THE

JOURNAL OF MENTAL SCIENCE

[*Published by Authority of the Medico-Psychological Association of Great Britain and Ireland.*]

No. 249 [NEW SERIES No. 213.] APRIL, 1914. VOL. LX.

Part I.—Original Articles.

The Complement-Deviation in Cases of Manic-Depressive Insanity[1].

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BEING personally satisfied by clinical observations that certain of the acute insanities are toxic in their ætiology, it occurred to me that it might be possible to demonstrate the presence of the toxæmia by means of the delicate test of complement-deviation. I argued that if a toxin existed in the blood, it would probably be excreted in the urine, and that at certain stages of the disease process a corresponding immune body would be found in the serum. In a series of observations carried out on these lines, I used urines as the antigen, and serum as the immune body.

During the past two years, I have examined the urine or the serum, often both, in every case of acute insanity admitted to Murthly Asylum, and—confining my remarks to cases of manic-depressive insanity—I found that when the serum of one case of manic-depressive insanity was mixed with the urine of another case in the proportion of ·2 c.c. serum to ·2 c.c. urine, the mixture frequently had the power of deviating from 3 to 4 M.H.D. of complement. This complement-deviating power was not present when the serum of a case of manic-depressive insanity was mixed with the urine of a sane healthy person,

https://doi.org/10.1192/bjp.60.249.177 Published online by Cambridge University Press

nor when the serum of a sane healthy person was mixed with the urine of a case of manic-depressive insanity.

It was noticed, however, that there was a very marked variation in the complement-deviating power of both the urines and serums of the same cases of manic-depressive insanity at different stages of the disease. This might be due to the use of serums and urines of varying and unknown quality. Chart No. 1, however, shows the average complement-deviating power

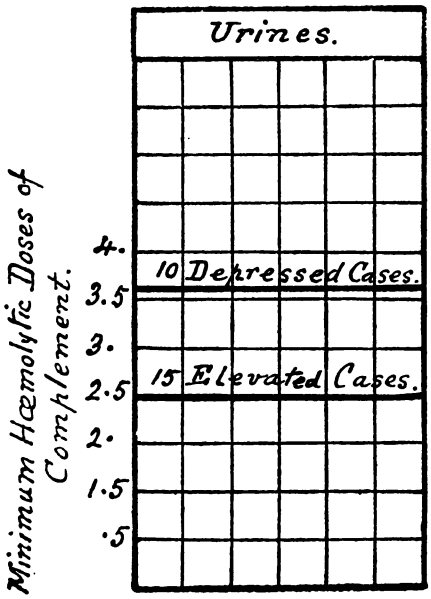


CHART 1.—The average deviation of complement by the urines of ten cases of depressed manic-depressive insanity and fifteen elevated cases.

of the urines of ten cases of manic-depressive insanity in the condition of depression, and of fifteen cases in the condition of elevation, all tested with the serum obtained from one patient suffering from manic-depressive elevation. The average complement-deviation of the ten depressed patients is 3·7 M.H.D., while that of the fifteen elevated cases is 2·5 M.H.D.

It is apparent from this observation that the urines of cases of depressed manic-depressive insanity have a greater complement-deviating power than the urines of cases in a state of elevation, and further, that the antigen, or complement-deviating

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substance in the urine, is always more or less present in the various stages of the disease.

Conversely, when the serums of six cases of manic-depressive insanity in the state of elevation, and six cases suffering from depression, were tested against the urine obtained from another case of the disease in the stage of depression, it was found that the complement-deviating power of the serum of the six elevated cases averaged 3 M.H.D., while the serum of the

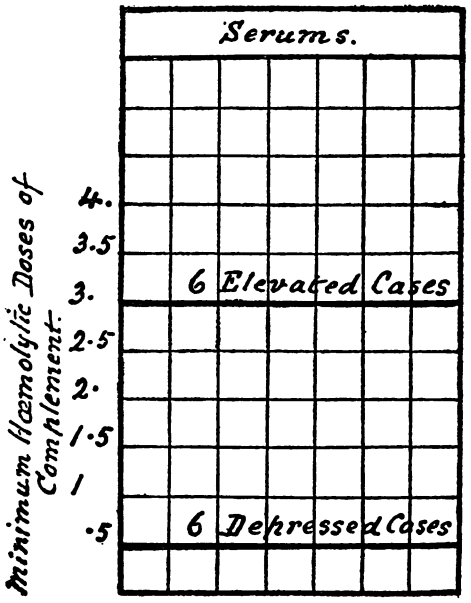


CHART 2.—The average deviation of complement by the serums of six cases of elevated manic-depressive insanity, and six depressed cases.

six depressed cases gave an average deviation of ·5 M.H.D. (Chart No. 2).

This observation would show that the immune body, or complement-deviating substance, in the serum of cases of manic-depressive insanity is greater during the stage of elevation than during the period of depression.

As these observations were carried out on cases of manic-depressive insanity as a class, a further observation was made on individual cases at the various stages of the disease, and the technique employed was as follows: The serum of a case of manic-depressive insanity was tested to ascertain that it held

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an appreciable quantity of immune body, and similarly the urine of another was tested to ascertain the presence of antigen. When it was proved that the serum contained immune body, and the urine the specific antigen, the serum and urine were stored in tubes, sterilised by heat at 55° C., and then hermetically sealed to prevent evaporation. Such tested and stored

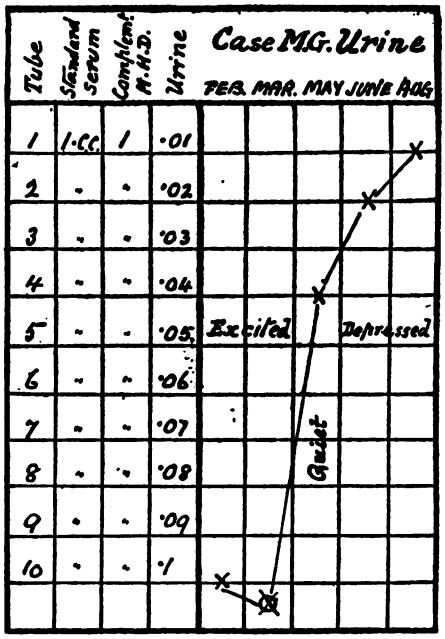


CHART 3.—Case M. G—, female, æt. 60. The patient had acute attacks, with long intervals of sanity. The chart shows that in February and March when the patient was acutely excited it took ·1 c.c. of her urine mixed with ·1 c.c. of the standard serum to deviate 1 M.H.D. of complement. She passed into a period of quiescence in May, when ·04 c.c. of her urine mixed with ·1 c.c. of the standard serum deviated 1 M.H.D. of complement. She became depressed in June, and was still depressed in August. The complement-deviating substance in the urine was increased during this stage, as it took only ·02 c.c. of her urine in June, and ·01 c.c. of her urine in August to deviate 1 M.H.D.

serum was designated standard immune body, and such urine as standard antigen.

Six cases of known manic-depressive insanity were selected, and their serum and urine was tested at various periods of their disease by means of the standard immune body, and the standard antigen. When the serum of any case was to be tested, a series of tubes numbered from 1 to 10 were taken, and in each

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was placed ·1 c.c. of the standard urine. The inactivated serum of the patient to be tested was added to the tubes as follows: to No. 1 tube, ·01 c.c.; to No. 2, ·02 c.c.; to No. 3, ·03 c.c., and so on. To each tube was then added 1 M.H.D. of complement. The M. H. D. in this observation was calculated as that quantity of fresh rabbit-serum which would completely

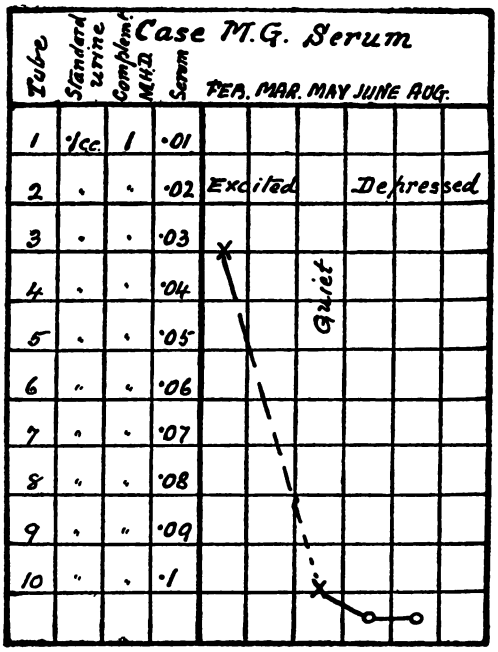


CHART 4.—Case M. G—. Patient whose urine deviation is shown in Chart 3. When excited in February, ·03 c.c. of her serum when mixed with ·1 c.c. of the standard urine deviated 1 M.H.D. of complement. In March, she would not permit me to take blood for observation. In May, during a period of quiescence, the complement-deviating substance in the serum was diminished, as it took ·1 c.c. of her serum mixed with ·1 c.c. of the standard urine to deviate 1 M.H.D. of complement. During June and August, when depressed, no complement was deviated by a mixture of ·1 c.c. of her serum and ·1 c.c. of standard urine.

hæmolyse ·25 c.c. of a 1 *per cent.* suspension of red blood-cells with an appropriate dose of its specific hæmolytic serum.

The tubes were incubated for two hours at 37° C., and then to each tube was added ·25 c.c. of the 1 *per cent.* suspension of red blood-cell emulsion, together with twice the amount of hæmolytic serum used to determine the M.H.D. of complement. The tubes were further incubated for two hours, and left at room

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temperature for twelve hours. The slightest trace of hæmolysis was recorded as a negative result.

When the urine of a patient was to be tested, tubes to the number of ten had each placed in them ·1 c.c. standard immune body, and then from a twenty-four hours' collection of the urine to be tested ·01 c.c. was added to tube No. 1, ·02 c.c. to tube No. 2, and so on, and to each tube was added 1 M.H.D. of

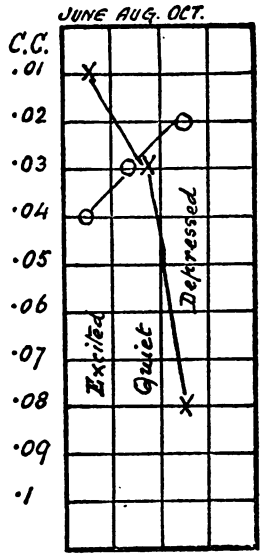


CHART 5.—Case A. A—, male, æt. 45. He suffered from acute attacks, with long intervals of sanity. When admitted in June he was excited; ·01 c.c. of his serum mixed with ·1 c.c. of standard urine deviated 1 M.H.D. of complement, and ·04 c.c. of his urine when mixed with ·1 c.c. standard serum deviated 1 M.H.D. of complement. He continued in the state of excitement during July, but during August he became quieter, when it was found that it took ·03 c.c. of his serum mixed with ·1 c.c. standard urine to deviate 1 M.H.D. On the other hand, the complement-deviating power of his urine had increased as it now took only ·03 c.c. of urine + ·1 c.c. of standard serum to deviate 1 M.H.D. During October he passed into mild depression; it now took ·08 c.c. of his serum + ·1 c.c. of standard urine to deviate 1 M.H.D. of complement, while the complement-deviating substance in his urine had still further increased as so small a quantity as ·02 c.c. of his urine when mixed with ·1 c.c. standard serum deviated 1 M.H.D. of complement. x = Serum, o = Urine.

complement. The remainder of the technique was as described above.

Control observations were made in each case of ·1 c.c. of the standard immune body, ·1 c.c. of the standard antigen, ·1 c.c.

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of the urine to be tested, and ·1 c.c. of the serum to be tested. In no case did any of these control tubes deviate one full dose of complement.

The results of this series of observations are shown in Charts Nos. 3, 4, 5, and 6. It was found that during the elevated

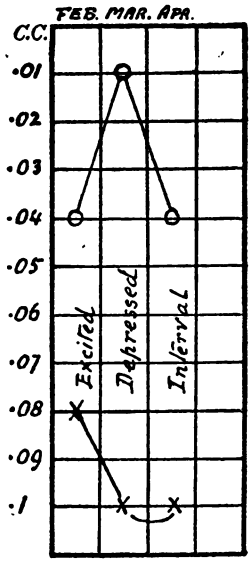


CHART 6.—Case A. L—, female, æt. 50. She suffered from frequent attacks of varying duration with short intervals of quiet which could hardly be called sanity. In February, during an attack of excitement, it took ·08 c.c. of her serum when mixed with ·1 c.c. standard urine to deviate 1 M.H.D. of complement, and ·04 c.c. of her urine mixed with ·1 c.c. standard serum to deviate 1 M.H.D. of complement. In March, she became depressed, when it took ·1 c.c. of her serum mixed with ·1 c.c. standard urine to deviate 1 M.H.D. of complement, and ·01 c.c. of her urine + ·1 c.c. standard serum to deviate 1 M.H.D. During April, she had a quiet interval, when it was found that her serum had not altered in its complement-deviating power, but that the complement-deviating of the urine was diminished, as it now took ·04 c.c. of her urine + ·1 c.c. of standard serum to deviate 1 M.H.D. This patient had such frequent attacks that it was possible to repeat the observations several times, and in all the observations made the complement-deviating power of serum and urine during each attack followed very closely the variations shown in this chart. The low complement-deviating power of the serum throughout the attack is characteristic of the chronic type of the disease, and is in marked contrast to the high deviating power of the serum of more acute cases whose intervals of sanity are marked and prolonged. x = Serum, ∩ = Urine.

period of the disease the complement-deviating substance in the serum was present in considerable amount, but that as the excitement passed off and depression set in, the immune body in the serum became markedly less, so much so that sometimes

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no complement was deviated by so large a quantitity of serum as ·1 c.c. + ·1 c.c. standard antigen. On the other hand, the complement-deviating substance in the urine of these patients was extremely scanty during the period of excitement, but became markedly increased during the periods of depression.

The test is not of diagnostic value, because I have found that the urines and serums of cases of acute insanity other than manic-depressive insanity will deviate up to 2 M.H.D. of complement with the urines and serums of cases of undoubted manic-depressive disease, but the results I have recorded are of interest, as they suggest a possible explanation of the varying mental states in the disease known as manic-depressive.

The suggestion is this, that during the excited period of the disease the defences of the body, in the form of immune body in the serum, are sufficient to neutralise to some extent the action of the toxæmia which causes the disease, but whenever the defensive power becomes exhausted, the toxin overwhelms and paralyses the nerve-tissues, so that the outward manifestation is depression, and, in some cases, even stupor.

(1) A paper read at the International Congress of Medicine, 1913.

Further Observations on the Influence of Toxins on the Central Nervous System (1).

By D. ORR, M.D., and R. G. ROWS, M.D.

FOR some years, we have been engaged in an investigation into the mode of action of toxins upon the central nervous system, and up to the present time have devoted our attention exclusively to the question of the upward passage of bacterial poisons along the sheaths of peripheral nerves to the spinal cord and brain. Experiment has shown us that toxins readily travel upwards in the perineural lymphatics, in which they induce an inflammation whose phenomena vary with the intensity of the irritant; and that this is continued without interruption to the central nervous system, granted that the toxins gain that level. Continuity of extension is, therefore, an important feature of lymphogenous inflammation, and is as constant in the central as in the peripheral nervous system.

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