

GOLD THERAPY IN PULMONARY TUBERCULOSIS.

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## INTRODUCTION.

In 1924 Holgar Møllgaard (1), introducing a double thiosulphate of gold and sodium under the term of "Sanocrysin", claimed the drug had a specific lethal effect on the tubercle bacillus of Koch and stimulated an enormous amount of trial and clinical work in many parts of the world; but there is yet a diversity of opinion as to its value.

An attempt to assess the value of any drug in pulmonary tuberculosis is fraught with many pitfalls - numerous and variable factors are concerned; an estimation of the resisting power of the patient, based on history and personal observation; the clinical state; the general mode of life, including observance of ordinary hygiene, climate, work and reaction; and the virulence of the attack. Walters (2) has stated the criteria to be observed in the estimation of the value of the drug; namely , a similar group of Control Cases under identical conditions (a Control experimentation of this type in a Sanatorium proving impracticable), and a knowledge of the action of the drug, how it should be employed and under what conditions. Other factors enter into account, for example, the combination of different methods of treatment (artificial pneumothorax), and the great value of modern sanatorium treatment. No standard of assessment/

assessment being available, a critical exposition and personal observations, based on physical signs, general condition and radiological evidence, is undertaken. It is the diversity of views expressed in the literature that makes this communication and critical exposition seem opportune.

Personal observations have been recorded in a hundred cases. In almost all instances a form of gold salt, "Crisalbine", synonymous with Møllgaard's "Sanocrysin", has been used intravenously. In certain cases and for specific reasons this has been replaced by an intramuscular injection of gold, Solganol-B-oleosum. All cases recorded were treated at a Sanatorium, patients not improving from such treatment were given gold injections. Crisalbine was also used in conjunction with collapse therapy, and in some cases gold only was employed, being the treatment deemed most suitable.

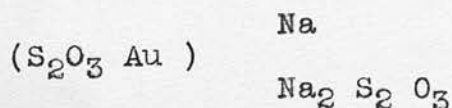
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HISTORICAL.

Gold salts have been employed in the treatment of Tuberculosis for hundreds of years and as far back as the 8th century we have records of their use in general Medicine. Abu Moussa the Wise recommended it for all diseases. The "elixir of life" of Paracelsus (1500 A.D.) contained gold and mercury, but following the usual historical fate of most drugs in medicine, the metal fell into disrepute until revived by Chretien in 1810. In 1810 Robert Koch (31) reported that gold cyanide completely inhibits the growth of tubercle bacilli in dilutions of 1 per 2,000,000 in vitro, but that in vivo it was entirely without influence. Thereafter White (4) employed a double chloride of sodium and gold combined with iodide of manganese with beneficial results, and this method was employed by many other workers including Bettman, Junker, Gibbes and Shurley and Mayer (5) who used "Borcholin" combined to gold to cause dissolution of the fatty sheath of the bacillus. Between 1912 and 1915 various workers, especially German, investigated the use of gold salts and favourable results were reported with gold potassium cyanide, especially in tuberculosis of the skin. A vast series of publications were being issued at this time and include Bruck and/

and Glück (6) and Spiers and Feldt (7) who eventually produced monocantharidyl-ethylenediamine-aurous cyanide under the name of "Aurocantan" for subcutaneous use. They employed cantharidin reduced in toxicity as it had a marked affinity for tuberculous tissues and found the aurous more efficacious than the auric salt. They had soon realised that the cyanides of gold were too toxic for human use, but as results were not proving very satisfactory with "aurocantan", Feldt (8) in 1917 recommended the sodium salt of P-amino-o-auro-phenol carbonic acid, under the name of "Krysolgan". In 1924 Møllgaard (1) introduced his inorganic salt of gold, a double thiosulphate of gold and sodium with the gold in trivalent form under the name of "Sanocrysin" having the formula of



Feldt (9) has continued experimenting and recommends "Solganol" on account of its low toxicity: it is an "alkali salt of a complex gold acid" with the formula  $\text{C}_7\text{H}_6\text{O}_6 \text{ NS}_3 \text{ Na}_2 \text{ Au}$  .

Crisalbine is identical with Sanocrysin in composition  $\text{Au}(\text{S}_2\text{O}_3)_2 \text{ Na}_3$ .

Various other gold salts, under trade names, (e.g. lopion, myocrisin, myoral, allochrysine) have been brought out by manufacturing firms, each claiming a diminished toxicity for the particular preparation.

MODE OF ACTION.

Chemotherapy is the introduction into an infected organism of a substance having a directly injurious influence on the bacillus at some distance from the seat of introduction. In the last quarter of a century numerous substances ranging from dye stuffs to heavy metals have been used in the treatment of Tuberculosis. The injection of a gold salt into the human organism is followed by various reactions, poisonous and/or otherwise, and a discussion of the various views advanced is undertaken. In culture the metals have been shown to have a growth-preventing influence on the bacilli, but most of them have been too toxic for use in man. Schumacher (10) explained Koch's supposition that gold was entirely without influence in the body (3) by the statement that the cyanides are broken down into gold protein compounds, colloidal gold being set free, and the cyanide group becoming non-toxic by uniting with the sulphhydryl group of cystine; while Schamberg and Brown (11) testing a large number of metals, found gold and mercury to be most adsorbed by tubercle bacilli but by body tissues as well.

J.B. White's treatment in 1894 caused a prolongation of life in both animals and human beings, with an improvement in the general and blood condition, in/

in physical signs and with the absorption of abnormal products.

"Krysolgan" according to Levy (12), exhibited a marked tuberculin-like effect on tuberculous lesions, but Koizumi (13) did not confirm this. De Witt, Cadwell and Leavall (14) showed the effect on animals of gold administration by mouth, intravenously and subcutaneously. Analysis of tissues formed a control to the results and more gold was found in the tuberculous tissues, but it is difficult to keep the concentration of gold in the body at or above the point required for inhibition of the bacilli (De Witt and Sherman (15) ).

Feldt and Spiers (7) introduced "autocantan" and thought its effect due to two factors - a direct inhibitory action on the bacillus and an indirect action on the defence mechanisms of the body - by stimulating connective-tissue formation and destroying disease products by oxidation. Feldt's idea was that gold had a catalytic effect which stimulated the natural defence reactions of the organisms causing autolysis of the tubercles. The theory that gold owes/



owes its effect to a toxic action on the capillary endothelium has been advanced chiefly by Heubner (17) with which however Feldt disagrees, though Gelpe has brought forward evidence to show the toxic effects of gold on the capillaries of dogs and cats in causing haemorrhage and hyperaemia in the pulmonary alveoli (18). De Witt and Sherman (14) found, as did Koch (3) that gold cyanide completely inhibited the growth of tubercle bacilli in vitro in a dilution of one in two million and Feldt believes that the bacilli develop a tolerance in vitro to gold though Shiga (19) completely contradicts this statement. A larger amount of gold is found in the liver and spleen than the amount of concentration required to inhibit growth in vitro. Voegtlen (20) and others state that the intoxication which is apparently dependent upon reaction with the S.H. group of the gluta thione is associated with hyperaemia, haemorrhage and oedema about the lesions, and resembles the tuberculin reaction.

There may be a lighting up of old tuberculin skin reactions during treatment with gold. This may be due to liberation of tuberculin; or in the nature of a non-specific allergic phenomenon due to disintegration products of the tubercle. It may be due to damage of the endothelium of the capillaries or to "gold/



"gold protein compounds"(31). The difficulty lies in the avascular nature of the tubercle and the fatty envelope of the bacillus; and also depends upon the diffusion of the drug through animal membranes.

That the gold does not act on the bacilli because it is outside the tubercles and in the reticulo-endothelial cells has been advanced by Kurosa (21) and Gallinal (22). An acute intoxication is apparently produced in the tuberculous animal by gold.

Møllgaard has himself modified his original statement of the specificity of the drug for the organism, and in 1927 stated that "the difference between the effects in vitro and in vivo, the latent period, and the importance of the condition of the infected organism, may be due to the fact that the chemotherapeutical compound is transformed into active bodies by chemical reactions in the organism and that the bodies thus formed are the true parasitotrophic substances which cause the death of the parasites".(23)

In 1924 Feldt (8) wrote that the toxic effects result from disintegration by increased autolysis in the tuberculous focus and increased absorption consequent upon the hyperaemia. It is analagous to mercury and iodides in syphilis in hastening autolysis of lesions independent of any bactericidal action. There may be a transient increased endothelial permeability due/

due to small doses followed by a relative impermeability (Petersen and Levinson (24) ). Gold has a high inhibitory value, but Sweany and Wasick (25) state that it has no bactericidal effect even in concentrations as great as 1 in 2000 for 2 hours. Lyle Cummins (23) has confirmed the experiments of Fry which show that the inhibitory effect of Sanocrysin is prevented to a fair extent by the presence of proteins in blood-clots.

Most of the earlier workers followed Møllgaard in his hypothesis of a direct specific bactericidal action but we must now abandon this specificity. Bang (27), Björn-Hansen (28) and many other workers do not substantiate the claims of Madsen and Mörch (29) in curing tuberculosis in rabbits with sterilization of the lesions. Small doses, according to Møllgaard (1) may stimulate the disease or have no action, and reduction of the dose does not always solve the question of intoxication; he originally prepared three types of antiserum to counteract the "shock" effects produced by Sanocrysin: (1) from a spontaneously infected animal, (2) by immunization with dead bacilli and (3) by defatted bacilli. Most workers of whom Secher (30) is the last, have long since abandoned the use of antisera.

More gold is apparently retained in tuberculous animals/

animals. It seems to be taken up chiefly in the reticulo-endothelial cells stimulating their immunological activity. Wells and Long (31) state that Sanocrysin does not differ from other gold compounds in toxicity, therapeutic effect and distribution in the tissues.

The intravenous introduction of heat-killed bovine bacilli into rabbits being treated with gold, protects them from lethal doses of tuberculin, and they develop less tubercle formation (Atkin (32) ) and he concludes that "Sanocrysin exerts an inhibitory effect on tuberculous lesions, apart from any bactericidal action it may have on the living tubercle bacillus".

Gold may be detected in the urine and stools after 8 months; in the body it loses its diffusible character and is slowly excreted behaving like other heavy metals (Hansborg (33) ). Gallinal (22) found gold microchemically in considerable amounts in a person who had received the drug 10 months before death. It is excreted in the urine for about 30 days, producing albuminuria, vomiting and diarrhoea as toxic effects (McCluskey and Eichelberger (35) ).

There is no absolute proof that gold has anything resembling a specific chemotherapeutic effect on the tubercle bacilli, nor that the toxic effects result from tuberculin liberated from the bacilli killed by the/

the metal.

There has long been a search among investigators for a gold compound that will have a minimum toxicity without the loss of the tuberculin-like effect.

"The tuberculin-like reaction might, if uniform and if it could be regulated and relied upon, produce certain beneficial connective-tissue changes in the neighbourhood of the tubercle, but the regulation seems too difficult and dangerous to make gold therapy ever a treatment of choice..

"Gold salts have a certain therapeutic value due to the tuberculin-like effect on tuberculous lesions and this effect may equally well be secured and with less danger by the proper use of tuberculin" (De Witt (14) ). In 1926 Philip and Murray Lyon (36) stated that the drug "unchanged or chemically altered may act on the tissues directly and that specific toxins might be liberated as a result of a selective action of the gold on the tuberculous tissues or organism."

The reticulo-endothelial system has come into prominence (as it has in immunology) for gold is taken up in the cells of the system, accomplishing thereby increased resistance to the infection, and acting mainly by stimulating these cells into transforming the metal into a more potent form. Metal therapy is therefore a method of stimulating the defence mechanism of the reticulo-endothelial system.

Lyle/



Lyle Cummins (37) concludes that the reactions of tuberculous persons to Sanocrysin are analagous to the tuberculin reaction and has suggested that the effects vary according to the patient's power to neutralise or tolerate the toxic substances liberated as the result of focal hyperaemia.<sup>(61)</sup> Descriptions by Sir Robert Philip and Murray Lyon (39) showed certain points of similarity in the reactions obtained to Sanocrysin and Tuberculin - there was a "general resemblance of events following Sanocrysin to those observed after the exhibition of Tuberculin in moderate amounts" (Philip (38) ).

Capillary hyperaemia may be sufficient to liberate toxins apart from any destruction of the bacilli: there is difference of opinion whether this is specific or due to a catalytic agent. The pathological changes in the organs are similar to those caused by tuberculin, and Møllgaard, as the result of animal experiments, believed that there was no injurious effects on blood vessels, corpuscles or organs of the body. Blood pressure and respiration were not affected and the kidneys injured only if large doses were suddenly administered. The action of Sanocrysin was due to the negatively charged ion of gold, dissociated in watery solution, and capable of penetrating the lipoid envelope of the bacillus, affecting its acid-fastness; but effects may vary with different strains/



strains of the bacilli. Stub-Christensen (40) sums up by stating that the "action of gold is partly a stimulation by the natural defences of the body - possibly of the reticulo-endothelial system - so that the bacilli are subject to a rapid phagocytosis, and partly to a stimulating effect on the formation of new connective tissue". The power of gold to stimulate the formation of new connective tissue is seen markedly in radiographs and in this series of cases some have been included. After splenectomy according to Jungeblutt and McGunn (41) the efficiency of gold is reduced.

Recently attention has been focused on the blood: particularly regarding the differential leucocyte count and sedimentation rate in attempting an assessment of the value and action of gold therapy in pulmonary tuberculosis and Houghton (42) suggests that the primary action of gold salts is probably on the tissues producing the white blood cells. This view is supported by Doan and Sabin (43).

Various advantages have been claimed for the different drugs employed e.g. Solganol and Lopion as the two least toxic. It is found that one preparation may produce a higher percentage of cases of albuminuria, while another causes particularly gastro-intestinal disturbances and cutaneous reactions, though generally all the reactions in greater or less degree are common to/

to the different types of drugs on the market. The method of administration and the dosage employed must also be taken into account, and on the evidence of blood changes small doses of gold have been found as useful as larger amounts (0.5 - 1.0 gm.). Feldt's(8) new compound, Solganol, is stated to be only one-tenth as toxic as his original "Krysolgan". We may hope therefore, apart from the results, beneficial or otherwise, claimed, that eventually the production of a drug of minimal toxicity, may be forthcoming, and Mayer (44) believes Crisalbine preferable to others.

We must abandon the theory of direct action and postulate that the effect of gold is an indirect one on the tissues of the body, in which many factors play a part; chiefly the reticulo-endothelial system, damage to the capillary endothelium and the liberation of tuberculin-like or disintegration products of the tubercle. It is not a chemotherapeutic substance but a form of "stimulation" therapy.

SUMMARY OF CASES.

In this section a summary of a hundred cases all treated at a Sanatorium is given. In all except seven cases (Nos. 36, 54, 77, 90, 92, 94 & 98) intravenous Crisalbine was used; in the others Solganol-B-oleosum was given by intramuscular injection. In 29 cases reduced points of X-Ray negatives have been included, realising however the relative value only of such owing to differences in density and exposure. In Case No.61 no negative prior to injections of Crisalbine was obtainable.

The amount of anatomical involvement and the degree of systemic disturbance have been noted according to the clinical classification of Philip - the Symbols L and S in capital or small letters with numerals denoting gradations represent the local or lung lesion and the systemic upset respectively.

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SUMMARY OF CASES.CASE NO. 1.

Female Age 18. Complained of loss of weight, haemoptysis, and night sweats. She had a cough and profuse expectoration, a temperature of 99° and a pulse of 120. Her sputum was positive. Radiologically she had extensive disease in both lungs, especially the left. (L<sub>2</sub>S) She had a left artificial pneumothorax performed and crisalbine was commenced with 0.05 gm. intravenously:-

1.8.35	0.05 gm.
5.8.35	0.1 "
8.8.35	0.1 "
12.8.35	0.1 "
15.8.35	0.1 "
19.8.35	0.15 "
22.8.35	0.15 "
26.8.35	0.15 "
29.8.35	0.2 "
2.9.35	0.2 "
5.9.35	0.2 "
9.9.35	0.2 "
12.9.35	0.2 "
16.9.35	0.2 "
19.9.35	0.2 "
23.9.35	0.2 "
27.9.35	0.2 "
30.9.35	0.2 "

and at intervals of 4 or 5 days (twice weekly) from 3.10.35 to 4.11.35 with 0.2 gm. i.e. 10 times; and from 7.11.35 to 9.12.35 with 0.2 gms. i.e. 10 times. Four and a half months after commencing this treatment with gold, she complained of ulceration of the mouth. After/

After the first four injections there was an initial loss of weight of 4 ozs. There was good collapse on the left side, and there was marked clinical improvement on the right side with apparent arrest of disease. The sputum diminished in amount very markedly and became negative for tubercle bacilli. She had a total amount of gold equal to 7.0 gms.

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CASE NO. 2.

Female Age 25. Had a cough for one year and pain occasionally in the left chest. She gave a history of haemoptysis, loss of flesh, dyspnoea, night sweating and weakness. She had expectoration, which was positive to Koch's bacillus. She had disease involving upper 1/3rd of the left lung with several cavities in the left upper lobe. There was also a recent spread from the right root involving the middle third right lung. (L<sub>3</sub>S) A left artificial pneumothorax was successfully induced. After 1.0 gm. she developed a red irritating measles rash on the chest, arms and legs. She had 6 hypodermic injections of adrenaline, one in a thousand, M 10, daily. She had no albuminuria but complained of diarrhoea. The rash desquamated and improved. Oedema of the face was very marked, and the temperature was normal. She however developed meatal eczema which was treated with ung. Hyd. Nit. and vaseline. She lost weight. There was no improvement clinically but radiological improvement of the right root. The sputum was still positive a year later.

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CASE NO. 3.

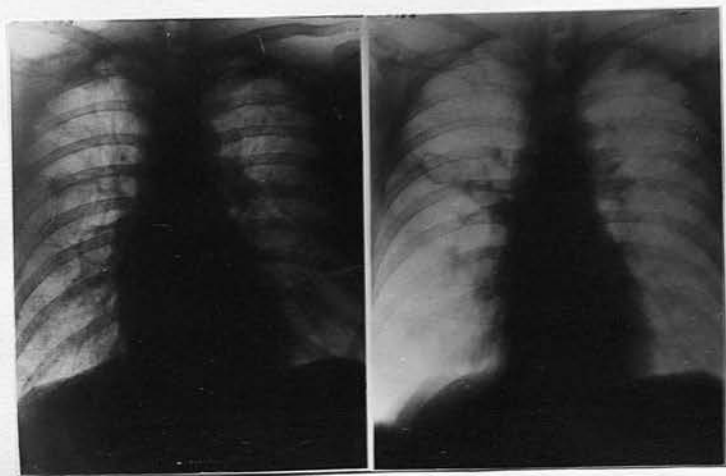
Male aged 13 who gave a history of pneumonia at 4 years of age and a family history of T.B., complained of a cough for 3 weeks. There was disease of the left upper lobe with a small cavity towards the left apex, and a spread from the right root. (L<sub>2</sub>s)

He was discharged after sanatorium treatment, having gained slightly in weight but with sputum still positive. He was re-admitted a year later when the condition of the right lung on the film did not justify thoracoplasty and crisalbine was started in the hope of controlling the right side sufficiently to allow of the operation later if an A.P. failed. There was an exudative infiltration in the lower half of the right upper lobe. A left A.P. and gold were started. With small doses, not exceeding 0.15 gm., he had a total of 7.0 gms., his sputum became negative and he gained weight. After injections he developed an occasional Febrile reaction to 99° but no other sign of toxicity. His general condition improved and his right lung appeared normal.

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CASE NO. 4.

Male aged 26 gardener, with cough for 6 months. Hoarseness for a few weeks and "touch of pleurisy" a month ago. He had streaks of blood 6 weeks ago. There was loss of flesh, profuse expectoration, dyspnoea, clubbing of the fingers and myxoedema. His sputum was positive. X-ray showed disease of



Dec. 1933

June 1935

exudative type in the left upper lobe. There was also a spread from the right root involving the middle lobe with cavity formation. (L<sub>1</sub>S) Crisalbine was commenced in January 1934 with 0.05 gm. mounting up to a dose of 0.25 gm. till the end of April when he complained of ulceration on the under surface of the tongue. The first course was then completed with a total of 5.05 gms. During this time his Arytenoids and cords were swollen and congested and he was kept on silence. His general condition was improving, adventitious/

adventitious sounds were diminishing and he was gaining weight. There was no albuminuria. In November both lungs showed improvement with a suggestion of fibrotic changes. A second course was then started which was completed by April 1935 with 6.6 gms. He was discharged with a negative sputum and with weight stationary. He lost 4 lbs in weight since commencing the second course and also complained of soreness of the mouth. His X-ray now showed that the right lung was markedly improved. There was now only a very small thick-walled cavity. He was re-admitted in September 1935 for another gold course, commencing with 0.1 gm. when he had another 3.7 gm. This was stopped on account of buccal ulceration. He therefore had a total of 15.35 gms. but the cavity was increasing, he was losing weight; and a right A.P. was induced. He had an occasional rise of temperature to 99° after the injections. He also had an unpleasant taste during the gold treatment. His left lung was stationary and gold therefore allowed of the performance of an A.P. on the right side, while keeping in check his left. His sputum became positive again in January 1936 though he was keeping fairly well.

CASE No. 5.

Male aged 42 with a family history of T.B., complained of cough and pain in the chest. He had occasional "staining", with loss of flesh, expectoration, night sweats, weakness and hoarseness. His fingers were clubbed and his sputum was positive. There was disease of the right upper lobe, exudative in type (L<sub>1</sub>S). He had a total of 3 gms. of crisalbine in two months when he has a trace of albumin in his urine and developed a rash on the trunk and limbs. He desquamated completely, alternating "dry and wet" types. This general exfoliative dermatitis was associated with oedema of the ankles and right arm which subsided after the first week. His scalp was affected and there was desquamation of the palms and soles. There was an itching and burning sensation. No tendency to acute infections was noticed. He desquamated several times and there were large raw, red blotchy areas over the whole body. He was given daily alkaline and bran baths and annointed with cotton seed oil. He had injections of whole blood, 5 c.c. intramuscularly at weekly intervals. Extracts of liver, glucose, potassium citrate, arsenic and "thiostab" were given with no great benefit. Contramine, as recommended by Stewart Smith, was not tried. Collosol sulphur by mouth/



mouth and strict milk diet seemed very beneficial, and for the weeping areas silver nitrate and aluminium acetate were of value. His general condition improved, including X-ray and physical signs. His sputum was negative but became positive again several months later. The skin condition cleared completely. He volunteered the information afterwards of being subject to "skin trouble".

CASE NO. 6.

Male aged 26 - shop assistant, with a positive family history, felt "run down" for several months and complained of a cough. He gave a history of haemoptysis, night sweats and weakness with a loss of weight. His sputum was positive. He had a total of 7 gms. of crisalbine, and an initial gain in weight. There was disease of the whole of the left lung and upper two-thirds of the right. (LgS) During the course he complained of diarrhoea. His sputum eventually became negative and he did very well.

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CASE NO. 7.

Male aged 30 - farmer - had a cough, occasional pain in the chest, dyspnoea and slight hoarseness. He had loss of weight and night sweats. His sputum was positive. Expansion of the left chest was poor. There was dullness of the left upper lobe and right apex. Breath sounds were weak in both lungs. His vocal fremitus and vocal resonance were increased at the apices. There were coarse râles in the upper half of the left lung. X-ray showed extensive disease of both lungs with the appearance of cavity formation towards the left apex. (L<sub>3</sub>S) After 2 gms. of crisalbine there was buccal ulceration and marked oedema of the face with a typical irritating erythematous type of rash, general in distribution. His palms and soles desquamated and there was an albuminuria which disappeared in a week as had the oedema. His sputum became negative and after desquamating twice the rash became scaly and chiefly on the legs. His general condition slowly improved though he had a temperature of 100° for 10 days. His weight after initial loss increased. He developed an acute appendicitis and after appendicectomy his rash had disappeared. His sputum however eventually returned positive.

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CASE NO. 8.

Male aged 18 had a cough for one year with poor appetite, dyspnoea, loss of weight, clubbed fingers, night sweats and weakness. He also gave a history of haemoptysis (June 1934). His sputum was positive. There was advanced disease of the whole of the left lung and upper two lobes of the right. (L<sub>3</sub>S)

He had two gms. of crisalbine which was stopped on account of ulceration of the mouth and a rash. He gained 5½ lbs in weight and slowly improved. His sputum was kept negative for many months following this amount of gold, but eventually became positive again and he developed a spontaneous pneumothorax.

CASE NO. 9.

Male aged 32 - tinsplate worker - gave a history of "pleurisy", cough, pain in the chest and dyspnoea. There was infiltration of the right middle lobe with a cavity opposite the right root. (L<sub>2</sub>S) He was given two grms. of gold while having the A.P. but he developed an irritating rash on the chest and back. His sputum became and remained negative; he gained weight. In view of the rather severe skin reactions with the two previous cases it was at this time thought advisable to stop treatment with the appearance of a rash.

CASE NO. 10.

Male aged 25 - chemist with a family history of T.B. and temperature of  $100^{\circ}/101^{\circ}$ . He had a cough for a year with slight weakness, dyspnoea and night sweats. He had disease of the upper two thirds of the right lung and upper half of the left. ( $L_3S$ ) His sputum was positive. There was granulation tissue on the vocal cords. Six months after admission and gold his general condition was slowly improving; by then he had had 5.05 gms. and was now complaining of ulceration of the tongue. His dose had reached 0.25 gms. twice weekly. A month later a second course was commenced with 0.1 gm. An X-ray report showed some tendency to fibrosis. He never once had a negative sputum. He was also on silence for ulceration in the interarytenoid region. In 3 months his second course of gold was completed, totalling 7 gms. His general condition was fair. There were no adventitious sounds. His larynx had improved. He was slowly gaining weight and 9 months later there was definite improvement radiologically with fibrosis of both lungs. There was however a small well marked cavity towards the left apex and a third course of crisalbine was started with 0.1 gm. After 6 gms. the course was completed owing to diarrhoea. After having 18.05 gms. he developed a spontaneous pneumothorax with effusion and began to lose weight and go rapidly downhill.



CASE NO. 11.

Male aged 34, had a bad family history, complained of cough and backache for 4 months. His general condition was rather poor with night sweats and weakness. He had a total of 7 gms. of crisalbine. After 3 weeks of gold he gained slightly in weight. He had poor lighting of the upper two thirds of the right lung and left apex with dense area of infiltration opposite the right root. (L<sub>2</sub>S) His sputum was positive at the beginning and remained negative for a year when there was a return of bacilli but a fortnight later it again became negative. He had an axillary abscess which was incised. This may have been due to infection resulting from the injection.

CASE NO. 12.

Male aged 20, with a T.B. family history, complained of feeling "run down" and pain in the right chest. He had a cough, night sweats and history of haemoptysis. There was disease of the upper half of the left lung and right upper lobe with a small cavity. (L<sub>2</sub>S) He was started with 0.05 gms. and had a total of 5.6 gms. of crisalbine. He gained weight; he had a febrile reaction after injection to 99.6 and also complained of diarrhoea and ulceration of the mouth, starting with a positive sputum. He remained negative for one year.



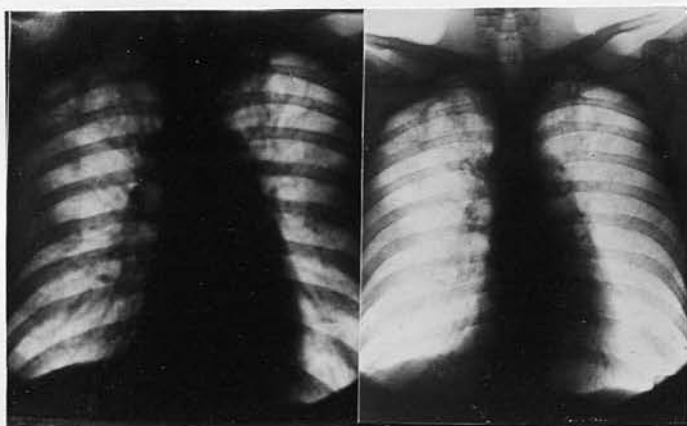
CASE NO. 13.

Male aged 14, with a previous history of measles and whooping cough, complained of slight cough and expectoration. Night sweats were not very marked and he gave a history of haemoptysis. The upper lobes of both lungs showed disease, the left exudative and productive; the right chiefly exudative. His sputum was positive. (12s) He was started with 0.05 gms. and had a total of 2.85 gms. when he was discharged after 10 months, having gained 5 lbs in weight and with sputum negative. There was evidence of spread in the middle third of the left lung, the upper lobes of both lungs however showing fibrosis. He returned a year later with a positive sputum and gold injections were again started to a maximum amount of 4.6 gms. At fortnightly intervals he gained weight steadily. He therefore had a total of 7.45 gms. but developed a rash in the groin and pruritus on the inner aspects of the thighs; not typical of or due to gold rash. His sputum became negative and remained so. Eventually an A.P. was induced on the left side; progress of disease in the right being stationary or arrested.

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CASE NO. 14.

Male aged 28 - had pleurisy with effusion 6 years ago, and complained of cough, spit, haemoptysis, night sweats, hoarseness and pain in the chest. His sputum was positive. There was disease of the right upper



Oct. 1934

May 1935

lobe and left apex. (1<sub>1</sub>S) A right A.P. was unsuccessful. He had a total of 6.75 gms. but developed a dermatitis in the groins and the injections were stopped. He had an initial loss of weight. His sputum became negative, his general condition improved, and also his physical signs. At the last examination a positive sputum was returned.

CASE NO. 15.

Male aged 18 - a labourer - had a cough, weakness, hoarseness, anorexia, loss of weight, night sweats and a history of haemoptysis. His sputum was negative but later positive. The right upper lobe showed disease. (1<sub>1</sub>S) He had a total of 7 gms. and his general condition improved very markedly gaining weight and expectoration diminishing. His sputum was negative and there was evidence of fibrosis in the right lung. He had an occasional febrile reaction to 99°.

CASE NO. 16.

Male aged 26 - policeman - complained of weakness and morning cough for 6 months. He had had haemoptysis, also night sweats and slight hoarseness. There was disease of the upper two lobes of the right lung, and a spread from the left root involving the middle third of the left lung. (L<sub>2</sub>S) After 2.5 gms. of crisalbine he complained of an unpleasant taste in the mouth with soreness of the gums. He gained weight and had a total of 7 gms. He had a left A.P. performed. His sputum was always positive except on one occasion after a year's treatment.

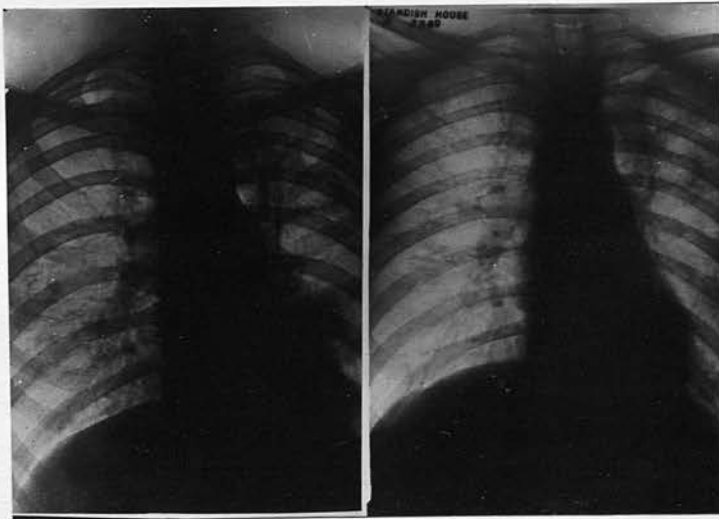
CASE NO. 17.

Female aged 27 - complained of cough and colds for 9 months with profuse expectoration. She had lost weight, had night sweats and had had haemoptysis. There was disease of the left upper lobe with ? cavity towards the apex and a spread from the right root involving the upper half of the right lung. (138)  
An A.P. was abandoned and after 4.4 gms. she developed a rash. She gained in weight, slowly improved, and lost the bacillary content of the sputum, having previously been positive.

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CASE NO. 18.

Male aged 21 - with a family history of T.B., had occasional cough and a history of haemoptysis. There was disease of both lungs with ? cavity left upper lobe. (L<sub>2</sub>s) Crisalbine was given to control spread in the right lung, considering afterwards a left A.P.



Oct. 1934

March 1936

or phrenic evulsion. In October 1934 the first course of gold was commenced with .05 gm. and by mid-February the following year he had had 7 gms. The right lung then showed little change and there was clinical improvement; the left lung showed some fibrosis. He had an occasional febrile reaction to 99° and gained weight. There were no other toxic symptoms. On commencing the second course in September with .1 gm. he lost slightly in/



in weight and by the end of December had received a further 7 gms. His sputum was negative on admission and negative on discharge though he had had positive sputum during treatment. He had a total of 14.0 gms. of Crisalbine, and also lost weight at the beginning of first course.

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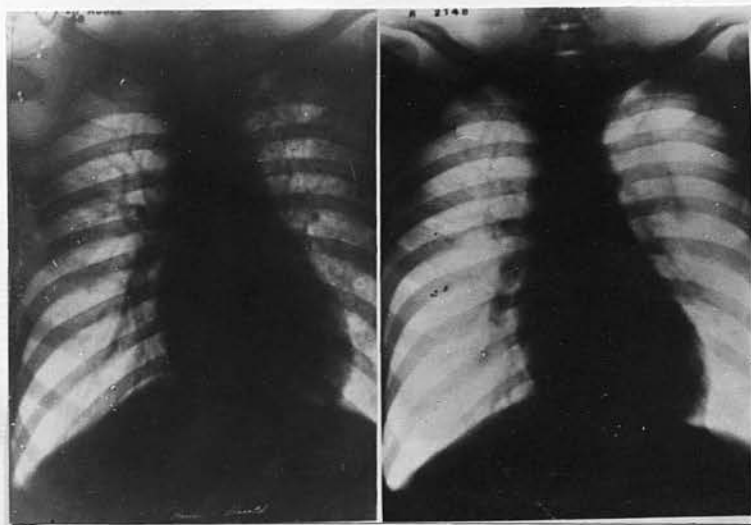
CASE NO. 19.

Male aged 39 - had a cough for 3 years which was getting worse and he was easily tired. There was loss of flesh, dyspnoea, weakness, hoarseness, expectoration, night sweats, occasional pain in the chest, haemoptysis and his fingers were clubbed. There was disease in the right lung with several cavities and an extension from the left root. (L<sub>3</sub>S) His sputum was positive. A right A.P. was unsuccessful owing to adhesions. When gold was started in August with .05 gm. he complained of anorexia and by December had received 7 gms. There was an initial loss of weight on commencing injections which was regained after a fortnight. The upper half of the right lung showed evidence of fibrotic changes and cavities showed signs of shrinking. His general condition was fairly good. The second course was commenced with 0.1 gm. in February and after 5 months reached a total of 7 gms. with a maximum dosage of 0.25 gm. twice weekly. He had a positive sputum from October 1933 at monthly intervals becoming negative for the first time in January 1936 on discharge. He had a total of 14 gms. of crisalbine. He has been doing fairly well since.

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CASE NO. 20.

Male aged 20 - with a family history of T.B. - complained of loss of appetite and lassitude; also haemoptysis, night sweats, weakness and hoarseness. There was well marked disease of the upper two thirds of the



Oct. 1933

Nov. 1934

left lung. The right upper lobe was suspicious of early T.B. ( $1_2S$ ) He had a total amount of crissalbine equal to 7.55 gms. and a left A.P. induced. He was admitted with a negative sputum but had one positive during treatment and after being discharged negative, he had remained so for a year. He gained weight very satisfactorily and had improved.

There was no toxicity.

CASE NO. 21.

Male aged 11 - came under observation in 1922 and there was no evidence of T.B. 4 years later. In 1934 he had a cough for 3 weeks, and a positive sputum. There was a spread from both roots involving the middle third of the left lung and lower two-thirds of the right lung with ? cavity opposite the right root. (L<sub>2</sub>S) A right A.P. was induced and crisalbine given to control the left side. He had 7 gms., and improved; he gained weight but was discharged with a positive sputum and not quiescent. There was soreness of the mouth with ulcers during treatment, and no other sign of toxicity.

CASE NO. 22.

Male aged 42 - with a history of nasal catarrh for years, cough for 3 weeks - anorexia - loss of flesh - weakness and dyspnoea. He had night sweats and haemoptysis. His sputum was positive. The upper half of the right side was the seat of disease with ? left root. (L<sub>1</sub>S) He had a total of 3.5 gms. of crisalbine when he developed a scaly rash on the left arm and fore-arm, discreet, and rather like psoriasis. The rash disappeared in 2 months; he gained weight and was discharged quiescent with a negative sputum. There was fibrosis of the right lung and clinical improvement. Ung. Chrysarobin did not prove of value in treating the rash but sphagnol ointment and alkaline baths were beneficial.

CASE NO. 23.

Female aged 24 - chambermaid - complained of cough with expectoration, haemoptysis, night sweats, weakness and dyspnoea. There was disease of the right upper lobe with a cavity, also a spread from the left root to the left upper lobe. (L<sub>2</sub>S) Her sputum was positive. A right A.P. was performed and she had a total of 7.0 gms. of crisalbine in 4 months, the highest dose not being above 0.25 gm. There was no gain in weight. There was no sign of toxicity. She was discharged, not quiescent, slightly improved and sputum negative.

CASE NO. 24.

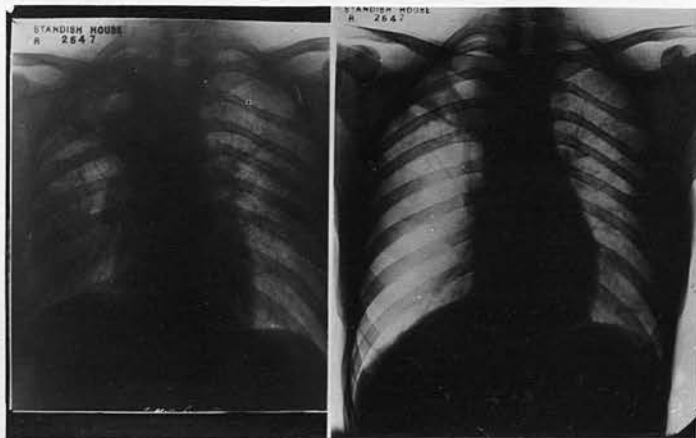
Male aged 32 - butcher - with haemoptysis; occasional night sweats and weakness and sputum positive. Disease upper half of both lungs with cavity towards the right apex. (L<sub>2</sub>S) Received 7.0 gms. of crisalbine and gained weight but had an occasional rise of temperature to 99° and buccal ulceration. His sputum became negative and he was discharged, not quiescent, though clinically he had slightly improved.

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CASE NO. 25.

Female aged 18 - with whooping cough in childhood, complained of cough, spit and haemoptysis, night sweats and weakness, slight hoarseness and dyspnoea. Her fingers were clubbed, there was loss of flesh and loss of appetite. Her sputum was positive. The right lung showed disease with a cavity at the apex. The left



Jan. 1935

Dec. 1935

lung showed spread from the left root involving the middle two-thirds. ( $L_2S$ ) She was on silence owing to ulceration in the interarythenoid region. She received 5.75 gms. of crisalbine and complained of diarrhoea and albuminuria which cleared up after a few days. She also had occasional rise of temperature to  $99^{\circ}$ . She was discharged with a positive sputum and no improvement. (Her weight was not recorded)

CASE NO. 26.

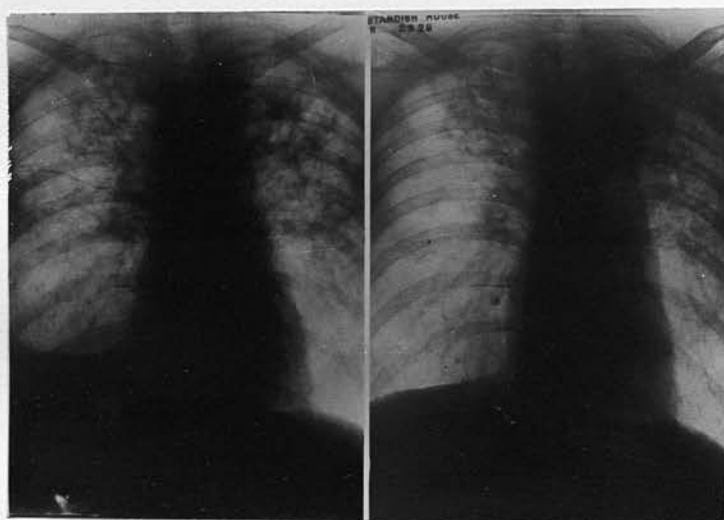
Male aged 35 - complained of husky voice for 6 months - cough 2 months, malaise and night sweats. He had profuse expectoration, weakness, dyspnoea and loss of appetite. There was disease of the upper half of both lungs, being rather more extensive on the left. (L<sub>2</sub>S) His sputum was positive. The vocal cords were reddened and he was kept on a whisper. He had a total of 7 gms. of crisalbine having only 4 injections of a maximum dose of 0.25 gms. He gained weight and improved. There was no toxicity of any kind and he was discharged with no sputum and which had become negative previously.

CASE NO. 27.

Female aged 16 - with a family history of T.B. and a previous history of cervical adenitis. She had a cough and hoarseness, expectoration, haemoptysis, dyspnoea, loss of flesh, night sweats and weakness. There was disease of the right upper lobe and spread downwards from the right root, and ? middle-third left lung. (l<sub>2</sub>S) She had a right A.P. and 7 gms. of crisalbine. She was discharged quiescent with no sputum, having gained weight and markedly improved. There was no toxicity of any description during the course.

CASE NO. 28.

Male aged 29 - had pleurisy on the left side 7 years ago, and complained of cough and expectoration which was positive to the tubercle bacillus. He had a



1.5.35

18.12.35

temperature of  $100^{\circ}$  and there was infiltration of the upper two lobes of the right lung and upper half of left, of exudative type. ( $L_2S$ ) He had a total of 7 gms. of crisalbine having gained weight and with some improvement though his sputum was still positive.

There was no toxicity.

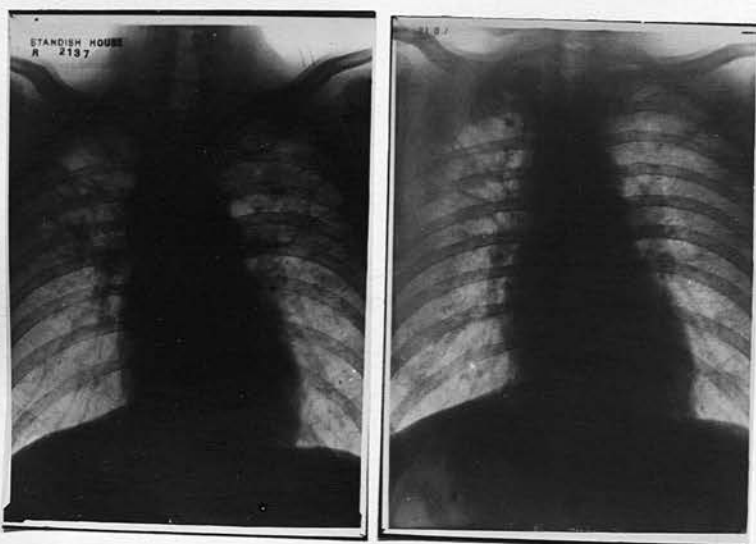
CASE NO. 29.

Male aged 23 - complained of a cough for 3 months, and had had haemoptysis, night sweats, weakness and hoarseness and occasional pain in the chest. His appetite was poor. He was dyspnoeic and there was general profound systemic disturbance. His sputum was positive. Upper lobes of both lungs showed disease, and a large cavity at the right apex. (L3S) A left A.P. was abandoned owing to adhesions, and gold commenced with 0.05 gms. following which he gained weight. He had a total of 7 gms. in 4 months. The cavity was apparently shrunken in size but there was little change in the right upper lobe. After an interval of 2 months a second course of gold was commenced but was completed owing to a slight rash at 6.45 gms. making a total of 13.45 gms. Subsequent X-ray showed marked improvement with evidence of fibrosis of both upper lobes, especially the right; the cavity on the left side remaining unaltered. He was discharged with a negative sputum. He commenced the course in August 1934 but died in February 1936.

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CASE NO. 30.

Male aged 25 - whose mother had died of T.B., complained of cough and pains in the chest. He showed a profound systemic factor with night sweats, dyspnoea, haemoptysis, weakness, anorexia and loss of flesh. There was fairly extensive disease in both lungs with a tendency to cavity formation at the right apex. (L<sub>2</sub>S)



Oct. 1933

Febr. 1935

His course stopped at 5.95 gms. in 4 months owing to buccal ulceration. (The course had been interrupted frequently owing to ulceration of the mouth). His general condition was fairly good. Adventitious sounds persisted in spite of rest but disappeared after commencing the injections. After an interval of 3 months gold was again started, but he commenced losing weight, complaining of soreness of the gums and eventually of diarrhoea/



diarrhoea and the injections were stopped at 5.5 gms. making a total of 11.45 gms. of crisalbine. X-ray then showed what appeared to be fibrosis of both lungs. The diarrhoea lasted two weeks and he was still losing weight. He was discharged not quiescent with a positive sputum but with radiological evidence of considerable fibrosis of both lungs. He died 2 years after commencing gold injections.

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CASE NO. 31.

Male aged 33 - with a bad family history of T.B. and a "previous trouble" related to the gastrointestinal tract. He had had streaks of blood in his sputum with cough, occasional night sweats, and dyspnoea. His fingers were clubbed and he was losing weight. Disease was evident in the upper half of the right lung and the left upper lobe with a multilocular cavity towards the right apex. (L<sub>3</sub>S) He was started on gold in January 1935 and gained 2 lbs in weight after 0.55 gms. He had a mild conjunctivitis in both eyes which was present before injections. By the middle of June he had had 7 gms. of crisalbine and he was improving. On admission his sputum was negative, became positive, and was discharged in October, still positive. The X-ray showed definite improvement of the right lung with evidence of fibrosis. In January 1936 he had been working for 12 weeks. There was no toxicity during the course of injections.

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CASE No. 32.

Male aged 26 - shop assistant - complained of loss of weight for one year. He had a cough, and occasional streaks of blood in his sputum which was positive. He also had dyspnoea, night sweats and weakness. There was extensive disease of the upper half of both lungs. (1<sub>3</sub>S) He was commenced with 0.05 gms. in 1933 and after 2 months complained of sore mouth. There were no true ulcers to be seen though areas of apparent vesication were present. His general condition however improved. A vomiting attack occurred once during the early injections but crisalbine was discontinued owing to persistent diarrhoea. There were no adventitious sounds and after an interval of 4 months, injections were again started but discontinued owing to persistent buccal ulceration. He had a total of 12.9 gms. There was not much, if any, change in the X-ray and he was discharged, sputum positive, at his own request; and a year afterwards he had been working steadily and keeping fairly well.

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CASE NO. 33.

Male aged 19 - a collier - came under observation in 1916 when no T.B. was found. He has complained of "bronchitis", cough and expectoration, dyspnoea, loss of flesh and weakness. The greater part of the right lung and left lower lobe showed disease with a cavity towards the right apex. There was a recent effusion at the right base. (L<sub>3</sub>S) An A.P. was unsuccessful. In October 1934, his sputum being negative, he was started with .05 gm. of crissalbine; he gained weight and by the end of February 1935 had completed his course of 7 gms. complaining only of sore tongue. The right upper lobe showed improvement with ? diminution in size of the cavity. The rest of the lung showed little change. His sputum became positive during treatment but was negative on discharge; and in February of this year in the usual follow-up attendance at the Dispensary, his condition was fairly satisfactory.

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CASE NO. 34.

Female aged 30 - complained of always being tired and a cough. She had had haemoptysis three times. She had pains in the right side of the chest, dyspnoea, night sweats and weakness. The radiogram showed extensive disease spreading from the roots and involving the middle-third of both lungs, especially the right. (13S) She was started in August 1934 with gold - gained weight and her general condition improved. After 6.5 gms. of crisalbine both the lungs, especially the right, showed definite evidence of fibrotic changes with hardening and shrinking of diseased areas. After an interval of a month she was started again and had altogether 13.5 gms. of crisalbine. There were no adventitious sounds and the disease was quiescent with indefinite signs. In February of this year she was keeping very well.

Her sputum was always negative, and there was no toxicity.

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CASE NO. 35.

Female aged 38 - had pleurisy with effusion in March 1934 and was off work for 8 months. She was losing weight and had haemoptysis on resuming work. Her sputum was positive, she had a cough, night sweats, weakness, pains in the left chest, dyspnoea, and was of a neurasthenic disposition. There was disease of the left upper lobe, fibrotic in type. (1<sub>1</sub>S) After one gm. of gold, crepitations were remarkably reduced. She had 6 gms. of crisalbine, complaining of buccal ulceration. The left upper lobe showed improvement with evidence of fibrosis. The disease was quiescent, she gained weight, and was discharged sputum negative.

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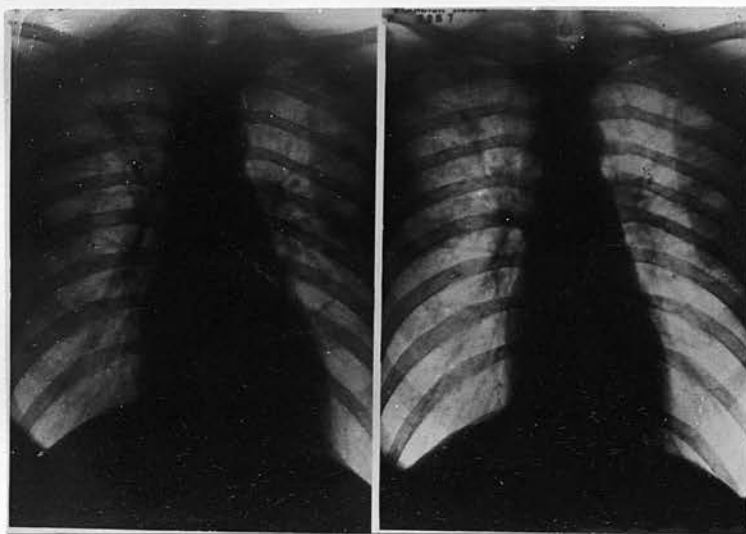
CASE NO. 36.

Male aged 22 - with a family history of T.B. - had pneumonia at the age of 14, and "chronic bronchitis ever since". In December 1931 he had had a troublesome cough and night sweats for 6 months. He had streaks of haemoptysis on one occasion, dyspnoea, loss of flesh and weakness, also slight hoarseness and pain in the chest; his fingers were clubbed. There was disease of the right lung and upper-half of the left. (L3S) In March 1932 crissalbine was started with .01 gm. and increased by .025 gm., but after .055 gm. he developed albuminuria. In August 1932 there was progression, viz. cavity at each apex and a smaller one opposite the left root. He was going down-hill. His sputum had been positive from December 1931 to June 1934. He was commenced in March 1933 with solganol B-oleosum intramuscularly, 0.01 gm., and increased by 0.1 gm. weekly. He had ulcers under the tongue after 3.97 gms. and reached a total of 5.2 gms. He was again given gold, making a grand total of 9.85 gms. In March 1934 there was some evidence of fibrotic changes in both lungs; his sputum was positive and he died in October 1934.

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CASE NO. 37.

Male aged 21 - with a family history of T.B. complained of a "nasty cough" for 2 months. He had lost flesh and there was slight weakness. There was no sputum on admission. The upper two lobes of the



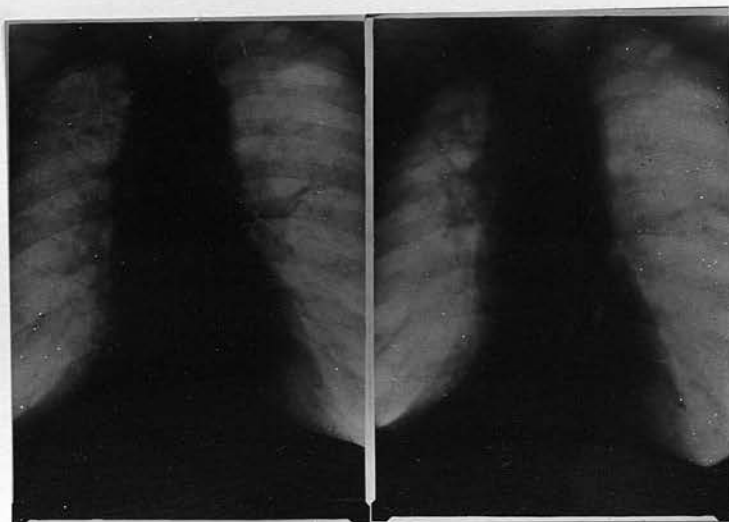
Dec. 1934

June 1935

right side were the seat of disease and also upper lobe of the left - fibrotic in type. ( $L_2S$ ) In  $3\frac{1}{2}$  months he had 7.15 gms. of crisalbine. Physical signs showed the disease quiescent, his sputum was negative and he had gained over a stone in weight, but radiologically there was little change in either lung. There was no toxicity.

CASE NO. 38.

Male aged 48 - collier - had pleurisy 6 months ago (November 1933) and a cough ever since. His sputum was positive - he had night sweats and weakness and gave a history of haemoptysis. There was disease of



22.11.33

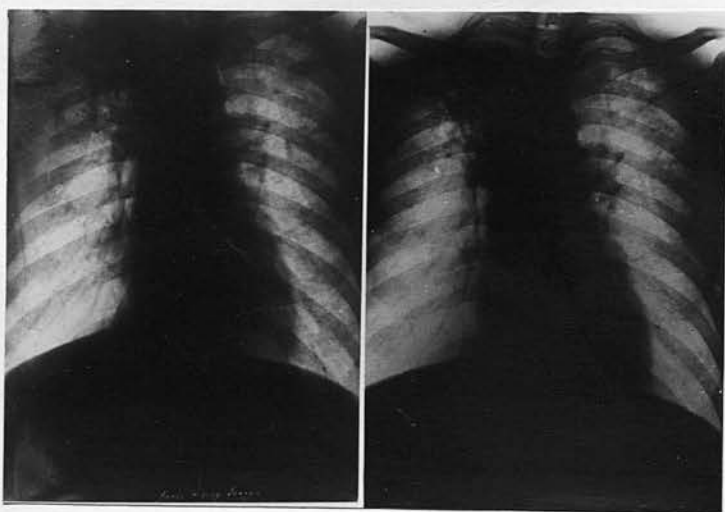
3.7.35

the upper two lobes on the right side and a dense shadow at the left root. ( $1_2S$ ) He was started with .1 gm. of crisalbine and reached up to 7 gms. in 4 months. There was an initial loss of weight on commencing treatment which was soon regained however, and no other sign of toxicity. There were fibrotic changes in the right lung. The course was repeated, making in all 14 gms. There was fibrosis in both lungs, his sputum was negative and he was discharged quiescent. In February 1936, however, it again became positive, though he was afebrile and doing well.



CASE NO. 39.

Male aged 23 - with a family history of T.B. - had a cough for 9 months, dyspnoea, loss of flesh, weakness, hoarseness, night sweats, and haemoptysis on two occasions. There was disease of the left lung in its



13.11.34

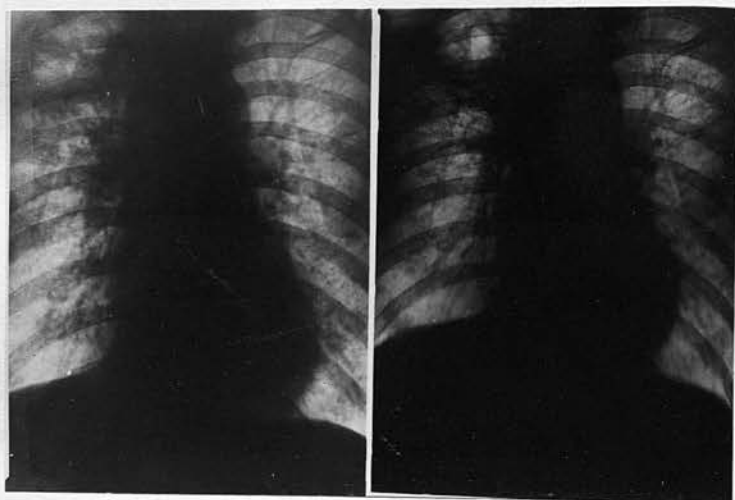
10.4.35

greater part and also in the right upper lobe. (L<sub>2</sub>S)  
 He had 6 gms. of Crisalbine in 3½ months but developed a macular rash. He had an initial gain in weight, which thereafter remained stationary. His sputum was originally negative but though there was a suggestion of fibrosis in the lungs and he was discharged slightly improved, his sputum was positive. In February 1936 he had been working steadily for 6 months and keeping fairly well.



CASE NO. 40.

Male aged 28 - complained of pains in the chest for 6 months with night sweats and occasional abdominal pain; slight cough and slight "staining", and profuse



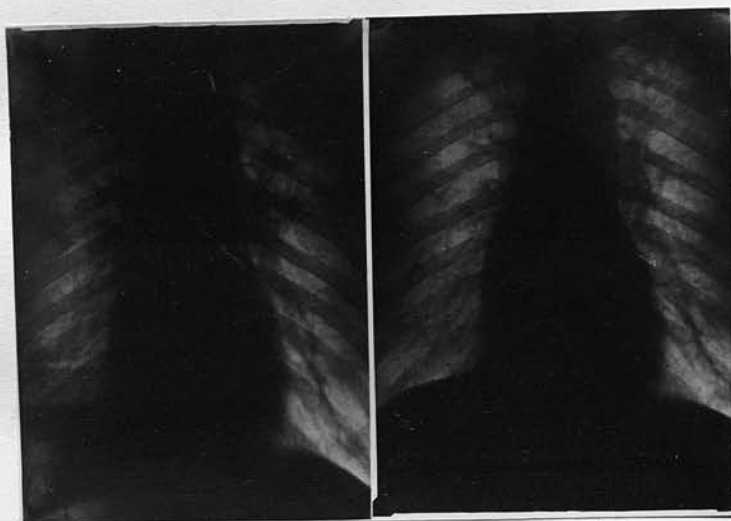
27.10.33

15.3.34

expectoration which was positive for T.B. There was disease of both lungs, especially the right upper lobe with a cavity towards the right apex. ( $L_3S$ ) The vocal cords were injected. In October 1933 crisalbine was started with 0.05 gms. and completed in 5 months at 6.95 gms. The larynx was now normal and there was improvement in both lungs. In August 1934 the course was repeated, making a grand total of 13.7 gms. He gained weight and his sputum was negative. He was discharged not quiescent with an unfavourable prognosis.

CASE NO. 41.

Male aged 32 - had a perianal abscess for one year and complained of abdominal pain and tightness in the chest. He gave a history of cough, spit and haemo-



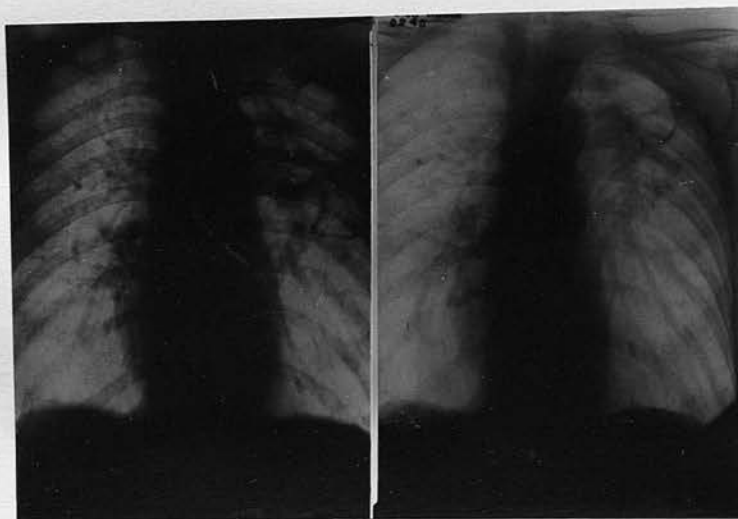
7.1.35

31.7.35

ptysis, loss of flesh, night sweats, weakness and hoarseness. His fingers were clubbed. There was disease of the whole of the right lung and the left upper lobe (L<sub>3</sub>S). His sputum was negative. He had 7 gms. of crisalbine in 5 months and gained weight. Both lungs showed fibrosis and he has been working regularly since discharge and with his sputum negative. There was no toxicity or idiosyncrasy.

CASE NO. 42.

Male aged 39 - complained of abdominal pain and sickness with a cough, sputum, which was positive for T.B., and with streaks of blood. He had dyspnoea and clubbing of the fingers. There was disease of the left upper lobe with several large cavities in February 1934, and there was more recent exudative infection in the upper half of the right lung. (L<sub>2</sub>S) No spec-



13.2.34

4.6.35

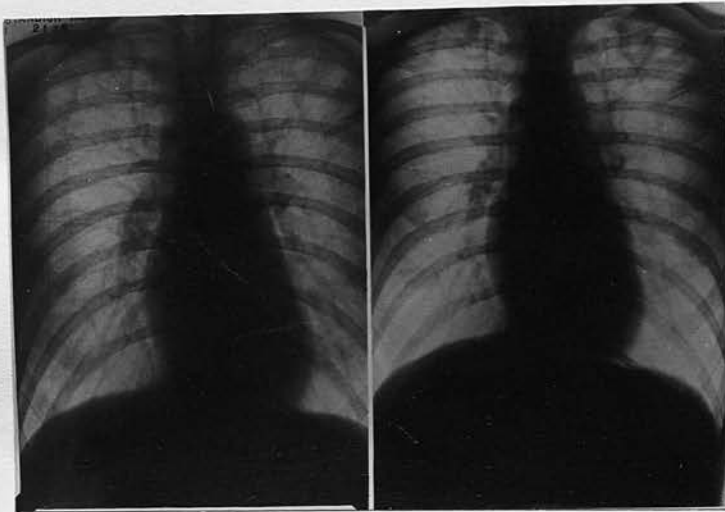
ific treatment was instituted. He gained weight, but his sputum remained positive. In January 1935 there was evidence of fibrosis in the left lung with the cavities pulled upwards the apex. Gold was given for the spread in the right side and in  $4\frac{1}{2}$  months he received 7 gms. The X-ray showed improvement. After 1.6 gms. of the second course an erythematous rash developed. He therefore had 8.6 gms. of crisalbine. Improvement was maintained and he had a negative sputum/

sputum which however became positive later. Eventually however on completion of the course it became negative and in February 1936 he had no sputum. He was provided with a shelter and was doing fairly well. There was X-ray evidence of fibrosis.

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CASE NO. 43.

Female aged 20 - stenographer - had broncho pneumonia and measles in childhood. She came under observation in June 1933; and complained that, since having a severe cold 8 months ago, she had always felt tired with a poor appetite and had had a cough ever since.



30.8.33

15.3.34

Her doctor reported her sputum positive but she had no sputum on admission. She had had profuse expectoration, and haemoptysis. There was loss of flesh; she was dyspnoeic and complained of night sweats, weakness and hoarseness. There was poor expansion of the left chest, flattening of the left apex and dullness over the left upper lobe and at the extreme right apex. The breath sounds were rather harsh and there were/

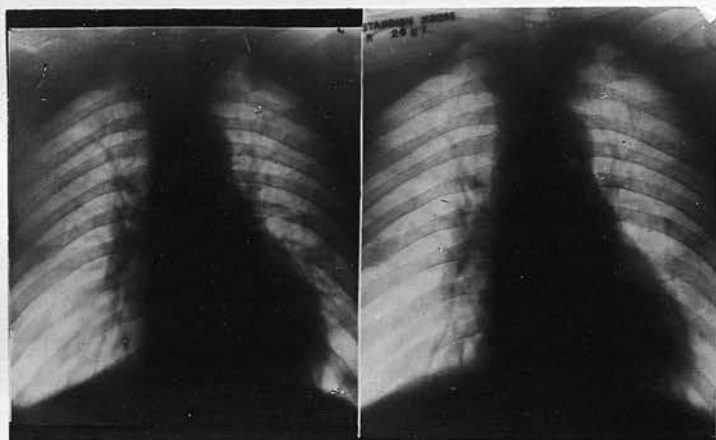


were no adventitious sounds. Radiologically there was an exudative type of disease of the upper lobes of both lungs. ( $1_2S$ ) It was decided that an A.P. was not suitable. She was started in September 1933 with gold 0.05 gm., the highest dose being 0.25 gm. She felt rather "faint" after the first few doses. By February 1934 she had had 9.5 gms. The course was extended as there were no signs or symptoms of intolerance. The X-ray report then showed fibrosis of both lungs. In May she was discharged as quiescent, having done well; and in February 1936 had been working for 9 months. She had gained weight during the course and there was no sputum on discharge.

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CASE NO. 44.

Male aged 47 - with a previous history of pneumonia and pleurisy, had a cough for 6 years and gave a history of haemoptysis, night sweats, weakness and pain in the left chest. His sputum was negative.



23.6.35

25.12.35

There was disease in the middle third of the left lung and a spread in the right upper lobe. (L<sub>1</sub>S)  
In 4 months he received 7 gms. of Crisalbine and there was improvement in the left lung. He was discharged quiescent, having gained weight and with sputum negative. There was no toxicity.

CASE NO. 45.

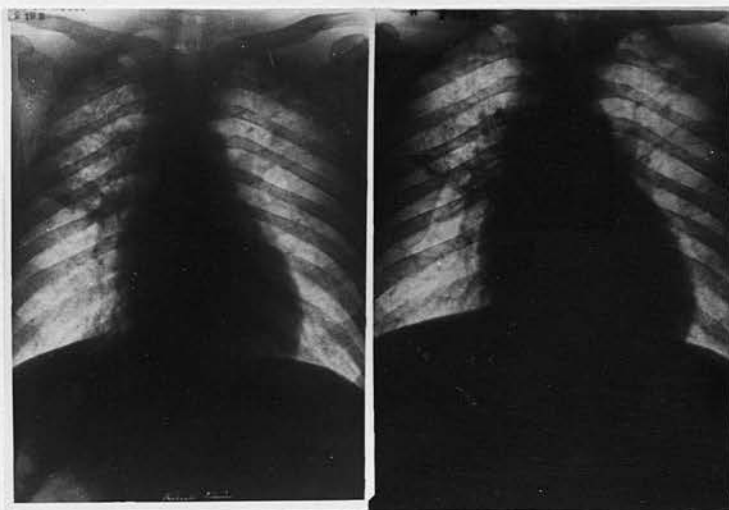
Male aged 32 - whose wife had T.B. - complained of laryngitis and cough. He had had a positive sputum for 3 years; loss of weight, dyspnoea, weakness and night sweats with occasional hoarseness. In January 1933 he was admitted with a spontaneous pneumothorax and 500 c.c. of the air removed. The left lung was almost completely collapsed except at the apex where there were cavities and adhesions. The right lung showed fairly extensive disease throughout. (L<sub>3</sub>S)

He developed an effusion on the left side and 3,195 c.c. of fluid were withdrawn and replaced with 2,170 c.c. of air. His urine was normal though rather diminished in amount for 2 days after commencing crisalbine. He had 7 gms. in all. He had gained weight, his sputum became negative. He had been lost trace of.

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CASE NO. 46.

Male aged 28 - family history of T.B. In January 1934 he had a cough for one year, one attack of haemoptysis, occasional night sweats and dyspnoea at times. His sputum was positive. There was disease of the



(1)

(2)

whole of the right lung, especially in the upper lobe, also in the left upper lobe. (1<sub>3</sub>s) He had 7 gms. of crissalbine, an A.P. having been discontinued. There was definite improvement in the right upper lobe and in July 1935 had been working for 12 weeks, having been discharged with a negative sputum and no loss of weight.

CASE NO. 47.

Male aged 24 - with a bad family history of T.B., had had several attacks of pleurisy, hæmoptysis and "influenza". His sputum was negative. He had a cough and expectoration, loss of flesh, hoarseness, weakness and poor appetite. There was disease of the Right upper lobe and Left apex, exudative in type. (1<sub>3</sub>S) There was a slight initial loss of weight on commencing crisalbine but he had a total of 7 gms. in 4 months. He was discharged sputum negative and improved.

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CASE NO. 48.

Male aged 38 - had pneumonia 10 years previously and frequent "bronchitis". He had "staining" on 3 occasions. In June 1933 had had cough, loss of flesh and dyspnoea with occasional night sweats and weakness. His sputum was positive. There was considerable disease in the whole of the left lung with a suggestion of cavity formation at the left apex. (L<sub>3</sub>S) There was spread from the right root. Crisalbine was given for right side and a left-sided A.P. tried. He had 7 gms. in 5 months. The left lung showed fibrotic changes and the cavity at the left apex "seemed smaller". The A.P. was unsuccessful - a second course of crisalbine was repeated, having only 2.5 gms. and making a total of 9.5 gms. He was discharged, sputum positive with fibrosis in the left upper lobe and a thick-walled cavity. He had gained weight. He has since been keeping fairly well.

He had no signs of toxicity.

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CASE NO. 49.

Female aged 19 - with a family history of T.B., complained of malaise, dyspnoea and dysphagia, and had loss of flesh and clubbing of the fingers. There was disease of the upper lobe of both lungs. (L<sub>2</sub>S)

In January 1934 she was started with gold, her sputum being positive, and after 5 months she had 7 gms. of crisalbine. Fibrosis was well marked; she was discharged quiescent and with sputum negative. There was no initial loss of weight and no signs of toxicity.

CASE NO. 50.

Male aged 33 - complained of abdominal pain and morning vomiting. He had pain in the left chest, cough, haemoptysis, dyspnoea and night sweating. There was disease of the upper two-thirds of the left lung and upper half of the right lung. (L<sub>3</sub>S) His sputum was positive. He received 7 gms. of crisalbine in 5 months, complaining of diarrhoea. The right lung, and to a lesser extent the left, showed some fibrosis. He was discharged for domestic reasons, not quiescent and with sputum positive though this was negative for 3 months during the course. In January 1936 he was keeping fairly well. He gained weight during the course.

CASE 51.

Male aged 29 - complained of pain in the right chest for 3 months with a cough and evening temperature of  $100^{\circ}$ . His sputum was positive; there was weakness, loss of flesh, dyspnoea and night sweats. There was disease of both lungs with a cavity in the right upper lobe. (L<sub>3</sub>S) A right A.P. was performed, gold 0.05 gm. started, totalling 7 gms. He lost weight and his sputum was positive on discharge. He complained of nausea after a few injections of crisalbine. Initially the A.P. and gold together gave a decided loss of weight.

CASE NO. 52.

Female aged 27 - barmaid - with a bad family history, had tonsillitis and cough. Her sputum was positive (February 1934). She had haemoptysis, night sweats and dyspnoea. There was dullness of the left upper lobe with moist râles. An X-ray showed disease in this situation. (l<sub>1</sub>S) An A.P. was abandoned owing to adhesions and gold started with 0.05 gm. totalling 7 gms. in  $4\frac{1}{2}$  months. She gained weight and the X-ray showed improvement. There were no symptoms of intolerance. She was discharged quiescent, with negative sputum which had become negative since commencing crisalbine and had remained so. In January 1936 she was keeping well and not complaining.

CASE NO. 53.

Male aged 29 with a family history of T.B. In August 1934 had complained of fistula-in-ano for 3 years and "pleurisy" 10 years earlier. He had a husky voice with cough and sputum which was negative on admission and with occasional streaks of blood. He had night sweats and weakness. There was extensive disease of both lungs with a large cavity in the right upper lobe and a smaller one at the left apex. (L3S) A right A.P. was discontinued as no satisfactory collapse was obtained. The right vocal cord was ulcerated. He had 7 gms. of gold and 6 months later both lungs showed improvement with evidence of fibrosis. There was a gain in weight. He was discharged owing to a breach of rules - sputum positive - though he had had a negative sputum during treatment.

There were no signs of toxicity.

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CASE NO. 54.

Female aged 23 - school teacher - complained of frequent "bronchitis" and pain in the left shoulder. Had a cough and expectoration with "staining", loss of flesh and occasional night sweats. She had bilateral infection (1<sub>2</sub>S) and in June 1933 was started with 0.05 gm. of crissalbine and reached a maximum dose of 0.25 gm., the total course equalling 7 gms., and discontinued owing to a slight rash on the arms and back of transient character and consisting of tiny raised macules and loss of weight. Her sputum was positive on admission and on discharge. She was given solganol at home by her own doctor and complained of diarrhoea. In January 1936 her sputum was still positive though it became very much less in amount and for some months was negative. There was very slight improvement, if any, with some evidence of fibrosis in both sides radiologically.

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CASE NO. 55.

Male aged 11 years whose mother died of T.B., came under observation in 1925 for "bad colds and coughs". In 1929 he was discharged from the sanatorium as non-T.B., but in May 1935, at the age of 19, his sputum was positive - he had had haemoptysis, night sweats and dyspnoea with loss of flesh. The right middle third and upper half of the left lung showed disease. (1<sub>3</sub>S) An A.P. was abandoned. After 1.5 gm. he complained of diarrhoea and was transferred sputum positive, with very bad prognosis.

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CASE 56.

Male aged 34 - had pneumonia at the age of 21, and now complained of a cough and husky voice. His sputum was positive and he had had haemoptysis. There was infiltration of the left upper lobe and spread from the right root. (L<sub>2</sub>S) Seven gms. of gold were given. There was an initial loss of weight; no toxic symptoms, but he had scrotal intertrigo (not due to gold) He was improved physically and radiologically. He was discharged quiescent, with a negative sputum. He did complain of a metallic taste during the injections of crisalbine.

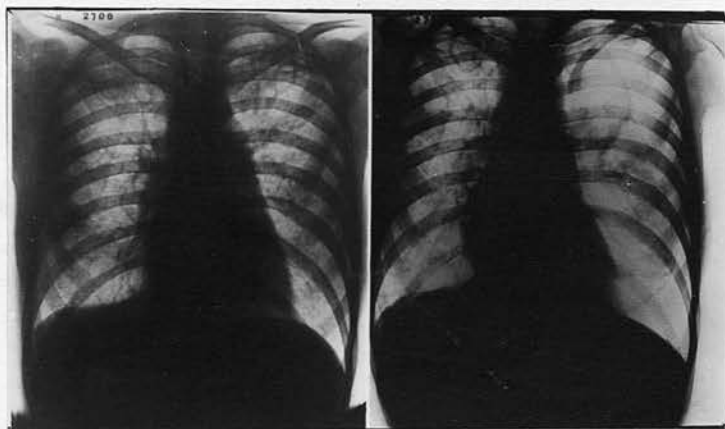
CASE NO. 57.

Male aged 27 - whose mother died of T.B., had a cough, spit, haemoptysis, weakness, loss of flesh and dyspnoea. His sputum was positive. The whole of the left lung and the upper half of the right show disease. (L<sub>3</sub>S) He had 5.2 gms. of gold and a left A.P. He gained weight. Gold was stopped owing to seborrhoeic dermatitis. There was no toxicity. His sputum was still positive on discharge.

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CASE NO. 58.

Female aged 19 - typist - (had an intraamniotic amputation of proximal third of the left forearm) - complained of always "feeling tired" and feeling unwell the last 6 months with a cough for 3 months and occasional pain in the right chest. Her sputum was positive. The menses were regular. She had night sweats, weakness and loss of flesh with dyspnoea. There was



30.7.35

6.1.36

bilateral infiltration of the apices with a cavity towards the left apex. There was unhealthy appearance of both roots. (L<sub>2</sub>S) After 1.6 gms. of Crisalbine she complained of diarrhoea and ulceration of the mouth; and of dizziness and headaches after injections which last for a few minutes only and made worse when injections and refills were on the same day. She had had a left A.P. induced; her sputum was less in amount but still positive though her general condition was good. There were no adventitious sounds and she gained weight. She had 3.7 gms. of Crisalbine and the X-ray showed the right lung stationary.

CASE NO. 59.

Male aged 34 - with pains in the chest for 2 weeks and a cough for one year - gave a history of haemoptysis. He was dyspnoeic, had night sweats and weakness though a good appetite. His sputum was positive. There was T.B. disease of the left lung with a cavity at the apex. Also infiltration from the right root towards the right apex. (L<sub>5</sub>S) There was an initial gain in weight. He had 6 gms. of crisalbine in four months. An A.P. was unsuccessful. The gold was stopped owing to a slight rash. He was only slightly improved and his sputum became negative.

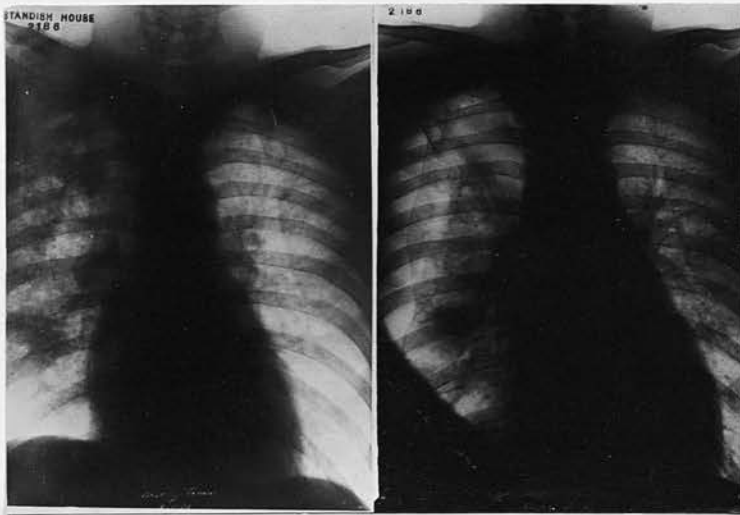
CASE NO.60.

Male aged 19 had a slight cough with loss of weight and weakness and positive sputum. There was an effusion on the left side and infiltration of both upper lobes. (l<sub>3</sub>s) A right A.P. was unsuccessful which had been tried for a cavity forming on the right side. He had 7 gms. of crisalbine in 4 months. There was no initial loss of weight, was improved, and his sputum became negative.

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CASE NO. 61.

Male aged 32 - a mental nurse - had not been feeling well for 6 months, complaining of nasopharyngeal catarrh. He had a slight cough - occasional streaks of blood in his sputum which was positive for T.B.,



8.1.34

9.7.34

weakness and slight dyspnoea. There was exudative disease of the right lung with commencing spread from the left root. <sup>(12<sup>s</sup>)</sup> A right A.P. was performed. He had 7 gms. of crisalbine in 6 months ending December 1933. In December 1934 his sputum was still negative and also remained so till March 1935. He had no loss of weight throughout the course and no toxicity. His X-ray at that time showed his left lung apparently free from disease, and fair collapse on the right side.



CASE NO. 62.

Male aged 25 - complained of "indigestion" and cough for 2 months. He had abdominal pain, night sweats, poor appetite and a history of haemoptysis. His sputum was positive. The upper two-thirds of both lungs with a large cavity in the right upper lobe and a smaller one towards the left apex were the seat of disease. (L3S) He had a bilateral A.P. and gold. There was an initial gain in weight but after this combination of treatment a slight loss for the first few weeks. He had 7 gms. of crisalbine and was discharged with a negative sputum. In January 1936 however - 2 years later - his sputum again became positive. There was no toxicity.

CASE NO. 63.

Male aged 27 - painter - had a T.B. ankle at 11 years of age and had been "unwell" for the last 6 months with cough and dyspnoea. His sputum was positive to Koch's bacillus. There was an exudative type of disease in the upper half of both lungs with a spread towards the right base. (L3S) An A.P. was discontinued. He gained weight and had a total of 4.4 gms. He developed a rash and stomatitis. His sputum was positive on discharge.

CASE NO. 64.

Female aged 30 - complained of not feeling well for the past 7 months with a cough and pains in the left shoulder. She had all the major symptoms and systemic disturbance was marked. There was disease in the middle third of the left lung with a cavity in the upper lobe and an area of disease in the right lung between the upper and middle lobes. (L<sub>3</sub>S) Her sputum was positive. In September 1934 a left A.P. was performed and gold to 5.55 gms. given. She complained of stomatitis, but gained weight and her sputum was negative. She was pregnant at this time and no adverse influence was noted on the kidneys.

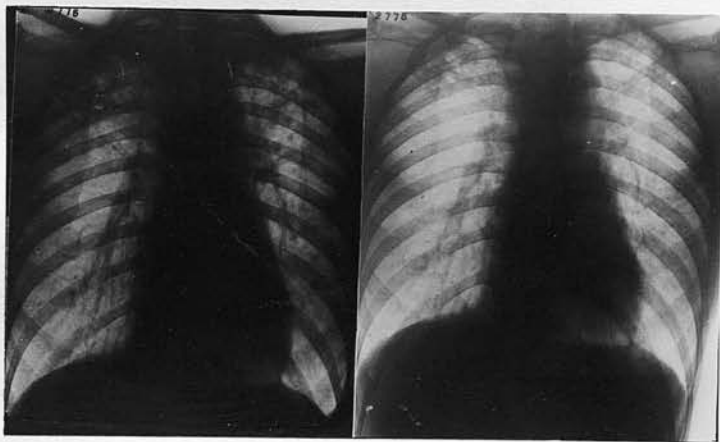
CASE NO. 65.

Male aged 45 - had a cough, haemoptysis, night sweats and dyspnoea. The upper lobes of both lungs with a large cavity at the right apex were the seat of disease. (L<sub>3</sub>S) His sputum was positive. After 3.5 gms. of crisalbine stomatitis was very marked, and his sputum was positive having had only one negative sputum. There was no improvement.

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CASE NO. 66.

Female aged 28 - with a family history of T.B. had pleurisy with effusion and frequent colds. She had no sputum. There was disease of the upper lobe of the right lung and upper half of the left lung. (1<sub>3</sub>s)



Nov. 1935

March 1936

An A.P. was unsuccessful. She gained weight during treatment. Though the dose of gold was never higher than 0.2 gms. she twice had a febrile reaction to  $101^{\circ}$  to  $102^{\circ}$ , with occasional shivers, headache and nausea immediately after the injections. Clinically and radiologically she was somewhat improved, having had a total of 7 gms. of crissalbine.

CASE NO. 67.

Male aged 24 - complained of general malaise, being easily tired and winter coughs. His sputum was positive in which were occasional streaks of blood. He was dyspnoeic on exertion, and had exudative disease of the left and right upper lobes. (L<sub>2</sub>S) He gained weight after having a left A.P. and 5 gms. of cris-albine. He was transferred with a positive sputum, not quiescent and died 18 months after coming under treatment.

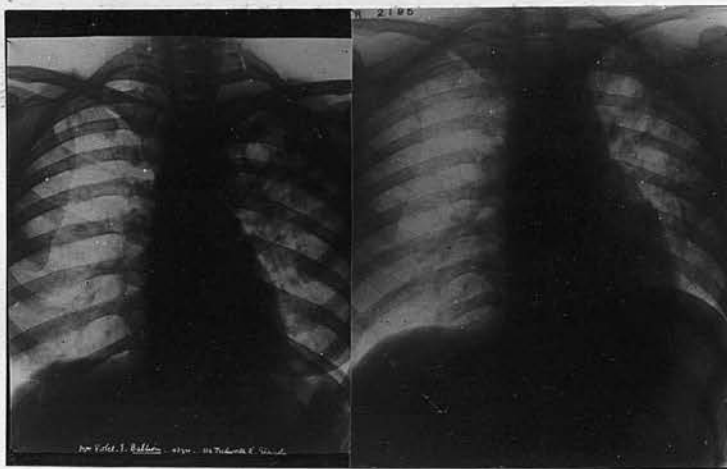
CASE NO. 68.

Female aged 20 - with a family history of T.B., complained of sore throat and cough. Her sputum was positive; she had had haemoptysis; she had lost weight and was dyspnoeic. Expectoration was profuse and there was disease of the upper two thirds of both lungs with a cavity in the left upper lobe. (L<sub>2</sub>S) She had a total of 1.7 gms. with febrile reactions to 100<sup>0</sup>F. Her sputum still remained positive and she died 9 months after commencement of gold treatment.

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CASE NO. 69.

Female aged 43 - had pleurisy with effusion, also haemoptysis and loss of flesh with dyspnoea and slight weakness. Her sputum was positive and there was old standing disease of the left upper lobe and more recent involvement in the upper lobe of the right lung. (12S) There was ulceration of the larynx. Two months after commencing gold her sputum became negative - for the



Jan. 1934

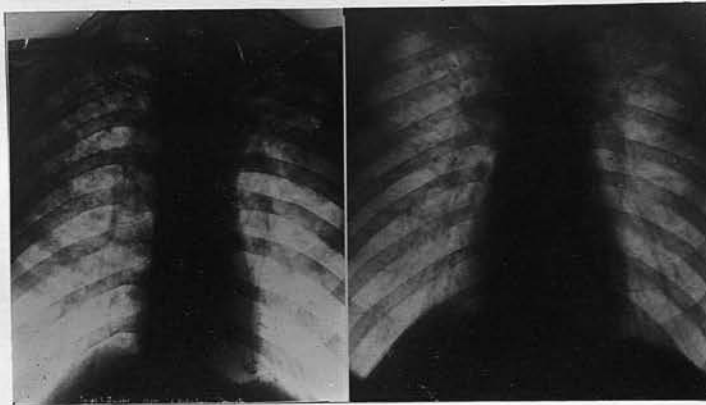
March 1935

first and only time, that is, once in two years. After 5 months she had 5.65 gms. but crisalbine was discontinued owing to stomatitis. After an interval of 7 weeks she was given a second course but only 0.1 gm. injected as the ulcers re-appeared, making a total therefore of 5.75 gms. Fifteen months after treatment X-ray of the right lung was deemed satisfactory, there being little change in the left lung; she gained weight and was discharged with a positive sputum.



CASE NO. 70.

Male aged 32 - had sanatorium treatment in 1928, that is, 5 years ago when sputum was positive on admission and negative on discharge. Developing "influenza" with a return of the cough and the sputum, dyspnoea, loss of flesh and a history of haemoptysis, he was



Nov. 1933

June 1934

re-admitted with disease of the upper half of both lungs. (L<sub>3</sub>S (1933) ) He had a total of 7 gms. of crisalbine in 4½ months and gained weight. There was tendency to fibrosis in the lungs and he was discharged sputum negative and quiescent, his sputum, however, again becoming positive.

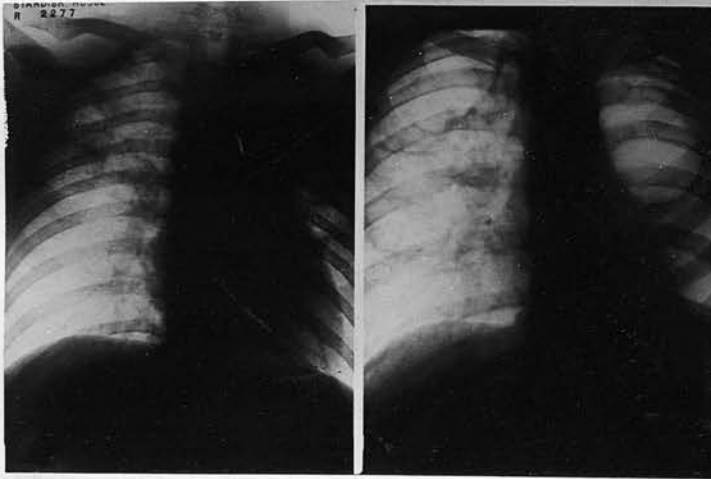
CASE NO. 71.

Male aged 28 - in 1933 complained of cough and "bronchitis for years" and abdominal pain for 3 weeks. His sputum was positive; he had had haemoptysis; occasional night sweats; pain at the right base and loss of weight. His right lung and left upper lobe showed disease with a cavity in the left lower lobe. (L3S) An A.P. failed; gold was started in March 1934 with 0.05 gm. and at the end of 3 months he had had 3.35 gms., complaining of diarrhoea and ulceration of the mouth. He was most anxious to continue with the injections and .05 gm. was given at fortnightly intervals; his sputum was positive; he was losing weight and diarrhoea had recommenced. He died in February 1935.

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CASE NO. 72.

Male aged 25 - complained of headaches and pains in the back for 4 months and a cough and gave a history of haemoptysis. He had lost flesh; was hoarse and dyspnoeic and his sputum was positive. There was



April 1934

June 1935

disease of the upper lobe on the left side and upper two lobes on the right. (L<sub>25</sub>). In April 1934 he had a left A.P. and crisalbine, totalling 3 gms. when he had stomatitis and by September 1934 had 6.9 gms. His sputum became negative in March 1935 but he died in November of the same year.

CASE NO. 73.

Male aged 42 - had a cough and spit with frequent streams of blood in his sputum which was positive to Koch's bacillus. There was weakness and dyspnoea with disease in the upper half of both lungs and a small cavity at the right apex. (L<sub>3</sub>S) He was started with 0.025 gms. and reached a maximum dose of 0.25 gm. totalling 9.86 gms. when he complained of ulceration of the mouth. On discharge his sputum was positive and he was not quiescent, though he gained weight. Both lungs showed improvement and he had been under observation for 4 years. During treatment his sputum had become negative.

CASE NO. 74.

Male aged 36 - farmer - with a family history of T.B., had a positive sputum, and complained of an emetic cough and loss of weight. He was dyspnoeic, with pain in the right chest, night sweats and history of haemoptysis. There was disease of the upper two thirds of the right lung and a spread from the left root involving the middle third of the left lung. (L<sub>2</sub>S)

In November 1932 he had a right A.P. and gold started with 0.1 gm. totalling 5.05 gms. in two months, when he complained of vomiting attacks, diarrhoea and albuminuria which cleared up within a week. His sputum became negative in March 1933 and remained so to March 1935 when he was doing very well except for slight "staining" of sputum on one occasion.

CASE NO. 75.

Female aged 29 - physical instructor - complained of being easily tired and not feeling well for 9 months with a cough and sputum which was positive, for 7 months. Her general condition was fair. She gave a history of haemoptysis and night sweats. The upper two lobes of the right lung with considerable cavitation and spread from the left root were the seat of disease. (L<sub>3</sub>S) She had a right A.P. performed and had 7.1 gms. of crisalbine, attending for refills and injections as an out-patient. She had gained weight, improved, and sputum became negative.

CASE NO. 76.

Male aged 30 - gave a history of haemoptysis and complained of pain in the right chest and weakness with a cough. His sputum was positive and profuse. There was disease involving the upper lobes of both lungs. (l<sub>2</sub>S) First course of gold was commenced in March 1933 with 0.05 gms. and totalled 5.6 gms. His second course commenced in October and altogether he had 15.25 gms. There was an initial gain in weight but he had an occasional "vomiting bout" during the second course. In May 1934 the disease was quiescent in both lungs; his sputum was negative and he was keeping well. In March 1936 he was all right but not working.



CASE NO. 77.

Female aged 28 - with a family history of T.B., after a cold at Christmas in 1932 developed a cough and started losing weight. She had night sweats, dyspnoea and weakness. Her sputum was positive (November 1933). There was disease of the right lung with a cavity at the apex. (13S) An A.P. was unsatisfactory. In January 1934 solganol intramuscularly was given with 0.01 gm. totalling 7.92 gms. and by August there was definite evidence of fibrotic changes in the right lung with retraction of the cavity towards the right apex. She was discharged quiescent, having had no toxic symptoms and with sputum negative. In February 1936 she was keeping well, and not complaining.

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CASE NO. 78.

Female aged 30 - with a previous history of bronchitis - came under observation in May 1934 complaining of cough for 9 months. She had cough, expectoration and slight loss of weight; night sweats, dyspnoea and slight weakness. There was disease of the upper two thirds of the left lung with a cavity at the apex and a localised area at the right base. (L<sub>3</sub>S)

In August 0.05 gm. of crisalbine was started and by January 1935 had a total of 7 gms. A left A.P. had been performed but was allowed to completely re-expand. There were fibrotic changes in progress in the right lung. She was discharged at her own request, not quiescent, and sputum negative in November 1935.

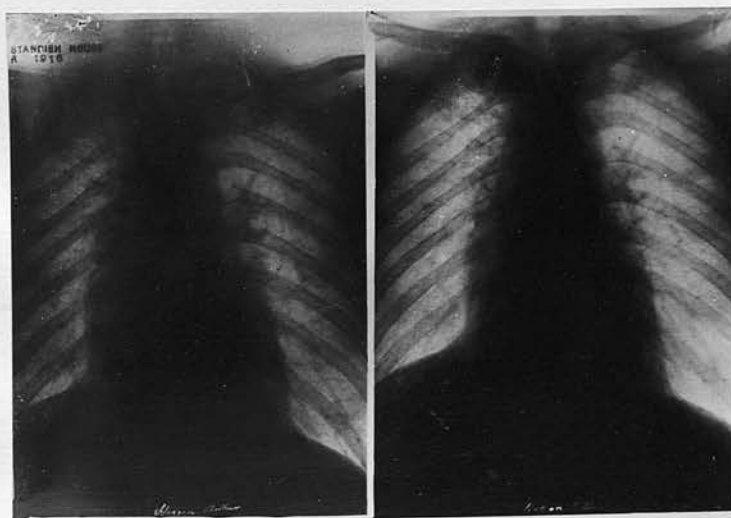
In March 1936 she was doing fairly well but her sputum was positive again. She had had no toxicity.

CASE NO. 79.

Male aged 37 with a family history of T.B., had had pneumonia twice and frequent bronchitis. He was losing weight and complained of praecordial pain for two months, also haemoptysis and slight dyspnoea. His sputum was positive; there was disease of both upper lobes. (L<sub>2</sub>S) Had 7 gms. in 4 $\frac{1}{2}$  months when stomatitis developed. There was an initial gain in weight, his sputum became negative but the X-ray showed very little change; and has since been keeping well.

CASE NO. 80.

Male aged 25 - with a family history of T.B. complained of a cough and haemoptysis, occasional night sweats and loss of weight. His sputum was positive. There was disease of the whole of the right lung and a spread from the left root to the upper lobe. (L<sub>3</sub>S)



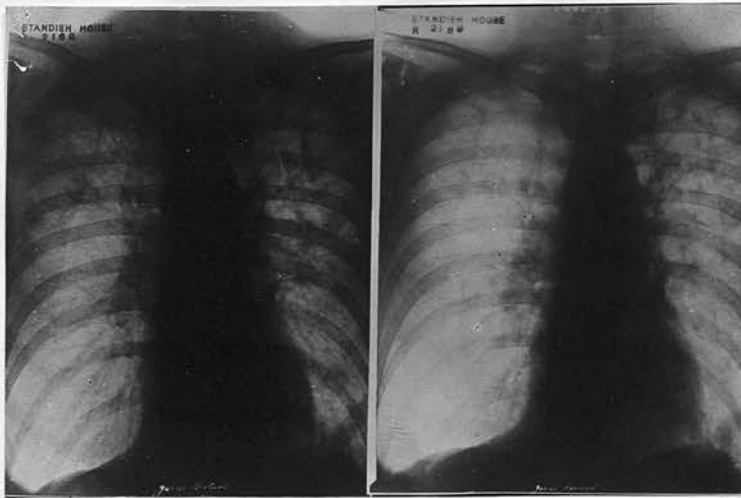
Nov. 1932

June 1934

The right phrenic dome was obliterated and an A.P. was abandoned. After the first injection of crystalline he had a sudden attack of shivering and weakness with a pulse of 120° and a temperature of 100°. Gold was continued and he had 7 gms., gaining weight, and with evidence of fibrosis in both lungs. He was much improved both clinically and radiologically but discharged with a positive sputum.

CASE NO. 81.

Male aged 33 - had typhoid fever in 1914 and "asthma" for 8 years, also pain between the shoulders for 5 years and a cough for the same period. He had had "staining" of sputum recently. His fingers were



Nov. 1933

April 1934

clubbed; he had a poor appetite and digestion and he was dyspnoeic and sputum positive. There was disease of the whole of the left lung, fibrotic in type and also in the upper two lobes of the right (November 1933). (L<sub>3</sub>S) By March 1934 he had received 6.75 gms. of crisalbine with no signs of intolerance or idiosyncrasy. In July 1934 he was discharged quiescent, having gained weight but with sputum positive and which was still positive a year later; he was slowly going downhill.

CASE NO. 82.

Male aged 23 - with a cough and haemoptysis, complained of weakness, night sweats and occasional pain in the chest. His sputum was positive. He received 6.85 gms. in 5 months with no signs of intolerance. There was a gain in weight. Disease was present in the left upper lobe. (1<sub>1</sub>S) A month after commencing injections his sputum became negative and remained so ever since. Two years later he was keeping well.

CASE NO. 83.

Female aged 22 - had an operation for goitre 1 year ago - complained of cough and occasional "staining" of the sputum which was positive to Koch's bacillus. She had slight weakness and occasional hoarseness. She was dyspnoeic and there was disease of the right upper and middle lobes and the middle third of the left lung. (L<sub>2</sub>S) She had 13.75 gms. of crisalbine, the sputum became negative, gained weight; but died 3 years after coming under treatment.

CASE NO. 84.

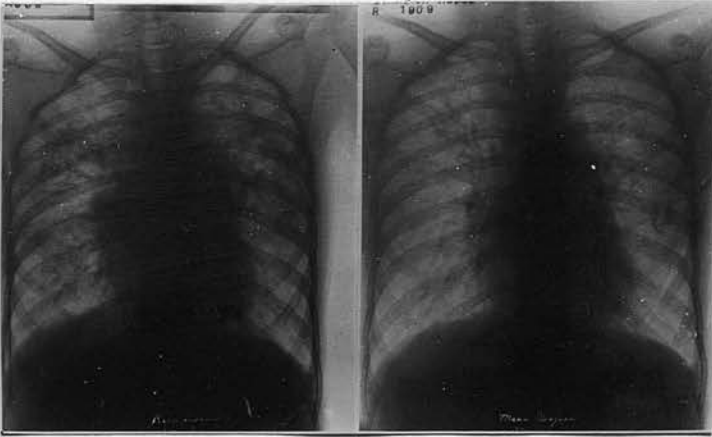
Female aged 33 - School teacher - had T.B. cervical adenitis, also malaise and loss of energy with cough, haemoptysis and night sweats. She had 2.35 gms. of crisalbine and developed a rash and diarrhoea. There was disease of the right upper lobe (1<sub>1</sub>S) an A.P. being discontinued. She had occasional shivers and nausea after injections. Her sputum had been negative and was negative when she took her own discharge - having been positive however while in the sanatorium.



CASE NO. 85.

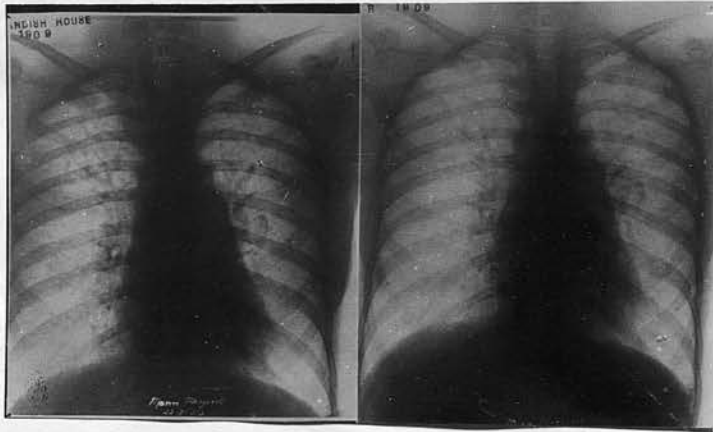
Female aged 13 - had measles and otitis media in childhood. Came under observation in 1932 - with temperature of  $99.2^{\circ}$  and pulse of  $130^{\circ}$  - complaining of getting thinner, easily tired and dyspnoea. She had no sputum; but a cough, loss of flesh, night sweats, pain in the chest and poor appetite. No impairment of resonance was detected and expansion was fair and equal. X-ray showed disease spreading out from both roots involving the major portions of both lungs apart from the apices which were free from disease. On screening the apices light equally, there was considerable mottling throughout the right lung and the left upper lobe. The right phrenic dome moves poorly, the angles were clear, the heart was normal and the trachea was central. (1<sub>3</sub>S) In December 1932 she was started with .025 gms. of crisalbine intravenously, the highest dose of crisalbine being .15 gms. In April 1933 a red weeping area in each axilla was present and gold was discontinued having received 3 gms. This rash was not attributed to gold but as she had so markedly improved gold was stopped as a prophylactic measure. There was no albuminuria. In July 1934 there was marked improvement in both lungs with fibrotic changes, all signs of the original disease having cleared up. In March 1936 both the lungs were free from disease. She was discharged quiescent having gained weight and T.B. negative.

CASE NO. 85.



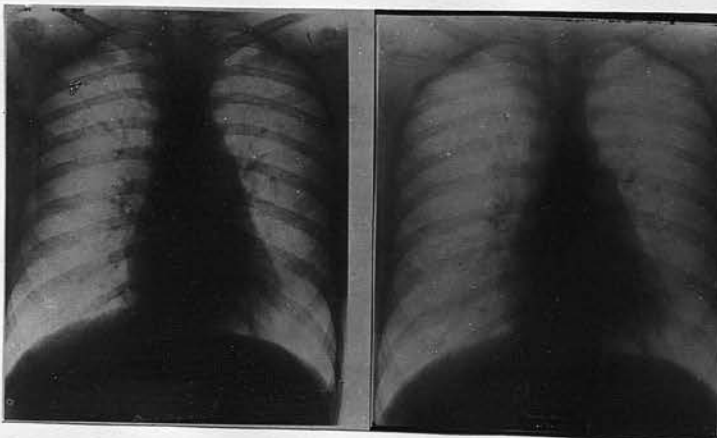
4.11.32

30.1.33



22.7.33

8.7.34



5.11.34

1.3.35

CASE NO. 86.

Female aged 23 - with a bad family history, came under observation in December 1931, complaining of always being tired after an attack of flu' a year ago with pains in the left chest, and cough for the last 6 months. Her sputum was positive; she had had haemoptysis, and occasional night sweats; there was hoarseness, weakness and dyspnoea. There was disease of the whole of the left lung with a large cavity towards the apex and more recent disease in the right side. (L3S) In April 1932 she had a left A.P. induced and gold started with 0.01 gm. to a dose of 0.5 gm. bi-weekly. She developed albuminuria which cleared up in 4 weeks and had a second course of 3.05 gms. making a total of 9 gms. She had gained weight and was much improved. A year later her sputum was still negative and the right lung was stationary. She was lost trace of.

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CASE NO. 87.

Male aged 33 - whose father died of T.B. came under observation in September 1932, having had pleurisy at the age of 11 and "influenza" 6 years ago. He always had a cough. He had a temperature of 99.2° and a pulse of 110°. He was thin, had recent streaks of blood in his sputum which was positive, occasional night sweats and dyspnoea. There was disease of the right upper lobe and a spread from the left root with the trachea pulled to the right. (1<sub>3</sub>S) He had a total of 5.5 gms. of crisalbine in 4 months and his general condition was satisfactory. There were no symptoms of gold poisoning. Radiologically there was very much improvement. He was discharged quiescent with a negative sputum and no further spread in the left lung and fibrotic changes in the right upper lobe. He was working for a year when his sputum again became positive (June 1935).

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CASE NO. 88.

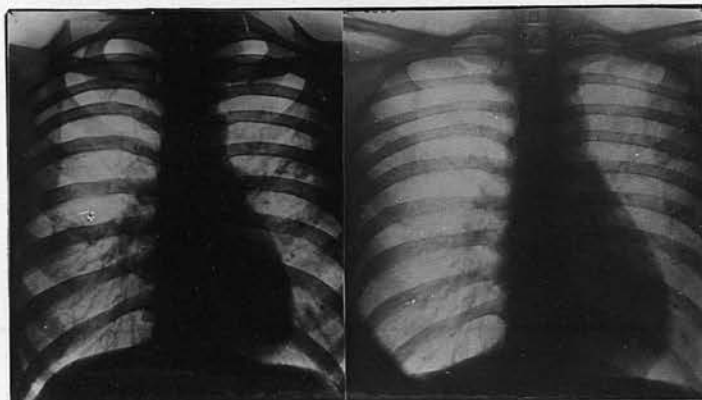
Male aged 45 - who had had malaria and dysentery; and a "chill on the liver" 6 years ago - complained of a cough for 6 months with night sweats, weakness, dyspnoea and loss of weight. His sputum was positive. There was disease of the upper-half of the right lung, and the left upper lobe, with the heart and mediastinum pulled to the left. (13S) He had a total of 2.1 gms. of gold which was stopped on account of a papulo-squamous rash on the chest and back. There was an initial loss of weight. His sputum was still positive and there was no improvement.

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CASE NO. 89.

Female aged 26 - bad family history - had "congestion of the lungs" at the age of 3 years - complained of a "nasty cough" for 2 years which was getting worse



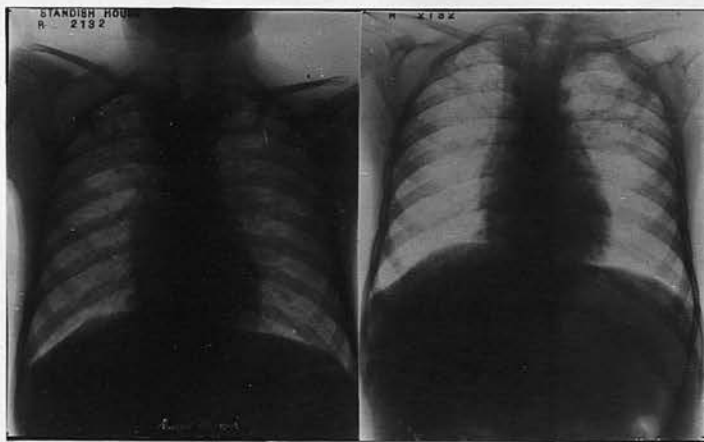
8.2.34

15.1.35

recently. She was afebrile, pulse 120<sup>0</sup> and dyspnoeic. She gave a history of haemoptysis and had lost weight. Her sputum was positive. There was disease spreading from the roots of both lungs. (12s) She improved under ordinary sanatorium treatment and was discharged quiescent (July 1933) but was re-admitted a year later with activation of the disease. She had 6.15 gms. of crisalbine, complaining of diarrhoea for 3 days towards the end of the course. Her sputum became negative 10 months later with clinical improvement, but with no influence on the cavity in the left upper lobe. She gained weight but sputum was returned positive for Koch's bacillus subsequent to discharge.

CASE NO. 90.

A male aged 8 years - came under observation in 1931 on account of a bad family history and "colds and coughs". He had a previous history of whooping cough. He had been in hospital 3 years ago with ? T.B. Peritonitis. There were shotty cervical glands and his



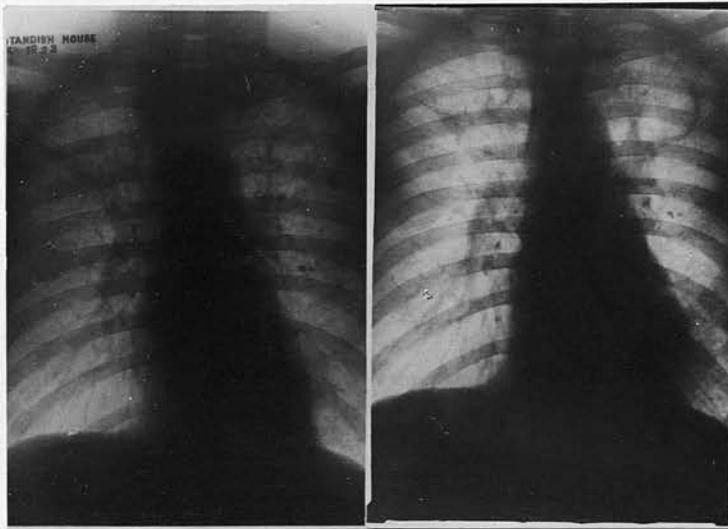
Oct. 1933

Sept. 1934

chest was full of bronchitic râles. In October 1933 there was disease of the upper third of the left lung and right apex. (1<sub>3</sub>s) He was given solganol, gaining weight and improving radiologically and clinically. In September 1934 his sputum was positive but he developed albuminuria and gold was stopped totalling 3.125 gms. His sputum became negative but 15 months later was positive again.

CASE NO. 91.

Male aged 26 with a family history of T.B. - complained of loss of weight and cough with expectoration for 3 months; he had haemoptysis, night sweats, pain in the right side of the chest and dyspnoea. His sputum was positive for T.B. The upper lobes of both lungs



Dec. 1932

Aug. 1934

show disease with a cavity at the left apex; and an A.P. was abandoned owing to adhesions. (L<sub>3</sub>S)

In January 1933 he had a total of 6.15 gms. during which he had diarrhoea once lasting 2 days and occasional pains in the limbs, headache and malaise after injections. After an interval of 6 months, he had a second course of 8.8 gms. making a total of 14.95 gms. There was no record of his weight. He was discharged, sputum negative and in January 1936 was keeping fairly well.

CASE NO. 92.

Male aged 38 - with a family history of T.B., complained of "pleurisy" 5 weeks ago and a slight cough at times (June 1932). His sputum was positive. There were occasional night sweats, dyspnoea and hoarseness and he gave a history of haemoptysis. There was disease involving the greater part of the left lung and also an area at the right root. (13S) After 0.4 gms. of crisalbine he complained of severe headache, vomiting, and a generalised macular rash, most marked in the flexor surfaces of the forearms. The face was red and somewhat swollen and the temperature was 102°. There was subsequent desquamation and gold intravenously was stopped. He was then tried on solganol, having a full course of 7 gms. by intramuscular injections. There was no record of his weight. He was improved clinically and radiologically with a negative sputum which, however, again became positive a year later.

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CASE NO. 93.

Male aged 19 - with a cough and streaks of blood in his sputum which was positive for T.B. Dyspnoea and expectoration were complained of, and there was disease of the right upper lobe and at the left apex. (L<sub>2</sub>S) He had a bilateral A.P. induced and had gold equal to 3.7 gms., developing stomatitis. His sputum was positive on discharge. There was no record of his weight. He died 2½ years after commencing treatment.

CASE NO. 94.

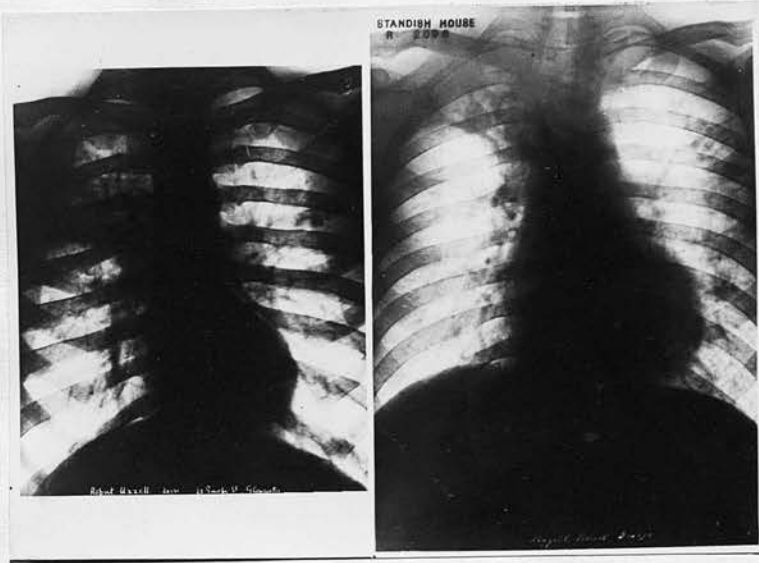
Male aged 27 - complained of insomnia, bronchitis, cough, and pain in the chest. He had dyspnoea, night sweating and a positive sputum. The upper half of both lungs show disease. (L<sub>3</sub>S) He had 5.46 gms of solganol intramuscularly in 9 months - his sputum still being positive with no change radiologically and a complaint on one occasion of vertigo and nausea.

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CASE NO. 95.

MALE aged 20 - had a previous history of "gastric stomach" 3 years ago, and "pleurisy" 10 weeks ago (August 1933). His sputum was positive. There was



1.

2.

profound systemic disturbance and a history of haemoptysis. There was disease of the upper two lobes of the right side, and a spread from the left root involving the middle third of the left lung (1<sub>3</sub><sup>S</sup>). He had 7.1 gms. of crisalbine in 6 months. He gained weight and there were fibrotic changes in the right lung with little change, if any, in the left. On discharge his sputum was negative, having improved clinically and radiologically. (November 1935)

CASE NO. 96.

Female aged 21 - complained of cough, expectoration, occasional "staining" of the sputum, which was positive - weakness and dyspnoea. There was disease of the left lung and upper half of the right lung with cavities at the apices. (L<sub>3</sub>S) An A.P. was abandoned. A total of 2.5 gms. were given and stopped on account of severe and recurrent stomatitis. Her sputum was still positive, and gained weight but she was not improved.

CASE NO. 97.

Male aged 35 - complained of cough and haemoptysis, pain in the chest, night sweats, weakness and dyspnoea. There was extensive disease in the upper two thirds of the left lung and spread from the right root involving the right upper and middle lobes. (L<sub>3</sub>S) His sputum was positive. An A.P. was performed on the left side. He had a total of 5.3 gms. of crisalbine; his sputum becoming negative and remained so with improvement radiologically and clinically.

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CASE NO. 98.

Female aged 24 - had been in a sanatorium before with a positive sputum - complained of cough, dyspnoea, loss of weight and night sweats. Her sputum was positive. There was disease of the left lung with a cavity towards the apex and a spread from the right root involving the middle third of the right lung. (L3S) Gold intravenously was discontinued owing to unsuitable veins but she had a course of 7 gms. of solganol intramuscularly. She had a left A.P. and was much improved. There was no toxicity; she gained weight and her sputum was negative on discharge.

CASE NO. 99.

Male aged 20 - with a family history of T.B., complained of a troublesome cough and expectoration for 3 months with weakness, dyspnoea and occasional night sweats; also of pains in the chest for 6 months. The upper two thirds of the right lung showed disease; also "mottling" at the left apex. (l3S) His sputum was positive. A right A.P. was performed and he had a total of 7.85 gms. of crisalbine. He was improved - his sputum being negative on discharge, and there had been no symptoms of poisoning due to gold.

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CASE NO. 100.

Male aged 39 - school master - complained of a cough and shortness of breath. He has lost weight and his fingers were clubbed. His sputum was negative and there was disease of both lungs, rather extensive, with a cavity in the right middle lobe. (Lgs)

He had a total of 6.5 gms. of crissalbine, occasionally suffering from shivering, headaches and vertigo.

His sputum was negative and he gained weight. He was not improved and died 6 months later.

-----

REACTIONS:

Numerous reactions are caused or have been attributed to gold. In this series the technique employed did not differ from any usual intravenous injection though Mayer (44) has used with considerable success 10% calcium gluconate as a solvent for Crisalbine in place of and to the same extent as distilled water, claiming that it "indubitably diminishes accidents of treatment by gold salts."

Crisalbine is a double thiosulphate of gold and sodium containing 37% of metallic gold. It is a crystalline substance, occurring in "fine white silky needles", easily soluble in water and forming a neutral solution.

Great care was usually taken to prevent any leakage of the gold salt into the perivascular tissues, and if such did occur, an area of infiltration formed which was however rapidly dispersed by the simple expedient of immediate massage and of hot fomentations. In no case did necrosis follow though in one (Case No. 11) an axillary abscess occurred which required surgical treatment. In Case No. 98, a female, the veins were found unsuitable and intramuscular injections of solganol were given. It was found that 20% of distilled water was suitable for dilution according to the dose e.g. 0.05 gm. in 1 c.c.; 0.15 gm. in 3 c.c.; and 0.25 gm. in 5 c.c..

There/



There is hardly any unanimity as regards the real value of the treatment and many believe that some type of reaction must be produced by gold injections if any beneficial results are to ensue.

In most cases the dose did not exceed 0.25 gm. and was not repeated if the effects of the previous injection had not passed off, but the majority of cases show some reaction; in this series 42.2% did not show any reaction at all (no toxicity); though figures of 84% are given by Beaumont and Dodds (16) for cases treated and exhibiting reactions (series of 93 cases).

Møllgaard's original doses were somewhat heroic and many accidents followed treatment (combined also with sera) causing a swing in the reverse direction and most observers now employ small doses (usually commencing with 0.05 - 0.1 gm.) at weekly intervals. Each case however must be judged on its own merits, but the latter method is safer and "thanks to the prudent methods employed, these (accidents) are reduced to a minimum, and cannot in any case offset the benefits obtained". (44).

Mayer (44) claims that accidental and incidental diseases due to gold do not amount to 10% of the cases so treated but most observers put this figure at a much higher level; in this series 57.8% and Beaumont and Dodds (16) give a figure of 55% showing evidences of/

of gold poisoning. The reactions may be attributed to the poison and/or to the liberation of tuberculin-like effects as a result of action on the tissues.

#### FEBRILE.

These reactions which occurred in 50.3% of cases treated, took various forms:-

- (1) rise of  $1^{\circ}\text{F}$  ( $99^{\circ}\text{F}$ ) unaccompanied by any other symptom except occasionally nausea, the same day or evening of the injection, which were given in the morning about 11 a.m. on an empty stomach.
- (2) rise of  $2^{\circ}\text{F}$  ( $100^{\circ}\text{F}$ ) and persisting for 24 to 36 hours and may or may not be associated with headache, malaise and feeling of "out of sorts".
- (3) those cases showing immediate vomiting, shivering, nausea, headache with temperature rise of  $2^{\circ}$  to  $3^{\circ}\text{F}$  (up to  $102^{\circ}$ ) and occasionally prostration.
- (4) A slow temperature rise 2 to 4 days after injection rarely reaching  $100^{\circ}\text{F}$  and falling by lysis. There may be a subsequent rise and appearance of other symptoms e.g. rash and albuminuria.
- (5) Others in which no rise of temperature occurred.

Those cases, with rigors and prostration and with temperature fairly high ( $102^{\circ}\text{F}$ ) and persisting up to one week, did not do well. Most of the cases receiving gold were originally afebrile; and many were up and about/

about during the course for certain hours each day; though it would appear to be safer to confine patients receiving gold to bed for 24 hours at least.

Any intravenous medication may cause a febrile reaction and in the tuberculous subject especially, care and discrimination is required in judging the effects produced.

A slight febrile reaction to 99.6° seems to be of benefit. Control of dosage according to this reaction is more difficult in the acute cases with fairly recent or active disease, and the productive cases on the whole showed less reaction. Actual rigors are not often encountered but call for a reduction usually of the dose.

#### GASTRO-INTESTINAL:

The tuberculous patient is very liable to gastro-intestinal disturbance, even apart from any gold injection; but a definite number of cases do occur with alimentary symptoms as a result of gold injections and take the form of nausea, vomiting and occasionally severe diarrhoea. Under this heading may also be included those cases with stomatitis which occurred in 40.4% of cases treated and ranging from an unpleasant metallic taste causing anorexia to buccal and lingual ulceration causing pain and interfering with food.

Oral/

Oral hygiene and a bitter tonic with temporary cessation of the injections usually allayed these toxic manifestations. Dental treatment is a useful prophylaxis before commencing gold therapy. Small greyish-white vesicles, discreet or in crops, which later become small shallow ulcers, usually develop on the under surface of the tongue and on the buccal mucosa; the patients complaining of soreness of the gums, necessitating cessation of gold for about 10 days. Persistent stomatitis, despite all treatment and lengthening of intervals between doses and reduction in subsequent dosage was usually a sign for withdrawal of the drug. The length of time before the appearance of these symptoms varied considerably, some arise within three weeks and others only after 6 to 8 weeks.

Vomiting may occur immediately or within 12 or 24 hours after injection: in many cases it was associated with nausea and seen most frequently with the higher febrile reactions. It was never severe nor persistent. An adverse influence was noted if the injections were given after a meal.

Diarrhoea was a fairly frequent sign of intolerance, in no case did it fail to respond to treatment and it was never of so severe a nature as to cause weakness and prostration. Under this term was included those cases with stools only somewhat unformed or/



or slightly loose occurring about three times in 24 hours, and by gradation to those cases where there was typical watery stools associated with mucus and frequent up to six times a day. In no case was blood observed in the stools. Cessation of the drug for a variable interval and treatment with Dover's powder in conjunction with a mixture of Bismuth and Tincture of Chloroform soon controlled this distressing symptom.

If the diarrhoea proved intractable - occurring with every exhibition of the drug even in smaller dosage - then complete withdrawal was indicated. These symptoms occurred in 34.6% of cases treated.

#### CUTANEOUS:

These usually took the form of an erythematous, scarlatiniform, or morbilliform reaction; in some cases macular or maculo-papular and urticarial but in no case pustular. Generally the eruption was widespread, irritating in character, and no area exempt. In the more severe forms the facial eruption is associated with severe oedema of the face and eyes and a blotchy appearance. In one case the eyes were completely closed. In two cases (Nos. 5 and 7.) the scalp was affected but there was no loss of hair. In these also a rather severe otitis externa was set up with a purulent discharge and pain over the mastoid region due/



due to post-auricular adenitis. A fine branny desquamation occurred in the milder cases, but in the two cases quoted above there was periodic desquamation of the whole cutaneous surface, including the palms of the hands and soles of the feet. A distressing feature was the alternation between the "wet and oozing" type of exfoliative dermatitis and the "dry and irritating" type. It is stated that there is an increased liability to acute infections during this exfoliative reaction but despite daily bran baths for some weeks no such tendency was noticed. In these cases good nursing is of the utmost importance and they are often very depressed and generally the prognosis should be guarded. They eventually recovered without any scarring or trace of the severe skin reaction. It is interesting to note that during this time the sputum in both became negative to Koch's bacillus but subsequently positive on the clearing of the acute skin condition, and that appendicectomy in one apparently hastened the recovery as regards the cutaneous reaction. As a prophylactic measure gold should not be given where there has been a previous history of skin disease. Various remedies may be tried but very few are of any benefit; with glucose, arsenic, liver preparations, intramuscular injections of whole blood (5 c.c weekly), calcium, and the usual skin/

skin emollients no appreciable result was experienced but sodium thiosulphate (0.5 - 1.0 gm.) intravenously may be given early. A strict milk diet and collosol sulphur by mouth seemed of benefit. Locally silver nitrate for the fissures and aluminium acetate for weeping areas judiciously employed are of value. Stewart Smith (45) recommends Contramine. Both the cases cited above had albuminuria which cleared up after three or four weeks in each instance. There was slight oedema of the ankles in Case No.7 which soon cleared and there was no haematuria or urinary casts.

A rash was present in 25% of the cases, but no case of pigmentation was noted. Pigmentation ("Chrysiasis") may occur as a lilac-blue or slate grey discolouration of the skin in patches where it is exposed to the light. Mayer (44) states that this ultimately disappears; it is due to gold being precipitated in the skin; it resembles argyria and may be permanent. Hansborg (26) states that reddish-blond persons are particularly liable. It may occur with exposure to ultra-violet rays or sunlight.

With the appearance of a rash it is wiser to discontinue gold injections as it is a definite sign of toxicity or idiosyncrasy.

#### ALBUMINURIA:

ALBUMINURIA:

It is more accurate to designate this type of reaction by albuminuria rather than renal as in no case was there any evidence of renal damage as shown by blood or casts in the urine and the albuminuria was transient, clearing up in every instance. It occurred in 13.5% of cases. This figure is much smaller compared with those recorded during the early years of treatment when almost every case showed a positive test for albumin in the urine and may be accounted for to some extent by the smaller dosage employed at the present time. It usually clears completely in 6 weeks at the most; and is often only slight. The severer forms of skin reactions are usually associated. The albuminuria is usually a late manifestation and there is some evidence that intramuscular injections of gold may lessen this form of reaction as well as reduction or a lengthening of the interval between doses. Oliguria occurred in one instance (Case No. 45).

FOCAL REACTIONS:

In early reports of the use of chrysotherapy focal reactions, as evidenced by pain and tightness in the chest, dyspnoea, increase in the amount of sputum, cough and râles, were very prevalent but in this series only 6 cases showed a definite focal reaction/

reaction after commencement of gold injections. This may similarly be accounted for by the reduced dosage now employed.

CARDIO-VASCULAR; MINOR CONSTITUTIONAL DISTURBANCES; ETC.

No case of heart failure or other manifestations such as pulmonary oedema, or syncope were observed. Blood pressure was not affected and no case of agranulocytosis, aplastic anaemia, purpura, leukaemia, excessive leucocytosis or punctate basophilia as mentioned by Witts (46) was noted. They are apparently not accompanied by the usual symptoms of gold poisoning and periodic blood examination should be carried out on patients undergoing treatment by gold. Witts mentions leucopenia and eosinophilia as warning signs. No case of jaundice, enlargement of the liver or pain in the right hypochondrium was observed. Beaumont and Dodds<sup>(16)</sup> mention a case of intractable sweating.

Malaise is usually associated with the injection and/or with the febrile reaction and is of no particular importance.

There was one case of pains in the limbs (No.91), with pain about the right knee joint: in association with cutaneous reactions this may be more frequent.

There was no case of abdominal pain, sore throat or conjunctivitis, delirium or aggravation of night sweats.

Headache/



Headache was very occasionally rather severe but extremely transient and reacting to the usual remedies. There was no general mental depression except where associated with exfoliative dermatitis and no case refused gold; psychologically there seemed to result a certain measure of benefit from the use of the so-called "gold dust". Most cases showed an initial gain in weight (76.2%): in 21.4% there was a loss and no change in 2.4% of cases - all received the benefits which follow the usual Sanatorium treatment. The severer grades of infection (those classified as L<sub>3</sub>S, L<sub>2</sub>S or l<sub>3</sub>S) showed on the whole a more severe type of reaction.

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No.	Sex	Age	(A.P.)	Class	Sputum o/A	Gold Grams	S.P. o/D.	Wt. Tox.	Result.
(1)	F.	18	(L.A.P)	L <sub>2</sub> S	+	7.0	-	Loss S.	(B.)
(2)	F.	25	(L.A.P)	L <sub>3</sub> S	+	1.0	+	Loss R.D.	(N.)
(3)	M.	13	(L.A.P)	L <sub>2</sub> S	+	7.0	-	Gain (F.R.)	(B)
(4)	M.	26		L <sub>1</sub> S + lar.	+	15.35	(+ later)	Loss (F.R.) S	(C.)
(5)	M.	42		L <sub>1</sub> S	+	3.0	+	Loss R.A.	(C.)
(6)	M.	26		L <sub>3</sub> S	+	7.0	-	Gain D.	(C)
(7)	M.	30		L <sub>3</sub> S	+	2.0	+	Loss A.S.R.	(N.)
(8)	M.	18		L <sub>3</sub> S	+	2.0	+	Gain S.R.	(N.)
(9)	M.	32	(R.A.P)	L <sub>2</sub> S	- (+ during)	2.0	-	Gain R.	(N.)
(10)	M.	25		L <sub>3</sub> S + lar.	+	18.05	+	Gain S.O.	(N.)
(11)	M.	34		L <sub>2</sub> S	+	7.0	-	Gain None	(C.)
(12)	M.	20		L <sub>2</sub> S	+	5.6	-	Gain S.D. (F.R.)	(B)
(13)	M.	14		L <sub>2</sub> S	+	7.45	-	Gain None	(N.)
(14)	M.	28		L <sub>1</sub> S	+	6.75	(+ later)	Loss None	(B.)
(15)	M.	18		L <sub>1</sub> S	- (+ during)	7.0	-	Gain (F.R)	(N.)

Class: = Classification: the symbol + indicates Concomitant local lesions followed by a reference to the focus (Philip) (lar: = larynx).

o/A; o/D = on/Admission; on/Discharge.

Wt. = Weight

Tox. = Toxicity

S. = Stomatitis

(F.R) = Febrile Reaction

D. = Diarrhoea

A. = Albuminuria

R. = Rash

An. = Anorexia

V. = Vomiting

(A) = Much improved.

(B) = Improved

(C) = Slight improvement

(D) = Deaths

(N) = No improvement.

No.	Sex	Age	(A.P.)	Class	Sputum o/A	Gold Grams	Sputum o/D.	Wt. Tox.	Result
(16)	M.	26	(L.A.P)	L <sub>2</sub> S	+	7.0	+	Gain S.	(C)
(17)	F	27		L <sub>3</sub> S	+	4.4	-	Gain R.	(C)
(18)	M	21		L <sub>2</sub> S	(+ during)	14.0	-	Loss (F.R.)	(N)
(19)	M	39		L <sub>3</sub> S	+	14.0	-	Loss An.	(B)
(20)	M.	20	(L.A.P)	L <sub>2</sub> S	- (+ during)	7.55	-	Gain None	(A)
(21)	M.	11	(R.A.P)	L <sub>2</sub> S	+	7.0	+	Gain S	(N)
(22)	M.	42		L <sub>1</sub> S	+	3.5	-	Gain rash	(B)
(23)	F.	24	(R.A.P)	L <sub>2</sub> S	+	7.0	-	..... None	(C)
(24)	M.	32		L <sub>2</sub> S	+	7.0	-	Gain (F.R.) S.	(C)
(25)	F.	18		L <sub>2</sub> S+lar.	+	5.75	+	..... D.A.(F.R)	(N)
(26)	M.	35		L <sub>2</sub> S+lar.	+	7.0	.....	Gain None	(B)
(27)	F.	16	(R.A.P)	L <sub>2</sub> S	+	7.0	.....	Gain None	(A)
(28)	M.	29		L <sub>2</sub> S	+	7.0	+	Gain None	(N)
(29)	M.	23		L <sub>3</sub> S	+	13.45	-	Gain R	(D) 1½ years
(30)	M.	25		L <sub>2</sub> S	+	11.45	+	Loss S.D.	(D) 2 years
(31)	M.	33		L <sub>3</sub> S	(+ during)	7.0	+	Gain None	(N)
(32)	M.	26		L <sub>3</sub> S	+	12.9	+	Loss S.D. V.	(N)

..... = No record or stationary; no sputum.

(Note: Minor degrees of Febrile Reaction not included in this Summary)

No.	Sex	Age	(A.P.)	Class	Sp. o/A.	Gold Grams	Sp. o/D.	Wt. Tox. Gain S.	Result
(33)	M.	19		L <sub>3</sub> S	(+ during)	7.0	-	Gain S.	((C))
(34)	F.	30		L <sub>3</sub> S	-	13.5	-	Gain None	((A))
(35)	F.	38		L <sub>1</sub> S	+	6.0	-	Gain S.	((A))
(36)	M.	22		L <sub>3</sub> S	+	9.85 (S)	+	Loss A.S. 1 $\frac{1}{2}$ years	((D))
(37)	M.	21		L <sub>2</sub> S	....	7.15	-	Gain none	((C))
(38)	M.	48		L <sub>2</sub> S	+	14.0	- (+ later)	Loss None	((B))
(39)	M.	23		L <sub>2</sub> S	-	6.0	+	Gain R.	((C))
(40)	M.	28		L <sub>3</sub> S + lar.	+	13.7	-	Gain None	((N))
(41)	M.	32		L <sub>3</sub> S	-	7.0	-	Gain None	((B))
(42)	M.	39		L <sub>2</sub> S	+	8.6	-	Gain R.	((C))
(43)	F.	20		L <sub>2</sub> S	.... (+ later)	9.5	....	Gain None	((A))
(44)	M.	47		L <sub>1</sub> S	-	7.0	-	Gain None	((A))
(45)	M.	32		L <sub>3</sub> S	+	7.0	-	Gain O	((N))
(46)	M.	28		L <sub>3</sub> S	+	7.0	-	Gain None	((B))
(47)	M.	24		L <sub>3</sub> S	-	7.0	-	Loss None	((C))
(48)	M.	38		L <sub>3</sub> S	+	9.5	+	Gain None	((N))

(S) = Solganol B-oleosum.

O = Oliguria.

No.	Sex	Age	(A.P.)	Class	Sp. o/A	Gold Grams	Sp. o/D.	Wt. Tox.	Result.
(49)	F.	19		L <sub>2</sub> S	+	7.0	-	Gain None	(B)
(50)	M.	33		L <sub>3</sub> S	+	7.0	+	Gain D.	(M)
(51)	M.	29	(R.A.P)	L <sub>3</sub> S	+	7.0	+	Loss N.	(N)
(52)	F.	27		L <sub>1</sub> S	+	7.0	-	Gain None	(B)
(53)	M.	29		L <sub>3</sub> S + lar.	-	7.0	+	Gain None	(N)
(54)	F.	23		L <sub>3</sub> S	+	7.0 (S)	+	Loss R.D.	(N)
(55)	M.	19		L <sub>3</sub> S	+	1.5	+	.... D.	(N)
(56)	M.	34		L <sub>2</sub> S	+	7.0	-	Loss None	(B)
(57)	M.	27	(L.A.P.)	L <sub>3</sub> S	+	5.2	+	Gain None	(N)
(58)	F.	19	(L.A.P.)	L <sub>2</sub> S	+	3.7	+	Gain S.V.D.	(N)
(59)	M.	34		L <sub>3</sub> S	+	6.0	-	Gain R.	(C)
(60)	M.	19		L <sub>3</sub> S	+	7.0	-	.... None	(B)
(61)	M.	32	(R.A.P.)	L <sub>2</sub> S	+	7.0	-	Gain None	(C)
(62)	M.	25	(R.A.P.) (L.A.P.)	L <sub>3</sub> S	+	7.0	(+ later)	Loss None	(C)
(63)	M.	27		L <sub>3</sub> S	+	4.4	+	Gain S.R.	(N)
(64)	F.	30	(L.A.P)	L <sub>3</sub> S	+	5.55	-	Gain S. (F.R.)	(C)

N = Nausea.



No.	Sex	Age	(A.P.)	Class	Sp. o/A	Gold Grams	Sp. o/D	Wt. Tox.	Result.
(65)	M.	45		L <sub>3</sub> S	+	3.5	+	..... S	(N)
(66)	F.	28		L <sub>3</sub> S	....	7.0	....	Gain (F.R.)	(C)
(67)	M.	24	(L.A.P.)	L <sub>2</sub> S	+	5.0	+	Gain None	(D) 1½ years
(68)	F.	20		L <sub>3</sub> S	+	1.7	+	Loss (F.R)	(D) 9 months
(69)	F.	43		L <sub>2</sub> S + lar.	+	5.75	+	Gain S.	(N)
(70)	M.	32		L <sub>3</sub> S	+	7.0	- (+ later)	Gain None	(B)
(71)	M.	28		L <sub>3</sub> S	+	3.5	+	Loss D.S.	(D) 11 months
(72)	M.	25	(L.A.P.)	L <sub>3</sub> S	+	6.9	-	..... S	(D) 1¼ years
(73)	M.	42		L <sub>3</sub> S	+	9.86	+	Gain S.	(B)
(74)	M.	36	(R.A.P.)	L <sub>2</sub> S	+	5.05	-	Gain A.D.V.	(A)
(75)	F.	29		L <sub>3</sub> S	+	7.1	-	Gain None	(C)
(76)	M.	30		L <sub>2</sub> S	+	15.25	-	Gain V.	(A)
(77)	F.	28		L <sub>3</sub> S	+	7.92 (S)	-	Gain None	(A)
(78)	F.	30		L <sub>3</sub> S	+	7.0	- (+ later)	Loss None	(C)
(79)	M.	37		L <sub>2</sub> S	+	7.0	-	Gain S.	(N)
(80)	M.	25		L <sub>3</sub> S	+	7.0	+	Gain (F.R.)	(C)



No.	Sex	Age	(A.P.)	Class	Sp. o/A	Gold Grams	Sp. o/D	Wt. Tox.	Result.
(81)	M.	33		L <sub>3</sub> S	+	6.75	+	Gain None	(C)
(82)	M.	23		l <sub>1</sub> S	+	6.85	-	Gain None	(A)
(83)	F.	22		L <sub>2</sub> S	+	13.75	-	Gain None	(D) 3 years
(84)	F.	33		l <sub>1</sub> S (+ during)	-	2.35	-	Gain (F.R.) R.D.	(M)
(85)	F.	13		l <sub>3</sub> S	....	3.0	-	Gain None	(A)
(86)	F.	23	(L.A.P.)	L <sub>3</sub> S	+	9.0	-	Gain A.	(A)
(87)	M.	33		l <sub>3</sub> S	+	5.5	(+ later)	Gain None	(C)
(88)	M.	45		l <sub>3</sub> S	+	2.1	+	Loss R.	(M)
(89)	F.	26		l <sub>2</sub> S	+	6.15	(+ later)	Gain None	(C)
(90)	M.	8		l <sub>3</sub> S	+	3.125 (S)	- (+ later)	Gain A.	(C)
(91)	M.	26		L <sub>3</sub> S	+	14.95 7.0	-	.... D.	(M)
(92)	M.	38		l <sub>3</sub> S	+	(S)	(+ later)	.... R.	(B)
(93)	M.	19	(L.A.P.) (R.A.P.)	L <sub>2</sub> S	+	3.7	+	.... S.	(D) 2½ years
(94)	M.	27		l <sub>3</sub> S	+	5.46 (S)	+	.... N.V.	(M)
(95)	M.	20		l <sub>3</sub> S	+	7.1	-	Gain None	(C)
(96)	F.	21		L <sub>3</sub> S	+	2.5	+	Gain S.	(M)
(97)	M.	35	(L.A.P.)	L <sub>3</sub> S	+	5.3	-	Loss None	(A)
(98)	F.	24	(L.A.P.)	L <sub>3</sub> S	+	7.0 (S)	-	Gain None	(C)
(99)	M.	20	(R.A.P.)	l <sub>3</sub> S	+	7.85	-	Gain None	(C)
(100)	M.	39		L <sub>3</sub> S	-	6.5	-	Gain (F.R.)	(D) 6 months.

RESULTS OF TREATMENT:

Wide divergence of opinion exists as to the relative value of gold therapy in pulmonary tuberculosis: for example Fishberg (47) states that "after a fair trial in various parts of the world Sanocrysin has been abandoned as a therapeutic agent in phthisiotherapy by nearly all of its enthusiastic advocates", and Pottenger (48) does not even mention the drug in treatment; but most European workers and many in this country have stated that it is of value in selected cases, having due regard to its limitations and dangers.

SPUTUM:

One of the most striking effects of Crisalbine is the "power" it has in rendering the sputum tubercle free - this with certain reservations however: this loss of bacillary content is extremely advantageous especially from the public health point of view but it is not in many instances permanent - of those sputum positive on commencing treatment 51.1% had a negative sputum on discharge, but 20.4% of these had a return of the bacillus in the sputum in varying periods from 3 to 15 months after discharge.

Mansell (49) records 45%; Stub-Christensen (50) 43.9% and Beaumont and Dodds 27% (16) but 26% of Mansell's cases were positive again within three months.

TABLE I.

	Sputum on Admission	Sputum on Discharge	Percentage of Cases (94).
(1)	+	-	51.1%
(2)	+	+	34%
(3)	-	+	3.2%
(4)	-	-	11.7%

TABLE II.CLASSIFICATION OF DISEASE AND SPUTUM CHANGE.

Classi- fication.	No. of Cases TB + on admission.	No. of Cases TB - on discharge.	Per Cent. of TB + cases treated losing TB from sputum
L <sub>3</sub> S	10	4	40%
L <sub>2</sub> S	14	8	57%
L <sub>3</sub> S	31	15	48%

More than half (54.5% of those in Group (4) i.e. Sputum T.B. - on admission, had a Sputum T.B + returned during treatment, and 37.3% in Group (2) were T.B - at some time during the treatment.

TABLE III./

TABLE III.

NUMBER OF CASES TREATED AND RESULTS.

Much Improved	13	14.4%
Improved	17	18.9%
Slightly Improved	27	30.0%

Total Improved = 63.3%. (Series of 90 Cases).

DEATHS:

Of the 100 cases treated there were 10 deaths (males 8), but in no case was it directly attributable to gold poisoning, death occurring from 6 months to  $2\frac{1}{2}$  years after treatment and exactly half of these were of the type classified as L<sub>3</sub>S.

TABLE IV.

TYPE OF CASE TREATED AND RESULTS.

Classi- fication.	No. of Cases.	No. of Cases Improved.	Per Cent.
L <sub>3</sub> S	13	8	61%
L <sub>2</sub> S	15	10	67%
L <sub>3</sub> S	32	15	44%

It was apparent throughout the series that the type L<sub>3</sub>S showed the least favourable response to gold, though occasionally very satisfactory improvement resulted. Moreover the A.P. cases were, on the whole, better/



better and the duration of stay in the institution much less. Many observers are agreed that gold is a valuable adjunct in Collapse therapy.

#### WEIGHT:

In the early records a majority of cases showed a definite loss of weight: in this series however there was a loss of weight in only 21.4%; while in 2.4% the weight was recorded as stationary. Pask (52) gives 66% loss in weight (series of cases). With regard to an estimation of the weight, the factors of treatment, rest, diet, sanatorium regime and gastrointestinal disturbances have a decided influence and the results are consequently only relative, and not comparable as no control experimentation was carried out.

#### DOSAGE:

In the majority of cases small doses were used (0.05 - 0.1 gm.) and usually did not reach higher than 0.25 gm. of Crisalbine per dose. There is some evidence to show that the "shock" effects experienced earlier may have been due to overdosage and with this smaller dosage the percentages of various reactions (e.g. albuminuria and cutaneous) are generally less than those recorded earlier with massive amounts, though the use of serum in these may have accounted for/



for some severe types to some extent. A dose which will not affect a healthy adult may have a decided reaction in the tuberculous subject, and the method of administration is important. The smallest amount of drug given was 1.0 gm. and the greatest 18.05 grams. For the hundred cases the average amount of gold per case equalled 6.92 grams. Case No.10 with 18.05 gms. of Crisalbine complained of stomatitis and diarrhoea and there was no improvement (LzS + larynx) and the case of 1.0 gm, (No.2), (LzS) had a rash and diarrhoea with likewise no change in her condition. 7 grams was considered the maximum for any course and an interval, other factors being equal, of at least 3 months should be allowed before commencing a second.

TABLE V. REACTIONS.

52 cases out of 90 (excluding 10 deaths) showed Reactions i.e. 57.8%.

(1) Stomatitis:	40.4%	(including all grades..)
(2) Rash:	25.0%	(All forms)
(3) Gastro-Intestinal:	34.6%	(Diarrhoea chiefly)
(4) Albuminuria:	13.5%	
(5) Febrile Reaction:	50.3%	(All types)

RELATION OF REACTIONS TO IMPROVEMENT:

The total number of cases improved was 57 ((series of 90) i.e. 63.3%; and 40 out of the 57 improved showed reactions i.e. 70.1%.

SEX:/

SEX:

Of the 10 deaths, 2 were females (one aged 22 (L<sub>2</sub>S) ; the other 20 (L<sub>3</sub>S) ).

Of the female cases (excluding 2 deaths) improvement occurred in 18 i.e. 72%.

TABLE VI.

RESULTS IN ARTIFICIAL PNEUMOTHORAX CASES.

A.P. Cases.	Improved.	Deaths.	Sputum + o/A	Sputum - o/D
23	14 (60%)	3	20	12 (60%)

1. DISCUSSION:

Various results have from time to time been brought forward showing the value or otherwise of gold in the treatment of pulmonary tuberculosis and "We are by no means at the end of the chapter. Clinical records do not have the finality of a test-tube experiment, but the fact that Sanocrysin is still in daily use in many institutions after a trial of five years and upwards, is evidence that its advocates have reason for believing in it" (51). The efficacy of the treatment will vary with the observer and is at present personal and clinical, though evidence is slowly forthcoming of a standard of comparison in an assessment of its value by examination of the blood - in this connection the work of Houghton (42) and Pesquera (68) as well as Hughes and Shrivastava (67) may be mentioned; the "leucocyte reaction" is chiefly concerned: in unfavourable cases there is a decrease in the total leucocyte count; a temporary fall in the sedimentation rate is regarded as a favourable reaction to gold and Pask (52) found an average diminution of the rate of fall of the red cells in the test of 18% after Sanocrysin and only 4% in controls (those receiving Sanatorium treatment alone). Oekonomopoulo (74) however states that the Sedimentation Rate shows no/

no difference either prior to or 24 hours after injection. Improvement in the Sedimentation Rate is regarded as a good response to the drug. It has been noted that the rashes were either preceded or accompanied by an eosinophilia; and we may hope that some definite ratio in assessment, dosage, and indications may be forthcoming.

In attempting an assessment of its value the indications for its use must first be set forth:-

(1) INDICATIONS resolve themselves into a consideration to some extent of the (a) type of Disease; cases being usually divided into the exudative or productive types and differences as regards results being noted by many observers. But it appears more satisfactory to employ the classification of Philip, as in this series: lesions in many cases are coexistent and many authorities agree that the fairly recent exudative type of case is likely to benefit to a greater extent, though there seems justification to state that the fibrotic case, generally, does show definite improvement in many cases equal to, if not more than, in the former. Some take into account the differentiation in acute, subacute and chronic types (based on the Temperature) and give figures showing the relative value of the treatment in these types.

Beaumont and Dodds (16) give the percentage of total/

total improvement in the recent exudative types as 73; whereas the fibrotic showed total improvement in 80% and the chronic cases in 92%. These figures are, on the whole, a great deal higher than those usually given; Møllgaard and Lyle Cummins both believe that the best results are given in the exudative type of disease though Pask (52) has obtained good results in cases with fibrosis, bearing in mind the difficulty in the differentiation of the types and that they are often mixed; and Henrichsen and Sweany (53) hold that when fibrous tissue has already been formed little good can be expected.

In this series where the cases have definitely been of either type, this has been stated in the Summary and consequently no figures are given of the relative benefit of different types, but as the classification takes into account both local and systemic factors, it has been possible to decide that those classified as L<sub>3</sub>S or l<sub>3</sub>S do not usually respond well to the drug; 44% of cases L<sub>3</sub>S were improved. Those with bilateral lesions, cavities and marked systemic disturbance were not good subjects for gold though occasionally radiographic evidence of apparent shrinking of the cavities was obtained in those with unsuccessful artificial pneumothorax. Gravesen (54) obtained excellent results in acute freshly spreading disease/



disease and Geoffery Marshall (23) found it unwise to give gold injections in the early stages of tuberculosis and advised waiting for one year, it being of greatest benefit in those cases febrile while at rest but Secher (30) institutes treatment as early as possible and even uses this treatment in tuberculous pleurisy which has however not found favour in this country. Sir Robert Philip (38) also advocates early commencement of the treatment. A "closed" type of lesion is often associated with severe reactions due probably to toxic absorption and it is wiser not to give gold in advanced cases (L<sub>3</sub>S) though it may be tried almost as a last resort in these patients. Good results are reported from Japan (55) in the proliferative or productive type but generally most workers consider the exudative case more favourable provided it is not too acute or too extensive.

The drug is a heavy metal and a poison to the body and should not be used indiscriminately; careful judgment is needed in the selection of cases:- factors of general "make up" or resistance of the patient, his mental outlook, the state of nutrition, the amount of toxæmia or systemic upset, the clinical and radiological evidences of disease and other methods of treatment must be taken into account before deciding on gold therapy. Sometimes it is the only means available at the hands of the physician and probably should/

should not be withheld and may be used tentatively in some cases where other methods of treatment prove of no avail whatever "type" of disease be present.

Stewart Smith (45) states that in agreement with Heaf and Burrell the cases of exudative disease give the best results and that the infiltrative type is also satisfactory though fibro-caseous disease does not respond and fibroid cases improve temporarily.

When some means of estimation of that elusive quantity - the resisting power or capability of "reacting" to stimulation on the part of the patient - is at hand, we may then be in a better position in the selection of cases and the assessment of the value of gold treatment in tuberculosis for at present it is largely a matter of experience and clinical trial and this divergence of opinion will still exist and vary with different observers.

Davidson (57) states that the "most striking results have been obtained in those cases in which the disease is active and of the exudative rather than of the productive type ---- ". Faber(58) in 1925 stated that "some good results may be obtained in old cases of apyretic fibrous phthisis and that the treatment is very effective on fresh pulmonary T.B. that has been manifest less than one year, but Beaumont and Dodds (16) are of opinion that "the recent exudative type of case does not do so well as the fibrotic type and the chronic case shows the best result.

In those cases with an acute almost overwhelming type of disease and no resistance, any beneficial result is not likely to ensue but it may be tried.

The general consensus of opinion is that a cavity is a detriment to good results though in conjunction with artificial pneumothorax treatment, satisfactory improvement may sometimes be obtained.

(b) Gold and Collapse Therapy.

Many results have been published showing the value of gold in conjunction with collapse therapy - the injections may be given before collapse is induced, rendering the "soil" more favourable in clearing up any fairly recent spread on one side in preparation for collapse on the other. It may be given simultaneously to control the contra-lateral lung and Capuani (56) finds it of value prior to induction in bilateral disease, proceeding with collapse if improvement ensues. It may be given some time after induction of artificial pneumothorax, anything from a few weeks to a few months, to control any recent infection in the contralateral side; also before proceeding to bilateral collapse and being continued while this is being undertaken; or to arrest disease already present. Gravesen (54) is of opinion that it arrests the spread of disease in the functioning lung in artificial pneumothorax cases.

Most/

Most observers in this country are of opinion that it is a useful adjunct in collapse therapy and Henrichsen and Sweany (53) state that "there seems to be a real indication for the drug's use as a supportive treatment in collapse therapy when patients are not doing well ---- "

It is wiser not to give gold injections and A.P. refills on the same day as loss of weight may be marked and minor manifestations of toxicity may become aggravated.

Those cases which fail to respond to ordinary Sanatorium treatment after a varying interval and those in whom collapse therapy is unsuccessful owing to adhesions or other cause , should be tried on gold; as should those in which the disease is progressing while under the regime of Sanatorium treatment and in whom an A.P. is deemed unsuitable. It may also be used with advantage in cases of Thoracoplasty and Phrenic Evulsion (Mansell (49) ).

(c) Temperature.

Good results are obtained in those cases febrile at rest, though some use the drug chiefly in afebrile cases. Generally it may be stated that of those febrile even at rest, the higher the temperature on commencing injections, the least satisfactory will the result be and the more likelihood of severe reactions/



reactions developing: with care a temperature of 100° F is not necessarily a contraindication and the drug may be used in both cases - with temperature or afebrile - if discrimination is exercised in the selection of cases.

(d) Economic Factor.

In those cases in which the economic factor is of importance, gold may be used to expedite the ordinary routine treatment and the time-period of institution stay is shortened. This "speeding up" of cases may be resorted to but is generally not to be recommended and is often unnecessary. The raising of a "hospital type of case" to the "Sanatorium level" is a factor sometimes stated to influence the use of Chemotherapy though most cases are now chiefly treated at a Sanatorium.

(e) Public Health.

Those cases where the general condition is improving but still with a sputum positive for Koch's bacillus may be tried on gold. From the Public Health standpoint this is eminently desirable but unfortunately in the majority of cases this bacillary loss is not permanent.

It is unlikely that treatment will be undertaken on a very large scale - it is expensive - and its indiscriminate/



indiscriminate use may be fraught with danger. Its use should generally be confined to Institutions where the results of treatment may be constantly watched and is not a drug that should be used indiscriminately by general practitioners as it requires constant supervision. In special circumstances the drug may be administered intramuscularly by others but only under strict supervision and control by the central authority.

(f) Mental and Psychological.

Occasionally cases occur where some "impetus" is required especially with regard to the mental outlook and in this Crisalbine may be given for its psychological effects - patients often "settling down" and feeling that something active is being undertaken in their particular case - none refused the so-called "gold dust" and some were even anxious for a repetition of the course.

It would appear that physiological factors are more important in deciding the indications for gold therapy than the "exact" anatomical state of the lesions. It should be based more on the individual - on his reactive capacity.

(2) CONTRAINDICATIONS.

It is wiser not to give gold in cases of myocardial and renal lesions: in cardiac cases with compensation and in cases of Hypertension with secondary effects on the heart and kidneys; also in cases of permanent renal damage with nitrogen retention, albuminuria and casts; in urinary infections (pyogenic) the drug is also contraindicated.

Careful consideration before employing the drug is required in cases with a previous history of cutaneous disease, e.g. dermatitis from any cause especially if extensive and in any cases with evident manifestations of the "allergic diathesis", e.g. hypersensitiveness to drugs and foods. It has been used in Lupus however with some benefit.

It should not be used in cases with Hepatic disease as shown by infection, jaundice or cirrhosis though Mollard (50) believes hepatic disease is not necessarily a contraindication.

It is unwise to employ Crisalbine in severe T.B. ulceration of the larynx; in those cases with high fever and in any cases of severe anaemia or blood dyscrasias as evidence is accumulating of delayed toxic effects as shown by purpura, agranulocytosis, etc. (Witts (46) ).

Cases of gastro-intestinal disturbance of any severity/

severity should make one extremely cautious in the employment of the salt. It may also aggravate any existing ocular disease - from slight hyperaemia or conjunctivitis a T.B. ophthalmia may be produced (Lyon (39) ).

In this series some of the cases did complain of hoarseness with tuberculous involvement of the larynx, yet no case showed any aggravation of the condition when given gold injections and some were benefitted combined with rest (silence).

Sebök and Horwath (59) however report good results as does Schröder (34) in laryngeal and ocular tuberculosis.

Gold Therapy in pulmonary tuberculosis should not be used indiscriminately and remains a treatment which should be confined to specialised institutions.

If other treatment proves wholly adequate - sanatorium, tuberculin, or collapse therapy, gold need not be given.

In cases of cachexia and wasting diseases gold therapy should not be instituted; similarly in amyloidosis. The treatment is expensive and recently an insoluble bismuth preparation has been used in conjunction with gold, rendering the cost less and showing favourable results.

Divergence of opinion exists as to indications in renal or intestinal tuberculosis, Hacker (60) stating that it is contraindicated.

Each/

Each case is to be judged individually and Secher (30) has stated that "an advanced stage is a contra-indication to Sanocrysin, as the patient will be unable to stand the intoxication produced by the treatment". No hard and fast rules can be laid down regarding the "type" of disease as forming a contraindication:- the patient, his resistance and reactions must be noted and treated.

### (3) PROPHYLACTIC MEASURES.

Prophylactic measures consist in securing an adequate history apropos of any pre-existing skin disease and any known idiosyncrasy to drugs, exercising consequently extreme caution in the exhibition of Crisalbine to these cases. Preliminary dental treatment and strict oral hygiene are useful measures. Examination of the urine should be carried out prior to using gold and thereafter daily examinations for the presence of albumen. If albuminuria be present a further dose should not be given till the urine is free.

In one case in this series associated with pregnancy no deleterious effect was noted on the kidneys with gold; the child was normal and there was no activation of the disease and Mayer (44) records two deaths/



deaths in a series of 36 cases of gold treatment and pregnancy - death resulting from acute evolution of the disease post-partum. It would appear that periodic blood examinations may be a useful measure in recording the results of treatment or indicating over-dosage.

#### (4) DOSAGE AND REACTIONS.

There has been almost from the inception of the "modern" therapy, two schools of thought and practice - those advocating the larger doses of 0.5 gm. - 1.0 gm., very frequent in the earlier years from 1924, but in 1927 Sir Robert Philip (38) stated that "the principle and scale of dosage recommended by Mollgaard and his colleagues require revision", and suggested that the intramuscular method of administration may be more advantageous than the intravenous route, and most workers nowadays employ much smaller doses and claim less toxicity as a result. Secher (30) is convinced that better results are obtained by giving large doses and has been the last worker to abandon serotherapy used in conjunction with chrysotherapy. Most workers are convinced that those with reactions show a greater improvement and it appears advisable that if this can be secured equally well with smaller doses there is less risk to the patient; and Heaf (62), Burrell (63), Clarke (64) and/



and Permin (65) advocate a "middle path" in dosage - between the high doses of Secher and the minute doses of 0.0001 gm. sometimes given; but each case should be judged individually; no rigid scheme should be adhered to; dosage depends on the patient, his resistance, and the reactions induced: it is wiser to commence with a dose of 0.05 - 0.1 gm. gradually increasing this, other factors being equal, to 0.5 gm. at weekly intervals which may be increased to fortnightly injections with less symptoms of intolerance or with less severity of these manifestations.

Any marked reactions should be avoided if possible and a subsequent dose should not be given till the effects of a previous injection have passed off. There is risk of storage and it is better not to exceed 7.0 grams in one course. Witts (46) attributes most of the ordinary reactions (e.g. albuminuria, stomatitis, diarrhoea and erythema) to overdosage; and on the evidence of blood changes, particularly the monocyte-lymphocyte ratio, small amounts, 0.1 gm., have been found as efficacious as larger doses (0.75 gm).

During a course of successful treatment an increased tolerance undoubtedly comes into play: this has been noted by the earlier workers: "in regard to the various (toxic) symptoms, the tendency to development increases with successive doses up to a maximum/

maximum and thereafter a decline occurs" (Lyon (39) ).

Secher (66) has stated that reaction following gold greatly activates the cure and believes gold causes a liberation of toxins which account for all the reactions produced and Sayè (70) divides reactions into three types: focal, (single rise of temperature, fleeting erythemas), those due to metallic intolerance (gastro-intestinal upset, dermatitis, persistent albuminuria) and lastly those which compel cessation of treatment - repetition or multiplicity of intolerance symptoms due to metallic saturation.

Not only is there no unanimity regarding its value after 12 years but also none regarding its action and the causation of reactions; the conception of its bactericidal power and the tuberculin effect from the dead bacilli have apparently been disproved (53). The toxic effects are apparently to be regarded as due to metallic poisoning in whole or in part but this simple statement will not entirely suffice - the poisonous effect of reabsorbed tuberculous tissue products may to some extent be a causal factor. A knowledge of the rate of excretion after an initial dose of gold is of distinct value in selecting those patients who may be expected to tolerate this drug (Stanbury (69)) and various methods of micro-analysis have been developed.

When used, it should be given in small dosage and effects carefully judged and controlled as far as possible/

possible. "In each individual patient there is an optimum scale of dosage which must be arrived at partly by a correct appreciation of the patient's condition and partly by the method of trial and error" (Lyle Cummins (23)).

Gold is apparently excreted both by the kidneys and intestines, the relative proportions varying with the different preparations employed. Fischer (79) found Sanoecrysin particularly toxic to the kidneys and Solganol more toxic to the intestines.

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(5) RESULTS OF TREATMENT.

Here again we find wide variations for many workers have recorded favourable results in varying percentage and some even "cure", and unfavourable reports are much in the minority. Thus the Japanese Commission (55) found 51% of cases improved by gold and 26% made worse; Koch (66) reported 62% as improved from the results of a large number of investigators and Lyle Cummins' (23) own experience with the drug has been definitely favourable and Secher (30) regards Chrysotherapy as the "best remedy that we have at the present time" and believes "that its use will mean recovery for many patients who would otherwise be without hope and considerable curtailment of the course of the illness for many months". Recently Lawrason Brown (71) stated that "the only hopeful result from Chemotherapy so far has been the gold salts. In certain instances they have been found helpful". An abstract of the late Professor Leon Bernard's paper at the Ninth Conference of the International Union against Tuberculosis in September 1934 (Hewat (72)) shows that "Gold Therapy has also proved its value. According to the author's latest personal statistics, this treatment brings about a clinical cure in 10-12% of cases and a favourable result with the social rehabilitation of patients in 51.6% of cases".

It/



It must be used with care and discrimination: large doses may in advanced cases surprisingly quickly cause disaster as in the earlier records of the treatment when the British Research Council reported 2 deaths in 30 cases and later 1 in 140 cases (77). There were also miraculous reports of the disappearance of encysted pelvic and peritoneal tuberculous fluids. At the International Congress on T.B. at Washington in 1926 it was stated that "Sanocrysin Therapy (23) was already dead", and in the United States generally opinion is against its use except with workers such as Henrichsen and Sweany: "Sanocrysin seemed to be the only form of gold which had not found its way into the States in large quantities during the last 10 years" (Dunlop (80) ).

Anderson, McMahon and Pinner (75) also found no advantage in a controlled series and Stephani (78) states that its use does not justify the risk entailed. MacNalty (76) has written that "the clinical results indicate that Sanocrysin is a form of treatment in Tuberculosis that is of limited application and which can only be given to carefully selected cases under constant medical supervision, and with due appreciation to its risks and contra-indications".

Peters and Short (73) in a statistical study (5 years) of gold treatment of Tuberculosis conclude that it is of no appreciable value, but Lyle Cummins believes/



believes that the risks and difficulties of the treatment have been exaggerated, and is a valuable adjuvant in the management of Tuberculosis.

There is also controversy over experimental work in animals and it is hardly surprising that we find such variations in clinical results for these must for the present remain a relatively personal matter. It was "brilliant with promise at its beginning" but has not fulfilled the great expectations it aroused and there seems "little justification for the use of Sanocrysin as a placebo". "We are not however justified in withholding the gold salt from those types of cases to which in the past its use has been associated with definite improvement". (Kayne (70)).

#### RADIOLOGY:

There is also difference of opinion regarding the interpretation of the radiological findings - whether the fibrosis often seen is in reality due to gold. Davidson (57) states that improvement has been accompanied by "definite radiological evidence of resolution and fibrosis". A series of reduced radiographic prints have been included and the majority show some evidence of fibrosis or clearing of the lung fields, and if we regard the treatment as a "Stimulation" therapy, we should apparently regard these findings as due to the action of gold, though it is equally true that some cases will show fibrosis in/

in the lung fields with ordinary routine sanatorium treatment alone.

Some observers treat ambulant cases and employ the facilities of the Tuberculosis Dispensary in this respect. These cases will vary with the patient himself and while there is apparently no great contra-indication to this type of treatment being instituted, having regard to the patient, his resistance and reactions, it would be wiser and safer to institute and continue treatment under complete supervision in a Sanatorium. If treatment as out-patients is undertaken, these cases will always be in the minority.

The ultimate difficulties of the treatment resolve themselves into a consideration of the structure of the bacillus - its fatty envelope - and the difficulty of securing penetration of this by medication; the structure of the tubercle - its avascularity - and the difficulty of reaching this by intravenous medication. The substance should be capable of diffusing through animal membranes at a greater rate than it is excreted by the body: it should have a maximum effect on the disease and a minimal action on the body as a whole.

The use of gold in pulmonary tuberculosis is still a highly controversial subject: a review of the literature shows that no unanimity has been reached regarding/

regarding its value even after 12 years, but there is a fairly large amount of clinical evidence in favour of its judicious employment in selected cases and that it should generally be included in the armamentaria of the Physician in his fight against Tuberculosis.

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SUMMARY AND CONCLUSIONS:

- (1) A survey of 100 cases and critical exposition of the literature has been undertaken.
- (2) Improvement was noted in 63.3% of cases of which 30% were slightly improved and 14.4% much improved.
- (3) Indications, contraindications, prophylaxis and the ultimate difficulties of the treatment have been discussed:
  - (a) Crisalbine may be given to cases pyrexial or apyrexial, not improving or stationary with sputum still positive for Koch's bacillus and undergoing routine Sanatorium treatment.
  - (b) it is useful in conjunction with collapse therapy, where an artificial pneumothorax is contemplated or has been induced to control disease in the contralateral lung.
  - (c) it may be used in both the exudative and productive type of case.
  - (d) it may be used where other treatment has proved unavailing; and where the time or economic factor is important.

(4)/



- (4) It is not a "cure" but is of value as an adjuvant in the treatment of Pulmonary Tuberculosis: its limitations and dangers must be recognised.
- (a) It produces evidences of Toxicity in 57.8% of cases.
  - (b) It is contraindicated in associated cardiac, renal or hepatic disease.
  - (c) Good results are not generally obtained in advanced cases of pulmonary tuberculosis.
  - (d) It will not replace other tried methods of treatment and is generally not required where other methods are satisfactory, but may be used in conjunction with these.
- (5) It is of limited value; a few selected cases show good results; a fair percentage are slightly improved and life prolonged, and no case of death was directly attributable to Crisalbine. It will not save life.

There is little, if any, value in the drug in uncollapsed cavities.

Each case must be judged on its own merits: the dose should be small (0.05 gm.) ; gradually increased; reactions should be carefully studied.

- (6) There is no proved experimental basis for its use in Pulmonary Tuberculosis.

Its/



. Its precise action in the human body is unknown: it is more a Stimulation Therapy than a true Chemotherapy.

- (7) Its value from a public health standpoint has been discussed: the bacillary loss of sputum is not generally permanent. It must still have a limited sphere and cannot be generally employed by all.
- (8) Results are based on clinical values; immediate and remote results are difficult to judge and often prove rather disappointing.
- (9) It is possible that remote reactions caused by gold may have a wider effect than is at present generally realised: there is also evidence that examination of the blood cells may afford a standard for the assessment of its value in this disease.
- (10) It is still a highly controversial subject; there is hope that a substance related to this gold compound, having a minimal effect on the human body, may yet be forthcoming.

It should not be withdrawn from clinical use, and should be employed with due regard to the resistance and reactions of the patient in certain/

certain selected cases. It should have a place in the armamentaria of the Physician in his fight against Tuberculosis.

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