A COMPARATIVE STUDY OF THREE COLLOIDAL REACTIONS ON THE CEREBROSPINAL FLUID.

BY D. O. RIDDEL AND R. M. STEWART, WHITTINGHAM.

THE colloidal-gold reaction introduced by Lange in 1912 is now generally accepted as one of the most important laboratory procedures in the examination of the cerebrospinal fluid. In neuro-syphilis it gives results which rival in value those of the Wassermann reaction, and its employment as a diagnostic aid in many non-syphilitic diseases has a wide sphere of utility which even at the present day does not appear to be fully appreciated.

Although the difficulties which at first surrounded the preparation of the reagent have now been largely overcome, there is still an element of uncertainty in its manufacture which cannot be altogether explained by failure to obtain a perfectly neutral solution. It occasionally happens that an apparently good reagent, fulfilling all the standard requirements laid down by Miller and his associates,¹ behaves in an irregular and mystifying manner, and, when such a misfortune arises, the worker must perforce reject his results and repeat from the beginning the rather laborious preparation of a new stock of solution. With a view to eliminating the risk of failure which attends the preparation of a solution of colloidal gold, proposals have been made to substitute other colloidal solutions which do not require the absolute purity of reagents and glassware which is so essential in Lange's test. It is perhaps too early to place much reliance on the trustworthiness of these modifications; but, judging from the few papers which have appeared, there seems to be a definite consensus of opinion that the colloidal tests in which gum mastic and benzoin are employed show a degree of parallelism to the gold test sufficiently close to justify their more extended use. One of the difficulties met with in attempting to apprise the value of these new tests is that few workers have carried out comparative tests, and in this country only Lange's reaction appears to have attracted attention. We have therefore thought it desirable to present the results of a short comparative study of the gold, the gum-mastic, and the colloidal-benzoin reactions, together with certain observations which may prove of interest to those performing these tests.

Material.—The comparative curves presented in this paper are 100 in number. The spinal fluids were obtained from asylum inmates, and, since the reactions with which we are here concerned find their greatest application in neuro-syphilis, a relatively large percentage of general paralytics have been included. None of the patients had received antisyphilitic treatment prior to examination of their fluids.

Technique.—

The Colloidal-Gold Reagent was prepared according to the standard method of Miller, Brush, Hammers, and Felton. Each fresh batch of reagent was tested with the spinal fluid of a known general paralytic, and the test was performed in the usual manner. All fluids were examined within a few hours of their withdrawal.

The Colloidal-Mastic Test of Emanuel was employed in the manner modified by Cutting,² using Smith's³ numerical scale to denote degrees of flocculation and precipitation. The emulsion was prepared from the stock solution (10 grm. gum mastic in 100 c.c. absolute alcohol) by diluting 1 c.c. of the latter with 9 c.c. of absolute alcohol; 40 c.c. of distilled water were placed in a small flask, and the diluted mastic solution rapidly added and mixed by rotation. To the first of eleven small test tubes ($3\frac{1}{2}$ in. $\times$ $\frac{1}{2}$ in.) there was added 1.5 c.c. of a salt solution containing 99 c.c. of 1.25 per cent sodium chloride plus 1 c.c. of 0.5 per cent potassium carbonate, and to each of the remainder 1 c.c. of the same solution; 0.5 c.c. of cerebrospinal fluid was next added to the first tube, and, after mixing, 1 c.c. transferred to the second tube, and so on to the tenth tube; from this 1 c.c. was rejected, the eleventh tube thus serving as a control. Finally, to each of the eleven tubes 1 c.c. of the mastic solution was added. The tubes were allowed to stand for twelve hours at room temperature and the results then read.

The Colloidal-Benzoin Test of Guillain, Laroche, and Lechelle⁴ is carried out as follows: Two stock solutions are prepared, one containing 0.01 per cent chemically pure sodium chloride, and the other a suspension of benzoin resin. One gramme of benzoin resin is dissolved in 10 c.c. of absolute alcohol, and after the lapse of forty-eight hours the supernatant fluid is decanted; of this, 0.3 c.c. is added drop by drop to 20 c.c. of distilled water, and the emulsion then heated to 35° C. in order to obtain a homogeneous suspension. The dilutions are carried out as follows: Sixteen small test tubes are set up in a rack; in the first tube there is placed 0.25 c.c. of the saline solution, in the second 0.5 c.c., and in the third 1.5 c.c.; each of the remaining tubes receives 1 c.c. of the same solution. Cerebrospinal fluid is next added: 0.75 c.c. to the first tube, 0.5 c.c. to the second and third tubes. From the latter, after mixing, 1 c.c. is transferred to the fourth tube, and so on until the fifteenth tube is reached. The cubic centi-

metre from it is rejected, the sixteenth tube thus acting as a control. Lastly, to each of the sixteen tubes 1 c.c. of benzoïn solution is added. The dilutions obtained are thus in geometrical progression, and range from 1-2 in the second tube to 1-16,384 in the fifteenth tube.

Graphic Representation.—

Gold-Sol Test.—In recording results the numeral 5 is used to indicate complete precipitation, and the lesser values to designate the graduated colour changes in the tubes where partial precipitation has occurred. In positive reactions precipitation always begins in tubes 3 and 4, and the tubes must be allowed to stand for twelve hours before the results are read.

A negative reaction is shown by an absence of colour change in all the tubes. The so-called paretic curve shows complete precipitation in the first few tubes, giving a colourless solution, with lesser changes in the remaining tubes. A typical paretic curve gives the following reading: 5555543100 (*Fig. 1*), but less marked precipitation may also be accepted where the general conformation of the curve

LANGE GOLD-SOL TEST.

FIG. 1.—Paretic curve.

FIG. 2.—Syphilitic curve.

is preserved; thus, a reading 444443210 is still fairly typical. In general it may be said that where reduction in the first three or more tubes is well marked it may be considered a paretic curve. The syphilitic curve shows a complete absence of precipitation in the first one or two tubes, with the maximum colour change (usually violet and seldom beyond pale blue) in the fourth or fifth tube. A typical curve would be 0023311000 (*Fig. 2*), and usually tabes dorsalis and cerebrospinal syphilis conform to this type.

Gum-Mastic Test.—The maximum change in this test is indicated by 4 (Smith's scale), and the lesser numerical values differ proportionately. A negative result is indicated by a total absence of precipitation in all the tubes, and a paretic curve is shown by complete precipitation in the first three or more tubes: 4444431000 (*Fig. 3*); but lesser degrees of precipitation may still be accepted provided the general conformation is preserved.

With regard to the syphilitic curve, the gum-mastic test does not appear to give any constant reading, and in this respect is much

inferior to the gold-sol test. In meningo-vascular syphilis, partial precipitation usually occurs in the first three or four tubes, but the first tube not infrequently remains unaltered. A curve such as 1332000000 (*Fig. 4*) might be interpreted as syphilitic or tabetic, but the wide variations encountered do not permit of a definite ruling on this point.

COLLOIDAL-MASTIC TEST.

FIG. 3.—Paretic curve.

FIG. 4.—Syphilitic curve.

The Colloidal-Benzoin Test.—A negative reaction is indicated on a vertical line by the figure 0; 1 indicates a weak positive where the fluid remains cloudy but shows precipitation; 2 indicates a positive reaction where precipitation is complete. The tubes are allowed to remain at room temperature for six hours before the results are read. As in the other tests, a negative result is shown by an absence of change in the fifteen tubes.

COLLOIDAL-BENZOIN TEST.

FIG. 5.—Paretic curve.

FIG. 6.—Syphilitic curve.

In their description of this test the authors recorded their results as positive or negative, no tables being provided to show the degrees of precipitation in positive reactions. They state that a paretic benzoin curve shows precipitation in the first nine or occasionally thirteen tubes. Apparently it is not essential that reduction should be absolute in all nine tubes, and the number showing complete precipitation may be increased or decreased somewhat without altering the interpretation. Duhot and Crampon⁵ regard as positive a reaction in which precipitation occurs in the first four tubes. In our series

we have accepted as paretic a curve in which precipitation is complete or almost complete in five out of the first six tubes (*Fig. 5*).

A syphilitic curve is indicated by a partial precipitation in tubes 1 to 3 or 4 (*Fig. 6*).

Limiting Factors in the Three Tests.—In all three tests cerebrospinal fluid which has been standing for some time will give curves differing from those made with fresh fluid. This effect is least noticeable with the colloidal-gold solution, and in this test fluids kept at room temperature may be used up to forty-eight hours after withdrawal. Blood-contaminated fluids introduce serious errors in interpretation and should not be employed. In the case of Lange's test, spinal fluid containing blood in macroscopic quantities may give reactions in the luetic zone, and in the other two tests blood-admixture gives rise to irregular curves. The colloidal-gold reaction may be performed with old solutions, provided they have been kept well corked in a dark cupboard. The colloidal solutions of mastic and benzoin require to be freshly prepared; those older than a few days give unsatisfactory results. It may also be mentioned here that not every sample of gum mastic appears suitable for the test, but we have found samples of ordinary commercial benzoin resin quite satisfactory.

Results of Authors' Tests.—In the following analysis we have grouped the cases for purposes of study under the following divisions: (1) Dementia paralytica; (2) Tabes dorsalis; (3) Cerebrospinal syphilis; (4) Disseminated sclerosis; (5) Non-syphilitic disease of the nervous system; (6) Miscellaneous.

Wassermann tests were performed only where the clinical diagnosis was in doubt or in cases in which the colloidal tests suggested an unsuspected syphilitic involvement of the nervous system.* For determining the presence or absence of globulin in the spinal fluid, reliance was placed on the Ross-Jones and Pandy tests. For the cell count the method described by Bybee and Lorenz⁶ was employed.

1. *General Paralysis (Table I).*—The spinal fluids of 30 cases of general paralysis were examined, and all three tests yielded typical curves in 28 instances. In the remaining 2 cases, which presented well-marked physical signs, the gold and benzoin tests were positive, and the mastic negative or atypical. The complete uniformity of the gold and benzoin reactions was very striking, and suggests that they are probably of equal value in the diagnosis of dementia paralytica. On the other hand, a paretic gold curve was obtained in four fluids taken from patients presenting no symptoms of general paralysis.

* The Wassermann reactions were performed at the City Laboratories, Liverpool, under the direction of Professor J. M. Beattie.

The first case was a demented female, 70 years old, who had suffered from a peripheral neuritis affecting the legs in 1916. Her blood and spinal fluid Wassermann were both negative. The second patient, although diagnosed general paralysis on admission, and in several other institutions, was unquestionably a case of disseminated sclerosis. He gave a negative Wassermann reaction in both blood and cerebrospinal fluid. The remaining fluids were from two cases of tabes, and in both the Wassermann reaction was strongly positive in the cerebrospinal fluid. The mental state of the first had been one of delusional insanity for nine years, and there was nothing to suggest an associated syphilitic involvement of the brain. The second case was one of progressive tabes with melancholia.

The gum-mastic reaction gave paretic curves in two non-syphilitic fluids—the chronic demented patient, and the case of disseminated sclerosis. The colloidal-benzoin reaction gave no paretic curves in non-syphilitic cases. From this brief analysis it is seen that in no instance were there paretic mastic and benzoin curves with a negative gold curve, and that, although the gold and mastic tests gave paretic curves in disseminated sclerosis, the benzoin reaction failed to do so.

It is not a little remarkable that in one instance two reactions gave paretic curves in the absence of other positive laboratory findings or clinical manifestations of syphilis. The patient was a woman, age 71, in an advanced stage of dementia; alcohol was the supposed cause of her insanity, and in 1916 she developed peripheral neuritis affecting the legs, which left them permanently paralyzed in a state of talipes equinus.

Tabes Dorsalis (Table 2).—The 3 cases that were diagnosed tabes dorsalis presented well-marked signs and symptoms of the disease. The mastic and benzoin tests gave syphilitic curves in the three fluids, but the colloidal-gold reaction gave in two instances paretic curves to which reference has already been made; in the other fluid a well-marked syphilitic curve was obtained.

Cerebrospinal Syphilis (Table 3).—The colloidal-gold reaction gave curves in the syphilitic zone in all 6 cases; the mastic test also gave curves which were interpreted as syphilitic. The colloidal-benzoin test showed syphilitic curves in 4 cases and negative in two fluids. The Wassermann reaction proved positive in 5 cases and negative in the sixth. We have included the latter case in the cerebrospinal group because the clinical history and physical state of the patient pointed clearly to a syphilitic infection of the nervous system. He contracted syphilis when 22 years of age, and had a transient attack of hemiplegia four years later. A mild dementia supervened, and he is now in his thirty-seventh year. Although both the Wassermann and

benzoin reactions are negative, it is probable that the positive gold curve is the more correct index of his condition.

Syphilitic Curves in Non-syphilitic Disease (Table 3a).—1. A primary dement with symmetrical wasting of the hands and slight spastic paresis of the lower limbs gave a syphilitic type of curve with the colloidal-gold solution, and negative results in the mastic and benzoin tests (Wassermann —, cells 4, globulin faintly +).

2. A patient with chronic tuberculous adenitis and recent symmetrical swelling of the parotid glands gave negative gold and benzoin curves and a positive mastic curve (Wassermann —, cells 6, globulin faintly +).

3. One case of insanity with epilepsy gave a syphilitic gold curve, slight reduction in the mastic test, and a negative colloidal benzoin reaction (Wassermann —, cells 0, globulin —).

4. In a case of confusional insanity the colloidal-gold reaction showed reduction in the syphilitic zone, a mastic curve which was interpreted as syphilitic, and a negative colloidal-benzoin reaction (Wassermann —, cells 8, globulin —).

The above four cases form too small a group on which to base any conclusions, but the parallelism between the Wassermann reaction and benzoin test is certainly noteworthy.

Disseminated Sclerosis (Table 4).—The first case gave syphilitic curves in all three reactions. The spinal fluid of the second case, to whom reference has already been made, showed a paretic curve in the gold and mastic tests, and a syphilitic curve in the benzoin test.

Organic Nervous Diseases (Table 5).—With two exceptions all three tests were negative. A patient suffering from pseudobulbar paralysis showed very slight reduction in the middle zone in the colloidal-gold test, slight reduction in the first two tubes of the mastic test, and a negative colloidal-benzoin reaction (Wassermann —, cells 4, globulin faintly +). In another patient suffering from paraplegia the gold test was negative, the mastic showed slight reduction in the first five tubes, and the benzoin test was negative (Wassermann —, cells 10, globulin faintly +).

Miscellaneous (Table 6).—A survey of this group shows that no positive results were obtained.

Relation of the Globulin Content and Cell Count to the Three Reactions.—In 30 cases of dementia paralytica, positive colloidal reactions were in all instances associated with pleocytosis and increased globulin content; but on the other hand, in 12 cases in which all three tests were negative there was a definite increase in globulin, and in 13 cases giving negative results the cell-count was increased. One fluid with no increase of globulin gave paretic curves in the colloidal-gold and gum-mastic tests, and in one case of dementia in whom all three tests

were positive the globulin content was within normal limits. In only one instance did we find all three reactions negative in a spinal fluid which showed a positive Wassermann reaction, pleocytosis, and increase of globulin. In other words, the three colloidal reactions failed to give evidence of a syphilitic infection in 1 per cent of the series. The patient was a woman with gummatous ulceration of the soft palate, and curiously enough her blood Wassermann was negative.

Table 1.—General Paralysis.

Case No.	Diagnosis	Cells per cmm.	Globulin Content	Colloidal-Go'd reaction	Mastic reaction	Colloidal-Benzoin reaction	W's'rman reaction CS.F. Bl'd
1	G.P.I.	98	+++	555555543	444420000	12222112221000	
2	G.P.I.	110	++	5555543200	4443000000	1222222222200000	
3	G.P.I.	68	+++	5555544444	4444433200	222222000022200	
4	G.P.I.	184	+++	555555554	4444321100	22222000222220	
5	G.P.I.	120	++	5555555443	4444430000	222222002222200	
6	G.P.I.	30	++	5544443220	4332200000	222222222222200	
7	G.P.I.	64	+++	555555554	4443232100	22222222222000	
8	G.P.I.	86	++	5555443332	4423210000	22222222222000	
9	G.P.I.	58	+++	5555555543	4444322210	222222001222210	
10	G.P.I.	—	++	5544443110	4443210000	12222222222100	
11	G.P.I.	82	+++	5555454333	4443210000	22222222222111	
12	G.P.I.	32	+++	444442100	4444432100	122222222222200	
13	G.P.I.	18	++	444443000	444420000	22222221000000	
14	G.P.I.	12	++	4443332000	4443222100	12222200000000	
15	G.P.I.	20	++	4444430000	4444000000	222222222221100	
16	G.P.I.	12	+++	4444332000	4431110000	222210221000000	
17	G.P.I.	292	+++	5555543434	4444433200	222222002221000	
18	G.P.I.	264	+++	5554434220	4444321000	122222222222000	
19	G.P.I.	38	++	5555432000	4444433200	222222012220000	
20	G.P.I.	38	+++	5553333210	4443310000	122222222000000	
21	G.P.I.	22	++	5555443200	4444211000	222222222000000	
22	G.P.I.	70	++	5553333310	4444422000	222222222200000	
23	G.P.I.	14	++	5555544200	4444443111	122222222200000	
24	G.P.I.	14	++	5554443221	4444443211	222222221000000	
25	G.P.I.	182	+++	5555555432	0444444330	222222112200000	
26	G.P.I.	16	++	5555555432	3444444443	222222222221000	
27	G.P.I.	48	++	5555543000	4444433211	122222222220000	
28	G.P.I.	34	+++	5555543100	4444444333	222222222200000	
29	G.P.I.	30	++	5443322000	4433333222	222221120000000	
30	G.P.I.	54	++	5544430000	4444321000	122212221000000	+

Table 2.—Tabes Dorsalis.

31	Tabes dorsalis ..	60	+	4443322000	4322000000	012200222100000	+	+
32	Tabes dorsalis ..	6	++	4433310000	3332000000	111102222100000	+	+
33	Tabes dorsalis ..	4	+	1133311000	2332100000	111111220000000	+	

Table 3.—Cerebrospinal Syphilis.

34	Cerebellar ataxia, congenital syphilis	54	+	0000333000	3322000000	111112112221000	+	
35	Syph. hemiparesis	—	++	0002332000	3210000000	000000222000000	+	—
36	Syph. hemiplegia	4	++	1112330000	3332221100	000000222000000	+	
37	Cerebral syphilis	8	+	1233300000	4322000000	111002222200000	+	
38	Erb's syph. spinal sclerosis ..	32	++	1112233100	2344432100	012002222210000	+	
39	Cerebral syphilis and gumma of palate ..	0	—	0002200000	3322100000	111111000000000	+	

THREE COLLOIDAL REACTIONS ON CEREBROSPINAL FLUID 333

Table 3a.—Syphilitic Curves in Non-syphilitic Disease.

Case No.	Diagnosis	Cells per cmm.	Globulin Content	Colloidal-Gold reaction	Mastic reaction	Colloidal-Benzoin reaction	W's'rmann reaction CS.F. Bl'd
40	Muscular atrophy —hands	4	+	0022210000	0000000000	000001222000000	—
41	Insanity with epilepsy	0	—	1122210000	3300000000	000000000000000	—
42	Confusional insanity	8	—	1123000000	4421002000	000002221100000	—
43	Tubercular adenitis	6	+	0023330000	3322110000	000002220000000	—

Table 4.—Disseminated Sclerosis.

44	Disseminated sclerosis	0	+	5444321000	4443210000	111002220000000	—
45	Disseminated sclerosis	4	—	1003444100	3320000000	111112222100000	—

Table 5.—Organic Nervous Diseases.

46	Motor aphasia ..	15	—	0000000000	0000000000	000002220000000	—
47	Pseudobulbar paralysis	4	+	0000111000	3200000000	000001222220000	—
48	Infantile cerebral paralysis	4	—	0000111100	0000000000	000002222220000	—
49	Spastic paralysis ..	6	—	0000000000	0000000000	000000211000000	—
50	Hemiplegia	0	—	0000000000	0000000000	000000222200000	—
51	Hemiplegia — epileptic imbecile ..	0	—	0000000000	0000000000	000000220000000	—
52	Hemiplegia	2	—	0000000000	1111113111	000001222000000	—
53	Paraplegia	0	—	0000000000	0000000000	000000211000000	—
54	Triplegia (mitral stenosis)	2	—	0000000000	0000000000	000000210000000	—
55	Hemiplegia and aphasia	2	—	0000000000	0000000000	000000200000000	—
56	Hemiplegia	0	+	0011100000	3000000000	000000221000000	—
57	Infantile polio-myelitis	0	—	0000000000	0000000000	000002220000000	—
58	Facial hemispasm ..	10	+	0000000000	1110000000	000000010000000	—
59	Sclerosis of cord ..	4	—	0000000000	0000000000	000002222000000	—
60	Lead encephalopathy	0	—	0000000000	0000000000	000000122200000	—
61	Optic atrophy	12	—	0000000000	0000000000	000000211100000	—
62	Paraplegia	20	+	0000010000	2200000000	000002222200000	—
63	Hemiplegia	0	—	0011110000	0000000000	000002222100000	—

Table 6.—Miscellaneous.

64	Secondary dementia ..	0	—	4444442100	4443200000	000112222222200	—
65	Idiocy	4	+	0000000000	3000000000	000000222220000	—
66	Tertiary syphilis (nasal bones) ..	2	—	0000000000	0000000400	000000222200000	+
67	History of syphilis ..	0	+	0000000000	0000000000	000001222000000	+
68	History of syphilis ..	0	+	0000000000	0000000000	000002221000000	+
69	Tertiary syphilis ..	8	+	0000000000	0000000000	000000111000000	+
70	Hypopituitarism ..	5	+	0000000000	0000000000	000000111000000	+
71	Chronic uræmia ..	6	+	0000000000	0000000000	000000000000000	+
72	Exophthalmic goitre ..	8	+	0000000000	0000000000	000002200000000	+
73	Pellagra	34	—	0000000000	0000000000	000012100000000	+
74	Secondary Dementia ..	18	—	0000000000	0000002202	000001100000000	+
75	to Cases of primary dementia ..	2	—	0000000000	0000000000	000000222000000	+
84	to Insanity with epilepsy ..	2	—	0000000000	0000000000	000000222100000	+
85	to Insanity with epilepsy ..	2	—	0000000000	0000000000	000000222100000	+
91	to Confusional insanity ..	6	—	0011100000	0000430000	000000010000000	+
92	to Confusional insanity ..	6	+	0011100000	3310000000	000000221000000	+
93	to Various psychoses ..	2	—	0000000000	0000000000	000000222100000	+
94	to	2	—	0000000000	0000000000	000000222100000	+
100	to	2	—	0000000000	0000000000	000000222100000	+

General Discussion.—The types of curve which we obtained when employing the colloidal-gold reaction appeared to follow exactly those which have been described by previous writers. The types of colour change in the various dilutions are certainly of great diagnostic value, but they are not specific for any one condition. A paretic curve was a constant finding in all the spinal fluids taken from general paralytics, but we also obtained four paretic curves in patients who were not suffering from general paralysis. Furthermore, in one advanced case (*Case 30*) of this disease a negative colloidal-gold reaction was obtained on the first examination of his spinal fluid; when a second examination was made six days later the curve was irregular, and only on the final examination made one month later was there a typical curve. This failure to obtain constant results cannot have been due to faulty solutions of colloidal gold, for the various samples used gave typical curves with other paretic fluids. Other writers have noted this peculiarity, and by some it has been attributed to the provocative effects of lumbar puncture which may determine an altered physico-chemical relation in the globulin of the cerebrospinal fluid.

The gum-mastic reaction has proved in our hands to be less sensitive than Lange's test and of less diagnostic value; but the possibility of technical error seems small, and readings may be rapidly obtained. Against this advantage must be placed the failure to obtain with any degree of constancy curves which could be interpreted as syphilitic.

From a study of 100 spinal fluids, E. Duhot and P. Crampon⁵ conclude that the colloidal-benzoin reaction is negative in non-syphilitic lesions of the nervous system, and positive in 90 per cent of cases of neurosyphilis. In our series the colloidal-benzoin test was positive in every case of general paralysis, and we did not obtain a paretic curve in any case of an obviously non-syphilitic character. In two cases of disseminated sclerosis the type of curve was syphilitic, and with these two exceptions the reaction appeared specific for neurosyphilis. The results were therefore not only in close agreement with those of the colloidal-gold reaction, but in some respects of greater diagnostic value.

When we came to chart the precipitation curves in the benzoin reaction we were at once impressed by the irregular behaviour of many fluids. Indeed, at first glance the test seemed to possess no value, for the presence of varying degrees of precipitation in one or more tubes was an almost constant finding with normal fluids. Thus, in a miscellaneous group of 35 normal spinal fluids the benzoin reaction showed a complete absence of precipitation in the whole 15 tubes in only two instances, a very different finding from the 27 entirely

negative gold reactions in the same series. However, on carrying our analysis a little further it became evident that this precipitation occurred almost constantly in the middle series, and with one exception was never found in the first five or six tubes. Another peculiarity was the incompleteness of precipitation in tube 1, even when reduction was pronounced in nearly all the remaining tubes of the series. The method of Guillain, Laroche, and Lechelle seemed, therefore, to stand in need of modification; but, by restricting the number of dilutions employed to five, we were able to obtain reliable information without altering the strength of the salt solution. Furthermore, the omission of the first tube of the series reduced the quantity of cerebrospinal fluid required for the test by nearly one-half. The benzoin curves in our tables were obtained by employing the original method; but, in the modification proposed, the dilution of cerebrospinal fluid in the first tube is 1 in 2, and is carried only as far as the fifth tube, the sixth serving as a control.* In the original method of Emanuel⁷ the mastic test was performed with five tubes, and since neither reaction appears to give positive results in cases of meningitis (non-syphilitic) we believe no advantage is obtained by using dilutions higher than 1 in 32.

Guillain and his associates recommend the use of the ultra-microscope for examining the benzoin reaction in its early stages. When the reaction is positive there is an immediate arrest of Brownian movement in the resinous suspension, followed by the appearance of a mass of refractile granules which agglutinate. We have found

FIG. 7.—Colloidal-benzoin reaction (modified). (a) *Negative curve*.

FIG. 8.—Colloidal-benzoin reaction (modified). (b) *Paretic curve*.

FIG. 9.—Colloidal-benzoin reaction (modified). (c) *Syphilitic curve*.

* Our investigation was complete before the appearance of a recent communication (*Presse médicale*, 1921, Sept. 28), in which Guillain, Laroche, and Lechelle describe a modification of their test, substantially the same as that outlined above.

that equally reliable information may be obtained by centrifuging the tubes for a few minutes. The control tube in a positive reaction shows no precipitation, and the degrees of reduction in the other tubes are strictly comparable with those obtained by the ordinary technique.

In this test the ease with which the degrees of precipitation may be read, the restriction to three numerals for designating these degrees, and the rapidity with which results can be obtained, may all be claimed as advantages which the colloidal-gold and gum-mastic reactions do not possess.

Conclusions.—1. In a comparative study of spinal fluids in 30 cases of general paralysis the gold-sol test and the colloidal-benzoin reaction of Guillain, Laroche, and Lechelle gave parallel results; the gum-mastic reaction was in less close agreement.

2. The colloidal-gold and the gum-mastic tests gave paretic curves in non-paretic fluids. The colloidal-benzoin test gave paretic curves only in paretic fluids.

3. Syphilitic curves were obtained in all three tests from cases that clinically were not examples of neurosyphilis.

4. In the colloidal-benzoin reaction a slight degree of precipitation in the middle series of tubes was often obtained with normal cerebro-spinal fluid.

REFERENCES.

- ¹ MILLER, BRUSH, HAMMERS, and FELTON, *Johns Hop. Hosp. Bull.*, 1915, xxvi, 391.
- ² CUTTING, *Jour. Amer. Med. Assoc.*, 1917, lxviii, 1810.
- ³ SMITH, *Med. Record*, 1917, xcii, 675.
- ⁴ GUILLAIN, LAROCHE, and LEHELLE, *Comptes rend. Soc. de Biol.*, 1920, lxxxiii, 1077.
- ⁵ DUHOT and CRAMPON, *Bull. Soc. méd. Hôp. de Paris*, 1921, xxxvii, 307.
- ⁶ BYBEE and LORENZ, *Arch. of Internal Med.*, 1911, July, 38.
- ⁷ EMANUEL, *Berl. Klin.*, 1913, lii, 792.