III.
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IV.
Attention
Speech
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Sentiment
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Instincts
Emotions
Temperament
Will-power

The Deviation of Complement in Cases of So-called Idiopathic Epilepsy. (Essay for which was awarded the Bronze Medal of the Medico-Psychological Association, 1911.)

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THE word "epilepsy" is used to describe a group of signs and symptoms which are associated with a disease that primarily affects the nervous system. We find grouped together under this name several diseased conditions which, so far as their clinical manifestations are concerned, bear a common relationship, but differ in regard to their exciting causes.

Dr. Aldren Turner in his Morison Lectures (*Lancet*, July 16th, 1910) has divided the manifestations of epilepsy, according to the exciting cause, into the following groups: (*a*) The organic epilepsies, (*b*) the early epilepsies, (*c*) the late epilepsies, and

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(*d*) idiopathic epilepsy, the last so named on account of there being no ascertainable cause found for the condition. It is the so-called idiopathic form of epilepsy alone and its exciting cause that I propose to discuss in this paper, and I shall therefore use the word "epilepsy" as indicative of idiopathic epilepsy unless otherwise stated.

Dr. Turner goes on to define epilepsy as "a chronic disease of the brain characterised by the occurrence of seizures in which interference with consciousness is an essential feature, associated either with convulsions or transient psychical phenomena occurring in persons with a hereditary neuropathic endowment, and eventually leading to a more or less permanent mental deficiency. This definition embraces the manifold symptoms usually included under the term epilepsy, such as psychical epileptic equivalents . . . ."

I do not intend to enter into the details of the convulsive and psychical elements or to discuss the predisposing causes of the disease, but as the direct or exciting cause of epileptic seizures plays an important part in the observations that I have made, a short summary of the theories which have been put forward in regard to this factor may not be out of place.

Such theories may be roughly divided into two groups—(*a*) toxic theories, and (*b*) non-toxic theories.

The following are perhaps the more important of the theories which have been advanced in support of a toxin being the direct or exciting cause of epileptic seizures.

Some years ago Magnam produced epileptic convulsions in animals by the intra-venous injection of small doses of essence of absinthe, these experiments being confirmed by Horsley, who carried out a long series of observations on similar lines.

Voison and Peron (*Archives de Neurologie*, vol. xxiv, p. 178) demonstrated certain toxic properties of the urines obtained from epileptic patients. These observers found that there was a hypotoxic condition of the urine before a seizure, and a hypertoxic condition of the urine after a seizure.

Haig, working on the uric acid content of the urine in patients suffering from epilepsy, found that before a seizure there was a diminution in the excretion of uric acid, and attributed the fits to an excess of uric acid in the blood.

Krainsky also has drawn attention to the diminution of uric acid in the urines of patients suffering from epilepsy, but carry-

ing his researches further, concluded that the presence in the blood of carbamic acid and certain of its compounds—substances closely related to uric acid—were the direct causes of an epileptic seizure.

Binswanger (*Die Epilepsie, Wien*, 1899) has called attention to a small group of cases which he considered might have a toxæmic origin, such cases being characterised by (*a*) marked premonitory symptoms of a psychical nature, (*b*) cases in which the fits were frequent and severe, and (*c*) cases in which there were more or less long intervals between the seizures.

In opposition to the theories of a possibly toxic origin, we find that there are a number of observers who attribute the exciting cause of an epileptic seizure to other factors.

A. E. Russell (*Lancet*, vol. i, pp. 963, 1031, 1093) regards cerebral anæmia due to cardiac inhibition and vaso-motor influences as the direct cause of epileptic seizures.

Dr. John Turner, of Brentwood, has demonstrated intravascular clotting in the cerebral arteries of epileptics, and attributes the fits to the formation of these clots.

Brown Séquard found that a few weeks after section of the spinal cord in an animal epileptiform seizures occurred, such seizures recurring at regular intervals, and further, that mechanical stimulation would cause a seizure in the animal whose spinal cord had been severed.

Whatever the cause of the so-called idiopathic epilepsy may be, whether it is a purely functional disorder, or the result of neuro-toxins, or a combination of these causes, a recent advance in the field of serum diagnosis—the complement deviation test—has made it at least possible to investigate as to whether specific toxins and their antibodies exist in the serum of patients who are subject to the symptoms of epileptic seizures. This method of diagnosis is based upon the axiom, that whenever a toxin is introduced or forms in the mammalian body, the body attacked protects itself by the formation of an anti-substance. It is reasonable from this known fact to argue that if epilepsy is in some cases caused by toxins acting upon the nerve centres, the presence of such a toxin would lead one to expect the presence of an antitoxin in the serum of the patient.

In 1902 Gengou showed that when an anti-serum was developed by the injection of various albuminoid substances into an animal, the mixture of the substance and the anti-substance

might not only give rise to a precipitate, but might also have the power of absorbing complement or alexine. (*Studies on Immunity*, Muir). Pfeiffer, Moreschi, Freiberger, Wassermann, and others, have done a great deal of work on the phenomenon known as the deviation of complement, and as it is perhaps the most recent method of serum diagnosis yet put forward, I propose to give a short summary of the reaction.

The deviation of complement depends upon the following facts: When an antigen or toxin is mixed with its corresponding immune body or anti-toxin, a union occurs between the two. If now complement, a constituent of every fresh serum, be at the same time added, it becomes fixed and held fast by the union of antigen and immune body. Whether or no such complement fixation has taken place may be easily determined by adding to the above mixture of toxin, anti-toxin, and complement, a hæmolytic serum obtained from an animal which has been injected with red blood-corpuscles, along with the homologous red blood-corpuscles. The hæmolytic serum, which has been heated to 55° C. to destroy its complement, is unable to produce lysis of the red blood-corpuscles by itself. If then upon adding the hæmolytic serum and red blood-corpuscles to the above-mentioned mixture of toxin, anti-toxin, and complement, no hæmolysis takes place, we may say that the complement has been fixed or deviated by the union of a toxin and its specific antibody. On the other hand, if hæmolysis does occur, it is evident that some at least of the complement has not been fixed or deviated, and this free complement has immediately entered into combination with the hæmolytic serum to produce the characteristic destruction of the red blood-corpuscles known as hæmolysis.

The test is a delicate one, and since its discovery had been used as a diagnostic sign in a number of diseased conditions in which ordinary clinical methods are uncertain. Professor Wassermann was the first to apply the test in the diagnosis of syphilis, and since then it has been used in the diagnosis of other infections in which toxins and their anti-substances exist.

Whilst it is true that complement is fixed or deviated by the union of an antigen and its antibody, it has been shown that other factors must be considered when carrying out observavations upon the deviation of complement. Professor Muir, of

Glasgow, has emphasised the following points regarding the causes of the disappearance of complement in a mixture: (*a*) physical and chemical means, (*b*) inhibition of complement by concentrated salt solution or certain proteins. Dr. Haswell Wilson has shown that albumen, by its power of deviating complement, could be demonstrated in solution in far greater dilutions than by any chemical method.

Observers have recently placed more value on the reaction when used as a quantitative one, that is to say by noting not only whether complement is deviated, but how much is deviated, and I have employed the latter method in carrying out the majority of my observations.

In approaching the question, therefore, of a toxin being a possible cause of epileptic seizures, I have done so under conditions which have been rendered more favourable by the discovery of such a delicate test as complement deviation, by means of which we may say that there is evidence in the individual affected of the existence of a substance which is capable of producing a specific anti-substance in such an individual, and possibly in other individuals similarly affected, although we may have no direct proof of its exact origin and nature.

It was the rapid strides in technique and the various methods of applying the reaction that have been recently made that induced me to use this test of complement fixation as a possible means of throwing light upon the causation of idiopathic epilepsy. I have mentioned a few of the theories put forward in support of the view that a toxin is the exciting cause of epileptic seizures, but so far as I am aware such theories have not been founded upon the use of so delicate a test as complement fixation.

In order to carry out observations on such lines two important factors had first to be considered (*a*) the source of antigen or toxin, and (*b*) the source of anti-substance, for the presence of both these substances is necessary in order to obtain a positive result or the fixation of complement.

The majority of workers who have employed this test have used mixtures of sera with their corresponding antisera, bacterial emulsions with the corresponding anti-bacterial substances, or extracts of certain organs with certain anti-substances as in Wassermann's reaction. In my series of

observations I have used the urines from patients suffering from epilepsy as the source of antigen, and the serum from epileptic patients as the source of anti-substance.

Urine was first used as the antigen or toxin in the complement deviation test by M. A. Bergeron in connection with tubercular infection. Lewis Bruce has used urine as the antigen in observations made in cases of mania (*Journal of Mental Science*, October, 1910). In both these observations the urine was chosen upon the supposition that if toxins were circulating in the blood they would most probably be eliminated in part by the kidneys, and under the same belief I have used the urines of epileptic patients as the antigen in my observations. I used the serum of epileptic patients as the anti-substance for the reason already stated, that if by any chance the disease was due to a specific toxin or group of toxins, there would almost certainly be some anti-body to that toxin found in the serum of those suffering from the disease.

In using the above-mentioned sources of supply of antigen and anti-body, we are probably working with toxins and anti-toxins in extremely dilute solution, but it has been proved by other observers that the success of the complement deviation test does not depend upon concentrated solutions, but is rather a very delicate method of detecting minute quantities of these substances when they are specific to one another.

Technique.

While not differing in the essentials and general principles of the reaction as used by Professor Wassermann and other observers, there are certain details in the technique employed which require description.

Specimens of urine.—The specimens of urine, which were used as sources of antigen throughout the observations, were treated in such a way before use as to reduce to a minimum any errors that might arise in carrying out the observations owing to the presence of organisms and other abnormal constituents in the urines. Accordingly, each specimen of urine before use was heated to a temperature of 70° C., in order to precipitate albumen and other substances, and then passed through a Berkefeld filter to remove organisms and substances precipitated by heat. The specimens were then kept in sterile flasks

in a cool place until ready for use. To avoid the possible complication of accidental contamination after filtration, the specimens of urine were never kept for more than twelve hours before they were required for use. Immediately before use each specimen of urine was examined for the presence of organisms, also the specific gravity and reaction were noted. In addition, the specimens were tested by the ordinary chemical methods for the presence of abnormal constituents.

Specimens of serum.—The specimens of serum, which were obtained from cases of epilepsy and used as the source of antibody throughout the observations, were taken in the following way. Blood was drawn from the patient by means of a sterile needle and syringe, the needle being passed into one of the veins of the forearm. The blood thus obtained was set aside in a sterile tube in a cool place, and the serum allowed to separate out from the clot. This serum was then removed from the tube, centrifuged to remove corpuscles, and heated at a temperature of 55° C. for one hour in order to destroy the complement which exists in all fresh sera.

Complement.—The serum from a normal rabbit was used as complement throughout my observations. The blood was collected in a sterile tube, and set aside in a cool place for twenty-four hours before use. At the end of this time the serum was pipetted off from the clot and centrifuged in order to remove corpuscles. The complement furnished by such a serum was found to be more potent in its action than the complement supplied by a serum which was obtained on the same day as it was required. Before making each set of observations the minimal hæmolytic dose (M.H.D.) of the complement to be used was tested. By the M.H.D. of complement I mean the smallest amount of complement which it would be necessary to add to a mixture containing a hæmolytic serum and ·5 c.c. of a 5 *per cent.* suspension of homologous corpuscles in normal saline, in order that the hæmolytic serum might completely hæmolyse the corpuscles in one hour. The method employed for estimating such a dose of complement was the same as that recommended in *Muir's Studies on Immunity*, pp. 4 and 5.

Hæmolytic serum.—A hæmolytic serum was obtained from a rabbit which had been injected with washed human red blood-corpuscles. Blood from the rabbit was collected in a sterile tube, set aside in a cool place, and the serum allowed to

separate out from the clot. The serum thus obtained was centrifuged in order to free it from corpuscles and then heated to a temperature of 55° C. for one hour in order to destroy the complement present in it. The M.H.D. of such a serum was always estimated before making each set of observations on lines similar to those used for the estimation of the M.H.D. of complement (*Muir's Studies on Immunity*, pp. 4 and 5).

Indicator.—As an indicator in my observations, I used ·5 c.c. of a 5 *per cent.* suspension in normal saline (·85 *per cent.*) of human red blood-corpuscles. The corpuscles were previously washed in normal saline in order to remove all traces of serum.

Observations.—These were carried out as follows: To each of a series of tubes was added ·2 c.c. of a specimen of urine, plus ·3 c.c. of a specimen of serum, plus a certain amount of complement. (I shall refer to the actual amounts of complement that were used when I give the details of the various groups of observations.) The above mixture of urine, containing a supposed antigen, serum, containing a supposed antibody, and complement, was placed in an incubator for one and a half hours at 37° C. in order to allow union to take place between antigen, antibody, and complement.

At the end of one and a half hours' incubation the tubes were removed from the incubator, and to each tube there was added ·5 c.c. of a 5 *per cent.* suspension in normal saline of human red blood-corpuscles, plus slightly more than the M.H.D. of a hæmolytic serum. The tubes were then returned to the incubator at 37° C. for one and a half hours, after which time they were removed and the results noted. The tubes were then set aside at room temperature for about twelve hours and the results again noted.

Control observations.—In each series of observations there were included control tubes containing—(1) antigen without antibody, (2) antibody without antigen, (3) antigen and antibody without complement, and (4) as antigen, urines from cases other than epileptics. These control observations were necessary in order to avoid certain errors. Thus, a specimen of urine which was being used as the antigen in an observation might, owing to the presence of some abnormal constituent, have deviated complement without the presence of anti-body in the mixture. In a similar way the serum which was used as the antibody might have deviated complement without the

presence of antigen in the mixture. A control tube, containing antigen and antibody but no complement, was included in order to determine whether complement, normally present in all sera, had been completely destroyed by heating to 55° C.

We may summarise the whole procedure thus: Antigen + antibody + complement, incubation for one and a half hours at 37° C.; the addition of hæmolytic serum + ·5 c.c. of a 5 *per cent.* suspension of human red blood-corpuscles, incubation for one and a half hours at 37° C. Results noted immediately after removal from incubator and again twelve hours later.

Results.—No hæmolysis in the corpuscles which had been added denoted a positive result or the deviation of complement, *i.e.*, the antigen had combined with its antibody and fixed or deviated the complement which had been added to the mixture so that there was not sufficient free complement in the mixture to enable the hæmolytic serum to cause lysis of the added corpuscles.

On the other hand, hæmolysis in the corpuscles which had been added denoted a negative result, *i.e.*, there had been no union between the antigen and its antibody, and therefore no complement had been deviated; free complement therefore existed in the mixture, the presence of this free complement enabling the hæmolytic serum to produce lysis of the red blood-corpuscles.

Much difficulty has been caused in the study of immunity by the employment of various names having a more or less synonymous meaning, and therefore it might be as well to point out in what particular sense I use the terms antigen and antibody throughout this paper. The word antigen is used to denote a substance which we may compare to a toxin, and which has given rise to, or stimulated in the individual affected, the formation of a specific anti-substance which I shall refer to as the antibody, the union of these two substances having the property of fixing or deviating complement which had been added to a mixture containing an antigen and its specific antibody.

Observations.

All the work in connection with the following groups of observations has been carried out in an asylum laboratory, and

therefore the specimens of serum and urine—with the exception of certain control urines—which were used throughout the observations, were obtained from epileptic patients who were certified lunatics, and who were suffering from some form of mental derangement as the result of, or in association with, epilepsy. In the course of the observations, specimens of urine from twenty-three cases of epilepsy, and specimens of serum from eleven cases of epilepsy, were used as sources of antigen and antibody respectively.

All the above epileptic patients were subject to fits, the number and frequency of which varied in each case.

The specimens of urine used for control observations were obtained from the following sources: (1) Members of the asylum staff; (2) cases of mania; (3) cases of melancholia; (4) cases of general paralysis; and (5) imbeciles and idiots.

The observations with the results that were obtained, may be divided into four groups, which I now propose to consider in detail, and as I have already described generally the technique employed throughout my observations, in dealing with the following groups I shall only mention such facts in regard to the technique as may have a direct bearing upon the results which are recorded.

TABLE I.—*First Series of Observations.*

Antibody.	Antigen.	Complement.	Results.	
			Positive.	Negative.
Serum from Epileptic A	Urines from 15 epileptic patients	1 M.H.D.	12 = 80 *per cent.*	3 = 20 *per cent.*
Ditto . .	Urines from 15 control persons *not* epileptic	1 M.H.D.	2 = 13·3 *per cent.*	13 = 86·7 *per cent.*

Antibody.—Throughout this series of observations the antibody employed was the serum of a male epileptic patient, A—, who was partially demented and who suffered from numerous epileptic seizures averaging three and four every twenty-four hours.

Antigens.—The sources of antigens were as follows: (1) The urines from fifteen patients suffering from epilepsy, and

(2) control urines, from (*a*) twelve members of the asylum staff, and (*b*) three cases of confusional mania.

Complement.—1 M.H.D. of complement was used in each observation of this series.

Example of Technique.—Series 1.

Tube.	Antigen.	Antibody.	Complement.	Hæm. serum.	5 *per cent.* suspension R.B.Cs.	Result.
1	·2 c.c. urine ep. 1	·3 c.c. serum ep. A.	1 M.H.D.	·04 c.c.	·5 c.c.	No hæm.
2	,, ,, 2	,, ,,	,,	,,	,,	Ditto
3	,, ,, 3	,, ,,	,,	,,	,,	,,
4	·2 c.c. urine control 1	,, ,,	,,	,,	,,	Hæm.
5	,, ,, 2	,, ,,	,,	,,	,,	,,
6	,, ,, 3	,, ,,	,,	,,	,,	,,

The M.H.D. of complement was ·01 c.c.

The antigens, antibody, and hæmolytic serum were all controlled as stated on p. 683 of this paper. (See paragraph on control observations p. 683.)

The double lines indicate incubation periods of one and a half hours each.

Results.—The results obtained were sufficiently striking; out of the 15 urines from epileptics 12, or 80 *per cent.*, gave positive results—that is to say the complement was deviated and no hæmolysis occurred—and 3, or 20 *per cent.*, gave negative results—the complement was not deviated and hæmolysis occurred.

Of the 15 controls only 2, or 13·3 *per cent.*, gave positive results, while 13, or 86·7 *per cent.*, were negative.

The 2 control urines, which deviated complement, were obtained from members of the asylum staff, and contained no abnormal constituent; but I found, on making further observations, that 1 M.H.D. of complement was occasionally deviated by the urines of apparently healthy persons, and therefore in the next series of observations I increased the quantities of complement.

TABLE II.—*Second Series of Observations.*

Antibody.	Antigens.	Complement.			Results.					
					Positive tubes.			Negative tubes.		
		Tube 1.	Tube 2.	Tube 3.	1	2	3	1	2	3
Serum from Epileptic A—	Urines from 18 epileptic patients	1 M.H.D.	2 M.H.Ds.	4 M.H.Ds.	18	15	8	0	3	10
Ditto	Urines from 18 control persons *not* epileptics	,,	,,	,,	6	3	1	12	15	17

Antibody.—The source of antibody in this series of observations was the same as that in Series 1, namely the serum of a male epileptic patient A—.

Antigens.—These were (1) the urines from 18 individuals, each the subject of epilepsy; and (2) control urines from (*a*) 4 cases of manic-depressive insanity; (*b*) 4 cases of confusional mania; (*c*) 2 cases of imbecility; and (*d*) 8 members of the asylum staff.

Complement.—Varying doses of complement, namely 1 M.H.D., 2 M.H.Ds., and 4 M.H.Ds. were used throughout these observations with each specimen of urine tested.

Example of Technique.—Series 2.

Tube.	Antigen.	Antibody.	Complement.	Hæm. serum.	5 *per cent.* suspension R.B.Cs.	Result.
1	·2 c.c. urine ep. 4	·3 c.c. serum ep. A	·02 c.c.	·03 c.c.	·5 c.c.	No hæm.
2	,, ,, 4	,, ,, A	·04 ,,	,,	,,	Ditto
3	,, ,, 4	,, ,, A	·08 ,,	,,	,,	,,
4	·2 c.c. urine control 4	,, ,, A	·02 ,,	,,	,,	,,
5	,, ,, 4	,, ,, A	·04 ,,	,,	,,	Hæm.
6	,, ,, 4	,, ,, A	·08 ,,	,,	,,	,,

The M.H.D. of complement was ·02 c.c.

The antigens, antibody, and hæmolytic serum were all controlled as described on p. 683 of this paper.

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The double lines indicate an incubation period of one and a half hours each.

Results.—A reference to Table II shows the following results:

The urines from all the epileptic patients—18 in number—deviated 1 M.H.D. of complement, the urines of 15 deviated 2 M.H.Ds., while the urines of 8 deviated 4 M.H.Ds.

Of the 18 control urines, 6 deviated 1 M.H.D., 3 deviated 2 M.H.Ds., and 1 deviated 4 M.H.Ds. of complement.

These results of complement fixation by the urines from epileptic patients are not very striking when looked at by themselves—no less than 55 *per cent.* failed to deviate 4 M.H.Ds. of complement—but when compared with the results obtained with the control urines, there can be no doubt that the urines of epileptics when mixed with the serum of epileptics have a greater power of complement deviation than the urines of non-epileptic persons when also mixed with the serum of epileptics.

The results are marked when stated in comparative form. The urines of epileptics, plus 1 M.H.D of complement, gave 100 *per cent.* of positive results, whereas the urines of the control persons, plus 1 M.H.D. of complement, gave 33 *per cent.* of positive results. With 2 M.H.Ds. of complement the urines of epileptics gave 83 *per cent.* of positive results, while the control urines gave only 16 *per cent.* of positive results. Lastly, with 4 M.H.Ds. of complement, the maximum amount of complement used in this series, the urines of epileptics gave 44 *per cent.* of positive results, and the controls only 5 *per cent.*

In looking at the above results, two factors must be considered. The first is that I have ample evidence that the toxin or substance in the urine of an epileptic, which has the power of deviating complement when mixed with the serum of an epileptic, varies greatly on different days, and as the urines from the epileptic patients were taken whenever it was convenient to carry out observations, it is more than probable that some of these urines contained a minus quantity of the toxin or deviating substance while others contained a plus quantity. (This factor is illustrated in Table IV.)

Secondly, the positive results obtained with some of the control urines may have been "group reactions," several of the controls being insane persons, and there is a known close affinity between the disease known as epilepsy and some of the diseases classed under insanity. (Prof. Muir, of Glasgow, in

the *Lancet*, November 5th, 1910, has recently drawn attention to the occurrence of a so-called "group reaction" in certain cases of trypanosome and other protozoal infections when using Wassermann's test for syphilis.)

TABLE III.—*Third Series of Observations.*

Antibody.	Antigens.	No. of observations.	Complement.		Results.			
					Positive tubes.		Negative tubes.	
			Tube 1.	Tube 2.	1.	2.	1.	2.
Serum from 10 different epileptics	Urines from 23 different epileptics	139	2 M.H.Ds.	4 M.H.Ds.	93	43	46	96
Ditto.	Urines from 41 control persons *not* epileptics	140	,,	,,	20	—	120	140

As the results of the observations of Series 1 and 2 were largely confirmatory, I made a third series of observations which are shown in the above Table III. This series of observations was more extensive than either Series 1 or 2, for I not only carried out a greater number of observations, but the antigen and antibody were obtained from a larger number of epileptic patients—10 supplied specimens of serum as antibody, and 23 supplied specimens of urine as antigen.

Antibody.—The antibodies were supplied by the sera of 10 different epileptic patients.

Antigens.—These were supplied by (1) 23 different epileptic patients, and (2) 41 persons who were not epileptic.

Complement.—2 M.H.Ds. and 4 M.H.Ds. were used with each urine tested.

In addition to the above ten specimens of serum which were used as sources of antibody in this series of observations, I used an eleventh specimen—serum K. This serum was obtained from a female epileptic who suffered from frequent fits and occasional attacks of epileptic mania. The observations made with serum K are not included in the results of this series, because I found that this serum caused the deviation of 2 and

4 M.H.Ds. of complement without the presence of an antigen in the mixture. Such complement fixation did not occur with any of the other ten sera that were used as sources of antibody and the results are therefore of interest, especially as specimens of urine obtained from the patient who supplied serum K failed to cause the deviation of 2 and 4 M.H.Ds. of complement when tested with nine different sera from epileptics upon nine different occasions, and only once did complement deviation occur when a specimen of this patient's urine was used as antigen, and this specimen was obtained after the patient had been in a "status epilepticus."

Example of Technique.—Series 3.

Tube.	Antigen.	Antibody.	Complement.	Hæm. serum.	5 *per cent.* suspension R.B.Cs.	Result.
1	·2 c.c. urine ep. 1	·3 c.c. serum ep. A.	·04 c.c.	·02 c.c.	·5 c.c.	No hæm.
2	" " 1	" "	·08 "	"	"	Ditto.
3	" " 2	" "	·04 "	"	"	"
4	" " 2	" "	·08 "	"	"	"
5	·2 c.c. urine control 1	" "	·04 "	"	"	Hæm.
6	" " 1	" "	·08 "	"	"	"
7	·2 c.c. urine ep. 1	" " B.	·04 "	"	"	No hæm.
8	" " 1	" "	·08 "	"	"	Ditto.
9	" " 2	" "	·04 "	"	"	Hæm.
10	" " 2	" "	·08 "	"	"	"
11	·2 c.c. urine control 20	" "	·04 "	"	"	"
12	" " 20	" "	·08 "	"	"	"

The M.H.D. of complement was ·02 c.c.

The antigens, antibodies, and hæmolytic serum were all controlled as in the previous observations.

The double lines indicate incubation periods of one and a half hours each.

Results.—With the urines of epileptic patients 139 observations were made; in 93 of these 2 M.H.Ds. of complement were deviated, and in 43 4 M.H.Ds. of complement were deviated.

With the urines of control persons 140 observations were made; of these 20 deviated 2 M.H.Ds. of complement and none deviated 4 M.H.Ds. of complement.

In this series of observations, as in those of Series 2, Table

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II, the results were not striking when regarded individually, but they are marked when regarded comparatively. For, whereas the total positive results with the urines of epileptics were over 90 *per cent.*, the total positive results with the control urines were only 14·2 *per cent.*

In this series of observations, also, allowance must be made for the same factors noted under Series 2, namely, the fact that the urines of epileptics vary from day to day in their power of deviating complement, and also the fact that certain of the controls in this series were insane and imbecile persons—conditions which are often associated with, and allied to, epilepsy—and therefore the urines of these persons would be quite likely to give "group reactions."

Table IV shows the results in tabular form of the actions of specimens of serum obtained from 10 epileptic patients upon the urines from 23 epileptic patients. The table is designed to show that the specimens of urine from the same patient apparently vary at different dates in the amount of toxin or deviating substance they contain.

TABLE IV.

	A	B	C	D	E	F	G	H	I	J
1	P	P	P	P	P	P	P	—	P	P
2	P	—	—	—	N	P	N	—	P	N
3	P	P	P	P	P	—	P	—	N	P
4	P	P	P	P	P	—	—	P	P	N
5	—	P	—	—	P	N	—	P	P	N
6	N	P	N	P	N	P	—	—	N	N
7	P	—	—	P	P	P	—	P	P	N
8	—	—	—	P	P	N	—	—	P	P
9	—	—	—	P	P	N	—	—	N	P
10	—	—	—	P	P	—	—	—	P	P
11	N	—	—	P	N	—	—	—	N	P
12	—	—	—	—	P	—	—	N	N	P
13	P	—	—	—	—	N	P	—	N	N
14	P	—	—	—	—	—	P	—	N	N
15	—	—	—	—	—	N	P	—	N	N
16	P	—	—	P	P	P	—	P	P	P
17	P	P	—	P	P	P	N	—	N	P
18	P	P	—	P	—	—	—	—	N	P
19	P	—	—	P	—	P	—	P	P	P
20	N	N	—	P	—	N	—	N	N	N
21	P	N	—	P	—	—	P	—	N	P
22	P	N	—	P	—	N	—	N	P	P
23	P	N	—	—	N	—	—	—	P	N

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The letters A, B, C, etc., refer each to the serum of a different epileptic patient, each serum being used as antibody and tested with urines from a number of epileptic patients represented on the left-hand side of the table by the figures 1, 2, 3, etc.

The urines from these epileptic patients 1, 2, 3, etc., were taken upon ten different days, and tested with the serum of one of the epileptic patients A, B, C, etc., so that the observations made with A's serum with the urines of epileptics 1, 2, 3, etc., were made with entirely different samples of urine from those tested with the sera of B, C, D, etc.

Positive results are indicated by P, negative results by N, while a stroke denotes that sample of urine was not tested against that particular serum.

In the total results it will be seen that out of 139 observations 93 were positive and 46 were negative.

The variation in complement deviation which occurred with samples of urine obtained from one particular patient on different dates is well shown. The urine of epileptic No. 6, for instance, gave alternate negative and positive results on six consecutive occasions when tested with sera A, B, C, D, E, and F; the urine of epileptic No. 17 gave five positive results on five consecutive occasions, then two negative results, and lastly one positive. It will be seen that in no one case were the results entirely negative, and that a single positive result was recorded in only two instances, namely in the case of patients Nos. 15 and 20.

Fourth Series of Observations.

This series of observations was made as a control series, in order to test the power of other sera than the sera of epileptics to deviate complement when mixed with the urines of epileptics.

These observations and their results are shown in Table V.

Antibody.—The antibody was supplied from the sera of two cases of insanity, one a case of confusional mania and the other a case of manic-depressive insanity.

Antigens.—The antigens were supplied by the urines of twenty epileptic patients. These urines had been used in the observations of Series 3 and given positive results.

TABLE V.

Antibody.	Antigens.	No. of observations.	Complement.		Results.			
					Positive tubes.		Negative tubes.	
			Tube 1.	Tube 2.	1.	2.	1.	2.
Serum from a case of confusional mania	Urines from ten epileptics	20	2 M.H.Ds.	4 M.H.Ds.	—	—	10	10
Serum from a case of manic-depressive insanity	,,	20	,,	,,	—	—	10	10

Complement. — 2 M.H.Ds. and 4 M.H.Ds. were used throughout the observations with each specimen of urine tested.

Example of Technique.—Series 4.

Tube.	Antigen.	Antibody.	Complement.	Hæm. serum.	*5 per cent.* suspension R.B.Cs.	Result.
1	·2 c.c. urine ep. 10	·3 c.c. serum (confus. mania)	·02 c.c.	·03 c.c.	·5 c.c.	Hæm.
2	,, ,,	,,	·04 c.c.	,,	,,	,,
3	,, ,,	·3 c.c. serum (manic-depress.)	·02 c.c.	,,	,,	,,
4	,, ,,	,,	·04 c.c.	,,	,,	,,
5	,, control 6	·3 c.c. serum (confus. mania)	·02 c.c.	,,	,,	No. Hæm.
6	,, ,,	,,	·04 c.c.	,,	,,	Ditto
7	,, control 8	·3 c.c. serum (manic-depress.)	·02 c.c.	,,	,,	,,
8	,, ,,	,,	·04 c.c.	,,	,,	,,

The M.H.D. of complement was ·01 c.c.

The antigens, antibodies, and hæmolytic serum were controlled as in previous observations.

The double lines indicate incubation periods of one and a half hours each. Control urines 6 and 8 were obtained from a case of confusional mania and a case of manic-depressive insanity respectively.

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Results.—The results obtained were uniform and entirely negative; in no observation did the serum from the case of confusional mania or the serum from the case of manic-depressive insanity deviate any complement when mixed with the urines of epileptic patients.

Conclusions.

As the result of these observations made upon the complement deviating power of the urines of epileptics when mixed in certain proportion with the serum of sufferers from epilepsy, I am led to the following conclusions:

(1) That the serum of persons the subjects of epilepsy contains some substance of the nature of a specific antibody.

(2) That the urines of persons suffering from epilepsy contain, very generally, a toxin or substance specific to the antibody contained in the serum.

(3) That the serum of persons who are not epileptic does not contain an antibody specific to the toxin which is generally present in the urines of epileptic patients.

(4) That the urines of some sane non-epileptic persons and some persons the subjects of insanity but not epileptic contain a toxin or substance, which when mixed with the serum of an epileptic is capable of deviating 1 and 2 M.H.Ds. of complement, but very rarely 4 M.H.Ds.—throughout the observations only 5 *per cent.* did so.

(5) That the urines of epileptic patients when mixed in certain proportions with the serum of patients also the subjects of epilepsy are capable in a much larger proportion of deviating 4 M.H.Ds. of complement. In the second series of observations 44 *per cent.* did so, and in the third series of observations 30 *per cent.* did so.

(6) The results are only striking when regarded comparatively, that is to say, when the positive results obtained with the epileptic patients are compared with the positive results obtained with non-epileptic persons. This method of observation, therefore, is of little value as a diagnostic of the disease known as epilepsy.

(7) The results of these observations are also of practical interest, because if further observations with improved technique and knowledge prove that some forms of epilepsy are of

toxic origin, it should be possible to extract the toxins from the urines of epileptic persons and to use the toxins as a specific vaccine in the treatment of the disease.

Occasional Notes.

The Annual Meeting.

After the lapse of seventeen years our Association has again held its Annual Meeting in Dublin.

There was much to remind members of the former meeting—an able and zealous President, scientific contributions of great importance and interest, and charming hospitality.

Dr. Dawson's Presidential Address, on a subject so judiciously selected and dealt with, his dignified and courteous conduct in the chair, and the enthusiastic support which he received from his fellow-workers in the cause of the insane, justified the confidence with which his friends had predicted for him a distinguished and fruitful occupancy of the office of Inspector of Lunatic Asylums in Ireland. We cordially renew our congratulations to him, and to those to whose welfare he will devote his life work.

Great advances have been made by our Association since 1894, and mainly on the lines which had the approval of our then President, the late Dr. Conolly Norman, to whose memory appreciative and affectionate references were made and whose loss is still so keenly felt.

The meeting extended over three days, and there was renewed evidence of the great amount of time which is devoted by the various committees to the work of the Association.

Much has been accomplished during the past year, as indicated by the several reports. The Sub-Committee on Post-Graduate Teaching and Diplomas in Psychiatry is to be congratulated on the result of its efforts—a result which must be very gratifying to those who have done so much to ensure it.

The Association is under a special obligation to the Chairman of the Housing Committee, who is also Chairman of the National Committee for Great Britain and Ireland *re* the