

THE COLLOIDAL GOLD REACTION OF THE CEREBROSPINAL FLUID IN ACUTE POLIOMYELITIS*

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The careful work of Peabody, Draper and Dochez,¹ in 1912, leaves little to be said, from a diagnostic point of view, concerning the cerebrospinal fluid of patients suffering from acute poliomyelitis. Abramson,² in 1912, and Neal³ and Klein⁴ in the recent New York epidemic obtained substantially the same results. Inasmuch, however, as the fluid from such patients has given uniform and significant reactions with Lange's colloidal gold, it has been thought worth while to record the results of the application of this test, as a further contribution to the laboratory knowledge of the spinal fluid in this disease.

The recent small epidemic in Baltimore afforded an opportunity to obtain spinal fluid from a number of patients with poliomyelitis. One of us had the opportunity of doing lumbar punctures on most of the suspects reported to the city health department, as an aid in establishing the diagnosis. Fluids in several early cases were thus obtained. A few were taken in cases diagnosed in the outpatient department of the Harriet Lane Home. The majority were patients held in the Children's Hospital School, the institution utilized by the city for the isolation of poliomyelitis patients. There the spinal fluids were obtained through the kindness of Dr. Rosenthal, the physician in charge.

No case in which the diagnosis was doubtful has been included in the series. All the patients showed paralysis in some form or had presented the typical clinical syndrome with the characteristic spinal fluid findings.

TECHNIC

Each cerebrospinal fluid was subjected to the following tests:

1. Cell count was made immediately after withdrawal of the fluid, when possible, and always within two hours.

2. The globulin-albumin content was estimated by means of the Pandy and the Ross-Jones methods. The usual technic was used both in preparation of the reagents and in the application of the tests.

3. The Wassermann reaction was done with 0.25 and 0.5 c.c. quantities with two antigens: A, plain alcoholic beef-heart extract, and B, cholesterinized alcoholic beef-heart extract. Antigen A bound 100 per cent. with a known positive syphilitic serum in dilution 1:400 and was not anticomplementary 1:5. Antigen B found 1:900 and was anticomplementary 1:5; used in dilution, 1:20.

4. The technic of the colloidal gold test both in the preparation of the gold solution and the carrying out of the test was the same as advised by Miller, Brush, Hammers and Felton,⁵ to whose paper those not

acquainted with the details of the test must refer, excepting two slight modifications used in the preparation of the gold solution: (a) in distilling the water there was added to each liter of the first distillate 5 c.c. of a saturated solution of barium hydrate. By this method the necessity of absolutely fresh first distillation was done away with. In fact, we have used with uniformly good results the single distillation of the day before; (b) in the use of oxalic acid, 1 drop of a 1 per cent. solution to the liter was added at 60 C., instead of 10 drops at 85 C.

The gold solution used was absolutely clear to direct and transmitted light.

Five c.c. of the solution were completely precipitated by 1.7 c.c. of a 1 per cent. sodium chlorid solution in one hour.

The entire series was tested by a single lot of gold solution, which on each day used gave a brownish-red color after the addition of 2 drops of alizarin red to 5 c.c. Too much emphasis cannot be laid on this point. Slight changes in the reactions of the reagent give widely diverging results.

The solution gave a typical reaction with a known parietic cerebrospinal fluid and absolutely negative reaction with four different known negative fluids.

RESULTS

Fifty-seven fluids from patients with poliomyelitis have been tested. These have been grouped into three tables according to the stage of the disease. Three fluids from normal children which were used as controls have been included, one being shown in each table. The cases in each table are arranged in order according to the day of the disease.

Table 1 is made up from fluids obtained during the acute illness. Of these cases, one (H. L. H. No. 10153) was nonparalytic; two (O. S. 7 and O. S. 4) were paralytic; and in the rest, the paralysis was either progressing or just arrested. The gold chlorid curve given in these cases is singularly constant and occurs in the so-called "luteic zone." Flocculation begins in the first tube in all but one, and reaches the maximum in from 1:40 to 1:160, in two instances persisting into 1:320. Decolorization usually proceeds as far as "blue."

In other words, in these fifteen cases in the acute stage of the disease, thirteen react with colloidal gold in the "luteic zone," and two (O. S. 7 and O. S. 5) show a slight tendency to precipitate in the higher dilutions, suggestive of the meningitic zone.

Johnston⁶ has recently published an article in which he used the colloidal gold test in four cases of acute poliomyelitis, the day of the disease not being mentioned, in which the reaction took place in the "luteic zone." That the reaction is not so transient a one as his work would seem to indicate is shown in Tables 2 and 3.

After the subsidence of the acute illness, as is well known, the cells tend to decrease in number very rapidly, but the globulin content may increase. Corresponding to this, we often found in the ensuing two weeks (from the eighth to the twenty-first day) a tendency for the gold to show more pronounced flocculation in the first tubes and to decolorize more intensely in the higher dilutions. This is well shown in Table 2. The gold chlorid curve for the period, consequently, may show a "meningitic curve," as is

* From the Laboratory of Immunology and Bacteriology and the Department of Pediatrics, the Johns Hopkins University, Medical Department.

1. Peabody, Draper and Dochez: Jour. Exper. Med., Monograph 4, June 24, 1912.

2. Abramson, H. L.: The Spinal Fluid in Poliomyelitis and Its Differentiation from Fluids of Other Infections, Am. Jour. Dis. Child., November, 1915, p. 344.

3. Neal: New York Med. Jour., 1916, 104, 167.

4. Klein: New York Med. Jour., 1916, 104, 219.

5. Miller, S. R.; Brush, N. D.; Hammers, J. S., and Felton, L. D.: A Further Study of the Diagnostic Value of the Colloidal Gold Reaction, Together with a Method for the Preparation of the Reagent, Bull. Johns Hopkins Hosp., 1915, 26, 391.

6. Johnston, M. R.: A Study of Normal and Pathologic Cerebrospinal Fluids in Children, Am. Jour. Dis. Child., August, 1916, p. 112.

illustrated by Case R. G. 3. One of the cases included in this table (P. 98) gave a "paretic" curve. The fact that the spinal fluid and blood of this child gave a positive Wassermann reaction might explain this reaction, although clinically there seems to be no sign of juvenile paresis.

From the third week, there is a strong tendency for the spinal fluid to clear, the cell count having returned

the terms "first," "second" and "third" zones be used. This would allow an exact description of the reaction without suggesting a probable etiologic relationship, and enable the clinician from his general knowledge of the reaction to correlate the laboratory with the clinical findings in arriving at a more exact diagnosis.

The term "paretic zone" does not have the objection that is so manifest in "luetic zone," inasmuch as the

TABLE 1.—ACUTE STAGE, FIRST WEEK

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No.	Name	Age, Years	Day of Disease	Cells per C.mm.	Ross- Jones	Pandy	Wassermann Reaction		Colloidal Gold Reaction									
							Antigen		Dilution of Cerebrospinal Fluid									
							A	B	1:10	1:20	1:40	1:80	1:160	1:320	1:640	1:1,280	1:2,560	
.25	.5	.25	.5															
A. L. H.	Catherine S.	5	3	70	+	+	0-0	0-0	1	1	1	2	2	1	0	0	0	
O. S. 1	Christy.....	1½	3	135	+	+	0-0	0-0	1	1	2	3	3	1	1	0	1	
O. S. 2	James M.....	2	3	110	+	+	0-0	0-0	1	1	2	2	1	1	0	0	0	
O. S. 6	Ernest C.....	1½	3	70	+	+	0-0	0-0	1	1	2	3	3	1	0	0	0	
O. S. 7	Robert S.....	4	3	45	+	+	0-0	0-0	1	2	2	3	3	3+	2	1	0	
P. 103	Korsunsky....	3	3	130	±	±	0-0	0-0	1	1	2	2	1	1	0	0	0	
O. S. 3	Lillian W.....	2	3	1	++	+++	0-0	0-0	1	1	2	2	1	1	0	0	0	
O. S. 4	Charles M.....	3	4	81	++++	+++++	0-0	0-0	1	1	2	2+	2+	2	1	0	0	
O. S. 5	Marjorie M....	3	4	10	+++	+++++	0-0	0-0	1	1	2	3	3	1	1	0	0	
O. S. 8	Thelma G.....	2	4	65	+	+	0-0	0-0	0	1	2	3	2	1	0	0	0	
O. S. 1	Christy N.....	1½	4	123	+	+	0-0	0-0	1	1	1	2	1	1	0	0	0	
P. 101	Benj. D.....	1½	4	32	±	±	0-0	0-0	1	1	1	2	2	1	0	0	0	
R. G. 1	Eugene N.....	2	5	30	±	±	0-0	0-0	1	1	2	3	3	2	1	1	0	
H. L. H. (10158)	Birtzal.....	¾	6	170	±	±	0-0	0-0	1	1	2	2	2	1	0	0	0	
O. S. 0	Adrian M.....	2	6	25	++	++	0-0	0-0	1	1	2	3	2	1	0	0	0	
H. L. H.	Pollock.....	4	0	5	0	0	0-0	0-0	1	1	0	0	0	0	0	0	0	

to normal, and the globulin gradually disappearing. The change has appeared in the gold chlorid reaction as early as the eighth day, but this is unusual. The first normal fluid encountered in our series was on the thirty-second day (P. 83), and we often found strong reactions as late as the eighth week after the onset, as is well shown by Case P. 83, which shows precipitation in the higher dilutions on the fifty-second day. In the main, however, "luetic zone" reactions are encoun-

precipitation in zone occurs practically only in paresis, tabes dorsalis and multiple sclerosis.

Regarding the "luetic zone" the following references are significant: Debenediti and Olivero,⁷ in a series of thirteen cases of tuberculous meningitis, give three in the "luetic zone." Eicke⁸ states that early tuberculous meningitis gives a reaction in dilutions from 1:40 to 1:80. Grulee and Moody⁹ give several reactions in the "luetic zone" in conditions other than syphilitic.

TABLE 2.—DISEASES IN SECOND AND THIRD WEEKS

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No.	Name	Age, Years	Day of Disease	Cells per C.mm.	Ross-Jones	Pandy	Wassermann Reaction		Colloidal Gold Reaction									
							Antigen		Dilution of Cerebrospinal Fluid									
							A	B										
							.25	.5	.25	.5	1:10	1:20	1:40	1:80	1:160	1:320	1:640	1:1,280
P. 99	Davis.....	21mo.	9	70	++	++	0-0	0-0	2	2	2+	3+	3+	2+	2	1	0	
P. 101	Droatman....	18mo.	9	5	+	+	0-0	0-0	+	+	1	1	1	+	0	0	0	
R. G. 8	Thelma G....	14mo.	10	33	+	++	0-0	0-0	2	2+	3	3+	3+	2	1	0	0	
H. L. H. (12000)	Edw. J.....	2	10	20	+	++	0-0	0-0	2	2	2	2+	2+	1	0	0	0	
P. 103	Korsunsky...	8	10	8	+	+	0-0	0-0	+	+	+	1	+	0	0	0	0	
P. 98	Bayton.....	4	11	11	++	++++	25-50%	25-75%	5	5	5	3	2+	2	2	+	0	
H. L. H. (12574)	Gladys B....	8mo.	11	20	+	+	0-0	0-0	1+	1+	2	2+	2+	1	+	0	0	
P. 104	Christy.....	15mo.	11	2	+	++	0-0	0-0	0	+	1	1+	2	+	0	0	0	
O. S. 6	Ernest C....	15mo.	11	1	+++	++++	0-0	0-0	2	2	2	2	3	3	2	1	0	
P. 96	Herbert L...	8	14	6	+	+	0-0	0-0	1	1	2	2	1	1	0	0	0	
P. 101	Droatman....	18mo.	14	2	++	++	0-0	0-0	1	1	1+	2	2	1	+	0	0	
H. L. H. (12574)	Gladys B....	8mo.	18	2	++	++	0-0	0-0	1	1	1+	2	2	1	+	0	0	
P. 81	Maffel M....	15mo.	21	4	+	+	0-0	0-0	2	2	3	3	2+	2	1	0	0	
P. 95	Banks G....	8mo.	22	12	+	++	0-0	0-0	2	2	2+	4	3	3+	2	1	0	
H. L. H.	Woolford....	8	0	3	0	0	0-0	0-0	1	1	1	0	0	0	0	0	0	

tered, and they persist and may be found as late as eight weeks after the onset of the disease. These facts are brought out by the study of Table 3.

In view of the foregoing significant reactions in the colloidal gold test, and from facts as tabulated in the recent work of Miller, Brush, Hammers and Felton⁵ and other workers, showing that clinical syndromes besides syphilis may give typical zonal reactions, and also because of the objections raised by the clinician that these terms are rather confusing, it is suggested that instead of the "paretic," "luetic" and "meningitic,"

Johnston⁶ gives several miscellaneous fluids reacting in the "luetic zone." In the compiled table of Miller, Brush, Hammers and Felton, 204 cases in the miscellaneous group, out of 1,808, give a precipitation in the "luetic zone." From these data, together with the series of fifty-seven cases of acute poliomyelitis here described, and the four cases described by Johnston,⁶

7. Debenediti and Olivero: *Riforma med.*, 1914, **30**, 906.
8. Eicke: *München. med. Wehnschr.*, 1913, **40**, 49, 2713.
9. Grulee, C. G., and Moody, A. M.: *Lange's Colloidal Gold Chlorid Test on the Cerebrospinal Fluid in Congenital Syphilis*, *THE JOURNAL A. M. A.*, July 5, 1913, p. 13.

it no longer seems desirable to continue the use of the term "lentic zone."

The term "meningitic zone" is not open to such strong objection as the others, inasmuch as it is but rarely that other conditions give curves simulating it. However, for uniformity's sake, we feel that it could well be called the "third zone."

CONCLUSIONS

1. In the acute stage of poliomyelitis, the spinal fluid reacts with colloidal gold in dilutions of from 1:40 to 1:160, producing a maximal decoloration of 3 ("blue").

2. In the second and third weeks the reaction is practically the same as in the acute stage, with a tendency to clear up in some cases and a precipitation in the higher dilutions in others. There is no constant rule.

3. In the fourth to the eighth week the colloidal gold reaction runs practically to the globulin-albumin content, persisting in some cases to the eighth week and

CLINICAL STUDY OF FOUR HUNDRED CASES OF ANTERIOR POLIO-MYELITIS*

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My object is to present the observations obtained by a close study of 400 cases of anterior poliomyelitis of the 1916 epidemic, seen at the clinic of the Hospital for Deformities and Joint Diseases.

These cases made their appearance at an average of about ten weeks after onset of illness, and show: (1) regional distribution; (2) a large amount of cranial nerve involvement; (3) muscular distribution; (4) unreliability of the reaction of degeneration to permit judgments concerning the extent of muscle paralysis, and (5) numerous deformities.

1. Of the entire series, thirty-two patients, or 8 per cent., showed no evidence of muscle paralysis. Of the

TABLE 3.—CONVALESCENT STAGE, FOURTH TO EIGHTH WEEK

No.	Name	Age, Years	Day of Disease	Cells per C.mm.	Ross- Jones	Pandy	Wassermann Reaction		Colloidal Gold Reaction									
							Antigen		Dilution of Cerebrospinal Fluid									
							A	B	1:10	1:20	1:40	1:80	1:160	1:320	1:640	1:1,280	1:2,560	
							.25	.5	.25	.5								
P. 93	Herbert.....	8	22	18	++	++	0-0	0-0	1	1	2	2	2	1	0	0	0	
P. 71	Lloyd B.....	3	27	1	+	+	0-0	0-0	1	1	1	2	2	0	0	0	0	
P. 100	Norman D....	3	28	4	++	++	0-0	0-0	1+	2	1+	2+	2+	2+	0	1	0	
P. 65	John J.....	8mo.	28	4	+	+++	0-0	0-0	1	1+	1+	3	2	1	0	0	0	
P. 91	Malcolm S....	3	28	2	0	+	0-0	0-0	1	1	1+	2	2	1	0	0	0	
P. 94	Elmer L.....	6	29	3	+	+	0-0	0-0	+	1	1+	1+	1	+	0	0	0	
P. 74	Mildred W....	9mo.	31	15	++	++	0-0	0-0	1	1+	2	2+	1+	1	+	0	0	
P. 88	James E.....	3	32	4	0	0	0-0	0-0	0	0	0	+	0	0	0	0	0	
P. 100	Norman D....	3	32	4	+	+	0-0	0-0	1	1+	1+	2	2	1	0	0	0	
P. 84	Luber F.....	3	35	2	+	+++	0-0	0-0	1+	1+	1+	2	1	1	0	0	0	
P. 47	Emily W.....	6mo.	37	4	++	++	0-0	0-0	1	1	1	2	3	2	1	1	0	
P. 56	Dillalunt....	21mo.	39	8	0	0	0-0	0-0	+	+	+	0	0	0	0	0	2	
P. 58	Hoffman.....	0	39	8	+	+++	0-0	0-0	2	2	2	2+	3	3	1	1	0	
P. 68	Fisher.....	3	39	1	+	+	0-0	0-0	+	1	1+	1+	1	+	0	0	0	
P. 70	Alfred E.....	6	39	1	++	++	0-0	0-0	+	+	1	2	2+	2	+	0	0	
P. 46	Gladys D....	4	40	2	++	++	0-0	0-0	0	0	+	1	1	+	0	0	0	
P. 42	Kathrine W....	2	40	4	+	+	0-0	0-0	1	1+	2	2	2	1+	1	0	0	
P. 30	John B.....	10	42	6	++	+	0-0	0-0	0	+	1*	2	2	1	+	0	0	
P. 37	Lillian L....	2	42	6	++	++	0-0	0-0	1	1	2	2	2+	1	0	0	0	
P. 45	Anna V.....	4	42	4	+	+	0-0	0-0	1	1	1+	2	2	1	0	0	0	
P. 43	Susie B.....	2	42	13	+	++	J-0	0-0	0	+	1	1+	+	0	0	0	0	
P. 55	Benj. B.....	15mo.	44	1	0	+	0-0	0-0	1	1	2	1	1	0	0	0	0	
P. 82	Naomi L....	1	46	2	++	++	0-0	0-0	1	1	1+	2	2+	2	1	+	0	
P. 26	Dorothy H....	4	50	2	++	++	0-0	0-0	1	1+	2	2	1+	+	0	0	0	
P. 27	Carr.....	3	52	3	+	+	0-0	0-0	1	1+	2*	3	3	1*	1	0	0	
P. 17	Eshbury.....	15mo.	52	4	+	+	0-0	0-0	1	1	1	1	1+	2*	3	0	0	
P. 19	Mildred.....	3mo.	54	3	+	+	0-0	0-0	1	1	2*	2*	1	0	0	0	0	
P. 48	Mary B.....	4	45	3	+	+	0-0	0-0	1	1+	3	3	2	1	1	0	0	
P. 90	William M....	2	0	2	0	0	0-0	0-0	1	1	1	1	0	0	0	0	0	

beyond, but still occurring in dilutions of from 1:40 to 1:160.

4. As the spinal fluid in acute poliomyelitis reacts constantly in the same zone, the gold chlorid reaction is helpful in the diagnosis of this disease.

5. We deem it advisable to use the following nomenclature in reading the reactions of Lange's colloidal gold test:

- Zone 1 (or paretic zone), maximum precipitation from 1:10 to 1:160, with complete decolorization.
- Zone 2, maximum precipitation from 1:40 to 1:160, with decolorization up to 4 (light blue).
- Zone 3, maximum precipitation beyond 1:160.

A Pessimistic View of Man.—What a chimera, then, is man! what a novelty, what a monster, what a chaos, what a subject of contradiction, what a prodigy! A judge of all things, feeble worm of the earth, depositary of the truth, cloaca of uncertainty and error, the glory and the shame of the universe!—Pascal, Thoughts.

remaining 368 patients, 286, or 78 per cent., showed some involvement in the lower extremities. Thirty-eight per cent. showed involvement of only one limb. Of this number, 10 per cent. were of the upper extremity and 28 per cent. of the lower. In 20 per cent. of the cases there was some form of trunk paralysis, showing that it has been quite a common occurrence. The right and left sides of the body were equally attacked.

The extent of paralysis differed from a part of one leg to an involvement of both legs, both arms, both sides of the abdomen and back, and also the larynx, which is slight. Between these two extremes there was seen every conceivable type of combination obtainable. Table 2 illustrates this very clearly.

2. In fifty-one cases, or 13 per cent., the cranial nerves were involved. In six cases, two different nerves were involved at the same time. The fifth nerve was affected 1 time; the sixth nerve, 1 time;

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