

## THE VALUE OF THE ROUTINE USE OF THE COLLOIDAL GOLD REACTION IN ACUTE EPIDEMIC POLIOMYELITIS\*

JOSEPH C. REGAN, M.D., AND G. W. HOLMES CHENEY, M.D.  
NEW YORK

In 1916 Johnston<sup>1</sup> reported on the use of the colloidal gold test on the spinal fluid in four cases of poliomyelitis. He found an early transitory reaction in the syphilitic zone during the acute stage, and he considered that the test might prove an important aid in diagnosis. In March, 1917, Felton and Maxcy<sup>2</sup> published an excellent and important contribution on the subject. These investigators examined the spinal fluids of fifty-seven patients during various stages of the disease, and came to the following conclusions: (1) In the acute stage of poliomyelitis, the spinal fluid reacts with colloidal gold in dilutions of 1:40 to 1:60 producing a maximum decoloration of 3. (2) In the second and third weeks the reaction is practically the same, with a tendency to clear up in some cases and a precipitation in higher dilutions in others. (3) From the fourth to the eighth week, the curve runs practically parallel to the globulin and albumin content, persisting to the eighth week and beyond but still occurring in dilutions of from 1:40 to 1:60. (4) As the reaction is constantly in the same zone, the test is helpful in diagnosis.

Jeans and Johnston<sup>3</sup> in the same month (March, 1917), reported the results of the examination of the cerebrospinal fluid in 100 cases of poliomyelitis in the acute stage. Fifty-five patients had definite paralysis and the fluids of the entire fifty-five gave a definite reduction of the gold chlorid solution in low dilutions of the spinal fluid. This reaction occurred with such uniformity that they believe the test is of distinct value in the diagnosis of poliomyelitis. In a few abortive cases and those in the preparalytic stage, the curve was not essentially different from that obtained in the clear cut paralysis cases. Jeans and Johnston emphasize the value of the test as a means of differential diagnosis from meningismus and other forms of meningitis.

---

\* Received for publication, Aug. 23, 1921.

\* From the Kingston Avenue Hospital, of the Bureau of Hospitals, Department of Health, New York City, Dr. Robert J. Wilson, Director; Dr. William T. Cannon, Resident Physician.

1. Johnston, M. R.: *Am. J. Dis. Child.* **12**:112 (Aug.) 1916.

2. Felton, L. D., and Maxcy, K. F.: *J. A. M. A.* **68**:752 (March 10) 1917.

3. Jeans, P. C., and Johnston, M. R.: *Am. J. Dis. Child.* **13**:239 (March) 1917.

Neal and Abramson<sup>4</sup> in a detailed and careful study carried out during the 1916 epidemic on the spinal fluid in poliomyelitis, reported, among other tests, the results obtained with the colloidal gold reaction. They examined 114 cases, and found the result in seventy-seven of the fluids to fall in one of six curves as follows:

In 40 cases.....	1122100000	In 5 cases.....	1121100000
In 8 cases.....	1123210000	In 14 cases.....	1111000000
In 6 cases.....	1112210000	In 4 cases.....	1121000000

The remaining thirty-seven fluids gave various curves similar to the six foregoing but not exactly classifiable under any of the headings. The composite curve of the 114 spinal fluids was 1122100000. Neal and Abramson did not consider the gold chlorid reaction of absolute diagnostic value since they found that a few of the fluids from epidemic or tuberculous meningitis cases may also fall in these groups. They emphasize the fact that in only one instance was a poliomyelitis fluid negative, even in the case of fluids with normal chemistry, while the curves from cases of meningismus have been normal, even with a slightly increased chemistry, although not a sufficient number of fluids had been examined to be sure that this latter fact holds true in all cases.

Kolmer, Freese, Matsunami and Meuse,<sup>5</sup> in a somewhat similar study of the spinal fluid from poliomyelitis cases, examined the fluids from thirty-eight cases by this reaction. The fluids from eighteen cases, removed from the second to the twelfth day after the onset of the paralysis, showed no color change at all; in four cases in the same stage there was only a slight precipitation in the first two tubes 1100000000—while all these fluids showed an increase in cells, and one of them in globulin. The fluids from ten cases, examined from two to twelve days after onset, yielded reactions of the syphilitic zone type with maximum precipitation in from 1:40 to 1:160; and decolorization usually terminating with blue. The fluids from six cases examined from twelve to nineteen days after the onset of paralysis yielded reactions of the meningitic zone type, characterized by maximum precipitation in from 1:80 to 1:320 to 1:640. In conclusion, Kolmer and his collaborators state that during the acute stage of poliomyelitis the fluid from 40 to 50 per cent. of the cases yielded a colloidal gold curve in the syphilitic and meningitic zone; a peculiar or definite curve of precipitation was not obtained by them.

Overholser<sup>6</sup> applied the colloidal gold test to twenty-one specimens of spinal fluid from cases of poliomyelitis. Fourteen, or 66

4. Neal, J. B., and Abramson, H. L.: *Arch. Int. Med.* **19**:341 (Sept.) 1917.

5. Kolmer, J. A.; Freese, A. E.; Matsunami, T., and Meuse, B.: *Am. J. Sc.* **154**:720, 1917.

6. Overholser, W.: *Boston M. & S. J.* **177**:480 (Oct. 4) 1917.

per cent., gave a typical curve of the acute stage (112331000), the other curves were so anomalous that this investigator believed some technical error must be invoked to explain them. Larkin and Cornwall<sup>7</sup> examined fifty spinal fluids by the colloidal gold test. In only two was a normal reaction obtained; 63 per cent. of the curves were humped, but they did not note any curve which was diagnostic of poliomyelitis. They found no parallelism to exist between the colloidal gold curve and the other spinal fluid or blood findings, but believed there was probably a tendency for the height of the curve to increase with the severity of the infection. Carr,<sup>8</sup> in writing of the same series of cases, states that the reaction was in the syphilitic zone in 70 per cent. of the cases and that low curves were the rule. Vogel,<sup>9</sup> in a general report of his work with this test, gives the result of its application in three cases of poliomyelitis; in one the curve was in the paretic zone and in two it was of a syphilitic type.

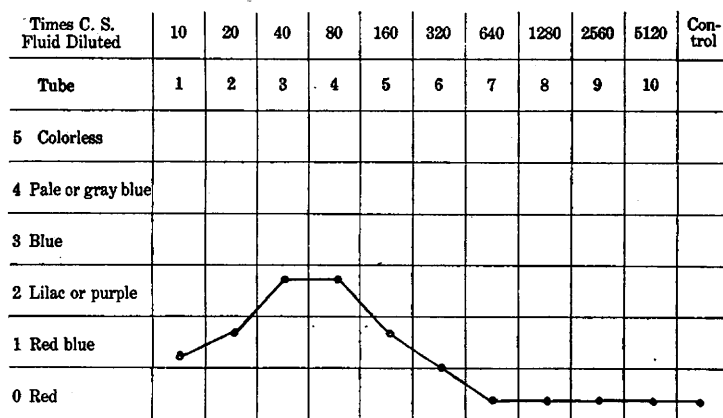


Fig. 1.—Average curve in first week of the disease.

During 1920, a small localized outbreak of poliomyelitis occurred in Brooklyn, and the Kingston Avenue Hospital admitted nineteen cases from August 24 to November 26. Subsequently two additional cases were received, making a total of twenty-one. In this series there were four fatalities, due to poliomyelitis, the four patients entering the hospital on or about the same date (November 11). The predominant type of the disease was that usually seen, the spinal or myelitic, with, however, an unusually high percentage of cases with moderate or marked polyneuritic symptoms, which in a few instances made up the most pronounced features of the malady.

7. Larkin, J. H., and Cornwall, L. H.: Arch. Pediat. **35**:459, 1918.

8. Carr, W. L.: Arch. Pediat. **34**:591 (Aug.) 1917.

9. Vogel, K. M.: Arch. Int. Med. **21**:496 (Oct.) 1918.

The colloidal gold reaction was performed in each of the twenty-one cases included in our series, and a total of seventy-four spinal fluids from these twenty-one patients were examined in various stages of the disease from the fourth to the one hundred and twenty-third day. Classified according to the week in which they were taken, the fluids were divided as follows:

First week.....	6 fluids	Eighth week.....	5 fluids
Second week.....	11 fluids	Ninth week.....	5 fluids
Third week.....	11 fluids	Tenth week.....	4 fluids
Fourth week.....	7 fluids	Eleventh week.....	3 fluids
Fifth week.....	6 fluids	Fourteenth week.....	1 fluid
Sixth week.....	10 fluids	Eighteenth week.....	1 fluid
Seventh week.....	4 fluids	Total .....	74 fluids

*Results Obtained.*—In this series, in no instance was the colloidal gold reaction normal when the spinal fluid was examined during the first three weeks of the disease. The curve obtained was constantly in the same zone.

In order to show the characteristics of the curve in poliomyelitis, we have separated our results according to the weeks of the disease in which they were obtained, and have on this basis separately constructed an average curve for each week up to the eighth. The curves for the first, second, fourth, sixth and eighth weeks are shown in Figures 1, 2, 3 and 4. These figures show the average characteristics of the reaction obtained at various periods of the disease in this series. It is noticeable that the curve for the first two weeks is very much the same, and is what we believe may be considered characteristic of this stage. In the first week it consists of an ascending curve presenting a gradual increase in reduction in higher dilutions starting in the reddish blue color in 1:10, extending into the lilac or purple color in 1:40 and 1:80, and then descending also gradually but more abruptly into the reddish blue again in 1:160 and reaching the nonreducing or red area in 1:640. In the second week, it differs only in that it remains in the lilac or purple area from 1:40 to 1:160.

As the disease progresses the average curve gradually falls, reaching normal in a minor proportion of the cases from the eighth to the ninth week of the malady. Thus, out of a total of ten fluids taken up to or beyond the ninth week, three showed a normal reaction before this period. One of these appeared on the twenty-eighth day, another on the fifty-third day, and a third on the fifty-fifth day. Of the seven fluids which remained elevated beyond the ninth week, three continued showing an acute poliomyelitis curve until the eleventh week, and one until the fourteenth week, to be exact, the one hundred and twenty-third day. In this series, therefore, 30 per cent. of the cases of poliomyelitis presented a normal reduction of colloidal gold at the end of the

ninth week. How long the curve remained elevated in the remaining 70 per cent. of the cases we were unable to determine, owing to the discharge of the patients from the hospital. We are cognizant of one case which is suggestive of the possible duration of a positive reaction in exceptionally severe attacks:

A young girl, 15 years of age, was admitted to the Kingston Avenue Hospital during the epidemic of 1916, with a very extensive paralysis involving the muscles of all the extremities, back and neck. After her discharge from the hospital, the patient had what she terms three relapses; in the first she was confined to bed two months, in the second for two years, and in the third for one year. She was admitted to the Kings County Hospital in 1920, suffering from chorea and residual paralysis of her left leg, back and some of the muscles of her neck. Two spinal fluids taken after admission showed a negative Wassermann, slight increase in cells and globulin, and a colloidal gold curve of 1122100000.

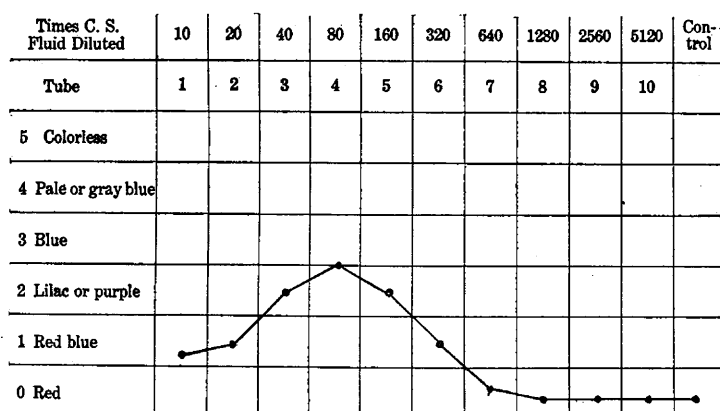


Fig. 2.—Average curve in second week of the disease.

This case is cited as an example of the possibility of a long persistence of colloidal gold reaction in a patient with severe infection. Of course, it cannot be absolutely proven that the curve was due to poliomyelitis, but the case is suggestive.

A very early subsidence of the curve, such as the twenty-eighth day (Case 1987) is exceptional. It occurred in a patient with moderate paralysis and slight polyneuritic involvement, who made a rapid recovery. On the other hand, patients with a persistence of a positive reaction of an acute type beyond the ninth week have usually presented a marked and extensive paralysis (Cases 1840, 1895 and 1990) with moderate or marked and persistent polyneuritis, or a mild paralysis with persistent and marked polyneuritis (Case 1011). It seems to us from this somewhat limited study, that there is a definite relationship between the duration of the positive colloidal gold reaction

and the persistence of polyneuritic symptoms and to a lesser extent paralysis. Patients who run an acute curve late in the disease usually present also some degree of persistence of the acute hydrocephalus which occur during the early weeks of the malady, and the fluid obtained on lumbar puncture continues to be increased in amount and in pressure. We are strongly inclined to believe that the period when the colloidal gold reaction returns to the normal indicates, as a rule, the end of the acute stage of the disease, and is, therefore, of great value in that one may determine more concisely than is done at present when the prolonged rest of the acute stage may be terminated, and the more active measures of treatment of the residual paralysis may be undertaken by massage, electricity, etc. The reaction seems to indicate better than any other means, such as the study of cytology and chemistry of the spinal fluid, or of the symptoms, when the acute generalized inflammation of the meninges, cord and brain has approximately subsided. It seems probable that all active methods of treatment for the subsequent paralysis are strongly contraindicated until this stage is passed. There is also another aspect, and that is that the extent of the paralysis which may remain and require treatment can best be judged when the reaction becomes normal, for throughout the period of its elevation great spontaneous improvement usually continues to occur.

In three of the seven cases presenting a curve beyond the ninth week, the reaction had begun to descend in the third or fourth week, but was subsequently found more elevated in the ninth, tenth or eleventh weeks. The average curve obtained, however, gradually falls as the disease advances. In the first and second weeks (Figs. 1 and 2) there is little variation. In the third week the average curve reaches high into the lilac area in 1:80 and the ascending line is definitely beginning to decline. In the fourth week (Fig. 3) there is a marked change in the curve consisting of a pronounced flattening out, and it is limited to the red blue area, from 1:10 to 1:320. From the fifth week to the ninth week (Fig. 4), the curve gradually continues to subside, the slight reduction obtained in the red blue color being gradually more and more limited to the lower dilutions.

There was only an inconstant relationship between the cytologic and chemical findings of the spinal fluid and the colloidal gold curve in this series. As a rule, as the reaction subsided, the globulin diminished, but, on the other hand, many cases presented a high curve late in the disease with a normal or almost normal globulin reduction. We did not note that in the first few weeks of the disease the augmentation of globulin and cells bore any relation to the height of the gold chlorid curve.

The average curve (Fig. 5) in the fatal cases is very similar to that obtained in the first and second weeks of the disease in the more severe nonfatal cases. Although in fatal cases it may tend to exhibit slightly greater precipitation and to be on the average a higher curve, there has not been sufficient difference in our series to make the test of any definite value from the prognostic viewpoint.

It is conceded by most workers who have studied the spinal fluid in cases of epidemic poliomyelitis, that there is nothing about the findings which is entirely characteristic of that disease. Thus, an increase in cells, lymphocytes or of globulin and a good (3+) reduction of Fehling's solution is merely confirmatory in a case in which the clinical diagnosis is clearly established. On the other hand, many

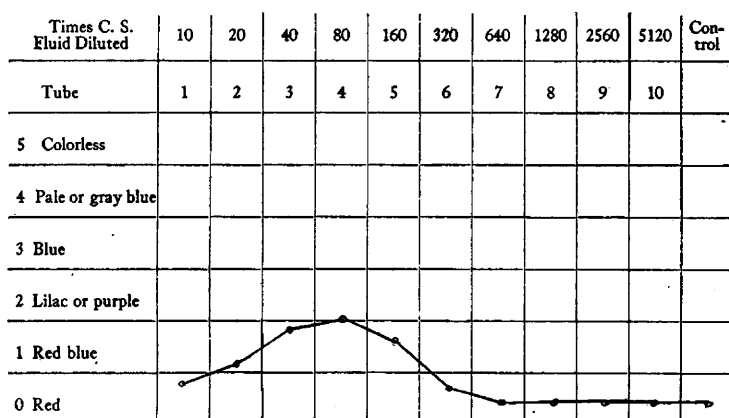


Fig. 3.—Average curve in fourth week of the disease.

cases of poliomyelitis do not present, when they come under observation any increase in cells, or if so, it is little above normal and the globulin may not be augmented. While in other conditions, such as meningismus or tuberculous meningitis, there may be an increase in globulin, as in the former, or an increase in globulin and cells, as in the latter. Hence, positive or negative findings in the spinal fluid as regards cytology or chemistry cannot be considered in the least conclusive. Especially is this the case if poliomyelitis is sporadic and the type atypical, presenting itself in one of its less common forms, such as the meningitic, encephalitic, ataxic, polyneuritic or abortive varieties, or in those cases in which it occurs as a Landry's paralysis, or in which a facial palsy may be the only paralytic involvement present. In such circumstances we need a finer laboratory test to establish the diagnosis, and we believe this is fulfilled by the gold chlorid reaction.

ANALYSIS OF CASES AS TO PRESENCE OF PARALYSIS ON ADMISSION AND ON DISCHARGE, AND DEGREE OF COLLOIDAL GOLD REACTION

Case No.	Date Admitted to Hospital	Days Ill on Admission	Type of Disease	Paralysis on Admission	Degree of Polyneuritis	Dates of Spinal Fluid Examination	Colloidal Gold Reaction										Paralysis on Discharge	Polyneuritis on Discharge	Degree of Improvement	Recovered or Died
1890	9/26	20	Myelitic, polynuritic, bulbar	Left arm, complete; legs, complete; back, complete; cranial nerves, involved	2+	10/5 10/15 10/29 11/5 11/17 12/8 1/5	1 2 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 1 1 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 1 2 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 2 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 2 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 2 2 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 2 3 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Right leg, complete; left leg, partial; back, complete; cranial nerves, involved	1+	Slight	Recovered									
561	2/18	4	Myelitic, polynuritic	Legs and neck, complete....	3+	3/1 4/18	1 1 2 3 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 2 2 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Right leg, complete; left leg, partial; back, complete	2+	Slight	Recovered									
1901	9/29	8	Myelitic	Right leg, partial.....	—	10/7 10/14 10/28 11/4 11/11	0 0 1 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	None.....	—	Moderate	Recovered									
2196	11/6	12	Myelitic, polynuritic, bulbar	Legs, complete; diaphragm, weak; back, complete; cranial nerves, involved	3+	12/2	1 1 2 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 2 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Legs and back, complete; cranial nerves, involved	2+	Slight	Recovered									
2005	10/2	6	Myelitic	Legs, partial.....	—	10/15 10/30 11/5 11/15	1 1 2 2 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 2 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Legs, weak.....	—	Moderate	Recovered									
2130	10/24	2	Meningitic	None.....	—	10/25 11/8 11/23	1 2 2 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 2 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 2 0 2 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0	None.....	—	Marked	Recovered									
1987	9/28	4	Myelitic, polynuritic	Legs and back, complete....	2+	9/30 10/21 10/28 11/4	0 0 2 3 2 0	Right leg, partial.....	—	Marked	Recovered									
1929	9/16	4	Myelitic, polynuritic	Right arm, weak; legs, weak; back, weak	2+	9/22 10/3 10/14 10/29 11/11 11/22	1 1 2 2 2 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 2 1 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 2 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 1 2 3 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 2 2 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0	None.....	2+	Marked	Recovered									
1011	10/4	9	Myelitic, polynuritic, meningitic	Legs, partial.....	3+	10/6 10/12 10/21 11/4 11/11 11/21	0 2 1 2 3 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 2 0 2 1 2 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 2 1 2 2 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 2 2 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 2 2 3 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 2 1 1 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0	Left leg, partial.....	2+	Marked	Recovered									



2266	11/18	2	Meningitic,	.....	2+	11/24 12/ 2 12/ 8	0 0 1 2 2 1 0 0 0 0 0 1/2 1 2 2 1 0 0 0 0 0 1 2 2 1 1/2 0 0 0 0	0 0 1 2 2 1 0 0 0 0 0 1/2 1 2 2 1 0 0 0 0 0 1 2 2 1 1/2 0 0 0 0	Legs, weak.....	2+	Moderate	Recovered
1895	9/ 6	4	Myelitic, meningitic, polynneuritic	Right arm and legs, partial; back and neck, weak; cranial nerves, involved	2+	9/20 11/ 5 11/ 8	0 1 2 2 3 2 1 0 0 0 1 1/2 3 2 2 1 0 0 0 0 1 1 2 2 2 2 1 0 0 0	0 1 2 2 3 2 1 0 0 0 1 1/2 3 2 2 1 0 0 0 0 1 1 2 2 2 2 1 0 0 0	Right arm, weak; right leg, partial; cranial nerves, involved	Moderate	Moderate	Recovered
2113	10/21	3	Myelitic, polynneuritic	Right leg, partial.....	2+	11/ 2 11/24	0 1/2 1 2 2 2 1 0 0 0 1 2 2 2 3 2 0 0 0 0	0 1/2 1 2 2 2 1 0 0 0 1 2 2 2 3 2 0 0 0 0	Left leg, weak.....	None	Moderate	Recovered
2019	10/ 5	7	Myelitic	Right leg, partial.....	2+	10/ 6 10/14 10/28 11/ 8 11/12 11/21	0 1/2 1 2 2 1 0 0 0 0 0 1/2 1 1/2 1 0 0 0 0 0 0 0 0 1/2 1 0 0 0 0 0 0 1 2 2 1 1 0 0 0 0 0 1 2 2 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1/2 1 2 2 1 0 0 0 0 0 1/2 1 1/2 1 0 0 0 0 0 0 0 0 1/2 1 0 0 0 0 0 0 1 2 2 1 1 0 0 0 0 0 1 2 2 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	None.....	None	Marked	Recovered
2320	11/26	7	Myelitic, polynneuritic	Legs, complete; back and neck, weak	3+	11/27 12/ 4 1/ 5	0 1/2 1 1/2 2 1 0 0 0 0 1 1/2 1/2 3 3 2 0 0 0 0 0 2 2 1 0 0 0 0 0 0	0 1/2 1 1/2 2 1 0 0 0 0 1 1/2 1/2 3 3 2 0 0 0 0 0 2 2 1 0 0 0 0 0 0	Right leg, weak; left leg, partial	None	Moderate	Recovered
1940	8/24	4	Myelitic, polynneuritic, bulbar	Arms and legs, complete; diaphragm and intercostals, weak; back and neck, complete; cranial nerves, involved	3+	10/21 10/28 11/ 5	0 1 1 3 1 0 0 0 0 0 0 0 1/2 2 3 1 0 0 0 0 1 2 2 2 1 0 0 0 0 0	0 1 1 3 1 0 0 0 0 0 0 0 1/2 2 3 1 0 0 0 0 1 2 2 2 1 0 0 0 0 0	Arms, partial; legs, complete; back and neck, complete; diaphragm and intercostal, weak; cranial nerves, complete	Moderate	Slight	Recovered
2035	10/ 7	8	Myelitic, polynneuritic	Legs, weak; back and neck, weak	3+	10/28	0 1 2 2 2 1 0 0 0 0	0 1 2 2 2 1 0 0 0 0	.....	.....	Moderate	Recovered of polynmyelitis
2044	10/ 9	5	Myelitic, bulbar	Arms and legs, complete; diaphragm and intercostals, weak; back and neck, complete	1+	10/12 10/21 11/11 11/24 12/ 2	1 1 2 3 3 1 0 0 0 0 1 1 2 3 3 1 0 0 0 0 2 3 3 3 1 0 0 0 0 0 1 2 3 2 1 0 0 0 0 0 0 1/2 1 1/2 1 1/2 1 0 0 0 0	1 1 2 3 3 1 0 0 0 0 1 1 2 3 3 1 0 0 0 0 2 3 3 3 1 0 0 0 0 0 1 2 3 2 1 0 0 0 0 0 0 1/2 1 1/2 1 1/2 1 0 0 0 0	Arms, partial; legs, partial; back and neck weak	Moderate	Moderate	Recovered
2273	11/19	2	Myelitic, polynneuritic, bulbar	Left leg, diaphragm, intercostals and neck, partial; cranial nerves, involved	1+	11/20	0 0 1 2 1 1/2 1 0 0 0 0	0 0 1 2 1 1/2 1 0 0 0 0	.....	.....	.....	Died, 11/21
2229	11/11	4	Ascending Landry's	Left arm and legs, complete; diaphragm and intercostals, partial; neck and back, weak; cranial nerves, involved	-	11/12 11/16 11/17	1 2 1/2 2 2 2 1 0 0 0 0 1 1/2 3 2 1 0 0 0 0 0 1 1 1 2 3 2 0 0 0 0	1 2 1/2 2 2 2 1 0 0 0 0 1 1/2 3 2 1 0 0 0 0 0 1 1 1 2 3 2 0 0 0 0	.....	.....	.....	Died, 11/19
2226	11/11	4	Myelitic, bulbar	Left arm and legs, complete; diaphragm and intercostals, partial; neck and back, partial; cranial nerves, complete	1+	11/13 11/18	1 1 2 1 0 0 0 0 0 0 1 1 2 3 3 1 0 0 0 0	1 1 2 1 0 0 0 0 0 0 1 1 2 3 3 1 0 0 0 0	.....	.....	.....	Died, 11/18
2230	11/11	2	Myelitic, meningitic, bulbar	Arms and legs, complete; diaphragm and intercostals, partial; neck, complete	1+	11/12	1 2 3 3 2 1 0 0 0 0	1 2 3 3 2 1 0 0 0 0	.....	.....	.....	Died, 11/13

In order to show the differential value of the curve obtained in the early weeks of the disease, we have placed in Figure 6 all reactions found during the first ten days or in what might be termed the very acute febrile stage. This, then, forms by its limitations what might be termed for descriptive purposes a poliomyelitic zone. It has been cross sectioned and is thus represented in the figure, and for comparison we have included the curves of various other well recognized meningeal conditions. The figure shows clearly that the zone of Heine-Medin's disease, as made out in this small series, is not identical with that of any other disease.

It is true, that a number of curves are obtained in cases of cerebro-spinal syphilis which run a low course, and in which there may be a close resemblance to a poliomyelitic reduction. But while such cases occur not infrequently, the clinical history and symptoms of the two diseases are so different that confusion is entirely improbable. The Wassermann test is moreover, available.

A typical curve of tuberculous meningitis would not be confused with any of our poliomyelitis curves. We have purposely selected as an example of a tuberculous meningitis curve for Figure 6 one which is of as mild a type as was obtainable and one which resembled as much as any which are ordinarily encountered the curve of Heine-Medin's disease. Yet even here the distinction is definite and clear cut, so far as the acute febrile stage of poliomyelitis is concerned. In tuberculous meningitis the curve begins to rise in higher dilutions, not lower commonly than 1:40, and is prolonged well into the meningeal zone in the vast majority of instances, rarely falling below the lilac purple in a dilution less than 1:640.

It must be stated, however, that occasionally one encounters cases, usually those with either marked polyneuritic or meningitic symptoms, in which the gold chlorid curve toward the end of the second week is prolonged slightly beyond the limits of the poliomyelitis zone (Cases 1929 and 1011). Obviously at this period of the disease the question of a differential diagnosis from tuberculous meningitis would not arise.

It must always be kept in mind that if a curve is obtained which transgresses definitely on the meningeal zone, tuberculous meningitis should be ruled out carefully, as the results of our work and that of the majority of our predecessors seem to show that such a reaction is altogether exceptional in the very acute stage of epidemic poliomyelitis.

The colloidal gold reaction is rarely required in the differential diagnosis of poliomyelitis and epidemic cerebrospinal meningitis or any other form of purulent meningitis owing to the entirely different macroscopic, cytologic and chemical characteristics of the spinal fluids in the two diseases. It is possible that in early cases the test might have to be invoked in so much as that in the preparalytic stage of

Heine Medin's disease the cell count is sometimes so augmented as to give a faint hazy appearance to the fluid, while, on the other hand, in the very early stage of epidemic meningitis the fluid may be almost clear, or have a faint opalescence. From Figure 6 it is evident how distinctly different the curves are in the two maladies

As previous work has shown, Lange's colloidal gold test provides the only certain method of differentiating poliomyelitis, and the various forms of meningismus. It was not uncommon during the 1916 epidemic to see cases in which a diagnosis of Heine-Medin's disease had been made in cases which were not such. Thus, occasionally, cases of scurvy, rickets, tetany, etc. were so diagnosed, and, still more commonly, cases of meningismus complicating diverse conditions such as bronchopneumonia, gastro-enteritis or colitis were confused with poliomyelitis. A negative spinal fluid did not absolutely exclude

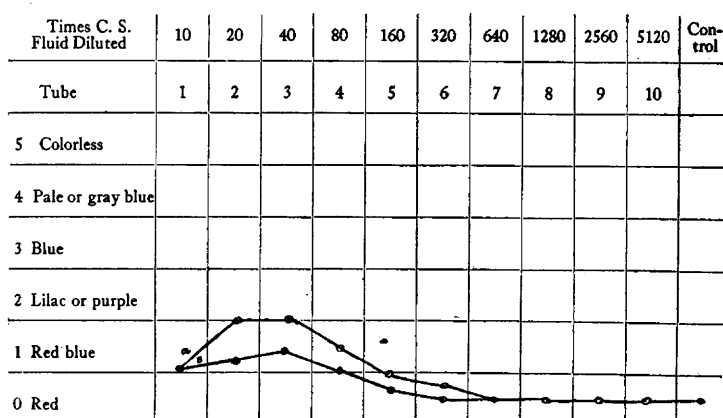


Fig. 4.—Average curve in sixth (a) and eighth (b) week of the disease.

poliomyelitis, while a positive fluid, as regards chemistry, did not prove it to be the latter. Had the colloidal gold chlorid test been employed as a routine in such instances there is no doubt the diagnosis would have been determined more accurately and more quickly. We have employed the test in this way in several cases during the past year, and in no instance did we obtain a reduction of colloidal gold in meningismus. In one case of scarlet fever and poliomyelitis (Case 2266), the diagnosis on admission was meningismus complicating scarlet fever, and we should not have recognized the fact that a mixed infection with the two diseases existed until a later period, after paralysis was definitely manifest, if it had not been for this test. In another patient (Case 24), in whom the physical signs of pneumonia were late in appearing, but who presented a pronounced meningeal syndrome including spastic paralysis of the left arm and leg, due to a lesion in the

course of the upper motor neuron, we were able to rule out Heine-Medin's disease in this way.

As to the value of the colloidal gold test in differentiating poliomyelitis and epidemic encephalitis, the literature gives no information. There has been relatively little work carried out on the use of this test in epidemic encephalitis. Among the few reports made on the subject are those of Tilney and Howe,<sup>10</sup> Davis and Kraus,<sup>11</sup> and Nixon and Sweetser.<sup>12</sup>

Tilney and Howe state that in the greater proportion of cases reported the spinal fluid has been normal and that the colloidal gold curve in the few cases in which it has been studied has been negative. In their case reports are included five cases in which colloidal gold reactions were performed. In three instances the test was negative, and in the remaining two the findings were 1223432100 and 11½22 1½00000.

David and Kraus reported thirty-four cases of epidemic encephalitis, in which forty-three examinations of the spinal fluid were made with the colloidal gold test. Nineteen were in the first three weeks of the disease. Fourteen spinal fluids were absolutely negative; in the remaining five cases the results were as follows: 1112100000; 0000110000; 0001210000; 0012231000; 1122100000. Of the fluids twenty-four taken in the later weeks of the disease, from the fourth to the sixteenth, negative results were obtained in ten, the remaining positive reactions being extremely variable.

Nixon and Sweetser, in an examination of ten spinal fluids obtained from five patients with encephalitis, found the colloidal gold curves exceedingly variable, as follows:

1	2	2	1	1	1	2	0	0		5	5	4	3	3	3	3	2	0
0	0	0	1	1	2	1	0	0		1	1	3	3	3	2	1	0	0
0	0	1	1	1	0	0	0	0		1	1	3	4	4	3	2	1	0
0	0	1	1	1	0	0	0	0		0	1	1	3	3	3	2	1	0
1	2	2	4	4	4	3	3	0		0	0	1	1	2	0	0	1	0

One of us has had five cases of epidemic encephalitis come under his observation and the curves in these cases were as follows:

0	1	1	1	1	0	0	0	0	0	½	1	1	1	½	0	0	0	0	0
0	0	1	1	1	1	0	0	0	0	0	1	1	½	2	1	½	½	0	0
1	1	½	1	½	1	½	1	0	0	0	1	2	2	2	1	0	0	0	0

It seems, therefore, that tentatively we may conclude that in a considerable proportion of cases of epidemic encephalitis, there is a negative colloidal gold chlorid curve, while in the remainder of cases in which a

10. Tilney, F., and Howe, H. L.: Epidemic Encephalitis, New York, 1920, p. 105.

11. Davis, T. K., and Kraus, W. M.: Am. J. M. Sc. **161**:109 (Jan.) 1921.

12. Nixon, C. E., and Sweetser, T. H.: Am. J. M. Sc. **161**:845 (June) 1921.

reduction occurs, the reaction is extremely variable sometimes presenting a tabetic, at others a paretic, meningitic, and at times a syphilitic curve. Judging by available information, therefore, only a small percentage of the curves of epidemic encephalitis fall entirely within the "poliomyelitic zone." Accordingly, it may be stated that while a mild syphilitic curve may indicate either one of the two diseases, a negative reaction, a paretic or meningitic curve, would be very strongly indicative of epidemic encephalitis, and as these latter are the usual reactions encountered, the test should be of distinct value in most questionable cases of differential diagnosis.

To realize the full value of this reaction in the diagnosis of poliomyelitis it must be taken into consideration with the history, physical findings and other laboratory data, in each case. It is a laboratory test and as such is subject to a personal equation of possible error, and it would

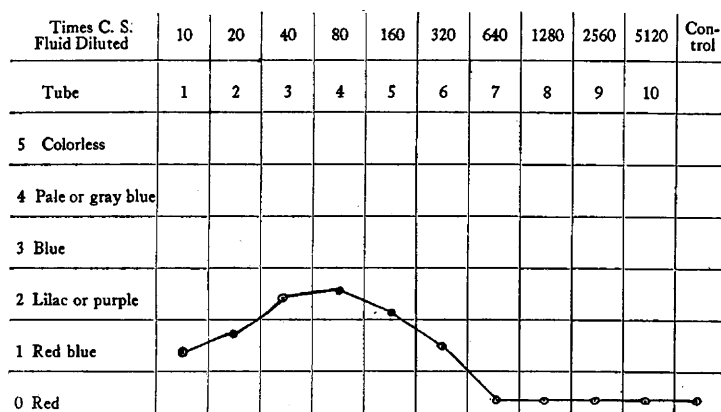


Fig. 5.—Average curve in fatal cases.

be poor policy to rely on it alone to the exclusion of all other information. We must recognize, however, that with a spinal fluid properly collected and preserved and with the test carefully performed by one familiar and experienced with the reaction, it is the most valuable laboratory means we possess at the present time, for the recognition of Heine-Medin's disease.

#### SUMMARY

The colloidal gold test was performed on seventy-four spinal fluids obtained from twenty-one cases of acute epidemic poliomyelitis. The fluids were examined at intervals varying from the fourth to the one hundred and twenty-third day of the disease. The predominant type of the malady was the myelitic with, however, a high proportion of

cases presenting symptoms of moderate or marked polyneuritis. The curves obtained have been classified according to the week of the disease in which the spinal fluids were taken. On this basis, an average curve has been constructed for each week from the first to the eighth (Figs. 1 to 4). Likewise, an average curve has been prepared from the reactions obtained in the fatal cases (Fig. 5). Finally, in Figure 6, we have placed all the curves obtained in the very acute stage of the disease, and have constructed by their limitations what might be called a poliomyelitic zone. For comparative study the curves of other well recognized meningeal conditions have been placed in the same figure.

#### CONCLUSIONS

We have drawn the following conclusions from a study of the colloidal gold reaction in this series of cases.

1. There was always a reaction with colloidal gold solution in the case of every poliomyelitic fluid examined during the acute stage of the malady. This reaction was constantly in the same zone (syphilitic zone).

2. The average curves for the first and second weeks of the disease were very similar, and consisted in a gradually rising curve presenting a graduated increase in reduction in ascending dilutions of the spinal fluid, starting in the reddish blue area in 1:10, extending into the lilac or purple in 1:40 to 1:80, and then descending somewhat more abruptly into the reddish blue again in 1:160 and reaching the non-reducing or red color in 1:640.

3. In the latter weeks of the disease the average curve gradually subsided, reaching normal in a minor proportion of the cases (three out of ten) by the eighth or ninth week, while in the remaining seven (70 per cent.) cases the curve remained still elevated at the ninth week. In two cases examined later than the eleventh week, one in the fourteenth and the other in the eighteenth, the curve was still elevated in both.

4. We have found a fairly typical poliomyelitis curve present in one chronic case as late as five years after the initial attack. This patient had a history of several relapses.

5. Of the three cases in our series, in which the curve reached normal before the end of the eighth week, this occurred on the twenty-eighth, fifty-third and fifty-fifth day, respectively. It is, therefore, exceptional for the reaction to become normal before the end of the fourth week of the disease.

6. When the curve has once reached normal, it has not been elevated again in the three cases in which this was determined.

7. Cases presenting a persistence of the very acute curve of the first few weeks up into the ninth week or beyond, commonly present at this time either considerable residual paralysis with slight, moderate or marked polyneuritis, or else slight paralysis with a polyneuritis, which still is or has been very marked. A definite persistence of the acute hydrocephalus commonly remains in these cases.

8. We are strongly inclined to believe that there is a relationship between the duration of the positive colloidal gold curve and the acute inflammatory stage of the malady, so that when the reduction of gold chlorid becomes normal, the acute period of the disease is over. If this is so, the reaction should be of value in determining when the rest of the acute period may be terminated, and the more energetic treatment by electricity and massage, etc., of the subacute stage begun.

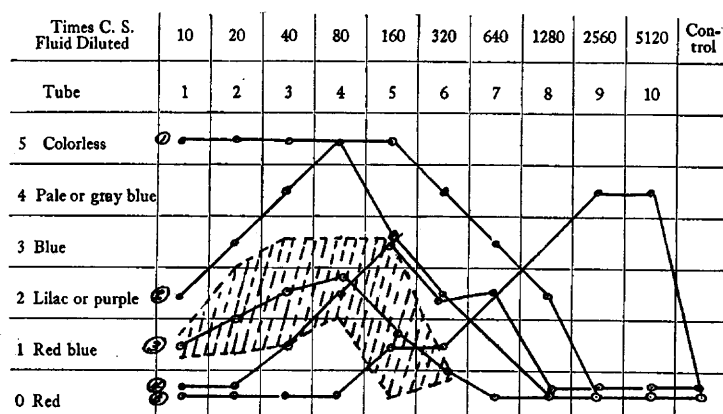


Fig. 6.—Comparative curve in (1) general paresis; (2) cerebrospinal syphilis; (3) Heine-Medin's disease; (4) tuberculous meningitis, and (5) epidemic cerebrospinal meningitis.

9. With the gradual subsidence of the colloidal gold curve there is usually a corresponding improvement in the patient's general condition, paralysis and meningeal symptoms. This relationship does not always hold true, and in patients who have had a marked polyneuritis, the curve may remain acutely elevated in the late weeks of the disease, despite the fact that the paralysis may have subsided entirely.

10. We found no close relationship, except in a general way, between the cytology and chemistry of the spinal fluid and the gold chlorid reaction. As the very acute symptoms subsided, the spinal fluid, in its chemical and cytologic contents, returned to normal. So, in most cases, does the gold chlorid curve return to normal, but more slowly, usually still remaining elevated at a period (eighth week) when

no other characteristic pathologic signs are to be found in the cerebrospinal fluid.

11. The average curve in the fatal cases, although showing a tendency to produce greater reduction, and to be prolonged slightly into the higher dilutions, did not differ sufficiently from that obtained in the nonfatal cases in the first few weeks, as to make the test of value in prognosis.

12. The gold chlorid curve began to fall in a few cases in the third and fourth week, and then was more elevated again in the ninth, tenth and eleventh weeks.

13. The reduction obtained in cerebrospinal syphilis will not usually be confused with that of poliomyelitis, except in a minor proportion of cases in which it runs rather low. In such instances the history and symptoms are so different as to cause no confusion in diagnosis, and the Wassermann test is available.

14. Typical curves of tuberculous meningitis should not be confused with those of poliomyelitis. Even the more unusual types of tuberculous meningitis curves rarely fall entirely within the poliomyelitis zone. If a curve is obtained from a clear fluid of a suspected poliomyelitis which is prolonged into the meningeal zone, a possible tuberculous meningitis should always be ruled out.

15. In the few instances in which poliomyelitis may be confused with epidemic encephalitis, the colloidal gold reaction may be of some use in differential diagnosis. The reaction in epidemic encephalitis is extremely variable, and a considerable proportion of cases present no reduction at all, while others yield a paretic, meningitic, tabetic or a very mild syphilitic curve. Often the latter two types (tabetic or luetic) fall entirely within the poliomyelitis zone. Hence we may say that in a given case, while such reactions may indicate either of the two diseases, any other type of reduction would point strongly to epidemic encephalitis. It would seem that the difference in reaction to gold chlorid is another point against the identity of the two infections.

16. Lange's reaction clearly differentiated in our series, the various forms of meningismus encountered from Heine-Medin's disease.

17. To realize the full value of this reaction, it must be taken into consideration with the history, physical findings and other laboratory data. We believe, however, that with a spinal fluid properly collected and preserved, and with the test correctly performed, it is the most valuable laboratory method we possess for the recognition of poliomyelitis, especially when the latter disease is sporadic or the type of case atypical.



The writers are indebted to Dr. W. W. Hala, Pathologist, Kings County Hospital, and Mr. F. J. Yonker, of the laboratory staff, for their generous cooperation in the laboratory portion of the work. Acknowledgment is made to Miss Meyers of laboratory staff and also Dr. S. Brody of the intern staff, Kingston Avenue Hospital, for assistance in the laboratory and clinical portion of the work.