

them, but I have met some who had been thus treated without any good resulting.

A large and important class may be called the syphilitic group. In this I place the general paralytic, the ataxic, and some para-syphilitic cases. Directly one is consulted by a middle-aged man for vague and uncertain nervous symptoms nowadays one not only asks if the patient has had any venereal disease, but one is not satisfied unless there is negative Wassermann reaction. I have met with several cases in which the history of syphilis was comparatively recent, and therefore the symptoms were treated as possibly removable, and these have done well. Very many cases of early general paralysis have occurred in the army, and the life of anxiety was just the one likely to start the more active symptoms. It is hardly necessary to say that no man with a clear history of nerve degenerative symptoms related to syphilis should be allowed to enter the army, but there are some of the patients whose symptoms are recent, and who after treatment may be allowed to enter the service.

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*The Compluetic Reaction (Wassermann) in Amentia: an Original Study of 100 Cases.*<sup>(1)</sup> By HAROLD FREIZE STEPHENS, M.R.C.S., L.R.C.P.

ALL the experiments for this investigation were carried out by me in the Bacteriological Laboratories at Guy's Hospital, and my thanks are due to Dr. Eyre, the Director, for having placed every facility at my disposal, and to Dr. Ryffel, the Chemical Pathologist, for his advice and assistance. I am also indebted to my Board of Management and to my Medical Superintendent, Dr. Caldecott, for their courteous permission to undertake this investigation in the case of patients resident under their care at the Royal Earlswood Institution, at Redhill, in Surrey.

A foreword is, perhaps, necessary in explanation of the title I have assumed for this paper, a title for which I beg your kind indulgence. By the "compluetic reaction" I mean the "Wassermann reaction." It ought never to have been called the "Wassermann reaction," for, as everybody should know,

and as our President has placed on record in his communication to the late Royal Commission on Venereal Diseases on this subject, not Wassermann, but the Belgian Professor Bordet was the first to "discover," to study and "establish" the essential principle of the test. As England to-day is at war for justice and fair play, it is only meet and right and, perhaps, our bounden duty that the Belgian should come to his own again! The proper name for the "Wassermann reaction" is the "Bordet-Gengou phenomenon in syphilis," but, although this is rightly its proper name, such a designation, however romantic the association of the things discovered with the names of their discoverers may be, is nevertheless not quite correct. For it is but a mere truism to maintain that natural processes exist and are not made; they always were and will be, in spite of their discoverers; and it is with the things themselves that science is concerned. The more correct phraseology, therefore, would be "the complement-fixation or deviation phenomenon in syphilis." For this rather cumbrous expression I have taken the liberty to make the simpler term the "compluetic reaction," coining the word "compluetic" from the two words "complement" and "luetic," and as such I beg leave to submit it to your courteous and generous consideration.

This paper is divided into two sections :

- (A) A summary of the technique employed in the experiments.
- (B) An analysis of the results obtained thereby.

#### (A) THE TECHNIQUE EMPLOYED.

The technique employed was that in current use at Guy's Hospital. It may be briefly summarised under the following three heads :

- (1) The reagents used in the test.
- (2) The preliminary preparations for the test.
- (3) The test.

#### *The Reagents.*

As is well known, the reagents required for this test are :

- (1) Antigen.
- (2) Reagin (blood serum or cerebro-spinal fluid).

- (3) Complement.
- (4) Hæmolysin.
- (5) Erythrocytes.
- (6) Saline solution.

The materials used in my experiments were as follows :

(1) For *antigen* a 1 in 10 saline solution of an alcoholic extract of human congenital syphilitic liver.

(2) For *reagin* only the blood sera were used. The sera were obtained from the peripheral blood of the patients. They were used undiluted.

(3) For *complement* a 1 in 10 saline dilution of fresh guinea-pig's serum.

(4) For *hæmolysin* a 1 in 20 saline dilution of the hæmolytic sera of rabbits immunised against human red blood corpuscles.

(5) For *erythrocytes* a saline suspension of fresh human red blood corpuscles, obtained always independently of the bloods to be examined, and diluted 100 times (1 in 100).

(6) A 0.9 per cent. saline solution, freshly made and sterile, was used for all dilutions in the test.

It may not be out of place here to note the following facts concerning the reagents :

(1) *Antigen*.—The strength and properties of a good antigen tend to remain constant. Its characteristics must, however, be redetermined and confirmed from time to time by testing the antigen against known syphilitic reagins. This practically consists in the performance of a test in which all the factors are known except the strength and properties of the antigen. The antigen used in my experiments had been used in the routine performance of many thousands of tests, in all of which it was proved to be neither hæmolytic nor anticomplementary, but truly antigenic in its properties.

(2) *Reagins*.—These were always tested against and compared with known "positive" and "negative" sera as "controls."

(3) *Complement*.—As is now fully recognised, the complement is the most important factor in this reaction, but unfortunately it tends to degenerate very easily. The strength of the complement therefore varies, and must be determined daily immediately before the tests are performed. The strength of the complement is best expressed in the terms of what is known as the minimal complementary dose (the

“M.C.D.”), the daily determination of which is one of the preliminary preparations for the test and will be described later. By means of the M.C.D. a scale of gradations can be obtained whereby what may be a purely qualitative test can be converted into a quantitative reaction. At Guy's Hospital both the qualitative and quantitative methods are in daily use. In every one of my cases, however, two minimal doses of complement were always employed, for by experiment I found that both from the qualitative and quantitative standpoints two minimal complementary doses were sufficient for each of my cases, a greater dosage resulting in the presence of an excess of complement, and, therefore, in the production of error. It is necessary to emphasise the amount of complement employed, as results with this test from the quantitative standpoint are only of value when expressed in terms of the M.C.D., from which it follows that, in my series of cases, even the definitely positive reactions are quantitatively very feeble.

(4) *Hæmolysin*.—The hæmolysin tends to remain constant. The strength of the hæmolysin is also best expressed in terms of what is known as the minimal hæmolytic dose (the “M.H.D.”). The M.H.D. for any given brand of hæmolysin therefore tends to remain constant. The M.H.D., however, should be confirmed from time to time in the manner of the method described later.

#### *The Preliminary Preparations.*

The compluetic test, it will be remembered, is an attempt to ascertain whether a given serum in the presence of syphilitic antigen is able to “fix” complement, that is, to de-ionise it, to rob it of its oxydases, and so to render it inactive. The test is not only a means of ascertaining whether a given serum can “fix” complement, but also how much complement it can so render inactive. The test is therefore both qualitative and quantitative. It is a means of ascertaining not only the *fixation ability*, but also the *fixation capacity* of the tested serum.

Now in order to be able to “fix” complement, the given serum must contain syphilitic reagin—*i.e.*, the syphilitic “antibody.” Therefore the test becomes limited to ascertaining whether a given serum contains syphilitic reagin and if so

the quantity of syphilitic reagin it contains. Thus, in my series of cases, I was able to determine that a certain proportion of the sera examined did contain syphilitic reagin, and that the reagin so contained was invariably in small quantities, being always enough to utilise two minimal doses of complement. To effect these determinations the method employed, as will be remembered, is :

(1) To free a given serum of any complement it will naturally contain—*i.e.*, to “inactivate” it.

(2) To add to a measured quantity of inactivated serum a measured quantity of antigen.

(3) To add to this mixture a measured quantity of fresh complement.

(4) A certain specified time is then allowed for these three substances to interact, and at the end of this time—*i.e.*, usually after one hour in the air incubator at 37° C.—the presence of “free” complement is looked for by means of a delicate “colour indicator.” If “free” complement is then found to be present, the serum does not contain syphilitic reagin, and is said to be “negative.” If, however, “free” complement is found to be absent (the added complement being “fixed”), the serum does contain syphilitic reagin, and is said to be “positive”; the degree of its “positivity” being determined by the quantity of added complement that has been “fixed.”

Such is the test. Its practical value depends upon the delicacy of the “colour indicator,” whose efficiency, in its turn, is dependent upon its ability to detect the smallest traces of complement. Therefore it will be seen the preliminary preparations for the test are three in number :

(1) The preparation of the reagin.

(2) The preparation of a delicate colour indicator.

(3) The determination of the smallest amount of complement that can be detected by means of this “colour indicator.”

These preliminaries will now be considered.

*The Preparation of the Reagin.*—In all my cases each specimen of blood for examination was taken from the peripheral circulation, about 5 c.c. of blood being withdrawn with aseptic precautions from the median basilic vein. Each specimen was allowed to clot, and the serum collected. The serum was then divided into two equal portions. One portion was heated by being placed in a hot-water bath at 56° C. for half an hour (*i.e.*,

“inactivation by heat”). The other portion was kept at room temperature for four days before being tested (*i.e.*, “inactivation at room temperature.”) The reason why each serum was divided into two portions, one being heated, the other not, is as follows: Every syphilitic serum is supposed to contain two substances, complement and syphilitic reagin (antibody); “inactivation by heat” eliminates the complement, leaving reagin for the purposes of the test. But many workers at Guy’s Hospital in a long experience of many thousands of cases have found that heat also tends to damage these syphilitic reagins, some more intensely than others, so that a possibly positive serum may declare itself as negative. It has therefore been the practice at Guy’s Hospital in all cases of doubtful reactions to re-test the serum, unheated, and after keeping for four days at room temperature. In my 100 cases, however, I have methodically pursued the double purpose, systematically dividing each serum into two equal portions, and regularly examining these after “inactivation by heat,” and after “inactivation at room temperature.” The outcome of this procedure has been that the results differed in fourteen of my 100 cases. Of these fourteen cases, four were negative heated, weakly positive unheated; ten were negative heated, definitely positive unheated. The results in all the other cases agreed both with the heated and the unheated portions of the sera. By testing the unheated sera in every case I was able to confirm the results obtained with the heated sera, and *vice versa*. Against the method of “inactivation at room temperature” it might be urged that normal sera tend to become positive on keeping, because of the factor of hydrolysis, which will naturally set free fatty and amino acids in the serum, an excess of such molecules having a decided anticomplementary action. But such a tendency would have been present in every one of the 100 sera examined, and yet in only fourteen cases did the results differ. Moreover, all these fourteen cases did not occur on the same day, under the same conditions of atmospheric pressure and temperature; and a further examination of the records showed that one occurred in a set of four, two occurred in a set of five, two occurred in a set of eight, four occurred in a set of eight, one occurred in a set of twelve, one occurred in a set of thirteen, and three occurred in a set of fourteen. So that the factor of hydrolysis does not seem wholly to explain why

under the same conditions more positive results should not have occurred.

*The Preparation of the "Colour Indicator."*—In the preparation of a delicate "colour indicator" for this test, advantage is taken of the well-known fact that in the presence of complement and hæmolysin red blood corpuscles are destroyed, the hæmoglobin escaping to colour the medium; but that in the absence of complement no hæmolysis occurs. On the basis of this fact a mixture of hæmolysin and erythrocytes is prepared. By this mixture the hæmolysin combines with the red cells and is said to render them "sensitive" to complement. The mixture is therefore called "a suspension of sensitised erythrocytes." In the actual making of the "sensitised erythrocytes" two stages occur: (1) The determination of the minimal dose of hæmolysin that with complement will produce in a definite period complete hæmolysis of the smallest convenient quantity of red cells; (2) the mixing of the components in these proportions.

*The Determination of the Minimal Hæmolytic Dose.*—The reagents required for this determination are: (1) A 1 in 20 saline dilution of hæmolysin; (2) a 1 in 100 saline suspension of fresh human erythrocytes; (3) a 1 in 10 saline dilution of fresh guinea-pig's serum; (4) saline solution (0.9 per cent.). The method is as follows: A series of small test-tubes are taken, marked A, B, C, etc. Into each of these are placed diminishing quantities of the diluted hæmolytic serum, thus: 0.10 c.c., 0.08 c.c., 0.06 c.c., etc. Then 0.50 c.c., the smallest convenient quantity, of the erythrocyte suspension is added to each tube, followed by the addition of an excess of complement, usually four minimal doses. Each tube is then filled with saline to a total volume of 1 c.c. The following example is appended as an illustration:

	Test-tube A.	Test-tube B.	Test-tube C.	Test-tube D.
Hæmolysin (1 in 20) ...	0.10 c.c.	0.08 c.c.	0.06 c.c.	0.04 c.c.
Erythrocyte suspension (1 in 100) . . .	0.50 "	0.50 "	0.50 "	0.50 "
Complement (1 in 10), four doses . . .	0.20 "	0.20 "	0.20 "	0.20 "
Saline solution (0.9 per cent.) . . .	0.20 "	0.22 "	0.24 "	0.26 "
	<u>1.00 c.c.</u>	<u>1.00 c.c.</u>	<u>1.00 c.c.</u>	<u>1.00 c.c.</u>

The tubes are placed in the air incubator for one hour at 37° C. The minimal hæmolytic dose (the "M.H.D.") is the minimal amount of hæmolysin giving complete hæmolysis of 0.5 c.c. of erythrocytes after incubation in the air incubator

for one hour at 37° C. In the above example the minimal amount of hæmolysin producing complete hæmolysis was found to be 0.08 c.c. (in test-tube B). Therefore the M.H.D. for the 1 in 20 saline dilution used was taken as 0.08 c.c.

*The Preparation of "Sensitised Erythrocytes."*—In the preparation of the "sensitised erythrocytes" used in my test, four minimal doses of the 1 in 20 saline dilution of hæmolysin were taken for each 0.5 c.c. of the 1 in 100 suspension of red cells. These proportions were used because in actual practice an excess of hæmolysin is found to be necessary on account of the varying numbers of red cells in each 0.5 c.c. of suspension, the varying capacity of the cells for combining with hæmolysin, etc. Thus if the M.H.D. were 0.08 c.c., the recipe for the preparation would be written as follows :

B	Erythrocyte suspension (1 in 100)	. . . . .	:	:	0.5 c.c.
	Hæmolysin (1 in 20), four times 0.08 c.c. (the M.H.D.)		:	:	0.3 "
					0.8 c.c.

Mix as much as is required in these proportions, and let the suspension stand at room temperature for fifteen minutes at least. For each dose of "sensitised erythrocytes" 0.8 c.c. of the above mixture is used.

*The Determination of the Minimal Complementary Dose.*—The "colour indicator" having been prepared as above, the next step is to find the smallest quantity of complement that will produce complete hæmolysis in a definite time of the estimated dose of "sensitised erythrocytes." The reagents required for this determination are: (1) A 1 in 10 saline dilution of the complement to be tested; (2) "sensitised erythrocytes"; (3) saline solution (0.9 per cent.). The method is as follows: A series of small test-tubes is taken, marked A, B, C, etc. Into each of these tubes diminishing quantities of the diluted complement are placed, thus: 0.09 c.c., 0.07 c.c., 0.05 c.c., etc., and then to each tube the dose of "sensitised erythrocytes" already estimated is added. Each tube is then filled with saline to a total volume of 1 c.c. The following example is appended as an illustration :

	Test-tube A.	Test-tube B.	Test-tube C.	Test-tube D.
Complement (1 in 10)	0.09 c.c.	0.07 c.c.	0.05 c.c.	0.03 "
"Sensitised erythrocyte"	0.80 "	0.80 "	0.80 "	0.80 "
Saline solution (0.9 per cent.)	0.11 "	0.13 "	0.15 "	0.17 "
	1.00 c.c.	1.00 c.c.	1.00 c.c.	1.00 c.c.



The tubes are placed in the air incubator for one hour at 37° C. The minimal complementary dose (the "M.C.D.") is the minimal amount of complement giving complete hæmolysis of 0.80 c.c. of "sensitised erythrocytes" after incubation in the air incubator for one hour at 37° C. In the above example the minimal amount of complement producing complete hæmolysis was found to be 0.05 c.c. (in test-tube C). Therefore the M.C.D. for the 1 in 10 saline dilution used was taken as 0.05 c.c.

#### *The Test.*

The test itself may now be described. As already stated, all the quantities of the reagents used in my reactions are the same as those employed at Guy's Hospital in the routine examination of cases with the exception of the complementary doses, which did not vary in my tests, two minimal complementary doses being always used, as these were found by experiment to be both necessary and sufficient for each of my cases. The method employed was as follows:

*The Patient's Serum.*—(1) For each serum two small test-tubes marked A and B were taken. (2) In each of these tubes was placed 0.1 c.c. of the patient's serum. (3) To each tube was then added two minimal doses of complement. (4) Into tube A, but not into tube B, was finally measured 0.1 c.c. of the antigen. Tube B was thus used as a "control" against tube A, for as tube B contained no antigen, one was able to note whether the patient's serum was naturally anticomplementary or not. (5) The volume of fluid in each tube was then brought to the same level by the addition, when necessary, of saline. Both tubes were then carefully shaken so that the contents of each were well mixed, the completest asepsis being observed in all the measurements.

*The "Control" Sera.*—Each patient's serum was always tested against and compared with two known sera, a syphilitic and a non-syphilitic serum, used as "controls." For each of these "control" sera two tubes were also prepared similar in every way to the two tubes containing the patient's serum.

For the testing of each patient's serum, then, six tubes were prepared—two for the patient's serum, two for the syphilitic serum, and two for the non-syphilitic serum. When these were ready they were placed in the air incubator for one hour at 37° C. The estimated dose of "sensitised erythrocytes" was then added to each tube, and all the tubes were replaced in the incubator at 37° C. for another sixty minutes. They were carefully examined at regular intervals, and the results finally recorded at the end of the hour.

A note may here be added with reference to the use of "control" sera in my series of cases. All my tests were performed at the same time and on the same days on which the routine Wassermann work of Guy's Hospital was undertaken. I worked side by side with the hospital serologists, and we used the same materials for our reagents. Therefore, in addition to my own "controls," I had the advantage of the hospital's series of tubes (*i.e.*, of those containing two minimal doses of complement) to check my reactions, and to confirm the accuracy of my results.

*Schema of the Test.*

	Unknown serum.		Syphilitic serum.		Non-syphilitic serum.	
	Tube A.	Tube B.	Tube A.	Tube B.	Tube A.	Tube B.
Reagin (undiluted)	0·10 c.c.	0·10 c.c.	0·10 c.c.	0·10 c.c.	0·10 c.c.	0·10 c.c.
Antigen (1 in 10)	0·10 c.c.	—	0·10 c.c.	—	0·10 c.c.	—
Complement (1 in 10), two doses	0·10 c.c.	0·10 c.c.	0·10 c.c.	0·10 c.c.	0·10 c.c.	0·10 c.c.
Saline solution (0·9 per cent.)	—	0·10 c.c.	—	0·10 c.c.	—	0·10 c.c.
The tubes are placed in the air incubator for one hour at 37° C.						
"Sensitised erythro- cytes"	0·80 c.c.	0·80 c.c.	0·80 c.c.	0·80 c.c.	0·80 c.c.	0·80 c.c.
	1·10 c.c.	1·10 c.c.	1·10 c.c.	1·10 c.c.	1·10 c.c.	1·10 c.c.

The tubes are replaced in the air incubator for thirty minutes at 37° C. They are then examined every ten minutes, and the results finally recorded at the end of another thirty minutes—*i.e.*, one hour after the addition of the "sensitised erythrocytes."

*Interpretation of the Results.*—The results in my series of cases were recorded as follows: (1) When no hæmolysis occurred the reaction was said to be "definitely positive." (2) When partial hæmolysis occurred the reaction was termed "weakly positive." (3) When complete hæmolysis occurred the reaction was called "negative."

*Summary of the Technique.*

In their preliminary report on the methods of carrying out this test, the Sub-Committee of the Section of Pathology of this Society defined what is generally understood to be "the

original Wassermann test" by its essential principles as follows:

"(1) The ingredients of the test (red corpuscles, 'antigen,' hæmolytic amboceptor, complement) are derived from *different* sources.

"(2) The serum to be tested is inactivated before use. An independent 'hæmolytic system' is employed, consisting of a suspension of red corpuscles, an inactivated hæmolytic serum, and a fresh normal serum containing complement. The hæmolytic values of the antiserum and complement are determined by a separate preliminary experiment.

"On general scientific grounds the Sub-Committee is unanimously of the opinion that, since the test is a quantitative reaction, the titre of the reagents ought, within practicable limits, to be accurately known."

From the above definition of the "original test" the technique herein described will be seen to differ, but it is sincerely hoped that the results so obtained will not therefore be very greatly impaired. Three points in connection with this technique must be briefly recalled, inasmuch as these points are directly concerned with the interpretation of the results obtained.

First, the serum. Each serum to be tested was always inactivated before use. Each serum was divided into two equal portions; one was subjected to "inactivation by heat," the other to "inactivation at room temperature." Each portion was then tested in exactly the same way and the results carefully compared, when it was found that in only fourteen cases did the results differ. In all other cases the results agreed both with the heated and the unheated portions of the serum. Thus by testing the unheated sera, in every case the results obtained with the heated sera were confirmed, and *vice versa*. As some observers would maintain that more correct results are obtained by "heating" the sera, and others by testing the sera "unheated," it was hoped to avoid the fallacies arising from both sources by systematically examining each serum in this way.

Secondly, the amount of complement used in each test. In every one of these determinations two minimal doses of complement were always employed, for by experiment it was found that two minimal complementary doses were necessary and

sufficient for each of these cases, a greater dosage resulting in the presence of an excess of complement, and therefore in the production of error.

Thirdly, the "controls." Three sets of "controls" were used. (1) Each serum, whether heated or unheated, was always tested with and without "antigen," to determine whether it was naturally anticomplementary, and so to avoid if possible an excess of "positive" results. (2) Each serum, whether heated or unheated, was always tested against and compared with two known sera, a syphilitic and a non-syphilitic, under exactly the same conditions. (3) All these tests were performed at the same time and on the same days and with the same materials as the routine Wassermann work of Guy's Hospital. Therefore, in addition to the above "controls," there was always the hospital's series of tubes (*i.e.*, of those containing two minimal doses of complement) by which to check the reactions, and to confirm the accuracy of the results.

#### (B) THE RESULTS OBTAINED.

In this section of the paper the results obtained by the above experiments are analysed as follows :

(1) *Total percentage.*—Of the 100 cases examined, forty-two gave positive reactions. None of the fifty-eight "negative" cases, after a thorough clinical examination, revealed any of the characteristic lesions of syphilis, so that this group of forty-two "positive" cases would seem to include all the patients with syphilitic amentia whose blood serums were examined. Of the forty-two "positive" cases, twenty-two were "definitely positive," and twenty were "weakly positive." To many workers on this subject these figures would appear to yield a large percentage of "positive" results. The following facts, determined by a closer analysis, must therefore be stated :

(i) That when the sera were *inactivated by heat*, the reaction was found to be present in twenty-eight cases, being—

"Definitely positive" in	.	.	22	—	10	=	12	cases
"Weakly positive" in	.	.	20	—	4	=	16	cases
"Negative" in	.	.	58	+	14	=	72	cases

(ii) That when the sera were *inactivated at room temperature*, the reaction was found to be present in forty-two cases, being—

"Definitely positive" in . . . 12 + 10 = 22 cases  
 "Weakly positive" in . . . 16 + 4 = 20 cases  
 "Negative" in . . . 72 - 14 = 58 cases

From which it will be seen—

(a) That in eighty-six cases the results *agreed* both with the "heated" and the "unheated" sera, being—

"Definitely positive" in . . . 12 cases  
 "Weakly positive" in . . . 16 cases  
 "Negative" in . . . 58 cases

(b) That in fourteen cases the results *differed* both with the "heated" and the "unheated" sera, so that—

In ten cases the reaction was "negative" heated, "definitely positive" unheated.

In four cases the reaction was "negative" heated, "weakly positive" unheated.

Now those workers who would maintain that heat tends to damage certain syphilitic reagins, some more intensely than others, so that a possibly positive serum may declare itself as negative, would regard the fourteen *differing* sera as yielding more correct results when tested after "inactivation at room temperature," and would therefore consider that a "definitely positive" reaction was obtained in twenty-two cases, a "weakly positive" reaction in twenty, and a "negative" reaction in fifty-eight, their total percentage of "positive" results being 42.

On the other hand, those observers who would urge that normal sera tend to become positive on keeping because of the factor of hydrolysis producing strong anticomplementary bodies, would consider the fourteen *differing* sera as yielding more correct results when tested after "inactivation by heat," and would therefore record them as "negative," or at best as being "doubtfully positive," and their total percentage would be 28 (16 "weakly positive," and 12 "definitely positive.")

Finally, there would be some observers who would hold that because only two minimal doses of complement were used in each of these determinations, only those cases in which the results were noted as "definitely positive"—*i.e.*, those cases in which absolutely no hæmolysis was observed—should be regarded as "truly positive." These would therefore discard the "weakly positive" and "doubtfully positive" cases as being "negative," and their total percentage of "positive" results would be 12, with which I personally am in agreement.

However the above figures may be interpreted, the point I wish to emphasise is this: that the results have been very carefully and accurately recorded; the "controls" have been numerous, strict, and efficient; and that under the conditions of the technique employed, as herein described, these results may be considered to be correct.

(2) *Sex*.—All the cases examined were males.

(3) *Age*.—The youngest of these patients was *æt.* 12, the five oldest were *æt.* 51, 52, 52, 73 and 78 respectively. There were fifty-seven patients between 12 and 21 years of age inclusive, twenty-one between 22 and 30 years inclusive, and seventeen between 30 and 50 years inclusive, so that the majority of the patients were boys. This fact is of some importance, for the compluetic reaction tends to vary with age, as shown in the following tables:

TABLE A.—Showing the Incidence of the Reaction at Different Age-periods.

Age-periods.	Number of cases examined.	Number of positive reactions at each age-period.	Percentage of positive reactions to cases examined at each age-period.	Percentage of positive reactions at each age-period to total number of positive reactions.
Under 12 years . . .	—	—	—	—
12 to 15 years inclusive	19	7	36·8	16·67
16 to 21 years inclusive	38 } 57	19 } 26	50·0 } 45·6	45·23 } 61·9
22 to 30 years inclusive	21	8	38·09	19·04
Over 30 years . . .	22	8	36·36	19·04

From this table it will be seen:

(i) That of all the positive reactions obtained twenty-six (or about 62 *per cent.*) occurred in patients between 12 and 21 years of age inclusive; while only eight (19 *per cent.*) occurred in those between 22 and 30 years inclusive, and eight (19 *per cent.*) in those over 30 years.

(ii) That positive reactions occurred in 45 *per cent.* of the patients between 12 and 21 years of age inclusive, in 38 *per cent.* of those between 22 and 30 years inclusive, and in 36 *per cent.* of those over 30 years of age.

Hence it would seem that the incidence of the reaction tended to diminish as the ages of the patients increased. But

a closer study of the cases revealed an interesting modification, which also is indicated in Table A, where it is shown :

(i) That a larger percentage of positive reactions occurred between the ages of 16 and 21 inclusive than at any other period—*viz.*, 45 per cent.

(ii) That 50 per cent. of the patients between the ages of 16 and 21 inclusive gave positive reactions, while about 37 per cent. of those below 16 years, and about 37 per cent. of those above 21 years, gave positive reactions.

From which it appears that the curve of the incidence of the reaction in aments tends to rise from between the ages of 12 to 15, reaching its maximum height between the ages of 16 to 21 and then gradually falling again as the ages increase.

Again, the intensity of the reaction at different age-periods is shown in Tables B and B<sup>1</sup> :

TABLE B.—*Being an Analysis of the Cases giving "Definitely Positive" Reactions.*

Age-periods.	Total number of positive reactions at each age-period.	Number of cases giving "definitely positive" reactions.	Percentage of "definitely positive" reactions to the total number of positive reactions at each age-period.	Percentage of "definitely positive" reactions at each age-period to the total number of "definitely positive" reactions.
Under 12 years . . . .	—	—	—	—
12 to 15 years inclusive	7	6	85·7	27·2
16 to 21 years inclusive	19	11	57·9	47·8
22 to 30 years inclusive	8	3	37·5	13·04
Over 30 years . . . .	8	2	25·0	8·7

TABLE B<sup>1</sup>.—*Being an Analysis of the "Weakly Positive" Cases.*

Age-periods.	Total number of positive reactions at each age-period.	Number of cases giving "weakly positive" reactions.	Percentage of "weakly positive" reactions to the total number of positive reactions at each age-period.	Percentage of "weakly positive" reactions at each age-period to the total number of "weakly positive" reactions.
Under 12 years . . . .	—	—	—	—
12 to 15 years inclusive	7	1	14·2	5·0
16 to 21 years inclusive	19	8	42·0	42·0
22 to 30 years inclusive	8	5	62·5	26·3
Over 30 years . . . .	8	6	75·0	31·5

From these tables it will be seen :

(i) That all the positive reactions, save one, occurring between the ages of 12 and 15 inclusive were "definitely positive," no hæmolysis being detected in any of the cases.

(ii) That the percentage of "definitely positive" reactions diminishes with the increasing ages of the patients.

(iii) That while there is only one "weakly positive" reaction between the ages of 12 and 15 inclusive, the percentage of such reactions increases with the increasing ages of the patients.

(iv) That if a composite graph were drawn illustrative of both these tables it would appear that the curve of the intensity of the reaction is similar to the curve of the incidence.

From this study, then, of the relationship of the incidence and intensity of the compluetic reaction in aments to the age of the patient, it becomes manifest that the reaction tends to be strongest and most frequent in patients between the ages of 16 and 21, and that it appears to be more frequent and stronger in those below 16 than in those above 21 years of age ; but it was not possible to determine exactly how either the incidence or the intensity curves should be drawn, the reason for this failure being shown in Table C. Such curves, however, ought to be realised when a very large number of reliable results have been tabulated and examined.

TABLE C.—*Showing the Number of Cases Examined, and the Number of Cases giving Positive Reactions for each Year of Age from 12 to 25 Years inclusive.*

Age.	C.	+	±	T.
Under 12 years	—	—	—	—
12 years old	2	—	—	—
13 "	2	2	—	2
14 "	9	3	1	4
15 "	6	1	—	1
16 "	7	1	3	4
17 "	8	3	1	4
18 "	6	1	1	2
19 "	7	2	—	2
20 "	4	—	2	2
21 "	6	4	1	5
22 "	2	—	—	—
23 "	6	2	—	2
24 "	1	—	—	—
25 "	2	—	1	1

C. = number of cases examined.

+ = number of cases giving definitely positive reactions.

± = number of cases giving weakly positive reactions.

T. = total number of cases giving positive reactions.



(4) *Social status*.—The fathers of forty-two of the patients were members of the skilled trades and labourers, thirteen patients were the sons of members of the professions, and thirty were born in the mercantile classes. As these cases were chosen spontaneously and more or less haphazard, it is interesting to remark that the parents of the smallest number of these aments are members of the most highly organised occupations, *viz.*, the professions; and it is also of importance to note that precisely those spheres of industry which have shown little or no manifestations of the social spirit contain the parents of the majority of these syphilitics (*vide* Table D).

TABLE D.—*Showing the Social Status of the Patients examined.*

Occupation of father.	Number of patients examined.	Number of patients giving positive reactions.
Skilled trades and labourers . . . . .	42	21
Professions . . . . .	13	4
Mercantile . . . . .	30	14
Dead and unknown . . . . .	15	3

All the 100 patients were born and bred in England (in her cities, towns, and villages) except seven. Of these seven, two were from the Channel Islands, one from the Isle of Wight, one from India, one from Barbadoes, one from Mauritius and one from Buenos Aires. The boy from Buenos Aires and the boy from the Isle of Wight gave "weakly positive" reactions; the sera of the other five were "negative."

(5) *Life-history*.—The compluetic reaction being an index of existing syphilitic infection, and not in the nature of an immunity reaction, the question arises as to whether the infection in this series of cases was an intra- or an extra-uterine one—*i.e.*, whether the syphilis was "congenital" or "acquired."

The fact that the majority of these patients came under institutional discipline and observation at a very early age, and were all of them under due protection when at home or with friends, together with the absence in them of all the physical signs and symptoms of "acquired" syphilis at any period of their lives, tends to dispose of the presence of this type of the disease in any one of these cases, the likelihood of which under the circumstances would be extremely remote. All the forty-two positive cases may therefore be said to be, in varying degrees, the victims of intra-uterine or "congenital" syphilis

But, save for the ophthalmoscopic and otological conditions, which unfortunately were not determined because of the obvious practical difficulties of such inquiries in aments, the most careful examination of the patients themselves failed to reveal the presence of any of the characteristic lesions of "congenital" syphilis in any one of them, a fact which has also been noticed by Dr. Plaut, of Munich, Major Mott, and other observers.<sup>(3)</sup> Nor did a study of the records of the parental and family histories adduce evidence of the disease in any of the parents or their forebears—a fact which is less surprising, for the histories in such cases are notoriously misleading. The compluetic reaction, being the only reliable evidence in forty-two of these cases of their being syphilitic at all, was also the conclusive testimony to the presence of syphilis in either or both their parents.

A note may here be introduced on the appearance of the stigmata of "congenital" syphilis in aments. It will be remembered that "congenital" syphilis is an intra-uterine affection, and it will also be recollected that the children of syphilitic parents need not necessarily be aments. So that apart altogether from the fact that certain central nervous systems are peculiarly prone to attack by this virus, the manifestations of "congenital" syphilis would appear to be dependent upon the time of onset of the infection *in utero*, bearing a direct relation to the structural condition of the developing organism. That the majority of congenital syphilitics bear evidences of epiblastic or mesoblastic infection would seem to show that the foetus is not attacked till late in its development, or, perhaps, that the maternal defences are able to protect it till then. The presence of an earlier neuroblastic infection is manifested by the cases of juvenile general paralysis of the insane, a condition to which any of the preceding cases may succumb, while the earliest embryonic infections would appear to result either in the death of the organism or in arrested development. Thus, consider those cases of "infantilism," free from all obvious syphilitic stigmata, in which Major Mott has seen in both ovary and testis myriad colonies of the *Spirochæta pallida*. Similarly retarded development of the other members of the endocrinic glands may be found to be due to the same cause, and how closely the endocrinic system is associated with the central nervous system is daily becoming more manifest.

Broadly considered, amentia may, perhaps, be interpreted as a symptom-complex of arrested brain development, such retardation being due either to an inherent inability on the part of the brain cells to grow and evolve, or to the effects of some factor inimical to their perfect fulfilment, such a factor being either traumatic, or toxic, or inflammatory in its appearance. In either case the syphilitic virus may be present as cause or coincidence—*e.g.*, the inherent inability of the brain cells to develop may be due to some occult influence of the virus, or the results of its toxicity may be more recent and pronounced. Our knowledge, therefore, of the “stigmata” of congenital syphilis requires some replenishing. How many, for example, of the so-called stigmata of degeneracy are in reality the stigmata of syphilis? We do not know. Those of the latter, so frequently described and portrayed, are mainly somatic in incidence, originating in fully developed structures (*e.g.*, nodes, scars, the syphilitic wig, interstitial keratitis, etc.). What is seriously needed is a more careful study of the germinal developmental stigmata (mainly microscopical in character), and the signs and symptoms with which these are associated, and by which they are rendered more evident to the naked eye—*e.g.*, as in “infantilism,” certain cases of cretinism, perhaps also certain groups of simple aments. In other words, evidences of arrested or deranged and irregular development, if shown to be directly due to the effects of the luetic virus, ought to be regarded as being in themselves “stigmata” of congenital syphilis. Again, what of the bio-chemical stigmata? One of these, surely, is that which has been studied in recent years on such a very extensive scale as “the Wassermann reaction.”

To continue with this analysis, the next point to be determined was whether the syphilitic virus acting alone was responsible for the mental defect in these forty-two congenital cases, or whether it attained that end with the assistance of other factors. An analysis of such factors, based on a consideration of the so-called “causes” of amentia, is given in Table E (see pp. 676 and 677), from which it will be seen :

(i) That in addition to syphilis certain reputed germinal and somatic defects are together present in seventeen cases ; that these germinal defects only are present in seven cases ; and the somatic defects only in eighteen cases.

TABLE E.—Showing the Factors concerned in the *Ætiology of Forty-two Possible Cases of Syphilitic Amentia.*

No. of case.	Germinal defects.												Somatic defects.											
	Neuropathic inheritance.			Alcoholism.			Tuberculosis.			Consanguinity.			Aged parents.			Other factors.			Fœtal.		Natal.		Infantile.	
	Ancestral.	Maternal.	Paternal.	Ancestral.	Maternal.	Paternal.	Ancestral.	Maternal.	Paternal.	Maternal.	Paternal.	Maternal.	Paternal.	Ancestral.	Maternal.	Paternal.	Adverse mental states of the mother.	Adverse physical conditions of the mother.	Other factors.	Firstborn.	Difficult labour, instrumental, &c.	Illness.	Injury.	
1	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
3	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
4	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
5	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
7	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
8	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
9	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
10	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
11	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
12	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
13	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
14	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
15	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
16	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
17	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
18	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
19	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
20	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
21	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
22	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	

(A) The *Ætiological Analysis of the Twenty-two Cases giving "Definitely Positive" Reactions.*



(ii) That in addition to syphilis, fourteen cases have at least one of these reputed defects, fourteen others at least two such defects, and eight have three. One case has as many as six germinal and somatic defects, another has five, and four have each four of such defects. In no case is the syphilitic virus unassociated with at least one of these ætiological factors.

Other points to be noted in Table E are :

(i) Of the forty-two positive cases the neuropathic diathesis occurs in seventeen. (Of the 100 cases examined a neuropathic inheritance was recorded in only forty-four ; so that syphilis was detected in seventeen of the forty-four cases with a neuropathic heredity. Of these seventeen cases the diathesis was recorded in seven in the parental histories only, in six in the family histories only, and in four in both family and parental histories. It appeared in seven cases on the maternal side only, in six on the paternal side only, and in four on both sides. Five of these cases gave family histories of amentia, three of insanity, and two of a "neurotic heredity." Eight of the parents were said to be "neurotic," one is insane, one had a spinal affection and was a cripple, and two died in apoplectic fits.)

(ii) There appears to be no family or parental history of alcohol.

(iii) Tuberculosis is seen to occur in the inheritance of six patients : in the family histories of four, and in the parental histories of three.

(iv) Consanguinity is present in two cases. (In one the parents were first cousins ; in the other the parental grandparents.)

(v) One of the patients, a cretin, has a paternal cousin who is likewise a cretin ; and the mother and sister of another patient, also a cretin, have suffered from exophthalmic goitre. Each of these cases also has a neuropathic inheritance, but, being instances of a metabolic inheritance as well, they are again noted here under a separate heading.

(vi) Adverse mental states of the mother were said to have been present during the foetal development of five cases, and adverse physical conditions of the mother in three. Six others are the children of aged parents.

(vii) Fifteen are firstborn children ; ten of these gave definitely positive reactions, the other five being weakly positive,

It is therefore very probable that a series of abortions may have preceded the birth of most of these patients, although such a history, unfortunately, was not recorded in any case either as positive or negative evidence.

(viii) Difficult and protracted labour with instrumental delivery is recorded in seven cases (four of which were firstborn children).

(ix) One patient was a premature birth, another was a ten months baby, and a third is the fifteenth child in his family, and the second of twins.

(x) Infantile illness is cited in seventeen cases, and infantile head injuries in five.

To what extent must now be considered does the syphilitic virus play its part in producing the mental deficiency in each of these cases? Its exact influence is, of course, difficult to estimate, but from a study of Table E it will be seen:

(A) That the virus is undoubtedly an *auxiliary* and *augmentary* factor in the ætiology of eleven cases—*viz.*, in Nos. 1, 2, 3, 6, 11, 23, 24, 25, 26, 28, 29.

(B) That it probably is the *exciting* or *determinant* factor in six cases—*viz.*, in Nos. 5, 9, 10, 27, 35, 36.

(C) That it appears to be the *essential* factor in twenty-five cases—*viz.*, in Nos. 4, 7, 8, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 30, 31, 32, 33, 34, 37, 38, 39, 40, 41, and 42.

(D) That in no case is it the *only* ætiological factor, for even on analysing Group C it will be seen:

(a) That though in two cases (*viz.*, 18 and 37) the syphilis appears to be wholly responsible for the amentia, it in reality has produced the mental defect by acting upon already degenerated germ plasm. Thus in No. 37 the boy's father was said to have died of phthisis; and No. 18, a Mongolian idiot, was the son of aged parents, being the eleventh child.

(b) In all the other twenty-three cases the syphilis appears to be associated with damaged nervous tissues. Thus No. 38, a Mongolian imbecile, and the second in his family, is said to have come of a healthy stock, being born under normal conditions, but two months previous to his birth his mother was shipwrecked and nearly drowned; while in the remaining twenty-two cases some adverse adventitious factor, occurring either at birth or during infancy, was always present. A study of these adventitious factors reveals the following interesting facts:

(a) Of the fifteen firstborn children giving a positive reaction, eleven are in Group C—*i.e.*, in the series of cases in the ætiology of which syphilis would appear to be the essential factor.

(b) Of the seven positive cases the amental condition of each of which was said to be due to difficult and protracted labour with instrumental delivery, six are seen to be in Group C.

(c) Of the seventeen positive cases in each of which the mental deficiency was attributed to a severe infantile illness, the syphilitic virus would appear to be the essential element in ten.

(d) While the five positive cases, in which infantile head injuries were cited as the cause of amentia, the essential ætiological factor in four would appear to be syphilis.

Obvious deductions, however, are disappointing, and, inasmuch as more than one of the above adverse adventitious factors of birth and infancy occur in many patients in Group C (as is shown in Table E), the obvious deductions should not be drawn, nor could they be accepted as true from the results already stated. Selecting, however, for a decisive examination only those cases in which, in addition to the syphilis, there occurred *one* other adverse adventitious factor of birth or infancy, the following tentative statements may, perhaps, be presented, *vis.*:

(a) That in three cases (19, 20, and 39), though the amentia was said to be due to the strain and stress of primogeniture, the mental deficiency was probably primarily and essentially the result of syphilis and not of the parturition.

(b) That syphilis was probably also the primary and essential factor in the two cases (27 and 22) in each of which the mental deficiency was directly attributed to difficult and protracted labour with instrumental delivery.

(c) That in two cases (40 and 41), perhaps also in three others (16, 17 and 31), where amentia was said to be produced by a severe infantile illness, syphilis and not the suggested illness, was probably the cause of the mental defect. (The illness recorded in the histories of Nos. 31 and 41 was "infantile convulsions"; while in the other three it was due to the onset of "epilepsy," a disease from which they still suffer.)

(d) That in No. 42, in whom the mental defect was said to have appeared from the date of a head injury received in



infancy, the essential cause of his amentia was probably not the injury but the syphilis, which, perhaps, was also the probable ætiological factor in No. 12, another alleged case of infantile traumatic amentia.

In conclusion, then, it should again be noted, and perhaps emphasised, that in none of these forty-two cases giving a positive compluetic reaction did the syphilitic virus acting alone appear to produce the amentia. In every instance it would seem that the virus was associated with and acted upon inherently defective, diseased and degenerated, or damaged nervous tissues. And this, perhaps, is only to be expected, for, as will be recollected, the children of syphilitic parents need not necessarily be aments, although, as is also known, a minority of congenital syphilitics, if untreated or ill-treated, are liable to become the victims of various nervous lesions under mental or physical strain and stress ; and this is especially so—in fact, it may even be said to be only so—in those patients in whom the central nervous system is in the least way defective. Given a healthy nervous system, congenital syphilis, as is proved by common medical experience, will not produce amentia. On the other hand, it is quite possible, and even reasonable, to suppose that given an exceedingly virulent neurotoxic type of syphilis *in utero* the healthiest nervous system would be likely to fall a victim to the virus. Between these two extremes, the various grades of syphilitic amentia may be found.

(6) *Classification*.—Mr. Tredgold, in his book *Mental Deficiency*, maintains that “there are two fundamentally different forms of amentia ; there are also innumerable degrees ; and it is convenient to describe certain distinctive clinical varieties.” The forms of amentia Mr. Tredgold has called primary and secondary ; the degrees are now jumbled together into four groups by Act of Parliament ; the clinical varieties are well known. In the following paragraphs the lines of classification suggested by Mr. Tredgold will be followed with slight modifications :

(a) The forms of amentia : Of the 100 cases serologically examined seventy-six were cases of primary amentia, and twenty-four cases of secondary amentia. Of the forty-two cases giving a positive compluetic reaction thirty-two were cases of primary amentia, ten cases of secondary amentia, so

that of all the cases of primary amentia examined, a little over 42 *per cent.* were positive, and of all the cases of secondary amentia examined, nearly 42 *per cent.* were positive. Moreover, as to the intensity of the reaction in each group, nine of the thirty-two cases of primary amentia gave "definitely positive" reactions, thirteen "weakly positive" reactions, and ten "doubtfully positive" reactions; while three of the cases of secondary amentia gave "definitely positive" reactions, three "weakly positive" reactions, and the remaining four "doubtfully positive" reactions.

(b) The degrees of amentia: By Act of Parliament the "innumerable degrees" of amentia are now legally grouped as four—idiots, imbeciles, feeble-minded, and moral imbeciles. All the 100 patients examined were either idiots or imbeciles. As a matter of fact, seventy of them may be considered to be imbeciles and thirty are idiots. Half of these thirty idiots gave positive reactions, in five the reaction being "definitely positive," in five "weakly positive," and in five "doubtfully positive"; while of the seventy imbeciles, twenty-seven gave a positive reaction, and of these seven were "definitely positive," eleven "weakly positive," and nine "doubtfully positive."

(c) The clinical varieties of amentia: No distinctive clinical type of syphilitic amentia has been described. Of the known clinical varieties the following occurred among the 100 cases examined:

(I) PRIMARY AMENTIA.

(1) Microcephalus . . . . .	<i>Nil.</i>
(2) Mongolianism . . . . .	11 cases.
(3) Simple amentia . . . . .	65 cases.

(IA) PRIMARY AMENTIA WITH COMPLICATIONS.

(1) With paralysis only . . . . .	2 cases.
(One Mongol and one simple primary ament.)	
(2) With convulsions only . . . . .	26 cases.
(All simple primary aments.)	
(3) With paralysis and convulsions . . . . .	<i>Nil.</i>

(II) SECONDARY AMENTIA.

(1) Hydrocephalus . . . . .	3 cases.
(2) Hypertrophicism . . . . .	1 case.
(3) Cretinism . . . . .	4 cases.
(4) Simple amentia . . . . .	16 cases.

## (IIA) SECONDARY AMENTIA WITH COMPLICATIONS.

- (1) With paralysis only . . . . . Nil.  
 (2) With convulsions only . . . . . 10 cases.  
 (One hydrocephalic, one hypertrophic, and eight simple secondary aments.)  
 (3) With paralysis and convulsions . . . . . 5 cases.  
 (One cretin, two hydrocephalic, and two simple secondary aments.)

Each of these varieties will now be considered (*vide* also Table F, p. 686).

(1) *Microcephalus*.—Unfortunately no case was examined.

(2) *Mongolianism*.—Of the eleven cases examined only three were positive. In other words, in over 72 *per cent.* of these cases the sera did not react to the test. Of the three Mongols giving a positive reaction two were doubtfully positive and the other was weakly positive. Brief records of the life-histories of these eleven Mongols are appended :

*The Negative Cases.*

CASE 1.—Idiot, æt. 14. (1) Ancestral history, *nil*. (2) Parental history, *nil*. Father a farm labourer. (3) Personal history: The third of five children; birth normal; infancy and childhood healthy.

CASE 2.—Idiot, æt. 25. (1) *Nil*. (2) *Nil*. Father a labourer. (3) The seventh of seven; fright of shipwreck to mother when three months pregnant; an eight months child; birth normal; infancy and childhood healthy.

CASE 3.—Idiot, æt. 20. (1) *Nil*. (2) Father somewhat dull; father and mother æt. about 35 when patient was born; father a clerk. (3) The second of three; fall of mother at seventh month; birth normal; infancy and childhood healthy.

CASE 4.—Imbecile, æt. 26. (1) *Nil*. (2) Father died of nephritis; mother healthy. (3) The fifth of six; fall of mother just before full term; birth normal; infancy and childhood healthy.

CASE 5.—Imbecile, æt. 20. (1) Paternal grandmother, aunt, and sister epileptic. (2) *Nil*. Father manager of brickfields. (3) The only child; birth normal; infancy and childhood healthy.

CASE 6.—Imbecile, æt. 18. (1) *Nil*. (2) *Nil*. Father an engineer fitter. (3) The fifth of eight; birth normal; infancy and childhood healthy.

CASE 7.—Imbecile, æt. 22. (1) *Nil*. (2) Mother always very delicate; father a policeman. (3) The eighth of nine; birth normal; infancy and childhood healthy; has right internal strabismus.

CASE 8.—Imbecile, æt. 23. (1) *Nil*. (2) *Nil*. Father a bank clerk. (3) The fourth of five; a seven and half months child; birth normal; infancy and childhood moderately healthy.

*The Positive Cases.*

CASE 9.—Imbecile, æt. 21. (1) *Nil*. (2) *Nil*. (3) The second of four; fright of shipwreck and drowning to mother two months before his

birth; birth normal; infancy and childhood healthy; C.R. weakly positive.

CASE 10.—Imbecile, æt. 17. (1) *Nil.* (2) *Nil.* Father a doctor. (3) The firstborn; birth normal; infancy and childhood healthy; C.R. doubtfully positive.

CASE 11.—Imbecile, æt. 27. (1) *Nil.* (2) *Nil.* Father a furniture remover (died from accident). (3) Eleventh of eleven; birth normal; infancy and childhood fairly healthy; C.R. doubtfully positive.

(3) *Hydrocephalus*.—Only three cases were examined, and one of these gave a doubtfully positive reaction. Their life-histories are briefly as follows:

CASE 1.—Imbecile, æt. 15. (1) *Nil.* (2) *Nil.* Father a labourer. (3) The sixth of ten; protracted labour and instrumental delivery; left hemiplegia, Jacksonian epilepsy; C.R. doubtfully positive.

CASE 2.—Imbecile, æt. 27. (1) *Nil.* (2) Mother died of erysipelas; father a doctor. (3) The second of seven; birth normal; infantile convulsions; C.R. negative.

CASE 3.—Imbecile, æt. 40. (1) *Nil.* (2) Father died of phthisis; mother died of "cancer"; father a schoolmaster. (3) The eighth of ten; worry to mother during pregnancy; birth normal; epilepsy when young; has left internal strabismus; C.R. negative.

(4) *Hypertrophicism*.—One case was examined, giving a definitely positive reaction. This boy is æt. 13, and the fourth child in a family of four. When he was born his father was æt. 70, and his mother æt. 40. No consanguinity existed between his parents; no phthisis, alcoholism, or insanity was said to be present in the life-histories. His father died of general peritonitis; his mother is alive and healthy. Instrumental delivery was necessary at his birth, but with the exception of recurrent convulsive attacks from which he at present suffers, he has always been in good health. Mentally he is an imbecile of a cheerful temperament and a happy disposition.

(5) *Cretinism*.—Four cretins were examined, and of these two gave positive reactions, one being definitely positive and the other doubtfully positive.

CASE 1 (giving a definitely positive reaction).—A boy, æt. 16, and the second of a family of six, all of whom are said to be normal. A paternal cousin is a cretin; the mother is said to "neurotic"; otherwise the life-histories are normal. Both his parents are healthy, his father being a fisherman. The mother attributes the patient's condition to the fright she sustained on seeing the cretin cousin for the first time while pregnant with the patient. His birth was normal. He has taken extracts of the thyroid gland since the age of 18 months. He was operated on as a child for cerebral abscess. At the present day he

is a strong, healthy, robust boy. He suffers occasionally from epistaxis, and recently he had two attacks of melæna. Mentally he is imbecile.

CASE 2 (giving a doubtfully positive reaction).—A boy, æt. 16, and the second of a family of three. No defect is recorded as present in his ancestral history. Both his parents are “neurotic,” but physically in good health. His father is a warehouseman. His mother and her eldest child, his sister, have had exophthalmic goitre. The birth of the patient was normal. He has had thyroid from an early age. He is and has always been in good health. Mentally he is imbecile.

CASE 3 (giving a negative reaction).—An idiot, æt. 16, with a history of “neurotic heredity.” His father, a parson, died of “heart disease”; his mother is alive and healthy. He is the only child, and instrumental delivery was necessary at his birth. He has had thyroid from an early age. He is epileptic. He also has a left otorrhœa, a right ptosis, and undescended testes.

CASE 4 (giving a negative reaction).—An imbecile, æt. 22, and the second in a family of five. Recorded in his family history is the fact that a maternal niece is feeble-minded and subject to epilepsy. His father died of “cancer of the kidneys.” His mother is in good health but she says she was unable to speak distinctly till the age of 12. His eldest sister is a cretin. His birth was normal, but his “mother used to think a great deal about a cretin when carrying him.” No infantile injury or other illness is recorded. He has had thyroid from the age of 2, and is to-day robust, strong, and in good health. He is very deaf.

(6) *Simple Amentia*.—In the book aforementioned, Mr. Tredgold writes: “The majority of persons suffering from primary amentia present no special distinguishing features other than the anatomical and physiological anomalies common to aments in general; they may therefore be termed simple aments, and they correspond to the ‘genetous’ group of Ireland.” “This term,” he adds in a note, “is open to the objection that all primary aments may in reality be called ‘genetous.’” In this paper both the “genetous” group of Ireland and the “simple aments” of Mr. Tredgold are called by the more exact name of “simple primary amentia.” It is here suggested that the term “simple amentia” should include a larger number of cases than those concerned in Mr. Tredgold’s definition; that so it should be capable of division into two classes, corresponding to the two forms of amentia, and that these two classes of simple amentia should be termed “simple primary amentia” and “simple secondary amentia” respectively. Mr. Tredgold’s definition, in fact, may be adapted as follows: Persons suffering from simple amentia present no special distinguishing features other than the anatomical and physiological anomalies common to aments in

general; they may be divided into two classes corresponding to the two forms of amentia and may be termed "simple primary aments" and "simple secondary aments" respectively. By simple primary amentia would be understood the "simple amentia" described by Mr. Tredgold, while simple secondary amentia would constitute all those cases of secondary amentia in which the mental defect is due to gross cerebral lesions that are the results of toxic, inflammatory, or vascular causes, but the patients themselves are not distinguished by any of the special characteristics peculiar to the clinical varieties of secondary amentia definitely known and described (*viz.*, hydrocephalus, cretinism, etc.).

TABLE F.—*Showing the Relation of the Reaction to the Clinical Varieties of Amentia Examined.*

Clinical variety.	Number of cases.	Number of "definitely positive" reactions.	Number of "weakly positive" reactions.	Number of "doubtfully positive" reactions.	Number of "negative" reactions.
(A) <i>Primary Amentia</i> —					
(1) Microcephalus	—	—	—	—	—
(2) Mongolianism	11	—	1	2	8 (72 per cent.)
(3) Simple amentia	65	10 (15·3 per cent.)	11 (17 per cent.)	8. (12·3 per cent.)	36 (55·4 per cent.)
(B) <i>Secondary amentia</i> —					
(1) Hydrocephalus	3	—	—	1	2
(2) Hypertrophicism	1	1	—	—	—
(3) Cretinism	4	1	—	1	2
(4) Simple amentia	16	—	5	1	10
(C) <i>Amentia with complications</i> —					
(1) Amentia with paralysis	7	—	—	2	5
(2) Amentia with convulsions	41	5 (12·2 per cent.)	9 (22 per cent.)	7 (17 per cent.)	20 (48·8 per cent.)

Each of these two groups of simple amentia will now be considered.

(a) Simple primary amentia : Of the hundred cases examined sixty-five were cases of simple primary amentia, and of these twenty-nine (or 44·6 *per cent.*) gave positive reactions. Moreover, of the sixty-five cases twenty-seven were cases of amentia with complications, and thirty-eight were uncomplicated cases.

Of the latter fourteen (or 36·8 *per cent.*) gave positive reactions, while of the former fifteen (or 55·6 *per cent.*) gave positive reactions. Again, of the twenty-nine cases giving positive reactions ten gave "definitely positive" reactions, eleven "weakly positive" reactions, and eight "doubtfully positive" reactions. Of all the "definitely positive" reactions 40 *per cent.* were given by the complicated cases, and of all the "weakly positive" reactions 45 *per cent.* were given by the uncomplicated cases.

(*b*) Simple secondary amentia: Sixteen of these cases were examined. Ætiologically, they may be classified as follows: Simple secondary amentia due to—(i) "infantile convulsions," seven cases; (ii) recurrent convulsions in early childhood, three cases; (iii) other illnesses in infancy, four cases; and (iv) head injuries in infancy, two cases. The first two of these groups will be considered in the section dealing with "amentia with convulsions." It may here be recollected that the ætiological group of simple secondary amentia due to "recurrent convulsions in early childhood" was known by the older writers as "eclampsic amentia." To-day Mr. Tredgold calls the same group of cases "epileptic amentia," distinguishing them from "amentia with epilepsy," where the convulsions are a complication and not the cause of the amentia. Both these terms, however, tend to confusion and are therefore not employed in this paper. Of the remaining two ætiological groups of simple secondary amentia, the sera of the four cases due to "other illnesses in infancy" gave negative reactions, the illnesses recorded being "sunstroke," "meningitis," "illness at teething," and "mastoiditis." Both the cases due to head injuries in infancy gave positive reactions, one being doubtfully positive and the other weakly positive. In the ætiological Table E these two cases are shown as Nos. 12 and 42 respectively, and they are very probably cases in which the syphilitic virus and not the alleged injury is the primary and essential cause of the mental defect.

(7) *Amentia with Complications.*—Of the 100 cases examined forty-three were cases of amentia with complications. Of these forty-three cases twenty-one (or 48·8 *per cent.*) gave positive reactions, while of the fifty-seven uncomplicated cases twenty-one (or 36·8 *per cent.*) gave positive reactions; so that of all the positive reactions obtained half were given by the uncomplicated

cases and half by the complicated cases. Again, of the seventy-six cases of primary amentia examined twenty-eight (or 36·8 *per cent.*) were cases with complications, while fifteen of the twenty-four cases of secondary amentia (*i.e.*, 62·5 *per cent.*) were complicated cases. Of all the cases of primary amentia with complications, fifteen (or 53·5 *per cent.*) gave positive reactions, while of the uncomplicated cases of primary amentia seventeen (or 35·4 *per cent.*) gave positive reactions. Of all the cases of secondary amentia with complications six (or 40 *per cent.*) gave positive reactions, while of the uncomplicated cases of secondary amentia four (or 44·5 *per cent.*) gave positive reactions.

The cases of amentia with complications will now be considered under two heads: (*a*) Cases with paralysis; (*b*) cases with convulsions.

(*a*) Amentia with paralysis: The physical condition of seven of the 100 patients was complicated with paralysis, the types of paralysis being as follows: Hemiplegia, three cases; strabismus, three cases; and ptosis, one case. Of these seven cases, two gave doubtfully positive reactions, both being hemiplegias and cases of secondary amentia. One of these two, a hydrocephalic, is also subject to "Jacksonian epilepsy."

(*b*) Amentia with convulsions: At the present day seventeen of the 100 cases examined suffer from recurrent convulsive attacks commonly designated by the convenient group-name of "epilepsy." In addition to these, eleven others have suffered from similar attacks when younger, but are not so affected now; and twelve others are said to have had "infantile convulsions." Moreover, one other case is subject to "Jacksonian epilepsy." In all, then, forty-one of the 100 cases examined have had convulsive attacks at some period of their lives. These cases are analysed in Table G.

From this table it will be seen:

(i) That, excluding the "Jacksonian epileptic," of the forty remaining cases of amentia with convulsions twenty (*i.e.*, 50 *per cent.*) gave positive reactions, five being "definitely positive," nine "weakly positive," and six "doubtfully positive."

(ii) That, excluding also the cases of "infantile convulsions," there are twenty-eight patients who are or have been subject to recurrent convulsive attacks. Of these sixteen (a little over 57 *per cent.*) gave positive reactions, five being "definitely positive," five "weakly positive," and six "doubtfully positive."



(iii) That of the seventeen cases suffering at the present day from recurring convulsive attacks, commonly designated by the group-name of "epilepsy," ten, or nearly 59 *per cent.*, gave positive reactions; and of these positive reactions 30 *per cent.* were "definitely positive."

TABLE G.—*Being an Analysis of the Forty-one Cases of Amentia with Convulsions.*

Clinical variety.	No. of cases.	Number of "definitely positive" reactions.	Number of "weakly positive" reactions.	Number of "doubtfully positive" reactions.	Number of "negative" reactions.
<i>Recurrent convulsions at present day—</i>					
(1) Simple primary aments . . . . .	15	2 (13 per cent.)	4 (27 per cent.)	3 (20 per cent.)	6 (40 per cent.)
(2) Hypertrophic . . . . .	1	1	—	—	—
(3) Cretin (with paralysis) . . . . .	1	—	—	—	1
<i>Recurrent convulsions in childhood—</i>					
(1) Simple primary aments . . . . .	7	2	1	2	2
(2) Hydrocephalic (with paralysis) . . . . .	1	—	—	—	1
(3) Simple secondary aments . . . . .	2	—	—	1	1
(4) Simple secondary aments (with paralysis) . . . . .	1	—	—	—	1
<i>"Infantile convulsions"</i>					
(1) Simple primary aments . . . . .	4	—	1	—	3
(2) Hydrocephalic . . . . .	1	—	—	—	1
(3) Simple secondary aments . . . . .	6	—	3	—	3
(4) Simple secondary aments (with paralysis) . . . . .	1	—	—	—	1
<i>"Jacksonian epilepsy"—</i>					
(1) Hydrocephalic (with paralysis) . . . . .	1	—	—	1	—

Hence it would seem from the above study that of all the patients who have had convulsive attacks at some period of their lives over 50 *per cent.* gave positive reactions; while of those who might have been designated "epileptic" at some period of their lives a little over 57 *per cent.* gave positive reactions; and of those diagnosed as "epileptic" to-day nearly 59 *per cent.* gave positive reactions.

Again, comparing the figures given in Table G with the total number of cases giving positive reactions (*viz.*, forty-two cases), it will be seen that of all the patients giving positive reactions twenty-one (or 50 *per cent.*) have had convulsive

attacks at some period of their lives ; sixteen (or 38 *per cent.*) might have been designated "epileptic" at some period of their lives ; and ten (or nearly 24 *per cent.*) are diagnosed as "epileptic" to-day.

Considering now the non-convulsive cases, it will be remembered that fifty-nine of the 100 cases examined have never had a convulsive attack of any kind at any period of their lives. Of these fifty-nine cases twenty-one gave positive reactions. In other words, half the total number of positive reactions in this series occurred in non-convulsive cases, and the other half in those who have had convulsive attacks at some period of their lives. To be more exact, 50 *per cent.* of the positive reactions occurred in non-"epileptic" cases, and 38 *per cent.* in those cases which might have been designated "epileptic" at some period of their lives. On the other hand, as already noted, a little over 57 *per cent.* of these "epileptic" cases gave positive reactions, while of the non-"epileptic" cases only 35·5 *per cent.* gave positive reactions.

Other facts to be noted are as follows :

(a) Seventy-six cases of primary amentia were examined, and of these twenty-six were cases with convulsions. Of the convulsive cases, fifteen (or 57·7 *per cent.*) gave positive reactions, while of the fifty non-convulsive cases seventeen (or 34 *per cent.*) gave positive reactions.

(b) Fifteen of the twenty-four cases of secondary amentia were cases with convulsions. Of these convulsive cases six (or 40 *per cent.*) gave positive reactions, while of the non-convulsive cases four (or 44·5 *per cent.*) gave positive reactions. Moreover, of the fifteen convulsive cases ten were cases with convulsions only, and of these five (or 50 *per cent.*) gave positive reactions.

(c) Eighty-one cases of simple amentia were examined, and of these thirty-six were cases with convulsions. Of the convulsive cases nineteen (or 52·7 *per cent.*) gave positive reactions, while of the forty-five non-convulsive cases sixteen (or 35·5 *per cent.*) gave positive reactions. Moreover, thirty-four of these cases were cases with convulsions only, and nineteen (or 55·8 *per cent.*) gave positive reactions.

Again, of the thirty-six cases of simple amentia with convulsions, twenty-six were cases of primary amentia and ten of secondary amentia. Of the twenty-six cases of simple primary

amentia with convulsions, fifteen (or 57·6 *per cent.*) gave positive reactions, while of the non-convulsive cases of this type fourteen (or 35·8 *per cent.*) gave positive reactions. Of the ten cases of simple secondary amentia with convulsions, four (or 40 *per cent.*) gave positive reactions; of the eight cases of this type with convulsions only, four (or 50 *per cent.*) gave positive reactions; while of the non-convulsive cases two (or 33·3 *per cent.*) gave positive reactions.

The last point to be investigated was the relation of the intensity of the "epilepsy" and the frequency of the convulsive attacks to the incidence and intensity of the reaction. Unfortunately, no such relations were obtained. Three of the "negative" cases, for instance, were the severest cases of "epilepsy" examined; while of the "positive" cases the most severe and the mildest gave "definitely positive" reactions, the serum of the second worst was only "weakly positive" and so on. One slight feature of this series of cases, however, should be noted. It was found that the convulsive attacks in the "positive" cases tend to be far more frequent during the night and the early hours of the morning than they are during the day, while in the "negative" cases they are most frequent during the day. The intensity of the convulsive attacks in each instance appears to be characterised also in the same way. This feature of the "positive" cases, therefore, tends to bring them into line with other syphilitic conditions—*e.g.*, the syphilitic headache, which is said to be most intense towards the early hours of the morning.

#### RECAPITULATION.

The main points of this paper may be recapitulated as follows:

(1) *The Incidence of the Complementic Reaction in the Cases of Amentia Examined.*—The blood sera of 100 aments were examined, and a "positive" reaction was found to be present in forty-two; but only twelve of these are to be regarded as "truly positive."

(2) *The Intensity of the Reaction in the Cases of Amentia Examined.*

(i) Sera were tested heated and unheated. Sera in which no hæmolysis occurred were recorded as "definitely positive"

those in which partial hæmolysis occurred as "weakly positive." Sera in which the results differed when heated and unheated were recorded as "doubtfully positive." Of the forty-two sera giving a positive reaction in twelve the reaction was found to be "definitely positive," in sixteen "weakly positive," and in fourteen "doubtfully positive"; but only the twelve "definitely positive" reactions are to be regarded as "truly positive."

(ii) Quantitatively, even the "definitely positive" reactions are to be considered as feeble reactions, for the syphilitic reagin present in each of these cases was invariably found to be in small quantities, being always enough to utilise two minimal doses of complement.

(3) *The Relation of the Presence of the Reaction to the Sex of the Patients Examined.*—This was not determined, as all the aments examined were males.

(4) *The Relation of the Presence of the Reaction to the Age of the Patients Examined.*—The reaction was found to vary with age. As a rule, it tended to diminish in incidence and intensity as the ages of the patients increased. It appeared, however, to be strongest and most frequent in patients between 16 and 21 years of age; and it tended to be more frequent and stronger in those below 16 than in those above 21 years of age. In considering the total percentage of the positive results obtained, it should be remembered that the majority of the patients examined were boys, 38 per cent. being between 16 and 21, and 57 per cent. under 21 years of age.

(5) *The Relation of the Reaction to the Forms of Amentia Examined.*—The reaction was obtained in a little over 42 per cent. of the cases of primary amentia, and in nearly 42 per cent. of the cases of secondary amentia. It tended to be a little stronger in the latter group of cases.

(6) *The Relation of the Reaction to the Degrees of Amentia Examined.*—Only idiots and imbeciles were examined. The reaction appeared to be more frequent and stronger in the idiots than in the imbeciles; thus, 50 per cent. of the idiots examined gave a positive reaction, and in 16.6 per cent. the reaction was found to be "definitely positive," whereas it was present in 38.5 per cent. of the imbeciles, being "definitely positive" in 10 per cent.

(7) *The Relation of the Reaction to the Clinical Varieties of Amentia Examined.*

(i) In over 72 *per cent.* of Mongols the serum did not react to the test. Of the eleven cases examined, a positive reaction was obtained in three, being "weakly positive" in one and "doubtfully positive" in the other two.

(ii) One of three cases of hydrocephalus gave a "doubtfully positive" reaction.

(iii) Only one case of hypertrophicism was examined, and this was found to be "definitely positive."

(iv) A positive reaction was obtained in two of four cretins, being "definitely positive" in one, and "doubtfully positive" in the other.

(v) Eighty-one cases of simple amentia were examined, and the reaction was found to be "definitely positive" in ten, "weakly positive" in sixteen, and "doubtfully positive" in nine. Excluding the "doubtfully positive" cases the reaction was found to be present in 32 *per cent.* of simple aments. It appeared to be more frequent in the cases of simple primary amentia than in the cases of simple secondary amentia.

(vi) Of the seven cases of amentia with paralysis, two, both hemiplegias, gave "doubtfully positive" reactions.

(vii) Excluding the "doubtfully positive" cases, the reaction was present in 41·2 *per cent.* of patients suffering at the present day from recurring convulsive attacks, commonly designated by the group-name of "epilepsy"; in 35·7 *per cent.* of those diagnosed as "epileptic" at some period of their lives; and in 23·7 *per cent.* of non-"epileptic" cases. It should also be noted that of the simple primary aments with recurrent convulsions to-day, a "definitely positive" reaction was obtained in only 13 *per cent.*

(8) *The Role of Syphilis in the Aetiology of the Cases of Amentia Examined.*—Three points are to be noted:

(i) That as the compluetic reaction is an index of existing syphilis, all the positive cases are to be regarded as weak syphilitic infections.

(ii) That these weak infections were intra-uterine or "congenital" in origin.

(iii) That the syphilitic virus did not appear to be wholly responsible for the amentia in each of these cases, but seemed rather to have been associated with and to have acted upon inherently defective, diseased and degenerated, or damaged tissues.

In conclusion, I should like to state how very grateful I am to Sir George Savage for his kindly interest in and generous appreciation of this my work, whereby it was submitted to the authoritative criticism of Major Mott, who, though he regretted that the technique employed was not in strict conformity with that of the "original" test, yet agreed the results obtained were of sufficient value to be placed before this meeting.

## APPENDIX.

Showing some of the results published.

Names of observers.	Number of cases examined.	Number of "positive" results obtained.	Percentage of "positive" results obtained.
<i>In France.</i>			
Raviart, Breton, &c. (1)	246	76	30.8
<i>In Denmark.</i>			
(a) Lippmann (2)	78	7	8.9
(b) <i>Idem</i>	(?)	(?)	13.2
<i>In Germany.</i>			
Kellner, Clemenz, &c. (3)	216	8	3.7
Dean (4)	330	51	15.4
Thomsen, Boas, &c. (5)	2,061	31	1.5
Kröber (6)	262	56	21.3
<i>In America.</i>			
Atwood (7)	204	30	14.6
W. C. Stoner and E. L. Keiser (8)	1,050	83	7.9
Dawson (9)	—	—	4.0
(a) Stevens (10)	21	2	9.5
(b) <i>Idem</i>	18	6	33.3
<i>In England.</i>			
Muirhead (11)	5	—	—
Schölberg and Goodall (12)	46	15	32.6
Chislett (13)	22	11	50.0
Gordon (14)	400	66	16.5
Fraser and Watson (15)	205	123	60.0
(a) Rees Thomas (16)	163	8	4.9
(b) <i>Idem</i>	—	—	10.0
Robertson and Findlay (17)	15	(?) 9	59.0
F. E. Batten (18)	2	—	—
(a) Mott (19)	257	21	8.1
(b) <i>Idem</i>	200	24	12.0
H. F. Stephens	100	12	12.0

## REFERENCES.

- (1) Raviart, Breton, Petit, Gayet et Cannac.—*Rév. de Méd.*, Par., 1909, xxviii, p. 840.
- (2) Lippmann.—*Münch. med. Wochenschr.*, 1909, lvi, p. 2417.
- (3) Kellner, Clemenz, Brückner und Rautenburg.—*Deutsch. med. Wochenschr.*, Leipz. u. Berl., 1909, p. 1827.
- (4) Dean.—*Proc. Roy. Soc. Med.*, 1910, iii (Neurol. Sect.), p. 117.
- (5) Thomsen, Boas, Hort, und Leschly.—*Berl. klin. Wochenschr.*, 11, xlviii, p. 891.

- (6) Kröber.—*Med. Klin.*, Wien, 1911, vii, p. 1239.  
 (7) Atwood.—*Journ. Amer. Med. Assoc.*, Chicago, lv, p. 464.  
 (8) Stoner, W. C., and Keiser, E. L.—*Cleveland Med. Journ.*, 1912, x, p. 251.  
 (9) Dawson.—*Journ. of Psycho-Asthenics*, Faribault, Minnesota, December, 1912.  
 (10) Stevens.—(a) *Journ. Amer. Med. Assoc.*, 1915, lxiv, p. 1636; (b) *Jour. Amer. Med. Assoc.*, 1916, lxvi, p. 1373.  
 (11) Muirhead.—*Journ. of Ment. Sci.*, 1910, lvi, p. 651.  
 (12) Schölberg and Goodall.—*Ibid.*, 1911, lvii, p. 218.  
 (13) Chislett.—*Ibid.*, 1911, lvii, p. 499.  
 (14) Gordon.—*Lancet*, 1913, ii, p. 861.  
 (15) Fraser and Watson.—*Journ. of Ment. Sci.*, 1913, lix, p. 640.  
 (16) Rees Thomas.—(a) *Report of the Commissioners of Lunacy*, 1912, p. 110; (b) *Lancet*, 1914, i, p. 1001.  
 (17) Robertson and Findlay.—*Glasgow Med. Journ.*, 1914, ii, p. 241.  
 (18) Batten, F. E.—*Quart. Journ. of Med.*, July, 1914, vii, p. 444.  
 (19) Mott.—(a) *Final Report of the Royal Commission on Venereal Diseases*, (Cd. 8189, 1916), Appendices, p. 144; (b) *Proc. Roy. Soc. Med.*, 1916, ix (Sect. of Psychiatry), p. 64.

(<sup>1</sup>) A paper read before the Royal Society of Medicine, and reprinted from its *Proceedings*, 1916, vol. ix (Section of Psychiatry), pp. 27-63.—(<sup>2</sup>) *Vide* the Appendices to the Reports of the Royal Commission on Venereal Diseases, printed separately in (Cd. 7475, 1914) and (Cd. 8190, 1916).

## DISCUSSION.

Dr. PERCY SMITH: Before the Wassermann test was discovered the percentage of definite syphilitic cases in mental defectives (idiots and imbeciles) appeared to be only 2 or 3 per cent., and the enormous difference in the percentages now shown by various observers raises doubt as to the real proportion of syphilitic cases. It is interesting that in the case of "mongol" idiots the percentage of syphilitics appears to be low, these cases being commonly the youngest child of a large family when the mother is approaching the limit of reproductive function.

Dr. SHUTTLEWORTH: In reference to the statistics of syphilis and mental defect quoted by Dr. Percy Smith, these were published by Dr. Fletcher Beach and myself in Hack Tuke's *Dictionary of Psychological Medicine* so long ago as 1892. They were based upon clinical signs and family histories of 2,380 cases investigated at the Darenth and Royal Albert Asylums, and gave a very low estimate (under 2 per cent.) of the influence of inherited syphilis as a factor of idiocy, etc. The late Dr. Langdon-Down also stated that in his large experience of idiots at Earlswood, as well as from pathological investigations as Physician to the London Hospital, he was of opinion that not more than 2 per cent. were the subjects of congenital syphilis. The *Spirochæta pallida* was, however, not discovered till 1905, and the earlier statistics rested solely on personal stigmata and family history. Subsequently the Wassermann reaction came into vogue as a test, and very varying reports have been issued by successive observers. In the new edition (just published) of *Mentally Deficient Children*, there appears a table of percentages obtained by fourteen different observers, varying from 1.5 to 60, in which positive reactions to the Wassermann test have been recorded in the blood of congenital cases of mental defect. Dr. Stephens apparently found such reaction in 42 per cent. of his 100 cases at Earlswood. Unfortunately I was prevented from arriving in time to hear the early part of the paper, in which presumably Dr. Stephens has described the technique he has adopted. But the discrepancies noted lead to the suspicion that the methods used by the various observers cannot

have been uniform, and consequently the results must be to some extent discounted. The inquiry is a most important one, and I trust that Dr. Stephens will utilise the material at Earlswood to the full. I am especially interested in the comparison made by Dr. Stephens as to reaction in certain characteristic types. The mongolian type, for instance, has shown comparatively little "compluetic" reaction, and this accords with clinical experience that such cases are "exhaustion products" rather than of toxic origin, though in exceptional cases a syphilitic taint may give rise to maternal exhaustion. I have always suspected that certain hydrocephalic cases are of syphilitic origin, and that is a point on which the compluetic reaction will shed scientific elucidation.

Sir GEORGE H. SAVAGE: I regret the smallness of the meeting, for I think the paper by Dr. Stephens one of the most important which have been read at the Section. It will be fully appreciated when it is in print. A very great change has taken place in the opinion of doctors in relationship to syphilis as a possible or partial cause of mental deficiency. Recently a paper has been read at the Medico-Psychological Society on the influence of toxins in producing mental deficiency. We all allow that syphilis is the most dangerous toxin to the nervous system, and we are prepared to recognise it as a cause of amentia. The former authorities on idiocy, such as Langdon-Down and Ireland, did not recognise it as a factor. The great difference between the percentage of positive Wassermann reactions met with at Earlswood from similar observations in Germany makes one feel, with our President, that the technique should be revised in some way so as to bring it into line with that of the Germans. It is again interesting to note the number of patients with a positive reaction yet with no external stigmata pointing to inherited syphilis. Recently I saw a case of a father who had had syphilis. He had had two children, one of whom died of epilepsy and the other is a very well-marked mental defective, yet without external signs of inherited disease. The paper is suggestive and gives evidence of good work in a field much neglected in England.

The PRESIDENT: I congratulate Dr. Stephens upon his paper, which is a valuable contribution to knowledge at the present time. I wish that it had appeared before the Report of the Royal Commission had been published. The high percentage obtained by Dr. Stephens may be due to several causes. It is necessary first of all to separate cause from coincidence; a positive Wassermann reaction of the blood, the cerebro-spinal fluid not having been examined, does not necessarily prove that the idiocy was due to syphilis. In support of this statement, I may mention that Sir John Collie has shown that 9·2 *per cent.* of males apparently healthy applying for employment in the various occupations connected with the administration of the L.C.C.—for example, tramway, fire brigade, etc.—gave a positive Wassermann reaction. The sera of these men were tested in the pathological laboratory of the L.C.C. under my direction, and the original technique (Wassermann's) was employed. I have tested the bloods from 200 cases of mental defectives, and have found a positive reaction in 12 *per cent.* I wish that Dr. Stephens had employed the original Wassermann technique, for it was laid down by the Royal Commission, strengthened by a report of a Committee of the Pathological Section of this Society, that short cuts were undesirable, and that it would be better if the original technique were employed in all investigations. I would accept the 12 *per cent.* of marked positive reactions of Dr. Stephens, for that about corresponded with the results obtained by Dean and others. I think the remainder of the cases which gave a partial or a weak reaction should be reinvestigated by the (approved) method of technique I have alluded to. I presume he considers that these positive cases were due to congenital syphilis, and not acquired. I am therefore surprised to learn that the larger number of positive cases occurred in adolescent patients. Plaut's observations on the children of general paralytics rather showed that the reaction tended to disappear with age. Dr. Stephens remarked that few cases showed any signs of syphilis on the body. Dr. Plaut only found one case out of twenty infants with a well-marked positive reaction showing any eruption on the body. Infantilism, imperfect development, or arrest of development of the reproductive organs, is very common in idiots and low-grade imbeciles; this may be due to syphilitic infection of the organ. I have found the spirochaetes in the testes of a foetus. The family history showed a number of pregnancies resulting in defective children,



and children born dead or dying in early infancy. The mother, however, was an imbecile; the dead children and abortions came after the living, so that probably the mental deficiency had nothing to do with congenital syphilis. Indeed, the history tended to show that the mother was syphilised after having given birth to living children, including the mental defective. The serological test in such a case would have been most valuable. I should like to ask Dr. Stephens whether he has made a comparative analysis of the family histories of the positive and negative cases, especially in regard to the result of pregnancies in the mothers. When I visited Darenth I found idiots of whom it was said there were no signs of syphilis, yet examination of the fundi showed choroido-retinitis. The reason why more mental defectives do not occur as a result of congenital syphilis is due to the fact that if the spirochaetes enter the central nervous system the child dies.

Dr. STEPHENS (in reply): The paper I have written, as you see, is a bulky one. I have therefore only chosen those sections of it that I thought would be easier to read, and questions concerning others I hoped to answer as they were raised in this discussion. I have also purposely omitted all reference to a few important aspects of the subject, hoping thereby to make certain of being asked about them. Dr. Percy Smith has raised an important issue, and in answer I should like to say that the patients have been very carefully examined from the clinical standpoint, and that in *no case* could I find any definite syphilitic stigmata, lesions usually considered to be characteristic of the inherited disease. I must, however, state—and this will answer the President's question also—that the ophthalmoscopic and otological examinations of these patients were unfortunately not undertaken because of the obvious practical difficulties of such inquiries in aments precluding one from making any general statements on these points. The family histories have also been carefully investigated and were "negative," from the information I had at my disposal; but such information is invariably deficient, and in the majority of cases unreliable. These observations, based on the clinical aspects and family histories, agree with those obtained by other workers, who may be divided into two groups—those who recorded their observations before the compluetic reaction was used in the investigation of amentia, and those who have themselves employed the test in such investigations. Dr. Shuttleworth (1) has given us his own results, published in collaboration with Dr. Fletcher Beach in 1892, when clear evidence of inherited syphilis was found in only 1.17 per cent. of their cases; while Dr. Langdon-Down (2) detected the stigmata in 2 per cent. of cases; and Dr. Ireland (3) recorded with some surprise that the disease was not concerned in the aetiology of amentia. Later, however, Dr. Sherlock (4) obtained satisfactory evidence of syphilis in one or other parent in 14.4 per cent. of ninety cases, and Professor Th. Ziehen (5), of Berlin, detected the disease in as many as 17 per cent. of aments. Therefore, before the advent of the compluetic reaction the percentage of syphilitic cases, based on clinical evidence alone, was considered to be small. Since the employment of the test, however, a larger number of syphilitic cases have been detected, but the same small percentage of clinical results has been obtained as shown in the writings of Dr. Plaut, Major Mott, and others. Therefore one of two conclusions is true—either that the reaction is not associated with syphilis, which in the light of our present knowledge would be considered absurd, or that the more obvious clinical stigmata of syphilis are not found in aments, which, with the testimony of the present and past experience of competent observers to support it, would appear to be correct. With Dr. Percy Smith's remarks on the causation of mongolianism most observers would to-day agree, but it was not so very long ago when this condition was considered to be parasymphilitic, and that is why I have emphasised the point that in the sera of over 72 per cent. of mongols I have found the reaction negative. In answer to the President I have to say that, with the exception of seven, the patients came from all parts of England—from villages, towns, and cities; and they were drawn from all ranks of society. These points I have mentioned in my paper. Both Major Mott and Dr. Shuttleworth have referred to the technique employed in these tests. One of the principles of the "original method," as defined by the Society's Sub-Committee, is that the ingredients of the test should be derived "from different sources." If this means "from different individuals," then the technique I employed agrees with that of the "original" test. But if it is intended to mean "from individuals of different species" (e.g., the rabbit, the sheep, the guinea-

pig), then the technique I employed does not agree with that of the "original" test, for I used in my "hæmolytic system" human red blood corpuscles (always obtained, it must be remembered, independently of the bloods to be examined). Otherwise my technique conformed with the principles of the "original" test, and as shown in my paper everything was done to render the determinations as accurate as possible. Major Mott questions the accuracy of the "unheated" reactions. I agree with him, but I do not think they in any way invalidate the final interpretation of the results obtained. I should like to emphasise the fact that 12 and not 42 should be taken as the total percentage of the positive results. I have recorded the other reactions merely to indicate that they have been obtained, and in my paper I have given reasons why they should be rejected as "negative."

## REFERENCES.

- (1) Hack Tuke's *Dictionary of Psychological Medicine*, London, 1892; also *Amer. Journ. of Insanity*, 1888, lxiv, p. 381.
- (2) *Mental Affections of Childhood and Youth*, Churchill, London, 1887.
- (3) *On Idiocy and Imbecility*, Churchill, London, 1877.
- (4) *The Feeble-minded*, Macmillan, London, 1911.
- (5) *Psychiatrie*, Leipzig, 1908, p. 613.

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*Reaction Time in Nervous and Mental Diseases.* By  
E. W. SCRIPTURE, M.D., Ph.D.

## I. Introduction.

OUR knowledge of whether a person is normal, or suffers from neuritis, or is a case of dementia præcox, is derived entirely from observations of how he reacts to his environment—that is, to various stimuli. The thought at the basis of these researches is that an attempt may be made to produce an environment where the results will be accurately recorded in a simple, direct way.

The study of the nervous and mental condition of human beings consists of a study of their reactions—that is, of their responses to stimuli. By using stimuli of sound or light to which the person must respond by a voluntary movement, some degree of simple mental activity is involved. By requiring discrimination between two stimuli, and choice between two actions, more complicated mental action is included. These researches have not gone beyond this rather simple degree of mental action involving sensation, perception, discrimination, choice, and volition. They should be extended to higher forms of reaction to include association of ideas, judgments, emotions, etc., in fact, to all and more than what is included in a regular examination.