TEETER (J. N.)

ON THE RELATION OF UREA TO EPILEPSY.

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ON THE RELATION OF UREA TO EPILEPSY.

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So much has been written upon epilepsy, its etiology, pathology, and treatment, that it is with great reluctance and hesitation these observations are presented to the medical profession, but in view of the fact that idiopathic epilepsy is one of the most obscure and therefore intensely interesting diseases we have to deal with, any research referring to its causation may be acceptable. Most observers, especially those of the present day, have dealt not so much with the etiology of this disease as with the treatment, and the whole pharmacopœia has been exhausted, from the old-time remedies down to the newer agents, in the extensive search for a specific. From time to time articles appear in our medical journals praising the efficacy of certain agents to the exclusion usually of others; but they all lack the proof of time, for the majority of these observations extend only over a few months, or a year at most. We have all noticed an improvement in our cases upon the exhibition of a newly vaunted remedy, and are inclined to be enthusiastic over its efficacy as an anti-epileptic, but further experience and careful observation bring disappointment, and we pass on to other drugs. Thus, the bromides, belladonna, nitrate of silver, anti-febrine, beta naphthol, sodium borate, and opium, which has been revived, have all proved unsatisfactory. Is it not time to commence the study of epilepsy à priori instead of heroically treating the great result — the convulsion — as if this were the root of the whole evil? Why should the convulsion be considered so much more important than other symptoms usually present — for example, the gradual mental enfeeblement which accompanies the progress of this disease?

Régis, in an article read before the congress of psychological medicine, incidentally speaks of the probable cause of epilepsy as an auto-intoxication, in proof of which he finds an increase in the toxicity of the urine subsequent to an epileptic paroxysm, and quotes similar results obtained by MM. Féré, A. Pérou, Chouppe, and Jules Voisin. This theory seems to be a very tenable one when we remember noticing in many of our cases considerable improvement for a time after thorough purgation or the exhibition of diuretics and exercise. Keeping in mind these facts, I was led to

believe that some definite constituent of the excretions of the body might be the cause of this auto-intoxication; that a continued and careful analysis of excrementitious materials would show a variation in amount before and after convulsions, and, perhaps, a lessening of the special poison during the whole course of the disease. Urea, it is well known, when not excreted by the kidneys in sufficient quantity, will give rise to great mental disturbance, often ending in severe convulsions, and finally bringing on coma and death. The convulsions in uræmia are very similar to those observed in epilepsy, so much so that they have been described as epileptiform in character. The peculiar epileptic cry, the fixation of the eyes, dilatation of the pupils, rigid features, congested countenance, and the tonic, followed by the clonic convulsion, have all been seen in the uræmic paroxysm. Upon examination of the urine, we find a lessened amount of urea excreted, and it is only after the accumulation of this special poison is gotten rid of by vicarious methods that the normal processes of the organism are again established. Uræmia is an auto-intoxication, and the special poison is urea. We notice in cases of status epilepticus convulsion following convulsion in rapid succession, bearing, as is often remarked, a close resemblance to the uræmic state. The fact that the most efficacious treatment is very similar in both cases — the administration of chloroform and the re-establishment of the functions of the excrementitious organs — suggested to me the strong presumption of a common origin of the two conditions. One need not necessarily assume for the production of uræmic convulsions a parenchymatous change in the kidney itself — might there not be a nervous origin for the impairment of its function? We notice in paralysis of muscles two origins, peripheral and central. In the peripheral there may be injury of the muscle itself, producing a temporary loss of power or disease of its parenchymatous substance, producing complete or partial destruction of the muscle, with a corresponding loss of function. To this I would liken the condition of the kidney substance in pure Bright's disease, uræmia being too comprehensive a term. On the other hand, a central origin may account for the muscular palsy. A degeneration, an injury of the motor area, or a tumor compressing it, may cause the trouble, and so it appears to me is the state in idiopathic epilepsy. There is a slowly progressing disease of some center or brain area not yet demonstrated, commencing often in early life and gradually extending to the rest of the brain substance, producing atrophy and sclerosis of important structures,

and finally ending in imbecility and terminal dementia. In epilepsy we have an actual disease of brain substance; no other process could bring about the pitable state of utter helplessness, such as some of the cases in our institution present. I have not had an opportunity for an examination of the epileptic brain, but the researches of Doctor Worcester, showing such changes as atrophy, with sclerosis of the hippocampus major; those of Barthez and Rilliet, finding sclerosis of the gray matter of the cortex; those of Bevan Lewis, showing degenerative changes in the second layer of the cortex, and of Eccheveria, describing changes in the sympathetic ganglia, as well as of Ziegler, revealing in some cases heterotopia, and of many other observers reporting various changes, warrant the belief that important alterations exist, although we have no exact data as to their special nature in all cases.

Treatment.	Date.	Reaction.	Specific Gravity.	Albumen.	Sugar.	Urea in Grammes per C. C.	Quantity of Urine in C. C.	Total Urea in Grammes.
None.	July 19.....	Slightly alk.	1015	None.	None.	.005	1184.0	5.920
"	" 20.....	Acid	1023	"	"	.01	1186.0	11.860
"	" 21.....	"	1022	"	"	.015	947.2	14.208
"	" 22.....	"	1010	"	"	.004	1420.8	5.683
"	" 23.....	"	1020	"	"	.011	660.4	7.264
"	" 24.....	Slightly alk.	1022	"	"	.015	1032.0	15.480
"	" 25.....	" .	1010	"	"	.006	1420.8	8.525
"	" 26.....	" .	1017	"	"	.008	1184.0	9.472
"	" 27.....	Acid	1020	"	"	.01	1006.4	10.064
"	" 28.....	"	1024	"	"	.01	948.4	9.484
"	" 29.....	"	1025	"	"	.012	1000.0	12.000
"	" 30.....	"	1024	"	"	.02	592.0	11.840
"	" 31.....	"	1030	"	"	.019	710.4	13.498
"	Aug. 1.....	"	1014	"	"	.011	1539.2	16.931
"	" 2.....	"	1025	"	"	.015	950.0	14.250
"	" 3.....	"	1015	"	"	.015	651.2	9.768
"	" 4.....	"	1030	"	"	.022	473.6	10.419
"	" 5.....	"	1022	"	"	.02	540.0	10.800
"	" 6.....	"	1023	"	"	.02	592.0	11.840
"	" 7.....	"	1025	"	"	.028	651.2	18.234
"	" 8.....	"	1025	"	"	.026	532.8	13.853
"	" 9.....	"	1023	"	"	.019	562.4	10.686
"	" 10.....	"	1015	"	"	.018	1716.8	30.903
"	" 11.....	"	1025	"	"	.024	710.4	17.049
"	" 12.....	"	1025	"	"	.025	478.0	11.950
"	" 13.....	"	1024	"	"	.02	680.8	13.616
"	" 14.....	"	1015	"	"	.008	1184.0	9.472
"	" 15.....	"	1020	"	"	.02	740.0	14.800
"	" 16.....	"	1015	"	"	.011	888.0	9.768
"	" 17.....	"	1015	"	"	.011	621.6	6.838
"	" 18.....	"	1012	"	"	.007	835.0	5.845
"	" 19	"	1015	"	"	.01	946.4	9.464

I wish to present the final result of some observations extending over a period of about six months upon two cases of idiopathic epilepsy — one of the grand mal and one of the petit type.

The first case, J. H., twenty-five years old, male, in good physical condition, has had attacks of major epilepsy since childhood. Family history negative. He came to the hospital in April, 1894, previous to which time he had been confined in two other State hospitals as a confirmed epileptic. He was very much demented upon admission, and subsequently had about three or four convulsions a week. Owing to the patient's greatly demented condition, considerable difficulty was experienced in collecting the urine, and it was finally necessary to confine him in a separate room before all the urine passed could be obtained. An examination of the urine of twenty-four hours, without treatment and with the ordinary hospital diet, for the first month, and without particular reference to convulsions, showed a large decrease in the total amount of urea from the normal, as is shown in the tabulated record on preceding page.

From this it will be seen that the amount of urea excreted is far below the normal average of 33.19 grammes per twenty-four hours — the average here being only 11.93 grammes. This is contrary to the results of Régis, who finds 25.17 grammes, which he says exceeds the normal by about two grammes. Observations were continued in this case, and particular attention was paid to the amount of urea excreted before and after the epileptic convulsions. All the urine passed by patient until the time of fit was considered to be before the convulsion — that excreted for eight hours after each attack was

	BEFORE.				AFTER.				TOTAL.	
	Specific Gravity.	Urea in Grammes per C. C.	Quantity of Urine in C. C.	Total Urea in Grammes.	Specific Gravity.	Urea in Grammes per C. C.	Quantity of Urine in C. C.	Total Urea in Grammes.	Total Urine in C. C. for 24 hours.	Total Urea in Grammes for 24 hours.
1	1020	.007	473.6	3.315	1022	.014	177.6	2.486	651.2	5.802
2	1020	.007	428.0	2.996	1024	.015	325.0	4.875	753.0	7.871
3	1022	.02	458.8	9.176	1020	.019	236.8	4.499	695.6	13.675
4	1006	.002	976.8	1.954	1010	.008	888.0	7.104	1864.8	9.058
5	1004	.001	1045.0	1.045	1028	.015	225.0	3.375	1270.0	4.420
6	1012	.003	478.0	1.434	1017	.01	472.0	4.720	950.0	6.154
7	1020	.019	450.0	8.550	1025	.02	200.4	4.008	650.4	12.558
8	1010	.004	505.0	2.020	1015	.007	855 0	5.985	1360.0	8.005
9	1020	.016	425.0	6.860	1022	.02	450.0	9.000	875.0	15.860

labeled as after the fit. A uniform variation in specific gravity and the amount of the urea present in the two specimens was invariable during a period of about four months' examination—the urine passed after the fit, having a higher specific gravity and a larger amount of urea per C. C., as shown in the foregoing table.

It will be seen by this table that, with one exception (Observation No. 3), the specific gravity and amount of urea was increased after each convulsion.

Case No. 2—L. F., a strong, healthy man, thirty-eight years old has had attacks of petit mal since the age of fifteen, which he believes were brought on by masturbation. The attacks occurred daily and were usually light, accompanied by the peculiar epileptic cry, but no convulsion occurred. At rare intervals he had convulsions of the grand-mal type. This patient was intelligent, and no difficulty was experienced in collecting all the urine, and the variation in amount of urea before and after the fit was more marked than in the previous case. The average amount of urea excreted was 11.57 grammes per twenty-four hours.

The following table shows the variation in amount of urea before and after convulsion :

	BEFORE.				AFTER.				TOTAL.	
	Specific Gravity.	Urea in Grammes per C. C.	Quantity of Urine in C. C.	Total Urea in Grammes.	Specific Gravity.	Urea in Grammes per C. C.	Quantity of Urine in C. C.	Total Urea in Grammes.	Total Urine in C. C. for 24 hours.	Total Urea in Grammes for 24 hours.
1	1012	.003	1243.2	3.630	1013	.005	769.6	3.848	2012.8	7.478
2	1007	.004	828.8	3.315	1017	.007	505.6	3.539	1334.4	6.854
3	1010	.005	888.0	4.440	1011	.007	562.4	3.937	1450.4	8.377
4	1010	.004	1657.6	6.730	1013	.006	296.0	1.776	1835.2	8.506
5	1011	.004	1420.8	5.683	1012	.007	769.6	5.787	1690.4	11.470
6	1008	.003	1685.2	5.056	1010	.008	450.3	3.602	2135.5	8.658
7	1011	.004	925.4	3.702	1012	.006	650.3	3.902	1575.7	7.603
8	1010	.004	940.2	3.761	1012	.008	1300.4	10.403	2240.6	14.164
9	1010	.006	1110.0	6.660	1014	.01	675.0	6.750	1785.0	13.310
10	1010	.006	1460.2	8.761	1010	.002	620.0	4.960	2082.0	13.761

These results led to the proposition that agents eliminating urea would have an influence upon the disease, and, with this idea in view, certain drugs were tried, combined with exercise. Particular attention was paid to digitalis, which was given in the form of the infusion, commencing with ʒ i and increasing to ʒ ss. Under this drug the

urine showed but little change — in Case No. 1 the urea fell below the average without drugs, being 9.30 grammes per twenty-four hours. In Case No. 2 the average was about the same as when no medication was used, being 11.32 grammes per diem. No decrease in the number of convulsions was noticed. Under the influence of the bromides the urea fell below the usual average in the first case, being 9.50 grammes per twenty-four hours. The convulsions were decreased in frequency, being six to nine of the previous month.

Sod. borate, used after the popular method of increasing the dose from time to time, caused in Case 1 no noticeable effect, either on convulsions or amount of urea excreted; in Case 2 it caused great loss of memory, anxiety, erotic dreams, and an alarming increase in frequency of the convulsions, and no effect on urea elimination; in two other epileptics marked eczema occurred, and in a fifth case catalepsy. In no case did the dose exceed gr. xxx T. i. d. Beta naphthol and belladonna showed but little influence over the disease. Opium in increasing doses is now being tried, and a decrease in the number of convulsions has been noticed, but no effect on urea has occurred, except to diminish it somewhat.

The purpose of these observations is, as I said in the beginning of my paper, to look more closely into the etiology of this interesting disease, idiopathic epilepsy. When we know the cause, then, and only then, can a rational treatment be advanced. Is the disease an auto-intoxication or one of central origin? Is it primarily an auto-intoxication with a poison which has a particular elective affinity for the brain structure, producing a gradual atrophy and deterioration of the latter? This latter theory seems to me the most tenable one, and the one toward which we should direct our observations — it is a cause of tangible origin, and gives to the etiology of epilepsy a rational and practical basis. Whether urea exercises a special influence in producing this auto-intoxication can not be stated from the above researches, but the fact remains that it is insufficiently eliminated, and this truth opens to us a new field — the study of the influence of toxic substances in the production not only of epilepsy, but all diseases of nervous origin.