THE COLLOIDAL BENZOIN REACTION IN THE CEREBRO-SPINAL FLUID COMPARED WITH OTHER TESTS.

BY

J. A. BRAXTON HICKS, M.D., M.R.C.P., D.P.H.,
PATHOLOGIST, WESTMINSTER HOSPITAL, AND CONSULTING PATHOLOGIST,
WEST END HOSPITAL FOR NERVOUS DISEASES;

AND

JOHN PEARCE, M.R.C.S., L.R.C.P.,
RESEARCH STUDENT, WESTMINSTER HOSPITAL MEDICAL SCHOOL.

THE object of this work was to test the colloidal benzoïn reaction (C.B.R.) under routine hospital conditions, comparing it with the other well known tests carried out simultaneously on the same specimens. The cases (over 200 in number) were chiefly derived from the wards and out-patient departments of the Westminster Hospital and the West End Hospital for Nervous Diseases, and we wish to acknowledge our indebtedness to the staff of both hospitals.

In classifying our results we have used the diagnoses received with the specimen of cerebro-spinal fluid. It must be clearly understood, however, that in many cases the diagnosis was admittedly tentative, and, indeed, depended on the result of the examination. Thus such comments as we may make on the diagnoses are entirely without prejudice.

The routine examinations made on every specimen of fluid were cytology, globulin reaction (G.R.), albumin percentage, Wassermann reaction (W.R., using Method 4 of the Medical Research Council). In many cases also the Wassermann reaction was done on the blood, but not in all cases. The full technique of the colloidal benzoïn reaction may be obtained from that most excellent pamphlet, *La Réaction du Benzoïn Colloïdal*, by G. Guillain, G. Laroche, and P. Lechelle (1922).

Technique (in brief).

(1) The gum benzoïn must be the *Sumatra* gum, obtained as the natural product in brown masses containing white or yellowish-white lumps. One gram of the freshly powdered Sumatra resin is dissolved in 10 c.cm. of absolute alcohol. This is well shaken and left to stand for forty-eight hours. It is then decanted and 0.3 c.cm. of the clear fluid slowly added to 20 c.cm. of twice distilled water at 35° C. A homogeneous suspension is thus obtained. This suspension must always be freshly prepared for each batch of tests.

(2) A 0.01 per cent. solution of chemically pure sodium chloride, in water twice distilled through a glass condenser.

(3) For each fluid to be examined a series of 6 or 12 test tubes is put up. Into the first tube 0.25 c.cm. of the saline solution (0.01 per cent.) is placed, into the remaining tubes 1 c.cm. of saline. Then 0.75 c.cm. of the cerebro-spinal fluid under examination is measured into the first tube and 1 c.cm. of the cerebro-spinal fluid into the second tube; 1 c.cm. from the second tube is put into the third tube, mixing thoroughly; 1 c.cm. from tube 3 is put into tube 4, and so on till the penultimate tube is reached, when, after mixing, 1 c.cm. is discarded. Thus the last tube contains only saline, which acts as the control tube. To each tube, including the control, add 1 c.cm. of the gum benzoïn suspension and mix thoroughly. Allow to stand on the laboratory bench some twelve hours before reading.

The reading of the tubes is simple, three degrees of precipitation being recognized, and these can be graphically represented by the numerals 0, 1, and 2. In the first of these (0) no change occurs, the fluid remaining as in the control tube without any precipitate. The next degree shows some precipitation, but the fluid still remains opaque; this is designated 1. In the third there is complete precipitation, the supernatant fluid being quite clear: this is called 2.

There are two types of readings which may be regarded as "negative" or "normal." One type shows no change whatever, reading as 0 in all five or eleven tubes (Chart 1); the other types give a precipitate in tubes 7 to 9 inclusive (Chart 2). In these tubes the reading may be either 1 or 2.

The readings which we have considered as being "positive" (that is, in tabes, general paralysis of the insane, etc.), and are classified as such in the following tables, consist of three types: (a) complete precipitation in all tubes (Chart 3); (b) certain

undoubted "positives" have shown a slight deviation from this rule, but usually only in tube 11, 10, or 9; while (c) some have remained opaque in the first tube, or three-quarters dilution. Thus the "positive" sign in the following results is used

CHART 1.—An example of a "normal" curve in a case of tuberculous meningitis (confirmed post mortem).

to represent a series of complete precipitation in the first five tubes at least, and in most of our cases the entire eleven tubes. In certain fluids, in which a trace of blood was present, the

CHART 2.—An example of a "normal" curve in a case of cerebral tumour (confirmed post mortem).

zone between tubes 7 and 9 is increased as far as 6 and 10. These have been regarded as negatives, but it must be remembered that the presence of much blood renders the fluid quite

CHART 3.—Composite chart of "positive" curves seen in cases of syphilis of the nervous system.

unsuitable for this test. Any other deviation—namely, precipitation, complete or incomplete—in tubes 1 to 6, which does not follow the rules above stated, has been separately recorded in the tables that follow.

Cases Diagnosed as Tabes (59).

Group.	No. of Cases.	Cerebro-spinal Fluid.			Blood.		
		G.R.	W.R.	C.B.R.	W.R. +.	W.R. -.	Not done.
A	21	—	—	—	4	13	4
B	30	+	+	+	16	13	1
C	1	+	+	—	1		
D	4	+	—	—		4	
E	3	—	+	—	1		2

In Group A of the cerebro-spinal fluid tests which were negative, only two showed a cell count of over 6 per c.mm.—namely, 8 and 17.3. One knows that in this particular group of cases the diagnoses were of a purely tentative nature. Thirteen of these "suspects" were negative in the blood also, and at the most four failed to respond to any of the tests for syphilis. As far as our efforts went to track the final diagnosis in this group (A) we only found two in which the clinical evidence was such that tabes could not be excluded.

In Group B there is no need for much comment, save that the cell counts ranged from less than 1 per c.mm. to 160 per c.mm. The percentage results of the blood Wassermann reaction are about the usual figure for tabetics. In Group C the cell count (examined twice on two separate samples) was 9 and 9.4 per c.mm. respectively. In Group D the cell counts were 5.4, 1.4, and 2.7 per c.mm.; and having regard to the blood Wassermann reaction these may be regarded as non-syphilitic, though we offer no explanation for the globulin reaction being positive. In Group E the cell counts were 8, 13.3, and 24 per c.mm., and in contrast to Group D these results are very interesting.

Cases Diagnosed as General Paralysis of the Insane (16).

Group.	No. of Cases.	Cerebro-spinal Fluid.			Blood.		
		G.R.	W.R.	C.B.R.	W.R. +.	W.R. -.	Not done.
A	12	+	+	+	5		7
B	1	-	+	-	1		
C	3	-	-	-		3	

In Group A the cytology varied from 4 to 101 cells per c.mm. In Group B the cells numbered 4 per c.mm.; in Group C the cell counts were respectively 1.4, 2, and less than 1 per c.mm.; this last group calls for no further comment since general paralysis of the insane is excluded definitely from the diagnosis.

Cases Diagnosed as Cerebral or Spinal Syphilis (16).

Group.	No. of Cases.	Cerebro-spinal Fluid.			Blood.		
		G.R.	W.R.	C.B.R.	W.R. +.	W.R. -.	Not done.
A	6	+	+	+	4	1	1
B	10	-	-	-	1	4	5

In Group A the cells varied from 4 to 6 per c.mm.—a very low figure considering the striking positive results. In Group B, with the exception of one case, the cells ranged from 1 to 6 per c.mm. In the single exception the cells were 72 per c.mm., and this case subsequently *post mortem* was found to have tuberculous meningitis.

Cases with a Diagnosis of Doubtful Syphilis of the Nervous System (27).

Group.	No. of Cases.	Cerebro-spinal Fluid.			Blood.		
		G.R.	W.R.	C.B.R.	W.R. +.	W.R. -.	Not done.
A	4	+	+	+	2		2
B	1	+	-	-	1		
C	22	-	-	-	2	18	2

In Group A the cytology varied from 3 to 95 cells per c.mm. In Group B the cells were 93 per c.mm., and *post mortem* the case was found to be tuberculous meningitis. The man gave also a history of syphilis, which is most interesting in view of the blood result. In Group C the cell counts were less than 6, with the exception of one case which showed 26.7 per c.mm., and subsequently proved to be an acute mastoid.

The diagnoses of Groups A, B, and C were made up as follows: cavernous sinus thrombosis, cerebral diplegia (2), frontal lesions (2), optic neuritis (2), functional monoplegia, hemiplegia (3), bulbar palsy, sciatic neuritis (2), spastic paraplegia, post-herpetic neuralgia, lower brachial root palsy, paraplegia, internal ophthalmoplegia, aortitis, congenital syphilis (2), trigeminal neuralgia, cerebral tumour, no diagnosis (3).

It seems to us that the results of the colloidal benzoïn reaction in this group of cases are of great value from a diagnostic point of view; and, further, Group B brings out a good point—that a positive blood Wassermann reaction should not be allowed to bias one's opinion in considering the results of cerebro-spinal fluid findings. Each case must be considered on its merits.

Cases Diagnosed as Disseminated Sclerosis (10).

Group.	No. of Cases.	Cerebro-spinal Fluid.			Blood.		
		G.R.	W.R.	C.B.R.	W.R. +.	W.R. -.	Not done.
A	6	-	-	-		3	3
B	1	+	-	-		1	
C	1	+	-	Slight		1	
D	2	-	-	Slight		2	

The cells in Group A varied from 1.4 to 8 per c.mm., the cells in Group B were 1 per c.mm., the cells in Group C 13.3 per c.mm., and in Group D 12 and 14 per c.mm., respectively. The graphic records of the colloidal benzoïn reaction curves are as follows: Group C case, 012210, and in Group D 021200 and 011000. These slight changes correspond to those found in some cases by G. Guillain and his co-workers.

Cases Diagnosed as Meningitis (10).

Group.	No. of Cases.	Cerebro-spinal Fluid.			Blood.		
		G.R.	W.R.	C.B.R.	W.R. +.	W.R. -.	Not done.
A	4	-	-	-		4	
B	6	+	-	Slight		5	1

In Group A the cells varied from less than 1 per c.mm. to 10.7 per c.mm., in Group B from 45.4 to 2,071 per c.mm., and all these 6 cases were confirmed *post mortem*. The graphic records of the colloidal benzoïn reaction in Group B are as follows: 211010, 111120, 111010, 011000, 011011, 010110; these, again, are similar to those found by other workers.

Cases Diagnosed as Cerebral Tumour (9).

Group.	No. of Cases.	Cerebro-spinal Fluid.			Blood.		
		G.R.	W.R.	C.B.R.	W.R. +.	W.R. -.	Not done.
A	3	-	-	-	1	2	
B	5	+	-	-		4	1
C	1	+	-	Slight		1	

The cells were not in excess in any group. In Group B the diagnosis was in all cases confirmed *post mortem*. The graphic record of the colloidal benzoïn reaction in Group C is 0112222222.

Cases Diagnosed as Encephalitis Lethargica (10).

Group.	No. of Cases.	Cerebro-spinal Fluid.			Blood.		
		G.R.	W.R.	C.B.R.	W.R. +.	W.R. -.	Not done.
A	1	+	-	-			1
B	9	-	-	-			9

The cells in Groups A and B varied from 4 to 253, and this last case three weeks later had completely recovered and had a cell count of 4 per c.mm.

Miscellaneous Diagnoses, Chiefly of Nervous System (50).

Group.	No. of Cases.	Cerebro-spinal Fluid.			Blood.		
		G.R.	W.R.	C.B.R.	W.R. +.	W.R. -.	Not done.
A	44	-	-	-	3	15	26
B	5	+	-	-		1	4
C	1	+	-	Slight		1	

The diagnoses of Group A were as follows: neurasthenia and hysteria 6, imbeciles 2, Parkinson's disease 3, epilepsy 3, cerebral thrombosis 2, spastic paraplegia 2, anterior poliomyelitis, lateral sclerosis, progressive muscular atrophy, pseudo-hypertrophic muscular dystrophy, syphilitic aortitis, hemiplegia 2, traumatic neuritis, syringomyelia, malignant endocarditis, incontinence, syncope, myopathy, gastric ulcer, no diagnosis 12. In Group B the diagnoses were: imbecile, myopathy, no diagnosis (3). In Group C the case was one of hemiplegia, and the graphic record of the colloidal benzoïn reaction was 011000. The cells were not in excess in any of these groups.

CONCLUSIONS.

1. In the colloidal benzoïn reaction we seem to have a simple test very nearly as sensitive to syphilis of the central nervous system as the Wassermann reaction.

2. It is not quite as sensitive as the Wassermann reaction, as the results of this investigation show. This is particularly well seen in the table relating to tabes.

3. We cannot agree, as is maintained by some, that there is a characteristic "luetetic" curve as contrasted with a "paretic" curve. It is true that some cases of tabes show less tendency to precipitate in tubes 9, 10, and 11, but so did one or two cases of undoubted general paralysis of the insane.

4. A positive result (that is, precipitates in tubes 1 to 6 at least) is not obtained with any disease other than

syphilis of the central nervous system so far as we have been able to ascertain.

5. Definite changes (other than a complete positive, and in the absence of blood) indicate apparently some definite pathological change in the cerebro-spinal fluid; but all pathological fluids do not necessarily show any colloidal benzoïn reaction.

AN EFFICIENT INTESTINAL ANTISEPTIC:

THE PERCHLORIDES OF MERCURY AND IRON
IN COMBINATION.

BY

T. STACEY WILSON, M.D. EDIN., F.R.C.P.,
CONSULTING PHYSICIAN, BIRMINGHAM GENERAL HOSPITAL.

SOME recent correspondence in the *BRITISH MEDICAL JOURNAL* has prompted me to bring forward the following evidence that a combination of the perchlorides of mercury and iron constitutes an efficient intestinal antiseptic.

My attention was first drawn to the value of this remedy by a short notice in this *JOURNAL* for May, 1894, by Dr. W. B. Wedgwood of King's Lynn, who wrote recommending its use in enteric fever, and suggesting a dose of 30 minims of liquor hydrargyri perchloridi and 20 minims of tinctura ferri perchloridi. Ever since that time I have used these two drugs as an intestinal antiseptic, combined with a little glycerin and chloroform water, but have found that 15 minims of each is quite sufficient to give a good result in those cases in which it is indicated, and I have every reason to be extremely thankful to Dr. Wedgwood for having drawn my attention to this remedy.

In Enteric Fever.

I first tried this prescription in a comparative test in enteric fever, for I took a hundred consecutive cases, of whom one-third had been treated with mercury and iron, one-third with sulphurous acid, and the remainder in various other ways. They were divided into groups according to the number of days that the pyrexia lasted after their admission to the hospital. The average height of the temperature was then ascertained for each group by dividing the week into two portions and taking the average morning and evening temperature for each case during each half-weekly period. The general run of the temperatures as thus averaged proved to be wonderfully uniform in all the groups, and so far as the morning temperature was concerned the average rate of fall of the temperature was not appreciably influenced by the treatment adopted. In the case of the evening temperature, however, where mercury and iron had been given, the average was more than a degree lower than where other treatment had been adopted.

The reliability of the test in this series of cases was enhanced by the fact that they were all in charge of the same two ward sisters, and the excellence of the nursing was shown by the fact that there were only three deaths out of the hundred consecutive cases.

Owing to the fact that few of the patients came into the hospital during the first week it was not possible to decide as to the effect of the mercury and iron treatment upon the total duration of the pyrexia, but where this treatment was adopted the case appeared to run a shorter and more favourable course. One of the fatal cases gave evidence as to the potency of the antiseptic action of this combination. It was complicated by acute nephritis, and during the first ten days of his illness the patient had given himself a liberal allowance of roast beef and mutton. He died somewhat suddenly a few hours after an injection of morphine given by a resident on his own initiative, and at the *post-mortem* examination over two hundred ulcers were found in the intestine, many of them quite deep, but all free from sloughs and all looking remarkably healthy and showing signs of healing. The unusually satisfactory condition of the ulcers considering their size and depth seemed to be distinctly traceable to the mixture which he had been taking every four hours for nearly two weeks.

In Colitis and Dysentery.

Evidence of the antiseptic value of the mercury and iron mixture is given also by its efficiency in acute and subacute colitis, especially when of the ulcerative type, and it often causes very rapid improvement in cases which have resisted other methods of treatment. The mixture proves of great service also in the treatment of dysentery. While I was acting as visiting physician to the First Birmingham War Hospital at Rubery, a convoy of over a hundred cases of dysentery was received and put under the charge of myself and the late Major Orr (of Ludlow). In consequence of my experience with ulcerative colitis I decided to give all my cases with three exceptions the mercury and iron mixture, and ordinary house diet consisting of beef and mutton and potatoes, etc., although not a few of them were having twelve to eighteen stools a day, and some still had a little pyrexia. Major Orr decided to put his cases on the same treatment.

The result of these somewhat heroic measures was, however, perfectly satisfactory, for there was not a man who did not make rapid progress to recovery. The three exceptions mentioned above were cases with high fever and extremely frequent evacuations; they also were given the mercury and iron mixture, but fed on finely divided raw meat and carbohydrate in the form of fresh juice expressed from pounded carrots after steeping for two hours in water at a temperature of 120° F. Carrot juice thus prepared contains albuminous material and vitamins free from vegetable fibre, and also inositol—a non-fermentable sugar which is of much value in such cases. The patients on house diet got on so well that no bacteriological investigations were made owing to the restricted laboratory service available, but the three severe cases were found to be due to Shiga's and to Flexner's bacilli. The *Amoeba coli* was not found.

Although I have had no experience of the treatment of acute dysentery I have little doubt that this remedy will prove of service, and this conviction is strengthened by the knowledge that a nurse whom I had treated with mercury and iron for colon trouble and who went out to a mission hospital in North Borneo introduced this mode of treatment of acute dysenteric conditions there with most satisfactory results. It is a remedy which proves of great value in cases where muscular disturbance of the colon is giving rise to tenderness and hardness of the bowel together with pain or other nervous symptoms. It is of special value where this type of colon trouble is causing mental depression, phobias, or obsessions, in place of pain, and in such cases its curative action is sometimes extraordinarily rapid.

In Addison's Anaemia.

The latest theories respecting the causation of "Addison's anaemia," as published by Dr. Arthur Hurst in this *JOURNAL* for January 19th, make it highly probable that this combination of mercury and iron may prove of value in this hitherto fatal disease. Naturally there has not yet been time to put this suggestion to a clinical test; I can, however, refer to a patient who recovered from a very severe second relapse of "Addison's anaemia," during which he was taking the mercury and iron for colon disturbance. I thought the cure of the relapse was due to the vaccine and dietetic treatment he was given, and it was a great disappointment to find that a year or two later this same treatment proved quite ineffective in averting the fatal termination of a third relapse of this complaint. On this occasion colon disturbance was not a prominent symptom, and if I remember right the mercury and iron mixture was not persevered with throughout the attack. Considering the powerful antiseptic action of mercury given in this way, it is possible that it may sometimes prove curative in this hitherto incurable disease, if it be really due to the action of streptococci in the duodenum or small intestine.

Precautions.

When using mercuric perchloride as an antiseptic certain things must be borne in mind.

1. Combination with albumin or alkalis will destroy its antiseptic value. It must therefore be given when the