the most usual sequela being perversion of conduct. Inquiry amongst my colleagues leads me to believe that such cases are not unknown in Belfast, as in other cities. These patients present a problem both to their parents and to the State, and are potential recruits for the criminal lunatic asylums. I wonder how soon a past attack of encephalitis will be urged as a defence on a criminal charge!

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The Colloidal Gold Reaction with Cerebrospinal Fluid.

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THE history of the colloidal gold reaction is one of great interest.

In 1901 Zsigmondy used the precipitation of colloidal gold by proteins as a means of determining quantitatively their amount in given solutions. He discovered that solutions of protein give protection to colloidal solutions of gold up to a certain point, and he determined the so-called goldzahl for various protein substances, by which is meant the number of milligrammes of protein employed, just sufficient to prevent the precipitation of 10 c.c. of colloidal gold of a percentage of ·0053 in the presence of 1 c.c. of 10 *per cent.* sodium chloride. By this method it can be determined whether a given protein is absolutely pure, or, granted that this is the case, how much of the protein is present in a given solution.

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In 1912 Carl Lange (1) endeavoured to apply this method to the study of the proteins in cerebrospinal fluid, and discovered that, instead of securing protection, quite the reverse occurred, and that this was especially true with the cerebrospinal fluid derived from patients with syphilitic disease of the central nervous system. Without coming to any certain conclusion about the cause of this aberrant phenomenon, he suggested that this method could be used as a means of diagnosing syphilitic from non-syphilitic cerebrospinal fluid.

In 1914 Miller and Levy (2), from the Johns Hopkins Hospital, emphasized the fact that the precipitations of colloidal gold by cerebrospinal fluids from cases of tabes and general paresis differ in a fundamental manner, so that the test could be used, not only to differentiate syphilitic from non-syphilitic conditions, but also to distinguish general paresis from tabes and cerebrospinal syphilis.

In 1914 Kaplan published his classical work on *The Serology of Nervous and Mental Diseases.* He investigated the colloidal gold reactions of many cases from the Neurological Institute in New York, and confirmed the results obtained in general paresis and cerebrospinal syphilis, but his cases of pure tabes showed either no reaction, or a very slight, insignificant change in the colloidal gold. He, however, emphasized the fact that in early tabo-paresis the paretic curve seemed to herald the symptoms of general paresis.

In 1915 Miller, Brush, Hammers and Felton (3) continued at the Johns Hopkins Hospital the work of Miller and Levy, and gave precise directions for the preparation of the colloidal gold. They differed from Kaplan in the curves which they obtained in cases of tabes.

In 1917 Hammes (4) regards the test as more delicate than any other as an index of pathological change in the cerebrospinal fluid.

The mechanism of the reaction has been subject to much investigation. Weston (5) showed that the substance producing the reaction is not the same as the Wassermann body.

In 1917 Felton (6) considered that the various types of reaction could best be explained by the antagonistic precipitating relations of albumen and globulin, the albumen exerting an inhibitory reaction, and the globulin a precipitating reaction.

In 1920 Cruickshank (7) put forward this same hypothesis independently. He assumed that the syphilitic reactions are in part due to the presence of albumen, sufficient in quantity to partially obscure the precipitating effect of globulin, and in part due to a specific alteration in the physical state of the globulin, which is associated with a positive electrical charge.

The great crux of this valuable reaction is the extreme difficulty

of making a satisfactory preparation of colloidal gold. This difficulty, no doubt, accounts for the fact that this reaction is not so generally used as it ought to be. Many serologists have spent much time and labour in futile attempts to prepare the test solution. We also think it possible that some of the results obtained, and the differences that have been recorded—for instance, in cases of pure tabes—may be due to the fact that the colloidal gold preparations used by different workers were not quite similar. This subject has been brought into relief by a valuable paper published in 1923 by Mellanby and Anwyl Davies.(8) They show that the exact reaction of the colloidal gold solution is a matter of great importance, and that by varying the reaction very slightly, great differences in the curves may be obtained. Thus, a normal fluid, if the reaction of the gold sol be faintly acid, will give the curve of cerebrospinal syphilis, and, if it be made more acid still, the curve of general paresis. In the published directions for the preparation of the test solution, only a few workers give any direction with regard to this essential point. Miller, Brush, Hammers and Felton recommend that the solution be titrated with alizarine red, and that the final product must be absolutely neutral, but the "change point" of alizarine red lies to the acid side of the strictly neutral point.

Cruickshank points out that an acid sol is very sensitive and an alkaline sol is insensitive, and, at his suggestion, Scott titrates his sols with bromo-cresyl purple, and brings them to a pH. of 5·5. Such a sol may, we fear, be dangerously acid, and too sensitive.

We have tried a number of the methods suggested, and found it almost impossible to get constant and reliable results. The solutions prepared on exactly similar lines seem to differ greatly in their sensitiveness, so that comparable results seem hardly possible. Since reading the paper on Mellanby and Anwyl Davies, and using their method, our results have been much more satisfactory. Any method of titrating colloidal gold seems very difficult, first, because of the red colour of the product; second, because the absorption of CO_2 from the air markedly interferes with the reactions. Thus, distilled water shaken up in the air or exposed for some time becomes distinctly acid to the usual indicators.

The method suggested by Mellanby and Anwyl Davies obviates this difficulty. Instead of using alkali and acid in making the colloidal gold solution, they use neutral potassium oxalate alone. Thus, if all the solutions be exactly neutral, the finished product must also be neutral.

In using this method we have found that the most essential point is the preparation of the distilled water.

Details of the Examinations of the Cerebrospinal Fluid in Cases giving a Paretic Curve.

Date	Name	Fluid Wassermann. 1 in 1	1 in 2·5	1 in 5	Sigma Units.	Cells per c.m.m.	Globulin.	Glucose	Colloidal Gold	NOTES
19/12/22	M. (3621)	X X	X X	X X	4·5	8	X	X	5553321100	Slurring speech, easily amused—tremor of lips. A.R. + K.J.s normal G.P.I.?
12/1/23	H_1 (x)	X X	X X	X X	2·2	8	—	X	5550000000	Incontinence of urine, loss of memory, anaesthesia of skin. Sluggish K.J.s A.R. + treatment with N.A.B & mercury begun
11/2/24	H_2	X X	X X	X X	8	16	X	X	4331000000	Before infection with malaria.
3/5/24	H_3	X X	X X	X	1·0		X	X	5432100000	Symptoms greatly improved after malarial treatment.
6/4/23	*T_1 Ward VI.	X X	X X	X X	4·8	13	X X	075%	4555143060	Dizziness and headaches of 7 weeks' duration, difficulty of speech, paresis, transferred to asylum.
4/1/24	*T_2	X X	X X	—	1·7	5	X	X	5555531000	Returned to venereal clinic greatly improved. Mental symptoms gone.
1/6/23	*M·I. Ward VI.	X X	X X	X X	35·2	60	X	X	5555110000	History of syphilis, epileptiform attacks, coma, died. Supposed gumma of brain.
24/1/24	W_1 (P.V.C.)	X X	X X	X X	4	124	X	X	5555543300	General Paralysis.
3/5/24	W_2 (P.V.C.)	X X	X X	X	1·7	24	X	X	5555543100	General Paralysis after malarial treatment.
24/1/24	B_1 (P.V.C.)	X X	X X	X X	6	7	—	X		General Paralysis.
23/3/24	B_2 (P.V.C.)	X X	—	—	1·5		X	X	5554320000	General Paralysis.
1/2/24	P. (P.V.C.)	X X	X X	X X	2	55	X	X	5555330000	General Paralysis.
1/2/24	M. (P.V.C.)	X X	X X	X X	10	99	X	X	5555544300	General Paralysis.
11/6/24	M_2 (P.V.C.)	X X	X X	X X	4·4		X	X	5553100000	General Paralysis.
1/2/24	P_1 (P.V.C.)	X X	X X	X X	2·1	13	X	X	4555431100	General Paralysis.
11/6/24	P_2 (P.V.C.)	X X	X X	X X	1·2		X	X	5553210000	General Paralysis.
1/2/24	B. (P.V.C.)	X X	X X	X X	9·1	37	X	X	5554332100	General Paralysis.
14/2/24	L. (P.V.C.)	X X	X X	X X	8	5	X	X	4443221100	General Paralysis.
28/2/24	*A. Ward 11	X X	X X	—	1·7	30	X	X	4553332100	Tabes.
4/3/24	*B. (6102)	X X	X X	X	1·4	33	X	X	4555332200	K.J.s—weakness of left leg.
4/3/24	*D (5317)	—	—	—	0	4	—	X	5430000000	History of syphilis, treated. K.J.s + ankle clonus tremor, eyes sluggish but react to light, R.V. 6/6 margin of disc blurred, vessels normal. L.V. hand movements—old iritis—posterior synechiae—choroido-retinitis
13/3/24	*McG. Ward 22	X X	X X	X	6·1	30	X	X	5555543200	Right sided hemiplegia.
23/3/24	L. (P.V.C.)	X X	X X	—	2	79	X	X	5555543100	General Paralysis.
23/3/24	McN. (P.V.C.)	X X	X X	X	2·9	123	X	X	5554321000	General Paralysis.
12/4/24	*H Ward V.	X X	X X	—	0	12	X	X	4444432100	Cerebral syphilis.
17/4/24	W. Ward 22	X X	X X	X X	4	26	X	X	5554443210	Weakness and tingling in arms. Delusions of persecution (G.P.I.)
17/4/24	R. (P.V.C.)	X X	X X	X X	10	25	X	X	5555544310	General Paralysis.
17/4/24	K. (P.V.C.)	X X	X X	X X	1	27	X	X	5555543310	General Paralysis.
27/4/24	*O'H. (4106)	X X	X	—	2·3	28	X	X	5433321000	Hemiplegia for 18 months.
15/1/24	M_1 (P.V.C.)	X X	X	—	·8	28	X	X	5555533210	General Paralysis.
3/5/24	M_2 (P.V.C.)	X X	—	—	·8		X	X	5554310000	General Paralysis (after malaria).
11/6/24	McC. (P.V.C.)	X X	X X	X X	4·7	40	X	X	5553343000	General Paralysis.
19/6/24	McD. (P.V.C.)	X X	X	—	·6		X	X	4555555310	General Paralysis.
25/6/24	*K. (5602)	X X	X X	X X	9·1	90	X		4555553210	A.R. + K.J.s—Romberg + Tabes.
15/12/22	*B. (X)	—	—	—	0	3	X	·09%	4443210000	Disseminated Sclerosis.
15/1/24	W. (P.V.C.)	X X	X X	X	2·1	107	X	X	3355430000	General Paralysis.
15/1/24	P. (P.V.C.)	X X	X X	X X	2·1	20	X	X	5555532000	General Paralysis.
15/1/24	McW. (P.V.C.)	X X	X X	X X	3·9	23	X	X	5555443000	General Paralysis.
15/1/24	R. (P.V.C.)	X X	X X	X X	49		X	X	5555554300	General Paralysis.
15/1/24	O'N. (P.V.C.)	X X	X X	X X	8	56	X	X	5555551100	General Paralysis.
15/1/24	I. (P.V.C.)	X X	X X	X X	7·3	26	X	X	5555430000	General Paralysis.
15/1/24	M. (P.V.C.)	X X	X X	X X	9·1	57	X	X	0005433210	General Paralysis—not typical.

The cases marked P.V.C. were sent for examination by Dr. Norman Graham from Purdysburn Asylum. A number of these cases were treated by infecting the patients with malaria. Cases marked ($_1$) and ($_2$) are before and after treatment with tertian malaria.

The other cases detailed occurred among 150 complete examinations of the cerebrospinal fluid of patients either attending the Venereal Clinic or in the wards of the Royal Victoria Hospital.

We use an all-glass still without any rubber connection. It would probably be even better to use a condenser with the central tube made of block tin, so as to prevent any absorption of alkali from the glass. Ordinary laboratory distilled water is taken, and a small quantity of carbonate of soda is added (1 grm. to the litre), and the water is re-distilled into a hard glass container which s scrupulously clean. The first 10 *per cent.* of the distillate is rejected, and the last 10 *per cent.* of the water left undistilled. This second distillate is then distilled a third time in exactly the same way, but without any carbonate of soda.

The other important point is that all the flasks and pipettes used should be absolutely clean and used for no other purpose.

It will be found that distilled water prepared in this way is absolutely neutral at the boiling-point, though it will, of course, absorb some CO_2 if left standing for any length of time.

With such precautions we have found that this method gives almost constantly a solution of colloidal gold of remarkable uniformity.

Conclusions.

1. The method described by Mellanby and Anwyl Davies is a satisfactory way of preparing neutral colloidal gold.

2. The so-called paretic curve is very characteristic of general paresis, but may occur occasionally with the cerebrospinal fluid from cases of cerebrospinal syphilis, and very rarely in that of disseminated sclerosis.

3. The number of sigma units in the fluid from cases of general paresis or cerebrospinal fluid usually gives a low reading.

4. Treatment by malaria, while often producing marked clinical improvement in general paresis, seems, at least in the cases detailed, to have little effect on the colloidal gold reaction. There is, however, in the majority of the cases a distinct lowering of the numbers of sigma units.

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The Spatz Test for Iron in the Brain. (1) By J. S. DUDGEON, M.D., D.P.H.Belf., Assistant Medical Officer, County Mental Hospital, Whittingham.

CONSIDERABLE interest has been shown of late in the occurrence of iron in the brain and its relation to certain nervous diseases.

The existence of the iron can be demonstrated by placing a section of brain in concentrated ammonium hydrosulphide solution. After a few seconds the globus pallidus and the substantia nigra become a greenish-grey colour. Later, the red nucleus, the corpus dentatus cerebelli, the putamen and caudate nucleus also darken. Still later, the corpus mamillare, the anterior part of the thalamus and the cortex cerebri, especially in the deeper layers, also become greenish-grey. These centres always follow in the same order, and it is important to watch the process, as at the end of the reaction they have all darkened to more or less the same degree, and the contrast is lost. In diseases of the extra-pyramidal system this reaction may be of considerable interest, and Spatz (2) reports a case with pyramidal lesion in which there was an abundance of iron in the globus pallidus and substantia nigra; in the majority of such cases, however, he did not find any increase of iron. Gans(3) mentions a case showing marked extrapyramidal motor symptoms, in which he found an increase of iron in the globus pallidus, putamen and caudate nucleus.

In general paralysis the cortex of the brain, especially in the frontal region, in addition to showing the greenish-grey darkening mentioned above, shows a number of fine black streaks and dots which, though easily seen by the naked eye, are more fully appreciated when a hand lens is used.

These are due to the presence of iron in the adventitial spaces of the cortical blood-vessels, and they have been demonstrated in two diseases only, *i. e.* general paralysis and trypanosomiasis.(1) As the latter can be disregarded in this country, the test remains a convenient and rapid method for the pathological detection of