THE THERAPEUTIC EFFECT OF COLLOIDAL MANGANESE IN CHRONIC PSORIASIS.

A Thesis

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By

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CHAPTER I.

OBJECT AND SCOPE OF THE INVESTIGATION.

In recent years numerous investigations have been made regarding the influence of Manganese on Psoriasis.

The results have been extremely contradictory, and varied from bad to brilliant. On the whole, however, it appeared that the administration of manganese was not sufficient without local therapy.

It is a familiar fact in the treatment of chronic cases of psoriasis that local applications, which have had a very favourable effect on the eruption, may a few months later give but little relief to the patient. The general condition of the patient has not apparently changed and the eruption has much the same appearance as before. Yet, due to some factor of which we are ignorant, the skin appears comparatively insensitive to topical therapy.

I have suffered from psoriasis myself and was impressed with the efficacy of manganese therapy by personal use. I therefore set out to inquire into its effects in

a series of cases of chronic psoriasis.

From previous reports it was hardly possible to consider manganese as a specific for psoriasis. The scope of my investigation was accordingly limited to two points:-

1. Does the administration of manganese to cases of chronic psoriasis consistently render them rapidly amenable to local treatment;

2. Does manganese prevent or retard recurrences of psoriasis.

CHAPTER II.

PHARMACOLOGY AND TOXICOLOGY OF COLLOIDAL MANGANESE.

Pharmacology.

Manganese, first discovered by Scheele, was isolated in pure form by Guhn in 1807. Von Schroeder in 1878 found it in the ashes of pine needles and bark. Since then a number of observers have reported its wide distribution in nature. Bertrand and Rosenblatt determined the amount of manganese in plant tissues. They found a much greater proportion was present in the green leaves compared with the faded ones, and came to the conclusion that manganese had an inseparable connection with the process of oxidation.

Bishop confirmed these findings, and in flowers found the highest proportion in the reproductive organs. He concluded there was a connection between manganese and the formation of chlorophyll.

Von Oettingen, in a survey of the literature, is of the opinion that manganese has an important function in plant metabolism, particularly in increasing the oxidase reaction.

Manganese appears to be a normal constituent of animal tissues. Its presence in blood was first discovered by Marchessaux. Bertrand and Medigreceanu estimated 0.2 mgm. to be present in 1,000 ccs. of blood. The plasma contained twice as much as the cells. The greatest proportion, however, is found in the liver, and Reiman and Minot found .17 mgm. per 100 gms. of wet tissue. According to Vairel a considerable proportion is found in the skin in rats, and this is increased compared with other tissues when additional manganese is added to a normal diet. Herrmann found that in man injections of manganese were followed by considerable increase in the residual ash of the skin and concluded that manganese was deposited in the skin.

When administered orally very little is absorbed and whether given orally or by injection it is chiefly excreted by the intestinal tract.

It has been claimed that manganese is an essential constituent of the blood, but the work of Waddell, Steenbock and Hart suggests that its influence on the synthesis of

haemoglobin is almost negligible.

McCarrison in 1926 reported that manganese had a favourable effect on the growth of rats. If, however, the dose was increased beyond .037 mgm. daily growth was retarded. Kamimura also found that large doses had a stunting effect on the growth of bone. Kemmerer, Elvehjem and Hart confirmed the views of McCarrison. On the other hand, Orent and McCollum found that on a manganese-free diet young rats grow to maturity in an apparently normal manner.

Relationship with the Ductless Glands.

Kemmerer, Elvehjem and Hart found that the absence of manganese from the diet prevented normal ovulation in the mouse, and Skinner, Van Donk and Steenbock reported that manganese decreased the time taken to reach sexual maturity and its absence affected the oestral cycle.

On the other hand, according to Orent and McCollum the oestral cycle of rats on a manganese-free diet was normal but the females failed to suckle their young. The male rats suffered from testicular degeneration which finally went on to complete sterility. They suggest as a hypothesis that manganese is concerned with the production of a hormone by the anterior lobe of the pituitary which is essential for the functioning of the testis and the mammary tissue.

Daniels and Everson, however, suggest that there is no failure in function of the mammae but rather a congenital weakness of the offspring so that they are too feeble to suckle.

Relationship to Body Ferments.

Katsunuma found a constant relationship between the quantities of manganese and oxidase in the tissues. He concluded that manganese, due to its power as an oxygen carrier, acted as a catalyst. Pautrier and Laumonier found the oxidase action increased after the administration of injections of manganese.

Gigon and Rosenberg report that manganese promoted the action of serum amylase and serum lipase, and Magnus found that it had a favourable effect on pancreatic lipase. According to Harpuder it aided the action of such proteolytic ferments as pepsin and trypsin, while Hamamato found that it increased the action of the glycolytic ferments carboxylase and lactodehydrogenase.

From the investigations of Piaux it would appear that manganese increases the rate of oxidation of uric acid in the body and Warburg found that it has a similar effect on cystein.

Relationship to Vitamins.

Guha and Ghosh found that parenteral administration of mannose produced ascorbic acid in rats chiefly in the liver. This was denied by Hawthorne and Harrison. But Rudra repeated the experiments of Hawthorne and Harrison but with this difference that the mannose contained .2 per cent. of manganese chloride. His results were then in agreement with Guha and Ghosh and he concluded that manganese is a determining factor in the synthesis of ascorbic acid by rat tissue.

Hamamato, from experiments on pigeons, was of the opinion that manganese had a prophylactic and therapeutic action in B_1 avitaminosis.

The Colloidal State.

A colloidal solution of a metal has an advantage in that the metal is permanently and evenly distributed through the solution.

Bayliss does not think that a metal administered in a colloidal state owes any part of its action either to electrical charges or to "surfaces". He points out that in the dilute solutions used these are insignificant compared with those that already exist in the protein systems of the blood and tissues.

The mode of action might be the ordinary action of the metal. Apart from a few free ions this, of course, is inert. But a change from a colloidal to an ionic condition can occur from various causes, e.g. bacterial action. As this occurs slowly the action of the metal would be exerted with a minimum of irritation. On the other hand, the action itself would be slight. The other possibility is that as the colloidal state gives the metal catalytic properties very small quantities of the metal might induce considerable reactions in other substances although it itself took no part.

Toxicology.

The toxicity of manganese varies for different salts. Kobert found that six to eight mgms. of MnO injected subcutaneously killed a dog in two days.

In monkeys after prolonged administration of manganese chloride Mella found on autopsy acute hepatitis and degenerative changes in the basal ganglia. The only post mortem on a human being was reported by Casamajor who found degenerative changes in the medulla and biliary cirrhosis.

Toxic symptoms from manganese are, however, fairly common among industrial workers. The symptoms are muscular weakness, a stiff clumsy gait, tremor, blurred speech and a mask-like expression and mental dullness. As Stoecker has pointed out there is remarkable resemblance to the clinical picture of progressive lenticular degeneration.

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CHAPTER III.

POSSIBLE MODES OF ACTION OF MANGANESE ON PSORIASIS.

Theoretically there are several ways in which manganese might influence psoriasis, depending of course on what we regard as the nature of psoriasis.

Thus Moore advanced the view that psoriasis was the result of a staphylococcal infection, and manganese exerted the same action as it did in furunculosis. Convincing bacteriological evidence to support this theory has not, however, been produced.

The view that retention of uric acid is a deciding factor in the development of psoriasis has been advanced by Le Coultre. He bases his conclusion on the following experimental observations: (1) all psoriatic patients he examined had an increased percentage of uric acid in the blood; (2) a decrease in the amount corresponded with improvement in the lesions. This explains the contradictory reports of others as they examined patients in

varied stages of the disease. (3) There was a marked increase of uric acid up to as much as 100 per cent. in the skins of sufferers from psoriasis. (4) He treated the patients with alkalies and the amount of uric acid decreased and the skin lesions improved.

If this theory is correct then manganese might have an effect by oxidising the uric acid as Piaux proved it capable of doing. Evidence to confirm Le Coultre's theory, however, has not been forthcoming and one cannot help feeling that if he were correct psoriasis would be much more amenable to treatment than it is.

As has been mentioned, manganese stimulates the action of both serum lipase and pancreatic lipase, and thus might exert a curative action on psoriasis providing the theory of Grutz and Burger is correct. According to their experiments the blood cholesterol in cases of psoriasis was increased up to 51 per cent. above the normal and they considered this to be the cause of the disease. Their results have been strongly disputed. Rosen, Rosenfeld and Krusnow actually reported a hypocholesterol-aemia in psoriasis and Madden in a large number of cases found the blood cholesterol in psoriasis about normal. Madden did, however, consider a fat-free diet beneficial,

but the work of Grutz and Burger is not generally accepted as correct. My own personal experience of a fat-free diet was very discouraging, nor have I seen any patient benefit.

A rather remotely possible mode of action depends on the suggestion by Orent and McCollum that there is a connection between manganese and the pituitary as the view has been advanced that the cause of psoriasis might lie in defective action of this gland. Gruneberg has reported favourable results from the use of a corticotropic hormone in a series of cases. No conclusive results have, however, been reached.

The question of psoriasis being a deficiency disease has been investigated in recent years. The work of Rudra in showing that manganese was a determining factor in the synthesis of ascorbic acid has already been mentioned. So that if psoriasis was caused by vitamin C deficiency another possible mode of action of manganese is suggested. In that case, however, the administration of vitamin C would produce striking results and Gruneberg reports absolute failure in a series of cases.

The most probable view as to the mode of action of manganese is advanced by Bohnstadt. He believes that colloidal manganese acting as a catalytic agent increases fermentative oxidative processes in the epithelial cells.

This conception is supported on the following strong theoretical grounds:

1. It has been shown by Von Kerchoff that the epithelial cells of the psoriasis papule constantly show a decrease in their oxidative function.

2. The close connection between manganese and the process of oxidation has been established by the work of Bertrand and Rosenblatt in plants.

3. As has been already mentioned Katsunuma and Pautrier and Laumonier found experimentally that manganese stimulated the action of oxidase.

4. The work of Hermann has established the fact that manganese is deposited in the skin after injection into the body.

5. Warburg, whose work was later confirmed by Bohnstedt, excised sections of skin from psoriatics who had been treated with manganese. The skin was suspended under anaerobic conditions in glucose saline. In five out of six cases there was an increase in the formation of lactic acid due to the increased oxidation power of the epithelium.

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CHAPTER IV.

RESULTS OF PREVIOUS INVESTIGATIONS.

Colloidal manganese was first used by James Moore in the treatment of psoriasis. He was treating two patients with furunculosis by injections of manganese. Both were in addition afflicted with psoriasis and he noticed that in one case the psoriasis cleared up after four injections and in the other after eight injections. He then treated a total of 35 patients. He gave two doses of ½ cc. colloidal manganese with a four day interval and then a weekly injection until the eruption disappeared. He concluded that psoriasis may be cured by six to sixteen injections of colloidal manganese without any local treatment.

The next investigation was made by Richter. He used a manganese preparation called Psormangan. He gave injections twice a week of 1 cc. gradually increasing the dose to 4 ccs. for a total of ten to sixteen injections. He used no local application and obtained excellent results

in twenty out of twenty-six cases.

Schmidt treated eleven patients in 1931 with a series of fifteen to twenty injections. None were cured until after the addition of local therapy. The lesions did, however, respond more rapidly to Chrysarobin than they had done before. Schmidt used Psorimangan and several of his patients had severe general reactions and local pain after the injections. He considered that increased oxidation made the lesions more sensitive to Chrysarobin, but owing to the severe reactions did not consider colloidal manganese suitable for routine therapy.

Abramson in 1931 treated twenty patients with Psorimangan combined with local therapy in the form of ½ per cent. Cignolin salve. He had no severe general reactions, but never used a bigger dose than 3 ccs. whereas Schmidt used as much as 4 ccs. He concluded that the results of combined therapy were much superior to local treatment alone.

Two months later Szego and Von Luka reported their results after treating 27 patients who received 12 to 16 injections in doses of ½ cc. to 2 ccs. All their patients had local therapy. Sixteen were completely healed and eight partly healed. Three remained refractory. The lesions began to clear after six injections and the time required for their disappearance was two months less than with local

treatment alone. Nine months after treatment there was no recurrence in any of the 16 who were cured, but there were fresh eruptions in two out of the eight who were improved. In both cases these disappeared after a few more injections. The authors concluded that "the comparatively great number of cures as well as the absolute margin of safety of the treatments assure to Psorimangan an important role in the battle against psoriasis."

Bohnstedt found intramuscular injections too painful and resorted to the intravenous route. Of 31 patients, 21 were treated locally with ammoniated mercury in addition to the manganese. Eight were cured and seven slightly improved. Six showed no benefit. Of ten treated locally with ugnolin in conjunction with injections only one got better more rapidly than was usual with ugnolin alone. In no case was a recurrence of the disease delayed. Bohnstedt did not regard the results as favourable. Richter reviewed the literature on the results of the manganese treatment of psoriasis. He considered that the superior results obtained by himself and others with intramuscular as compared with intravenous injections might be due to a slow continuous absorption from the intramuscular deposit. He stressed the fact that as with arsenic the

optimum dose for each patient must be found. He concluded that manganese alone was effective in the treatment of psoriasis, and that when combined with local therapy it appreciably shortened the period of treatment and permitted much milder local applications to be employed.

Fruend and Ravalico treated 18 patients with intramuscular injections of manganese dioxide. Eleven were healed and three improved. Four were unaffected. They obtained a better and quicker response when the injections were combined with local therapy.

Geyer and Wesener, on the theory that with other methods of treatment improvement occurs in psoriasis in about three weeks, observed patients who had had manganese injections at this period. Seven were improved and ten no better. In general they concluded that improvement was not more rapid and remissions no longer than with other remedies. They concluded that there was no particular advantage in manganese therapy.

Bowden gave injections of manganese to 34 cases of psoriasis. Sixteen to 24 injections were given over a period of two to three months. The initial dose was $\frac{1}{2}$ cc. and this was gradually increased to 2 ccs. Twenty seven were completely cured and the remaining seven were improved.

Barr in 1935 gave a detailed report on seven patients treated with intravenous injections of manganese chloride and calcium chloride in normal saline. Five were cured and two were improved, without any local therapy. Three remained clear for over a year. There were no severe reactions. Barr stated that he had used this preparation for two years and of 95 cases 68 per cent. showed total improvement and 21 per cent. partial improvement. He concluded that manganese chloride was the most effective remedy available for the treatment of psoriasis.

Niles treated 72 cases with a weekly injection of 1 cc. colloidal manganese. Thirty four were improved. Thirty three showed no improvement and five were not determined. Only two of those improved were completely cured, and one of these had a recurrence in three months. Fifty two of the cases were treated with Boric ointment only as a local application. Eleven used an active ointment while five used boric ointment for a time and later on a more active preparation. Four had no local therapy. The manganese did not appear to enforce the effect of active external treatment as the results were poorest in these cases. Niles concluded that while results were occasionally good the treatment was too long and too uncertain to be valuable. Further, he found no evidence that it prevented

or delayed recurrences.

Oliver and Crawfurd treated 125 patients with colloidal manganese. They had 125 patients as controls. An average of twenty injections was given, with a total dose of 30 ccs. of manganese. Local treatment varied but all had at least Paraffin mollis. After six months 8 per cent. of the treated group were completely clear and only 1.6 per cent. of the controls. Thirty one per cent. of the treated group were 75 per cent. clear compared with six per cent. of the controls. Twenty six per cent. were 50 per cent. clear compared with nine per cent. of the controls.

At the end of 18 months 20 per cent. were absolutely healed. Three quarters of these, however, were patients who had continued active external treatment along with the injections. On the other hand, these local measures had not been effective until the manganese therapy had been started.

No unfavourable reactions were experienced by any of the patients and the authors concluded that manganese was of definite value in the treatment of psoriasis especially if it is combined with local treatment.

It must be pointed out, however, that when they say 20 per cent. were completely clear after 18 months they mean

20 per cent. of those patients still attending at that time. A number of patients had defaulted, and as these would probably consist largely of those discouraged by lack of improvement 20 per cent. cured is possibly an over optimistic result.

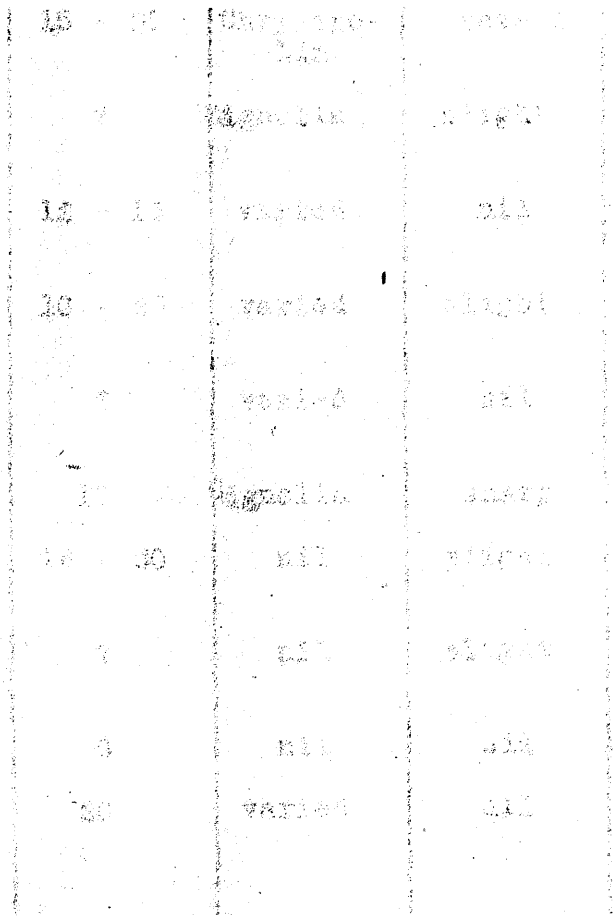

Table of Results obtained by Various Authors.

Author	No. of Patients	No. of Injections	Local Treatment	Reactions	Results
Moore	37	6 - 16	nil	nil	All cured
Richter	26	10 - 16	nil	slight	Excellent in 20
Schmidt	11	15 - 20	Chrysarobin	severe	Nil with injections alone
Abramson	20	?	Cignolin	slight	100% cured with combined therapy
Szego & Von Luka	27	12 - 16	varied	nil	10 cured 8 improved
Bohnstedt	31	10 - 20	varied	slight	9 cured 7 improved
Fruend & Ravaliso	18	?	varied	nil	11 cured 3 improved
Geyer & Wesener	26	10	Cignolin	sharp	7 improved
Bowden	34	16 - 30	nil	slight	27 cured 7 improved
Barr	95	?	nil	slight	68% cured 21% improved
Niles	72	9	nil	nil	36 improved
Oliver & Crawford (after 18 months)	125	20	varied	nil	20% cured

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CHAPTER V.

THE PRESENT INVESTIGATION.

The plan proposed in the present investigation was to administer an average of 25 ccs. of colloidal manganese to about fifty cases of psoriasis. Controls were not used, but recent cases of the disease were avoided and the patients were all chronic sufferers from whose previous history it was possible to form some estimate of the value of the treatment.

In view of previous reports all the patients used some local application. This consisted of a weak tar and salicylic acid ointment. In the majority of cases the patients had been using an ointment of this type prior to the commencement of manganese injections. In my own case as I had been in the habit of using Cignolin I continued to do so.

The initial dose was 1 cc. of colloidal manganese and thereafter 2 ccs. were injected at weekly intervals. An average course lasted 13 weeks, with a total dose of 25 ccs.

Details of the cases are as follows:-

Case No. 1. A.M.S.(self). History of psoriasis of 15 years' duration. Maximum period of remission three months. From 1933 to 1938 there had been no complete remission.
Family History: Nil.
Effect of Sunlight: Beneficial.
Extent of Disease: Involvement of scalp and trunk.
Local Treatment: Chiefly agnolin ointment. Over a period of three months 25 ccs. of colloidal manganese were injected in the spring of 1938. Complete cure was obtained and no further lesions appeared for three months. The eruption then began to slowly appear but did not reach its former severity and reacted favourably to Cignolin in the spring of 1939. After three months remission it re-appeared and no local treatment made any impression. After 4 ccs. of colloidal manganese had been given there was a marked improvement and the lesions were completely healed after a total of 16 ccs. had been injected. After four months there was a mild recurrence.

Case No. 2. E.K. Female. Aged 43.

Had a history extending over 32 years. Remissions had occurred during pregnancy only.

Family History: Nil.

Effect of Sunlight: Beneficial.

Extent of Disease: Scalp, forearms and both legs.

Local Treatment: Tar and salicylic acid ointment.

25 ccs. of colloidal manganese were administered over a period of three months. Her condition improved greatly, but the lesions did not completely clear up. The treatment could be described as 90 per cent. successful. She relapsed in two months.

Case No. 3. A.G. Female. Aged 70.

Gave a history of 28 years with maximum remission periods of five months.

Family History: nil.

Effect of Sunlight: Bad.

Extent of Disease: Feet and ankles.

Local Treatment: Tar and Salicylic acid ointment.

She was given 26 ccs. of colloidal manganese over three months. At the end of that time the patient was 90 per cent. better but relapsed in two months.

Case No. 4. J.M. Male. Aged 68.

Gave a history of 14 years' duration. During that time he had a remission of five years. The present attack had lasted about three years.

Family History: Nil.

Effect of Sunlight: Beneficial.

Extent of Disease: Numerous lesions on back and legs.

Local Treatment: Tar and salicylic acid ointment.

After 25 ccs. of colloidal manganese had been given he was completely clear. The disease, however, recurred after about four months.

Case No. 5. A. M'T. Male. Aged 62 years.

Gave a history of 40 years' duration. The maximum remission period was three months.

Family History: Nil.

Effect of Sunlight: Beneficial.

Extent of Disease: Numerous lesions on the back and the left leg.

Local Treatment: Tar and salicylic acid ointment.

He received 25 ccs. of colloidal manganese, but without any benefit apart from some reduction in the scaliness such as would occur from the use of ointment.

Case No. 6. E.O. Female. Aged 22.

Gave history of two years' duration, during which she has never been free from the disease.

Family History: Nil.

Effect of Sunlight: Unknown.

Extent of Disease: Chiefly on the legs and a few spots on the thighs.

Local Treatment: Tar and salicylic acid ointment.

After 25 ccs. of colloidal manganese had been given there was considerable improvement and within a month of the cessation of the injections. the lesions had disappeared. She relapsed in three months.

Case No. 7. E.F. Female. Aged 23.

Gave a history of seven years' duration. There were no complete remissions.

Family History: Nil.

Effect of Sunlight: Beneficial.

Local Treatment: Sulphur and salicylic acid ointment.

Extent of Disease: Scalp and arms and legs.

After 25 ccs. of colloidal manganese the condition was about 75 per cent. better. She did not relapse, but the condition remained stationary with a few spots in evidence for about six months. It then cleared completely but re-appeared three months later.

Case No. 8. E.B. Female. Aged 65.

Gave a history of 20 years' duration. She had a complete remission of one year, but for three years prior to treatment had no remission.

Family History: A brother and a niece were affected.

Effect of Sunlight: Bad.

Extent of Disease: Buttocks, knees, legs and a few spots on the arms.

Local Treatment: Tar and salicylic acid ointment.

After 15 ccs. of colloidal manganese had been given there was considerable improvement. A further 4 ccs. were given and then owing to illness attendance ceased. The patient, however, reported two months later to express thanks for complete recovery. She was later lost trace of.

Case No. 9. P.C. Male. Aged 71.

Gave a history of 50 years' duration with no remissions.

Family History: A son and daughter were affected.

Effect of Sunlight: Not known.

Extent of Disease: Numerous lesions over back, thighs and legs.

Local Treatment: Tar and salicylic acid.

After 25 ccs. of colloidal manganese had been given improvement was so slight that the patient could not be said to have obtained any benefit at all.

Case No. 10. E.M. Male. Aged 48.

Gave a history of 14 years' duration. He had one remission of six months.

Family History: Nil.

Effect of Sunlight: Bad.

Extent of Disease: Scalp, trunk, elbows and knees.

Local Treatment: Tar and salicylic acid ointment.

After 25 ccs. of colloidal manganese no appreciable improvement took place in the patient's condition.

Case No. 11. M.E. Female. Aged 15.

Gave a history of seven years' duration, but had had a remission of two years during that period.

Family History: Her mother was affected.

Effect of Sunlight: Beneficial.

Extent of Disease: Generalised over the body, including the face.

Local Treatment: Tar and salicylic acid ointment.

This patient was completely well after 25 ccs. of colloidal manganese had been given. There was a recurrence, however, in three months.

Case No. 12. S.K. Male. Aged 63.

Gave a history of ten years' duration with no remissions.

Family History: Nil.

Effect of Sunlight: Unknown.

Extent of Disease: Numerous confluent lesions involving the trunk and all the limbs.

Local Treatment: Tar and salicylic acid ointment.

After 25 ccs. colloidal manganese had been given no benefit was apparent, but during the next three months there was about a 50 per cent. reduction in the extent of the disease. It has remained almost stationary since then for 12 months.

Case No. 13. M.K. Female. Aged 17.

Gave a history of five years' duration. She had no remissions.

Family History: Nil.

Effect of Sunlight: Beneficial.

Extent of Disease: Knees and legs.

Local Treatment: Tar and salicylic acid ointment.

After a total of 15 ccs. colloidal manganese this patient was 75 per cent. better. Owing to extraneous circumstances no further injections were possible and a subsequent history was not obtained.

Case No. 14. G.J. Female. Aged 26.

Gave a history of eight years' duration with no remissions.

Family History: Nil.

Effect of Sunlight: Beneficial.

Extent of Disease: The brow, scalp, elbows and knees.were all affected.

Local Treatment: Tar and salicylic acid ointment.

The patient responded slowly to the injections, and after 25 ccs. had been given was about 50 per cent. improved.

Case No. 15. K.P. Male. Aged 11.

Had an attack of psoriasis at the age of six and then remained free until the present attack which had lasted about a year.

Family History: His mother and sister were affected.

Effect of Sunlight: Not known.

Extent of Disease: Patches on the scalp and trunk.

Local Treatment: Tar and salicylic acid ointment.

In view of the patient's age the amount of the injection was limited to 1 cc. He responded rapidly, and after 10 ccs. had been given was completely free of the disease. He had, however, a recurrence in four months.

Case No. 16. H.H. Male. Aged 11.

Gave a history of a year's duration with no remissions.

Family History: A brother was affected.

Effect of Sunlight: Beneficial.

Extent of Disease: Chiefly the scalp with a few scattered lesions on the arms and legs.

Local Treatment: Tar and salicylic acid ointment.

Owing to his age injections of 1 cc. only were given. Response was rather sluggish and after a total of 18 ccs. had

been given he was only 50 per cent. better. As this represents a period of about four months the manganese therapy cannot be said to have been of any benefit.

Case No. 17. W.F. Male. Aged 23.
Gave a history of 14 years' duration. He had had repeated remissions, the longest being for a year.
Family History: His father was affected.
Effect of Sunlight: No appreciable effect.
Extent of Disease: Generalised, including the face.
Local Treatment: Tar and salicylic acid ointment.

The patient responded rapidly to the injections and was completely free from the disease after 25 ccs. had been given. He considered it the most satisfactory treatment he had experienced. The lesions recurred in about four months and within a year he was as bad as ever, but once more responded to manganese and required only 15 ccs. to render him free. He has remained clear for five months.

Case No. 18. M.L. Female. Aged 52.
Gave a history of two years' duration with no remissions.
Family History: Nil.
Effect of Sunlight: Good.
Extent of Disease: Numerous lesions on the back and patches on the knees and elbows.

Local Treatment: Tar and salicylic acid ointment.

Response to manganese injections was fair, but after 25 ccs. had been given the patient was only about 75 per cent. better. She was still a sufferer a year later, though not so severely.

Case No. 19. G.C. Female. Aged 35.

Gave a history of 30 years' duration.

Family History: A sister was affected.

Effect of Sunlight: Beneficial.

Extent of Disease: Numerous patches on the scalp, knees and elbows.

Local Treatment: Sulphur and salicylic acid ointment.

25 ccs. of manganese were given with a very slight response at first and practically none later on. The patient derived no real benefit from the treatment.

Case No. 20. J.T. Male. Aged 50.

Gave a history of 23 years with no complete remissions.

Family History: Nil.

Effect of Sunlight: Doubtful.

Extent of Disease: Numerous lesions, scattered over the scalp and limbs.

Owing to irregular attendance it took about four months to give 25 ccs. of colloidal manganese. He responded briskly at first and then more slowly. At the completion of the course of injections he was about 50 per cent clear, but within three weeks was completely better. He had a recurrence after two months.

Case No. 21. B.M. Negro. Aged 56.
Gave a history of 20 years' duration with no complete remissions.
Family History: Nil.
Effect of Sunlight: No appreciable effect.
Local Treatment: Tar and salicylic acid ointment.
Extent of Disease: Generalised, including the face.

The patient responded very little to manganese therapy, and after 25 ccs. had been given had obtained no real benefit.

Case No. 22. J.McV. Male. Aged 40.
Gave a history of two years'duration with no remissions.
Family History: His son was affected.
Effect of Sunlight: Beneficial.
Local Treatment: Tar and salicylic acid ointment.
Extent of Disease: Numerous lesions scattered over the arms and legs.

The patient responded fairly well at first, but after 23 ccs. had been given was only 50 per cent. clear. He was subsequently lost trace of.

Case No. 23. J.D. Male. Aged 48.

Gave a history of 16 years' duration with no complete remissions.

Family History: A sister was affected.

Effect of Sunlight: Doubtful.

Extent of Disease: There were scattered lesions over the scalp, the trunk and limbs.

Local Treatment: Tar and salicylic acid ointment.

Attendance was irregular, and the response to treatment slow. A total of 23 ccs. was given with no appreciable benefit.

Case No. 24. J.C. Male. Aged 17.

Gave a history of 12 years' duration with no complete remissions.

Family History: Nil.

Effect of Sunlight: Bad.

Extent of Disease: A few spots on the scalp and abdomen. Patches on elbows and arms.

Local Treatment: Tar and salicylic acid ointment.

There was a fair response to the injections. After 25 ccs. had been given the patient was 75 per cent. better and six months later had only two spots, one on each elbow.

Case No. 25. M.F. Female. Aged 20.

Gave a history of seven years' duration with maximum remission periods of three months.

Family History: Nil.

Effect of Sunlight: Doubtful.

Extent of Disease: Scattered lesions over the scalp, chest and limbs.

Local Treatment: Tar and salicylic acid ointment.

After 25 ccs. of manganese had been administered the patient was about 90 per cent. clear, but within a few days of the cessation of treatment fresh spots appeared on the forehead.

Case No. 26. E.G. Female. Aged 56.

Gave a history of six years' duration with no complete remissions.

Family History: Nil.

Effect of Sunlight: Doubtful.

Extent of Disease: A few spots were present on the scalp. Numerous lesions were distributed over the back and thighs.

Local Treatment: Tar and salicylic acid ointment.

After a complete course of injections which was prolonged over the average period of three months owing to irregular attendance the patient's condition was about 75 per cent. better, but within three months tended to deteriorate again.

Case No. 27. B.B. Female. Aged 38.

Gave a history of 15 years' duration. She had one remission period of seven years. The present attack had lasted two years.

Family History: Nil.

Effect of Sunlight: Doubtful.

Extent of Disease: The disease chiefly affected the elbows, hands and legs, but a few spots were present on the back.

Local Treatment: Tar and salicylic acid ointment.

After 25 ccs. of manganese had been given there was 75 per cent. improvement, and in the following weeks the condition cleared up completely. There was, however, a recurrence four months later.

Case No. 28. L.D. Male. Aged 65.

Gave a history of two years' duration with no remissions.

Family History: Nil.

Effect of Sunlight: Beneficial.

Extent of Disease: Lesions were present on the scalp, elbows and knees.

Local Treatment: Tar and salicylic acid ointment.

The patient made a fair response at first, but improvement later was slow and after 25 ccs. had been given was only 75 per cent. clear and tended to relapse within a few weeks of treatment.

Case No. 29. M.S. Female. Aged 17.

Gave a history of a year's duration with no remissions.

Family History: Her mother was affected.

Effect of Sunlight: Doubtful.

Extent of Disease: Numerous lesions on the scalp, face and back.

Local Treatment: Tar and salicylic acod ointment.

This patient received a total of 21 ccs. of colloidal manganese. At the end of treatment her face and back were clear, but there was no improvement in the scalp. Her condition was 75 per cent. better. She was lost trace of.

Case No. 30. K.McK. Male. Aged 17.

Gave a history of four years' duration with no remissions.

Family History: Nil.

Effect of Sunlight: Beneficial.

Extent of Disease: Numerous patches scattered over the trunk, arms and legs.

Local Treatment: Tar and salicylic acid ointment.

Any response to treatment was very slow and slight. 25 ccs. of manganese were given with no real benefit.

Case No. 31. A.T. Female. Aged 21.

Gave a history of about five years' duration with no complete remissions.

Family History: Nil.

Effect of Sunlight: Bad.

Extent of Disease: There were numerous patches on the scalp. A few on the chest, arms and legs.
Local Treatment: Tar and salicylic acid ointment.

The early response to treatment was satisfactory, but later became less marked. After 25 ccs. had been given the patient was about 75 per cent. better but in three months was as bad as ever.

Case No. 32. A.C. Female. Aged 26.
Gave a history of three years' duration during which time she had a remission lasting six months.
Family History: A cousin was affected.
Effect of Sunlight: Doubtful.
Extent of Disease: The lesions were confined to the scalp.
Local Treatment: Tar and salicylic acid ointment.

Response to treatment was moderate and after 25 ccs. had been given the scalp was about 75 per cent. better.

Case No. 33. E.C. Female. Aged 47.
Gave a history of 35 years' duration, with one remission five years ago which lasted for three years.
Family History: Nil.
Effect of Sunlight: Doubtful.
Extent of Disease: Numerous patches were present on the scalp only.
Local Treatment: Tar and salicylic acid ointment.

A satisfactory improvement occurred at first, but was not maintained and the scalp was only 75 per cent. clear after 25 ccs. had been given. Within four months the disease was active again.

Case No. 34. L.G. Female. Aged 23.
Gave a history of five years' duration with no remissions.
Family History: Nil.
Effect of Sunlight: Doubtful.
Extent of Disease: Numerous lesions on the scalp and back and a few on the arms and legs.
Local Treatment: Sulphur and salicylic acid ointment,

The patient responded briskly to treatment, and after 25 ccs. had been given there were only a few spots on the legs. She was considered to be 90 per cent. better. Within two months her condition was relapsing again.

Case No. 35. J.G. Male. Aged 51.
Gave a history of twenty years' duration. He had a remission lasting three years which occurred three years ago.
Family History: Nil.
Effect of Sunlight: Beneficial.
Extent of Disease: The back, abdomen, elbows and legs were all affected.
Local Treatment: Tar and salicylic acid ointment.

There was a fairly steady response to treatment, but this tended to fall away latterly. After 25 ccs. had been given the patient was about 75 per cent. clear. He never improved after that and indeed fresh lesions tended to appear.

Case No. 36. L.W. Female. Aged 21.

Gave a history of seven years' duration with no remissions.

Family History: Nil.

Effect of Sunlight: Beneficial.

Extent of Disease: The scalp was severely affected, and there were numerous patches scattered over the trunk.

Local Treatment: Tar and salicylic acid ointment.

There was a fair response to treatment and the lesions on the trunk cleared up. The condition of the scalp was not so satisfactory. The patient was about 75 per cent. clear after 25 ccs. Fresh lesions appeared in two months.

Case No. 37. H.T. Male. Aged 57.

Gave a history of 20 years' duration with one complete remission of two months ten years ago.

Family History: Nil.

Effect of Sunlight: Beneficial.

Extent of Disease: There were numerous patches on the back, abdomen, thighs and knees.

Local Treatment: Tar and salicylic acid ointment.

There was a satisfactory response to treatment and the condition was about 75 per cent. clear, but even before the cessation of treatment fresh lesions were appearing.

Case No. 38. L.R. Female. Aged 50.

Gave a history of 24 years' duration. During that time she had two remissions each lasting a month.

Family History: Nil.

Effect of Sunlight: Doubtful.

Local Treatment: Tar and salicylic acid ointment.

Response to treatment was slow and after 25 ccs. had been given the patient was only 50 per cent. improved.

Case No. 39. H.C. Female. Aged 22.

Gave a history of eight years' duration with no remissions.

Family History: Nil.

Effect of Sunlight: Beneficial.

Extent of Disease: The scalp, trunk, arms and legs were all affected.

Local Treatment: Tar and salicylic acid ointment.

During the first eight injections improvement was satisfactory, but it was not maintained and after 25 ccs. had been given the patient was only 75 per cent. free and fresh lesions were appearing within two months.

Case No. 40. F.W. Male. Aged 17.

Had suffered from psoriasis five years ago and then remained clear until this year.

Family History: His mother and sister were affected.

Effect of Sunlight: Doubtful.

Extent of Disease: The scalp, forearms and legs were severely affected.

Local Treatment: Tar and salicylic acid ointment.

For six weeks the patient improved rapidly and was about 75 per cent. better, and then even before treatment with manganese ceased fresh lesions were appearing.

Case No. 41. G.H. Male. Aged 36.

Gave a history of about one year's duration.

Family History: Nil.

Effect of Sunlight: Unknown.

Local Treatment: Tar and salicylic acid ointment.

Extent of Disease: The scalp, elbows and forearms were affected.

After having received 11 ccs. of manganese this patient had an acute exacerbation of the disease and no more injections were given.

Case No. 42. W.H. Male. Aged 22.

Gave a history of 14 years' duration. He had one remission of four years two years prior to the present attack.

Family History: An uncle was affected.

Effect of Sunlight: Beneficial.

Extent of Disease: There were patches on the scalp and arms and legs.

Local Treatment: Tar and salicylic acid ointment.

There was a favourable response to treatment, and the patient was completely clear after 25 ccs. had been given. He was later lost trace of.

Case No. 43. E.W. Female. Aged 33.

Gave a history of seven years' duration with no complete remissions.

Family History: Nil.

Effect of Sunlight: Doubtful.

Extent of Disease: The lesions were chiefly distributed on the back with a few on the arms and legs.

Local Treatment: Tar and salicylic acid ointment.

Response to treatment was fair at first, but the improvement was not maintained. The patient was about 75 per cent. better after 25 ccs. had been given, but shortly afterwards fresh lesions appeared.

Case No. 44. N.J. Female. Aged 36.

Gave a history of 19 years' duration with remissions during pregnancy only.

Family History: Her mother was affected.

Effect of Sunlight: Beneficial.

Local Treatment: Tar and salicylic acid ointment.

Extent of Disease: The scalp and arms were chiefly affected with a few spots on the trunk.

During the first seven injections there was a satisfactory response to treatment, but the patient only became about 75 per cent. clear. She was later lost trace of.

Case No. 45. F.C. Male. Aged 27.

Gave a history of 18 months' duration with no remissions.

Family History: Nil.

Effect of Sunlight: Nil.

Extent of Disease: There were numerous lesions on the scalp, trunk and limbs.

Local Treatment: Tar and salicylic acid ointment.

Response to treatment was slow, and after 25 ccs. had been given the patient was only about 50 per cent. better.

Case No. 46. D.B. Female. Aged 29.

Gave a history of 19 years' duration with no complete remissions.

Family History: A brother was affected.

Effect of Sunlight: Beneficial.

Extent of Disease: The scalp, trunk and limbs were all affected.

Local Treatment: Tar and salicylic acid ointment.

There was considerable improvement during the first six injections, but afterwards fresh lesions appeared in numerous places while injections were still being given. No benefit was derived from manganese therapy.

Case No. 47. C.F. Female. Aged 31.

Gave a history of 13 years' duration with remissions lasting about three months.

Family History: An aunt was affected.

Effect of Sunlight: Doubtful.

Extent of Disease: There were numerous patches on the scalp and a few on the trunk.

Local Treatment: Tar and salicylic acid ointment.

This patient responded rapidly to treatment. She made very little attempt to treat the scalp with ointment, but she became completely clear. She was lost trace of later.

Case No. 48. R.C. Male. Aged 55.

Gave a history of 30 years' duration with several remissions, the longest of which was for 15 months.

Family History: Nil.

Effect of Sunlight: Doubtful.

Extent of Disease: There were lesions on the scalp, face and a few on the forearms and legs.

Local Treatment: Tar and salicylic acid ointment.

Response to treatment was very satisfactory. After 25 ccs. had been given there were only a few spots on the scalp. The patient was about 90 per cent. clear. Some fresh lesions appeared within three months.

Case No. 49. J.P. Male. Aged 13.

Gave a history of six years' duration with no complete remissions.

Family History: A brother was affected.

Effect of Sunlight: Bad.

Extent of Disease: There were numerous patches on the scalp and trunk.

Local Treatment: Tar and salicylic acid ointment.

Owing to the patient's age not more than 1 cc. of colloidal manganese was given at a time. Twelve ccs. were given with no appreciable benefit.

Case No. 50. M.P. Female. Aged 59.

Gave a history of 27 years' duration with remissions of three months at varied intervals.

Family History: Nil.

Effect of Sunlight: Doubtful.

Extent of Disease: The arms and legs were chiefly affected, but a few spots were present on the back.

Local Treatment: Tar and salicylic acid ointment.

Response to treatment was very slow, and 20 ccs. were given with hardly 50 per cent. improvement.

In view of the impression that the face is almost immune from psoriasis it is interesting to note that five patients, or ten per cent. of the total, were affected on the face.

Seventeen, or roughly a third of the patients, gave a history of some relative being affected with psoriasis.

Twenty one patients found sunlight beneficial, while 23 were doubtful about its effect. Six considered it definitely harmful. Probably the most severe and intractable case in the series was B.M. who is a deeply pigmented West Indian negro (Case No. 21).

As a result of treatment 11 patients became completely free from the disease. Eight of these were clear at the cessation of treatment and three became so shortly afterwards. Three patients out of the 11 were lost trace of. The maximum period of complete remission among the remaining eight was four months, and the average was three months.

Five patients were 90 per cent. better as a result of treatment. This almost complete remission lasted in one case for three months and in three cases for two months. The remaining one had an exacerbation within a few days of the termination of treatment.

Seventeen patients were about 75 per cent. better after treatment.

Seven patients were about 50 per cent. improved.

Nine patients showed no appreciable improvement and one became definitely worse while treatment was being given.

CHAPTER VI.

SUMMARY.

The pharmacology of manganese is described and its possible mode of therapeutic action in psoriasis is discussed.

The results of previous authors are tabulated.

An investigation into the action of colloidal manganese on fifty cases of psoriasis is described.

CHAPTER VII.

CONCLUSIONS.

On theoretical grounds alone there is a strong prima facie case for the use of manganese in psoriasis. Support for this is given by the enthusiastic reports of the majority of investigators. On the other hand, the results obtained by Niles in a prolonged investigation were poor, and while Oliver and Crawford write in favourable terms of their experience with 125 cases I do not think their results when analysed justify their complacency.

The injections are not as a rule painless, but do not appear to be associated with any danger otherwise. In one of my cases the disease was apparently aggravated although this may have been a coincidence.

A remission period of three to four months is common in psoriasis treated or untreated, so that my results do not give the slightest grounds for the belief that manganese prevents or even delays the re-appearance

of the lesions.

As regards its curative value consideration must be given to the fact that over a period of three months which the treatment occupies remissions may occur in psoriasis without any treatment at all. Also in that time very considerable improvement may be produced by the use of an ointment alone.

On the other hand, the patients chosen were as far as possible those in the more chronic stages of the disease who had been applying local remedies without much success. Again, the majority suffered from scattered lesions and my experience is that in these cases the ointment is applied in such a perfunctory manner as to lose much of its effect.

However, allowing for the fact that some degree of local therapy was attempted in every case I do not think that manganese therapy could be claimed to be of any value unless the patient became free of all manifestations of the disease. This occurred in eleven patients only, i.e. less than a quarter of the cases, and it is a fair assumption that a proportion of these would have become clear with local measures alone. Still the majority gave histories of two, three, five and even 23 years since they were last free from the disease, and during that period local therapy

had not succeeded.

In my own case, observing as I had the opportunity of doing the course of the disease very closely, I found colloidal manganese extremely valuable not as a complete remedy in itself but rather as a powerful adjuvant to local measures and superior to any other methods I have tried which include sodium salicylate, arsenic, thyroid, mercury, saponin, vitamines, vegetarianism, fat free diets, ultra-violet rays and x-ray therapy.

But viewing the results as a whole it is hardly justifiable to advise a long series of injections which may cause considerable discomfort and which even when combined with local measures give promise of recovery in less than a quarter of the cases.

I find myself in agreement with Niles that while isolated cases may derive considerable benefit the treatment is too prolonged and uncertain to be adopted as a routine measure.

I wish to express my thanks for permission to conduct this investigation to:

Dr. F.A. Pond, Hon. Dermatologist to the Liverpool Hospital for Diseases of the Skin, and to

Dr. F. Glyn-Hughes, Hon. Dermatologist to the Liverpool Hospital For Diseases of the Skin; Senior Dermatologist to the Liverpool Corporation Hospitals.
