THE COLLOIDAL BENZOIN CURVE IN THE CEREBROSPINAL FLUID.

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THE following investigation of the colloidal benzoïn curve was made on a series of cerebrospinal fluids from the wards and outpatient department of Guy's Hospital over a period of about eighteen months.

The technique followed was that of the modification described by Riddel and Stewart.¹

A stock solution of benzoïn is prepared by mixing 1 grm. of powdered benzoïn resin with 10 c.c. of absolute alcohol, allowing it to stand for forty-eight hours and then decanting the clear supernatant fluid. The colloidal emulsion is made by adding 0.3 c.c. of the stock solution slowly to 20 c.c. of distilled water heated to 35° C. This method gives a better emulsion than that originally described, in which the alcoholic solution is added to cold water and the mixture then heated to 35° C.

A second stock solution containing 0.01 per cent. pure sodium chloride is made; this solution occasionally grows micro-organisms and should then be discarded.

One c.c. of this salt solution is placed in each of six small test tubes and 1 c.c. of the cerebrospinal fluid to be examined is placed in the first test tube and the whole mixed. One c.c. of the mixture is removed and placed in the second test tube and the whole again mixed. One c.c. of this mixture is then transferred to the third test tube, and so on to the fifth tube, from which 1 c.c. is taken and discarded, the sixth tube being used as a control. One c.c. of the colloidal benzoïn solution is now added to each tube, mixed, and allowed to stand for twenty-four hours at ordinary room temperature. The tubes are inspected at the end of six hours and twenty-four hours. The method of reading is as follows: Complete discharge of the suspension, giving a white precipitate with a clear fluid above, is called 2.

Partial discharge, giving a fluid still opaque, but not so opaque as the control, is called 1, and no discharge, the fluid equalling the control in opacity, is called 0. No advantage is gained by grading the degree of partial precipitation as described by Wright and Kermack² in two papers containing an excellent discussion of the theory of the reaction. A comparison of results by both methods failed to furnish any increased information from a diagnostic point of view with the more elaborate technique.

Special care as to the distilled water or the washing of the glass-ware used is not required, ordinary laboratory technique being all that is necessary.

TABLE I.—*Tuberculous Meningitis.*

No.	Case.	Cells. Per c.mm.	Protein. Per cent.	Benzoin curve.		Notes.
				6 hours.	24 hours.	
1	J.B.	10	0.18	00000	00000	
2	S.C.G.	20	0.10	01002	12002	
3	J.D.	58	0.20	00000	00000	
4	M.H.	52	0.11	00002	00002	
5	E.J.	86	0.10	00002	11002	
6	S.H.	258	0.18	02212	...	
7	T.R.	++	0.10	11112	22222	
8	A.F.	66	0.085	00002	00002	

TABLE II.—*Septic Meningitis.*

No.	Case.	Cells. Per c.mm.	Protein. Per cent.	Benzoin curve.		Notes.
				6 hours.	24 hours.	
9	N.R.	++	0.14	22211	22211	Mastoid.
10	A.D.	640	0.05	...	10002	Mastoid, before operation.
	...	2000	0.11	11000	...	Mastoid, after operation.
						This case recovered.
11	M.K.	> 400	0.15	00001	...	Otitis media.
12	E.M.	+	+	22222	22222	Pneumococcal meningitis.
13	W.G.	640	0.20	22200	22211	Cerebrospinal meningitis.

TABLE III.—*Encephalitis Lethargica.*

No.	Case.	Cells. Per c.mm.	Protein. Per cent.	Sugar. Per cent.	NaCl. Per cent.	Benzoin curve.		Notes.
						6 hours.	24 hours.	
14	G.W.	0	0.02	...	...	00000	00000	Acute stage passed.
15	A.R.	7	0.015	...	...	00000	00000	Acute stage.
16	B.	0	0.01	...	...	00002	00002	Acute stage.
	...	1	0.04	0.086	0.73	...	...	Acute stage passed.
17	S.H.	0	0.04	0.083	0.81	00001	00001	Acute stage passed.
18	B.G.	0	0.025	...	...	00000	00000	
19	E.P.	2	0.03	0.076	0.82	00002	00002	Acute stage passed.
20	R.E.	3	0.04	0.088	0.80	00002	00002	Acute stage passed.
21	E.M.	0	0.04	0.081	0.79	00001	00001	Acute stage passed.
22	E.J.	4	0.04	0.073	0.82	22112	22122	Acute stage passed.
23	F.B.	1	0.04	...	...	00002	00002	
24	E.T.	0	0.05	...	...	00001	...	Subacute.

TABLE IV.—*Fits (Jacksonian, Epileptic, Idiopathic).*

No.	Case.	Cells. Per c.mm.	Protein. Per cent.	Wassermann.		Benzoin curve.		Notes.
				Blood.	C.S.F.	6 hours.	24 hours.	
25	A.R.	2	0.025	...	...	00000	00000	Age 1 year. Idiopathic fits.
26	E.J.	0	0.025	—	—	00000	00000	Petit mal.
27	B.	0	0.02	—	—	00000	00000	Epilepsy.
28	F.V.	1	0.02	+	—	00001	00002	Fits. ? Epilepsy.
29	G.F.	1	0.02	...	—	00001	00001	Epilepsy.
30	G.G.	0	0.03	...	—	00001	00002	Epilepsy.
31	W.R.	0	0.02	—	—	00000	00000	Jacksonian epilepsy.
32	G.F.	0	0.02	...	...	00000	00000	Age 2 years. Idiopathic fits.
33	L.R.	1	0.02	—	—	00002	00002	Epilepsy.
34	S.G.	0	0.02	—	—	00000	00000	Epilepsy.

TABLE V.—*Disseminated Sclerosis.*

No.	Case.	Cells. Per c.mm.	Protein. Per cent.	Wassermann.		Benzoin curve.		Notes.
				Blood.	C.S.F.	6 hours.	24 hours.	
35	F.T.	2	0.08	—	—	00000	00000	
36	J.H.	0	0.06	...	—	00001	11001	
37	E.B.	0	0.07	...	...	00000	01002	
38	M.T.	0	0.03	—	—	00000	00000	
39	R.K.	0	0.05	—	—	00000	00000	

TABLE VI.—*Miscellaneous Lesions of C.N.S.*

No.	Case.	Cells. Per c.mm.	Protein. Per cent.	Wassermann.		Benzoin curve.		Diagnosis.
				Blood.	C.S.F.	6 hours.	24 hours.	
40	B.C.	2	0.18	...	—	11222	22222	Polyneuritis.
41	S.L.	0	0.025	—	—	00002	00002	Peripheral neuritis.
42	R.C.	0	0.02	...	...	00002	00002	Polyneuritis.
43	F.C.	0	0.025	—	—	00000	00000	Polyneuritis, ataxic.
44	A.W.	?	0.035	—	—	10000	21001	Peripheral neuritis, blood present.
45	A.A.	4	0.05	...	—	00000	11001	Midbrain tumour.
46	M.Y.	0	0.025	—	—	00000	...	Tuberculoma.
47	M.J.	0	0.02	±	—	00000	00000	? Tumour. Cerebral.
48	M.D.	0	0.15	—	—	00000	00000	Tumour. Spinal.
49	W.B.	1	0.24	—	—	00000	00000	Tumour. Spinal.
50	E.B.	1	0.06	—	—	00000	00000	? Tumour. Cerebral.
51	A.M.	4	0.025	+	—	00000	00000	Amyotrophic lateral sclerosis.
52	M.D.	1	0.02	—	—	00002	...	Progressive muscular atrophy.
53	H.B.	1	0.04	—	—	00000	00000	? Progressive muscular atrophy.
54	R.B.	1	0.045	—	—	00000	00000	Subacute combined degeneration.
55	J.B.	0	0.03	...	—	00000	00000	Lateral sclerosis.
56	A.S.	1	0.03	—	—	00000	00000	Progressive double hemiplegia.
57	G.T.	2	0.035	++	—	00000	00000	Erb's spastic paraplegia.
58	A.S.	25	0.04	—	—	00001	10001	Subarachnoid hæmorrhage. Fluid tinted yellow. Van den Bergh's reaction indirect positive. Some blood present.

TABLE VI.—*Miscellaneous Lesions of C.N.S.—(Continued.)*

No.	Case.	Cells. Per c.mm.	Protein. Per cent.	Wassermann.		Benzoin curve.		Diagnosis.
				Blood.	C.S.F.	6 hours.	24 hours.	
59	F.P.	2	0.035	+	—	00000	00000	Aphasia.
60	W.T.	0	0.08	—	—	00000	00000	Hemiplegia : arteriosclerosis.
61	G.M.	2	0.04	—	—	00000	...	Cerebral arteriosclerosis.
62	W.S.	1	0.04	—	—	00000	00000	Cerebral arteriosclerosis.
63	A.H.	2	0.035	—	—	00000	00000	Cerebral arteriosclerosis.
64	F.J.	3	0.045	—	—	00000	00000	Cerebral thrombosis.
65	G.W.	4	0.04	—	...	00012	00022	Hydrocephalus : septicæmia.

TABLE VII.—*Miscellaneous Diseases.*

No.	Case.	Cells. Per c.mm.	Protein. Per cent.	Wassermann.		Benzoin curve.		Notes.
				Blood.	C.S.F.	6 hours.	24 hours.	
66	S.W.	0	0.06	...	...	00000	11112	Uræmia. Urea in C.S.F., 0.45 per cent. (Stale specimen.)
67	J.S.	1	0.02	...	...	00001	00002	Septicæmia.
68	F.C.	0	0.04	...	—	...	00000	Diabetes. Sugar in C.S.F., 0.20 per cent.
69	A.C.	0	0.02	—	—	00000	00000	? Congenital syphilis.
70	A.G.	0	0.025	—	—	00000	00000	Chronic alcoholism.
71	P.T.	2	0.025	—	—	00000	00000	Mitral stenosis.
72	C.R.	0	0.025	—	—	00001	10001	Gastric ulcer.

TABLE VIII.—*Neuroses, etc.*

No.	Case.	Cells. Per c.mm.	Protein. Per cent.	Wassermann.		Benzoin curve.		Notes.
				Blood.	C.S.F.	6 hours.	24 hours.	
73	E.S.	1	0.04	—	—	00001	00002	Hysterical vertigo.
74	C.M.	0	0.03	—	—	00000	00000	Psychasthenia.
75	G.J.	0	0.02	...	—	00000	00001	Persistent headache.
76	M.G.	0	0.03	...	...	00000	00000	Normal.
77	R.L.	2	0.025	—	—	00000	00000	Psychoneurosis.
78	P.H.	0	0.03	—	—	00000	00000	Syphilophobia.
79	A.H.	0	0.03	—	—	00000	00000	Anxiety hysteria.
80	J.K.	1	0.02	—	—	00000	00000	Hypochondriasis.
81	C.B.	0	0.025	—	—	00002	00002	Normal.
82	C.G.	2	0.04	...	—	00000	00000	Hysterical vertigo.
83	F.P.	0	0.04	—	—	00000	01000	Anxiety neurosis ?
84	J.D.	0	0.05	—	—	00000	00000	Hysteria.
85	T.S.	0	0.025	++	—	00000	00000	Neurosis.
86	W.G.	2	0.04	++	—	00000	00000	Neurosis.

TABLE IX.—*G.P.I.*

No.	Case.	Cells. Per c.mm.	Protein. Per cent.	Wassermann.		Benzoin curve.		Notes.
				Blood.	C.S.F.	6 hours.	24 hours.	
87	W.A.	3	0.09	++	++	22222	...	
88	E.L.	22	0.09	++	++	22222	...	
89	E.S.	6	0.04	++	++	22222	...	
90	J.H.	89	0.10	++	++	22222	...	
	...	37	0.10	...	...	22222	...	
	...	18	0.07	...	...	22222	...	
91	W.B.	40	0.09	++	++	22222	...	
92	T.G.	?	0.06	++	++	22222	...	Much blood. No blood.
	...	23	0.04	++	++	12222	...	
93	A.B.	124	0.06	++	++	22222	...	
94	H.F.	56	0.09	++	++	12210	22220	
95	E.V.	9	0.07	++	++	22222	...	
96	W.M.	55	0.07	++	++	22222	...	
97	H.M.	7	0.05	++	++	22222	...	
98	J.P.	7	0.04	++	++	22200	...	

TABLE X.—*Meningovascular Syphilis.*

No.	Case.	Cells. Per c.mm.	Protein. Per cent.	Wassermann.		Benzoin curve.		Notes.
				Blood.	C.S.F.	6 hours.	24 hours.	
99	C.M.	0	0.04	+	—	00000	00000	
100	J.C.	45	0.04	+	—	00000	00000	
101	W.O.	0	0.025	+	—	00000	00000	
102	A.T.	0	0.02	++	—	00000	00000	
103	A.K.	4	0.08	++	—	00000	00000	
104	A.C.	12	0.03	++	—	00002	00002	

TABLE XI.—*Tabes Dorsalis.*

No.	Case.	Cells. Per c.mm.	Protein. Per cent.	Wassermann.		Benzoin curve.		Diagnosis.
				Blood.	C.S.F.	6 hours.	24 hours.	
105	E.P.	?	0.07	++	++	00001	11102	Blood present.
106	G.J.	48	0.08	++	++	12222	22222	
107	A.F.	0	0.025	+	—	00000	00000	
108	F.D.	9	0.045	++	++	00000	01101	
109	E.S.	3	0.085	++	++	02210	12221	
110	W.B.	0	0.02	++	—	00000	00000	Had intensive antisyphilitic treatment.
111	L.C.	44	0.35	+	++	11112	21112	Fluid had yellow tint.
112	W.B.	1	0.07	+	+	00000	11000	
113	C.W.	0	0.035	++	—	00000	01100	
114	G.G.	8	0.04	++	++	00000	00000	Had intensive antisyphilitic treatment.
115	T.H.	84	0.06	++	++	11102	22212	Had intensive antisyphilitic treatment.
116	A.M.	35	0.04	—	—	12100	22210	

TABLE XI.—*Tabes Dorsalis*.—(Continued.)

No.	Case.	Cells Per c.mm.	Protein. Per cent.	Wassermann.		Benzoin Curve.		Diagnosis.
				Blood.	C.S.F.	6 hours.	24 hours.	
117	W.M.	35	0.06	++	++	12212	12212	Had intensive antisyphilitic treatment.
118	H.P.	0	0.048	++	—	11211	22211	
119	W.P.	5	0.04	++	++	...	12102	
120	Y.	18	0.04	++	++	01101	12201	Had intensive antisyphilitic treatment.
121	F.W.	0	0.02	++	—	00001	01000	
122	A.S.	0	0.06	++	++	22210	22221	
123	M.T.	3	0.04	—	+	01100	01100	
124	M.L.	12	0.04	++	++	11110	11210	
125	M.G.	19	0.04	++	++	22220	22220	
126	K.A.	8	0.025	++	++	01212	12212	
127	F.S.	0	0.04	++	—	00001	00002	

SUMMARY OF TABLES.

I. In meningitis, both tuberculous and septic (Tables I. and II.), a positive result is obtained, usually of the tabetic, but occasionally of the paretic type.

II. In encephalitis lethargica (Table III.), with one exception (Case 22), a negative curve is obtained. The figures obtained for sugar and sodium chloride are recorded in some postencephalitic cases as perhaps being of some interest, both being somewhat above normal.

III. In epilepsy and allied conditions (Table IV.) negative results are obtained.

IV. In disseminated sclerosis (Table V.) all are negative at six hours, a slight precipitation occurring after twenty-four hours in two cases.

V. In Table VI. a series of miscellaneous cases with some lesion of the C.N.S. are recorded, the majority of which are negative. A definite positive in six hours is obtained only once in a case of polyneuritis (No. 40), and in twenty-four hours weak positive results are obtained in two other cases: peripheral neuritis (No. 44), midbrain tumour (No. 45).

VI. In Tables VII. and VIII. are recorded cases having presumably no lesion of the C.N.S. In six hours all are negative, and at the end of twenty-four hours one positive result only occurs—No. 66, a case of uræmia.

VII. In general paralysis (Table IX.) in all but two cases complete precipitation of all five tubes occurs in six hours. In the remaining two cases there is precipitation in three or four tubes only. The Wassermann test is positive in all cases.

VIII. In meningovascular syphilis (Table X.), on the contrary, no precipitation occurs, even after twenty-four hours. In every case the Wassermann reaction in the C.S.F. is negative. Riddel and Stewart, however, record some cases of meningovascular syphilis in which there was a positive Wassermann reaction and a tabetic type of curve.

IX. In tabes (Table XI.) thirteen out of twenty-three cases show precipitation in the second and third tubes or more, within six hours. In twenty-four hours, seventeen cases show precipitation of the second and third tubes and two others precipitation of the second tube, but not the third.

Several curves (Nos. 107, 118, 123, and 126) give results closely resembling the typical paretic curves in six hours, and at the end of twenty-four hours No. 107 resembles the typical paretic curve, and in many others there is complete precipitation in four tubes and partial precipitation of the remaining one.

The Wassermann reaction is positive in sixteen cases, being positive twice when the benzoïn curve is negative, and negative three times when the benzoïn curve is positive.

DISCUSSION.

The benzoïn curve, except in such gross disturbances of the C.S.F. as occur in meningitis, is positive in this series only in general paralysis and tabes, with the following three exceptions—Case 22, encephalitis lethargica; Case 40, polyneuritis; and Case 66, uræmia. On the other hand, it is negative in six cases of tabes. There does not appear to be any sharp dividing line between the curves in tabes and general paralysis, but omitting, as before, cases of meningitis, no case other than G.P.I. gives complete precipitation in all five tubes in six hours. If reading is delayed to sixteen or twenty-four hours this useful point of distinction is lost. In tabes greater ease of reading and a larger percentage of positive results is obtained by waiting twenty-four hours. The maximum amount of information is obtained by reading at both six and twenty-four hours. While the type of reaction in G.P.I. is quite definite, that in tabes is much less well defined. An inspection of the results shows that partial or complete precipitation in at least both second and third tubes should occur before the curve can be labelled tabetic. In some of the cases of tabes which failed to give a tabetic curve, precipitation occurred in the second tube, but not the third; as a similar precipitation occurred in several non-tabetic cases, not much importance can be attached to such a result in the diagnosis of tabes. Precipitation in the first, or first and second tubes, also occurred several times in non-tabetic cases having some organic lesion of the central nervous system. The exact significance of such a typical curve is not yet apparent.

Precipitation in the fifth tube occurs in about 20 per cent. of the apparently normal cases and would seem to have no significance; there is, however, a tendency for precipitation to occur more frequently in encephalitis lethargica and epilepsy.

With regard to the Wassermann reaction, in ninety-seven cases in which both the benzoin curves and the Wassermann reaction were obtained both were negative in sixty-four, both were positive in twenty-seven, in four cases (three cases being tabes) the Wassermann was negative and the benzoin curve was positive, and in two cases (both tabes) the Wassermann was positive and the benzoin curve negative.

This gives a somewhat too favourable comparison, however, as the Wassermann reaction was not done in all cases of meningitis and encephalitis, while the benzoin curve often gave a positive result. There would appear, however, to be quite a marked parallelism between the two reactions.

CONCLUSIONS.

I. A typical reaction is obtained in most cases of G.P.I. in six hours.

II. Curves of the tabetic type are obtained in about 70 per cent. of tabetics at the end of twenty-four hours.

III. Negative curves are obtained in meningovascular syphilis.

IV. The results of the benzoin curve, while not being absolutely diagnostic, are sufficiently reliable to be of considerable value in the diagnosis of G.P.I. and tabes.

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