REVIEW OF SYPHILIS WITH ESPECIAL RELATION TO HEREDITARY SYPHILIS *

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Part Two — Newer Therapy

The foundation on which the newer therapy of syphilis rests is composed, in largest part, of material derived from the results of the serum tests which we have just been considering in Part One. It follows that, as the solidarity of a structure is affected by the strength or weakness of its foundations, so must the opinions expressed in Part Two for and against salvarsan and neosalvarsan be judged in accordance with the estimates formed of the strength or weakness of the serum tests.

CRITICISMS

Having seen that criticism of the serum test method exists, it cannot occasion surprise that the newer therapy of syphilis should also be criticized. Klotz⁶⁷ is most outspoken in his objection to an employment of salvarsan or neosalvarsan as a routine method of treatment of syphilis. He admits that, occasionally, the newer remedies do possess a certain value, but, speaking generally, the indications for their use will be reduced to a minimum if mercury and iodids are prescribed with proper judgment and administered with thoroughness. Gaucher⁴⁷ uses the Ehrlich remedies as a last resort, i. e., when mercury has failed. He considers them both untrustworthy and dangerous. Hoffman⁵⁹ states that, if we may judge the efficiency of the newer therapy by its success in protecting the offspring of syphilitic unions, we are not yet justified in abandoning the ancient rule of forbidding syphilitics to marry until they have been under observation for at least three years. The most that we are permitted to hope from the new remedies is that we shall be able to substitute two or three injections of salvarsan for five or six courses of mercury. Experience leads Levy-Bing and Duroeux⁷³ to write that they cannot recommend the new remedies as the best method of treatment in hereditary syphilis. Müller⁹⁰ is in doubt as to which method is superior, mercury or salvarsan. Langford⁷⁰ favors mercury when there is visceral involvement. Noeggarath⁹⁴ considers mercury

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superior to salvarsan if the infant's physical condition is not good, or if a septic process exists, even one not syphilitic. Watrazewski¹³⁰ much prefers mercury to salvarsan. Shields¹⁰⁸ was so disappointed with the results of salvarsan that he doubts if it can either abort or cure. Nichols and Mutot⁹² call salvarsan a useful adjunct to mercury. Wilson¹³⁴ opposes the routine employment of salvarsan and neosalvarsan. The present popularity he ascribes to a lamentable international hysteria, the result of "an over-riding of science by commercialism." He warns the profession that unless it takes a saner view of the uses and limitations of the new remedies, five or ten years hence every child born of syphilitic parents will inherit the disease.

De Aja replies that the criticisms prove only that the critic lacks the courage to use the remedies as they should be used. If he would only give them in adequate doses, his opposition would disappear at once. De Azua,⁶ Dreyfus^{33, 34} and Iverson⁵⁷ agree with de Aja that such insufficient dosage cannot be expected to give proper results. Spiethoff¹¹³ even declares that if the total dosage is too small, salvarsan is dangerous, but that the same reproach cannot be made if adequately large. Whitehouse and Clark¹³³ are so enthusiastic over salvarsan therapy that they assert that a disease which salvarsan does not at least relieve cannot be syphilis.

METHODS

Almkvist³ says that, in his opinion, a combination of salvarsan and mercury is the best method of treatment. He reasons that the cure of syphilis is produced by the continuous action of substances on the spirochetes. Salvarsan cannot exert such an effect for, acting in the blood-stream, it does not reach the spirochetes hidden in the tissues. Mercury used alone cannot cure for the reason that it is impossible to give it in sufficiently large amounts without doing damage to the patient. Therefore, the only logical method is to reinforce the action of salvarsan by the supplemental effect of mercury. Barduzzi¹⁰ says that, without mercury, salvarsan is powerless to cure. According to de Azua,⁶ frequent injections are necessary if salvarsan is not supplemented by mercury. Corbus²⁷ believes that it is possible to cure with either salvarsan or mercury alone, but a quicker result is obtained if they are used in combination. Fordyce,⁴² Mortimer⁸⁷ and Morton⁸⁹ advocate the combined method, the last because he doubts the effectiveness of salvarsan therapy. Nicholas and Mutot⁹² always give salvarsan in combination with mercury. Eisenstaedt³⁵ and de Favento³⁸ get better results when the drugs are used together. Gougerot and Parent⁴⁹ say that it is immaterial which of several approved methods is chosen

provided the scheme of treatment adopted includes daily injections of some soluble mercurial salt.

Dreyfus³³ concluded that salvarsan is most effective when a total of 5 or 6 gm. is injected within six or eight weeks and followed by a course of mercurial inunctions.

Gardner⁴⁶ quotes Schreiber as advocating the administration of a total amount of 6 gm. divided into four doses and one dose injected every other day. It is to be noticed, however, that, in a more recent paper Schreiber¹¹⁰ advises the very different procedure of an initial dose not to exceed 0.3-0.4 gm., and, instead of every other day, subsequent injections once in two weeks. Schreiber explains his changed attitude on the ground that he has come to the conclusion that the customary dose in Germany is too large and that the too frequent repetition predisposes to undesirable cumulative action. Iverson,⁶⁰ following Schreiber's earlier method, gives one injection every other day up to the number of four. Four, McDonagh⁸² thinks, is the smallest number of salvarsan injections which is likely to cure. Lueders⁷⁶ reports that, to relieve deafness, he had to give six injections of salvarsan in the course of ten weeks in order to secure the result.

Gardner⁴⁶ found 1.5 gm. in 20 c.c. water a satisfactory dose of neo-salvarsan. McIntosh and Parker⁸⁴ injected 0.6 gm. in a solution of 150 c.c. of bacteria-free distilled water. In the primary stage they give two initial doses, with a third after three weeks. In the secondary stage, they first inject three doses and, after an interval of eight weeks, a fourth. Tertiaries they treat by an injection every two or three months until the W. R. becomes negative. Stühmer¹¹⁸ advises doses of neosalvarsan of not over 0.4-0.6, repeated at intervals of ten days.

Scholtz and Riebes¹⁰⁹ have adopted as a routine method two successive injections of 0.4-0.5 gm. of salvarsan within twenty-four hours, followed by daily inunctions of mercury for three or four weeks together with a subcutaneous injection of mercury once every five to eight days. Then, they repeat the series for a second time. They report that, by using this method, they have had but one accident in 1,200 cases and neurorecurrences have been eliminated. They also report that they have recently given three successive injections of 0.4-0.5 gm. of salvarsan within a period of twenty-four hours with no untoward result. Marshalko and Veszpremi⁸⁰ do not think such large amounts of salvarsan are necessary, as smaller doses are just as effective and likewise safer. It is interesting to read in this connection that Szametz¹²¹ obtained a brilliant result in a case of chorea from a dose of only 0.2 gm. of salvarsan. Wechselmann¹³¹ urges giving smaller doses of salvarsan than is customary at the present time. Spiethoff,¹¹³ on the other hand, states that if salvarsan is to be used at all, at least

in secondary syphilis, the dose should certainly not be small. He would follow salvarsan with mercury in order to prevent recurrence.

Müller⁹⁹ states that intramuscular injections of salvarsan produce more lasting effects than intravenous.

Gruenberg⁵² prefers salvarsan to neosalvarsan when it is desired to try to abort the disease, to treat secondary cases, to give large doses or frequent injections or to obtain a rapid effect. Whitehouse and Clark,¹³³ from one or more injections of salvarsan, obtain the same effects as with four or more injections of neosalvarsan.

The newer remedies do not protect the offspring from his syphilitic parents much more effectually than the older (Hoffman⁵⁹). The children of the next five or ten years will be subjects of inherited syphilis if the present blind confidence in salvarsan and neosalvarsan continues (Wilson¹³⁴). Experience does not commend the Ehrlich remedies as the best treatment for inherited syphilis (Levy-Bing and Duroeux⁷³). It is a question whether the newer therapy is more efficient than the older (Müller⁹⁹). The administration of salvarsan was followed by death in two cases of hereditary syphilis (King-Smith⁶⁶). Salvarsan is more dangerous in the presence of visceral, inherited syphilis (Langford⁷⁰). While Ehrlich's warning that salvarsan should not be used in infants has received little support in fact, nevertheless, it is true that poor physical condition and septic disease of any origin constitute contraindications to its employment (Noeggarath⁹⁴). Salvarsan should never be used under any condition for the deafness of hereditary syphilis (Beck¹¹). Salvarsan may be used in such cases, but, probably, better after mercury (Voorhees¹²⁷). Only the future can prove that large doses of salvarsan in concentrated solutions are really as harmless as they seem and alone can teach us in which forms of the inherited disease salvarsan is not to be used (Noeggarath⁹⁴). Although he obtained the result in two of his nine cases, Welde¹³⁸ is impressed by the obstinate resistance which the positive serum reaction of hereditary syphilis offers to the injections.

Opinions differ as to the value of the new remedies in the special manifestations of inherited syphilis. In interstitial keratitis, general opinion is not favorable to them. Post¹⁰¹ reports that his results were good. In the hereditary syphilis of bones, skin and mucous membranes, Langford⁷⁰ found salvarsan, as a rule, less efficient than mercury. In the exceptional cases, resistant to mercury, salvarsan was more efficient. Steiger¹¹⁴ was well pleased with salvarsan in hereditary syphilis when given intramuscularly in the form of a 40 per cent. suspension in iodopin. Swift and Ellis¹¹⁹ were impressed by the results from the administration of the milk of salvarsanized mothers to nurslings. On the other hand, King-Smith⁶⁶ was unfavorably impressed.

HEREDITARY SYPHILIS AND DOSAGE

The literature contains very little concerning the most effective dose of the newer remedies in the treatment of inherited syphilis. Noegarath⁹⁴ estimates that, in syphilis of children, the initial dose should correspond to 0.0002 gm. salvarsan per each kilo of body weight. Succeeding doses should be gradually increased in amount until they reach 0.1 gm. per kilo of body weight. King-Smith⁶⁶ likewise advises beginning with small doses and increasing the size gradually. Compared to adults, children bear relatively large doses of salvarsan (King-Smith⁶⁶) and of mercury if the liver and kidneys functionate perfectly (Levy-Bing and Duroeux⁷³).

Ordinarily, salvarsan is, as in adults, injected intravenously. The choice of a vein for the operation differs with the preference of the individual operator. Some use the veins of the head. King-Smith⁶⁶ prefers the jugular vein. Weil, Morel and Moriquand¹³² tried, experimentally, rectal injections. Somewhat to their surprise, they found that children bore rectal injections well if a little laudanum was added to the salvarsan solution. The disappearance of the visible signs of the disease proved that, contrary to the experience in adults, the drug was, in children, actually absorbed from the rectum. Neither local nor systemic reactions occurred.

ACTION OF SALVARSAN AS SHOWN BY THE URINE

Hitherto, we have considered the action and effect of salvarsan and neosalvarsan only from the clinician's point of view. There have been published, however, reports showing that attempts have been made to secure evidence from other sources. Capelli²¹ thinks that his investigations of the nitrogen excretion by the kidneys demonstrates that salvarsan is a disturber of metabolic processes. Capelli found the nitrogen output was increased (2 gm.) for twenty-four hours after an intravenous injection of salvarsan notwithstanding a decrease in the nitrogen intake of 6 gm. After twenty-four hours, the nitrogen excretion fell to 1.8 gm. below the ingestion. The excretion urea was perceptibly reduced. Capelli attributes the primary increase to a "Herxheimer reaction" and the presence of a slight fever. His final conclusion is that salvarsan alters the metabolism in syphilitic subjects, producing a temporary increase and a subsequent, more lasting decrease in the excretion of nitrogen. Greven,⁵¹ using a so-called "biological method," reported that salvarsan could be detected in the urine within an hour after its injection. He found evidence of its continued presence for fourteen days after subcutaneous injections and for seventeen to eighteen days after intramuscular. He thought that mercury hin-

dered excretion while the iodids favored. Lorenz⁷⁵ found arsenic in the urine one-half hour after an intravenous injection of salvarsan. Twenty-eight to fifty-seven hours later he could discover only a slight trace.

SALVARSAN IN THE BLOOD

Scholtz and Riebes¹⁰⁹ failed to discover a trace of salvarsan in the blood-serum four to six hours after the injection.

SALVARSAN AND THE CEREBROSPINAL FLUID

Lorenz⁷⁵ found that the lymphocytosis and increased globulin content in the cerebrospinal fluid was reduced by salvarsan. Levy-Bing, Duroeux and Dogny⁷¹ report that there occurs, after salvarsan, a true hypertension of the cerebrospinal fluid which is always accompanied by an increase in the amount of albumen. They do not doubt that salvarsan causes meningeal reactions more frequently than mercury.

SALVARSAN AND BLOOD-PRESSURE

In twelve cases of mental disease, McKinnes⁸⁸ could not demonstrate that salvarsan increased the blood-pressure even when given in so large a volume as 195 c.c. of the solution.

LETHAL DOSE

Merian, Girauld and Duret⁸⁵ endeavored to determine the fatal dose of the two substances in rabbits. The lethal level of neosalvarsan was approximately in the proportion of 0.42 gm. per kilo body weight. The toxic dose varied from 0.14 gm. upward. With salvarsan, the lethal level was reached at 0.10 gm. per kilo body weight.

CAUSE OF THE SALVARSAN REACTIONS

Marshalko and Veszpremi⁸⁰ do not believe that the so-called "water-error" plays any part in the production of the systemic symptoms of reaction after salvarsan. Nobl and Peller⁹³ could not demonstrate the bacterial contamination of the solution to be a cause of the fever. They doubted also if the fever after salvarsan was due to circulating endotoxins. They concluded that the more recent the generalization of the systemic symptoms of syphilis and the larger the relative dose of salvarsan, the greater was the febrile reaction. Wachenfeld¹²⁹ considers it still remains to be proved that salvarsan reactions are due either to the solvent, to bacteria or to bacterial toxins.

Schreiber¹¹⁰ suggests that the untoward symptoms which occur after injections of salvarsan and neosalvarsan may be due to a species of anaphylaxis. Plausibility is lent to the idea by Swift's success in

reproducing the symptoms of anaphylaxis in guinea-pigs by means of repeated injections of salvarsan. In this connection it is not to be forgotten that Gradwohl's⁵⁰ explanation of the luetin reaction was that it was a phenomenon of anaphylaxis. Stühmer¹¹⁸ ascribes the salvarsan reactions to "auto-anaphylaxis," a state especially favored by certain conditions such as, for example, the increased susceptibility of the auto-intoxication of pregnancy.

De Aja¹ has observed that immediate and late reactions after salvarsan injections occur more frequently in cases in the secondary stage of syphilis. De Azua⁸ agrees that the secondary stage favors relapse. Nicholas and Mutot⁹² and Gruenberg⁵² have seen neurorecurrences develop in cases of secondary syphilis in spite of energetic treatment. Rimini¹⁰⁷ is convinced that the secondary cases offer a peculiarly stubborn resistance to curative treatment.

It is an accepted fact that the secondary stage of syphilis yields the greatest percentage of positive results to the serum test. The writers just quoted assert that the greatest frequency of neurorecurrences is in secondary syphilis. The question is unavoidable, What is the connection between these facts?

DEATHS AFTER SALVARSAN

Several fatal cases have been reported during the past year, one by de Favento,³⁸ one by Keyes,⁶⁵ three by Hirsh⁵⁷ (of which one case was his own and two Hammer's), two of hereditary syphilis by King-Smith,⁶⁶ one by Newmark⁹¹ and one by Marshalko and Veszpremi.⁸⁰

The number of salvarsan injections is in the thousands. The fatalities can almost be reckoned in single figures. Nevertheless, it is not disputed that a certain small number of patients have died under circumstances which threw suspicion on the injected remedy as the cause. The partisans of salvarsan maintain that the remedial substance should not be held responsible, but preexisting forces with which it has no connection except in so far as it may have acted as the exciting agent which stimulated these forces into fatal activity. The opponents declare that the direct cause of death is the toxic action of salvarsan. To the ordinary reader the conclusion would seemingly be unavoidable that occasionally salvarsan is the cause of death, perhaps directly, perhaps indirectly.

AUTOPSY EVIDENCE

Marshalko and Veszpremi⁸⁰ concluded that, in their case, changes found at the autopsy pointed to the fact that the fatal encephalitis was caused by the toxin action of the salvarsan. They could find no actual signs of inflammation, but only multiple hemorrhages into the brain from stasis or thrombosis without any changes of especial significance

in the substance of the brain. De Faventa³⁸ thinks that the bacterial contamination of the solvent was the cause of the findings in his fatal case. Newmark⁹¹ reports the autopsy of a patient dying after an intramuscular injection of 0.3 gm. salvarsan into each buttock in which a softening of the cord was present.

NEURORECURRENCE

As ordinarily used, neurorecurrence refers to the symptoms which develop in some part of the nervous system after a considerable time has elapsed since the last treatment. The question of the comparative frequency of the condition after salvarsan and neosalvarsan and after mercury and the iodids has been sufficiently discussed above. The theories of the relationship of the action of the remedial substances to the development of the symptoms of neurorecurrence demand more attention. Some say that they are the direct result of the toxic action of the drugs. Some say that they are not the result of toxicity, but of insufficient dosage; that the symptoms are not to be attributed directly to the action of the remedies themselves, but to the latent foci of disease which they have accidentally stimulated into action.

Wechselmann¹³¹ considers neosalvarsan more neurotropic than salvarsan, and at the same time, clinically and serologically less active. De Aja¹ thinks salvarsan is less able to prevent neurorecurrences than is mercury. Ellis³⁶ denies that salvarsan in any way predisposes to these nervous relapses. Fordyce⁴² has never had a case of neurorecurrence in the auditory nerve after salvarsan. Gardner⁴⁶ thinks there is no choice between salvarsan and neosalvarsan so far as relapses are concerned. Gruenberg⁵² considers the effects of neosalvarsan more cumulative and more toxic than of salvarsan. Kall⁶² believes neosalvarsan is the more neurotropic and, in ambulant, the more dangerous. Mortimer⁸⁷ does not think it is proved that salvarsan harms the nervous system. Müller⁹⁰ reports that, in 200 salvarsan cases, 7.5 per cent. of the patients developed symptoms of neurorecurrence within seven to twelve weeks. Dreyfus^{33, 34} states that neurorecurrences have become more frequent since the introduction of salvarsan. Ravaut¹⁰³ says that, in the presence of spirochetes salvarsan is neurotropic, that is, predisposes to affections of the nerves. Whereas, under ordinary conditions, without salvarsan, syphilis causes a meningeal reaction in 67 per cent. of all cases, after salvarsan medication, the figures are raised to 87 per cent. He therefore concludes that salvarsan should be used with caution if the cerebrospinal fluid shows signs of meningeal reaction. Spiethoff¹¹³ agrees that since the introduction of salvarsan, neurorecurrences have become more frequent, not, however, because of the salvarsan, *per se*, but because of the timidity of the operator.

Schreiber,¹¹⁰ once the advocate of high dosage, now believes that the massive and frequent doses customary in Germany are dangerous. Marshalko and Veszpremi,⁸⁰ from the autopsy evidence of their fatal case, conclude that salvarsan is safer in small doses. Nobl and Peller⁹³ say that salvarsan is toxic. Wolff and Melzer¹³⁸ concluded that neosalvarsan is more toxic than salvarsan. Gruenberg⁵² thinks neosalvarsan the less toxic and its effect the less cumulative. Kall⁶² belongs to the group of those who, advocating one, refer incidentally to the toxic properties of both. He advocates salvarsan on the ground that it is *less* dangerous and *less* neurotropic than neosalvarsan. Noeggarath⁹⁴ wonders what the future will show is the effect of concentrated solutions injected intravenously. Levy-Bing and Duroeux⁷³ say that the symptoms of toxicity are largely dependent on the functional perfection of the liver and kidneys. Rimini¹⁰⁷ declares that the symptoms of neurorecurrence which follow after salvarsan are due to the lighting up, by the injections, of old foci of disease. Mortimer⁸⁷ also attributes the symptoms of nervous involvement to the reawakening of a previous luetic process, possibly an accumulation in the nerve tissue of spirochetes which have escaped destruction (Müller).⁹⁰

DOSE AND NEURORECURRENCE

De Aja¹ says that it is not the salvarsan to which neurorecurrence is due, but to the use of too small an amount to prevent the event. Almkvist³ argues that if it were only borne in mind that it is necessary to sterilize the organism to prevent neurorecurrences, more frequent injections would be given. De Azua⁶ proportions the frequency of repetition to the urgency of the case. Ravaut¹⁰⁸ once wrote that the likelihood of neurorecurrence went hand in hand with the frequency of the injections (the dosage). Dreyfus,³³ replying to Ravaut's later paper,¹⁰³ does not deny the accuracy of Ravaut's observations, but says that they are based on the results of a too timorous use of the remedy. Spiethoff¹¹³ states that neurorecurrences occur in inverse ratio to the intensity of the salvarsan therapy. Iverson⁶⁰ declares that, rather than favoring neurorecurrence, high doses of salvarsan are preventative. Scholtz and Riebes¹⁰⁹ concur.

AUDITORY SYMPTOMS OF NEURORECURRENCE AND SALVARSAN

Rimini¹⁰⁷ reports eight cases of hereditary syphilis in which the auditory symptoms of neurorecurrence seemed to have been the direct result of salvarsan medication. Not one patient had ear symptoms before salvarsan. One to three months after the injections all had developed symptoms of aural disease. According to J. C. Beck,¹² the symptoms of neurorecurrence in the ear may appear at any time from

two to eight months after the salvarsan. As salvarsan may possibly predispose to the conditions, Beck thinks it inadvisable to give it to hereditary syphilitics with symptoms of aural involvement or to adults whose ear symptoms have developed within six to eight weeks of a previous injection. Biggs¹³ reports a case in which deafness developed within forty-eight hours after salvarsan was injected. Carpenter²³ thinks that salvarsan is least effective in the treatment of syphilitic affections of the organs of special sense.

THE EYE

In the diagnosis of hereditary syphilis, the ocular manifestations of the disease have a peculiar importance. One result of the Ehrlich remedies has been to give us a more accurate conception of the changes which hereditary syphilis produces in the eye. Many symptoms which earlier were attributed to the deleterious effect of salvarsan medication have been shown by recent careful study to have resulted from pre-existing syphilitic processes and not from the action of the remedy.

Stiern has drawn from statistics the conclusion that only one-half of all syphilitic fetuses are born alive, and that 80 per cent. of the living half develop some form of ocular syphilis, most often an interstitial keratitis. Neumann is said to have found that 81.9 per cent. of the syphilitic infants in his clinic had symptoms of iritis. Oscar Dodd³² estimated that, of every 5,000 cases of all forms of eye disease, one will be a manifestation of syphilis which, in 1 or 2 per cent. of the total, is some form of disease of the orbit. He says, the primary manifestation may be either an involvement of the orbital margin, a periostitis or a gumma of the orbital wall. The prognosis is worse in hereditary syphilis than in the acquired form.

The eye symptoms indicative of involvement of the central nervous system are even more serious. According to Knapp,⁶⁸ if it is desired to avoid irreparable damage, the symptoms must not escape immediate recognition. In the diagnosis of ocular syphilis, Knapp found the W. R. of inestimable value. Monradian⁸⁸ thinks its value in these cases is doubtful.

Otchaposky's results from the salvarsan treatment of ocular syphilis were disappointing, which is contrary to Post's experience. Of the 120 cases reported by Otchaposky, only forty-five showed any improvement. He even saw the other eye attacked while treatment was in progress. His best results were obtained in iritis, although, at that, the best were not so good as with mercury and the iodids. Relapses were more frequent. Reese¹⁰⁵ considers that salvarsan is an indispensable adjunct to mercury in the treatment of ocular syphilis without, however, being able to replace mercury.

NEURORECURRENCE; SITES OF PREDILECTION

Returning to the general subject of neurorecurrence, the fact is at once interesting and suggestive that when its symptoms develop after treatment, they seem to exhibit a distinct tendency to limitation to some one nerve trunk and that certain nerves seem to be particularly susceptible. Thus, de Aja² says that a very large majority of the cases of relapse affect one of three nerves which, in order of frequency, are the facial, the acoustic and the trigeminal. Fully 50 per cent., he says, occur in the facial nerve and are peculiarly obstinate to treatment compared to the ease with which other nerve systems respond.

DO SALVARSAN AND NEOSALVARSAN CURE?

A committee once met to consider how patients afflicted with syphilis might be cared for most efficiently. In the course of the discussion the question was raised as to whether a specialist in syphilis was to be preferred to a general practitioner. A physician of more than ordinary attainments rose and stated as his opinion that the care of the syphilitic to-day is not the intricate and complex problem of a few years ago which a specialist alone could handle. Then we had nothing to guide us but clinical experience. To-day, our position is different. With means of testing the blood at command, the detection of the disease is assured. By injections of salvarsan, its cure is easy.

The climax of the speech is in the last three words, "cure is easy." Whether we shall agree or disagree with the speaker, depends on our interpretation of the discussion of salvarsan and neosalvarsan in Part Two and of the serum test in Part One.