stance and he is perfectly right. I reported the first case of paresis that I ever treated with salvarsan and I reported another exceptionally good result in a case treated three years later. Both cases were remarkably good results. If you can get such results in any cases of paresis with salvarsan you are fully justified in using it.

The intravenous injection of salvarsan will not cure every case of paresis or tabes dorsalis, but it will cure some cases.

The first case of paresis I reported was treated nearly four years ago and he was rational and able to attend to his business inside of five months after the injection of salvarsan. We might have obtained the same results with three or four years of mercurial treatment, provided the patient could have stood it.

Dr. Roberts says that a nerve cell cannot regenerate. We all realize that that is so, but a great deal of the loss of reflexes that we get in tabes and paresis is due to pressure on the nerve trunk from the infiltration due to the inflammation and not due to a degeneration. You get an inflammation which causes a pressure on the nerve trunk and gives the same symptom as a degeneration of the nerve trunk. All you can expect to do is to stop the inflammation before it destroys the nerve, and where you can do this you get a quick result.

You can take some cases of tabes dorsalis who can hardly see to find a chair in a room, give them salvarsan and they can read the headlines in a newspaper in twenty-four hours. This simply means that the inflammation has been reduced until the reflex of the nerve has been re-established after having been lost, not through destruction of nerve tissue, but through pressure due to inflammation. In these cases it is certainly better to give the patient the benefit of the immediate stoppage of this destruction with salvarsan, than it is to wait several weeks or months for mercury and the iodides alone to take effect.

Some say that there is no use in using mercury when you use salvarsan. We treat malaria with arsenic and quinine; we do not need the arsenic in most cases but we use both. If you have two or three good agents that work together for a certain result, use them all. Every syphilitic patient, no matter what stage he may be in, should have two or three full doses of salvarsan with full doses of mercury in between, and the salvarsan about ten days apart. If a patient has any of the late manifestations of syphilis he should have iodine in some form in connection with the mercury.

I do not believe in treating any patient with straight mercury or straight salvarsan. Unless for some special reason, I think we should always use both.

SOME FACTS PERTAINING TO THE WASSERMANN REACTION IN RELATION TO DIAGNOSIS AND TREATMENT.*

By R. B. H. GRADWOHL, M.D.

Director, The Ricord Hospital and Gradwohl Biological Laboratories, St. Louis, Mo.

Since the advent of the Wassermann reaction of blood serum and spinal fluid into the realm of diagnostic and prognostic medicine, some very interesting and instructive lessons have been taught. We have learned first to consider no case of syphilis as "cured" until a definite study of blood and spinal fluid has been made. Secondly, we have also refrained from discharging patients until a "provocative" salvarsan administration has occurred with a Wassermann test of blood serum in the following week. Thirdly, we have learned that a serological curve of blood serum is essential during the course of treatment of any case. Again, we have learned to classify neurological disease better by making a study of the serology of blood serum and spinal fluid in all such cases. We have also learned that a series of Wassermann tests is far more rational and instructive in clearing up obscure cases than is the old method of application of the "therapeutic test."

We have learned to control our treatment of these reactions, and more especially we have been interested in more closely following the reactions during the course of the more laborious method of treatment of cerebrospinal syphilis by salvarsanized serum injections into the intra-rachidian space.

*Read before the Physicians' Club, St. Louis, Mo., January 14, 1915.

These are, in brief, the lessons that have so far been taught. It shall be my task to go over some of these lessons, speaking from the standpoint of the consulting serologist and syphilologist. Our work here in this institution has been singularly interesting in that many of the results of our laboratory data have been obtained, as it were, in the dark, with no clinical history, hence with no bias, conscious or unconscious. Afterwards the clinical data were given us by our consulting friends. We have been furnished opportunities time and again to follow out serological curves.

The problem of stating when a "cure" of syphilis has been established is one that has been for years the "bête noire" of the practicing profession. It would be interesting reading to ask every physician who has been handling syphilis before and since the advent of the Wassermann reaction just what his answer would be to the question of "when is the syphilitic 'cured' of this disease?" Let us cite a case: A patient has been pronounced a syphilitic. He has had a secondary skin manifestation. He has taken say two years "mixed treatment," salvarsan and mercury and iodide of potassium. He has had a series of Wassermann reactions performed. For a year they have been negative. What ought we to tell him? He may wish to marry. What shall we say? We may be asked by him what are the chances for a later neurological complication, tabes or paresis. How much of a "risk" is he, viewed in the light of an insurance policy?

We would state, first, that he must have been adequately treated for at least two years. By "adequate" treatment I mean vigorous and intensive treatment with salvarsan and mercury. I am free to confess that I am one of those who regards salvarsan as a most important adjunct to our modern therapy of syphilis. Some there are within our ranks, some of high and some of low degree, who unmercifully condemn this agent. The curses of

high heaven have been invoked against Ehrlich and his remedy. No less an authority than Finger, of Vienna, has inveighed against it, and in a voice of equal force and bitterness Gaucher, the dean of the active syphilologists of Paris, has protested against its use and has doubted its usefulness. And there are others, too, lesser lights, men of but little experience with either mercury or salvarsan, who say they do not believe in it. Predictions have been frequently made by some of these lesser lights of all kinds of dire consequences that will accrue to those of our patients into whose veins this dreadful remedy is injected. Their arguments have ranged from the possibility of instant death following its administration, down to total blindness, the onset of precocious brain syphilis, the disintegration of brain and spinal cord and a waiting crowd of paretics and tabetics in future years to stand as mute witnesses of our iniquity in treating this disease with this agent. Without entering too deeply into this question, I must admit that my belief in salvarsan is based upon its wonderful immediate effects upon cutaneous and mucous membrane lesions; upon its rapid action in hurrying the patient through a disagreeable and contagious period of the disease; in rapidly getting rid of tertiary lesions, and finally in assisting in ameliorating certain types of cerebrospinal syphilis. As for the predicted increase in the number of cases of "precocious" brain syphilis that is certain to follow the use of salvarsan, I would point to the fact that salvarsan has been in use now for something over four years, and I do not believe that the profession has yet been struck by any unusual number of cases of precocious brain syphilis. And in four years the term "precocious" becomes outlawed if brain syphilis has not occurred. Finally, as to the predicted increase in tabes and paresis I have no answer as yet to make. Time alone will answer that. But in passing I would ask those who stoutly believe in a non-salvarsan course of treatment to explain away the multitude of cases of cerebral and

spinal syphilis that now crowd our consulting rooms and institutions. And, too, to these very same men who presume to deny to these brain and cord victims the benefit of salvarsan medication I would ask for evidence of *their* ability to make any kind of restoration or improvement whatsoever among these people with their mercurial or iodide therapy. I will take up later the benefits that can be shown in the treatment of cerebrospinal syphilis by means of salvarsanized serum.

Getting back to our original proposition it can be said that with the adequate treatment should be coupled the fact that Wassermann reactions of blood serum should be made from time to time during the course of treatment.

How often this should be done is a matter of choice with different workers. Ordinarily, every three months should suffice. Not only the Wassermann test should be used but also one which gets rid of the natural amboceptor found in 98 per cent of people, and one, too, that deals with unheated sera. The presence of natural amboceptor and the heating of blood sera serve to convert many weakly positive Wassermann into negatives. This has been shown by me to give a difference of 15 per cent as regards positive findings. For this purpose the writer utilizes a method called the Hecht-Weinberg test, a working modification of which having been reported by him in a paper published in *Journal A. M. A.*, July, 1914. A present experience of over two thousand comparative serological tests, using the Wassermann and the Hecht-Weinberg methods, has convinced me that the Wassermann alone is inadequate in our "control" of treatment by serology. Therefore, I would insist that the ideal negative reaction is a negative Hecht-Weinberg as well as a negative Wassermann. Six months after the termination of the two years, a lumbar puncture should be performed and a complete examination made of the spinal fluid, a Wassermann, a cell count and an estimation of excess of globulin and albumen. The Wassermann should be performed, using the Hauptmann

method of rising strengths of fluid, 0.2, 0.4, 0.6, 0.8 and 1.0cc. The cell count may be made with the Fuchs-Rosenthal counting chamber.

Granting that all these tests result negatively, in the absence of any clinical symptoms, we may tentatively say that we have restored the patient to as nearly a normal condition as we can hope to do. Some there are who may take exception to even this position, asserting that proof positive of "cure" cannot be gained even by this method. We believe, however, that if every physician followed out a routine of this kind he would have done his full duty by his patient. If possible, further observation of the case is timely, and should be practiced. The average patient, however, will not remain under treatment more than two years.

The use of the "provocative" injection of salvarsan has been advocated in estimating the "cure" of a patient. This means the injection of salvarsan into a patient who has given a series of persistent negative Wassermann reactions. It has been claimed that if such a patient is given salvarsan and the infection still exists, it will make itself manifest by the appearance after a few days of a positive reaction. Our policy is to ask patients to go through with this test. Many refuse. They are champing at the bit at the end of two or three years, and want no more of treatment even if it is in the form of a test. Those who consent should be given this test as it seems to be very useful in clearing up the question of "cure."

Those cases which show persistent positive Wassermanns during the course of treatment, sometimes after a year, sometimes after even a longer period, dishearten and discourage many physicians and patients. Our belief is firm that they represent cases that require more intensive and more prolonged treatment than the average one just cited. In no case in our experience has a case failed to become negative that was treated from the inception of the malady along the line of combined salvarsan and mercury therapy. They should

not be discharged or permitted to marry until their Wassermann becomes negative, no matter how long this may be.

The reaction may persist and hover for a long time on the border line, but the enemy will surely be routed if more fire is concentrated upon him. I believe that the earlier the case is put under treatment, the more probable it is that "sterilization" of the disease may be accomplished.

This brings us to a consideration of the value of the Wassermann in the treatment of the latent case, the obscure case, the tertiary case, the case that has had syphilis a long time ago, the case that had little or no treatment, either through the patient's own neglect or through the negligence of the medical attendant who failed to appreciate the necessity of intensive treatment. In these cases a Wassermann reaction will often make the diagnosis where all else fails. Cases are legion that have gone the rounds and have been treated for everything but syphilis. Some there are that deny ever having had syphilis, denying either a primary sore or a secondary skin manifestation. Some lie and others don't know. Some are late congenital cases that naturally know nothing of their parents' infection. *Possibly the most monumental sin that besets the profession today is its readiness to accept any statement from any patient regarding the history of a past syphilitic infection in so far as it has any bearing on the inclusion or exclusion of syphilis in explaining a present obscure disease.* We are too prone to ask a patient whether he ever had syphilis, and on being told "no" to accept this as final proof that he cannot possibly now have the disease. We are also too much inclined to regard the patient's respectability as offering a bar to the existence of syphilis.

We are too prone to think of syphilis as the last explanation instead of the first in seeking the cause of something obscure. Some of us are overawed by the apparent or real chastity of our patients, particularly of the female sex. Sex, age, social position, marital status,

nothing should stand in our way in investigation of disease. And there should be no hesitation once the diagnosis is made in telling the patient the real nature of his disease. It is in this class of patients that the Wassermann looms up as the great hope of diagnosis. The blood serum examination usually suffices to pin down the existence of a stomach or liver or heart or lung syphilis.

So far as a means of control in such a case, we can only state that the treatment of a latent or tertiary syphilis means continual and continuous observation over many years, checked from time to time with Wassermann reactions. No statement of any kind touching upon the length of time necessary to "cure" or "sterilize" tertiary syphilis can be made. Our policy should be one of intermittent attack, possibly throughout the patient's entire life. In this way, and in no other, is the physician performing his full duty. Any deviation from this policy exposes the latent or tertiary syphilitic to a fresh outbreak of his disease.

The study of syphilis of the nervous system with serological methods has thrown new light on this subject. We have clinched the theory that paresis and tabes are due solely to syphilis. We have been enabled to recognize these diseases in their pre-paretic and pre-tabetic stages. The Wassermann reaction of blood serum and spinal fluid has permitted us to better classify many neurological conditions. The serology of spinal fluid, as a rule, gives us much more information than does a similar study of the blood serum. Many cases of tabes show no reaction in blood but a very definite reaction in spinal fluid. Many cases of tabes in the incipency are not recognized. The profession has not yet learned to suspect tabes when the patient complains of pains in the legs, of failing sexual power, of vague gastric symptoms. Close inspection of these cases will show tabetic pupils, absent knee jerks, Rombergism, etc. A spinal puncture will do the rest. A Wassermann of blood will often fail to help the clinician in his search

for tabes, and what is worse, will often make him dismiss the diagnosis completely from his mind. Many physicians regard a lumbar puncture as too serious an operation to be suggested except in very unusual cases. They fail to appreciate two facts, first, that it is not a severe or serious operation; secondly, that without it we cannot accurately make a diagnosis of syphilis of the nervous system. I would rather not see them make a Wassermann test at all if only the blood serum is searched. A failure to find it in the blood serum too often takes their mind off the possibility of syphilis of the nervous system. Lumbar puncture is necessary and imperative in these cases. Beware of the comfortable old diagnosis of "rheumatism." Beneath its venerable clothing lurks often a luetic affection of the cord, masquerading as a harmless although painful affection. A failure to heed this advice will enable the patient's street acquaintances to make a diagnosis of tabes before his medical man. We ought naturally to try to recognize disease before the layman does for the sake of our own self-respect if for nothing else. While not in any way wishing to endorse indiscriminate lumbar puncture, we certainly must maintain that it is a procedure by far too much neglected in searching for syphilis.

Attention must also be called to the necessity of a serological curve of spinal fluid. More than once have we seen a variation in spinal fluid as regards the Wassermann at different times independent of treatment. In one case of suspected gumma of the cord which the gentlemen present saw at our last meeting, we found a positive reaction in the spinal fluid at one sitting. One week later, the spinal fluid showed a *negative reaction*, there having been no treatment in this interval. A few weeks later, after an intra-spinal injection, a strongly positive Wassermann was found. We have seen four cases of outspoken tabes that had never had treatment, with negative Wassermann reactions. In one case, we saw a positive supervene after two weeks. This em-

phasizes the need of repeated lumbar punctures when the occasion demands it.

This brings me to the last consideration, namely, the usefulness of the Wassermann in controlling our treatment of syphilis of the central nervous system by means of the injection into the subarachnoidal space of salvarsanized serum. Swift and Ellis, who have been foremost on this Continent in advocating this method, have given it as their opinion that the injections should be continued until negative reactions occur; when the reaction becomes negative, then it usually remains so and we may speak of the case as having been arrested. After an experience of something like one hundred and seventy-five intraspinal injections in fifty-two cases, I must in a measure disagree with this statement, although my earlier opinion as given in a paper read before the Cincinnati Academy of Medicine in May, 1914 (see Cincinnati Lancet Clinic, July 11, 1914), practically supported the above writer's belief. In some of my cases reported at that time as having become negative under the influence of treatment and having remained so, subsequent lumbar punctures have shown a reappearance of the Wassermann reaction. The reappearance of this reaction in no way was indicated by any backsliding on the part of the patient, so far as physical signs go. On the contrary, there had been in these cases even after the cessation of treatment a progressive improvement. I wish, therefore, to be understood as going on record in denying that the changing of a spinal fluid from positive to negative during the course of the intra-rachidian injection of salvarsanized serum means complete arrest of the process or a serological indication for stopping treatment. Our policy should be to reduce the reaction from positive to negative, to watch the physical signs, and, above all things, to continue making lumbar punctures and Wassermans and, on the reappearance of a reaction, to be prepared to continue the treatment again with subsequent watching and waiting. In this way and in no other can we hope to arrest

and to stay the progress of these cord changes.

Briefly, then intensively treat syphilis and have your serological curve at hand, both of blood serum and spinal fluid. Look for syphilis with laboratory methods when the case is obscure, just as you would use your stethoscope or your ophthalmoscope.

Remember that sparing the lumbar puncture needle means spoiling the patient's chances for relief and your own diagnostic reputation. And when you are dealing with salvarsan medication in the spinal canal, remember that many lumbar punctures are to be made before treatment should be stopped and that there are eccentricities in spinal fluid reactions just as there are in blood serum.

803 N. Garrison Ave.

A SIMPLE AND EFFICIENT CONTRAST STAIN FOR B. DIPHTHERIAE.

By G. McF. MOOD, M.D.,
Charleston, S. C.

PRELIMINARY REPORT.

Several years ago, it being observed that old alkaline methylene blue would at times color some of the polar granules of *B. diphtheriae*, red, attempts were made to produce this contrast staining effect constantly. Many methods were tried, each of which produced either no contrast stain at all, or gave a decided polychrome effect.

A few months ago, however, a method was finally perfected by which methylene blue is converted by oxidation into methylene red, within the polar granules, during the process of staining.

The stain as perfected is as follows:

Sat. Alcoholic Sol. Methylene-blue
(Koch for Bact.)..... 1 part
Hydrogen peroxide 9 parts

Should be kept in a well-stoppered bottle.

Methylene-blue, Koch for bact. has been specified, because other forms used failed to give the desired result.

Any peroxide which we have tried was found to be efficient.

The stain may be kept for several weeks after mixing, provided it be placed in well-stoppered bottles; samples placed in white glass bottles upon shelves in the open laboratory for six weeks were unaffected in any noticeable way, and retained the specific staining properties unaltered.

In using the stain, the specimen is prepared and fixed in the flame, as for ordinary specimens, and the stain allowed to act for from thirty seconds to three minutes. Upon its application, there occurs usually in about ten seconds a rise of small gas bubbles to the surface, this continuing for from thirty seconds to three minutes. As soon as this rise of bubbles ceases, the specimen is sufficiently stained. One minute has been found best for the majority of specimens, and is recommended for routine work. There is no danger of over-staining, as a half hour's exposure will not darken the *B. diphtheriae* appreciably, but has the disadvantage of staining some of the other organisms present in cultures from throats darker than when the time of exposure is shorter. The contrast effect upon the *B. diphtheriae* is, however, unaltered.

The specimen may be dried, either in the air or with the application of a small amount of heat—the latter not altering the contrast effect—and mounted in balsam.

B. diphtheriae will be stained as follows:

Bodies a pale pigeon egg blue, polar granules a bright red.

Other throat organisms ordinarily present usually take a very pale blue color, even paler than the bodies of the *diphtheriae* organism, in some specimens, forming here an almost homogenous pale blue background. When these various organisms stain darker, they are quite clear enough not to be confused, morphologically, with the *diphtheria* organism. A coccus has been encountered occasionally