 yrs. Physical signs--swelling & limitation of movement. X-ray--periarticular swelling, cartilage & bone destruction. Progress--irregular variations of the sedimentation rate & joint swelling but without any permanent improvement. Final result--"possibly less pain & stiffness."

Case 7. Gold case, large doses.



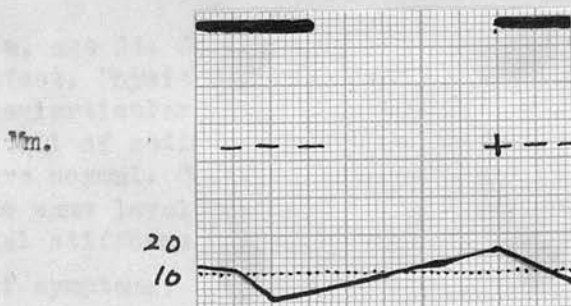
Female, age 43. Joints affected--fingers, wrists & right knee. Duration $1\frac{3}{4}$ yrs. X-ray--decalcification & periarticular swelling. Progress--the sedimentation rate fell from 10 mm. to 2 mm. in the first month & remained at 1 or 2 mm. throughout the remainder of treatment. Steady improvement in joint pain & swelling occurred. Final result--no swelling, no pain on walking etc.. Slight stiffness in the mornings.

Case G. Control.



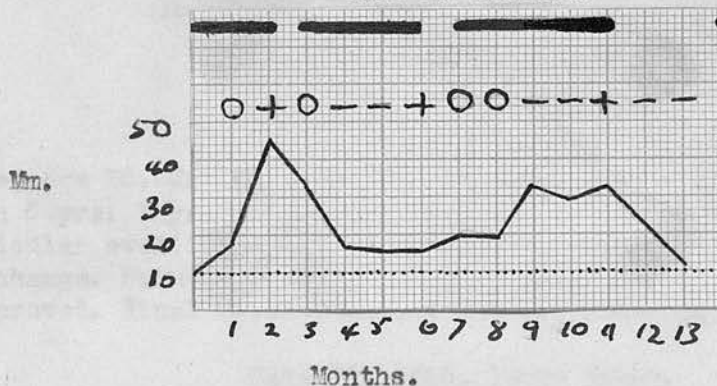
Female, age 35. Joints affected--hands, right knee & ankle. Duration 3 yrs. Physical signs--swelling & limitation of movement. X-ray--periarticular swelling & cartilage destruction. Progress--irregular variations in the sedimentation rate but no definite improvement. Pain & stiffness better while injections were being given, worse after injections stopped. Itchy papular eruption developed towards end of second course. Course not completed.

Case 8. Gold, large doses.



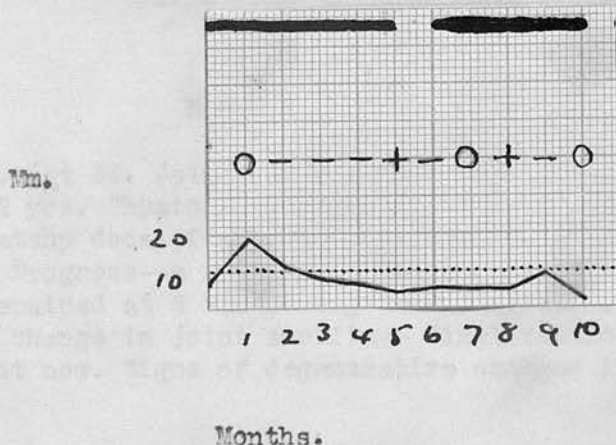
Male, age 41. Joints affected--hands, elbows, knees & feet. Duration 16 yrs. Physical signs--swelling & limitation of movement. X-ray--cartilage destruction. Knees show eburnation & osteophytes. Progress--drop of sedimentation rate to normal with relief of pain & stiffness. Went away for six months. On return, pain worse & sedimentation rate increased. Rapid improvement again on resuming treatment.

Case H. Control.



Female, age 25. Joints affected.--fingers, knees, wrists & toes. Duration 1 yr. X-ray--decalcification, periarticular swelling. Progress--the sedimentation rate shows considerable variations but no definite improvement. Although starting at a normal figure it rises rapidly during the 1st two months. Compare with the two gold cases nos. 1 & 7, which show a commencing sedimentation rate of the same value. Final result--pain much less.

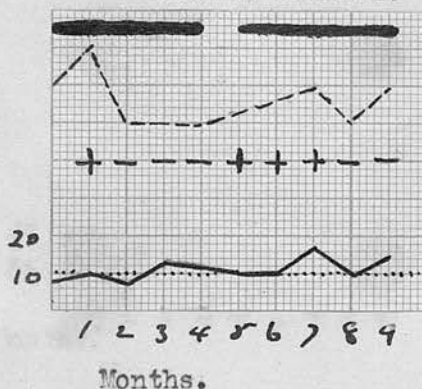
Case 9 Gold large doses.



Female, age 34. Joints affected--hands, wrists, shoulders, knees, ankles & feet. Physical signs--swelling & limitation of movement. X-ray--periarticular swelling. Duration 6 months. Progress--a gradual fall of sedimentation rate to normal after an initial rise above normal. Compare with control case H which started at about the same level. Final result--all pain gone apart from occasional stiffness in the left wrist. seen 6 months later, no return of symptoms.

Case I. Control.

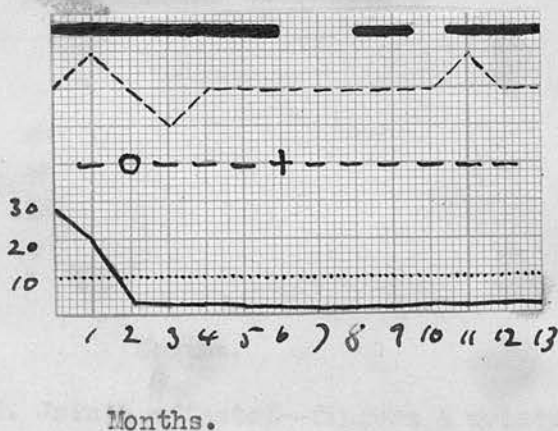
mm.



Female, age 35. Joints affected—fingers, wrists & ankles. Duration 5 yrs. Physical signs—swelling & pain on movement. X-ray—periarticular swelling. Progress—the sedimentation rate shows little change. Pain was worse at the beginning of each course & then improved. Final result—ankles better, other joints unchanged.

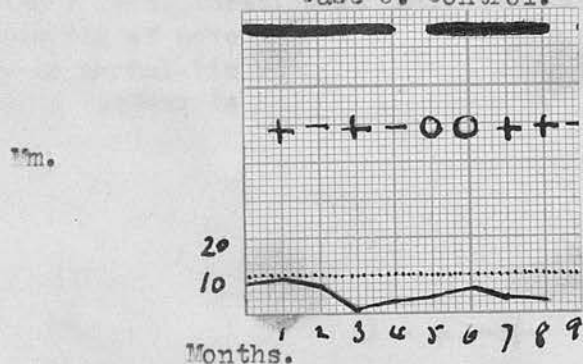
Case 10. Gold, large doses.

mm.



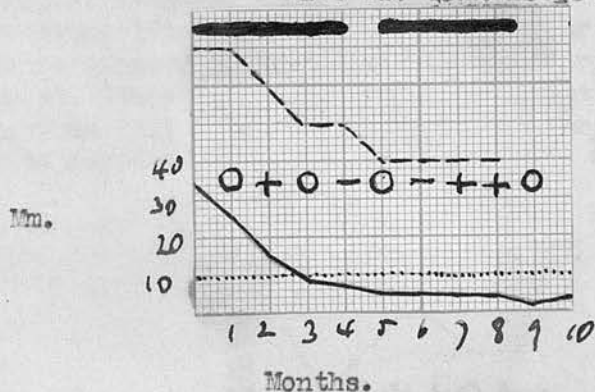
Female, age 38. Joints affected—fingers, wrists, knees & feet. Duration 2 yrs. Physical signs—swelling & limitation of movement. X-rays—patchy decalcification, diminished joint space & periarticular swelling. Progress—a rapid fall of sedimentation rate to normal limits. Remained at 2 mm. during the remainder of treatment. No permanent change in joint swelling. Final result—pain much better, only slight now. Signs of degenerative changes in wrists.

Case J. Control.



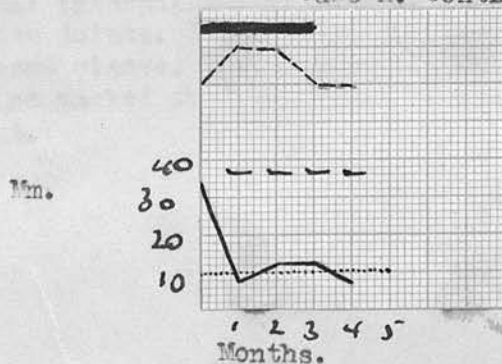
Male, age 32. Joints affected--fingers, wrists, knees, ankles & toes. Duration 5 yrs. Physical signs--pain on movement & slight limitation. X-rays--periarticular swelling. Progress--sedimentation rate remained within normal limits throughout the period of observation. Final result--no pain or stiffness now for 3 months.

Case 11. Gold. Large doses.



Female, age 56. Joints affected--fingers & wrists. Duration 3 months. Physical signs--swelling & limitation of movement. X-ray-----decalcification, periarticular swelling. Progress--a rapid fall of the sedimentation rate to normal limits & constant low level thereafter. Rapid reduction of joint swelling after a preliminary increase in one. Final result--pain much less. Joints freely movable. Slight degenerative changes in the left wrist. Decalcification disappeared. Arthritic changes in one finger joint.

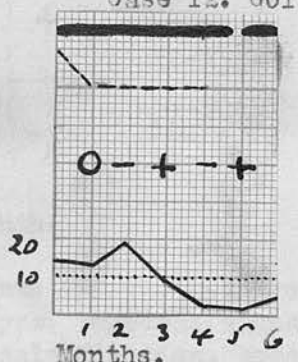
Case K. Control.



Female, age 43. Joints affected--fingers, wrists, shoulders, knees, ankles & feet. Duration 18 yrs. Physical signs--swelling & limitation of movement. Progress--a rapid fall of the sedimentation rate to normal limits followed by a slight rise above this level & then a further fall.

Case 12. Gold. Large doses.

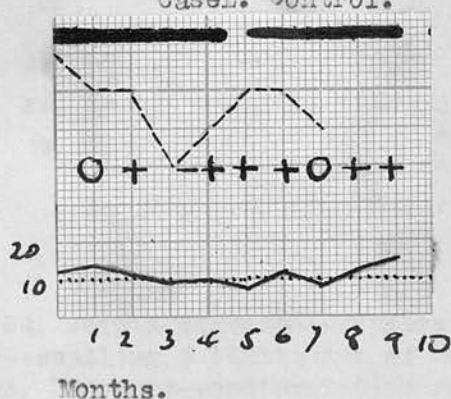
mm.



Male, age 35. Joints affected--fingers, wrists, elbows, shoulders, knees, ankles & feet. Duration 6 yrs. Physical signs --spindle swelling of fingers. Pain & limitation on movement of other joints. X-ray--decalcification, destruction of cartilage, erosion of bone. Progress--improvement in swelling of interphalangeal joints & one wrist. Other wrist unaltered. Sedimentation rate rose at 2nd month, then fell to normal & remained there. Treatment stopped owing to onset of exfoliative dermatitis. **Final result--all pain gone.**

Case L. Control.

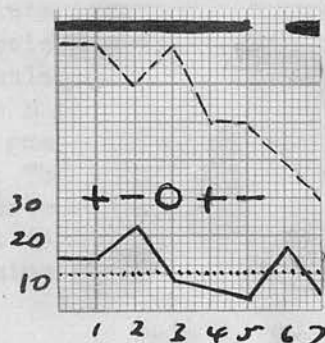
mm.



Female, age 62. Joints affected--fingers, wrists, elbow, shoulder, knees & ankles. Duration 14 yrs. Physical signs--spindle swelling proximal interphalangeal joints. Pain & limitation of movement in other joints. X-ray--destruction of cartilage, bone atrophy & in some places, hypertrophy. Progress--the sedimentation rate shows no marked change. Final result--pain much better but still present.

Case 13. Gold, large doses.

mm.

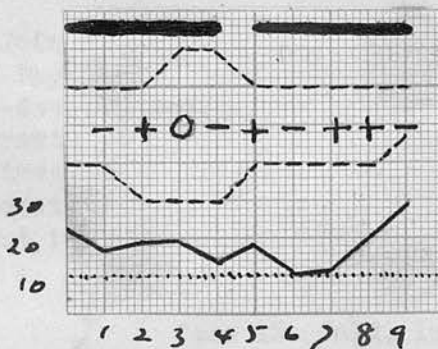


Months.

Female, age 56. Joints affected—fingers, elbows, shoulders, ankles & feet. Duration 25 yrs. Physical signs—swelling & limitation of movement. X-rays—decalcification, some hypertrophy of bone. Progress—increase of sedimentation rate during the second month followed by a fall to normal. A secondary rise during the interval between the courses. A marked reduction of joint swelling. Final result—all pain gone.

Case 11. Control.

mm.

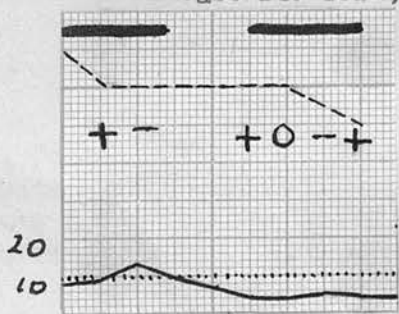


Months.

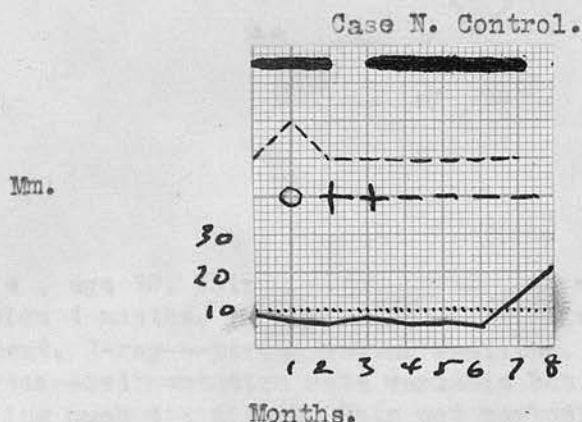
Female, age 54. Joints affected—fingers & wrists. Duration 3 months. Physical signs—swelling & limitation of movement. X-rays—decalcification. Progress—sedimentation rate variable, but not becoming normal at any time. Joint swelling variable but not showing any permanent improvement. Final result—pain & stiffness about the same as before the injections.

Case 14. Gold, large doses.

mm.

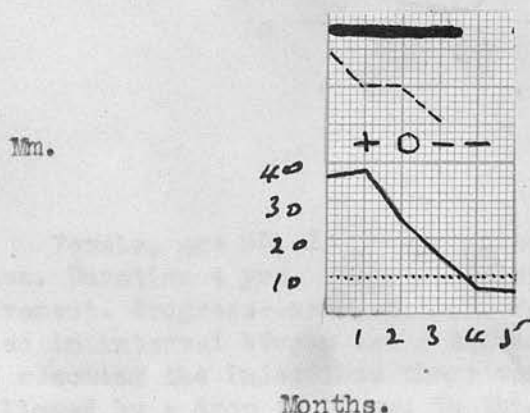


Female, age 27. Joints affected.--fingers, wrists, neck & toes. Duration 7 yrs. Physical signs.--swelling & limitation of movement. X-rays--periarticular swelling. Progress--- treatment had to be discontinued for 3 months during an attack of cystitis. This occurred after 1.1 gms. had been administered. The first course was then completed. The onset of pregnancy occurred before a second course could be started. The sedimentation rate rose at the second month, fell to normal limits during the attack of cystitis & afterwards maintained this level. Joint swelling diminished.



Female, age 40. Joints affected--fingers, wrists, elbows & feet. Duration 15 yrs. Physical signs--spindle swelling, limitation of movement. X-ray--decalcification, destruction of cartilage, osteophytic outgrowths. Progress--gradual fall of sedimentation rate throughout treatment followed by a sudden rise at the last estimation. No constant change in joint swelling. Final result--marked improvement in joint pain & in general health. Decalcification increased.

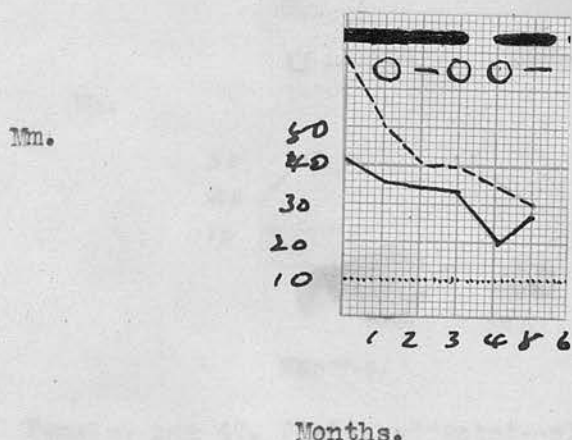
Case 15. Gold, large doses.



Female, age 55. Joints affected--wrists, radio-ulnar joints, ankles tarsi & toes. Duration 37 yrs. Physical signs--swelling & limitation of movement, wrists ankylosed. Progress--rapid fall of sedimentation rate to normal after initial rise. Improvement in joint swelling &

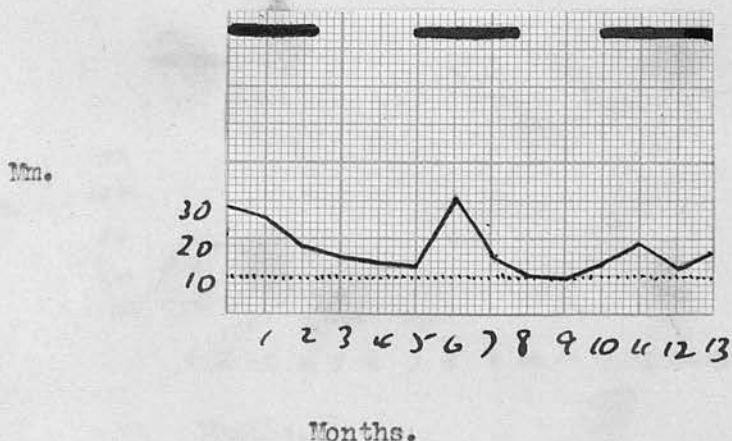
pain. Gold had to be discontinued owing to stomatitis.

Case 0. Control.



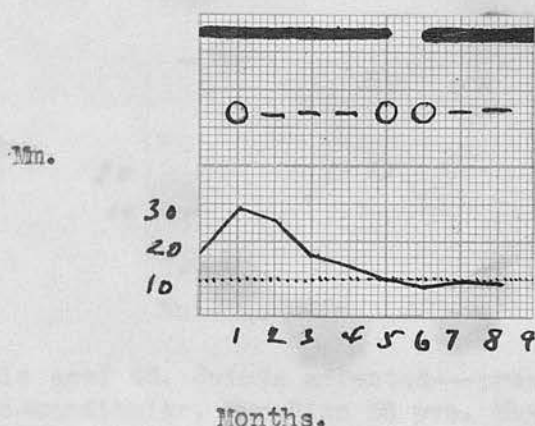
Male, age 70. Joints affected—hands, wrists, shoulders & feet. Duration 4 months. Physical signs—swelling & limitation of movement. X-ray—periarticular swelling. Slight hypertrophic change. Progress—sedimentation rate variable but no definite improvement. Joint swelling much diminished. Pain not markedly affected. Patient discontinued treatment himself. Transient stomatitis.

Case 16. Gold, large & small doses.



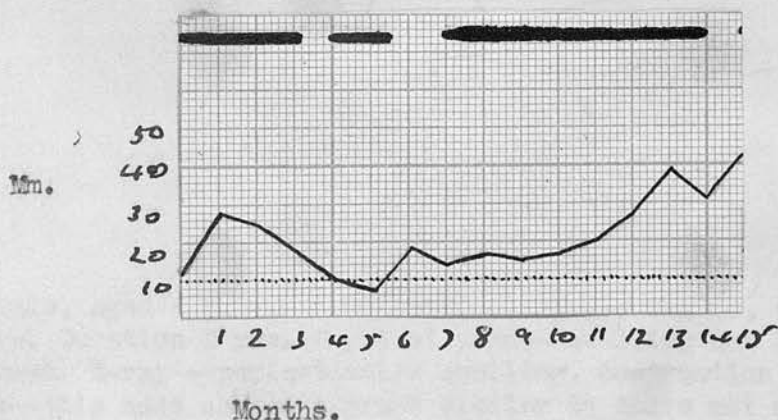
Female, age 50. Joints affected—fingers, wrists, ankles & toes. Duration 4 yrs. Physical signs—swelling & limitation of movement. Progress—sedimentation rate fell during 1st course & also in interval between 1st & 2nd course but did not reach normal. On resuming the injections there was a temporary aggravation followed by a drop to 10 mm. In this case a 3 month interval was tried with the idea of reducing the chances of a high degree of sensitivity having developed when the second course was started. A smaller dose was also employed in the second course, viz. 0.1 gms. weekly. The results were not so satisfactory. Final result—pain & stiffness definitely better than before injections.

Case P. Control.



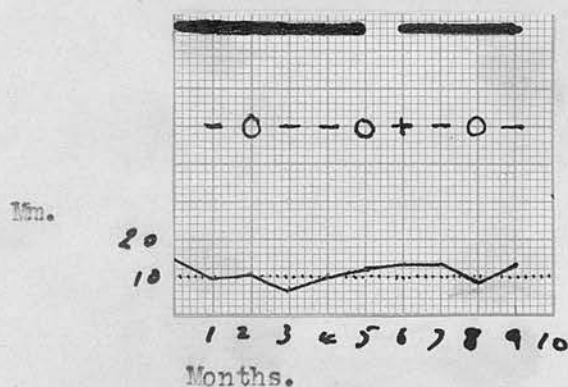
Female, age 47. Joints affected--elbows and wrists. Duration 2 years. Physical signs--pain & limitation of movement. X-rays--areas of decalcification. Diminished joint space. Progress--although this case had no gold, the sedimentation rate responded in a very typical manner. There was an initial rise in the 1st month, followed by a fall to normal levels which were then maintained. We must put this case down as the exception which proves the rule. Final result--pain & stiffness much better. "Only a slight nagging pain remains."

Case 17. Gold, large & small doses..



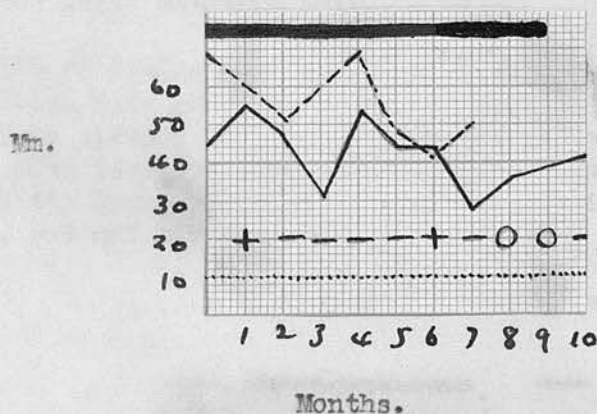
Female, aged 57. Joints affected--proximal interphalangeal, wrists, elbows, & right shoulder, cervical & dorsal spine, left knee. Duration 4 yrs. Physical signs--swelling, pain & limitation of movement. Progress--an initial rise in the sedimentation rate occurred in the 1st course, followed by a rapid fall to normal limits. In the second and third courses, smaller doses were used. The sedimentation rate rose to 20 mm., maintained this level for 5 months, and then rose to 40 mm., where it remained. This confirms the unsatisfactory result obtained in case 16, where also the smaller doses of gold were substituted for the large doses after a 3 months interval. Final result--pain and stiffness lessened.

Case R. Control.



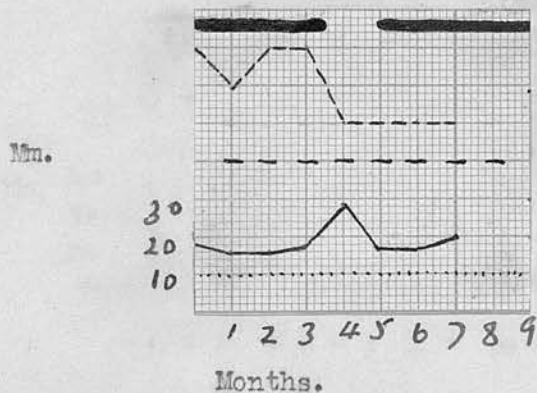
Female aged 43. Joints affected—proximal interphalangeal, left temporo-mandibular. Duration 35 yrs. Physical signs—pain and limitation of movement. X-ray—areas of rarefaction, loss of joint space. Progress—sedimentation rate variable, no definite change, joints improving most of the time. Final result—pain better than at commencement of treatment, and has cleared up in joints originally affected and moved to others.

Case 18. Gold, large doses.



Female, aged 46. Joints affected—fingers, wrists, elbows and shoulders. Duration 2 yrs. Physical signs—swelling and limitation of movement. X-ray—periarticular swelling, destruction of cartilage. Progress—this case showed a graph similar to those met with in the control cases. The sedimentation rate underwent marked variations but never reached normal limits. The joint swelling likewise failed to show any definite improvement. The dose of Solganol was reduced to 0.1 gms. in the middle of the first course, when a papular eruption appeared on the arms, chest and face. Later, with onset of stomatitis and an eruption on the face, it was reduced to 0.05 gms. Final result—pain less but still present.

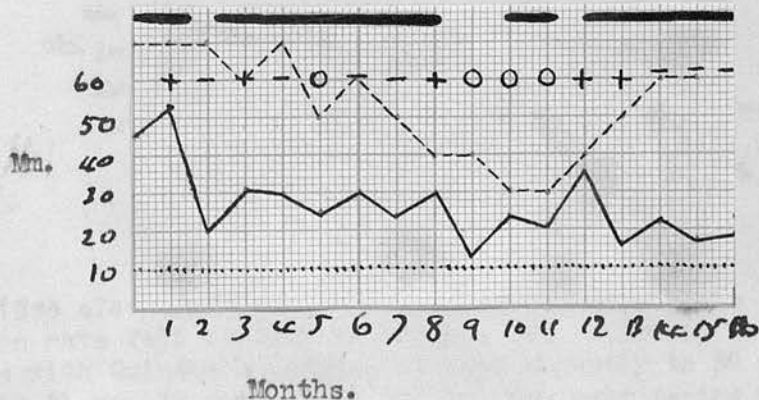
Case 8. Control.



Female aged 39. Joints affected--phalangeal, wrists, right ankle, tarsal. Duration 14 yrs. Physical signs--swelling, pain and limitation of movement. X-ray--patchy decalcification, periarticular swelling, diminished joint space. Progress--sedimentation rate variable, no definite improvement. Joint pain steadily improving each month better than the one before. Joint swelling somewhat improved in one joint, unaltered in another. Final result--better, but still has some pain.

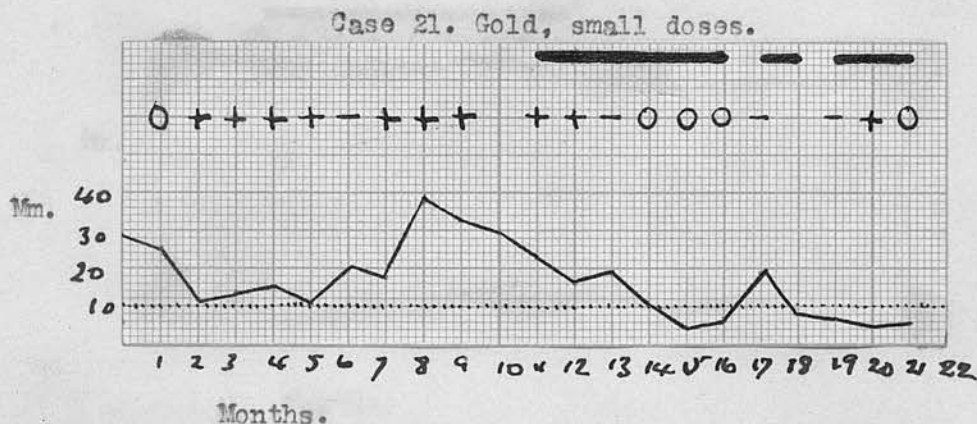
The following cases are those having small doses of gold and which have received 9 or more months treatment. Some of these have already been used as control cases, in which circumstance the graph also includes the original figures for comparison. In this group the heavy black lines on the graphs indicate the period when gold, and not almond oil, was being used.

Case 20. Gold, small doses.



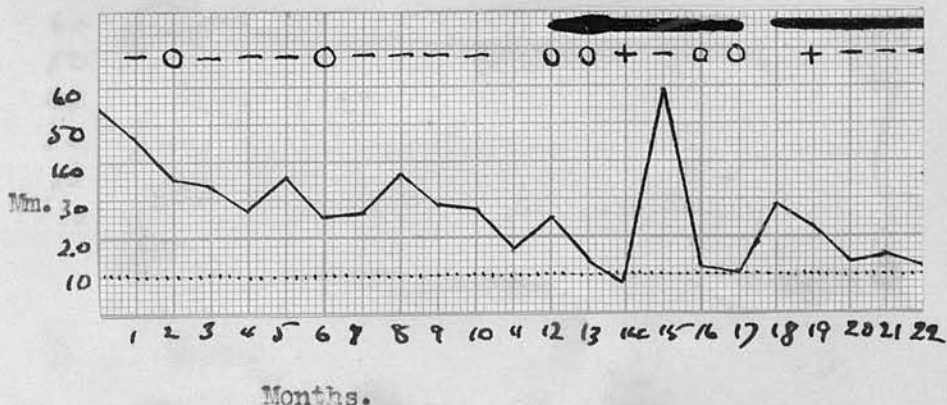
Female aged 37. Joints affected--proximal interphalangeal joints of fingers, knees. Duration 2 yrs. Physical signs--pain, swelling and limitation of movement. X-ray--periarticular swelling, patchy decalcification. Progress--considerable fall in sedimentation rate following 1st course, which unfortunately was cut short by intervention of holidays. Thereafter, variable course, never reaching normality. Final result--pain worse than at commencement. Joint

swelling considerably reduced. Total 3.75 gms.



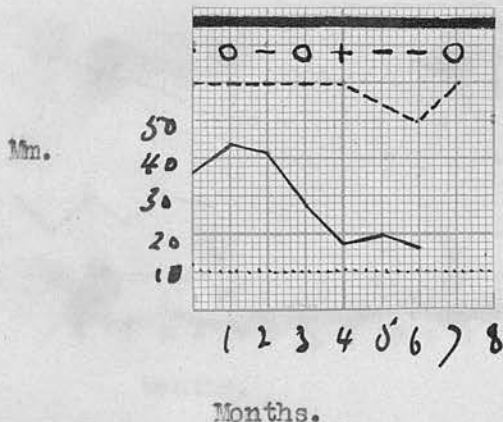
This patient was first used as a control case (see case D). During this time, as has been seen, her sedimentation rate ran a variable course, never reaching below 10 mms. When gold was administered, however, it slowly fell from 22mm. to 5 and thereafter only rose above normal limits during the interval between the 1st and 2nd courses. There was a striking contrast in her replies to questions about joint pain. During the control period, the pains were always "getting worse", but when gold was being administered she became much more cheery, although in the belief that she was having the same injections as before. And, latterly, she has stated that she is quite free from pain.

Case 22. Gold, small doses.



(See also control case B) On starting gold, the sedimentation rate fell rapidly to normal, but following an attack of urticaria with Quinke's oedema, it rose abruptly to 59 mm. and fell again to 11 mm. It rose again during the rest period and is now falling again. Joint pain has now entirely disappeared.

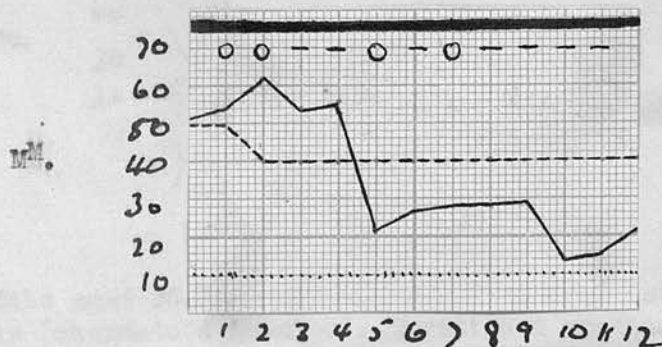
Case 23. Gold, small doses.



Months.

Female, age 56. Physical signs--pain and limitation of movement. Joints affected--interphalangeal, wrist, cervical spine, knees, and toes. Duration 5 yrs. X-ray--areas of rarefaction, periarticular swelling, diminished joint space. Osteophytes distal interphalangeal joints. Progress--after a preliminary rise the sedimentation rate fell considerably but has not yet reached normal limits. The joint swelling has as yet not shown any improvement. The pain is much better.

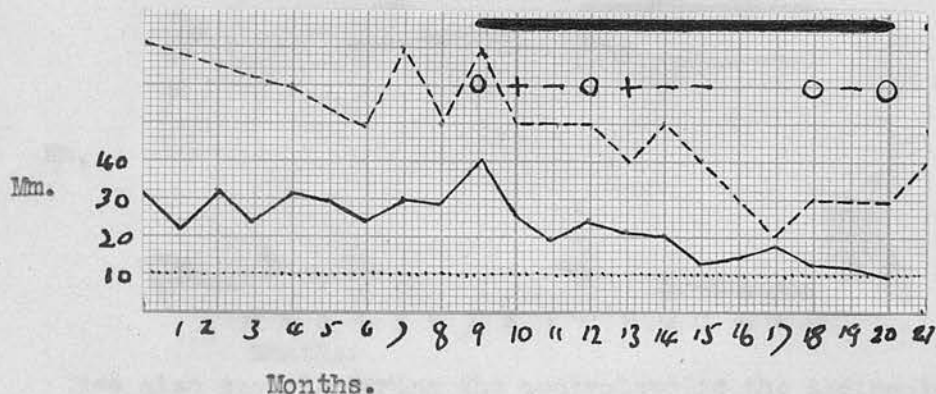
Case 24. Gold, small doses.



Months.

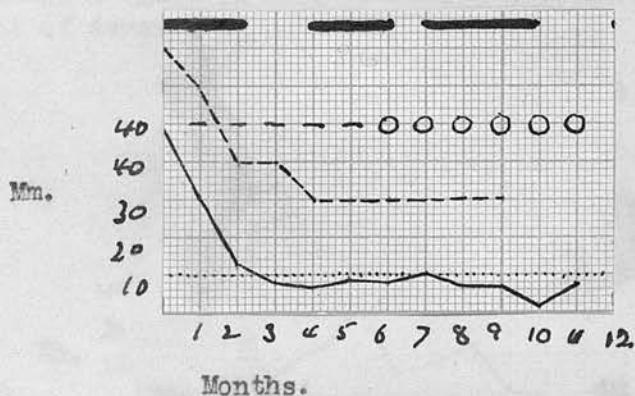
Female aged 53. Joints affected--fingers, wrists, shoulders, knees, neck and jaw. Duration 5 months. Physical signs--pain, swelling and limitation of movement. Right knee--fine crepitus. X-ray--decalcification, periarticular swelling. Progress--initial rise of sedimentation rate at 2nd month to 62 mm.; rapid fall to 20 mm., followed by stationary period and further fall. Joint swelling which was never large, now practically disappeared. Pain much less, but still present in slight degree.

Case 25. Gold, small doses.



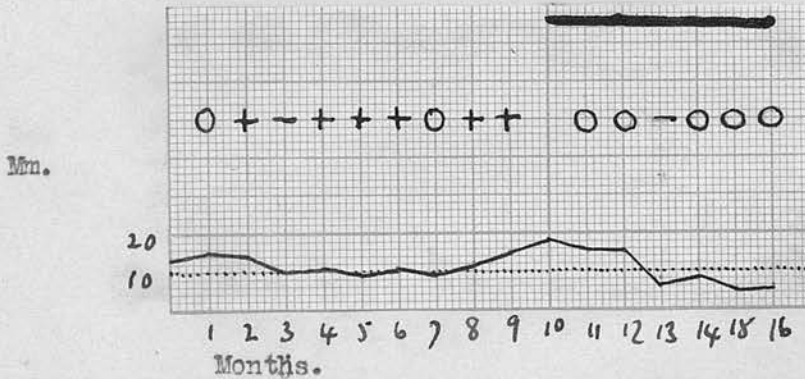
(See also case F) Sedimentation rate and joint swellings, which showed no constant change during control period, both began a gradual and prolonged fall when gold was started, but have not so far become normal. Pain, which was possibly "slightly better" after 9 months control period is now "much better".

Case 26. Gold small doses.



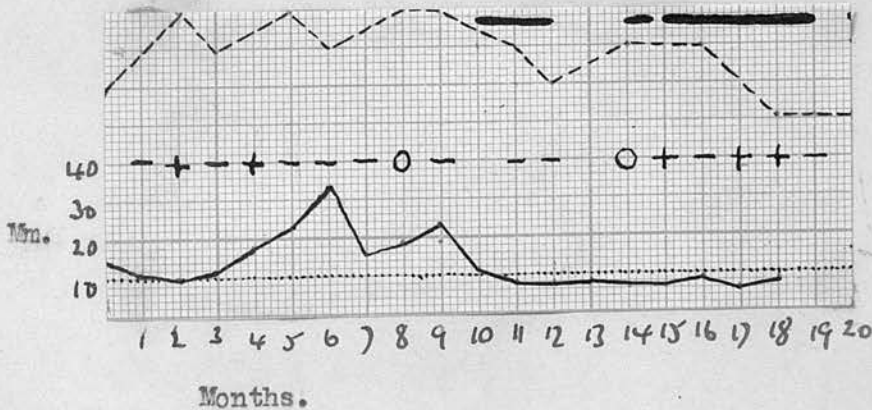
Male aged 35. Joints affected--right wrist, ankles, tarsi and heels (rheumatoid nodules). Duration 2 months. Physical signs--pain, swelling and limitation of movement. X-ray--no bony change. Periarticular swelling. This case is particularly interesting (a) because he had very septic tonsils. These were not interfered with; (b) he had no physiotherapy. Progress--rapid diminution of joint pain and swelling, and also of sedimentation rate. Sedimentation rate normal at 3rd month, joint swelling gone at 4th month and pain at 6th month. No recurrence.

Case 27. Gold small doses.



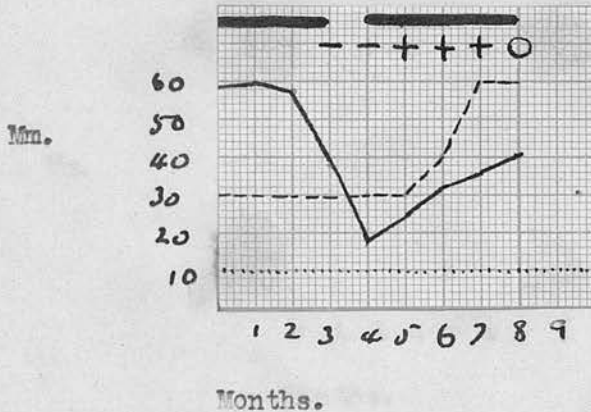
See also case I. During the control period the sedimentation rate ran a variable course between 9 and 28 mm. At the ^{3rd} month of gold treatment it fell to 6 mm. and has remained at about this figure since. The leucocyte count fell to 2,400 during the 2nd month of gold, polymorphs 28%. A test dose of 0.01 gms. Solganal was given and the blood examined 24 hours after. No further drop in the granulocyte count had occurred, and a week later a count showed 11,300 leucocytes and 67% polymorphs. There has been no recurrence, nor did granulopenia occur during the control period when the patient was having injections of sterile oil. Treatment eventually discontinued on account of dermatitis.

Case 29. Gold, small doses.



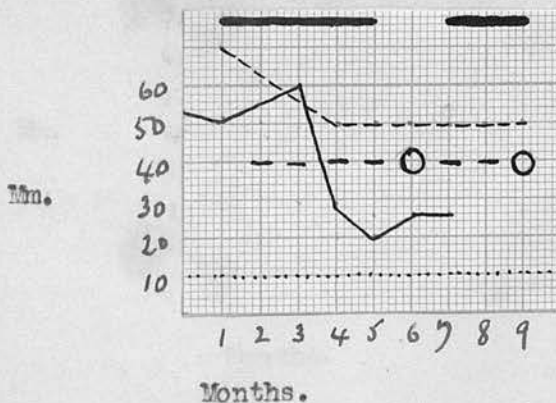
See also case C. Note the marked difference between the undulating course of the sedimentation rate before gold and the constant normal figures obtained after gold treatment had been started; also the rapid diminution of the swollen joint. Final result--all pain and swelling gone.

Case 28. Gold small doses.



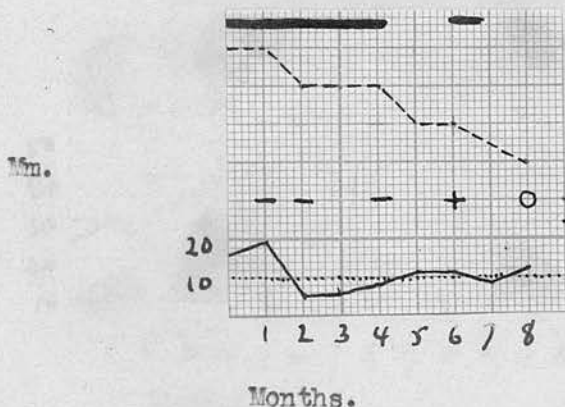
Female aged 50. Joints affected--metacarpo-phalangeal, wrists, right knee. Duration 2 yrs. Physical signs--pain, swelling and limitation of movement. X-ray--decalcification, diminished joint space. Progress--unfortunately in this case the patient stayed away for 3 months between the 1st and 2nd courses. The sedimentation rate fell considerably during the 1st course and the interval and almost reached the normal level. During the 2nd course, however, it again rose and eventually, at the end of 9 months, stood at 40 mm. The joint pain and swelling also increased during the 2nd course. Final result--pain worse than at commencement of treatment.

Case 30. Gold, small doses.



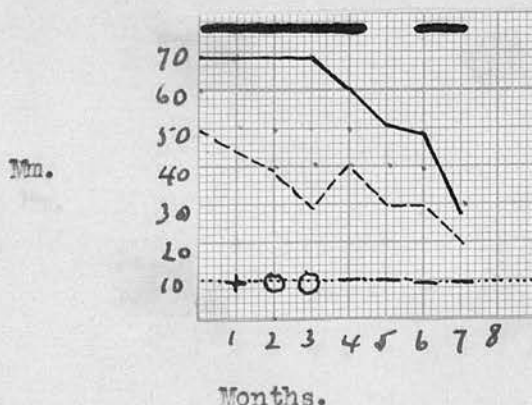
Female age 69. Joints affected--interphalangeal, metacarpo-phalangeal, wrists, knees, ankles, tarsi and toes. Duration 12 months. Physical signs--pain, swelling and limitation of movement. X-ray--decalcification, diminished joint space and periarticular swelling. Progress--Gradual reduction of sedimentation rate but did not reach normal during the period of observation. Joint swelling also reduced. Final result--pain much better.

Case 31. Gold, small doses.



Female aged 40. Joints affected--phalangeal, wrists, shoulder, tarsi. Physical signs--pain, swelling and limitation of movement. Progress--despite very irregular attendance and dosage which was for the most part very small on account of stomatitis, there was considerable reduction in joint swelling and the sedimentation rate became rapidly normal. It rose, however, during the interval of 6 weeks in which the patient did not attend, and also on the occasion of the last test following a similar default. The patient has not been since.

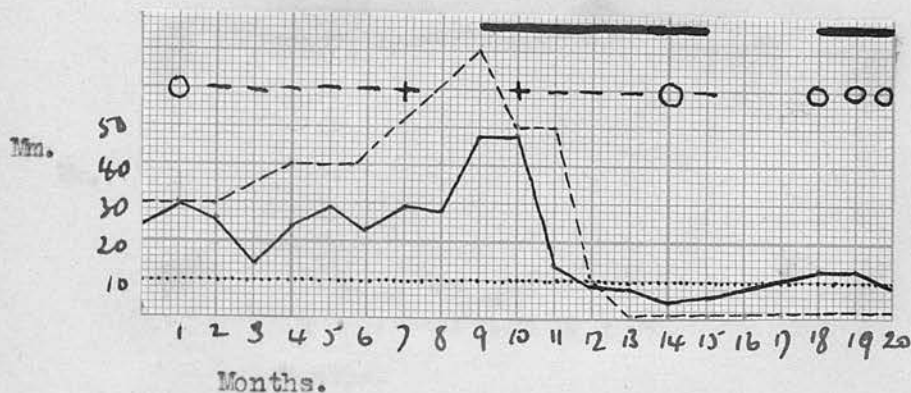
Case 32. Gold, small doses.



Female age 49. Joints affected--fingers, wrists, elbow, knees, ankles, tarsi and toes. Physical signs--pain, swelling and limitation of movement. Duration 2 yrs. Progress--although the tendency is for the sedimentation rate to fall in this case there is in reality very little change. There is however some reduction in the joint swelling. Final result--after 9 months treatment, pain much less.

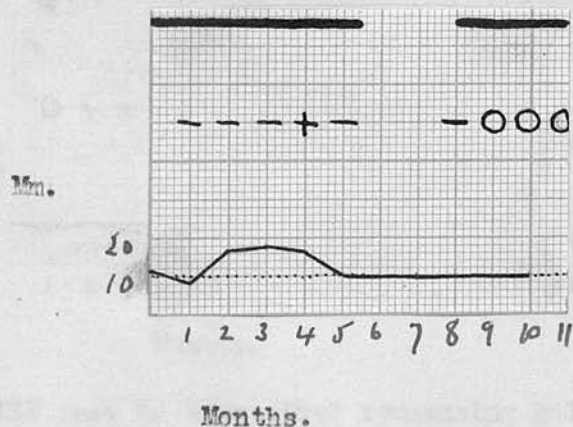
Case 33. Gold, small doses.

Case 33. Gold, small doses.



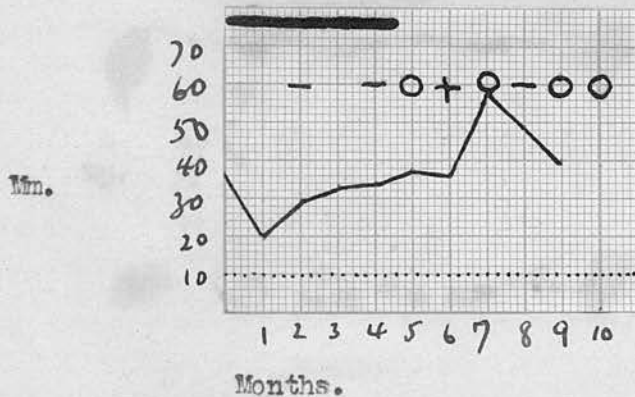
See also case G. This case shows very dramatically the affect of gold, the figures for the blood sedimentation rate and joint swelling both dropping rapidly. Unfortunately, the patient did not attend for several months in the middle of the treatment and during this time the sedimentation rate rose above normal limits, and has not yet remitted. The patient states that the joint pain, at the present moment, is about the same as at the commencement of gold therapy. The joint swelling, however, has completely disappeared.

Case 35. Gold, small doses.



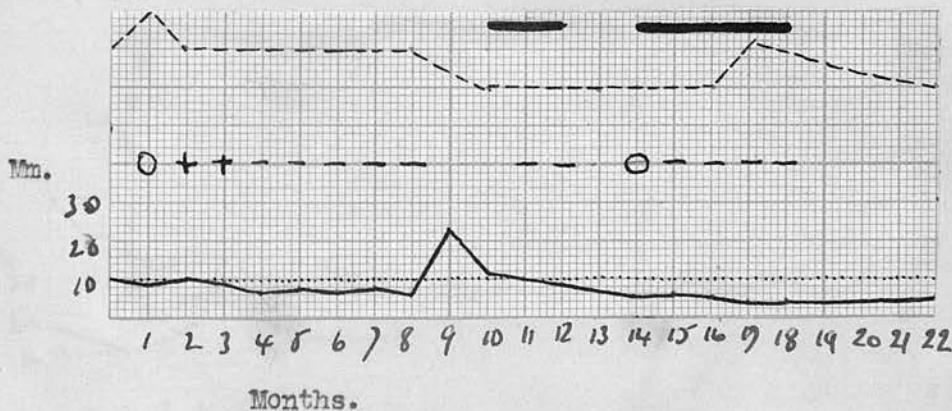
Female aged 39. Joints affected--wrist, elbows, knees, ankle and tarsus. Duration 8 yrs. Physical signs--pain and limitation of movement. X-rays--decalcification and loss of joint space. Progress--initial fall in the sedimentation rate followed by a slight rise and then slow fall to normal. Final result--only occasional slight pain now. Pain had quite disappeared after 1st course but slight exacerbation occurred with commencement of the 2nd course.

Case 36. Gold, small doses.



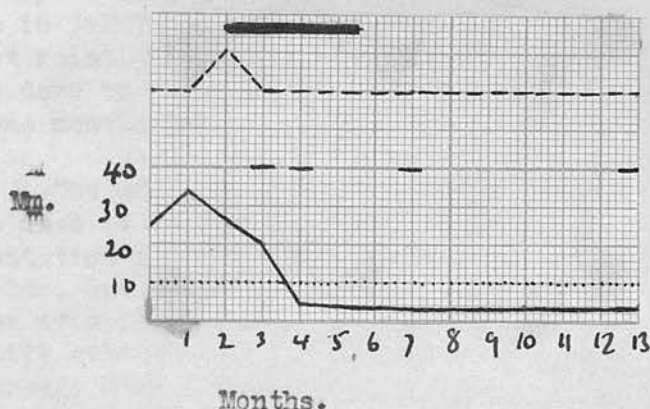
Female aged 49. Joints affected--fingers, wrists, elbows, knees, ankles, tarsi, and toes. Duration $2\frac{1}{2}$ yrs. Physical signs--pain and limitation of movement. Knees ankylosed. X-ray--marked decalcification, diminished joint space. Progress--in this case the injections were stopped after 5 months and have not been resumed. The sedimentation rate showed no marked ^{change} during the course of gold, and has risen somewhat ^{swell}. Final result--pain better than at commencement of treatment.

Case 37. Gold, small doses.



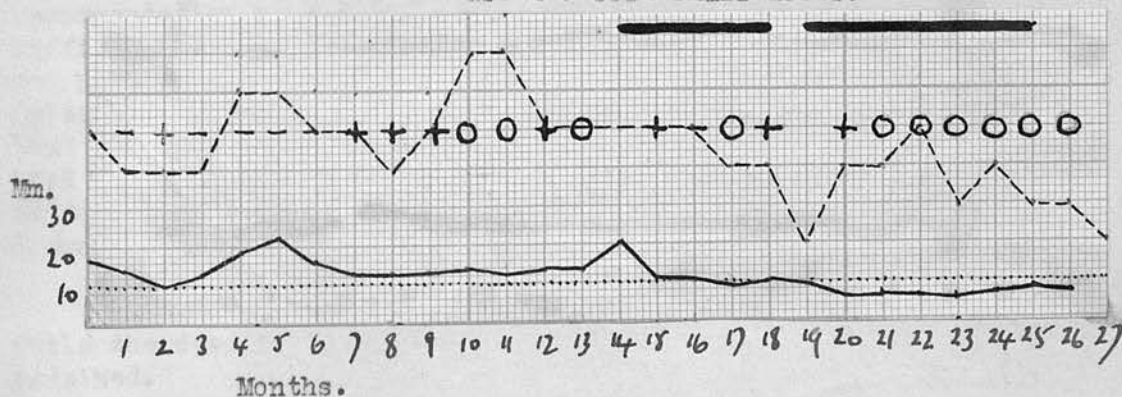
SEE case N. Soon after commencing gold a dermatitis set in so that the treatment had to be discontinued. Since resuming it, only minute doses have been given (max. 0.03 gms.) The joint swelling has not responded well. The sedimentation rate is very interesting in this case, as it was for the most part normal during the control period, averaging about 8 mm. On giving gold, however, it fell to still lower figures, eventually becoming stationary at about 4-5 mms. Final result--pain much less.

Case 39. Gold, small doses.



Female aged 18. Joints affected—proximal interphalangeal wrists. Duration 3 yrs. Physical signs—pain, swelling and limitation of movement. X-ray—decalcification, periarticular swelling, diminished joint space, areas of rarefaction. Progress—treatment had to be discontinued after $3\frac{1}{2}$ months on account of axillary dermatitis. The sedimentation rate had by this time become normal and the joint pain was very much better. Examined 6 months later, she was found to have lost all pain and limitation of movement. The swelling of the proximal interphalangeal joints, however, had persisted, although the sedimentation rate was still normal, and all other signs of disease had disappeared.

Case 40. Gold small doses.



See case E. Although the sedimentation rate was never high, during the control period it never fell below 10 mm. When gold was started, it fell rapidly to 9 mm. and eventually became constant at between 6 and 8 mm. The joint swelling, although still variable, shows a much lower trend. Final result—all pain gone.

General Commentary on Study of Individual Cases.

The study of the different cases individually brings out several interesting points. In the first place it shows that there is no direct relationship between joint pain, swelling and sedimentation rate. The sedimentation rate may

rise suddenly or fall suddenly without there being any marked alteration in joint pain or swelling. On the other hand there is an indirect relationship in that a patient whose sedimentation rate comes down to normal and stays there, eventually, though perhaps some months later, loses the pain and swelling.

The effect of gold on the sedimentation rate in the individual case is also of interest. In a case not under treatment the sedimentation rate runs a variable course, sometimes high and sometimes low, but seldom showing any final improvement. When small doses of gold are given the variable course of the sedimentation rate is still evident in the majority of cases but there is a downward trend. When large doses of gold are given there is, not only a more rapid downward trend but the peaks of the sedimentation rate are considerably flattened out. In one case, in 20, there is apparently no response at all to gold treatment whether small or large doses are given (though possibly doses larger than 0.2 gms. might prove effective).

If the 1st course is stopped before the sedimentation rate has become normal, recrudescence is likely to occur during the rest period and the case be more refractory subsequently. No harm results from prolonging the 1st course, no matter how large the total amount of gold given, provided the sedimentation rate remains high and the white cell and platelet counts are satisfactory. The present practice of limiting the 1st course to 1.0 gms. is likely to lead to numerous failures and even Forfestier's recommendation of 2.5 gms. maximum for the 1st course is not sufficient for some cases. The interval of 3 months between courses now usually recommended is also too long and frequently allows a relapse to occur. An interval of 6 weeks is ample, and provided that the sedimentation rate is still below 10 mm. only minute doses need be given during the second course (max. 0.05 gms) and should be continued till the sedimentation rate has been normal for about 6 months.

If smaller doses are substituted for large doses while the disease is still active very disappointing results are obtained.

Mode of Action

Various theories have been brought forward to account for the action of gold. Houghton(1932) considers that the beneficial effect is due to a stimulation of lymphocyte production. According to Raund(1931 2) there is a 20% increase in the oxidation rate on administering gold. Fehlow(1933) believes that gold produces a general shock to the body and a specific shock to the joints, while Feldt(1926) thinks that either the gold compound or some other substance formed from it in the body acts chemically on the exciting cause of the disease. His alternative theory is that it may possibly stimulate the defensive powers of the body. He showed how when sodium-gold-chloride was mixed with dog's serum and spirochaete *recurrens*, in vitro, no action

occurred, whereas when gold was injected into mice infected with the spirochete it produced a definite result. So far, however, no definite proof of the mode of action in cases of rheumatoid arthritis is forthcoming.

Toxic Phenomena.

Toxic phenomena are of fairly common occurrence in gold therapy, especially in cases of rheumatoid arthritis, and it is very necessary to be on guard against them. Forestier(1932) reports that in treating 22 cases he found toxic symptoms in 3, i.e. 14%. Copeman and Tegner(1937) report 23% and Hartfall et. al. (1937) 43%.

These toxic phenomena may be divided, according to the system affected, into 7 groups as follows:--

- (a) effects on the skin.
- (b) effects on the kidneys.
- (c) effects on the liver.
- (d) effects on the haemopoietic system.
- (e) effects on the mucous membranes.
- (f) effects on the central nervous system.
- (g) effects of a psychotic nature.

There are also certain immediate phenomena which occur only when intravenous injections are given. Nausea, vomiting, vertigo and headache are the chief of these. Temporary pyrexia and aggravation of joint pains are very frequently met with, especially if large doses are given. Occasionally the pyrexia becomes excessive--- the so-called "grippe aurique".

Effects on the Skin.

These are divided by Hinault and Mollard(1934) into 5 groups. (a) erythemata, which are frequently associated with pyrexia; (b) exfoliative dermatitis, which is frequently followed by pigmentation; (c) pruritus, urticaria and Quincke's oedema; (d) eczema; (f) pigmentations. Freund (1928) found that adrenaline in the form of asthmolysin was effective in removing the rashes and even in preventing their recurrence during further gold treatment. The following skin lesions have also been described by various observers:--pustular dermatitis, erythema nodosum, lichen planus, erythema pernio, psoriasis, herpes zoster and alopecia. The exanthemata occurred in 4% of Huhn's cases, 15% of Fehlow's (1930), 7 - 10% of Freund's (1931), and 20% of Faber's. Hartfall and Garland report pruritus in 36% of cases, erythema in 28%, and desquamation in 4%.

Erythema, according to Forestier, does not contra-indicate further treatment, for if the injections are continued it is found to disappear. As an antidote he gives magnesium hyposulphite, 0.6 gms., per diem, orally, or sodium hyposulphite 10 cc. of a 20% solution intravenously. He does not stop giving the gold unless hyperpyrexia occurs.

Hartfall and Garland (1935) treated their complications with sodium hyposulphite and did not consider that any benefit was derived from it.

Mucous Membranes.

In our experience by far the commonest lesion of the mucous membranes produced by gold is stomatitis. The ulcers are small and usually multiple. They are situated on the inner surfaces of the cheeks and lips and the under surface of the tongue. Their course is frequently protracted.

Other lesions of the mucous membranes which have been described are bronchitis, enteritis, and conjunctivitis. Solganal B we have found, is particularly liable to produce bronchitis and tracheitis, especially in cases which show marked clinical improvement. Pneumonia, as a subsequent complication, has been reported by Coste.

Kidneys.

Albumen and casts may appear in the urine. Hartfall and Garland (1935) report it in 13% of cases and Huhn (1932) in 10%. It generally passes off in spite of continuation of treatment. Some, however, regard this phenomenon as an indication that the dose should be reduced. Diuresis following injections has also been recorded. Israelski (1931) found albumen, casts and red blood cells in 50% of his cases and hyperglycaemia in one. A true nephritis associated with oedema, raised blood pressure and albuminuria has also been reported.

Coste et al. (1932) consider that kidney damage is not liable to occur with Solganol, provided the courses do not exceed 3 gms.

If a patient has albuminuria prior to gold therapy it may disappear when gold is given.

Liver.

Jaundice due to a degenerative hepatitis is reported by Brailion. The patient, who had a case of tuberculosis, also developed purpura and agranulocytosis with ulceration of the palate. She had had 2.8 gms. of chrysalbin.

Haemopoietic system.

Owing no doubt to the frequency with which complications of this system lead to a fatal issue, they have been fairly fully reported in the medical literature.

Emil-Weil and Bousser in 1932 collected 30 cases from the literature and classified them as follows:--

- (a) purpura simplex. This has not caused any fatalities.

- (b) purpura haemorrhagica. Sometimes fatal and often associated with pyrexia.
- (c) isolated haemorrhages such as epistaxis, haemoptysis and menorrhagia. Not fatal.
- (d) agranulocytosis. Nearly always fatal.
- (e) aplastic anaemia. Nearly always fatal.

These observers consider that, in view of the large number of patients being treated with gold for various complaints, the frequency of these accidents is probably very low, possibly even lower than the percentage of accidents occurring from arsenobenzol injections. Apparently no single preparation of gold is particularly responsible for the fatal results as deaths have been reported following allochrysin, chrysalbine and solganal.

McCarthy and Wilson (1932) who have made a special study of the blood dyscrasias following the arsenicals gave a further small injection to a patient who had already had an attack of purpura. This was followed by an immediate relapse, thereby proving that the purpura was actually due to the drug.

The following are a few short summaries of some of the cases reported in the literature.

Griveaud (1932) reported a case of purpura simplex in a patient suffering from lupus erythematosus. The rash appeared following the second injection of 0.05 gms. of chrysalbine and it disappeared in this case after 3 weeks.

Emil-Weil reports in 1931 a case of purpura with profuse epistaxis in a male aged 38, suffering from pulmonary tuberculosis. It followed the second injection of 0.25 gms. of chrysalbine. The patient had had several courses of other gold preparations before. The leucocyte count was not affected, the platelets were 50,000, coagulation time was 14 minutes, bleeding time 20 minutes, the tourniquet test positive. There was a previous history of asthma and urticaria and a family history of bleeding in the mother and sister. This patient recovered. Emil-Weil (1931) also quotes Mollard and Bonafe who have recorded a case of purpura with uterine haemorrhage. The patient was a woman aged 28. The haemorrhage started after the 4th injection in the second course.

Laignel, Lavastine and Reyt report a case of purpura haemorrhagica, in which the patient was being treated for pleurisy and in which all the blood findings and tests were normal, except for a slight diminution of the red blood count. The bleeding stopped after a transfusion of 150 cc. of blood. The anaemia improved with liver therapy. There was no previous history of metrorrhagia or rashes.

(1932 I)

Emil-Weil and Bousser report four cases. The first subject was aged 18. Epistaxis and haemoptysis developed after the second injection of chrysalbine. Apart from an eosinophilia of 5%, and 8% of myelocytes the blood count was normal. The

antecedents were suggestive, there being a slight haemorrhagic tendency. The second subject was also aged 38 and epistaxis occurred during the first course of crisalbine. The bleeding stopped but death followed. The blood count was normal, platelets 200,000. No haemorrhagic tendency. The third case, aged 50, developed purpura after 6 injections of allochrysin and 2 of crisalbine. Red blood cells 1,610,000 polymorphs 40%, myelocytes 4%, otherwise normal. The patient was suffering from chronic rheumatism. There were no haemorrhagic antecedents. The result was fatal. The fourth subject, aged 38, was a case of pulmonary tuberculosis, who developed purpura after the second injection of the third course, which cleared up, however, after a blood transfusion. There was a family history of haemorrhages. The sensitivity to gold of these four patients was tested by means of intradermal and cutaneous reactions. Three of them gave a positive result.

(1935)

Hudson reports a case of purpura haemorrhagica due to gold (crisalbine) and a similar case due to arsenobenzol. The first was a woman of 21 suffering pulmonary tuberculosis. The purpuric eruption appeared after the first injection of the second course. Recovery occurred after a transfusion of 500 cc. of whole blood.

(1935)

Hartfall and Garland have reported 3 fatal cases occurring in a series of 100 rheumatoid arthritides. The first, a case of purpura haemorrhagica commenced after 0.36 gms. of crisalbine had been given. 0.15 gms. had been administered on a previous occasion. The second case, also one of purpura haemorrhagica occurred 7 weeks after the last injection of crisalbine. 0.75 gms. had been given in all. Previously this patient had had several short courses. The third was a case of agranulocytosis. There was an interval of 3 months between the final injection and the onset of the blood condition. Eight injections of crisalbine had been given.

Angeras and Ginsbourg (1932) reported a fatal case of purpura haemorrhagica with agranulocytosis in a girl aged 19, suffering from pulmonary tuberculosis. She had just started her second course of crisalbine. No eosinophilia was present.

Achard, Coste and Sahen (1932) have reported 2 cases, one a fatal purpura haemorrhagica with agranulocytosis occurring in a woman aged 38. It developed after 4.85 gms. of Solganol B had been given in doses of 0.25 gms. The patient died of meningeal haemorrhage. The other case was a pure agranulocytosis following the 8th injection of Solganol B in a case of rheumatoid arthritis. The polymorphs fell to 4% and the eosinophils rose to 34%. The patient recovered after daily injections of 5 cc. of 4% sodium nucleate.

Jacob and Douady (1930) had a tuberculous patient with 13 injections of crisalbin (0.1) when she developed a fatal agranulocytosis.

Dameshek (1934) reported a case of aplastic anaemia following the treatment of lupus erythematosus with gold. During the course an erythema had appeared and was followed by desquamation. The injections were continued despite this and, after the 19th injection, the anaemia gradually developed and was eventually fatal though the patient was kept alive for some months by means of blood transfusions.

Jacquelin and Allonic (1932) also reported an aplastic anaemia following gold. The patient was a young woman suffering from tuberculosis. The anaemia occurred during the second course of crisalbine and after the 9th injection (maximum doses 0.25 gms.) There was nothing of note in the personal or family history.

It is noticeable in studying the reports of series of rheumatoid arthritis treated with gold that toxic phenomena develop in a large percentage of cases. This coincides, moreover, with our own experience for we have rarely observed such phenomena in pulmonary tuberculosis. Coste^{Forrester} and Bourderon (1932) consider that rheumatoid patients are more sensitive to gold than tuberculous or syphilitic patients. We found that when oily preparations are used the toxic symptoms take longer to develop and last correspondingly longer. We do not consider that they have, necessarily, any relation to dosage as accidents occur at any time from the third injection onward. They are commoner in women than in men, 18 out of 25 cases being female. Haemorrhagic troubles in the personal and family history or an allergic history are very common. It was noted that 2 cases had had previous treatment with radioactive substances.

(1932 2)

According to Emil-Weil and Bousser the disease for which the patient is being treated is not a determining factor in producing the accidents, though there is considerable doubt as to how these accidents are produced. Feldt (1926) points out that animals killed by overdosage of gold preparations do not develop any of these toxic phenomena but die of respiratory and vasomotor paralysis.

It has been suggested that the toxic phenomena may be produced, not by the gold but by the rapid absorption of pathological products, possibly of the histamine or peptone type set free by the dissolution of the diseased tissues.

Emil-Weil and Bousser (1932 2) consider that they are due to sensitivity to gold, as is shown by the positive cutaneous reactions which they obtained in their cases.

Van Noordén considers that the exanths are anaphylactoid in nature and that they are produced by protein or lipid breakdown products.

Central Nervous System.

Toxic effects on the central nervous system appear to be comparatively rare. There have, however, been numerous cases reported during the last few years. Peripheral neuritis, affecting the upper and lower limbs, manifested by loss of power, hyperesthesia, muscle tenderness and atrophy, diminished reflexes and slow electrical responses, has been reported by Alajouanine, Mauric and Fauvert (1934). The face also was involved in a case reported by Lescher (1936). Tzanck, Pautrat and Klotz (1934) reported a case of pain in the right scapular region with loss of power in the right arm followed by erythema and Jacob (1934) a case of pain in the back and legs. Lebeuf, Petouraud and Mollard (1931) reported a case of pain and hyperesthesia in the palms and soles with erythema and desquamation in the same parts.

A peculiar and very distressing syndrome characterised by severe pains in the limbs, loss of power, generalised fibrillary contractions in the muscles, and in some cases wasting of muscles and altered electrical reactions has been described by Chavany and Chaignot (1934), Gernez (1935) and Bernard and Morin (1936). The severity of the pain can be judged by the fact that little relief could be obtained from morphia, and other hypnotics were useless. The condition lasts about 3 months.

Gougerot (1931) describes a case in which pain started in the leg 6 hours after the injection and spread all over the back and limbs. It lasted 24 hours.

Psychic manifestations---asthenia, melancholia and mania following gold have also been described.

Prophylaxis and Treatment of the Toxic Manifestations.

Phil-Weil and Bousser (1932 2) consider that the most important point in the prevention of these accidents is to avoid giving gold to any patient with a personal or family history of purpura or bleeding.

Coste and Bourderon and Forestier (1932) also stress this point and recommend that gold should not be given after substances which affect the bone marrow, such as thorium. Special warning should be taken from haemorrhages or petechiae appearing during treatment. When toxic symptoms have occurred an eosinophilia is, they find, frequent but it does not appear till after the onset of the toxic symptoms and when it does occur they do not regard it as a contra-indication to further treatment.

Dumaret, Mollard and Pavie (1931) on the other hand, consider that care in dosage should be considered whenever the eosinophil count rises above 5%. Since taking this precaution they themselves have had fewer complications.

Lacapere (1932) recommends that the injections should be discontinued when the eosinophil count reaches 6%. Three cases of mucous aurides had eosinophil counts of 7, 8 and 10% respectively. one among them developed purpura and haemorrhage although the treatment was discontinued. No aurides occurred with eosinophil counts of less than 6%. One patient who had an eosinophilia before treatment, developed toxic symptoms after 0.15 gms. had been given. Other features which developed in toxic cases were a diminution of lymphocytes and an increase of transitionals, myelocytes and mast cells.

Freund (1927) and others caused a gold rash to disappear by doubling the dose of gold at the next injection.

The most effective treatment in the case of the blood dyscrasias is blood transfusion, repeated as often as a relapse occurs, although its value, according to recent opinions, is very doubtful in cases of agranulocytosis. Subcutaneous injections of whole blood have also been recommended, besides adrenaline, liver and sodium or magnesium hyposulphite.

TOXIC PHENOMENA IN OUR OWN CASES.

The commonest toxic phenomenon observed in our cases was stomatitis. It occurred in 43% of the gold cases and 35% of the controls. In our opinion the frequency of stomatitis in the control cases is definitely higher than might be expected in a random sample of the population but we attribute this, not to the almond oil injections which these cases were having, but to the fact that the majority of these patients have been submitted to dental extractions before coming under our care and had in consequence been recently fitted with dentures. Although the frequency of stomatitis was almost identical in the gold and control series the severity and extent of the trouble was much greater in the cases having gold treatment. A study of table 10 shows that it occurs for the most part towards the end of the 1st course or during the subsequent courses and but seldom during the early stages of treatment. As will be seen from a study of the sedimentation rate column it is most liable to occur when the sedimentation rate has reached normal figures. All the severe attacks of stomatitis have occurred in conjunction with a low sedimentation rate. The average figure at the onset of stomatitis was 8 mm. whereas the average of all sedimentation rates obtained in our gold cases was 17 mm.

The eruptions of the squamous and exfoliative type which were the next most frequent accident to occur in our series, have been grouped together as they all have a similar prognosis. They tend to be of lengthy duration, are resistant to treatment, and, like the cases of stomatitis, do not occur during the early stages of treatment. They may take the form of an eczema, a psoriasis, an exfoliative dermatitis, or an intertrigo. They occurred in 22% of our gold cases and in none of the control cases. A curious feature is their onset in two of our cases during the interval between the 1st and second courses. This was not met with in any of the other "accidents" (see table 10). The sedimentation rate was low at the time of onset in all except one. The scaling in this case was very slight being rather a fine branny desquamation. The most marked case of exfoliative dermatitis we have seen occurred in a case of gout treated with gold. The sedimentation rate was, of course, normal. The average sedimentation rate in the cases with this complication was 8 mm.

The erythematous and papular eruptions occurred in 20% of the gold cases and 10% of the controls. In the gold cases they appeared for the most part soon after the commencement of treatment and were in consequence associated with a high sedimentation rate (average 24 mm.) They cleared up rapidly and did not return on resuming the treatment. It has been our practice to discontinue the injections temporarily or give minute doses in these cases with a view to making certain that an exfoliative type of eruption was not in course of development.

Complications met with during Treatment.

Complication.	Stage of treatment at which it occurred.	Sedimentation rate immediately prior to its occurrence.
Stomatitis.	1st month. 1st course. 3rd " 1st " 3rd " 1st " 4th " 1st " 4th " 1st " 5th " 1st " 5th " 1st " 5th " 1st " 5th " 1st " 1st " 2nd " 2nd " 2nd " 2nd " 2nd " 3rd " 2nd " 3rd " 2nd " 5th " 2nd " 6th " 2nd " 2nd " 3rd "	19. 2. 6. 8. 8. 18. 5. 6. 16. 3. 6. 5. 6. 7. 2. 11. 4.
Exfoliative Eruptions.	2nd " 1st " 4th " 1st " 4th " 1st " 4th " 1st " 6th " 1st " Interval. Interval. 2nd month 2nd " 6th " 2nd "	10. 3. 2. 9. 4. 12. 5. 28. 3.
Erythemaatons & papular eruptions (non-exfoliative)	1st " 1st " 1st " 1st " 1st " 1st " 1st " 1st " 2nd " 1st " 5th " 1st " 6th " 1st " 2nd " 3rd "	16. 36. 19. 38. 3. 8. 20. 55.

TABLE X. (Cont.)

57 B.

Herpetic eruptions.	1st month.	1st course.	27.
	4th "	2st "	2.
	5th "	1st "	7.
	2nd "	2nd "	7.
	3rd "	2nd "	6.
	3rd "	2nd "	18.
Albuminaria.	1st "	1st "	23.
	3rd "	1st "	28.
	3rd "	1st "	3.
	6th "	2nd "	18.
Urticaria.	1st "	1st "	23.
	2nd "	1st "	19.
	2nd "	1st "	20.
	3rd "	1st "	9.
Vomiting.	3rd "	1st "	14.
	5th "	1st "	13.
	7th "	1st "	17.
	1st "	2nd "	3.
Agranulocytosis	@ 3rd "	1st "	5.
	1st "	2nd "	8.

@ Not a patient in present series.

Herpetic eruptions --herpes labialis, and dermatitis herpetiformis occurred in 15% of our gold group and 20% of our control group. We therefore consider that they were not due to the gold injections. Albuminuria occurred in 10% of the gold cases and none of the control cases. It occurred most frequently in the early stages and was not associated particularly with a low sedimentation rate (average 18). It was not associated with any evidence of impaired kidney function and in only one case did it become so heavy as to necessitate reduction in dosage of gold.

Urticaria occurred in 10% of gold cases and no control cases. It always occurred during the early stages of treatment, and did not recur. Average sedimentation rate 18 mm.

Pruritus unassociated with any eruption occurred in 2 gold cases and 1 control, and was probably not due to the gold treatment. Nausea, vomiting and diarrhoea occurred in 10% of gold cases and 10% of controls.

Agranulocytosis occurred in one case in this series and has been fully reported elsewhere (Ellman and Lawrence) (1935) Another case which did not occur in this series is also included in table 10 for comparison. The latter developed the condition at an early stage in the treatment. She had a normal sedimentation rate from the start. The former who had a raised sedimentation rate at first did not become agranulocytic till the beginning of the 2nd course when the sedimentation rate had reached normal limits. It was associated in this case with purpura haemorrhagica. Both were fatal.

Granulopenia occurred in one of our cases. The leucocyte count fell to 2,400 per cu. mm. (polymorphs 38%). It rapidly returned to 12,000 leucocytes per cu. mm. (polymorphs 67%) despite a provocative injection of 0.01 gms. of solganal and has not recurred despite continuation of the treatment (0.04 gms. Solganal B once weekly).

The following complications have also been met with occasionally:- furunculosis, blepharitis, conjunctivitis, erythema pernio, psychotic symptoms, tracheitis and bronchitis, epistaxis, cystitis, menorrhagia, Quincke's oedema, metallic taste, and paresthesiae in the extremities. Apart from the furunculosis, these symptoms have not been noted in the control cases.

Witts(1936) has divided the "accidents" caused by drugs when in non-toxic doses, into two groups:- (1) those due to idiosyncrasy and (2) those due to abnormal sensitivity to the drug. In the latter group he includes stomatitis and exfoliative dermatitis, and in the former, erythema and agranulocytosis. Our results bear out these views. Stomatitis and the exfoliative eruptions occur after prolonged treatment, erythema and urticaria occur in the early stages. They also suggest a

factor in this abnormal sensitivity to gold. It is apparently when the sedimentation rate is low that patients are particularly liable to develop stomatitis or exfoliative dermatitis. We have observed that those who have a normal sedimentation rate at the commencement of treatment are liable to develop these complications at an early stage. But while a patient's sedimentation rate is high he appears to be immune. In the case of agranulocytosis there is unfortunately not much evidence available. In the cases reported in the literature the sedimentation rates are not given. All however have occurred after a considerable number of injections. Of our own 2 cases, the one who developed the trouble fairly early had a low sedimentation rate right from the start of the treatment and the other one, who was high at first, developed the trouble after the sedimentation rate had become normal.

On reviewing all the serious or prolonged toxic effects that we have seen resulting from gold we find that in no case have any of these occurred till the sedimentation rate has fallen to 10 mm. We would therefore recommend that great care should be exercised once this point has been reached. Possibly the dose of 0.05 gms. which we have been using at this stage is too high as we have seen an extensive dermatitis of trunk and limbs following weekly doses of 0.04 gms. in a patient whose sedimentation rate was 4 mm. A dosage of 0.02 - 0.03 gms. might have avoided this. Fortunately at this stage in the progress of the case these small doses seem to be sufficient to complete the cure.

In some typical cases of rheumatoid arthritis the sedimentation rate will be found to be low at the start although the disease appears to be in an active stage. In these cases when gold treatment with very small doses (0.01 - 0.03 gms.) is instituted the sedimentation rate will usually be found to rise to higher figures. Larger doses of gold may then be given in safety.

In suggesting this method of regulating the dosage we realise of course that in a large proportion of cases we are being overcautious, for many patients can be given moderate doses without harm, although the sedimentation rate is very low. Unfortunately, however, we have no means of recognising the sensitive patient until the catastrophe occurs; and then it may be too late. Such conditions as agranulocytosis and aplastic anaemia are usually fatal, no matter what treatment is adopted. Our only alternative is to be cautious in every case, even though we may by this means render the "cure" a little less dramatic.

DISCUSSION

As each of our results has been fully discussed already, it will not be necessary to go into them again here. In considering the results we have obtained, it is advisable to study first the results in the control series. In the consideration of any beneficial effects obtained in the control series, three main factors have to be taken into account: (a) the natural course of the disease; (b) the effect of the physical treatment; and (c) the psychological effect of the injections.

The natural course of the disease is one of frequent remissions and relapses, but with a tendency eventually to reach a stage of inactivity. The final result depends on how soon this stage is reached. In some early cases, the remissions may be complete, all symptoms and signs disappearing for a short time. In others, the joint condition never completely disappears, but follows a subacute course, with occasional exacerbations.

That physiotherapy has by itself a beneficial effect in cases of rheumatoid type of arthritis, there can be no doubt. In addition to relieving the pain, it is also said to exert a curative influence by increasing the circulation of blood in the diseased tissues.

The marked improvement which has occurred in many of the control cases during the first few weeks of injection treatment is probably due to the psychological factor, which is stronger during the early stages, when the patient's expectations are high. Many too, of the control cases, have noticed a considerable reduction of pain and stiffness immediately after the injection. This lasts several days, and has usually passed off by the time the next injection is due.

We can therefore draw the following conclusions from our results in cases treated with Solganal. The gradual reduction of pain and stiffness is not wholly due to the effects of local treatment, and the psychological effect and the natural tendency of the disease to get better. There is, in addition, an effect due to some inherent property in the gold compound itself. That this effect is not simply analgesic is shown by the fact that the improvement is gradual and steady and not simply a temporary palliation such as is obtained with the analgesic group of drugs.

Of the effect of gold on the sedimentation rate in these cases, there can be no doubt, as the course which it takes is quite different in the two groups.

The general impression gained was that, when gold is given the disease is made to run its course much more rapidly than is normally the case. At first it becomes more active; the joint pain and stiffness increase and the sedimentation rate goes up. After, there is a gradual reduction in all symptoms and signs, the disease becoming inactive finally in 1 - 2 years instead of the usual 10 - 20 years which is necessary when physical treatment alone is given.

With regard to the comparison of those cases treated with large and those with small doses of gold, we consider that there is definite evidence of a greater and more rapid effect with the large doses. We are, of course, comparing in these two groups cases who have had the same length of treatment but not the same amount of gold. Possibly, later on, when we are able to compare cases which have all had 5 gms. of gold, in the 1st group in large doses and in the 2nd in small doses spread over a longer time, we may find no marked difference. At the present stage it is useless to speculate further on this point.

With regard to the dangerous reactions associated with gold treatment, we consider that it may be possible to avoid these in the future. In order to do this we would make the following suggestions. The urine should be examined every week and the blood every 4 weeks. The sedimentation rate and the differential count are the essentials in the examination of the blood. When the sedimentation rate is low, (below 10 mm.) large doses of gold should on no account be given and are not, in fact, necessary, as these cases respond to very small doses. When, however, the sedimentation rate is high, larger doses (0.2) may be given and increased if necessary. The 1st course may and should be prolonged till the sedimentation rate is normal, but as soon as this occurs the dose should be reduced (say to 0.05 gms.) This small dose should also be used throughout the 2nd course, provided the sedimentation rate is still within normal limits. If stomatitis or a squamous eruption occurs, the injections should immediately be discontinued or a minute dose (0.01 or 0.005 gms.) substituted, and after it has cleared up only very tentatively increased. For erythematous eruptions, non-squamous papules and urticaria, the dose need only be reduced until the diagnosis has been definitely established (by which time the eruption will probably have disappeared) when the large doses may be resumed.

SUMMARY

1. A series of cases of arthritis of the typical rheumatoid type have been carefully studied. The detailed results in 60 cases of this series which have been under observation for not less than 9 months have been recorded.
2. These cases were divided into three equal groups. Group I was given large doses of gold; Group II was given small doses of gold; and Group III was given injections of sterile oil as a control series.
3. The disease was rendered inactive in 50% of cases in Group I; 38% of Group II; and 5% of Group III.
4. Joint swelling was reduced in 81% of Group I; 79% of Group II; and 16% of Group III.
5. No changes were noted in the radiological picture, apart from diminution of periarticular swelling and certain slight changes in the areas of decalcification in Groups I and II. Group III was entirely unaffected.
6. The sedimentation rate became normal in 83% of Group I; 43% of Group II; and 26% of Group III.
7. The toxic manifestations, which were numerous, have been discussed and methods for avoiding the more serious of them in the future suggested.

I wish to express my great indebtedness to Dr. Phillip Ellman, honorary physician to the St. John Clinic and Institute of physical medicine, Ranelagh Road, London, SW1, under whose supervision this work was carried out.

RESEARCH PAPERS

- Achard C., Coste F., and Cahen R.,-----Bull. et Mem. Soc. Med. d'Hop.
de Paris 1932 48 547.
- Alajouanine Th., Maurie G., et Fauvert R.--Ibid 1934 50 128.
- Angeras et Ginsbourg.-----Le Sang 1932 6 798
- Bach F., -----St. Barts. Hosp. Journ. 43 206
- Bernard E., et Morin M.,-----Bull. et Mem. de la Soc. Med.
d'Hop. de Paris 1936 52 469
- Bertier L., et Bocquillon -----Bull. Soc. franc. de Derm. et
Syph. 1933 39 1335
- Baillon J. -----Le Sang 1934 8 356
- Chavany J. -A., et Chaignot A.-----Presse Med. 1934 42 488
- Copeman W. S. C., and Tegner W. ----Lancet 1937 1 554
- Coste F., Forestier J., et Bourderon T.--Paris Med. 1932 2 478
- Crosby G.J.V.-----Lancet 1936 1 1463
- Dameshek W. -----New England Journ. of Med.
1934 210 687
- Denier -----Rev. d'Actinol 1930 6 610
- Dumaret F., Mollard H., et Pavie P.--Soc. Biol. 1931 2 794
- Ellman P., and Lawrence J.S. -----Brit. Med. Journ. 1935 2 622
ELLMAN P. "THE RHEUMATIC DISEASES" *edited by Sir L. Hill*
and Philip Ellman
E. Arnold & Co 1936
- Emanuel S. -----Derm. Z. 1933 67 24
- Faber K. -----Ungeschrift f. Laeger 1932 47
- Fehlow W. -----Munch. Med. Wschr. 1930 77 2215
- " -----Dtsch. Med. Wschr. 1933 59 1206
- Feldt A. -----Klin. Wschr. 1926 no. 8 299
- " -----Ibid 1927 no. 24 1137
- " -----Med. Welt. 1930 12
- " -----Ibid 1930 13 437
- Forestier J. -----Bull. Soc. Med. d'Hop de Paris
1929 323
- " -----Therapeutique Moderne. Personal
communication.

- Forestier J. -----Lancet 1932 441
- " -----Gazette Med. de France no. 8
(15 avril 1932)
- " -----Ligue française contre la Rhumatisme
Séance scientifique du 13 mars 1933
- " -----Lancet 1934 2 646
- Freund A. -----Klin. Wschr. 1927 19 903
- " -----Beitrag zur klinik der tuberculose
1928 68 606
- " -----Med. Klin. 1931 5 186
- " -----Ibid 1931 27 992
- Gernez Ch. -----Rev. de Tuberc. 1935 1 386
- Gougerot M.H. -----Bull de la Soc. Franc. de Derm. et Syph.
1931 38 53
- Griveaud E. -----Ibid 1932 39 822
- Griffiths G. and Race J. -----Lancet 1935 Sept 28 714
- Hartfall S.J. and Garland H.G. -----Ibid 1935 2 8
- " " " and Goldie W.-----Ibid 1937 2 784
- Hinault V. and Mollard H. ---Le Traitement Aurique de la Tuberculose
Paris 1934
- Houghton L.E. -----Tubercle June 1932
- Hudson E.H. -----Lancet 1935 2 74
- Huhn D. -----Zeit. f. klin. med. 1932 121 485
- Israelski E. -----Dtsch. Med. Wschr. 1931 57 1280
- Jacquelin A., and Allonic A. ---Bull. et Mem. de la Soc. Med. d'Hop.
de Paris. 1932 48 539
- Jacob M.P. -----Ibid 1934 280
- Jacob M.P. et Douady -----Ibid 1930 9th May 788
- Lacapere Jean -----Le Sang 1932 6 221
- Laignel, Lavastine et Rayt -----Ibid 1932 6 452
- Lebeuf F., Petouraud Ch. et Mollard H. ---Bull de la Soc. franc. de
Derm. et Syph. 1931 38 142

- Lescher F.G. ----- Brit. Med. Journ. 1936 2 1303
- Mallie H. ----- J. de Med. de Bordeaux 1933 110 797
- Maliwa E. ----- Wien. klin. Wschr. 1932 45 1313
- McCarthy F.P. and Wilson R. ----- J. Amer. Med. Ass. 1932 99 1557
- Pemberton H.S. ----- Lancet 1935 1 1037
- Schiemann and Feldt A. ----- Zeit. Hyg. 1926 106 83
- Secher K. ----- Ugeskrift f. Læger 1932 44
- Slot G. and Deville P.M. ----- Lancet 1934 1 73
- Taylor A. Brian ----- Ibid 1937 2 73
- Tzanck A., Pantrat J. and Klotz H.-P. --- Bull. et Mem. de la Soc. Med.
d'Hop. de Paris 1934 50 332
- Umber F. ----- Med. Welt. 1929 no.18 635
- Weil P.E. et Bousser J. ----- Le Sang 1932 6 800
- " " ----- Ibid 1932 6 825
- " Iach Wall ----- Presse Med. 1923 31(2) 657
- " ----- Paris Med. 1931 81 102
- Witts L.J. ----- Brit. Med. J. 1936 2 211