Therapeutics of syphilis : including preliminary observations with the Ehrlich-Hata preparation, dioxydiamidoarsenobenzol or salvarsan / by Victor C. Pedersen.

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THERAPEUTICS OF SYPHILIS.

*Including Preliminary Observations with the Ehrlich-Hata Preparation, Dioxydiamidoarsenobenzol or Salvarsan.**

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Mr. President, and Fellow Members of the Medicosurgical Society of New York:—It is a peculiar pleasure and honor to be invited to read a paper on so important a topic as the therapeutics of syphilis before a society like ours, comprising personal, professional friends who have reached or are reaching positions of prominence and importance in the medical community of our city. This paper is based on personal experience gained in genitourinary work in the outpatient department of the New York Hospital and the House of Relief, and as attending genitourinary surgeon at the People's Hospital, New York. It seems, therefore, fitting to suggest a series of practical points on the subject with more or less the authority of a specialist. By your leave, therefore, the paper will be planned on this basis.

The first point of practical moment for every practitioner to remember is, as already pointed out in another paper (1), by the writer: "In general, the treatment of syphilis must recognize the three broad types of invasion met with, namely: First, the benign form from which patients fully recover, go on to have healthy children, and live fully unaffected by the disease. Second, the relapsing form not infrequently benign in general characters, but severe and uncertain enough to tend toward recurrence of symptoms, unless the patient is careful of himself and the physician is duly watchful. Third, severe form of infection leading to great deterioration of health and not infrequently to death, more or less attributable to the syphilis itself, its complications or its sequels. In modern days, owing to early diagnosis and better management, this form is fortunately uncommon. Hereditary syphilis is the product of the last two forms as a rule."

It is to be remembered that the second or relapsing, and the third or grave form of syphilis may defy all known forms of treatment or their combinations or correlations.

The second dictum for full recognition by all is, that the treatment of syphilis is not merely a matter of medication, but also a matter of management. In other words, it is better to treat the patient as a diseased human being than to treat the disease as having a certain victim in its clutches. Someone has aptly said "It is well to realize not only what kind of disease the patient has, but also what kind of patient the disease has got": very bad English, but a very great truth. This means that in managing a syphilitic, various details must have constant attention by physician and patient. In general, the life habits must be in moderation those of the athlete as to regular hours, exercise, diet, etc. Bad habits should be reduced to their minimum, with special reference to alcoholism, smoking, and eating. The hours of exercise, work, and sleep should be, as far as possible, well balanced. The systemic condition of the patient should ever be a matter of concern. Strength and resistance should be maintained at the highest possible level, and nutrition, exemplified by body weight and the condition of the blood, should be fully in mind. Tonics in the form of medicinal and nonmedicinal measures should always be available.

In all patients the facts of loss of weight, the onset of anæmia, and the invasion of nephritis should be observed and known. Of the several guides as to how the patient is doing clinically, the foregoing, therefore, are the most important in the early stages. The weight of the patient should be observed every week; later every fortnight, and finally once a month. The blood should be similarly examined for anæmia, and also for that new blessing, the complement fixation test discovered by Wassermann, and greatly improved by Noguchi. The nephritis of syphilis is a much more constant and important entity than even syphilographers appear to recognize. This is not due to medication as many claim; otherwise one would see hardly any escape in common experience. The writer has frequently observed patients with marked kidney lesions before any treatment of the syphilis had been taken which improved or even disappeared under treatment and relapsed with a decline of treatment and with a return of the syphilis; also cases which never develop nephritis no matter how hard the mercurial and iodide treatment is pushed; also cases of nephritis which, like the syphilis itself in the given patient, is comparatively unaltered by treatment either to increase or decrease the symptoms. Various German authors have also reported cases of nephritis of nonsurgical type greater in one kidney than in the other during active syphilis. A third practical point which I have proved to my satisfaction is that in the general management of syphilitics better progress is made if the so called alkaline measures of treatment are applied, namely, the drinking of the various alkaline mineral waters with or without well known alkaline mixtures. This probably seems to recognize the fact that alkaline is the normal reaction of the body fluids in

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the main and that an increase thereof or a maintenance thereof to the full normal strength augments the body resistance against disease.

The fourth warning to be given the general practitioner is that the diagnosis of syphilis is of importance. Without offense to the title and aim of this paper, it is well to point out that there are four stages of syphilis, requiring careful recognition: a. The primary or chancrous period, usually easy of determination from clinical appearances, the presence of the *Treponema pallidum*, the Noguchi or Wassermann reaction in the blood, and early lymphangeitis and lymphadenitis.

b. The secondary period, likewise easy of recognition from the presence of signs of syphilis in the skin, mucous membranes, lymphatic glands, blood, and the like.

c. The tertiary period, likewise diagnosticated easily, if symptoms are present. Usually a positive serum diagnosis is very helpful.

d. A fourth or parasyphilitic period is aptly described by French authors, in which the infection of syphilis as an entity is absent, but in which the body damage and late sequels of syphilis are positive and absolute.

The most momentous period of all in syphilis as to diagnosis is that which, beginning with the second period and extending through the fourth, has no symptoms in virtue of competent and energetic treatment. This period is called the most dangerous because it is exactly the period when so many family practitioners deny the existence of syphilis at any time in the patient, because at the moment of examination there are no symptoms of the disease. This leads the patient into a position of false hope and not infrequently to the insane asylum, or to his grave, when a continuance of the treatment might totally change or save him. I believe that the most important warning of this evening's paper is to have all understand that the diagnosis of syphilis should be accepted and confirmed by a good history, carefully taken, in virtue of which it has been ascertained that the previous diagnosis was given by a competent observer or in a first class institution. A diagnosis thus established is absolutely and amply proper grounds for a continuation of the treatment. Absence of clinical symptoms and even in many instances of a positive Wassermann or Noguchi test are not grounds for withholding treatment, if the usual two or three years' duration thereof have not been fulfilled.

5. The fifth axiom for the general practitioner concerns diagnosis also. He should realize that diagnosis of syphilis means not only a proof of the presence of the disease, but also an estimate of the effect that this dreadful scourge is having on the body of the patient. This repeats what has been said a moment ago that diagnosis, if conscientiously made, must comprise knowledge of the presence of the organism of syphilis, *Treponema pallidum*, serodiagnosis, variations in body weight, changes in the quality of the blood, and in the condition of the kidneys, and finally a reasonable measure of the response by the constitution to treatment.

This appreciation of the effects of treatment is in a certain sense the most important detail, because without it, many elements in the subsequent treatment and management are not controlled.

The sixth principle to state for general application is that every syphilitic must have a most careful physical examination, which cannot possibly be considered complete unless all details are duly investigated. This physical examination cannot be recorded as conscientious and final, unless it includes bacteriology, hæmatology, and urology, together with a minute investigation of the body as a whole, beginning with the skin and ending with the nervous system. One need not take time in this paper to describe the details of such an examination; it should be borne in mind, however, that it cannot be made too conscientiously and searchingly. It is very easily possible to make it superficial, hasty, and negligent of some little thing which may mean much to the patient and the doctor. In the end result, due attention must, therefore, have been given to the general condition, nutrition, and digestion, lungs, heart, vessels, blood, lymphatic system, skin, and nervous system, which includes the various reflexes of the pupil, ocular muscles, and fundus. A rapid and convenient suggestion, though not proof of anæmia, may be made with Tolquist's scale. If the findings of this method so indicate, a more positive and scientific proof of anæmia may be secured.

The seventh title for discussion in the interest of the nonspecialist concerns the time of beginning treatment. Probably many in this audience were taught never to begin the treatment of syphilis until the appearance of the rash proved the diagnosis beyond controversy, This was sound doctrine for the days when it was established, respected, and taught, namely, in the prebacteriological epoch. Although for centuries syphilis has acted the part of a bacterial disease the nature of the organism was not proved until the *Treponema pallidum* (*Spirochæta pallida*) was discovered by Hoffmann and Schaudine in 1906. To-day, therefore, it is as sound doctrine to delay treatment of tuberculosis until signs of systemic loss of ground by the patient against the disease are present, as to delay treatment of syphilis until the signs of systemic invasion are present as exemplified in skin and mucous membrane lesions. I would lay down the rule that no one should attempt to treat syphilis at all who has not in his office a first class microscope with a dark field illuminator, or a bacteriological outfit, suitable for staining the *Treponema pallidum*. This diagnosis must be made at the first visit if possible. If there is doubt, a thin section of the lesion of a chancre or a deep scraping of a mucous patch duly mixed with one per cent. sodium citrate in sterilized salt solution, may be sucked into a capillary tube and sent to a competent pathologist for confirmation. Thus treatment may be begun on the day of or within a very few days of the first visit. Combined with the finding of the organism there should be present also by preference a Noguchi or Wassermann complement fixation test, and clinically a more or less typical lymphadenitis and lymphangeitis. How terrified would you and I feel if we were told to-day that we were the victims of syphilis, but that treatment would have to be delayed from six to seven weeks until the organism had spread through our systems

and had made deposits not only in the skin but everywhere in the body. Gentlemen, I regard the old doctrine of delay until the secondaries are established as a crime, in virtue of the modern scientific diagnosis of syphilis.

The eighth element in our title is properly a brief review of the various methods of treatment. So far as my experience goes, these should be arranged in their order of merit as follows:

(a) Ingestion;
(b) Inunction;
(c) Fumigation;
(d) Injection;
(e) Combined or alternating;
(f) Mixed treatment.

If reports of literature all over the world based on about one year's experience with the Ehrlich-Hata arsenical compound, dichlordioxydiamidoarsenobenzol (salvarsan) are correct, this should be at the top of the list in merit, at least in the acute and subacute degrees of the disease.

As to the ingestion method, the following facts may be briefly touched upon. Of the common preparations the following are most usually employed in tablet, pill, or powder form. The best in my opinion are in their order of merit mercury and chalk, bichloride, tannate, and cyanide; of less merit are calomel, the biniodide, and protiodide of mercury. If the ingestion method is adopted, it is of primary importance to bear in mind that alkalies should always be given with any of the foregoing preparations and also various digestive aids. For this purpose, pepsin and pancreatin are of great value. Frequent interchanges among the various forms of mercury available should be made, in order to prevent failure of the digestive tract to absorb any one form after a time. Thus, a tannate is usually a good reserve against the advent of diarrhœa from any of the other forms. The chalk present in mercury and chalk is a good antacid and renders this preparation perhaps the best of all internal medication, especially if alkalies, such as sodium biçarbonate in vichy water, are given with it. The so called tonic dose of mercury was developed as a part of the ingestion method. It is determined as follows: the dose of mercury is advanced rapidly from day to day until the earliest signs of diarrhœa or salivation appear. The tonic dose is half the dose required to produce these unfavorable symptoms. The therapeutic ladder by which this determination is reached is as follows: for the first day or two usually one grain of mercury and chalk for example are ingested three times a day, for the second day or two the noon dose is raised to two grains while the morning and evening doses remain at one grain; for the next day or two the morning and evening doses are raised to two grains while the noon dose is decreased to one grain; for the fourth day or two all the doses are two grains each. If slight symptoms of overdose do not now appear, the increase is resumed by the same method, a grain at a time, until said symptoms do occur. Comparatively little can to-day be stated in favor of the ingestion method, beyond the facts that it is most convenient and if properly balanced, usually causes the patient little inconvenience. In brief, it is the most convenient of all methods, but it is probably the least effective, because one cannot tell how much ingested medicine of any kind is really absorbed by the body. On account of its convenience and relative inexpensiveness, in that the patients once having had a prescription, do not report frequently to their doctor for observation, the ingestion method has become that which is most commonly employed. If the writer's observation carefully made in clinical and private practice is a guide it may be said that 75 per cent. of all syphilitics have received chiefly the ingestion method. I think, therefore, that the question is normally and properly raised, Is not the ingestion method at least in part responsible for the present status of society, with regard to syphilis in the following points?

(a) That it is steadily spreading throughout the world;

(b) That it accounts for fully 25 per cent. of insanity by statistical records in asylums;

(c) That it accounts for fully 50 per cent. of all organic nervous disease besides insanity;

(d) That thus syphilis has become a more potent factor in the death rate of the community, than any one has yet attempted to compute statistically;

(e) That to-day any patient who has had syphilis and is later the victim of another disease almost invariably requires consideration of this fact in the treatment of said other disease.

The inunction method of treating syphilis is very efficient, but invariably it is also one of the most laborious and dirty processes. It is very difficult to get a patient who is able to rub the salve into his own body conscientiously. Hence the loss of mercury through this fact is indeterminate. If a masseur can be engaged for the rubbings, there is a loss also upon the gloves or hands of this operator, unless he is careful and conscientious. Not many patients, therefore, will give this method its proper, fair trial. I believe it is second in the ascending scale of merit. If the inunctions are to be undertaken the zones of the body, described by Taylor (2), should always be respected, changing from zone to zone, night after night, until the entire body has been covered once or twice, after which the skin should be given a week's rest, when another period of rubbing may be undertaken just like its precedent. I consider highly unfavorable to the inunction method individuals who have a great deal of hair on their bodies, as an unavoidable result is a general folliculitis. Commonly the blue ointment is employed; it may be diluted with or replaced by ammoniated mercurial ointment if the skin becomes intolerant.

Fumigation would be the ideal method but for the fact that it requires special apparatus, is rather expensive, and involves loss of time to the patient. It also takes the patient more away from the observation of the doctor than in my opinion is desirable. Convenient volatilizing lamps for these medications are on the market; likewise patent cabinets which remove some of these difficulties. In fumigations we do not know how much of a given dose is absorbed by the skin and how much lost through dissipation within the cabinet or

through its crevices, nevertheless for rapid mercurialization it remains one means of choice.

Injection as a method of treatment is undoubtedly the best of all if the physician will only study the proper details and if the patient can be convinced that the pain it sometimes causes is worth while. Is it not in a sense significant that the Ehrlich-Hata preparation is to be given by injection? To discuss minutely the various advantages of injection in syphilis would make this paper repeat a previous contribution (1). It is fitting to say, however, that the gluteal region is the region of choice, and that it should be divided into eight or ten points of injection, two inches apart, each to be taken in turn from dose to dose so that it is ten or twelve weeks before the starting point is used again. I regard it as professional stupidity to use much the same point repeatedly at frequent intervals. Necrosis or abscess formation must occur in such instances, sooner or later. Since writing the foregoing article, the writer has decreased the interval between the doses from seven to four or five days, and has increased the strength of suspension of salicylate of mercury from 10 per cent. to 66⅔ per cent. or 10 grains in one c.c. Thus, a tenth of a c.c. (one and one half drop) of the suspension will deliver one grain of the medicine. The quantity of fluid injected and the secondary nodes are greatly decreased.

Combined or alternating method of treatment is the term applicable to that form which recognizes that all other forms must be employed in turn for some patients in order to keep them controlled. For example, if a given injection is painful beyond the usual experience, one may turn to ingestion or inunction until the painful node disappears. I have seen patients in whom this alternation was enacted week by week and who did not do well in any other way. It is extremely important to remember this, otherwise the patients will not improve at all under treatment, or, becoming discouraged, pass to the care of another practitioner.

Mixed treatment is the term commonly applied to the addition of potassium iodide to the mercury in whatever form the latter has been exhibited. I believe that under this heading there should also be included the addition of arsenic to the mercury alone or to the mercury and potassium iodide or to the potassium with the mercury excluded. I am personally, however, apt to give mercury with the iodide followed by mercury with arsenic the next week, thus alternating the iodide and the arsenic more or less regularly from week to week. This is particularly valuable in patients whose digestions are rapidly upset by the iodide. The period at which mixed treatment is commonly taken is the later months of the secondary period and practically always in the tertiary period. Many then omit mercury altogether in the later manifestations of the disease. I believe this to be a mistake and am urgently of the opinion that whenever the diagnosis of syphilis has been established, mercury should always be administered, as it is up to the present time the one fully established curative measure against the disease, aside from the great possibilities of dichlordioxydiamidoarsenobenzol.

The therapeutic ladder for giving potassium iodide is no doubt so familiar to all as hardly to bear repeating. Nevertheless, in consultation work I find so many practitioners who do not climb this ladder carefully that the following points must usually be described: The usual initial dose is five grains three times a day. After this has been well borne the dose is increased one grain each day until the total increase of ten grains is reached, thus: first day five grains, second day six grains, third day seven grains, etc., until fifteen grains are given on the tenth day three times. A recession of five grains is then made a grain at a time day by day so that on the fifteenth day ten grains three times a day are being taken, thus: eleventh day fourteen grains, twelfth day thirteen grains, thirteenth day twelve grains, fourteenth day eleven grains, fifteenth day ten grains three times a day. From this point of ten grains another ascent of ten grains is made so that on the 25th day twenty grains three times a day are being taken. Then a descent of five grains is made in just the same way as previously. The writer adopts the little plan of not increasing the dose for a whole week whenever a total advance of thirty grains is made —the patient uses the dose thus secured, by fixed advances of thirty grains each. In this way is it possible gradually to give large doses of iodide without disordering the digestion. Not uncommonly one finds patients who suffer iodism from small but not from large doses of the iodides. In such individuals it is well to begin the medication with thirty grains, from which ascent is then made as described.

It is true in the periods of temporary indigestion from medication of this kind that good management plays itself a part in holding the patient up to the discipline of good treatment and in controlling the disease indirectly. This statement means that the patient will not be discouraged by temporary indigestion. In this management the use of alkalies must not be forgotten.

Periods of rest from the treatment of syphilis have for many years been prescribed. I believe in such periods of rest but am reasonably convinced that most practitioners exaggerate their necessity. I believe the indication for the period of rest lies not in some theoretical rule but rather in observing the signs given from patient to patient, as to the effect of the medicines upon his system and the disease. Again we repeat the rule that we treat the patient as well as the disease. I believe that one may thoughtfully ask the question, May not the terrible record of syphilis as to insanity or organic nervous disease in the community be partly due to the blind following of such rules which would of course mean entirely deficient treatment? Are we not dealing with an infectious disease, a veritable scourge on the face of the earth comparable to tuberculosis in its ravages? We do not give the tuberculous periods of rest from treatment, excepting for special indications furnished by the disease and not by theoretical rules. Why should we deviate from this rule of common sense in syphilis? Personally, therefore, I give the medicines continuously until, for a given reason directly

furnished by a given patient, it seeems advisable to cease the treatment temporarily or to modify it. In this way I find that the average patient has about one month's rest from treatment in the year, which is ample, and, being determined by direct indications, is in my opinion wiser and safer than guesswork or arbitrary rules.

This brings us to the final subdivision of this paper which I trust will be accepted in the spirit of a preliminary report on personal observations with the new arsenical preparation of Ehrlich-Hata, dichlordioxydiamidoarsenobenzol.

Historically, to Professor Conrad Alt, of Uchtspringe, in September, 1909, were delivered specimens of this arsenical preparation. Bertheim, a colleague of Ehrlich, chemically produced the substance; a Japanese, Hata, a pupil of Kitasato, established the effect of the preparation on animals. Especially, Hata established the facts that a single injection will cure relapsing fever in rats and mice and that syphilis in rabbits is wonderfully relieved. The odd term "606" arose from the fact that previously 605 different preparations of the same chemical class had been tried and discarded. In man the first injection was given in Uchtspringe by Hoppe. The scientific precaution, however, was taken to try it first on a larger animal, a dog, as to toxicity. To the honor of our profession be it noted that two physicians without the disease received a dose of the medicine by injection in order to prove still further its harmlessness in man. Fortunately all they suffered was pain and swelling for several days. Ehrlich's description is probably correct that the drug has active parasitotropic powers but is not organotropic.

It seems to me that the logical points of this part of this paper must include forecare of the patient before the injection, the preparation of the drug for the injection, the surgical technique of the injection, the range variations and repetitions of doses, the reactions to the injection, the aftercare of the patient, and finally a brief description of the cases within the writer's experience, which will include a brief discussion of the effects of the drug on the various stages of syphilis as reported in literature.

(a) Forecare of the patient is so closely synonymous with selection of the patient as proper for the injection that we will not divide these two topics. It is needless to add also that all the points given under the previous topics of diagnosis and management, in brief, that everything which can possibly be known about the syphilitic patient must be known before dichlordioxydiamidoarsenobenzol is exhibited. The present consensus of opinion from existing experience is that this preparation should not be given in the presence of advanced progressing organic disease: a true statement which includes particularly organic lesions of the heart, arteries, kidneys, and nervous system. The reason is probably that syphilitic lesions of this type have already produced cellular changes which no power on earth can improve or alter. Another reason, particularly with regard to advanced nephritis, is that the action of the kidneys in eliminating the arsenic may induce an exacerbation of the disease and death may follow. Ehrlich did wisely and well in not giving the drug prematurely for universal use by the profession, simply because had he done so no such careful discussion of cases as proper to receive it would ever have been reached. "We could not see the woods for the trees," in other words the records of accidents and failures would have been so numerous that this drug, which may be wonderful in its benefits to man, would have been distrusted if not discarded.

(b) The preparation of the drug is important. At the present time that recommended openly by Ehrlich is a modification of the original method of Alt. This I employ in the following manner: Every implement is sterilized in boiling distilled water for at least five minutes; the drug is then rubbed up carefully with ten c.c. of the recently boiled distilled water until a perfect solution is obtained. This requires fully ten minutes of patient work and is greatly aided by the hot pestle and mortar and the hot distilled water. After this preliminary solution has been obtained, sterilized normal sodium hydrate solution is added, about 2 c.c. for a dose of 0.6 gramme of the drug. The sodium hydrate solution throws down a peculiar stringy precipitate, looking a little like yellow vaseline in water. The mixture is then rubbed up until all precipitation stops. After that the sterilized normal sodium hydrate solution is again added, drop by drop, until the fluid is perfectly clear. This requires at least another five minutes, and is again greatly facilitated by the hot pestle and mortar.

From time to time, more hot, boiled, distilled water may be added until the total fluid is increased to 20 c.c. An injection of more than 10 c.c. into each buttock adds greatly to the pain. For this reason I use a 10 c.c. antitoxine syringe for the purpose of measuring the fluids used in preparing the drug and then for the injection, with the result that I now usually give a trifle less and never more than 20 c.c. total.

While the last stage of preparing the medicine is being completed the skin of the patient should be cleansed, preferably with tincture of green soap, alcohol, and iodine. The iodine is daubed over an area about one inch in diameter at a point one inch above the imaginary horizontal line passing through the upper limit of the intergluteal cleft, about three inches outward from the cleft. This, in my opinion, is the safest point to use, as the injection is then well above the exit of the great sacrosciatic nerve. One may parenthetize the statement that cases of paralysis of this nerve have been reported due to injecting mercury too deeply and too low down into the buttock.

The position of the patient is preferably flat on his face, and a precaution never to be forgotten is that one finger of the operator must be on the gluteus about to receive the injection, determining whether the patient hardens the same or not. If the muscle is held rigid the injection must cease momentarily until the patient relaxes it. Injection into the rigid muscle is extremely painful and moreover forces the injection within the muscle into the fat and in part even upon the skin. Just after the injection, gentle massage for about twenty minutes should be given the part by the nurse. The

patient should then lie in bed for an hour or two. The balance of the aftercare will be discussed later. I use a No. 18 needle with a pyramidal point, three inches long under head, as described in my paper concerning the injection treatment of syphilis. The penetration secured with this needle depends on the size of the individual, the amount of fat, etc., all of which are matters of common sense.

The range, variation, and repetition of dose are not yet determined. The consensus of opinion, however, is that the safe rule to follow is 0.6 gramme for adult male and 0.4 gramme for women. Factors in this decision are obviously activity of the disease, general health of the patient, previously known susceptibility to other drugs. The reported limits of dose are 0.3 gramme, and 1.0 gramme in a few cases. Repetition of dose, according to Schreiber, may be safely 0.5 gramme. A case referred to me through courtesy of Dr. Noguchi received 0.6 gramme on the 2nd and 26th of October by Dr. Noguchi, and the same dose by me December 13, 1910. Further notes on this case are later given in this paper. A most important detail is that it is better to err on the side of a full dose than of a deficiency, the theory being that the spirochætæ become arsenofast unless the dose is sufficient to destroy them at once. This is with reference to arsenic, a dictum which I hold to be the fact with regard to mercury in the internal treatment of syphilis, namely, the amount of mercury absorbed during the first few weeks of the disease is so little that the *Treponema pallidum* becomes more or less indifferent to the mercury and the disease goes on. The best region for the injection is undoubtedly the buttocks, although the back below the scapula has been used and the abdomen when the subcutaneous method was in vogue. The intravenous method is very active, but seems to have had less favor with Ehrlich and most authorities than the intramuscular, chiefly because the absorption and the elimination of the arsenic are so rapid. The first five of my cases received the intravenous method largely from the fact that Dr. Krug, of Magdeburg, Germany, agreed with Neisser's dictum in preferring this method. Dr. Krug was presented to me through one of my former associates and had only a few days on shore before returning. Since then I have given the medicine subcutaneously once and intramuscularly twenty times.

(c) Reactions to the injection are both immediate and remote. The latter come on after a few days. In their order of onset, the reactions are pain, swelling, fever, digestive disturbances, nervous irritation, and cutaneous eruptions.

The pain may be unbearable and require morphine. The more slowly the injection the warmer the preparation up to body heat, the more accurately neutral the solution, and the greater the softness of the gluteus, the less will be the pain, as a rule. One element in the pain, concerning which I have written Professor Ehrlich, is whether or not the use of a normal salt solution in distilled water is not preferable to plain distilled water. No chemical reaction can occur, as the salt is already the dichlordioxydiamidoarsenobenzol. As pointed out in my paper on the injection method of treating syphilis, gentleness and deliberation in the injection of the material will greatly decrease the pain. Radiating pains, which are occasionally observed down the backs of the legs, may possibly be due to the proximity of the injection to the sacrosciatic nerves. After the first few hours of active pain it is replaced by a dull distress; thus the whole process simulates the pain of a severe bruise. In fact, that is what it is, with certain chemical reactions added.

The swelling is of two classes, superficial and deep. If the injection has been properly landed within the muscle, only the deep swelling appears, feeling much like a hæmatoma just after the blood is clotted and before it breaks down within the muscle. If the injection has been subcutaneous or, what means the same thing, forced by a rigid muscle into the subcutaneous region, a severe inflammatory reaction may occur, greatly resembling a phlegmon in its early stages. The tissues about the points of injection may become swollen, boggy, and tender over a very large region, as described in one case. These subcutaneous masses are readily movable on the deeper parts as a rule, and commonly break down into aseptic abscesses, that is to say, no germs are found in them, although detritus and pus from fat necrosis are found.

Fever is not frequent, the range being that commonly seen during the first twenty-four hours after most aseptic surgical procedures, 100° to 101°. In some cases fever may be sharp and severe during the first twenty-four or forty-eight hours and then quickly or slowly fall to the normal.

Digestive disturbances are seen at times. Constipation is the most common, perhaps due to the rest in bed. Diarrhœa has been reported. In one of my intravenous cases, there was vomiting of a fluid which closely resembled the medicine injected into the patient. Unfortunately it was not preserved by him for me to see.

Nervous irritation, such as headache, restlessness, thirst, hysterical fear, and the like, have been seen Eruptions of the skin directly of the arsenical type in patients who did not have an eruption at the time of injection seem to have been reported. Changes, however, in syphilitic eruptions are remarkable. A roseolar syphilide increases its congestive redness and size and may add to it macular spots. Papular syphilides show a kind of red zone surrounding them and look irritated.

The Jarish-Herxheimer phenomenon is peculiar. It consists in increased redness and swelling of macules and the papules. Its significance has not yet been determined. Inasmuch, however, as it is a manifest disturbance of the lesions, Wechselmann's view may be correct, namely, that too little of the drug has been given to destroy the *Treponema pallidum*, hence its obvious activity in the lesions in resisting the drug.

The clinical effect of salvarsan should be considered in series as to the period of the disease under treatment. In open lesions the *Spirochæta pallida* may disappear in from one to seven days. Siesskind, Gérrone, and Huggenberg and Neisser have observed that during this period their common characteristics of activity, form, refringence, coils, and the like become altered. The serum test is all im-

portant in watching the disappearance of the infection; as a rule, the change is constant and regular and in from two to six weeks a positive becomes negative. In the nervous lesions this change is a little less marked.

Chancres, condylomata, and other secondary lesions of syphilis heal with great rapidity. Secondary signs upon the skin disappear as a rule with a similar promptness. Forms, however, with mixed infection, such as rupial syphilides, are much slower and require local treatment in addition. Tertiary lesions, particularly gummata, heal with renewed activity. Tertiary lesions with pain, such as periostitis and in the nervous system, appear to be little affected by the injection unless it be that the process is brought to a standstill. Even if this proved to be true in the future, the method will be acknowledged one of great value because in cases with early diagnosis subsequent ravages of syphilis in the nervous system will be stopped. All this, however, seems to be too good to be true. Time and only time will tell. Syphilis of important organs, particularly the liver and the kidneys, is undoubtedly benefited by injections of 606 according to the literature. When the eyes are attacked, the medicine may not be advisedly given in all forms. The theory that optic neuritis prevented its administration was probably evolved from the fact that some injections were harmful. It has been found, however, that these injections usually contained wood alcohol which was used in some of the original methods for preparing the medicine for injection.

In hereditary syphilis the medicine seems to be of value. Pregnant women, nurslings, and syphilitic children of tender years have been injected. The writer has had four cases, in two husbands and their wives, all giving positive blood tests and a history of repeated miscarriages of syphilitic children. It is too early to give the final data concerning these cases so far as the results are concerned.

A brief detail of the cases in the writer's hands is now in order:

Case I. A. G. (referred by the courtesy of Dr. S. Rottenberg). Married, Russian, housewife, admitted November 17th to the People's Hospital. Diagnosis, early syphilitic locomotor ataxia. Family history negative. Previous history, very alcoholic. Has had the ordinary diseases of childhood. Occupation, housework, but has been a prostitute. Venereal history, syphilized three years ago. Locomotor ataxia appeared two years ago. Treated off and on with internal and injection methods during the past two years. Physical examination, general condition poor. Locomotor ataxia with symptoms of optic neuritis. One half gramme of 606 was injected on or about November 20th. The results have been that the early symptoms of locomotor ataxia very greatly improved so that the patient has been able to get back to her work. The eye symptoms have also improved. It is hoped only that this ground fully gained will be increased. The serum test was very strong on November 17th, 28th, and December 13th, and strong on December 20th and January 3d.

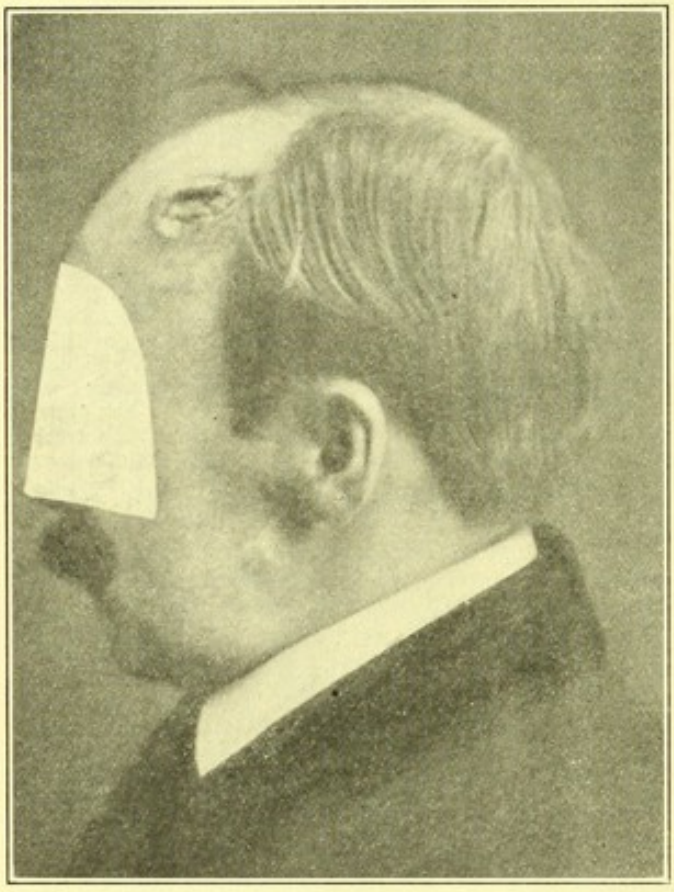
On December 27th, her weight was 151½ pounds, blood pressure, 117. January 3d, weight, 152½ pounds; blood pressure, 117. January 10th, weight, 153 pounds. January 17th, weight, 157½ pounds; blood pressure, 112. Rather recent retinal hæmorrhages were in the eyes prior to the treatment.

Case II. H. B., married, Denmark, saloon keeper, forty-four years old. Admitted, November 16th, to the People's Hospital. Diagnosis, early tabes dorsalis. Family history, negative. Previous history, excessive alcoholism. Can remember no disease of childhood or acute illness. Gonorrhœa six years ago, cured in about two months. Syphilis about four years ago. Secondaries acknowledged. Treated by internal medication for a short period about one year. No history of gumma, complains of pain in the right knee and thigh and of constipation, and at times difficult micturition with straining. Physical examination, fairly well nourished, rather alcoholic appearance. Inequality of the pupils, right reacts to light and distance but left does not. Vision, normal. Reflexes for the most part exaggerated, also the Romberg signs of ataxia. After considerable treatment with mercury without effect on any of his symptoms during which what appeared to be a syphilitic myositis appeared; it was determined to give the patient 606, although it was realized that no benefit to his ataxia would be established. On November 16th, 0.5 gramme was injected. After this the patient's temperature varied from normal to 102.2°. Returned to normal on November 22d, when he was discharged. Since that time the patient's general condition has improved a good deal. His tendency toward nervousness, headache, ataxia have improved. The ataxia is still present, but in a much less degree. The patient states that he feels a good deal better and the pains in the thighs, which seem to me to be a myositis, and not an evidence of locomotor ataxia, have disappeared. The muscles were somewhat thickened where the pain was. The serum test on November 18th and 22d was positive; November 30th, weak; December 8th, negative. The blood pressure in this patient on admission was 65. Varied from 101 to 117. His weight increased from 149 pounds to 164¼ pounds.

Case III. M. B. Referred by Dr. I. M. Rottenberg. Admitted November 7, 1910, to People's Hospital. Married; thirty years old. Family history, negative. Previous history, formerly an excessive, at present a very moderate smoker. No alcoholism. Diseases of childhood not remembered. Venereal diseases denied, especially syphilis, no acute illnesses. In the last six weeks has lost a great deal of weight. Present illness, a large mass protrudes from rectum causing bleeding on defæcation, duration three years. Bleeding may have weakened patient. Appetite and sleep fair. No symptoms referable to the abdomen or chest. Physical examination, patient shows signs of gumma on the brain, is greatly reduced, is of slow mentality, speaks slowly and has a left hemiplegia, combined with loss of kneejerk and other signs of cerebral difficulties. After a consultation with two of the visiting physicians of the People's Hospital, it was decided that the patient probably had gumma of the brain, as his Wassermann test was strongly positive. After the family had been told that probably no treatment would avail for more than temporary relief, it was at their request decided to give him a dose of 606. On account of his depreciated condition on November 15th only 0.45 gramme was injected. The patient after this ran a temperature which varied from 99° to 101° until November 23c, when it reached 102° and on the 25th had declined again to 100°. His mentality in this period picked up wonderfully so that he could answer questions with almost normal promptness and correctness. His defæcation and urination which had been involuntary, became voluntary and the whole aspect of the man was one of great improvement. Reasonable hopes were held out to the family that if present condition continued the patient might improve a good deal. Unfortunately, however, through circumstances that cannot be fixed the patient's blood pressure must have risen, because he died of symptoms of cerebral hæmorrhage, November 26th, nineteen days after his admission and twelve days after the injection. It cannot be said in any sense that the injection contributed to his death; quite to the contrary, if his toxæmia could have been foreseen his cerebral hæmorrhage might have been prevented. His kidneys were in reasonably good condition. On November 20th the uranalysis showed the presence of albumin. November 22d and 23d the same. The serum test on November 16th was positive; November 27th, weak. Examination of the eyes showed vision for two fingers at twenty

feet, and old multiple retinal hæmorrhages on November 22d.

Case IV. J. M., U. S., white, forty-eight years old, male, married, merchant. Syphilis, tertiary stage. Referred by Dr. Johnathan G. Wells. Gonorrhœa thirty years ago, followed by stricture, cured by dilatation. Apparently infected with syphilis eight years ago, although he does not remember a chancre and denies distinct secondaries. On the elbow and calf two years ago small gummata appeared which were relieved by mixed treatment. Three years ago syphilitic leucoplakia appeared on the tongue which resisted treatment. Has also had a

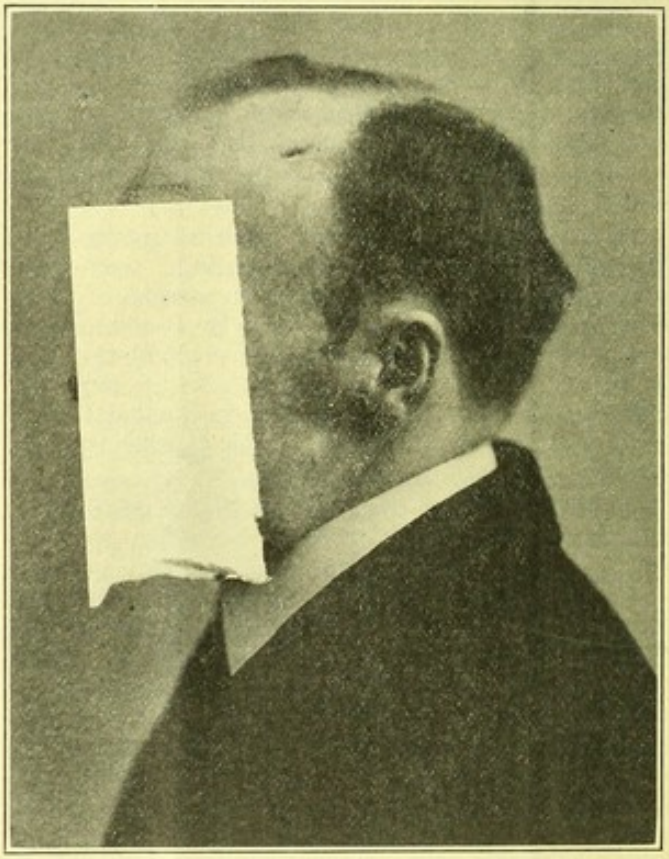


Case VI.—J. J. H., exhibiting conditions before injection, namely, gumma of forehead, excavation of mandible, and gumma formation there.

serpiginous syphilide of the palm. Kidneys negative excepting for a little albuminuria. Is intensely nervous and desired relief of tongue and hand. Injected with 0.45 gramme, December 16th. Complained extremely of the pain, to which he appeared to be very susceptible. The hand was dressed with five per cent. ichthyol, with ammoniated mercurial salve, which with the 606 yielded remarkable results. The change in the tongue was much less definite, although a certain degree of the dryness and stiffness seemed to have disappeared. Blood test, November 19th, weak, positive, which tests on December 23d and January 3d, increased to positive. This sometimes happens under 606. Later blood tests finally showed negative. It is too early in this case to state how permanent these results are.

Case V. Mrs. W. Referred by the courtesy of Dr. A. L. Weindrug. Diagnosis, disseminated syphilis of the cord. Has had several syphilitic babies, stillborn. Latterly, developed paresis of the lower extremities more marked on the left side, also paresis of the left upper extremity. Tendency to involuntary defæcation and urination. About seven weeks ago, 0.5 gramme of 606 was injected. Involuntary defæcation and urination have ceased, and an obvious gain in weight and general nutrition has occurred. About three weeks after the injection, began to move the right leg well and the left less so, also to lift herself up by the arms to the sitting posture in bed. On January 21st, arsenic had disappeared from the urine. In a short time another injection of 606 will be given. She is now four months pregnant and has not aborted.

Case VI. J. J. H., Ireland, thirty-eight years old. Male. Now married. When first seen in 1906, single. Porter. Diagnosis, syphilis, tertiary stage. First seen August 4, 1906. Gonorrhœa and chancroid each once, many years ago. Initial lesion appeared in June, 1906. Apparently eight days' incubation. Treated regularly with injections, up to October, 1909. At this time two gummas of the forehead developed, which improved under treatment. At this time he withdrew from treatment going to the Postgraduate Hospital Dispensary, where, under antisyphilitic measures, the gummata disappeared. Then his jaw bone began to show signs of osteomyelitis, abscess and sequestrum all requiring surgical treatment. In June, 1910, gumma of the forehead relapsed. Has also had a great deal of neuritis, chiefly on the left side of the face and the forehead. Has considerable nasal catarrh, ozœna, and a small perforation of the hard palate, well forward. He came to me begging to receive a dose of 606. Admitted to the People's Hospital, December 5th, received on that same date an injection of 0.5 gramme of 606. He ran a moderate temperature for two days, gradually declining to normal on the seventh day. There was considerable pain at the point of injection. The gumma immediately began to improve in which the surgical dressings may have been an important factor. The weight rose from November 30th at 138 pounds to 144¼ pounds on December 28th. The gumma was three quarters healed by December 28th; other features are shown by the photograph. The serum test on November 30th was strong;

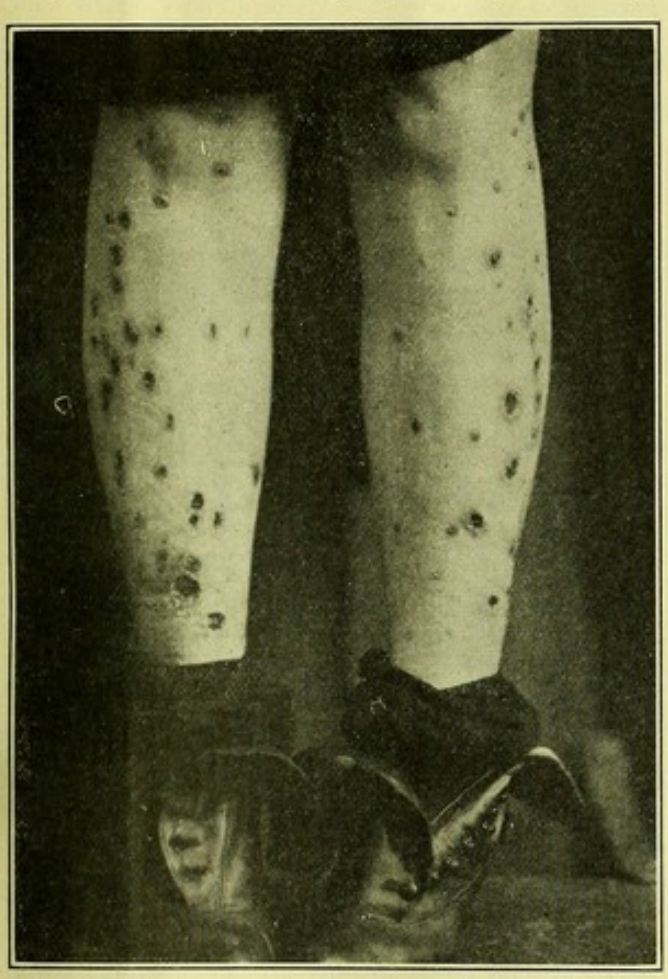


Case VI.—J. J. H., about six weeks after injection; gumma of forehead virtually healed, and that of mandible reduced.

December 12th, weak; and negative on December 19th. Albumin was present in the urine on December 6th, 8th, and 11th. Eyes, normal.

Case VII. O. A. F. Referred to me by the courtesy of Dr. Pasternak. Single, U. S., ticket speculator, twenty-six years old. Admitted November 28th to the People's Hospital. Diagnosis, tertiary syphilis, periostitis of the shins. Family history, negative. Previous history, moderate alcoholism. Gonorrhœa five years ago. Secondaries of the skin denied. Mucous patches prompt and persistent. Has lately had pains in the shins, breaking his rest.

Treatment has been mercury and iodide internally. Admitted November 29th; 0.5 gramme of 606 was injected. The result has been an apparent decrease in the shins, especially at one point on the right shin, where a distinct softening and sensitiveness have occurred. As was expected, this was not an ideal case for a remarkable result, but we believe the presence of the pain in his shins justified the injection. The blood pressure in this patient was 117 on admission. Varied from 111 to 118 while in the hospital and decreased to 105 after discharge. His weight

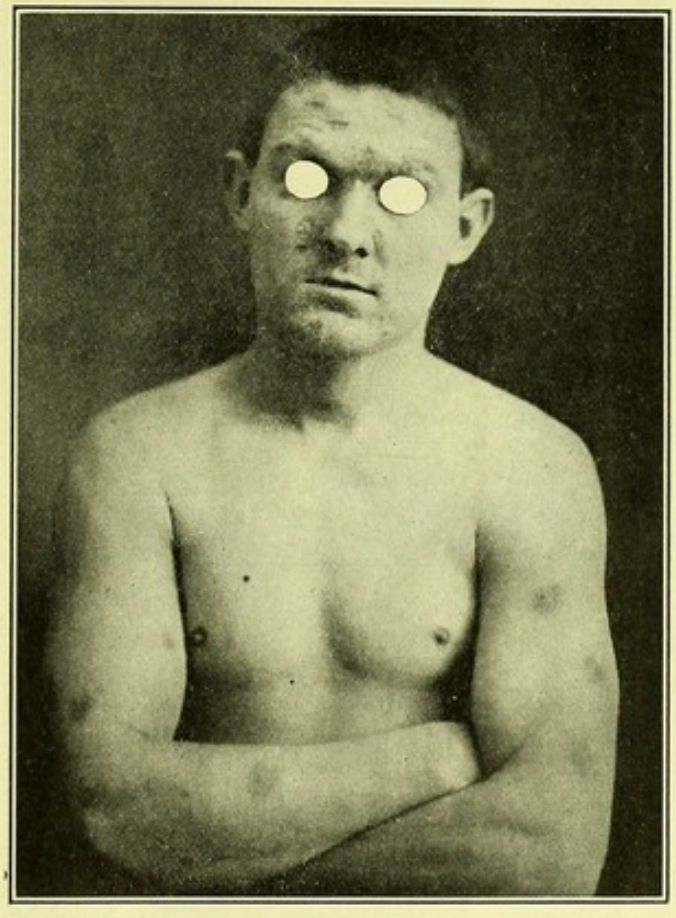


Case II.—E. B., presenting ulcerating and scaling lesions of lower extremities; similar conditions were elsewhere on the trunk. All healed in about four weeks after injection, leaving the usual atrophic scars. Unfortunately the patient returned home before a second photograph could be made.

remained the same at 159 to 160 pounds. The serum test was negative on November 28th, December 1st, 5th, and 12th, almost negative on December 19th, and weak on December 27th. Eyes, normal.

Case VIII. J. G., married, Spaniard, porter, twenty-nine years old. Admitted to People's Hospital, December 12, 1910. Diagnosis, syphilis, tertiary stage. Family history, negative. Previous personal history, negative. Syphilis acquired twelve years ago. Reasonably good history of mucous patches and alopecia, but not of rash. Gonorrhœa six years ago. Chief complaint, wife has had seven miscarriages varying from third to seventh month, never went to full term. Several children have been macerated as though syphilitic. Referred to me by Dr. Hideyo Noguchi, of Rockefeller Institute, for medical research for 606. Injected, December 12th, 0.55 gramme. Ran a variable temperature about 100° for the second and third days, about 102° on the fourth and fifth days, normal on the sixth day. There was considerable pain, which disappeared when the patient was discharged on the seventh day. The blood pressure was highly variable being 155 December 13th and 16th; 152, December 27th; 142, December 15th; 138, December 19th. The serum test on December 10th was strong; December 16th and 17th, positive; December 21st, almost negative; December 27th, very weak. Eyes, normal. There has been slight increase in weight. It is too early to state whether the injection is going to control the syphilis in this patient sufficient to permit his wife to have healthy, living children.

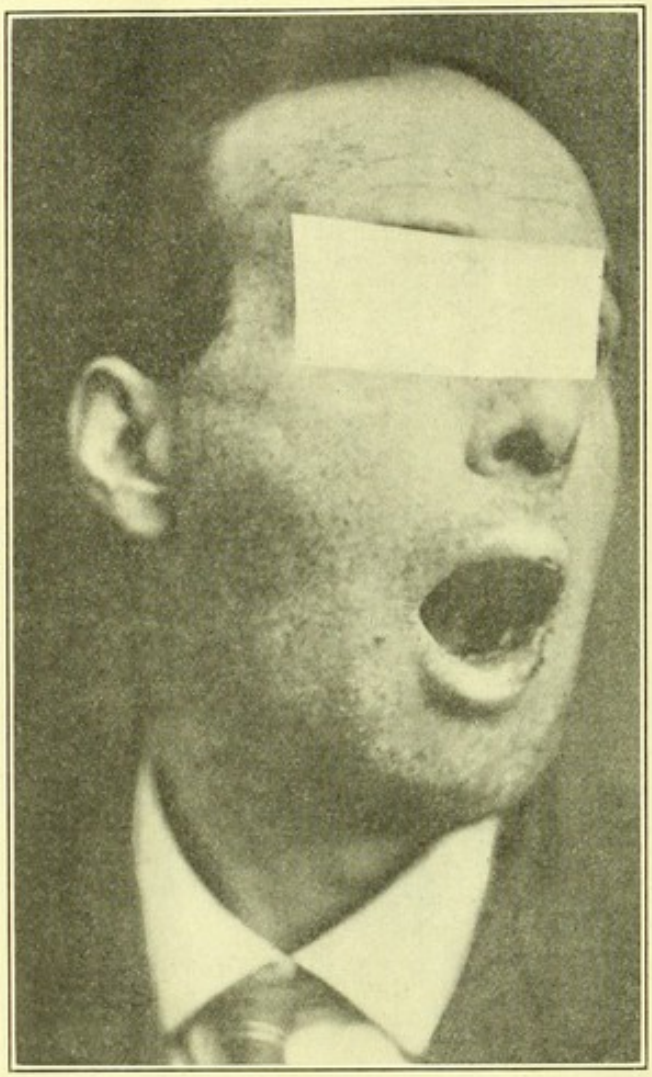
Case IX. R. G., the wife of the preceding patient. Spanish, housework; twenty-six years old. Admitted December 12, 1910, to the People's Hospital. Diagnosis, syphilis, tertiary stage. Family history, negative. Previous personal history, negative. Venereal disease denied. Can recall no signs of syphilis after marriage. Married eight years, has had seven miscarriages, as previously stated. Is now pregnant possibly for two months. Is in good general condition, and complains of her childlessness; 0.5 gramme of 606 were injected, December 12th. The patient held the muscles of her buttock very tense so that some of the injection was forced out into the fat where it quickly formed a large node, which at the end of the third week at the present writing seems to be slowly disappearing. Physical examination at the New York Hospital shows that she has a very small fibroid in the anterior surface of the womb, the size of a hazel nut. It is possible that further fibroids within the womb may account for her miscarriages, but they would not account for the syphilization of the children. Blood pressure is stated constant at about 105. The temperature rose to 101° F. on the fifth day after varying previously between 99° F. and 100° F. and then declined to normal on the seventh day when she was discharged. The serum test on December 12th was strong; December 16th, positive; December 17th, almost negative; December 27th, weak. The node referred to above subsequently broke down into a sterile abscess, that is, necrosis of the fat occurred without infection.



Case XIV.—C. K., showing deep scars of early rupial syphilides. These were ham color, similar to early secondaries just before the third injection and did not change color much after, although a positive became a negative blood test.

Case X. S. S., Russian, white, about forty-five years old, male, married, merchant: tertiary syphilis. Referred by Dr. Max Wolper. Chancre of the anus. Acquired about fifteen years ago. At this time he was treated by Dr. Abraham Jacobi. Although his history of secondaries

is not definite, the statement that Dr. Jacobi treated him should be accepted as good evidence that he had the disease, together with the facts that his blood test is positive and that his wife has borne four dead syphilitic babies; 0.6 gramme of 606 was injected, December 23d. On the 24th, his blood test had decreased from strongly positive on December 6th, to positive on December 23d and 26th, and remained so when next tested, December 26th. Blood



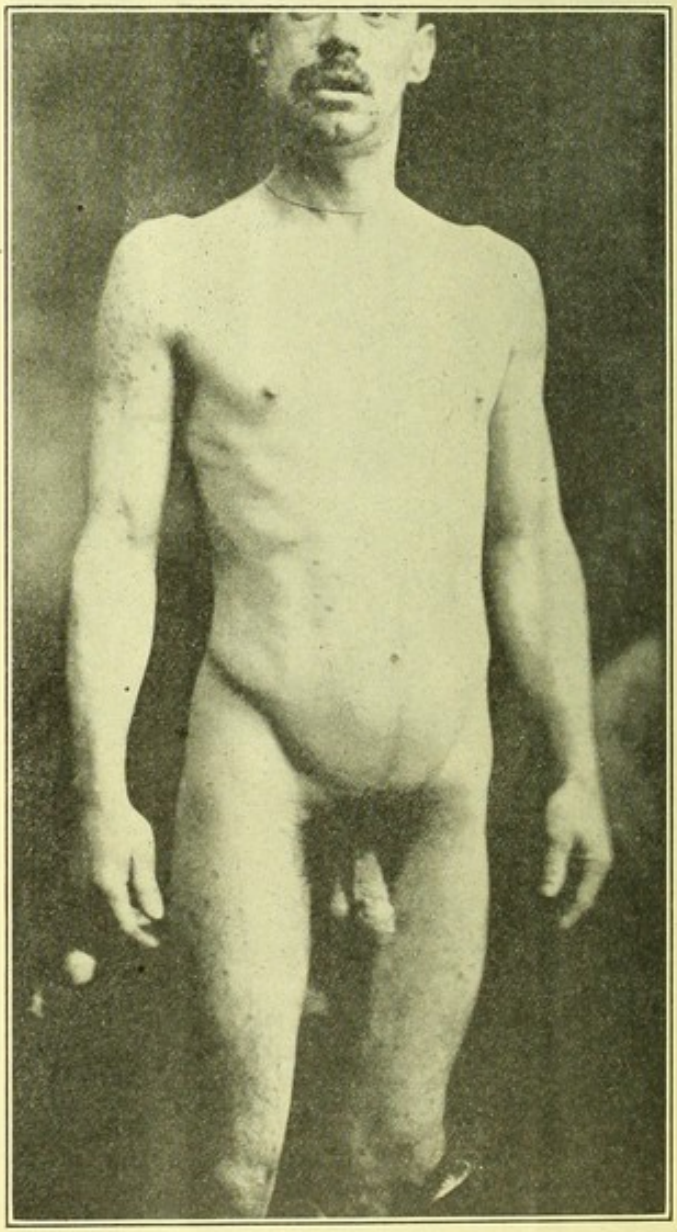
Case XVI.—C. H., indicating very extensive chancre of the lip rather well, but not so well as the prominent lymphadenitis on same side of neck.

pressure on December 24th was 142, declined to 138 on December 26th, and rose to 162 on December 30th. What the result will be in this case is impossible to state for a year or two, or until the wife again conceives. The wife of this patient is to receive an injection early in January.

Case XI. E. B., U. S., white, twenty-three years old, female, single. First seen December 17, 1910. Diagnosis, syphilis of the innocent. Second stage. Source of infection seems to have been eating utensils of her brother. Site of infection seems to have been on the tonsil. Of this positive signs were absent on examination. Has had seven months of active treatment by the ingestion and inunction methods during which chancre and throat recovered but upper and lower extremities remained the seats of large and small scaling or rupial syphilides. Has lost perhaps fifteen pounds in the past six months. Has a moderate albuminuria, but no casts. The photograph shows the punched out, ulcerating rupial syphilides with scabs removed, and a few of the scaling lesions above nearer the knee. December 18th, received 0.6 gramme of 606, which resulted in a very prompt relief of the skin lesions so that in two weeks nearly all had healed, and the patient's general condition had improved. In addition to the 606, the lesions were treated locally.

The skin lesions were covered with mercurial plaster, if scaley. Scabs were removed from the rupial ulcers and wet dressings of 1 in 5,000 mercury bichloride applied until the pus had disappeared. Then five per cent. ichthyol in ten per cent. ammoniated mercurial ointment was applied. No doubt this treatment had a very beneficial effect. The blood test was negative upon admission and has so remained. This anomaly of a negative test in the presence of active skin lesions is not by any means uncommon. The case is to be marked one in which the diagnosis of syphilis must be accepted on its clinical signs. The serum test on December 20th, negative; December 23d, almost negative. Eyes, normal.

Case XII. I. W., single, Pole, shirt maker, twenty-four years old. Admitted to the People's Hospital November 29, 1910. Family history, negative. Previous history, had the diseases of childhood. Recalls no other sicknesses. Constipated. Appetite and sleep only fair. Venereal disease, denied, other than the present condition.

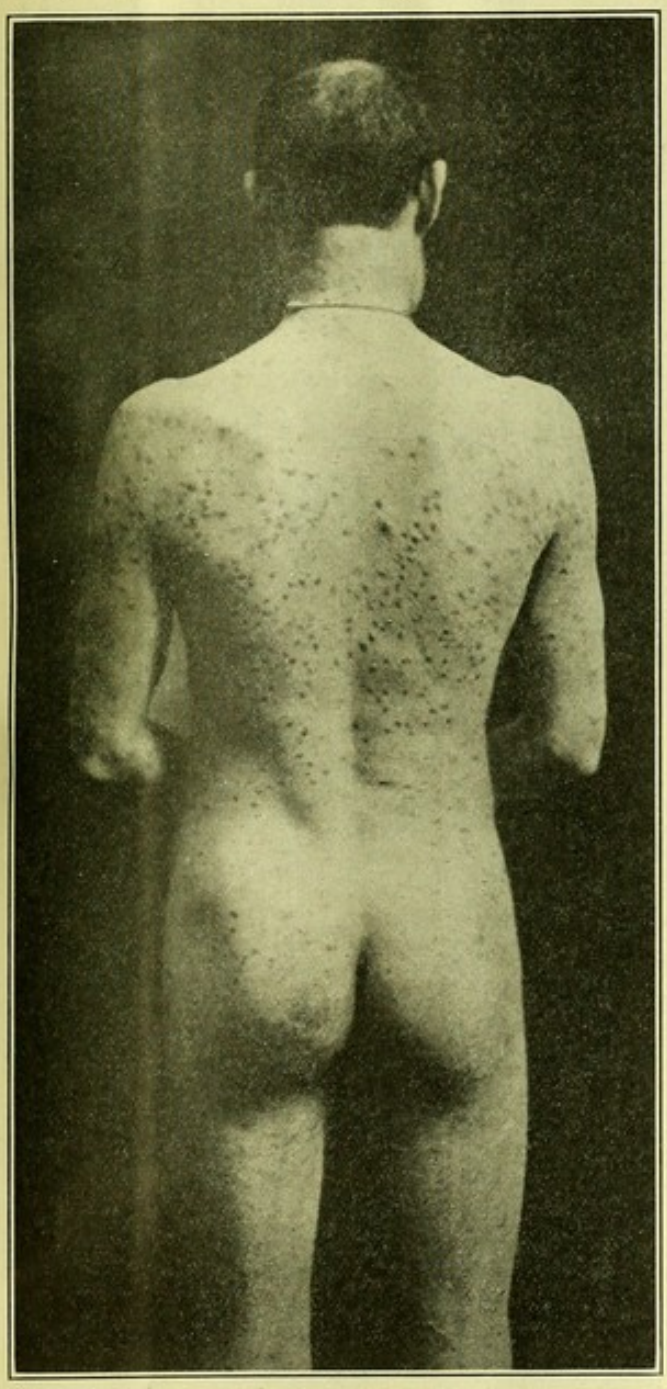


Case XVII.—J. McL., shows chancre of mouth, pronounced cervical lymphadenitis, pustules and rupials of body, extremities, and genitals.

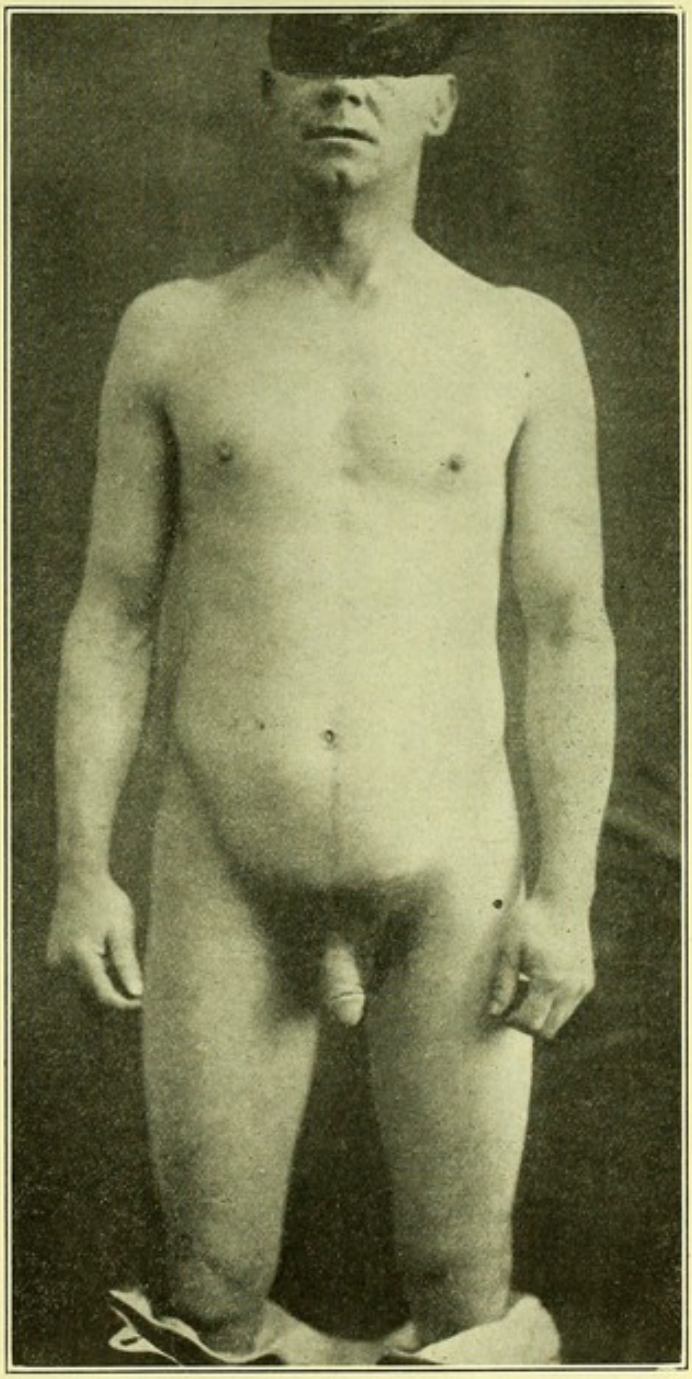
Three months previous to admission chancre appeared on the abdomen, just above the pubes, followed by a bubo on the right side. Two days later, surgical dressings were applied to the chancre followed by a course of internal and intramuscular treatment. A peculiar punctate, papular rash appeared, four or five weeks after the chancre, on

the legs and body. Mucous patches on the tongue showed themselves five or six weeks after the chancre. Physical examination, evidently a man in poor health and of ill nourishment. Pupils react to light and distance. Tongue coated and tremulous. Mucous membrane pale Heart, lungs, and abdomen, negative. The foregoing is the physical examination upon admission. When first seen, October 20th, at my office there was in addition to the foregoing a distinct rash, a glandular involvement, with patches everywhere in the mouth. The patches were treated in the usual manner and intramuscular injection of the mercury cyanide given without very much effect on the rash except very slowly. The patient learned ot 606 and was from visit to visit threatening suicide. It was to control this decidedly nervous depression that I consented to give it to him. The benefits upon his general feeling and attitude were manifest, also upon his throat in which the patches cleared up. The blood pressure varied from 120 to 142. The weight gained a few pounds from 123½ to 124¼ pounds. The Wassermann test on this patient was negative. Notwithstanding this fact he insisted on 606, which was given him rather than run the risk of his destroying himself. I have never in many years in the practice of syphilis seen a patient who was so mentally disturbed. It is not possible to say whether this was a psychic effect or the result of the toxines.

Case XIII. C. G., referred to me by Dr. Charles Kennedy. Married, U. S. police officer, twenty-six years old. Admitted October 26, 1910. Family history, negative, except father died of heart disease at the age of forty-nine years. No chronic disease, tuberculosis, or syphilis. Previous history, bowels, appetite, and sleep normal. Excessive steady smoker. Measles and diphtheria in childhood. Malaria and dengué during his twentieth year in the Philippine Islands in the army. Gonorrhœa seven and two years ago. Cure established in four or five weeks on each occasion. Present history, a year ago, eight days after intercourse, gonorrhœa began. Followed in two days by four sores and right inguinal adenitis. The gonorrhœa and sores were well in about two months. At this

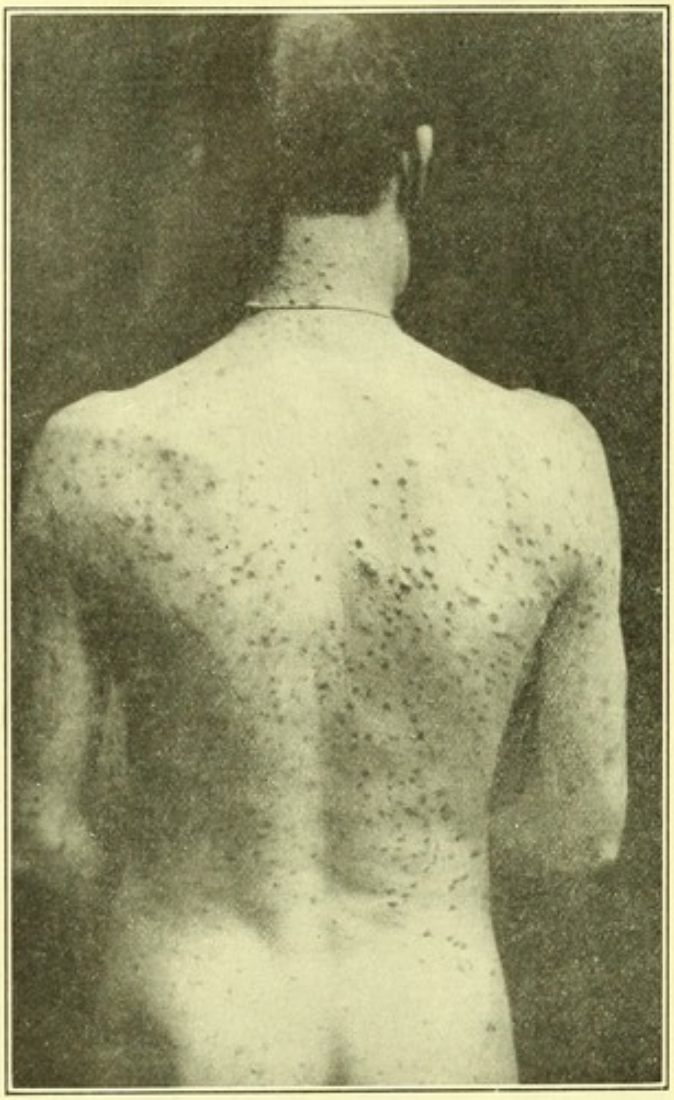


Case XVII.—J. McL., showing distribution of skin lesions.



Case XVII.—J. McL., about eight weeks after injection.

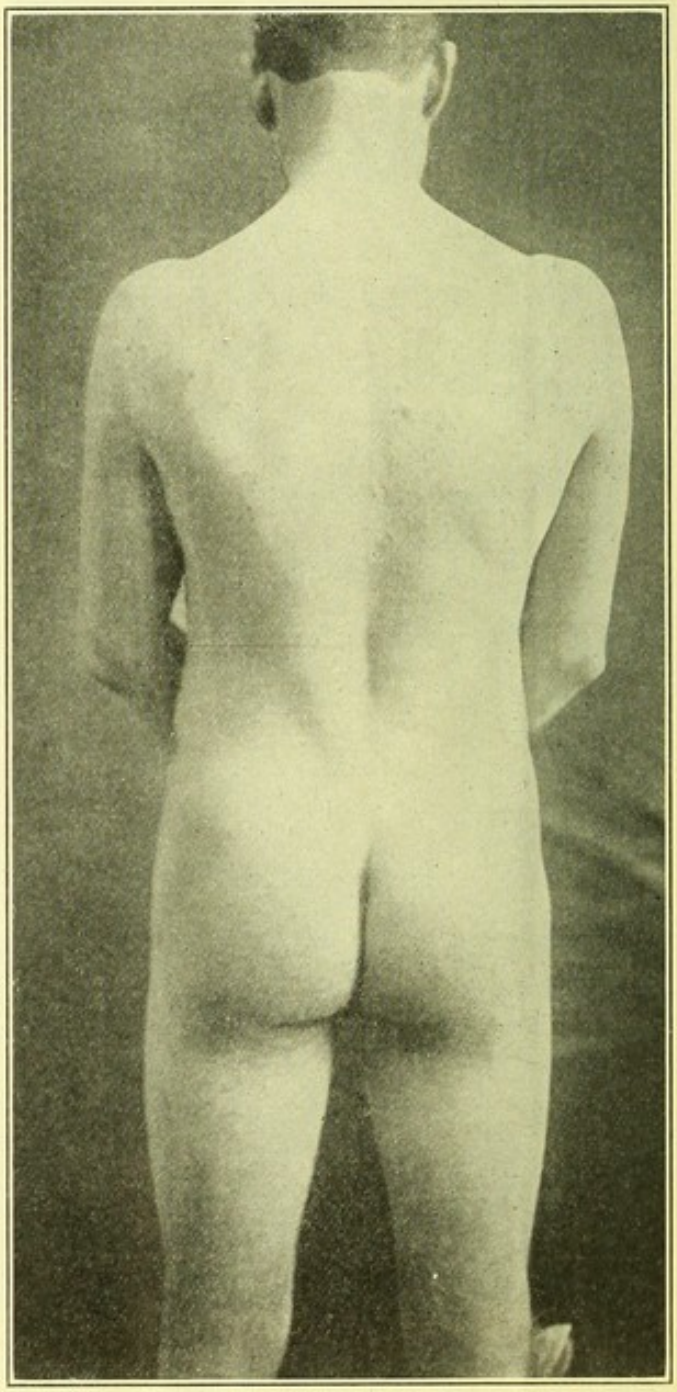
time a chancre developed on the mouth, involving upper and lower lips. This was followed by patches and the rash which lasted a short time. The treatment has been internal and despatched the symptoms, excepting the patches which have been persistent ever since. October 27th, 0.6 gramme was injected. In this case the method



Case XVII.—J. McL., presenting pustules and rupials.

of Herxheimer was used and the medicine injected in the form of an emulsion. The injection was followed by a very prompt disappearance of the obstinate lesions on the tongue. The serum test became negative in a few days. The injection was made subcutaneously into the fat of the abdomen. This was followed by a very unusual degree of redness, œdema, and infiltration, which extended downward upon the thigh and upward toward the navel, making a mass, eight or ten inches in diameter. Under wet dressings this slowly disappeared, so that six weeks after the injection nothing remained but the point of softening in the centre where the medicine had been deposited. Examination here showed deep peculiar feeling similar to fluctuation. The patient had at no time ran a temperature above 99° and except for the temporary pain at the point of injection suffered no inconveniences. The serum test, October 22d, was positive; October 31st, November 2d, and November 7th, almost negative; December 14th, negative. The blood pressure in this patient was 142½ on admission, remained at 137 from October 27th to 31st, and until January 14, 1911, varied from 122 to 132. His weight increased from 191 to 208½ pounds. The urine on admission showed a slight trace of albumin, which decreased to negative on second examination. Arsenic was also present on October 27th in the urine. The site of the injection became a necrotic centre with a black slough, very little pus, no visible infection, and a very sluggish course. The slough was hard to remove and had in part to be cut away.

Case XIV. Referred by the courtesy of Dr. Hideyo Noguchi. C. K. U. S., white, twenty-three years old, male, single. Plumber. Syphilis, second stage. Gonorrhœa twice; last attack one year ago. Infected with syphilis six months ago. Incubation nearly five weeks. Very active secondary lesions began within four weeks, resulting in deep scars on the body and face, as shown in the photograph. Was treated at Bellevue Hospital for a few weeks with mercury and potassium iodide, by each of which he was greatly poisoned. Received his first dose of 606 October 1st; second, October 26th, and third, December 13th, 0.5 gramme. Temperature rose slowly to 100.6° on



Case XVII.—J. McL., about eight weeks after injection.

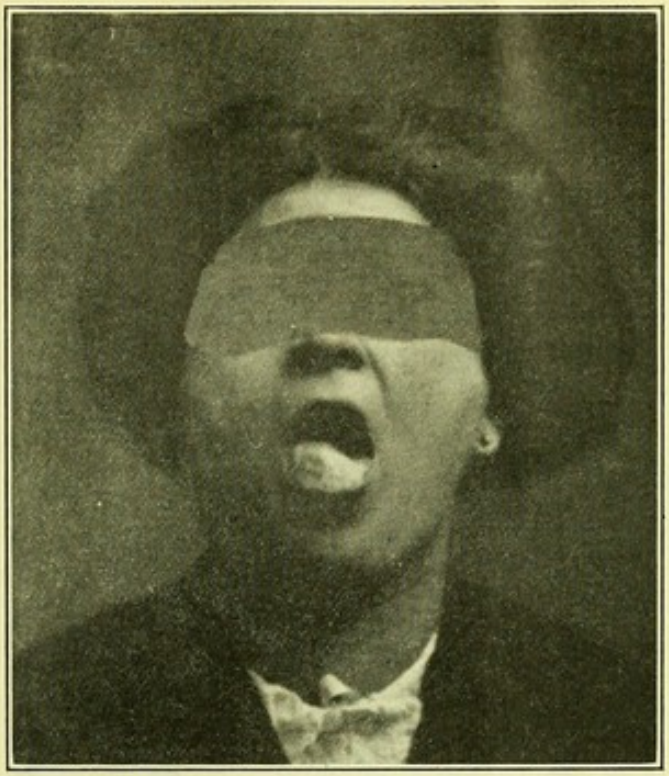
the third and fourth days. Returned to normal on the sixth day. No definite change took place in the scars, as was to be expected. The blood test ran as follows: Strong reaction a few days prior to December 12th when Dr. Noguchi referred the case to me. Weak positive De-

cember 16th and 27th. Blood pressure has varied between 134 on December 15th, 122 on December 16th and 19th and 137, January 2d. Weight has slowly increased from 147¼ pounds on December 16th, to 149¼ pounds on January 2d. The patient says he feels better but there are no clinical signs to mark this progress except the fact that the serum test on January 3d was negative. Eyes and vision, normal. O. S. old hæmorrhagic chorioiditis from below, pigmented hæmorrhage near nerve head and macula.

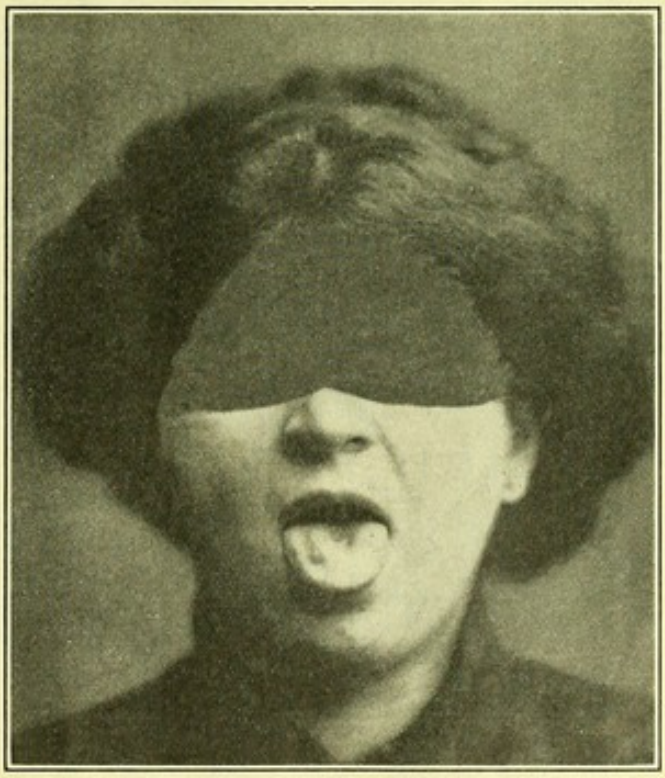
Case XV. H. W., referred by the courtesy of Dr. G. I. Miller, single, Russian, clerk, nineteen years old. Admitted, November 27th, to the People's Hospital. Family history, negative. Previous history, negative. Gonorrhœa four years ago. Present illness, syphilis contracted about eighteen months ago. Clear history of secondaries. Treated with the usual mercurial injections, twenty-six in number. Iodide by mouth for fourteen months. Present condition, positive Wassermann reaction. A feeling of malaise and a laryngitis. November 29th, 0.25 gramme injected into each buttock. Slight rise of temperature for three days, never above 101.4°. The Wassermann test declined until it became very weak on December 29th. The laryngitis improved somewhat and the patient's general feeling of being ill and out of sorts disappeared. The serum test was strong on December 1st, 5th, and 12th, and weak on December 19th and 29th. The blood pressure in this patient on admission was 135; varied from 135 to 138. His weight has remained practically at about 127½ pounds.

Case XVI. C. H., single, U. S., machinist, thirty-eight years old. Admitted to the People's Hospital November 30, 1910, in fair health with a large chancre in the left angle of the mouth involving both lips. Family history, negative. Previous history, negative. Had the usual children's diseases. Uses tobacco and alcohol to excess. Venereal history: Had gonorrhœa fifteen years ago, also chancroid fourteen years ago. Present history, was bitten on the lip by a prostitute while kissing her. Chancre came about three weeks later, accompanied by very great swelling of the lymph glands on the left side of the neck. The chancre is shown in the photograph, but the lymph glands are only slightly within view owing to the angle from which the photograph was taken; 0.5 gramme of 606 was given November 30th. The results were disappearance of pain in the chancre within a few hours, softening and loss of pain in the lymph glands within twenty-four hours, and, on the fourth day, the lymph glands had almost entirely disappeared and the chancre had already greatly decreased in size and had begun to heal. Within twenty-four hours the patient was able to eat with more freedom than he had in ten days or so. The blood reaction was negative. The spirochætæ were not found in the chancre, because caustic had been used by another physician. In my effort to get the specimen I probably did not scrape in deeply enough. The spirochætes travel to the deep parts of the lesion after a caustic. This patient was most ungrateful and did not return for observation after December 5th, notwithstanding written requests. The serum test was negative on November 29th and December 1st, and almost negative on December 5th. On November 30th patient's weight was 134½ pounds, blood pressure, 124.

Case XVII. J. M., widower, U. S., driver, thirty-three years old. Admitted November 14th to the People's Hospital. Diagnosis, chancre of the mouth. Family history, negative, except one brother who died of tuberculosis of the throat. Previous history, excessive smoker and drinker. Frequent venereal disease. Present illness, chancre noticed nine weeks before admission, followed by rash all over the body. Six weeks ago was treated for a short time with injection of mercury without benefit at the House of Relief for the chancre and lymph glands in the neck. 606 was recommended; injected, November 15th, with 0.5 gramme. Improvement in the lesions immediately occurred so that when discharged, November 18th, the lymph glands, which had been one mass, became distinct nodes and the rash began to get paler. This patient was seen twice during the next two weeks at the clinic of the House of Relief. In that time the chancre had nearly healed and the lymph glands had nearly disappeared from the side of the face and the rash had nearly faded. Subsequent to this the patient disappeared so that the final results cannot be stated at this writing. (This patient reappeared on January 4th in excellent condition, as is shown by the photographs.) The serum test was strong on November 16th, positive on November 18th, and almost negative on November 29th. The blood pressure in this patient was 105 on admission. Varied from 105 to 117 and decreased to 105 on November 18th. His weight remained constant at about 133 pounds.

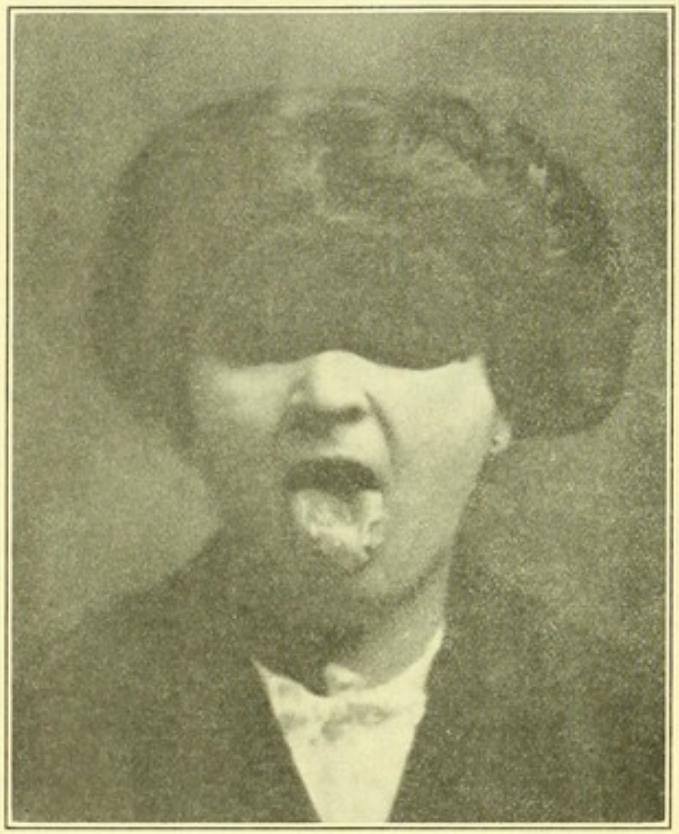


Case XVIII.—S. R., degree to which the chancre enlarged the tongue is shown very well. (From front.)

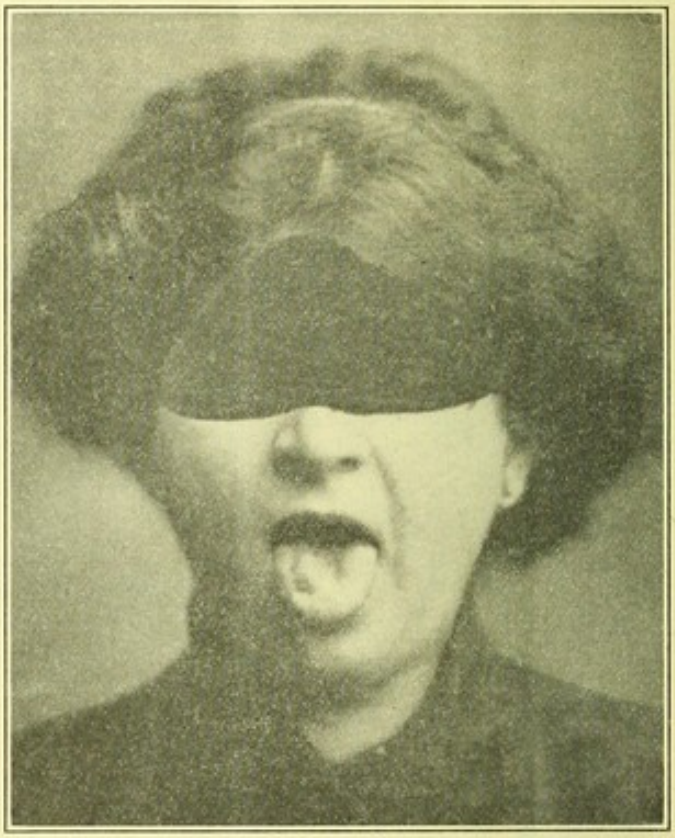


Case XVIII.—S. R., about four weeks after injection the tongue was nearly normal, and in about another week was normal. (From front.)

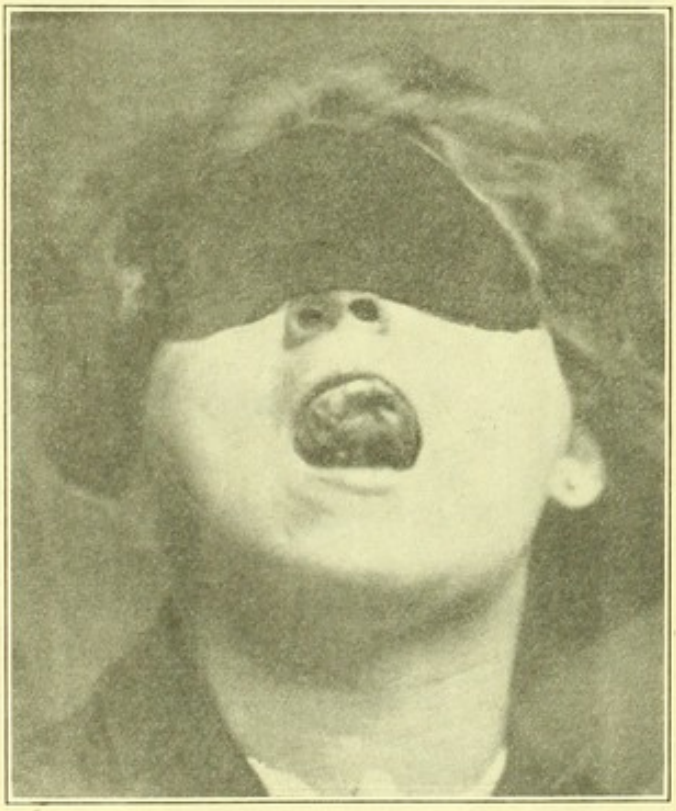
Case XVIII. S. R., referred by the courtesy of Dr. Solomon Rottenberg. Russian, saleswoman, twenty-one years old, single. Admitted November 30, 1910, to the People's Hospital, when 0.5 gramme was administered. Diagnosis, chancre of the tongue (*syphilis insontium*). Family history, negative. Has not the slightest idea as to how she became infected. Is not engaged to be married or receiving the attentions of any young men. The photograph shows the excavated chancre very well. Likewise the result at the end of about four weeks. The treatment of the chancre was surgical. Owing to the great sloughing in its walls no *Treponema pallidum* was found in



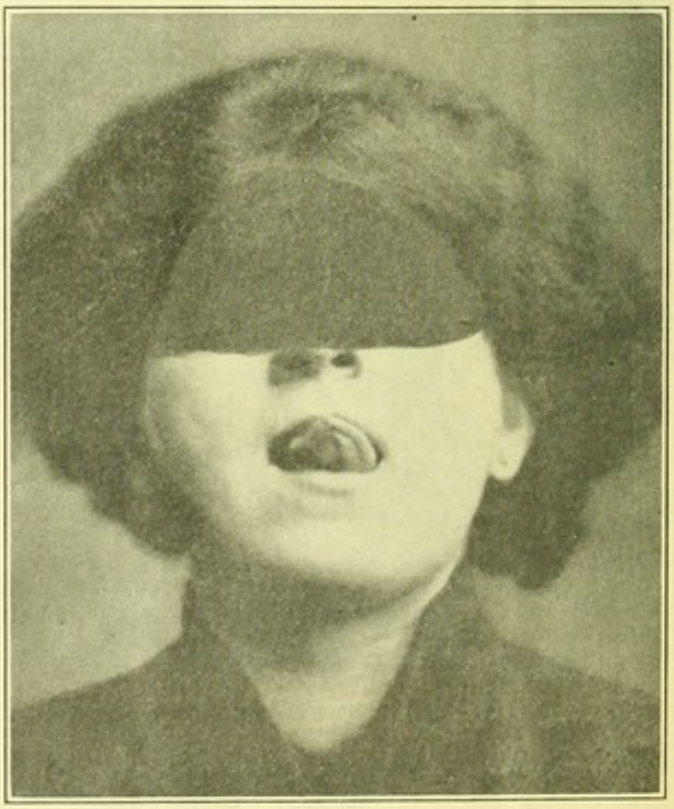
Case XVIII.—S. R., enlargement of chancre is well shown, involving much of tip of tongue. (From above.)



Case XVIII.—S. R., about four weeks after injection, the enlargement of the tongue is slightly present, but disappeared completely in about another week. (From above.)

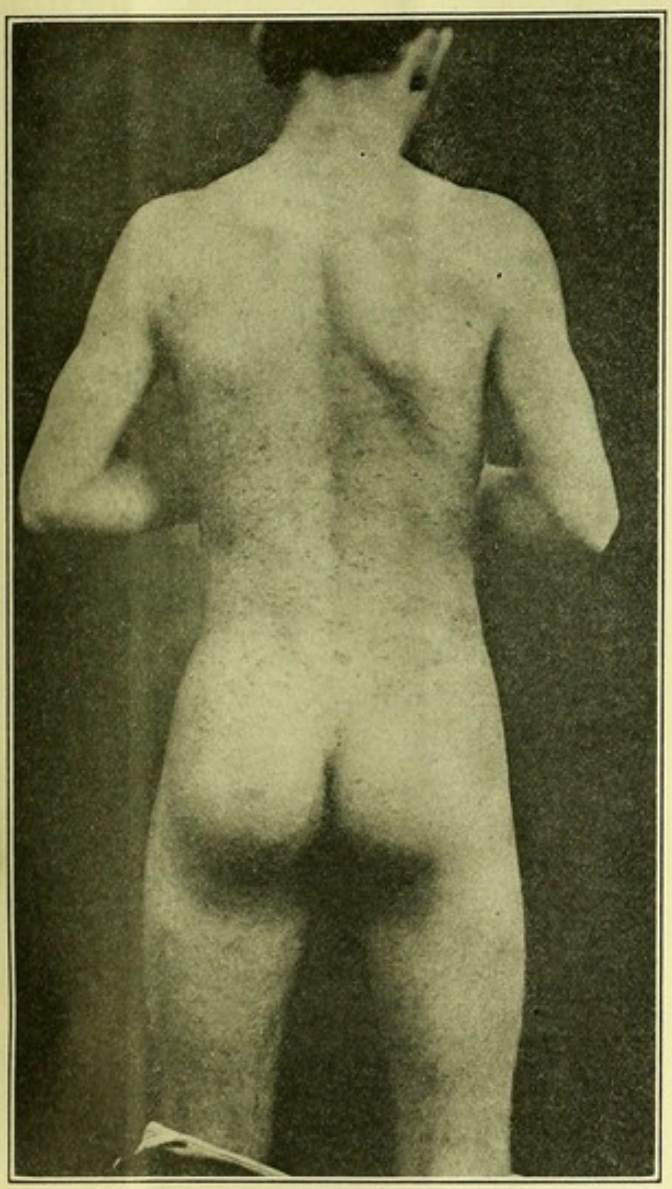


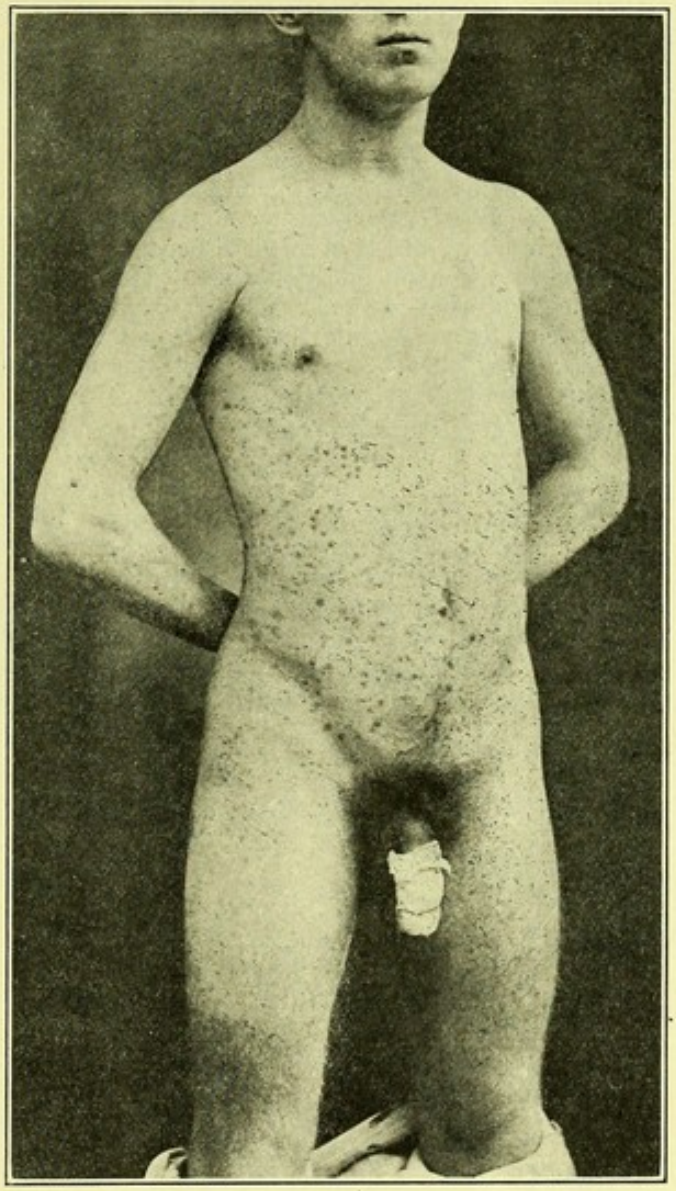
Case XVIII.—S. R., showing excavation of chancre and thickening of tongue. (From below.)



Case XVIII.—S. R., about four weeks after injection, showing excavation healed and enlargement decreased. (From below.)

scrapings. The patient refused to allow a piece to be cut out from the tongue for examination. The chancre has healed completely and at present writing, January 3d, even the induration is gone. The patient has gained about four and a half pounds in two weeks and looks greatly improved in health. This will be a very valuable case to follow as the years progress because of the immediate benefit. The serum test on November 17th and 21st, strong; December 3d, positive; December 19th, almost negative; January 3d, negative. No syphilis of eyes.





Case XIX.—J. M., showing very marked large and small macular eruptions almost universally distributed, although mercurial injections had been given regularly for several weeks.

Case XIX. J. M., single, U. S., clerk, nineteen years old. Admitted to the People's Hospital November 20, 1910. Diagnosis, syphilis second stage. Family history, negative, also previous history. Drinks and smokes moderately. Has had usual diseases of childhood. Present history, always has had a marked phimosis for which circumcision was suggested, in his childhood. About week after intercourse a large chancre involving the whole of the mouth of the foreskin appeared. Treated by mercury injection with little effect on the chancre or the skin lesions. Rash appeared, which did not yield well to the mercurial treatment; 606 decided on. Injection was given November 21st, 0.6 gramme Circumcision also done. Improvement in the conditions immediately appeared, the circumcision healing promptly and the rash disappearing positively but rather slowly. The blood pressure was not materially affected by the injection, the range being from 103 to 110. The weight remained constant at about 163 pounds. The photograph shows the rash just before the admission to the hospital. The serum test on November 19th, 22d, and 28th was positive; on December 1st and 5th, weak; December 12th, very weak; December 19th, almost negative; December 31st, negative. This patient was ungrateful and disappeared before a second photograph could be secured. He was last seen January 7th, when rash was still faintly present.

Case XX. A. A., German, forty-one years old, single, brassworker. On February 1, 1909, at three o'clock in the morning, patient was awakened by a severe pain in the right thigh above the knee. A few days later the leg from the knee to the groin was swollen and remained so until an abscess which had formed at the knee was cut, after which the swelling at the knee disappeared, but the swelling near the groin remained. Various doctors treated him for rheumatism of the muscles, but was never treated for syphilis or skin disease of any description, as far as he knew. In August, 1910, he went to Sharon Springs, N. Y., to take the sulphur baths and massage. After the first massage there was a slight discoloration which became gradually darker. On September 9th it was lanced by a physician at Westport, N. Y., releasing about a cupful of bloody water. The wound was permitted to close without being thoroughly drained. On September 19, 1910, Dr. Lewson again opened the wound, after which he

referred the patient for 606. The serum test was weak to positive. The blood pressure varied from 119 to 142. 0.5 gramme 606 was given November 17th. Patient remained in bed until November 21st, and was subsequently observed at short intervals. No effect on the limb was observed. The lesion later proved to be an osteomyelitis.

CONCLUSIONS.

Syphilis has been historically known for many hundred years and its well established characteristics have been studied during this time, as to chronicity and tendency to relapses. Many cases have been cured permanently by mercury and potassium iodide. Hence, it would be premature and immature to think that these drugs may be supplanted as if by magic. Since the observation of the cases reported in this paper in January, 1911, the writer has administered salvarsan to about thirty other patients in all of whom immediate benefit occurred. This leaves the main question open: How permanent and enduring are the results of salvarsan? If permanent, then a wonderful discovery for the relief of syphilis has been made. But this question remains for the next twenty years to decide.

Another question still unanswered is: What is the best dose? Originally 0.3 gramme was proclaimed as correct. Now it is 0.6 gramme; indeed, some of the German observers have given more. Here, again, only patient study and long continued observation will answer the question.

If the results of salvarsan shall be shown to be temporary rather than permanent, by relapses which have already been appearing in the hands of many careful observers, then the question arises: How frequently may the medicine be repeated in the correction of such relapses? Here, again, only many careful observations, distributed of necessity widely the world over and persisting through the next twenty years, can in human experience furnish the solution of this problem. Again, only time reckoned in many years can answer the question, through the study and record of many cases: Given a relapse, will a repetition of salvarsan be better than a resumption of mercury and iodide? Such a question is of far reaching importance!

Finally, in closing, the words of Marshall (*Lancet*, February 25, 1911) cannot be improved: "The two main questions to be decided are: First, is arsenobenzol capable of replacing mercury and iodides in the treatment of syphilis? Secondly, if it is incapable of doing this, is it of value as a third weapon against syphilis? Before any drug can replace mercury and iodides it must be proved capable of producing one or more of the following effects: (1) The realization of an abortive cure of syphilis; (2) the prevention of tertiary or parasyphilis manifestations; and (3) the healing of syphilitic lesions with greater rapidity, greater constancy, and, at the same time, with less liability to relapse and recurrence than is the case with mercury and iodides. It must compare favorably with the latter as regards dangerous toxic effects."

In the main, it is rational and conservative to leave all these points for settlement by many years of time and by a larger and larger record of carefully studied cases.

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