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THE ADMINISTRATION OF SALVARSAN IN SYPHILIS *

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Before the introduction of the Wassermann reaction the treatment of syphilis was more or less a matter of guess-work. While it is doubtless true that some patients were cured by the methods then in vogue, and others possibly treated for too long a period, the observations which I have made during the past three years show that the majority of such patients still retained their infection. The idea which prevailed among physicians and is still prevalent among the laity, that one attack of syphilis confers immunity, is chiefly if not entirely due to the fact that syphilis was seldom cured under the old methods of treatment. It is impossible to give the average percentage of cures formerly obtained, but from my findings and the application of the Wassermann test to cases treated five to twenty-five years ago I should say not more than 20 to 25 per cent.

The great rarity of a second infection in these patients supports the contention that cures were then infrequent. Since the beginning of the salvarsan era reinfection is being reported with growing frequency, and, as recent laboratory and clinical studies tend to show that immunity in syphilis does not exist, except perhaps in certain cases covered by Profeta's law, the number may be expected to multiply. The failure, then, to develop a second attack is not due to true immunity, but to an insusceptibility because the disease is still present. This insusceptibility or anergy is said to develop soon after generalization of the infection and lasts until it is cured spontaneously or by specific remedies.

Cases of reinfection after a cure had been established with salvarsan alone or in combination with mercury have been reported by various continental observers, and I mention Gennerich particularly, as he employed the more intensive combination-therapy from the beginning and controls his cases by means of provocative treatment, or the biologic reactivation of the Wassermann reaction. Both Gennerich and Milian found that by injecting patients with 0.3 gm. of the remedy six months or a year after a supposed cure and by examining their blood every day thereafter for two weeks a transient positive reaction was procurable if any evi-

dence of the infection was left, while it remained negative if cure was absolute.

In my own experience I have met a case of possible reinfection giving the following history:

CASE 1.—A. B., aged 30, developed a primary lesion Dec. 9, 1910; Wassermann was double plus, Dec. 30, 1910; Jan. 1, 1911, 0.5 gm. salvarsan was given intravenously; Feb. 17, 1911, Wassermann was weakly positive. About the middle of March, ten days after exposure, patient developed an induration like the original chancre on the opposite side of the glans penis. Spirochetes were found in the lesion. On April 15 the Wassermann reaction was strongly positive; April 17 and 24 patient received 0.52 gm. The serum reaction May 6 was plus minus, July 14 negative and has remained negative. Neither instance was followed by a generalized rash.

The treatment of syphilis is no longer the control of symptoms, but should be undertaken with a full appreciation of the serious nature of the infection. Furthermore, it should be undertaken with a thorough understanding of what is to be accomplished with the remedies employed. The amount of treatment in lues cannot be arbitrarily fixed, as the infection varies within wide limits in different individuals. In some its course is so mild that it is possible to eradicate it with a minimum amount of the drugs, while in others—and they are in the majority—it persists with treatment increased many fold.

The perfunctory administration of protoiodid pills, a practice only too much in vogue, accomplishes little in the eradication of the disease and leads to an immunity to the drug. Day after day we see patients, the victims of paresis, tabes or other serious disease, all giving an identical therapeutic history, namely, two, three or more years of pill-taking. The method stands condemned by its eloquent results.

If practitioners follow the rules of treatment laid down in certain modern text-books on therapeutics, one as recent as 1911, the number of cures will certainly not increase. On the contrary the late manifestations will continue to show as large a percentage as in the past. It is time a campaign of education is instituted as to the proper administration of our standard drugs in the treatment of syphilis. When a physician who pretends to be an instructor of students states that the treatment of syphilis by mercury given internally is still the method of choice, it is, to say the least, far from the truth. In the light of the results shown by the Wassermann reaction, as I have reiterated time and again, few patients treated in this manner are actually cured by the drugs employed; on the contrary, an increasing immunity to mercury is produced so that its subsequent administration is absolutely without effect except to impair the nutrition of the patient. I have repeatedly seen cases of obstinate syphilitic infection of the skin, as scaling syphilids of the palm, treated for years internally with-

* Because of lack of space this article is somewhat abbreviated in THE JOURNAL. It appears in full in the Transactions of the Section and in the author's reprints.

* Read before the Joint meeting of the Section on Dermatology and the Section on Pathology and Physiology of the American Medical Association at the Sixty-Third Annual Session, held at Atlantic City, June, 1912.

out any effect, yield after four or five injections of salicylate of mercury. It is not sufficient to know that mercury influences the syphilitic lesions, but one should be familiar with the methods of administration which influence the disease in the most rapid and permanent manner and this certainly cannot be said of mercury by the mouth. It is true that when it is administered in large doses combined with potassium iodid, the so-called mixed treatment, it is efficacious in many of the late cutaneous manifestations, but I have seen few cases in which even a persistent use of the remedies given in this way would permanently change the serum reaction.

The efficiency of the modern treatment of lues is attested by hundreds of experienced observers all over the world. It is now known that criticism of the specific action of salvarsan when given in single doses is of no value nor are the conclusions based on imperfect methods of preparation and administration. Since its introduction several modifications in the technic have taken place. Subcutaneous and intramuscular injections have entirely given way to the intravenous method, although, as I have observed previously, the intramuscular injection of an alkaline solution was the more efficacious of the two. This statement is borne out by the results obtained in some of the early patients treated, several of whom I have been able to keep under observation to the present time.

Salvarsan is a specific spirochetal poison the efficiency of which is in direct ratio to the age of the infection. One of its most pronounced points of superiority over mercury, in my estimation, lies in the treatment of the early cases in which in the primary stage it is possible to prevent the development of secondary symptoms and a positive Wassermann, or, in the event of its being already positive, to change it to negative. In the old days it was the rule for the practitioner to await the development of secondary symptoms to corroborate his diagnosis or to justify various superstitions such as proneness to nerve syphilis or an inhibition of antibody formation, if treatment were instituted in the early period of the disease. The latter had a certain amount of support from pathologists who believed that the natural defenses of the body would rally to the fore more quickly and strongly if the combat were not interfered with by drugs. Such views have long since been discredited and it has been proved that the best interest of the patient is served by the earliest possible treatment. With laboratory aids, such as the dark-field microscope and the Wassermann reaction, a diagnosis need not long remain in doubt. Of the significance of antibodies in syphilis, Thalmann's view is perhaps the prevalent one, namely, that early in the disease, especially after the destruction of the spirochetes by treatment and the liberation of their endotoxins, there is corresponding formation of antibodies and with it an increase in immunity. This antibody production may be so considerable that even without further treatment an arrest and improvement of the disease may result. As the living spirochetes gradually continue to proliferate, immunity decreases, and later when the foci are smaller in number they contain weaker spirochetes and few antibodies. According to this author, the endotoxins have so weakened the tissue cells that in tertiary syphilis only slight amounts of the virus are sufficient to cause a destruction of tissue and ulcerative processes. Wolff-Eisner,² however, attributes the severe clinical alterations

to a hypersensitiveness brought about by the repeated absorption of heterogenous albumin.

It cannot be too strongly emphasized that in the treatment of the various stages of the disease different problems confront us. In the early period it may be possible with one or two or three doses of salvarsan, alone or in combination with mercury, completely to sterilize the patient and eradicate the infection. This has been demonstrated in my experience in the following cases:

CASE 4.—Patient (S), who had three initial lesions of the lips, and secondary eruption, was treated May 19, 1910, with 0.3 gm. alkaline solution intramuscularly. Prior to this treatment he had had two intramuscular injections of hydrarg. salicylate. Since then he has had no other treatment; no clinical signs of the disease; his Wassermann reaction was negative Oct. 23, 1910, and the last one made March 15, 1912, was likewise negative.

CASE 5.—The patient (C) had a chancre Oct. 12, 1910. Treatment was given Nov. 17, 1910, 0.55 gm. alkaline solution; Dec. 23, 1910, 0.6 gm. alkaline solution. The serum reaction, strongly positive before the first treatment, was only weakly so before the second and became negative on March 30, 1911. Repeated examinations made to Feb. 17, 1912, have all been negative. This patient never developed secondaries.

CASE 6.—The patient (P) developed a primary lesion Feb. 10, 1911; Feb. 25, 1911, he received 0.6 gm. salvarsan intravenously. The Wassermann reaction was negative at the time of treatment and continued so with no further development of symptoms.

CASE 7.—The patient (B) had an initial lesion Dec. 9, 1910; received treatment Jan. 1, 1911, April 17, 1911, and April 28, 1911, 0.5 gm. each. Reaction, negative in July, has remained so since.

CASE 8.—The patient (B) developed a primary lesion Sept. 21, 1910. On Oct. 24, 1910, he received 0.6 gm. salvarsan in alkaline solution. Reaction was negative March 11, 1911.

CASE 9.—The patient (S) had a primary lesion September, 1910, with beginning secondaries. He received treatment Dec. 27, 1910, 0.6 gm. alkaline solution followed by a course of inunctions. Reaction was negative January, 1911, and is still negative.

CASE 10.—The patient (N) had two initial lesions on hand November, 1910. No. 28, 1910, he received 0.6 gm. alkaline solution. Reaction has been negative since March, 1911.

CASE 11.—The patient (W) had an initial lesion Dec. 1, 1910, began treatment Dec. 30, 1910, 0.6 gm. alkaline solution followed by mercurial injections. March 17, 1911, he received 0.55 gm. salvarsan intravenously, followed by mercurial injections. The Wassermann reaction has been negative from June 12, 1911, to the present.

CASE 12.—The patient (E) had a tonsillar lesion Jan. 1, 1911. On Feb. 21, 1911, he received 0.5 gm. salvarsan intravenously, and on March 10, 1911, 0.4 gm. intravenously, followed by mercurial treatment. The Wassermann became negative March 29, 1911, and has continued so.

CASE 13.—The patient (D) had a chancre in March, 1911; he was treated March 10 and April 7, 1911, receiving 0.5 gm. salvarsan each dose intravenously, followed by two courses of mercurial injections. He never developed any secondaries and his Wassermann reaction is negative.

CASE 14.—The patient (B) had a primary lesion in July, 1911; received treatment Aug. 22, 1911, 0.58 gm., followed by mercurial injections; and Oct. 2, 1911, and Nov. 18, 1911, 0.5 gm. each. His reaction is now negative.

CASE 15.—The patient (M) was infected Aug. 16, 1911. At the time of treatment he had an indurated lesion containing numerous spirochetes; reaction was positive. Sept. 2, 1911, he received an intravenous injection of 0.58 gm., followed by a course of inunctions. No other manifestations developed and the reaction Nov. 23, 1911, and Feb. 11, 1912, was negative.

2. Wolff-Eisner: *Clinical Immunity*, 1911.

While it is demonstrated that it is possible to cure syphilis within six months with two to four doses of salvarsan alone or with mercury, it will not do to rely too confidently on accomplishing this result; in patients in whom a negative reaction has been obtained, I insist on serologic observations for at least a year after the first negative reaction has been obtained, and when practicable I advise a provocative injection of salvarsan.

Excision of the initial lesion is advocated by a number of modern syphilographers as an aid in ridding the patient of a focus of spirochetes, but as yet we have not accumulated sufficient evidence to show whether the infection in patients thus treated pursues a milder course or not. In former years there were many claims made as to the possibility of aborting syphilis by excising the initial lesion and communicating lymph-nodes, but after many trials the procedure was abandoned, as it was definitely shown that the disease in such patients followed the same course as in those who had not undergone excision. If all of the spirochetes were concentrated in the initial lesion, it would be an entirely rational procedure to excise it and remove the focus at once; it is known that this is not the case, but that early generalization takes place through the lymphatic system and the blood, and that at best we are only ridding the patient of a small nest of spirochetes. When the chancre is situated on the foreskin or an easily accessible region, however, there is certainly no objection to excising it.

During the secondary period of the disease with a strong, positive Wassermann reaction the infection is more difficult to eradicate in a short time, but it is possible even then by more intensive treatment—let us say, five or six doses of salvarsan at intervals of from one to four weeks, followed by a course of mercurial injections or inunctions. That it is possible to cure the disease in from six months to a year in this stage I have demonstrated by cases which have been under observation for from eighteen months to two years. As the disease grows older, the time required for its eradication grows progressively longer, as in cases in which the infection dates back, five, twenty or thirty years. In these it may require ten or twelve injections of salvarsan combined with several courses of mercurial injection to reverse the serum reaction permanently, but, if we pursue our treatment with a definite plan and have confidence in our drugs, persistent treatment, extending over a period of a year, will change the reaction. The question is sometimes rendered more difficult by the failure of patients to cooperate with the physician in their treatment. Usually, however, when the problem is placed before intelligent patients in a clear and definite manner, their cooperation can be secured and, when this is so, salvarsan, supplemented by mercury, will in the majority of cases change the reaction. It may be that there is a certain class of cases in which no amount of treatment will reverse the reaction.

Salvarsan has a much more rapid action on the organism than mercury. This is demonstrated most strikingly in cases with mucous membrane lesions and in those of malignant syphilis. In the latter the extreme cachexia, which characterizes this type of the disease, disappears within two or three weeks, and lesions which have persisted for months promptly recede. It is a common experience to see patients whose cases were absolutely hopeless under the old method restored to health in a few weeks.

CASE 16.—I recall a patient seen a year and a half ago, in a state of extreme physical and mental depression, with ulcerative lesions, joint involvement and a nephritis. His lesions yielded in a surprising manner; at the end of a month his weight had increased from 105 to 121 pounds and under continued treatment he became entirely well. He has now had no drugs for a year, weighs 145 pounds and has had a continuous negative reaction.

CASE 17.—In another case in which the patient was cachectic, had been running a high temperature for a year, had multiple cutaneous lesions and a specific orchitis, all symptoms resolved under two doses of salvarsan and the patient's physician writes me that his nutrition and strength improved to such an extent that for months he has been able to do hard work in a lumber camp, whereas he had been an invalid for nearly a year and a half before treatment. This patient had a decided idiosyncrasy against both mercury and potassium iodid, the latter producing edema of the tongue. His Wassermann reaction, made a few weeks ago, was still strongly positive, as might be expected with only two doses of the drug at his stage of the disease.

In controlling the treatment by the Wassermann reaction it must be borne in mind that from 10 to 15 per cent. of the active late manifestations of syphilis give a negative reaction, so that, in the face of positive clinical findings and a negative test, the latter may be disregarded in the late stages of the disease. I have on several occasions administered salvarsan to patients with a negative Wassermann with the very best results. In the case of a physician with a marked onychia involving the nails of his hands and feet, a decided change took place after the second injection. The nails, which had been thickened, discolored, fissured and every now and then shed and replaced by the same deformity of these structures, were after the treatment reproduced in an absolutely normal manner. The explanation of a negative reaction in the presence of clinical symptoms is based on the fact that the spirochetes are too few in number to give rise to the Wassermann-producing substances.

In disease of the nervous system the administration of salvarsan should be undertaken only with the full knowledge of the possible effects. That great prudence must be exercised was taught by the accidents which occurred in cases with advanced disease of the nervous system during the trial period of the drug. Professor Ehrlich is of the opinion that the former dreaded reactions in late lues of the nervous system are to be referred entirely to faulty technic and the use of old water containing the proteid products of dead organisms. In a letter recently received he states that Dreyfuss of Frankfort has treated hundreds of cases of late nerve syphilis without any reaction whatsoever, except in a single instance in which a spinal puncture had been made just prior to the salvarsan injection. In this patient the puncture was regularly followed by meningeal manifestations lasting several days. When the injection was delayed until such symptoms had subsided, absolutely no by-effects were noted. In syphilis of the brain the possibility of the development of the Herxheimer reaction should always be kept in mind. Although we have no pathologic findings in such cases, the occurrence of convulsions and localized paralyses after the administration of the drug points to an intensification of the inflammatory process about certain focal brain lesions, which in the majority of cases is only transient. Where the remedy is indicated, it should be given cautiously in small repeated doses or preceded by several injections of mercury. In this way a gradual effect on the lesion is produced and we avoid a too rapid disso-

lution with dangerous consequences. Even with a positive Wassermann reaction and an active process, when combined with degenerative changes in the brain cord, its administration is rather a delicate question to determine.

It is, however, indicated in tabes with a very positive serum reaction and a lymphocytosis of the cerebrospinal fluid. In these cases its administration in repeated small doses at proper intervals offers more than the treatment with mercury and potassium iodid. But to be satisfied with one or two injections is not giving the patient the full benefit of all that may be accomplished. It relieves the pains, increases the efficiency of the bladder function and stimulates the body nutrition. In several patients with inequality of pupils the latter have become equal and in two cases in which they were unresponsive to light the reflex returned. In the old degenerative types with a negative reaction and absence of lymphocytosis, the active specific process is probably entirely replaced by degenerative and sclerotic changes, and the administration of salvarsan or any other remedy can accomplish little or nothing.

The most marked improvement is seen in cases of cerebrospinal syphilis which simulate tabes.

CASE 18.—I have under observation a patient who had had a hemiplegia and epileptiform convulsions. His knee-jerk was absent on the right side, locomotion was impaired, his pupils were unequal and sluggish to light and he suffered from incontinence of urine. These symptoms have all practically disappeared. He has regained control of his bladder, his pupils are equal and responsive and he walks now a distance of several miles with little fatigue. His blood reaction has been persistently negative for six months.

In the treatment of paresis my experience has been limited to only a few cases.

CASE 19.—In one with a very positive Wassermann reaction the administration of three doses was followed by a marked remission in all of the symptoms. The reaction remained positive and I strongly urged the family of the patient to continue the treatment. The advice went unheeded and within a month or two the patient's symptoms reappeared and progressed in a rapid manner.

CASE 20.—At present there is under my care a patient who came to me with the diagnosis of paresis from one of the best-known neurologists in New York. He had marked delusions of grandeur; his pupils were unequal and sluggish to light, and his knee-jerks were absent. There was no speech disturbance and no change in his handwriting. His serum reaction was strongly positive. Up to this time he has had seven injections at intervals of from three to four weeks. His delusions have entirely disappeared, his pupils are practically equal and more responsive to light and in every way he acts like a normal individual. His reaction is still strongly positive and guided by this index I am advising persistence in treatment. In addition to his salvarsan injections he has had several courses of mercurial inunctions. He was lately seen by the consulting neurologist, who was inclined to change his diagnosis of paresis on account of the improvement that had taken place.

All neurologists have emphasized the difficulty of differentiating between the early stages of paresis and other forms of cerebral lues which simulate paresis. Reports of autopsy findings in these two classes of cases are perhaps too meager to enable us to draw deductions as to whether any essential differences exist between the two, other than the cerebrospinal cell count. It has long been held by Dr. Dana that the prognosis in early paresis is not wholly hopeless, as many of these forms develop from a preexisting cerebrospinal syphilis which can be arrested by treatment.

Regarding the permanency of results in nerve syphilis I might refer to a case reported a year and a half ago.

CASE 21.—The patient was suffering from an obliterating endarteritis of the base of the brain involving both pyramidal tracts and the sympathetic. His pupils were unequal, very nearly Argyll Robertson, and his speech was thick. There was general involvement of the muscles of the pharynx, tongue and face on the right side with anesthesia, partial paralysis of the right leg, marked Babinski, clonus of both knee and ankle and incontinence of urine. The Wassermann reaction was positive. A decided improvement took place after the first two injections. The treatment was carefully controlled by repeated Wassermann tests and when the strength of the reaction increased, the patient was immediately given another injection. This method of procedure has been kept up to the present time and the man may be considered practically well, with only slight evidence of his former hemiplegia. He has been able to resume his professional duties, which he conducts as well as formerly.

Intense headaches, often so persistent during the secondary and tertiary stage of the disease and due to a low-grade meningitis, are influenced by salvarsan in a most gratifying manner. They usually remit with remarkable rapidity, patients stating that within from twenty-four to forty-eight hours or a few days after the injection the pains have entirely disappeared. Occasionally they are intensified for two or three weeks after treatment and then suddenly disappear.

The drug has been criticized owing to the relapses which have occurred, affecting chiefly the nervous system, and which the critics attributed to a toxic action and a special affinity for nervous tissue. That this view was not justifiable is shown by the experience of the past year, for since the adoption of more intensive treatment such reports have become comparatively rare. The reasonable deduction therefore is that these complications were true relapses, as has been proved by further observation of the cases and in some instances by examination of the cerebrospinal fluid.

The latest word on salvarsan concerns the new product neosalvarsan. This preparation, which bears the laboratory number 914, is a very soluble form of salvarsan obtained by the addition of formaldehydesulphoxylate of soda. It is claimed to be fully as efficacious as the old remedy and possesses certain decided advantages in the simplification of the technic of its preparation and the greater tolerance to it, permitting much larger doses at shorter intervals, thus concentrating the attack on the disease. Neosalvarsan is extremely soluble in water. Neutralization with caustic soda is not necessary as with old salvarsan, as the new product is neutral when in solution. It is prepared by dissolving 0.15 gm. in 20 c.c., or 1.5 gm. in 200 c.c. of freshly distilled water; 0.8 gm. in 22 c.c. gives an isotonic solution. Schreiber, who has been entrusted with the preliminary trials and has given over 1,200 injections since last October, advises that the temperature of the water be about 20° C. (68° F.). As the preparation oxidizes readily and the oxidation products are more toxic than the drug itself, the following precautions are suggested: In making the mixture it should be gently agitated and not vigorously shaken. It should not be warmed after it is made up, and it must be used immediately.

Four doses are administered in succession with an interval of one day between. Schreiber's procedure is to give 0.9 gm. for the first dose, 1.2 gm. for the second, 1.35 gm. on the third day and 1.5 gm. on the fourth. This equals 6 gm. of neosalvarsan or 4 gm. of salvarsan

within one week. Women receive from 0.75 to 1.2 gm., children 0.15 to 0.35 and infants 0.05 gm.

In cases of meningitis or involvement of the cerebro-spinal system the patient's susceptibility should be cautiously tested with small doses. Owing to its less irritating properties neosalvarsan lends itself more readily to intramuscular use. For this purpose 0.9 gm. are dissolved in about 30 c.c. of water. Several c.c. of a 1 per cent. novocain solution are first injected; the needle is left *in situ*, and the neosalvarsan injected through it several minutes after. Schreiber⁴ has observed edema after its use, but never infiltration or necrosis. He prefers, however, the intravenous method.

Two weeks after treatment the Wassermann reaction is to be taken and, if negative, is to be repeated at monthly intervals. If it becomes positive, an intensive course of mercury is to be inaugurated followed by two more injections of neosalvarsan. If it still is positive two weeks after the first series of injections, the above plan is to be put into immediate effect.

Through the kindness of Professor Ehrlich I received a supply of neosalvarsan and have used it in about thirty cases, including early and late manifestations. The data relative to these cases will be published in a subsequent article, as the time which has elapsed since the administration of the remedy is now too short to permit of a definite expression of opinion.

In all the patients except one the clinical symptoms were influenced very promptly. In the exception, a gummatous ulcer of the leg, the lesion remained unaffected two weeks after the fourth injection, but yielded readily to mixed treatment. In none of the cases with a strong Wassermann was the reaction reversed at the end of two weeks. An initial lesion of the lip with secondaries completely resolved in three weeks with a negative Wassermann. A case of early syphilis with a marked iritis and chorioiditis, after 5 gm. of neosalvarsan were given in one week, gave a negative Wassermann after two weeks of mercury. In three other cases the Wassermann reaction has become progressively weaker in from four to six weeks after neosalvarsan has been given.

Of ninety-seven treated by Schreiber sixty-one became negative and thirty-six remained positive; one-third of the former were negative at the end of fourteen days. Five of these cases were still negative after four months and seven after three months.

Schreiber has but seldom noted by-effects after neosalvarsan. He had observed an elevation of temperature after the first injection in the florid stage, and drug rashes were also seen in a few patients, but in the majority the reaction was negligible. In my own experience a sharp febrile reaction has occurred sometimes after the first and sometimes after succeeding injections. In three cases a trace of albumin appeared in the urine, but it disappeared again in a few days. In a few cases slight vomiting or diarrhea was also complained of.

Assuming that the solution of salvarsan is properly prepared and that one is familiar with the technic of its administration, it may safely be stated that, given to an individual with intact kidneys, circulatory and nervous system, it is free from danger, and in the majority of cases causes less disturbance than an intramuscular injection of a mercurial salt. Patients repeatedly state to me that they much prefer to take an injection of salvarsan rather than one of salicylate or bichlorid. As

the kidneys are chiefly concerned in the elimination of the drug, a nephritis is much more apt to occur when they are not in a healthy condition, and this emphasizes the importance of carefully ascertaining their state before its administration. I have not found albuminuria a contra-indication, but the remedy must be given in small doses.

It is important that the organs of circulation be in a fairly normal condition. The blood-pressure in some cases drops suddenly after the administration of the drug, and the heart's action becomes slow and feeble. In several cases I have noted that the pulse fell to forty. For this reason it is advisable that patients be kept in the recumbent position for several hours after an intravenous injection. From Auer's animal experiments to determine the cause of the fall in blood-pressure, he found that the heart might be so affected that a slight extra strain would throw it into fatal fibrillation. As this did not occur regularly in his animals, he attributed it to an inherent weakness of the cardiac muscle brought out by the injection of salvarsan. The contention of Ehrlich that myocarditis be regarded as a contra-indication for the intravenous injection of the drug, therefore, has experimental support. Whether this action is exerted on the cardiac muscle, on the vagus endings or on both structures could not be definitely stated.

CONCLUSIONS

The efficiency of salvarsan bears a direct relation to the age of the infection.

In the early stage three or four doses supplemented by mercury will in many cases cure the disease in from six months to a year.

The florid stage requires more intensive treatment; five or six doses followed by several mercurial courses are necessary.

In some forms of syphilis of the nervous system the effects of salvarsan are more satisfactory than mercury and potassium iodid.

In malignant syphilis, when mercury has been given over a long period continuously without changing the clinical manifestations or the blood reaction, not infrequently all of the manifestations disappear after one or two doses of the drug. These patients probably develop more or less immunity to mercury, or their strains of spirochetes are more amenable to arsenic treatment.

A reaction uninfluenced by a long course of mercury may be changed by one or two injections of salvarsan. In other words, a combination of salvarsan and mercury is more efficient in changing the blood reaction than either alone. In the primary stage it is possible permanently to reverse the blood reaction with salvarsan, but, as the disease grows older, the probabilities of changing it with only a few doses grow less. The introduction into the system of such large quantities of the drug as is possible with neosalvarsan may so concentrate the treatment that all or most of the organisms are destroyed, but it has not yet been used long enough to enable us to draw definite conclusions.

8 West Seventy-Seventh Street.

The Special Care of the Nervous Child.—The special care of the nervous child should begin in early infancy and be continued until after puberty. Many of the children are wholly or to a considerable extent bottle-fed babies. Every nervous baby should be fed exclusively on mother's milk for the greater part of the first year if it is possible for sufficient nourishment to be obtained from this source. If not, properly modified cow's milk is the best substitute.—Perry in *Jour. Missouri Med. Assn.*

4. Schreiber, E.: Ueber Neosalvarsan; München. med. Wchnschr., April 23, 1912, p. 905.