THE LÆVULOSE TOLERANCE TEST IN PARALYSIS AGITANS.*

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THE publication, in 1912, of Kinnier Wilson's monograph on progressive lenticular degeneration⁸ first directed attention to the remarkable association of cirrhosis of the liver with softening and cavitation in the lenticular nucleus. Since that time it has been conclusively established that this association was by no means accidental but that liver disease is of constant occurrence in progressive lenticular degeneration and in the closely allied condition of Westphal's pseudosclerosis.

Of equal interest are the facts elicited concerning industrial poisoning by manganese. It is well known that a small proportion of workers in ores containing this metal develop, after a longer or shorter period of exposure, a clinical syndrome closely resembling that of paralysis agitans; in the one case which has come to autopsy Casamajor^{1, 2} found a condition of biliary cirrhosis in the liver, but made no mention of the state of the lenticular nucleus. Mella⁶ produced symptoms referable to the basal ganglia by the injection, into monkeys, of manganese chloride; after death cirrhosis of the liver and cellular changes in the basal ganglia were found.

In the more common diseases affecting the basal ganglia no gross damage to the liver has been observed, but the question has arisen whether this organ suffers from a functional disturbance during the course of the malady.

In encephalitis lethargica, of which Parkinsonism is so frequently a sequel, various writers have described histological changes in the liver, while others have studied the liver functions with varying results. O'Flynn and Critchley,⁷ who have made the most recent contribution to the subject, have not succeeded in demonstrating any definite failure in the activities of the liver.

The field for research in this direction, offered by idiopathic paralysis agitans, has not yet been exploited. Dresel and Lewy,³ investigating Vidal's hæmoelastic crisis in this condition, observed a post-prandial fall in the circulating leucocytes in each of thirteen cases. They also found that, while the fasting level of the blood sugar was not altered,

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the rise in it after 25 grm. of saccharose was greater than in controls suffering from other nervous and systemic diseases.

Giacomo,⁴ in a series of five cases, determined a slight and inconstant hyperglycæmia which he regards as due, not to the malady itself, but to associated arteriosclerotic and senile changes.

The present investigation, carried out upon a series of eighteen cases of idiopathic paralysis agitans, was made with the object of determining whether liver deficiency was demonstrable in any of these patients.

TECHNIQUE.

As the majority of the cases were out-patients of the hospital and often came from a considerable distance, it was impossible to perform upon each the complete series of tests for liver efficiency. One reaction was therefore chosen for the purposes of this research, and as the lævulose tolerance test is probably the most sensitive and satisfactory of those in use at the present time, it was the one selected.

The patient to be investigated was starved for a period of five hours and, after the percentage of sugar in the blood had been determined, was given 30 grm. of lævulose by the mouth. Readings were then taken at intervals of thirty minutes for one and a half hours. The sugar was estimated by Maclean's method⁵ immediately after removal of the blood.

The controls fell into two groups. The first group consisted of five organically healthy subjects, the second of four patients suffering from the effects of cerebral and general vascular disease.

RESULTS.

The figures obtained in the examination of five organically healthy subjects are given in the following table :—

TABLE I.

No.	Sex.	Age.	Blood Sugar percentage.			
			Fasting.	$\frac{1}{2}$ Hour.	1 Hour.	$1\frac{1}{2}$ Hours.
1	M.	37	0·120	0·134	0·130	0·120
2	F.	43	0·112	0·132	0·128	0·116
3	M.	56	0·130	0·160	0·145	0·126
4	M.	49	0·130	0·170	0·166	0·144
5	M.	39	0·126	0·158	0·136	0·133

The average age of these subjects was forty-five. The fasting level of the blood sugar varied from 0·112 per cent. to 0·130 per cent., the average being 0·124 per cent. The maximum rise after the administration of lævulose was in all cases obtained after half an hour and varied from 0·014 per cent. to 0·042 per cent., with an average of 0·029 per cent.

The results in the four cases of cerebral vascular disease were of a somewhat different order, and are shown in Table II.

TABLE II.

No.	Sex.	Age.	Blood Sugar percentage.			
			Fasting.	$\frac{1}{2}$ Hour.	1 Hour.	$1\frac{1}{2}$ Hours.
1	M.	68	0·160	0·150	0·150	0·158
2	M.	49	0·162	0·170	0·172	0·164
3	F.	35	0·150	0·162	0·168	0·154
4	M.	45	0·137	0·177	0·109	0·104

The average age of these patients was forty-nine. The fasting level of the blood sugar varied from 0·137 per cent. to 0·162 per cent., with an average figure of 0·152 per cent. In the first case the level of the blood sugar fell 0·01 per cent. after the administration of lævulose. In the remaining three cases the rise in blood sugar was respectively 0·01, 0·018 and 0·040 per cent., the average rise being 0·015 per cent. In the second and third cases the maximum rise was not obtained before the end of the hour.

The results obtained in the cases of paralysis agitans are given in Table III.

TABLE III.

No.	Sex.	Age.	Duration of Disease.	Blood Sugar percentage.			
				Fasting.	$\frac{1}{2}$ Hour.	1 Hour.	$1\frac{1}{2}$ Hours.
1	M.	50	$2\frac{1}{2}$ years	0·130	0·140	0·133	0·128
2	M.	50	8 "	0·124	0·140	0·136	0·126
3	M.	53	10 "	0·130	0·147	0·137	0·127
4	M.	60	3 "	0·134	0·140	0·137	0·134
5	M.	63	2 "	0·124	0·134	0·134	0·124
6	F.	49	2 "	0·106	0·112	0·106	0·106
7	M.	50	$1\frac{1}{2}$ "	0·106	0·122	0·112	0·104
8	M.	58	4 "	0·116	0·120	0·118	0·116
9	M.	45	3 "	0·144	0·164	0·154	0·150
10	F.	53	$1\frac{1}{2}$ "	0·130	0·152	0·144	0·132
11	M.	54	3 "	0·154	0·162	0·154	0·150
12	M.	58	3 "	0·134	0·153	0·153	0·143
13	F.	57	$1\frac{1}{2}$ "	0·142	0·166	0·156	0·138
14	M.	57	7 months	0·138	0·144	0·154	0·150
15	F.	66	9 "	0·136	0·180	0·156	0·130
16	F.	53	6 years	0·120	0·144	0·154	0·120
17	F.	39	2 "	0·158	0·184	0·184	0·168
18	F.	60	2 "	0·118	0·200	0·186	0·154

The average age of these patients was fifty-four. The fasting sugar

varied between 0·106 per cent. and 0·158 per cent., the average being 0·130 per cent. A more detailed analysis is shown below :—

Fasting Blood Sugar percentage.	No. of Cases.
Under 0·120	4
0·120 to 0·129	3
0·130 „ 0·139	7
0·140 „ 0·149	2
0·150 „ 0·159	2

The maximum rise in the blood sugar, attained in all but two cases after half an hour, varied between 0·004 per cent. and 0·044 per cent., except in Case 18, in which the rise was 0·082 per cent. The average rise was 0·021 per cent.

Rise in Blood Sugar percentage.	No. of Cases.
Under 0·01	4
Over 0·01 and under 0·02	7
„ 0·02 „ 0·03	4
„ 0·03 „ 0·04	1
„ 0·04 „ 0·05	1
„ 0·082	1

DISCUSSION.

A consideration of these results shows that, as regards the fasting level of the blood sugar, the average figure in paralysis agitans was slightly higher than that in normal controls; on the other hand, the average age of these cases was higher than in the controls. The maximum resting blood sugar found in the healthy controls was 0·130 per cent.; of the cases of paralysis agitans, seven exceeded this slightly (0·130 per cent. to 0·139 per cent.) and four considerably (0·140 per cent. to 0·159 per cent.). In the four controls suffering from cerebral vascular disease the average resting blood sugar was 0·152 per cent., the highest value being 0·162 per cent. It cannot therefore be assumed that the hyperglycæmia found in some of the cases of paralysis agitans is a distinctive feature of the disease; rather is it probable that the rise in the blood sugar level is due to coincident vascular disease, which is a common accompaniment of paralysis agitans.

The average rise in the blood sugar following the administration of lævulose was 0·021 per cent. in the cases of paralysis agitans as compared with 0·029 per cent. in the healthy controls. In Case 18 the rise was relatively enormous, amounting to 0·082 per cent.; the patient suffered from the effects of a myocardial degeneration of moderate severity, but otherwise appeared to be healthy except for the nervous affection. Apart from this case there was no material difference in reaction between the cases of paralysis agitans and the healthy controls; the rise in the blood sugar was, on the whole, less in the former.

CONCLUSIONS.

1. A certain degree of hyperglycæmia is commonly observed in paralysis agitans but is inconstant, while a similar degree also occurs in cerebral vascular disease; it seems probable, therefore, that this hyperglycæmia is the effect of coincident vascular disease and not of the nervous affection.

2. In paralysis agitans there is no definite evidence of liver deficiency as detected by the lævulose tolerance test. In only one of eighteen cases was an abnormal rise in the blood sugar found after the administration of lævulose.

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REFERENCES.

- ¹ CASAMAJOR, *Jour. Amer. Med. Assoc.*, 1913, lx, 646.
- ² CASAMAJOR, in *Diseases of Occupation and Vocational Hygiene*, by KOBER and HANSON, 1916, Sect. 6, 119-125.
- ³ DRESEL and LEWY, *Zeits. f. d. g. exp. Med.*, 1922, xxvi, 87, 95.
- ⁴ GIACOMO, *La Riforma medica*, 1925, xli, 1.
- ⁵ MACLEAN, H., *Modern Methods in the Treatment of Glycosuria and Diabetes*, London, 1924.
- ⁶ MELLA, H., *Arch. of Neurol. and Psychiat.*, 1924, xi, 405.
- ⁷ O'FLYNN and CRITCHLEY, *Lancet*, 1925, ii, 1329.
- ⁸ WILSON, S. A. K., *Brain*, 1912, xxxiv, 295.