

2. Oligospermia or azoöpermia may occur without obvious cause.

3. The production or ejaculation of spermatozoa may be intermittent for reasons as yet unknown.

4. A single examination of the semen is insufficient. At least two, perhaps three or four specimens, each taken after a considerable period of sexual continence, must be seen, before a prognosis can safely be given.

5. Marriage may continue to be sterile even with the finding of active spermatozoa in the husband, and a normal genital tract in the wife. Experience has shown us all that for some reason best known to herself, Nature delays procreation often for years.

6. It is noteworthy that in no case of male sterility regardless of the cause, is masculinity in the least impaired. This is to be explained by the fact that even though the spermatogenetic function of the testicles is inhibited, the internal secretion continues in full force.

#### STATISTICAL NOTES ON A SERIES OF 6000 WASSERMANN TESTS FOR SYPHILIS PERFORMED IN THE HARVARD NEUROPATHOLOGICAL TESTING LABORATORY, 1913.

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THE value of the present series of Wassermann tests is enhanced by the interest which the laboratory officers have taken in the clinical diagnoses of the cases tested and by the courtesy with which the clinicians submitting specimens have given important data.

Since the Harvard Neuropathological Testing Laboratory is not a commercial institution and has performed much charity work in addition to its other work (paid for virtually at cost), a spirit of cooperation has grown up which has helped in the solution of many problems of individual diagnoses.

The Testing Laboratory, of which the last year of work is here summarized, was, I believe, the first to be established in Massachusetts to make use of the ingenious discovery of Wassermann, and, since it has been in continuous action under its various heads, (1) Professor F. P. Gay (now of the University of California) who established the standards since maintained, (2) the late Dr. Emma W. D. Mooers, who brought to the work a great interest in both the technique and the clinical significance of the tests, derived from her work with Plaut in Munich, (3) Professor W. P. Lucas, (now of

the University of California) who turned his attention to numerous clinical problems, not only of children, but in general, and (4) their successors (see below), the Laboratory has had a very varied experience and has sustained most of the shocks which the numerous pitfalls of the test provide. The result has been an increasing confidence in the tests as made, and fewer and fewer complaints of lack of congruence between the results of the tests and clinical findings, especially when these latter are reviewed.

My own interest in the tests was in the first instance psychiatric and neuropathological, and I believe that the laboratory would hardly have survived, had it not been for the interest in these tests taken by the state institutions for the insane. The work published heretofore, based on this laboratory's tests, has been largely psychiatric, as the following titles illustrate:

Lucas, W. P. The Wassermann Reaction in its Application to Medicine. *BOSTON MEDICAL AND SURGICAL JOURNAL*, clxix, 1913, No. 4, pp. 116-121, July 24, 1913.

Paine, H. L. Results of the Wassermann Test in Two Hundred Consecutive Admissions to the Danvers State Hospital. *BOSTON MEDICAL AND SURGICAL JOURNAL*, clxviii, No. 14, pp. 501-503, April 3, 1913.

Morse, M. E. Correlations of Cerebrospinal Fluid Examinations with Psychiatric Diagnoses: A study of 140 Cases. *BOSTON MEDICAL AND SURGICAL JOURNAL* (in press) Worcester State Hospital Contributions No. 20, 1914.1.

I believe the value of the Wassermann reaction will always remain even more critical in the neurological arts than in those of the syphilographer who has so many more clinical data immediately accessible to him. It is to be hoped that some state agency will take over the entire task of Wassermann-testing on a scale commensurate with its value. If so, it is the experience of the present Laboratory, which has been virtually supported by cooperation of several of the larger hospitals for the insane, that psychiatric and neurological cases will absorb the lion's share of attention, although from time to time many series of sera will be submitted by physicians having special therapeutic tests (salvarsan, neosalvarsan) in hand.

There are Wassermann tests and Wassermann tests! In comparing our results with others, we often find tests described as Wassermann tests which are somewhat essentially different therefrom. Needless to say some workers omit various precautions and controls which are essential to reliable work. To make clear the policy of this laboratory, which has been managed in common by the writer, by Professor H. M. Adler, and by Dr. Annie E. Taft under the Department of Diseases of the Nervous System of the Harvard Medical School, I propose to set down (without description) the steps, precautions, and controls used in the series of tests, which are now being executed by Dr. W. A. Hinton.

(A.) *Materials:*

- (1) washed sheep corpuscles, 5% suspension, 5 c.c. to tube.
- (2) antishoop amboceptor, 2 units.
- (3) complement (guinea-pig serum, 10%), 2 units.
- (4) patient's serum inactivated at 56°, 0.1 c.c. with each antigen.
- (5) antigens (a) human heart reinforced with cholesterol (0.1 c.c.)
  - (b) human heart reinforced with cholesterol (0.05 c.c.)
  - (c) alcoholic extract of syphilitic fetal liver (0.25 c.c.)

(B.) *Controls:*

- (1) antishoop amboceptor unit tested daily.
- (2) Complement unit tested daily.
- (3) 0.2 c.c. inactivated patient's serum used in addition to test with 0.1 c.c.
- (4) each specimen tested with three antigens.
- (5) control to exclude the (rare) occurrence of natural hemolytic power in complement.
- (6) same hemolytic power in amboceptor.
- (7) same, salt solution.
- (8) control sera six in number (strong positive, slight positive, negative; each antigen doubled in amount.)

(C.) *Remarks:*

- (1) period for fixing complements, 1 hour.
- (2) doubtful cases repeated with double amount of serum and appropriate controls.
- (3) cerebrospinal fluids used in five times the amount of sera.
- (4) attention may be called to the "slight positive control (v. B., 8 above) which prevents many slightly positive cases from being overlooked on a given day.
- (5) attention is especially called to the use of *three* antigens (This is not usual in many American laboratories), excluding technical error, perhaps indicating slight quantitative changes in a given patient's reaction, and excluding certain false positions.
- (6) supervision and control, (highly important where so important a diagnosis as syphilis is being rendered) are obtained by the direct contact of (a) secretary, (b) technician, (c) laboratory boy, in addition to medical expert diagnostician (during 1913, Dr. W. A. Hinton) under general direction of Dr. Annie E. Taft, Custodian, Neuro-pathological Laboratory, Department of Neuropathology.

## GENERAL STATISTICS.

Total Wassermann tests, 1913 . . . . .	6139
Blood sera . . . . .	5282
Cerebrospinal Fluids . . . . .	857
Total tests repeated . . . . .	228
Blood sera . . . . .	186
Cerebrospinal Fluid . . . . .	42
Total individual blood sera . . . . .	5096
Cerebrospinal Fluids . . . . .	815

An important question is always raised by tests which have to be classed as doubtful by result. These doubtful tests occupy a large share of attention and inspire requests for new specimens. I was surprised to learn the low percentage of such doubtful results when all the tests were summed up. The percentage (2.4%) is somewhat like what might be expected of a biological test. The fact that there are more such doubtful tests in sera than in cerebrospinal fluids signifies doubtless the larger number of confusing substances in the blood as well as other technical difficulties. The figures follow:

Total blood sera . . . . .	5282
"Doubtful" results (4%) . . . . .	202
Total cerebrospinal fluid . . . . .	857
"Doubtful" results (2%) . . . . .	19

It may be properly inquired what is the result of repeated tests in connection with these "doubtful" cases. The following table demonstrates cases in which a change in result was registered involving "doubtful" tests in sera:

"Doubtful" became negative . . . . .	17
Negatives became "doubtful" . . . . .	4
"Doubtfuls" became positive . . . . .	2
Positives became "doubtful" . . . . .	5

This table would incline one on statistical grounds to prefer to call "doubtfuls" negative. Suppose we look at a group of non-"doubtful" cases to see how they turn with repeated tests.

Negative cases become positive . . . . .	15
(of which 3 had also been positive also before the initial negative and one had been "doubtful.")	

Positive cases become negative . . . . .	33
(of which three became positive again later and one had been negative before the initial positive.)	

If we leave out the anomalous examples of one dissimilar test in a triad, we arrive at

Negative cases become positive . . . . .	11
Positive cases become negative . . . . .	29
Comparing this with data above:	
"Doubtfuls" become positive . . . . .	2
"Doubtfuls" become negative . . . . .	17

we see that, statistically at least, "doubtfuls" resemble negatives more than positives. This also confirms the qualitative suspicions of many workers. Nevertheless it must be pointed out that this general trend toward negative is partly due to natural immunizing or spirochaete-destroying factors at work in the individual and partly to therapeutic efforts.

The figures with respect to "doubtfuls" and changes of reaction in cerebrospinal fluid are as yet too small to make tabulation profitable.

If we exclude "doubtful" tests and limit consideration to the positive and negative tests alone, we have the following denominators:

Blood sera . . . . .	5096
Cerebrospinal fluids . . . . .	815

Concerning these blood sera in our laboratory it is not at all certain that they represent the community fairly; indeed it is highly probable that they are a picked class of sera derived from patients in whom syphilis was seriously suspected.

Positive blood sera (23%)	1161
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And it is certain that the cerebrospinal fluids are a still more highly selected class

Positive cerebrospinal fluids (33%)	267
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It is an interesting speculation to consider how far this 33% of positive cerebrospinal fluids represents the chance that an "organic" disease of the nervous system has of being syphilitic.

From the community's point of view it is clear that the percentage of outstanding syphilis is not so high as alarmists have sometimes thought. It is probable from such data as these that the percentage of syphilis in the community is far below 23%.

A curious fact is illustrated by the figures from the Worcester State Asylum, a transfer institution for chronic patients. This institution harbors syphilitics (3 in 103) not quite to the extent of 3% (2.9%). Here is a community from which the luetic organic cases have largely never been sent. The chances are that this percentage is lower than that of the community at large.

On the other hand, if we consider the girls of the Massachusetts Reformatory for Women, we find the extraordinary percentage of 44, that is, 112 positives in 254 cases.

Some facts concerning the Psychopathic Hospital data were worked up more particularly for the benefit of the White Slave Commission, and the following paragraphs are reproduced from a report to Dr. Walter E. Fernald, Chairman of that commission.

"I. The general average for the whole state of cases thought by the hospital physicians to be due to syphilis is 5.49% for the three years

1910-1912, and 6.28% for the year 1912 itself. This figure can be safely stated to be far too low because the average percentage of general paresis during the same three years (1910-1912) was 8.43% (for 1912, 8.65%). This latter figure is also beyond question too small since a certain proportion of coarse brain lesions of epileptic insanities and of imbecilities are undoubtedly due to syphilis, although they are classified outside the syphilis group in the figure presented by the Board of Insanity from which I make the above extracts.

"II. The best information available to me as to the general percentage of syphilis to be found in mental cases is that afforded by our experience at the Psychopathic Hospital covering 1671 separate random tests on different persons. 264 of these 1671 persons were determined to show syphilis so far as the Wassermann reaction carried out under the precepts of the original method can be trusted. I consider that there is no better set of data available for Massachusetts. This will be found to work out a percentage of 14.7% for our Psychopathic Hospital intake. I think our Psychopathic Hospital intake may be regarded as more representative of the general population than any admissions in previous years to other insane hospitals. An indication of this for example, is the fact that we discharged 250 persons during the last year alone as "Not Insane" although every one of these cases presented some kind of mental problem. It is rather curious that the percentages which we here work out, viz., approximately 15%, correspond to the idea prevalent I believe among dermatologists as to the general percentage in the community which they deduced from cases resorting to skin clinics.

"III. In a series of random "organic" cases 321 in number, I found cerebrospinal fluids positive in 118 cases or about 37%. You will of course wonder how I determine cases to be "organic." My general policy has been to have examination of the blood serum made in all cases having severe mental symptoms. If the serum is positive, I proceed as a rule to an examination of the cerebrospinal fluid by the Wassermann and other methods, believing it to be of importance to determine whether a case is one of General Paresis or of some other form of cerebrospinal syphilis. In case the serum is negative but the patient shows signs of disorder in the projection system, or as we say, looks "organic," then I proceed to a cerebrospinal fluid examination, despite the negativity of the serum. It is from these two groups that my random organic series of 321 cases is made up."

Following is not intended as a complete account of the Wassermann technique but only to record the particular materials and main steps used in this laboratory in 1913, so that it may be known exactly what we mean by "Wassermann" tests.

## SUMMARY.

1. On account of the varying standards and criteria which have held or will in future hold in the matter of Wassermann tests for syphilis, it has been thought wise to summarize the materials, controls, and special precautions used in the Harvard Testing Laboratory.

2. General doubts are often raised as to the reliability of Wassermann's test on account of the "great number" of "doubtful" reactions; this "great number" resolves in our large series to 4% of the blood sera and 2% of the cerebrospinal fluids.

3. On statistical grounds we find the "doubtfuls" resolve much more frequently into "negatives" than into "positives."

4. 23% of all sera examined were positive, and since the cases are in many instances picked as likely to be positive, this percentage is doubtless much higher than the community's total percentage.

5. 33% of all cerebrospinal fluids examined were positive. The principle of selection of these cases was such (positive serum or symptoms of "organic" nervous or mental disease) that the result is of practical value, stateable as follows: The chances of a syphilitic origin for a case of "organic-looking" nervous or mental disease are not more than one in three.

6. The Massachusetts Reformatory for Women yields 44%, a partial index of the infected nature, though not necessarily of the infectivity, of prostitutes and other delinquent women.

7. The Danvers State Hospital (for the insane) yields between 19 and 22% positive sera in its routine intake of cases from Essex County.

8. The Worcester Asylum, a transfer institution (to which are transferred chiefly *non-paretic* cases), yield less than 3% positive. If this percentage should be maintained in future work, one might infer that, from the group of persons in the community with insane tendencies and infected by syphilis, cases are drained off into the frankly parietic group, in such wise that a population of asylum *transfers* will be likely to show a *low* syphilis index. But this conclusion can be only tentative on account of many other issues.

9. The Psychopathic Hospital index (15%) is perhaps somewhat closer to the general community index than the others just mentioned on account of the large number of cases "not insane" that are tested, but it is evident that 15% would be too high an index to assign to the syphilis of the general population.

10. Aside from its capacity to solve problems of individual diagnosis, the Wassermann method is obviously of such value to the community that a community Wassermann service might well be undertaken by a state agency such as the Board of Insanity or the Board of Health.

## CYSTITIS—AN INCOMPLETE DIAGNOSIS.\*

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THE number of proprietary and semi-proprietary remedies for "cystitis," "catarrh of the bladder," "inflammation of the bladder" which are advertised to the profession and to the public is equalled only by those for "indigestion," "dyspepsia," and "rheumatism." This can mean but one of two things, either the profession fails to make a complete diagnosis followed by curative treatment or else the condition leading to the symptoms is either extremely resistant to treatment or incurable.

People in pain and with physical handicaps go to some doctor at some stage in their disease as a rule. If they are then told what they already know and given some treatment from which they obtain but little relief, they try other men or clinics until they are relieved or they class all medical help as futile and turn to proprietary medicines or extra-medical delusions. It has been said before that the list of remedies for a given disease was a fair indication of our uncertainty in the treatment of the disease, and it may be said with equal truth that the number of proprietaries and semi-proprietaries advertised as cures corresponds somewhat with the failure of the general profession to promptly and permanently relieve the pains and other handicaps of people who are not well.

Some things are still beyond prompt or permanent relief, but more human ills are controllable now than ever before and a large part of our gain has come from perfecting our diagnosis. A completed diagnosis based on findings apart from the patients' statements and not inconsistent with the statements leads to a choice between a small number of therapeutic measures—often to a choice between mechanical treatment or none.

An incomplete diagnosis leads nowhere, but leaves both doctor and patient in a fog of uncertain and changing therapeutics until nature kills or cures.

To return to the title of this paper, the diagnosis of cystitis is made on one or more of the following symptoms and signs.

1. Frequency of urinating.
2. Pain in connection with urinating.
3. Pus, red corpuscles, and shreds in the urine.
4. Tenderness of bladder to pressure.
5. Appearance through cystoscope.

Three of these can be studied apart from the patient's statements.

1. Frequency in urination depends on the distensible capacity of the bladder quite as much as on the rate of kidney excretion. In urinary tuberculosis and some stages of urethral ob-

\* Read before the Somerville Medical Society, May 7, 1914.