

usually clears up unless it has advanced too far, when the condition is exceedingly deplorable and difficult to relieve.

THE URINE IN TUBERCULOSIS OF THE GENITAL TRACT

The occurrence of tubercle bacilli in the urine of patients with tuberculosis of the epididymus, the seminal vesicles, or the prostate, has never been thoroughly investigated. Marwedel found tubercle bacilli in the urine in four cases of prostatic tuberculosis. My own experience is very limited, but in three cases no acid-fast rods were found in the urine. When the prostate or seminal vesicles are involved, massage may produce a secretion containing tubercle bacilli. The constant presence of the occurrence of tubercle bacilli in large numbers would suggest tuberculosis of the urinary tract as well.

Fortunately the diagnosis of tuberculosis in the genital tract rarely depends on the discovery of tubercle bacilli in the urine. An enlarged globus major with a thickened or slightly enlarged seminal vesicle or irregular or nodular prostate in a patient with a preexisting tuberculosis can be diagnosed as tuberculous. Barney's²⁰ paper on this subject should be consulted.

CONCLUSIONS

1. No staining method differentiates absolutely tubercle bacilli from smegma bacilli, but cultural methods may aid greatly.
2. Animal inoculation, with the production of tuberculosis, is an absolute test, but of value only when positive.
3. The same care about the collection of urine should be exercised as about the collection of sputum.
4. Tubercle bacilli can be excreted through apparently normal kidneys.
5. Radiography may aid in the quick detection of caseous foci when the urine contains no tubercle bacilli.
6. Spontaneous healing is often fictitious.
7. The final, and often the best, treatment for renal tuberculosis on diagnosis, is nephrectomy followed by the use of tuberculin.
8. Tubercle bacilli occur in the urine in genital tuberculosis usually late in the disease and are consequently of little aid in diagnosis of the condition.

20. Barney, J. D.: Ultimate Results of Genital Tuberculosis in the Male, *THE JOURNAL A. M. A.*, Dec. 26, 1914, p. 2274.

Infectious Diseases an Unnecessary Waste.—Sir Frederick Treves believes that the time will come when hospitals for infectious diseases will be empty and not wanted. This is to be accomplished by hygiene. The fight is against millions of microbes, and the weapons are sanitary regulations, municipal government, the sanitary inspector and the health officer. The mystery of the ancient doctor, with his long words and extraordinary prescriptions, is passing away. The multitude of shelves of bottles which surrounded lives also is passing away and being replaced by simple living, suitable diet and plenty of sun and fresh air. The time will come when it will be as anomalous for persons to die of scarlet fever, typhoid, cholera or diphtheria as for a man to die of a wolf's bite in England. Personal hygiene is only beginning to be generally exploited. It is manifest destiny that a wise economy of vitality will sooner or later be practiced. Waste of vital resources is as irrational as waste of natural resources. Neither is inexhaustible and both must be conserved. Thoughtlessness and ignorance are the reasons for the appalling waste of both now going on.—Irving Fisher, "Report on National Vitality."

FAMILIAL SYPHILITIC INFECTION IN GENERAL PARESIS*

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In view of the fact that so little definite information concerning the importance of familial syphilitic infection in paresis has been brought before the American medical public, it has been thought desirable to present briefly certain observations which we have been able to make in this connection during the past three years.

The material on which our observations have been made includes, first, fifty-five clinically unquestionable cases of general paralysis in married individuals admitted during this time in which we have been able to test the presence of syphilitic infection in the other mate, and secondly, eighty-six cases in which the anamnesis concerning intimate family matters of absolute sterility, pregnancies with early abortions, total number of living-born children, with additional abortions, miscarriages, etc., could be accepted without question.

We have been able to examine the blood serum of the conjugal mate in fifty-three married paretics. Seventeen, or 32.7 per cent., of these cases showed a positive Wassermann reaction. Although this figure is sufficiently high to be striking, it yet does not represent the whole situation. One wife, acknowledging a severe infection following a lip chancre, had had careful treatment and presented at the time of our examination a negative Wassermann reaction. The first wife of a patient, whose second mate now has a strongly positive reaction, herself died of syphilitic disease. Of two female paretics, the husband of one preceded her in the development of paresis by about one year, while the husband of the other died of tabes about two years before. Since both of these husbands must have had syphilis, they should be added to the total. Although there are other possible factors, such as, for example, a wife showing a repeatedly negative Wassermann reaction and yet a history of repeated abortions without living children, or where the wife has a negative reaction but with children showing a positive Wassermann, which would justify assuming an additional number to swell this figure, at the present time we will add only these unquestioned cases. These additions show that in the families of fifty-five paretic patients there is a total of at least twenty-one mates infected with syphilis.

Separating this group into the two sexes, we find that in forty-nine cases in which the husband is paretic, seventeen wives are infected with syphilis; in six cases in which the patient is a woman, there are four husbands who are known to have syphilis.

While these figures are high, they are not greatly higher than other investigators have found and, as already suggested, probably underestimate rather than exaggerate the real situation. In a study of fifty-four cases of married paretics Plaut and Göring¹ found the other mate showing a positive Wassermann reaction in 32.6 per cent., a slightly smaller number than our figures of 38.18 per cent. Hauptmann² includes among forty-three cases where he investigated whole families serologically, eighteen cases of paresis in which

* From the Psychiatric Clinic, University of Michigan.

1. Plaut and Göring: *München. med. Wchnschr.*, 1911, No. 37, p. 1959.

2. Hauptmann: *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1912, viii, 36.

he found a positive Wassermann in twelve mates, or the enormously high figure of 66 $\frac{2}{3}$ per cent.; but, inasmuch as he picked these cases for a special purpose and did not take them as they came, as in Plaut and Göring's study and in our own, this figure does not concern us.

The number of these infected mates who had previous knowledge of any infection, or who could tell us of any suspicious signs of secondaries, was the extremely small figure of two. Only one of them had had any antisyphilitic treatment. The matter of regularly mild or no skin and mucous membrane lesions appears to be about as common as similar observations on paretics themselves.

At the time these paretic patients entered the hospital, excepting the two where the other mate was known to have already had paresis and tabes, respectively, there was only one case in which ordinary clinical methods, such as could be used in examining a visitor, gave sufficient grounds for assuming organic disease of the central nervous system in the conjugal mate. This was in a wife with the Wassermann reaction on her blood strongly positive, apparently regularly moderate and occasionally excessive in her alcoholic habits, who showed a slightly sluggish reaction of her pupils to light and unequally diminished knee jerks. She showed some difficulties in her speech, an ataxic tremor in her writing, mild defect in retentive memory, spreading of impulses through her facial muscles under mild emotion, and some difficulties in solving involved mathematical tests. Though one appears justified in making a clinical diagnosis of conjugal paresis in her case, yet in view of her showing signs of mild alcoholic intoxication on each of two visits, in itself a very significant fact, until we shall have been able to examine her cerebrospinal fluid we shall not include her further in our statistical consideration.

It so happens that in our material we are quite certain in each case which mate was infected with syphilis before marriage, and from now on in this paper that individual will be spoken of as the infecting member. In only three cases was the woman the first infected; in two of these the serum examination on the husband was negative, while in the third the reaction was positive.

The relation of already developed metasymphilitic disease in the other mate is interesting. In one case both mates were paretic; in the other case the original infecting mate was tabetic, with the infected member paretic. How many metasymphilitic mates should we expect? This query leads us immediately into the big question of the existence of a *lues nervosa*, but it is well perhaps merely to state the results of some other careful observations. Mattauschek and Pilcz,³ from observations on 4,134 army officers infected with syphilis between 1880 and 1900, found 4.67 per cent. to have developed paresis by 1912 and an additional 1.6 per cent. to have developed tabes, a metaluetic total of 6.27 per cent. These figures concern, however, a rather specialized group and one exposed to many of the factors supposed to tend to metasymphilitic disease. Pick and Bandler found that among 2,066 syphilitics coming to the Prague Skin Clinic during 1879-1899, twenty-eight had become paretic in 1904, a percentage of 1.3. O. Fischer⁴ separates these into the two sexes

and shows that among 1,178 men 25 had paresis and 12 tabes and among 888 women 3 had paresis and 2 tabes, or 3.7 per cent. of the men and 0.55 per cent. of the women had in that interval developed a metaluetic disorder. What proportion of these had obtained their syphilis in the first place from one who had, or later developed, a metaluetic disorder is unknown. In his own 500 cases of paresis Fischer had 395 married individuals. Among the 319 men 1 wife developed paresis and 2 tabes, while among the 76 women 5 husbands had paresis and 2 tabes; that is, a total of 10 metaluetic individuals, or 2.5 per cent. of the infected mates developed some metaluetic condition. Mönkemüller among 741 married paretics found 18 cases, or 2.14 per cent., of conjugal metaluetics. These figures, even when applying only to the cases of conjugal paresis, 6 in Fischer's cases and 14 in Mönkemüller's, are considerably higher than Hannard and Gayet⁵ found among 2,429 married paretics in two French institutions where only 23 mates developed conjugal paresis.

In our material, starting with 51 metaluetic husbands, whom we are justified in assuming to have been the infecting agents, and of whom we grant that possibly one was only a tabetic, we find that among 19 infected wives 2 have already developed general paralysis. In this smaller number of cases the percentage of wives to have already developed paresis is 3.9 per cent. when figured on the entire number, but when figured on the number of wives shown by the Wassermann reaction to be infected with syphilis, it reaches the astounding figure of 10.5 per cent. It so happens that this figure agrees exactly with the percentage Fischer reaches in studying his 76 female paretics, where he assumes, rightly or wrongly, that all these wives got their syphilis from their husbands after marriage.

We have further been able to study the matter of sterility and the number of abortions and living-born children in 86 cases in which the accuracy of the anamnesis, furnished by the wife or husband of the patient and confirmed in many cases by the patient, could be definitely depended on. The conditions found are clearly illustrated in the accompanying table.

DATA CONCERNING FERTILITY IN PARETIC MARRIAGES

	Total Number	Sterile Completely	Abortions Only	Total Number of Abortions	Living-Born Children
Male G. P...	76	22	10	43	110
Female G. P.	10	6	1	1	13
Total	86	28	11	44	123

This table shows that of 86 marriages among paretics, 39, or 45.4 per cent., were absolutely childless. Of this number 28 marriages, or 32.5 per cent., were completely sterile, while the additional 11, or 12.7 per cent., resulted only in abortions. This total number agrees almost exactly with Heubner's figures of 45.7 per cent. of childless marriages, although his percentage of completely sterile marriages is about 7 per cent. higher. This percentage is considerably higher than Kraepelin's⁶ findings of about 18 per cent. of unfruitful marriages in his Munich material, which is not much higher than the figure for the whole Ger-

3. Mattauschek and Pilcz: *Ztschr. f. d. ges. Neurol. u. Psychiat.*, Orig., 1912, viii, 133; 1913, xv, 608.

4. Fischer, O.: *Ztschr. f. d. ges. Neurol. u. Psychiat.*, Orig., 1913, xvi, 120.

5. Hannard and Gayet: *Ann. Medico Psychol.*, 1911, xiii, 200, 403; xiv, 36.

6. Kraepelin: *Lehrbuch der Psychiatrie*, Ed. 8, iii.

man population, and yet distinctly lower than Regis gives, who assumes that three-fourths of paretic marriages are childless.

Even more interesting and startling is the matter of the living-born children. The average number of living-born children in this group is 1.4 to each family. If we consider only those families with living-born children, we find the average to be 2.24 children per family. In this group, however, are included 2 instances in which there is the unusually large number of 10 and 12 children, respectively. If we exclude these two abnormally large families we find that 75 families of male paretics have 98 living-born children and 9 families of female paretics have 3 living-born children. The average would then become 1.2 children per family, or where the father was paretic, 1.3 children per family, and where the mother was paretic only 0.3 children per family. Our number of paretic wives, we grant, is extremely small and not sufficient in itself to warrant drawing conclusions from it alone, but it is found quite generally that when the mother is the paretic the influence on the matter of sterility, number of abortions and small number of living-born children, together with their character, is more marked than where the father is paretic.

Further study of the histories of these 84 families with 101 living-born children shows that at the time the paretic patient entered the hospital, in this series averaging a period of 11.6 years after marriage, 20 children of this extremely small total of 101 died. Usually these deaths were in early infancy, as in the following instances, in which definite statements are noted: "1 immediately and 1 at the end of the first day," "1 at the end of the first week and the other of hydrocephalus at 5 months," "1 of spasms at 5 weeks," "1 of convulsions in early infancy." Subtracting these 20 children already dead from the total number, we find that in 84 families after a married life averaging 11.6 years, there were living only 81 children or less than one living child per family.

There is no statistical compilation of similar conditions in the general population which will allow satisfactory comparison of these figures. The nearest approach to this end is the tables of the United States Census in which we find that the average family in the State of Michigan in 1910 consisted of 4.3 individuals. With the two parents subtracted from this figure it leaves a total of 2.3 living children per family of the entire population. We do not know the average length of married life in these families entering into this general statistical compilation, but it would appear quite justifiable to assume that it at least equaled the period of 11.6 years found in our present series. Granting this assumption, we are able to conclude that the number of living children in the average family throughout the State of Michigan is 2.38 times as large as the average number of living children in the families of our series of paretic patients.

It would be desirable to know just when the original syphilitic infection occurred, the position that each pregnancy and miscarriage bore to that time and the relation which the three different types of marriages outlined above bore to this varying interval before marriage. All who try to obtain accurate histories from this type of patients know such information is very unsatisfactory at best, and inasmuch as we are not at this time going deeply into the matter of the character of the living offspring, we have purposely minimized its importance.

Our examinations of the serum of the children in these cases have not as yet been extensive enough to warrant drawing any conclusions. Plaut and Göring found among 100 children of their 54 cases a positive Wassermann reaction in 26 instances. They found in some families children showing a positive reaction where the mother's serum gave a negative reaction, and again, some children with positive and others in the same family with negative reactions. Similar observations can be found in Hauptmann's series and in our own cases. Although only 26 per cent. of Plaut's cases gave serologic evidences of syphilitic infection, 45 per cent. showed some defect in their physical conformation or signs of a psychopathic constitution, although as a rule they were intellectually well gifted. In many cases these defects are degenerative physical states no different from similar conditions found in children in whom other toxic agents, such as alcohol, have impaired the normal development of the germ plasm. The negative reaction in such cases, Hauptmann, drawing on bacteriologic distinctions, would explain as due to the condition being purely an intoxication, and assumes such children not to be infected with the treponeme. Such children do not show signs of definite specific disease. Theoretically they should not later develop juvenile paresis or even non-nervous specific disease. Whether they can later develop a primary sore is highly interesting. It is assumed that the Wassermann reaction and other of the four signs long precede the development of paresis. Since juvenile paresis and other evidences of lues hereditaria may not appear until the second and third or even fourth decade, it will require longer observation to prove whether this assumption holds true. Since this problem is very closely allied to the influence of constitutional syphilis on the descendants, we will leave it with the statement that competent observers have found about one-fourth of the living children of paretics to be actually infected with syphilis and approximately another fourth to show definite evidences of degenerative influences in their physical or mental constitution.

The number of cases in our series is admittedly small, but since they are taken as they came over a space of three years, and since they agree very closely with similar deductions made from larger numbers, one is justified in believing that they present a truthful picture.

With so much said, the next pertinent question is, What are you going to do about it? We have already commented on the pitifully small number of the infected mates of our paretics who had any knowledge of their disease. The same condition obtains, to be sure, in a large majority of all paretics. Treatment as ordinarily carried out with pills, even in those cases that are recognized, is the harmful factor. Some competent syphilologists have said that in those cases in which they have had control of the treatment of their syphilitics from the beginning, they have never seen tabes or paresis develop. Recent years have shown an unusually high percentage of early involvement of the central nervous system even in the secondary stages, particularly from the work of Ravaut and of Wile. Correct diagnosis of the syphilitic condition should be made and careful, persevering treatment given, with attention to the newer findings in the cerebrospinal fluid. If these pathologic changes do not permanently disappear under acceptable mercurial and salvarsan treatment, direct intraspinal introduction of

salvarsanized serum in some form, with proper Wassermann control before permitting marriage and then similar careful observation, serum examinations and, if necessary, treatment in the case of the wives and children of all syphilitics, should theoretically offer some relief.

CONCLUSIONS

The large number of 38.18 per cent. of conjugal mates of paretic patients is shown to be infected with syphilis. In most of these mates the condition courses unrecognized as lues latens.

A pitifully small number of them ever receive treatment.

The proportion of these infected mates who later develop paresis appears to be higher than those who receive their infection from non-metasyphilitic sources.

The number of completely sterile marriages in syphilitic families in which one individual later develops paresis is abnormally high, constituting 32.5 per cent. This percentage is higher when it is the female mate that later becomes a paretic.

The number of marriages in which repeated pregnancies result only in abortions is likewise abnormally high, constituting in our series 12.7 per cent.

Of our series of eighty-six marriages 45.3 per cent. were absolutely childless.

Among 167 pregnancies there were forty-two abortions, miscarriages and stillbirths.

Among 123 living-born children twenty had already died before their eleventh year.

The number of living children per family is abnormally small.

A large number, in some investigations reaching as high as 25 per cent., of these children are actively syphilitic.

An equally large additional number show signs of degenerative physical conformation and psychopathic tendencies without a positive Wassermann reaction.

Much of all this is preventable.

State Psychopathic Hospital.

A REVIEW OF THE PRINCIPAL METHODS USED TO STANDARDIZE BACTERINS (BACTERIAL VACCINES)

WITH SPECIAL REFERENCE TO THE USE OF THE
HEMOCYTOMETER *

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The use of bacterins in the treatment and prevention of disease has steadily increased since their introduction by Wright in 1902. "Vaccine therapy," so called, is now used by nearly every practitioner of human or veterinary medicine. Much more attention, however, has been paid to the extension of the application of this branch of medicine than to the study of its underlying principles and the perfection of its technic. One of the first requisites is an accurate and reliable method of estimating the number of dead bacteria inoculated. There are a few workers who will doubtless claim that it is quite immaterial whether a few million bacteria, more or less, are injected, and furthermore, that no method is absolutely accurate. These criticisms are not con-

firmed by careful scientific work. Those who are familiar with the use of bacterins know that often their injection is followed by unexpected results due to the toxicity of the bacterin, the idiosyncrasy of the patient or too large a dose, further, that while it is true that probably no method gives the exact number of bacteria, certain procedures lead to more accurate results than others.

During the last few years, I have prepared many bacterins for human and veterinary use. In their preparation the great inaccuracy of the methods of standardization has been thoroughly impressed on me. The more reliable methods were used and finally one was adopted, that is, the hemocytometer, which seemed to give by far the most reliable results. This method has been employed for the past three years.

On the publication of the article by Glynn, Powell, Rees, and Cox,¹ in which they give the results of very careful comparisons of the different methods, these results were compared with those obtained by me and found to agree in practically every instance. The technic which gave the most reliable results with them was the one used by me with several minor modifications. So far as known this method is not widely used in this country and it has been thought advisable to review the different methods of bacterin standardization with the relative advantages and disadvantages of each.

I. WRIGHT'S METHOD

Wright² first described his method in 1902. In its original and simplest form it consists in mixing measured and usually equal volumes of bacterial suspension and normal human blood with a small capillary pipet on a glass slide. From this mixture films are made on glass slides, stained, and a number of fields are examined microscopically. The number of bacteria and corpuscles are counted in each field and the ratio of the bacteria and red corpuscles found. The average number of red corpuscles is known to be 5,000,000 per cubic millimeter in a normal individual. Therefore, if there are two bacteria to each corpuscle in the different fields then the bacterial suspension is assumed to contain 10,000,000,000 per cubic centimeter. Allen³ modified this method by using two or three volumes of a 2 per cent. sodium citrate solution as a further diluent for the bacterial suspension and blood. This was employed in order to prevent coagulation of the blood during the mixing process. He also used 5,500,000 as the average number of corpuscles per cubic millimeter. Nearly all of the stock bacterins now on the market are standardized by this latter modified method.

The criticisms of Wright's methods are many, among them we quote from Glynn, *et al.*:

Wright's standard of comparison, namely, 5,000,000 red-blood corpuscles per cubic millimeter, is not altogether accurate; thus Cabot⁴ states: "At the level of the sea and in adult life the normal number of red cells per cubic millimeter is about 5,000,000 for men and 4,500,000 for women. This is frequently exceeded in vigorous healthy persons; 6,000,000 is by no means rare among healthy young men, and higher figures are seen occasionally."

1. Glynn, E.; Powell, A. A.; Rees, and Cox, G. L.: Observations upon the Standardization of Bacterial Vaccines by the Wright, the Hemocytometer and the Plate Culture Methods, *Jour. Path. and Bacteriol.*, 1913, xviii, 379.

2. Wright, A. E.: On Some New Procedures for the Examination of the Blood and of Bacterial Cultures, *Lancet*, London, 1902, ii, 11.

3. Allen: Vaccine Therapy and Opsonic Treatment, Ed. 4, Philadelphia, P. Blakiston's Son & Co., 1912.

4. Cabot, R.: Clinical Examination of the Blood, Ed. 5, New York, William Wood & Co., 1904.

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