

In reference to the treatment, it is difficult to foresee whether it will be possible to find an antisyphilitic vaccine which, by increasing the opsonic index, will render the organism capable of disposing entirely of the treponema. One thing is sure: that in the mercurial preparations we have a remedy which directly attacks the spirochete and improves the general condition of the system, rendering it able to cope with the virulence of these germs.

In the meantime we can find the means to attack the treponema directly on the initial lesion where it is developing. We can either destroy it in the locality or at least succeed in modifying syphilis to such a point that it may have a mild course. The local and the general action of atoxyl has been greatly praised by Salmon and Hallopeau. The last named author⁴ has called its use the novel local treatment of syphilis in its primary period. A salve containing 50 per cent. of atoxyl has been used on the initial chancre and at the same time there have been given injections with an atoxyl solution from 10 to 20 per cent. with satisfactory results.

In my service at the City Hospital in two cases of initial lesion the application of the atoxyl salve dissolved the hardness, cleaned the surface and healed up the ulcer in a much shorter time than has been possible with any other means.

The action of the atoxyl on the syphilitic pathologic products has been recognized by Hoffman⁵ not only on man but also on the animals. Hoffman and Uhlenhuth have found in the application of atoxyl a preventive action against syphilis in the animals, and this was later confirmed by Metchnikoff. But it seems that the atoxyl treatment does not protect the patient from the relapses of syphilitic manifestations. In my practice the atoxyl injections in cases of severe symptoms did not give me the results which the mercurial preparations have afforded. We can say then that to-day we believe there has been found another remedy which has antisyphilitic action. Time and experience will show whether it is to replace mercury, whether it is to be given in conjunction with mercury, or whether the greatest of all antisyphilitic remedies will still be mercury.

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THE INFLUENCE OF THE DISCOVERY OF THE SPIROCHÆTA PALLIDA ON THE TREATMENT OF SYPHILIS.*

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The brilliant results of the work of Schaudinn and Hoffman, following the researches of so many able investigators, and confirming pre-existing opinions that syphilis was due to a specific micro-organism, are certainly a cause for congratulation on the progress of pathologic study. To the general practitioner, however, it presents the question: "What advantage is gained and what difference should it make in the management of a case of syphilis at any stage?"

This is a pertinent question and deserves consideration. In connection with the recent work done by

French investigators in the prophylaxis and treatment of syphilis by calomel ointment and atoxyl, a partial answer to the question is found. Metchnikoff¹ has conclusively shown that syphilis may be aborted by the inunction of calomel ointment, provided it be used sufficiently soon following inoculation. Such a prophylactic use of the ointment, while interesting and useful on rare occasions, is impracticable and of no service in general practice; nor can it be used in any case in which a diagnosis has been made by the demonstration of the presence of the *Spirochæta pallida*.

In the same article the abortive power of atoxyl in syphilis was proved. With this drug the interval elapsing between the time of the inoculation and the use of the drug was much lengthened, such an interval having been as long as fifteen days, following which no manifestations of infection appeared. This again, as in the prophylactic use of calomel ointment, is an interesting fact, easily demonstrated in laboratory experiments, but of little more service in general practice than the use of the calomel ointment, so far as aborting the disease following a laboratory diagnosis with the presence of *Spirochæta pallida*.

Among the various laboratory experiments on apes, two animals were inoculated, together with controls, with syphilitic virus and later given prophylactic doses of atoxyl. The control animals contracted the disease, while the two inoculated animals did not. After an interval of two to three months these two apes were re-inoculated and both developed typical primary sores. These experiments went to show that after the first prophylactic dose of atoxyl there is neither a dissemination of the virus nor a lasting immunity.

If further work goes to demonstrate the truth of the claims of these men as to the prophylactic power of atoxyl, given soon after inoculation, such a fact can be made of practical use in one way at least. If all persons who have been exposed to a possible syphilitic infection were to submit themselves for treatment by prophylactic doses of atoxyl, it would be possible to wipe out the disease. Such a line of treatment, however, would have to be instituted before the infection had been generally disseminated and before its presence could be demonstrated by finding the *Spirochæta pallida*. In general practice, of course, such a line of treatment would be purely empiric and the infected and uninfected must needs be treated alike. In this connection it might be said that such a dose of atoxyl, however, is harmless.

The prophylaxis and the treatment of an actually existing syphilis, of necessity, are two different things. Having a patient presenting a suspicious lesion, what is the general practitioner to do in the light of present knowledge? Weight of authority up to this time has held that no constitutional treatment should be begun until the diagnosis is confirmed by the appearance of secondary symptoms in some form.

In the presence of a lesion, to-day, in which an unsuccessful search for the *Spirochæta pallida* has been made, it would seem that the active constitutional treatment should still be delayed, pending confirmation of the diagnosis. With such a lesion, scrapings from which show the *Spirochæta pallida*, their presence is of sufficient confirmative weight to warrant the immediate institution of antisyphilitic treatment. Again the question arises: "Of what advantage is this to general

4. Hallopeau, H.: Nouveau traitement local de la syphilis dans sa première période, rev. scient., 11, Jan. 11, 1908.

5. Berl. dermat. Gesellschaft, July, 1907; cited in Dermat. Ztschr., 1907, p. 656.

* Read in the Section on Cutaneous Medicine and Surgery of the American Medical Association, at the Fifty-ninth Annual Session, held in Chicago, June, 1908.

1. Ann. de l'Inst. Pasteur, October, 1907.

practitioners, practically none of whom are able to demonstrate or differentiate the *Spirochæta pallida*?" Granting, however, that the micro-organisms have been demonstrated, what difference will it make in the line of treatment? The primary lesion from which you can first recover the *Spirochæta pallida* is but the first anatomic evidence of a condition already more or less systemic and unquestionably disseminated quite beyond the localized area of the primary sclerosis.

What has been previously demonstrated as to the inadequacy of surgical excision in such lesions is quite as true to-day as ever. The only change from pre-existing methods of treatment which could be wrought by the finding of the *Spirochæta pallida* would be in advancing the time in which one would feel warranted in beginning constitutional treatment, and even then one of the chief objections to early constitutional medication previously existing would still hold true; that is, early mercurial treatment may abort or delay secondary symptoms and the patient be lulled into a false sense of security after an insufficient course of medication and ultimately develop serious after-effects as a result of medication early instituted following a microscopic diagnosis of syphilis.

If, however, further observations go to show that atoxyl eliminates all evidences and possibilities of a lasting syphilitic disease, then surely much will have been gained.

A study of an exhaustive article by Paul Salmon² on arsenic in syphilis leads one to a conviction of the sincerity of its author and the truth of his claims regarding the results of the administration of atoxyl in syphilis. From it the following observations and conclusions may be made:

Atoxyl must be admitted to an equal footing with mercury as a specific in syphilis, and as an abortive in the disease it is much more reliable. As a remedy it is preferable in all stages and possibly can be depended on to destroy all spirochetes if used even after the primary manifestation. It is of special service in the graver and more malignant types of the disease. It is not contraindicated in the parasymphilitic manifestations, but even ameliorates many of the symptoms, such as pains and neuralgia in tabes and paresis.

Syphilis may be aborted by the prophylactic use of atoxyl administered as late as from one to two weeks following inoculation. The failures of previous investigators along these lines have largely been due to insufficient doses of atoxyl.

That atoxyl administered by injection proves to be a true prophylactic is demonstrated by the fact that an animal in which syphilis has been aborted by atoxyl, and later was again inoculated with syphilis, developed a typical chancre. The same experiment goes to show that prophylaxis does not carry with it an enduring immunity.

In the use of the remedy, during any of the stages of syphilis, more rapid improvement than one gets from the use of mercury usually followed.

When the disease has become disseminated—that is to say, at any time following the appearance of the primary lesion—constitutional treatment, be it with atoxyl or mercury, must be carried on for a prolonged period, and, while the improvement of particular syphilitic manifestations is more rapid with atoxyl than with mer-

cury, recurrences appear on the cessation of the treatment.

The explanation of the action of mercury or atoxyl on the spirochete must still be found. It is probably through the effects of the drugs in attenuating the germs or in stimulating phagocytosis.

Beyond a certain dose, the amount given has no further effect on the destruction of the micro-organisms. The small doses are ineffective and useless, while large ones produce toxic effects, varying from slight headache, nausea, vomiting, colic and possibly ocular effects and subsequent paresis.

The ordinary dose should be 50 centigrams. This should be given hypodermically at intervals of one or two days and repeated from four to eight or ten times, after which an interval of rest should be observed, or treatment may be continued by one of the other specifics of mercury or iodine.

Very good results have been observed in the alternation of these remedies, or even in using them together at the same time. At present, atoxyl, as a remedy, promises much.

In unusual dermatoses of uncertain character, the recovery of the *Spirochæta pallida* establishes a positive diagnosis and indicates the necessary treatment. The failure to find spirochetes, however, proves nothing and we are then no better off than we were years ago. In such cases, the Wassermann test may be used as a necessary diagnostic resort.

Outside of the larger medical centers, such diagnostic measures are quite impracticable, and in the hands of the general practitioner impossible. The fact remains that in many cases a diagnosis must and will depend entirely on the clinical picture presented.

To the attending physician still remains the necessity of recognizing syphilis from the symptoms manifested by the patient.

The discovery of the *Spirochæta pallida* undoubtedly marks one of the greatest steps forward in the knowledge and literature of syphilis. The immediate practical benefit of this discovery, however, will be limited to a comparatively few cases, and even in these few cases its presence usually seems to be a confirmatory evidence of a diagnosis previously made by the clinical presentation.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DRs. BREAKEY AND RAVOGLI.

DR. HERMANN G. KLOTZ, New York: My experience with primary sores of syphilis has been very similar to that of Dr. Ravogli. I particularly recall one case of a very malignant type in which the primary lesion consisted of a slight abrasion which healed within a week and which I had not recognized as a chancre at all. In connection with Dr. Breakey's paper, I emphatically warn from depending too much in practice for the present on these new discoveries. In time we shall learn more about the spirochete and about the part it actually plays in the development of syphilis, but it is much too early to draw practical conclusions. Long before the spirochete was discovered we knew that some micro-organism must be the causal factor in syphilis, but from clinical experience most syphilologists had come to the conclusion that it was safer to wait until the secondary symptoms appeared before beginning treatment. Until we know more about the spirochete and its life history there is no reason to recede from the former practice. From clinical observation we knew, long before this fact was explained by the study of the life history of the malaria plasmodium, that quinin was most effective in malaria if given at a certain time. So in time we may learn

2. Ann. de l'Inst. Pasteur, January, 1908.

why the results of the mercurial treatment are more favorable when it is withheld until the secondary symptoms have appeared.

DR. WILLIAM A. PUSEY, Chicago: I endorse Dr. Klotz's caution against attaching too much importance to the spirochete in a diagnostic way. I also protest against the present vogue of atoxyl. There is no reason to believe that arsenic is more efficient against syphilis than mercury, or that there is anything except arsenic in atoxyl that could be beneficial in syphilis. The only claim for the preparation is that by it arsenic can be given in enormous doses, but it is not established that the molecule of atoxyl has the same therapeutic effect as arsenic. There are a variety of opinions as to the safety of the preparation; dangerous results have been reported from its use, and the testimony regarding it is not all in accord. I believe that we are not justified in relying on it to any extent in the present state of our knowledge regarding it. Metchnikoff believes that syphilis can be aborted by the use of a calomel ointment, and certain French writers assert that this is efficacious when applied within eight hours after exposure. The statement that atoxyl or any other preparation of arsenic will abort syphilis if used within fourteen days or even longer after exposure is, in my opinion, absurd. If mercury will not do it—and it will not—there is no reason to believe that a new preparation of arsenic will display such potent action against syphilis.

DR. A. KAVOGLI, Cincinnati: I do not in my paper recommend the use of atoxyl. I selected six cases of recent syphilis in my hospital service and subjected the patients to three injections per week of a syringeful of a 10 per cent. solution of atoxyl; one of these patients developed an iritis, and the others were at times a little better, at times a little worse. I then changed the injections to bichlorid, and my experience showed that the three weeks I had devoted to atoxyl treatment had been wasted. After three injections of bichlorid the eruption in all the cases cleared up. Atoxyl, used locally, seems to hasten the healing of a hard chancre. Calomel would probably have the same result. My experience has led me to take a lukewarm attitude toward atoxyl.

HEMOLYSIS WITH SPECIAL REFERENCE TO CANCER AND TUBERCULOSIS.

FURTHER OBSERVATIONS ON ITS CLINICAL ASPECTS*

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The literature of the work hitherto done to discover some blood test for cancer is presented by Richard Weil.¹ The technic followed in our work at Lakeside Hospital is based on that in current use, modified to meet clinical requirements.

I have heretofore reported for the American Society of Cancer Research our observations on hemolysis in malignant tumors. This is in the nature of a report of progress in our investigation. The technic has been greatly improved and now seems to be quite accurate. It is exacting, must be precisely done, and every step amply surrounded by checks and controls.

Dr. D. A. Prendergast made the first series of observations, after which Miss Ora Lewis took all the responsibility of the technic for seven months and made many improvements during the period of her painstaking work. Dr. A. M. Tweedie has been carrying on the work since Miss Lewis' service and has made extremely valuable suggestions and alterations in the technic. My resident physician, Dr. H. G. Sloan, and members of my staff at Lakeside Hospital, Drs. Gamble, Eisenbrey and Pomeroy, have assisted in the clinical side.

THE NATURE OF HEMOLYSIS.

The red corpuscle is covered by an exceedingly thin and delicate membrane, which prevents the escape of its contents, the most important being hemoglobin. This investing membrane is very susceptible to chemical or thermal changes in its environment. If impaired by such changes a part or all of the hemoglobin will escape and become freely diffused in the serum. The corpuscles then become proportionately paler, and if all the hemoglobin is lost there will remain only the framework of the cell, designated as "shadow cell" or "ghost."

Free hemoglobin may be detected in the urine and other secretions. If in quantity, it stains all the tissues, causing a brilliant jaundice. This process is known as hemolysis and the agents causing hemolysis are known as hemolysins. Hemolysins may be roughly classified as inorganic and organic. Among inorganic hemolysins are ammonia, soaps, ether—any agent that will change the isotonicity of the blood serum. Among organic hemolysins are normal blood and tissue juices of alien species, and blood and tissue juices in certain pathologic states. In pernicious anemia, in certain fevers, occasionally in chronic suppuration, and in other general diseases there is such a change in the blood serum that when the red corpuscles from normal individuals are suspended in this serum hemolysis occurs. It may be at once asked why such hemolytic serum does not destroy the corpuscles of the patient *in vivo*. Two reasons suggest themselves why this does not always occur. The first is that the corpuscle undoubtedly shares the universal attribute of living matter whereby it is able, to a certain degree at least, to adapt itself to its environment. The second reason why hemolysis may not occur in the presence of hemolytic serum is that the process *in vitro* is not identical with that *in vivo*. A corpuscle, having adapted itself to a certain environment, may itself become so altered that when it is again suspended in normal blood serum it may undergo hemolysis.

The medical importance, if any, that these facts assume is determined by correctly answering the following questions: Is there a reliable technic for the determination of hemolysis? Are the changes in the serum and in the corpuscles thus produced by disease of a specific nature? Are they constantly present?

CONDITION OF THE TEST.

Many difficulties beset the technic. There are many inorganic hemolysins that must be avoided. The blood must be drawn and kept absolutely free from these. Red blood cells are extremely sensitive to changes in temperature. Provision for absolute control of the temperature must be made. As the corpuscles are very delicate, extreme care must be exercised in applying the mechanics of the technic. Experience has shown that if the serum and corpuscles are immediately separated, either by drawing the blood in sodium citrate solution or by immediate centrifugalization, the hemolytic action is either minimized or negative. The maximum reaction is obtained when the serum and the corpuscles are separated by clotting. The serum attains its maximum hemolytic power in about twenty-four hours. In securing normal blood one must bear in mind the fact that it is not possible absolutely to determine, except by an actual blood test, whether a given individual's blood will react as normal. But if these samples of supposedly normal blood are used and are tested against each other as well as against the blood of the patient, there is then but

* Read before the American Society of Obstetricians and Gynecologists, Baltimore.

1. Jour. Med. Research, October, 1908.