

Another group of cases in which the results seem to be very satisfactory is that in which the patients have received the drug following a vigorous course of mercury for periods of from a few months to a year, with the disease under control at the time. None of the cases in this group have so far recurred clinically, and in all that we have been able to follow serologically, the Wassermann reaction has remained negative. Some of the cases have been under observation now for six months.

Cases with active secondary or florid syphilis, however, although all of the lesions and clinical manifestations have promptly disappeared following the treatment, and in many cases the Wassermann has become negative, almost invariably recur at some later date.

In cases with the late recurring secondary and tertiary lesions, or in which more or less diffuse syphilitic processes are present in the body, an absolute eradication of the disease with one or more doses of the drug can scarcely be expected. In none of our cases of this type have we been able to accomplish permanent results with salvarsan alone, although a marked beneficial effect on the lesions has almost always been observed.

In one case of congenital syphilis, with severe double keratitis in a girl 12 years old, no benefit resulted from an intramuscular injection of 0.2 gm. of salvarsan. In one tabetic receiving 0.5 gm. of salvarsan the painful crises disappeared and remarkable improvement in the general condition followed.

In six cases which were followed in order to observe the effect on the *Spirochæta pallida* in open lesions, the organisms were seen to disappear in from five to twelve hours.

COMPLICATIONS

In no cases have any untoward effects been observed directly attributable to salvarsan, with possibly one exception. In this patient ten weeks after the injection a palsy of the iris and accommodation in the right eye developed. The patient has been under treatment with potassium iodid, but the lesion is still present. A sufficient interval has not yet elapsed to make clear whether the palsy was syphilitic or caused by the salvarsan. In another case two months after injection, a paralysis of the external rectus of the right eye, such as is often seen in syphilis, was noted. The Wassermann reaction never became negative. The paralysis disappeared gradually under treatment with mercury and potassium iodid, so that it seems fair to assume that it was syphilitic in nature. No ear disturbances have been observed.

CONCLUSIONS

From our experience with this drug, we are convinced that it is an important addition to the therapeutics of syphilis. In almost every case in which visible lesions were present complete disappearance followed the injection and marked improvement in the general condition of the patient was a constant feature. In all cases refractory to mercury, the response to salvarsan has been prompt and striking. The drug is indispensable for the treatment of patients who do not tolerate mercury. A study of our statistics does not warrant us in expecting a complete cure of syphilis and absolute immunity from recurrences in the majority of cases after the use of only one or two injections. A small number of cases which have been followed by us for four or five months without recurrences justifies the belief that one injection of salvarsan will effect a complete cure in some cases. Salvarsan is without doubt of equal value with a long

course of mercury and potassium iodid in the cure of lesions. It has, however, the very great advantage of simplicity of administration, and causes the lesions to disappear with great rapidity. Moreover, it saves the patient from the damage done by the luetic toxin during the period necessary for the control of the disease by means of mercury.

We want particularly to emphasize the fact that the use of salvarsan has now passed beyond the experimental stage. One should no longer make it his object to see how much good can be done with one or more injections of this drug, but rather of how much value it can be made to assume in the treatment of syphilis when combined with other drugs.

The superior ability of salvarsan over mercury to kill rapidly the *Spirochæta pallida* in the tissues has been demonstrated beyond question, and salvarsan is therefore indicated in every case of syphilis, when not specially contra-indicated, even in those cases in which it seems advisable to supplement it with the subsequent use of mercury.

From our experience at present, we strongly advocate a vigorous course of mercury following the injection of salvarsan, continued for about six months and possibly then followed by another dose of salvarsan. In the primary cases, and those already well under control with mercury, it seems fairly probable that salvarsan may be sufficient to eradicate the disease.

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THE DISADVANTAGES INCIDENT TO THE ADMINISTRATION OF SALVARSAN *

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Salvarsan in its present form can never become a popular remedy. Paul Ehrlich, however, is so ingenious that any day he may invent a modification that will be more easily administered, and will be even less toxic.

There are three determinations of salvarsan that are of fundamental importance; its poisonous action on the *Spirochæta pallida*; its selective action on epithelial tissue; and its selective action on the tissue of nerves. Its stimulating action on epithelial tissue is shown in the marvelous way mucous patches and luetic ulcers epidermize under its influence. Its selective action on nerve tissue, however, is what immediately interests us in this paper.

On the introduction of salvarsan, the attention of observers was fixed on the optic nerve, as it was feared that salvarsan might, like atoxyl, cause amaurosis. But experience accumulated, and as no reports of disagreeable ocular symptoms were at first recorded it was hoped that at last an arsenic preparation had been discovered which had no attendant grave toxic disadvantage. Still later experience tends to show, however, that salvarsan is not entirely free from poisonous influences on the nerves in the orbit. Finger was among the first to draw attention to these, but the instances reported are not so typical as those from atoxyl and arsacetin. They have been observed very infrequently, and it seems often to be a question whether they are owing to syphilis, to salvarsan, to a previous treatment with atoxyl, or to some other cause. It must be remembered that the hope and the interest aroused by the new drug have induced

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thousands of old syphilitics to apply for treatment for all sorts of chronic ailments not necessarily caused by syphilis at all, and that among these old ambulatory pathologic museums there would necessarily be a great number suffering from ocular disabilities.

But while attention was fixed on the eye, the ear seems to have suffered, as since the introduction of salvarsan an unusual number of troubles with the vestibular apparatus have been observed in early syphilis. It would seem that the arsenic in salvarsan acts true to kind and that we cannot entirely escape the predilection of this metal for nervous tissue. Implications of other nerves have also been reported, but, of course, of infinitely less consequential gravity. In any fair consideration of the detrimental effect of salvarsan on the nerves, however, we must always take into account the patients with whom we are dealing. Besides having syphilis, which itself attacks the nerves, they, as a class, habitually over-indulge in drugs that are strongly neurotropic, such as alcohol, tobacco, coffee and tea, and in addition put their nervous systems to the hardest kind of use, such as exposing the eye night after night to strong electric lights.

It is most interesting to consider for a few moments the selective action of arsenic on the nervous system. Arsenic has been used by therapeutists for ages as a nerve tonic, and although this experience has not the definiteness of a laboratory experiment, it, nevertheless, has value as indicating this metal's neurotropic nature. Accumulated clinical impressions always have a value. Furthermore, the marvelous action of salvarsan as a tonic is common to it and to the other arsenic preparations, and is probably due to its combined stimulating effect on epithelial and nerve tissue. The frequent occurrence of herpes zoster in those who are taking arsenic is another expression of the stimulating effect of this drug on the nerves. Then we have the selective action of atoxyl and arsacetin on the optic nerve, causing amaurosis. Furthermore, dentists constantly use arsenic to kill nerves. Arsenic has also been used for ages as a topical necrotizing agent in the treatment of epithelioma, and those who so employ it almost invariably come to the conclusion that the metal exerts a selective action on the diseased epithelial cells. At the same time, the atrocious pain that it causes when used on epitheliomas impels to the belief that the nerves at the same time are receiving special attention. The intolerable pain sometimes felt when salvarsan is employed, either subcutaneously or intramuscularly, is easily recognized by the experienced as the same kind of pain complained of by patients when arsenic is used topically in epithelioma.

Therefore, we recognize the neurotropic action of arsenic as a nerve tonic, as a herpetogen, as an amaurotic, as a nervocide and as a dolorific. Accordingly, it follows that when an unusual number of vestibular affections are reported in early constitutional syphilis, and therefore at a time of life, as well as at a stage of the disease, when such affections are rare, there naturally arises a grave suspicion that salvarsan may be the cause.

But the surprise lies in the fact that it is so little toxic. It is long since anything so dramatic as the introduction of salvarsan has occurred in the practice of medicine. The metal forming its main ingredient has played a romantic part in the world's history as a poison. Ehrlich, by combining this metal with other elements, changed at will its mode of action as regards this or that kind of animated protoplasm, so that it became almost indifferent even to its beloved nerve-cells and yet retained

a strong affinity for the cells that constitute the virus of syphilis.

At present very few men rely solely on salvarsan in the treatment of syphilis. It is now used in conjunction with the two other great specifics, mercury and iodid of potash. On informing a patient that salvarsan is not an absolute specific for syphilis, clearing up the disease and all its manifestations at one stroke, it is interesting to watch the mental reaction that takes place. The patient almost invariably concludes that the remedy is worthless. Yet a medical man, for the sake of his own reputation, must tell the facts of the case. Furthermore, it is dangerous to tell a patient that he is cured, for then he is thrown off his guard in case further manifestations of his disease should appear.

Another feature tending to diminish the popularity of this remedy is the difficulty surrounding its administration. It cannot be taken by the mouth, and if given either intravenously, intramuscularly or subcutaneously, it has to be prepared with minute care, and the injection has to be carried out under the strictest antiseptic, as the drug itself is an irritant, but not an antiseptic.

Many drugs such as morphin and cocain are so bland in their action on the tissues that we never expect any local trouble to follow their hypodermic use. Others, while irritant and harmful, are at the same time antiseptic, and therefore the injured or necrosed tissues are not exposed to the additional danger of sepsis. One of the great points in favor of the administration of salivlate of mercury intramuscularly is that this particular preparation is slightly soluble and a good antiseptic, and yet so slowly soluble as to act almost as powerfully as an insoluble mercurial salt. Among the drugs used subcutaneously or intramuscularly, salvarsan is distinguished by its injurious action on the tissues, and often gives rise to local necrosis. K. Martius found that it did so in every case he investigated. Once, where the injection was thrown into the gluteal muscles, there was no tendency to heal, although three months had elapsed. In two instances the necrotic mass had to be excised. Salvarsan, however, although it acts so injuriously, is not an antiseptic, and therefore if the technic is not perfect and germs happen to be included in the injection, they have an excellent opportunity to develop in the injured or helpless tissues. Septic infection, sometimes fatal, may therefore be a consequence of the administration of this remedy.

When salvarsan causes an arsenic necrosis that involves the whole skin, an ulcer results that is very slow in healing, and there is no telling when such an ulcer may develop. I have seen a patient get a necrotic ulcer from an injection of salvarsan who, several weeks before, had received an injection that passed off without any more than the ordinary inconveniences.

Then again, when salvarsan is given either subcutaneously or intramuscularly, the drug may not be absorbed. Schreiber had a patient, a doctor, who became so tired of the annoying deposit of salvarsan as to beg to have it cut out, and over 80 per cent. of the drug was removed from the local deposit. I have seen a number of these deposits, and the percentage of their occurrence must be quite high. In many instances they lie almost inert in the tissues causing pain only when pressed on, while in other cases they are very annoying. When the deposits are very annoying, the patient may ask to have the sac emptied, and the affair ends. When such a deposit

J. Martius, K.: Local Action of Salvarsan at Point of Injection, *München. med. Wchnschr.*, Dec. 29, 1910; abstr. in *THE JOURNAL*, A. M. A., Feb. 4, 1911, p. 388.

is inert it is a question what to do with it; whether to leave it alone or to advise its removal. If left alone it might possibly give rise to arsenic poisoning by slow absorption, although I have never seen it do so. When the remedy lies unabsorbed, it, of course, does not act as an antisypilitic, and may, if solely relied on to combat a progressive, destructive gumma, occasion serious loss of time. In other words, it constitutes a delay in treatment, possibly at a critical moment.

The intravenous method is undoubtedly to be preferred, as when the patient receives the dose, he has it then and there in sufficient quantity, and with little fear of any local trouble. But this way of administering salvarsan constitutes a surgical operation, demanding skill, intelligent care, and the strictest antisepsis, and more care and time indeed are here necessary than in many more pretentious operations. Above all things, an absolutely perfect solution must be obtained, as the injection of solid particles into the venous circulation is not permissible. So important is it to get a faultless solution that Schreiber always kept this step under his direct supervision. I never saw him give the actual injection into the vein, but I never saw an injection given in his clinic wherein he did not supervise the dissolving of the salvarsan. The greatest care is also necessary to keep adventitious particles out of the fluid. Sterilized distilled water should be used in making the solution, and no cotton should be employed in stoppering the bottles or in wiping the instruments lest cotton threads get into the fluid. The solution injected into the veins should not be a concentrated one, as it is an axiom that even harmless salts, when employed intravenously, should be well diluted. Furthermore, if by accident some of the salvarsan solution should escape into the subcutaneous tissues, it irritates far less when highly diluted than when concentrated. A concentrated deposit of salvarsan at the bend of the elbow where it may annoy for weeks is not pleasant.

Another important point in the intravenous injection is that the lumen of the needle should be free of rust. The blood in flowing out through a rusty needle is far more apt to clot than if the bore of the needle is smooth. This clot would naturally be injected into the vein in the course of the operation. I have also seen thrombus of the vein, presumably from the mere injury of the operation. The only symptoms were edema of the arm with some functional incapacity, and a cord-like hardening that cleared up in a short time.

An annoying feature, although a fleeting one, is the severe pain at the shoulder that patients often complain of after about 100 c.c. are injected. This may necessitate stopping the injection for a few moments in order to allow the circulation to readjust itself.

What is called a Herxheimer arsenical reaction may occur on the skin in the course of the first few days. It is a bright red erythema, usually best observed on the trunk, and I have never seen it give rise to any further disturbance. It is as well to know of its existence, however, as misunderstandings may otherwise occur.

The salvarsan reaction in the syphilitic lesions themselves is highly important. When, for example, there are a great number of very active syphilitic lesions, as in early malignant syphilis, the temperature reaction may run as high as 105 F. It is, therefore, important to be careful when there are many lesions, and when there is a low cachectic condition. I have never seen any deaths arise from this source, but at times there are serious inconveniences. In such cases Schreiber advises giving half the usual dose, followed in a week

by the other half. Usually, the temperature reaction comes on quite early in all syphilitic lesions excepting those of the central nervous system. The temperature reaction in lesions other than those of the central nervous system occurs at about four or five hours after the injection, while in lesions of the central nervous system it occurs at about from eight to ten hours afterward. This difference is so regular in its occurrence that it may be used for diagnostic purposes. When no syphilis is present, no temperature reaction occurs. The experience of Schreiber is particularly interesting in this respect. Knowing how frequently arsenic is prescribed in psoriasis, and how excellent the results sometimes are, and knowing also that in many instances the favorableness of the result bears some relationship to the size of the dose, he hoped to achieve success in psoriasis by injecting salvarsan which contains such an enormous quantity of arsenic. The psoriatic patients injected showed no temperature reaction whatever, nor had the drug the least effect on the eruption.

There is not alone a temperature reaction in cases of syphilis in which salvarsan is injected, but there is a marked reaction in the lesions themselves. They become redder and more swollen. The drug acts in this respect somewhat like tuberculin in tuberculosis. As may readily be seen, this is an important matter when it comes to the question of administering salvarsan where the affected organ is of great dignity, as in cases of gumma of the heart or of the brain. If a patient has gumma of the brain, from which he is suffering severely from the pressure of the tumor, the sudden enlargement of this tumor, consequent on the local reaction, may be of the greatest importance. For the same reason, if a patient has gummatous softening of an artery, giving rise to an acutely dilating aneurysm, a dose of salvarsan by increasing the quantity of blood sent to the part may cause irremediable damage. The action of mercury and of potassium iodid is quite a contrast to this, as under these remedies there is no increased afflux of blood to the affected part, but rather a slow melting down of the syphilitic infiltration. Of course, in a patient suffering with aneurysm the drug would not be administered intravenously, as the fluid itself would dangerously raise the arterial pressure.

Finally we come to a disadvantage in the administration of salvarsan, which may count for nothing in an altruistic or scientific sense, yet from a practical point of view is of great importance. It is not a remedy to use in office practice or in an ambulatory clinic. The patient should be sent to a hospital, and this in itself constitutes an expense which many patients cannot afford. Even when given intramuscularly or subcutaneously, the administration of salvarsan consumes considerable time, and the physician's time counts for something. When given intravenously a very considerable amount of time is consumed, as the administration amounts to a surgical operation, making its administration still more expensive. This expense the patient might cheerfully undergo if the physician were able to assure him that his troubles would thereby be ended, but we are far from being in a position, even after several injections of salvarsan, to assure the patient that he is permanently cured. In the present state of our knowledge, we still are compelled to advise the patient, although he has taken salvarsan, to take mercury and potassium iodid also.

An enumeration of the disadvantages of this new drug serves only to throw into still bolder relief its great advantages. The wonder grows that such a powerful

spirillicide can be thrown in such quantities into the circulation with such little risk to the host. In contemplating this marvel, we begin to appreciate the fine scientific imagination of the man who made this possible.

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ABSTRACT OF DISCUSSION

ON PAPERS IN THE SYMPOSIUM ON SYPHILIS

DR. D. W. MONTGOMERY, San Francisco: I agree with Dr. Fox that it is unnecessary to dissolve salvarsan in normal salt solution. It is best dissolved in warm distilled water. But salt solution should be injected into the vein before injecting the salvarsan solution, in order to make sure that the point of the needle lies free in the vein. The making of the salvarsan solution is a most important step. The solution should be perfectly clear. I never saw Schreiber give the actual injection, but on the other hand I never saw this drug administered in Schreiber's clinic when he did not himself personally superintend the making of the solution. One of the speakers has accentuated a fact that I think cannot be successfully disputed, that mercury is a true specific for syphilis and that it constitutes the best means that has yet been found for treating the disease. I also believe that iodid of potash is a specific for syphilis, although inferior to mercury. Mercury is a poison. This, to my mind, is as clear as any fact in therapeutics.

DR. HOWARD FOX, New York: In our work at the New York Skin and Cancer Hospital we have observed one case of herpes zoster following the use of this drug. In the course of 128 injections we have not had any serious ill effects. In two of the cases the treatment was followed by a general toxic erythema, accompanied by high temperature, lasting three days. Necrosis at the point of injection occurred in five cases, twice after subcutaneous injections, once after an intramuscular injection of an alkaline solution, and twice after intramuscular injections of oily suspensions. I cannot agree with the previous speaker that the intravenous injection of salvarsan is a difficult or complicated procedure. With a little experience the proper introduction of the needle into the vein can readily be learned. It is hardly necessary to say in addition that the usual aseptic precautions should be strictly observed. In the interest of simplicity I think it best to use sterile water instead of physiologic salt solution for diluting the salvarsan. Furthermore, the gravity method is in my opinion much simpler than the method originally suggested by Schreiber. In the course of sixty-nine intravenous injections we have noted the appearance of small nodules in the vein in eight cases. In six of these cases the nodules disappeared very shortly after the injection.

DR. W. J. BUTLER, Chicago: In regard to the treatment of the disease under consideration, I wonder if we all have similar ideas on this question. When is syphilis cured? I do not think that any of us can answer that question; I do not think that we can saturate a patient for two or three years and then say that the patient is cured; we all know that he is not cured. I agree with what has been said regarding the value of mercury; I can also see certain advantages that result from the administration of this agent hypodermically. How do you know when a patient is saturated? This we do not know clinically. Too much importance has been given in past years to the disappearance of external manifestations and their continued absence in judging the results of treatment of syphilis. The possibility of visceral syphilis existing or appearing at any time should always be kept in mind. I cannot emphasize sufficiently strongly the above points. If we ask ourselves when are these patients cured, we can only say, recollecting the possibility of recurrence at any time, they are cured when they are dead. We can, however, determine the activity or inactivity of the specific virus in a syphilitic by resorting to the serum reaction for syphilis. This is the only means of judging early activity of the specific process in internal organs, before clinical symptoms have manifested themselves. In the treatment of syphilis the serum reaction should not be applied for one, two or three months, or even years, but indefinitely as a control on the activity

or abeyance of the disease. We should never assume that we can treat a patient with this disease for two or three years and then say positively that he is cured. The serum reaction should be resorted to when treating these patients to see that the treatment is being pushed sufficiently. We should never assume that a cure has taken place because there is a negative reaction. Such patients should not be allowed to go out of the care of the physician even when the serum reaction is negative after two, three or four years of treatment, but should occasionally receive further treatment to protect them against recurrences, and their blood should be examined three or four times a year. When found positive, treatment should be resumed.

DR. C. F. HOOVER, Cleveland, Ohio: During my student days I was profoundly impressed by an autopsy on a young man who died from pulmonary syphilis shortly after his return from Switzerland where he was sent six months before on account of an hemoptysis supposedly of tuberculous origin. Ever since that experience I have endeavored to avoid such a diagnostic error by always considering the possibility of syphilis whenever a chronic pulmonary disease is under consideration. Thus far I have seen only three instances of pulmonary syphilis in adults. That it does not oftener occur seems strange, but it seems more strange to me that our colleagues who practice in regions frequented by tuberculous patients have not a goodly number of cases of pulmonary syphilis to report.

Every variety of fever curve is encountered in syphilis. I remember one instance in which the rise from normal to 106 F. and return to normal was accomplished within a few hours. There were sufficient signs to show that the disease was located in the liver and on account of the extremely rapid rise and fall of temperature a diagnosis of suppurative pyelitis was made. This patient promptly recovered after mercury was given. Another patient with syphilitic fever (whom I saw through the kindness of Dr. Buswell of Buffalo) had relapsing fever for a period of fourteen years and during all that period never had more than ten consecutive days without having at least one or two days of fever. Recently a woman who was referred to the medical ward of Lakeside Hospital from the gynecologic service had a daily evening rise of temperature to 104 F. This patient was infected with syphilis ten years previously and had been often treated for some manifestation of the disease since that time. Within forty-eight hours after mercury was given in large doses all fever ceased.

I think the experience we have had with salvarsan has taught us that the proper method of employing mercury is to give large doses up to the point of tolerance for short periods of a few weeks. Lesser doses of mercury are probably harmful when long continued.

DR. HARRY REEVES OLLIVER, San Francisco: I have had one case of lung syphilis, in a young man 34 years old. He had been treated for six years for tuberculosis of the lungs. He had been sent to different climates. He had had hemorrhages, but no tubercle bacilli were ever found in the sputum. About six months ago he came to me to see if I could find any tubercle bacilli. He was very despondent. When in the laboratory I questioned him; he was asked if he had ever had syphilis. He smiled and revealed a perfect set of Hutchinson's teeth. The Wassermann reaction was positive. He was placed on mercury and the improvement was rapid. The radiographic plates showed pulmonary lesions. At this time salvarsan came into use and the patient was given injections, beginning them on January 8. The improvement that followed was remarkable. He gained 19 pounds in weight in three weeks; his gain was steady. The day after his first injection of salvarsan he did, however, have a hemorrhage. So far as I can determine he is now in perfect health. Subsequent x-ray examinations of the thorax have shown that the shadows have markedly decreased in size. This man had a sister with large glands over her body and I suggested that an examination of her blood be made. The Wassermann reaction was positive and I gave her salvarsan; within two weeks the enlarged glands had entirely disappeared, and she quickly gained in weight.

The mother of these two individuals was in bed with a very pronounced myocarditis. Her blood also gave a positive Wassermann reaction. On questioning her I learned that her husband had died with evidences of a brain tumor. I think that the history in this case was complete.

I have seen four cases of nephritis in which a very large percentage of albumin and granular and hyaline casts in the urine, general anasarca, ascites, etc., were present, and these patients all made a good recovery under the use of mercury and salvarsan. The first patient was to me of particular interest. She was a young woman with general anasarca, ascites, 1 per cent. albumin and with a tumor in the pelvis. I placed her on mercury and Epsom salts. The albumin dropped to 0.1 of 1 per cent. and the casts rapidly disappeared and she greatly improved. She was operated on by Dr. George B. Somers and an ovarian cyst was removed. Ether was the anesthetic used. After the operation she had considerable pain in the back and legs; this was supposed to have been due to this tumor. After the removal of the tumor, however, the pains continued. She was a frail woman and I hesitated to give her salvarsan. The pain continued so severe, with no relief in spite of the mercurial rubs, that I decided at last to give her salvarsan. Four-tenths of a gram was given and within twenty-four hours she had no pain; it is not three weeks since the injection was given and she has not had any pain since. The patient has remained well and gained in weight.

The second case was one that appeared in the medical clinic with sciatica which had persisted for fourteen years. There was a positive Wassermann reaction. The use of salvarsan entirely cured her in a few days.

With regard to what has been said about the dosage of mercury I agree entirely, the best and most lasting results being thereby obtained. As to the saturation guide, I think we should give the full dose for twenty days and then make a Wassermann reaction test. If this is negative we have probably reached the saturation point. We should then keep the dose of mercury at this point; but if there is any indication that there is not enough mercury given, the dose should of course be increased until the Wassermann reaction is negative.

In regard to salvarsan, the resulting reaction depends on the amount of infection before salvarsan was introduced. If a patient has but a mild infection, the quicker will he become negatived after the salvarsan injection. The more positive the reaction before the introduction of salvarsan, the longer will it take for him to become negative to the Wassermann reaction test. I think this is explained by the fact that a large number of spirochetes are killed and thrown into the circulation where their endotoxins give rise to the formation of antibodies. Consequently the more spirochetes present, the stronger will be the reaction and the longer the time required for their elimination from the blood.

DR. HARVEY G. PARKER, Portland, Ore.: It is interesting to note the large sums of money advised to be spent in Wassermann tests during the treatment of lues, one of the speakers mentioning sufficient to count into the hundreds of dollars, at \$25 per test; it seems to me the essential thing is to treat the patient very thoroughly and when satisfied that this has been done, after waiting a period of three months without treatment, try the Wassermann test; if negative, later try another. The more frequently early Wassermans are disregarded and all effort placed on saturating treatment, the better permanent results we will get in treatment. In line with some of the cases reported of long standing hidden syphilis, undiagnosed, I wish to report a case. A patient came to the coast under the advice of his physician who pronounced him tuberculous. He had a severe cough, loss of weight, rapid breathing, and yet expectorated very little; he wandered about from place to place and finally, quite at the end of his resources, he arrived in Portland. He gave a history of a soft chancre eighteen years previously, and was satisfied that there had been no infection since. On general principles among the things resorted to to give relief from the severe cough was protoiodid of mercury; he got some relief but fell dead in a lodging house about this time. Post-mortem revealed a gumma of the arch of the aorta with the right lung also involved. The giving way of the arch caused death. In regard to some of the

skin eruptions following the use of salvarsan, I have noticed two erythematous eruptions of a bullous type appearing after the injection, one after the second dose of the drug and aggravated after the third. In another case, on the third day after injection, there developed an itching, oozing eruption, somewhat like psoriasis in appearance as far as color and elevation go, in spots from a dollar to a half in size; at the end of three weeks under astringents it disappeared. I have given salvarsan in several cases in which there was an apparent idiosyncrasy against mercury; also in cases in which mercurial treatment had been long and carelessly used with practically no results, getting gratifying and rapid results with, so far, no bad results. I heartily speak for the intramuscular injection of salvarsan, especially in old cases, but always in conjunction with proper mercurial treatment.

DR. WILLIAM LITTERER, Nashville, Tenn.: I take issue with the statement that salvarsan produced no reactions in cases other than syphilis. I have observed the use of salvarsan in five cases of pellagra, and in three marked reactions were obtained. In one the reaction was very severe, the temperature going to 104 F. while in the other two the temperature reached 102 F. All gave negative clinical history as to syphilis as well as a negative Wassermann. I have also used salvarsan intravenously in two cases of sarcoma; in one only was there a slight reaction. The patient vomited twice the next day while the temperature was 100 F. The Wassermann test was negative. In two cases of psoriasis, salvarsan was given intravenously with the result that in one case the temperature went to 99.8 F. two days after its administration. The Wassermann test was negative. In the pellagra cases good results followed its administration in one case only. In all of the others the general nutrition was improved, but there was no permanent improvement. I should like to report a unique case, which I believe to be one in which Ehrlich's "therapia sterilisans magna" was attained. This patient gave a typical clinical history of chancre on the penis. *Spirochetes pallide* were found in large numbers three days after the appearance of the primary lesion. The Wassermann was negative. The chancre was excised and the spirochetes were demonstrated in the tissues by the Levaditi stain. After the method of Iversen, an intravenous injection (0.5 gm. salvarsan) was given, followed four days later by another (0.5 gm.) intravenous, and five days later an intramuscular injection (0.6 gm.) by Lesser's method was given. No other antisyphilitic treatment was instituted. The patient felt perfectly well in every respect. Wassermann tests were made every month for ten months with negative results. Three weeks ago this patient developed another chancre on the penis, which came nineteen days after a suspicious intercourse. The chancre was typical in every respect and numerous spirochetes were found in the lesion. One intravenous of salvarsan caused its disappearance in two weeks. To my mind this is a case in which the first three doses of salvarsan produced a complete sterilization of all the spirochetes in the body. Ten months elapsed without the slightest symptoms and repeated negative Wassermann tests were always recorded. The appearance of the second chancre is a probable demonstration of an instance of Ehrlich's "therapia sterilisans magna."

DR. GEORGE H. AIKEN, Fresno, Cal.: I should like to say something from the standpoint of the general practitioner. I have been treating syphilis for over thirty years and have had a large number of cases. I feel somewhat humiliated in being told that I have really never cured a patient. I rise especially to ask the gentleman who says that no patient is ever cured to listen to the recital of this case: A young man 20 or 25 years old, having been treated for this disease for two years, marries a healthy young woman, who bears four or six children. These children grow up healthy and strong, they never develop any local or constitutional evidences of syphilis, and they are under observation constantly for over twenty years. What should be our conclusion in this case? Was this patient not cured?

DR. WILLIAM W. GRAVES, St. Louis: If there is anything the medical profession of this country is united on, it is the belief in the curability of syphilis; yet recent serologic investigation and more accurate clinical observations indicate that many individuals whom we have considered cured have not been cured at all, and this is true whether from our recognized

specific or from the much lauded salvarsan. Aside from accurate clinical studies of the syphilitic, similar studies of his wife and his progeny further show the inadequacy of our therapy. During the last five years I have made what I have called comparative clinical studies of families in which the fathers were syphilitics; likewise of families in which the fathers were free from syphilis. These studies have shown what is everywhere recognized, that healthy parents beget offspring, as a rule, quite equal to themselves in physical and mental endowments. "A chip off the old block" is expressive of our expectation of the offspring of healthy parents. My studies of families in which the fathers were syphilitic have shown: first, the wives, like the husbands, are rarely free from some of the more subtle manifestations of syphilis, such as pupillary anomalies, sensory loss, arterial changes, pallor, alterations in reflexes, etc.; second, the offspring rarely compare favorably with either parent or with each other. These studies have further shown the infrequency of the heretofore recognized signs of congenital or so-called hereditary syphilis, such as Hutchinson's teeth, interstitial keratitis, deafness without otitis, joint, skin and mucous membrane affections. Now the absence of these signs is one of the main props to our belief in the curability of syphilis. When such signs fail in the progeny, we point to them as living examples of the triumphs of our therapy in the parents. Similar comparative clinical studies of a few families in which the fathers are tabetics or paretics or known syphilitics will prove to anyone who will take the time to make such studies the inadequacy of our therapy, and, at the same time, the evil effects of syphilis on the progeny. I wish to indorse all that has been said by Dr. Butler. We must look the issue squarely in the face and not be afraid to look more closely at the progeny and to make clinical studies of them and of their mothers. We consent to a syphilitic's marriage three, four or five years after his infection, provided he has had adequate treatment and no recent manifestations; yet no man can say when a syphilitic has had adequate treatment nor when he is cured. The repeated use of the Wassermann reaction indicates that not more than 35 per cent. are apparently cured, and more accurate studies of the syphilitic, his wife and progeny will show that he is seldom, if ever, cured. It is safe to say that not more than 10 per cent. of syphilitics who apply to the medical profession for treatment receive what is considered adequate treatment; so that Nature must take care of the 90 per cent., and comparative studies of families will show that she does it almost as well as we do. These studies have caused me to admire Nature's resources in the care of syphilitics and at the same time to believe that our hope for a cure lies neither in mercury nor salvarsan, but in prevention.

DR. B. H. ORNDORFF, Chicago: I wish to relate the experience I have had with salvarsan. In a series of nearly 100 cases of syphilis intravenous injections of salvarsan were given and without any unfavorable symptoms. In nearly all of the cases the Wassermann reaction test was positive. I also gave salvarsan in three cases of leukemia. The first was a case of myeloid leukemia, with 450,000 white cells. The full dose was given. There were no beneficial or deleterious effects for about three months following the injection; then the patient had trouble with the auditory apparatus. This patient died one month later when he was totally deaf. The second case was one of lymphatic leukemia with 600,000 cells of the mononuclear type. Three weeks following the injection of salvarsan, this patient died, having slight auditory disturbances. The third case was one of chronic lymphatic leukemia; the white cells were less than 200,000. No advantageous nor deleterious results followed the injection of salvarsan.

DR. L. S. SCHMITT, San Francisco: The discussion has been somewhat apart from the subject of my paper, the laboratory diagnosis of syphilis. By using laboratory methods, particularly the dark-field condenser, one can corroborate the point made by Dr. Graves that the injection of salvarsan reduces the contagious condition of the initial lesion, and of the secondary syphilids within twenty-four hours. With regard to the point brought up by Dr. Butler, it is difficult to tell when a patient with syphilis is cured. In the examination of the serums of the offspring of syphilitics I have found positive reactions in a number when there were no clinical manifestation in the par-

ents. In syphilis, with a return of the reaction one can anticipate a return of the clinical symptoms. To bring out a point made by Dr. Graves and Dr. Butler, I have in mind a patient who without doubt had syphilis; the Wassermann reaction made shortly before death was positive. The history brought out the fact that the primary sore dated back forty-one years before his death.

DR. FRANK BILLINGS, Chicago: Visceral syphilis is very prevalent in the large cities, but is not much found in the country towns. There is no doubt that any man who has access to the big hospitals will find many cases of visceral syphilis, cases that have not been discovered previously. Dr. Hoover mistakes me when he states that I said I had never met with a case of pulmonary syphilis. I did say, however, that I had never seen cases that were called in the literature "interstitial forms of pneumonia of the syphilitic type." Such cases I have not seen. I believe Dr. Graves' statement is true, that probably a very small portion of people applying for treatment are properly treated. Therefore, late syphilitic lesions are presented to us. How many of you have cases of locomotor ataxia come for treatment and in taking the history you find that the patients have not had adequate treatment? How many of you have found locomotor ataxia develop among your own patients? I have practiced medicine over thirty years and I have seen many patients with visceral and nervous syphilis who have not been cured. Perhaps I have not cured these patients. Can any of you say that your malarial patients are cured? Yet I do not want our old friends and patients to believe that one suffering from syphilis will be condemned to an eternal attack of this disease. I believe enough in drugs to feel that mercury will absolutely cure syphilis. If I can keep patients long enough under observation, I believe I can prevent further signs of the disease appearing. I have had some experience with salvarsan chiefly in late syphilis. I have given salvarsan to thirty-three patients. I have repeated the dose in several patients. One patient received four doses. Three patients each received two doses. The results from the use of salvarsan have not been as good as from the use of mercury in my hands. In patients suffering from locomotor ataxia salvarsan seems to have an analgesic effect. Those suffering from the crises seem to be relieved in a few hours after receiving this agent. I recall one man who came from Milwaukee with a very severe neuritis of the brachial plexus; he had been confined to his bed for many months; the Wassermann reaction was positive. This patient was entirely relieved of his pain in eighteen hours and he was able to use his hand again within one week after the injection. I have seen many instances which show the analgesic effect of salvarsan. I believe in the use of mercury. As to what form of mercury to use I believe that is, to a certain extent, a matter of individual choice. During the last few years I have come to resort to the intramuscular method; I feel that I can command the dosage better in this way than in any other. I can keep my patients better under command. I think the value of mercury is greatly enhanced when the patient is absolutely at rest; this applies to any case of syphilis, whether primary or late. Mercury should be pushed to the point of saturation; this means at least to the point of salivation. I give large doses—as much as one-half a grain of corrosive sublimate; by repeating this again and again we conserve the best interests of our patients. I look on the iodids not as a specific in any sense, but as a helpful means of driving out the waste material. When we meet with gumma, for instance, the administration of the iodids will clear it up quickly as a rule, and without intervention from mercury.

Ointment Bases.—W. T. Corlett, in the *Cleveland Medical Journal*, calls attention to the importance of adapting the base of an ointment to the disease for which it is prescribed. If an ointment is intended as a vehicle for an internal remedy, the base should be absorbable, such as lanolin or lard. On the other hand, if the remedy is to act locally, a non-absorbable base should be chosen, such as petrolatum. In conclusion the author criticizes some of the ready-made ointments, especially those "made in Germany," which have been devised to replace the time-honored ointments of the pharmacopeia.