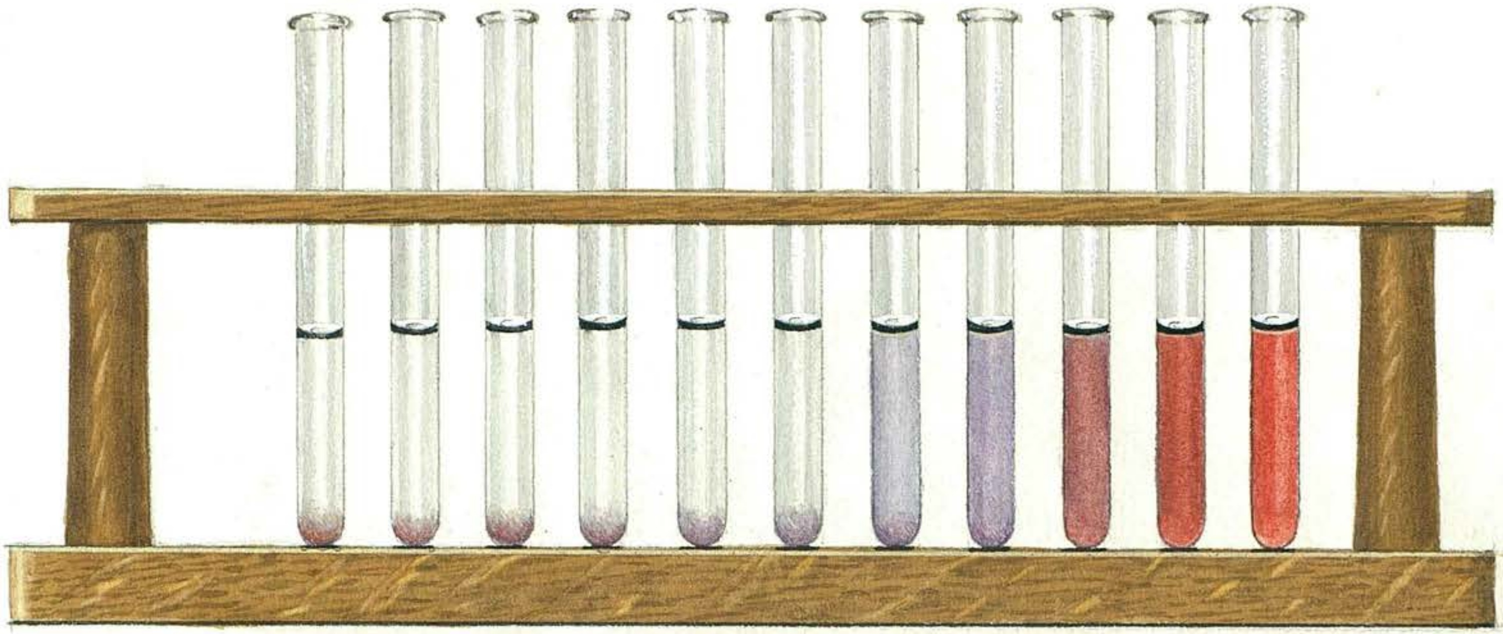
Frontespiece.



A "Positive" Goldsol Reaction in General Paralysis.

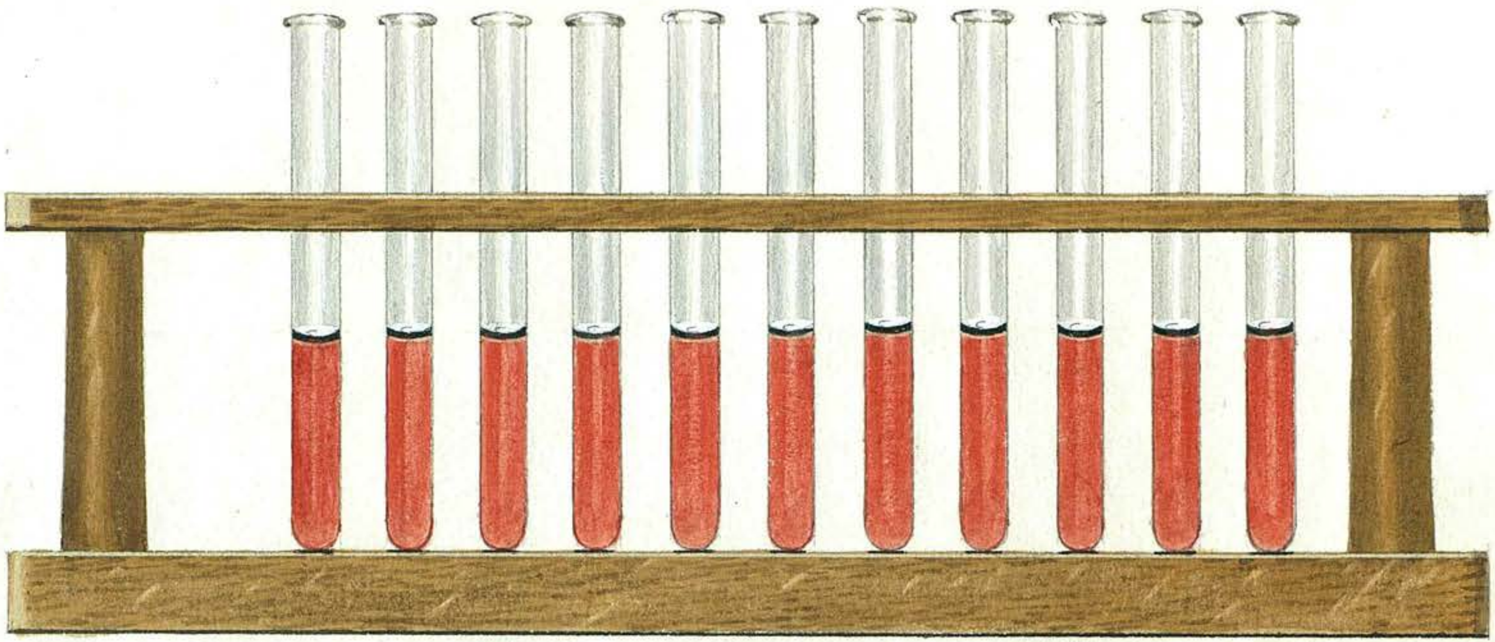
THE GOLDSOL TEST IN MENTAL DISEASE.

Thesis for the degree of M.D. 1920.

by

P. W. BEDFORD, M.B., Ch.B.

Figure. 1.



A Negative Goldsol Reaction

THE GOLDSOL TEST.

I N T R O D U C T I O N.

"Dimidium Scientiae prudens quaestio."

The increasing prevalence of the plea of insanity in criminal prosecutions, and the frequency of its failure as a defence, would seem to indicate that there are mental diseases from the Medical standpoint which are not equivalent to the legal status of insanity.

According to Southard, of 119 cases diagnosed as General Paralysis, post-mortem examination showed a diagnostic error of 26%.

It follows that the diagnosis of the form of Mental disease may become a social function of the greatest delicacy, and the margin of error a matter of very great importance.

General Paralysis is often very difficult to diagnose, and the responsibility of coming to a decision is not lessened by the fatal character of the disease.

It is a problem in the present tense and imperative mood.

Robertson puts the case very clearly in his Morison Lectures. He says - "In the whole field of psychological/

psychological Medicine there is still not a more responsible problem, nor one requiring the exercise of more prudence and caution, than the early and definite diagnosis of General Paralysis. ------
The anxiety produced by this uncertainty (of diagnosis) was often very trying, and, when important matters are at stake, it has been found so intolerable that the skull has been trephined and a small portion of the cortex removed and examined microscopically to settle the question one way or another."

Nowadays such heroic measures are uncalled for. The modern method of diagnosis consists of the clinical examination of the patient in the usual way, supplemented, but not supplanted, by the laboratory examination of his spinal fluid. For laboratory tests have come to play a greater guiding part in the diagnosis and treatment of syphilis than in that of any other bacterial disease.

If anyone had been able to devise a less intricate test for the recognition of active Syphilis in all its stages, the Wassermann Reaction would never have survived to the present day.

The general utility of any test, and in a measure its reliability, is determined chiefly by the simplicity of its unspecialised technique. It is from this point of view that I have made the Goldsol test the/

the subject of my thesis; for any simple test which promises increased precision in diagnosis is worthy of that careful investigation which is the half-way house to knowledge.

As will be shown later, the Goldsol Test is more delicate than the Wassermann Reaction, cell count, or globulin estimation, and the margin of error quite small. Its technique is so simple that the performer cannot make a mistake without bringing the most ingenious carelessness to his aid.

ORIGIN OF TEST.

The most delicate known method of protein analysis is the outcome of a successful attempt to use Colloidal Gold as a means for the quantitative estimation of protein substances. The Goldsol test has its origin in certain unexpected results that were obtained in experiments on the differentiation of proteins by this process. It was known that Colloidal Gold was electrically charged and could be precipitated by a suitable electrolyte. Zsigmondy then discovered that the addition of a very small quantity of protein to the Goldsol conferred "protection" on it, and prevented the gold from being precipitated. He found, further, that different proteins/

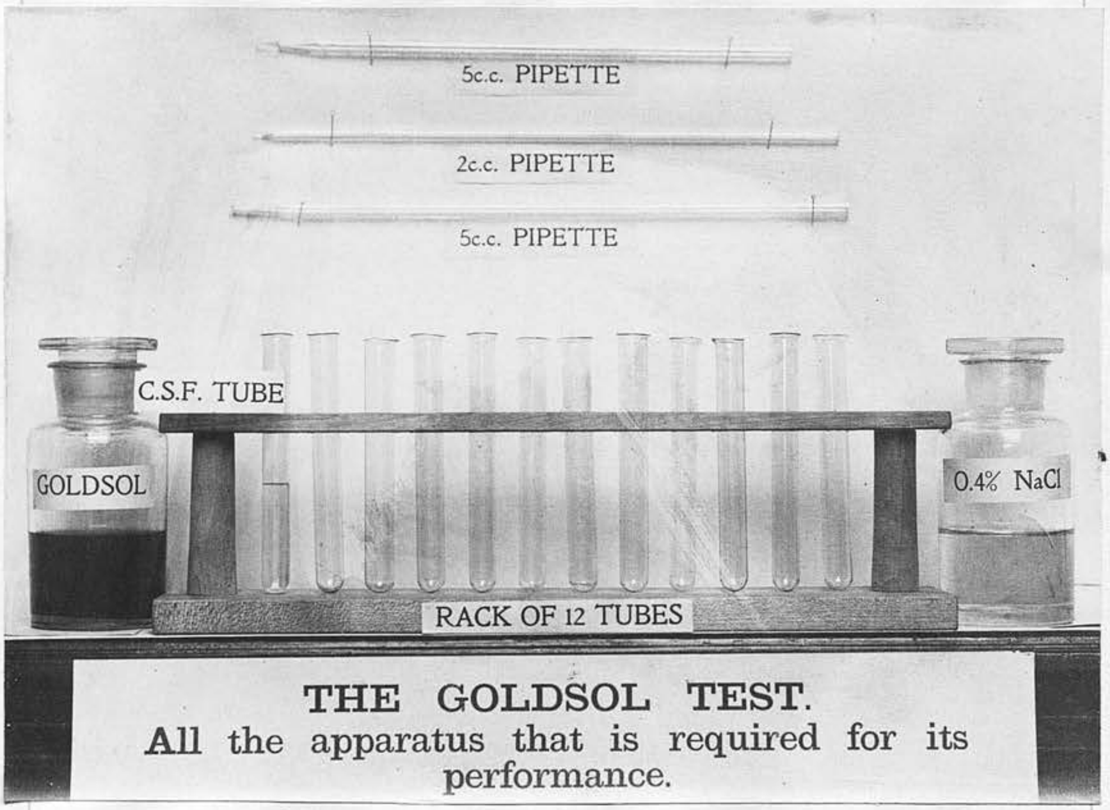
proteins differed in this protective action, and he was able to determine the so-called "Gold Number" for the various proteins; that is, the measure of their relative protecting power. Using this as an index, he was able to estimate the quantity and purity of a known protein in a given solution.

Lange then attempted to apply this method in investigating the nature of the proteins precipitated from spinal fluid by Ammonium Sulphate solution. Contrary to his expectation he discovered that spinal fluids containing an excess of protein precipitated the Goldsol instead of protecting it.

He was unable to explain this occurrence, but the reaction suggested the possibility of using Goldsol as a test for Neurosyphilis.

The practical application of this idea resulted in the Goldsol Test and his discovery that General Paralysis had an absolutely typical reaction; that without any clinical data, he could tell from the Gold test alone whether or not the fluid under examination was from a case of General Paralysis.

Further, the test appeared to differentiate Cerebrospinal Syphilis from Suppurative Meningeal inflammations. Since that time, the reaction has been tested by many observers, and has yielded consistent results. It is now generally agreed that in the Goldsol test we have a diagnostic method of greater precision and discriminative value than any other hitherto in use.



THE GOLDSOL TEST.
All the apparatus that is required for its performance.

Photograph. 1.

TECHNIQUE OF THE TEST.

(1) Apparatus required -

All the apparatus necessary for a single test is as follows:-

A rack with eleven test tubes.

Bottle of Saline Diluent (0.4%)

Bottle of Goldsol.

A 1 cc. pipette for C.S.F. - graduated in 1/10th to tip.

A 5 cc. pipette for Goldsol - graduated to tip.

A 5 cc. pipette for Saline - graduated in 1/10th to tip.

Two small beakers.

For the test-tubes, the size 5" x ½" is convenient. They are cleaned in the usual manner for glassware; namely, boiled in Bichromate Solution and then brushed with soap and water, being finally rinsed out with running water. They are then inverted and allowed to dry at room temperature, or more rapidly in an oven. Sterilisation is not essential.

The Saline diluent is made up with doubly distilled water and chemically pure Sodium Chloride. A 0.4% solution is required, so that 1 gramme of $NaCl_2$ to 250 cc. of water will give a sufficient quantity for twenty-two tests.

The/

The Stock-bottle should be carefully cleaned and then rinsed out with distilled water before receiving the saline.

The bottle for the Goldsol should be glass-stoppered, and preferably of hard glass. The preparation of the Goldsol will be described later.
500 cc. is sufficient for ten tests.

The pipettes are most easily cleaned in the first instance with Aqua Regia and then kept in distilled water in a tall glass jar. Just before use they may be shaken free of water and allowed to drain, or dried more rapidly in an asbestos-lined box in the hot-air steriliser.

Of the two small beakers, one is required to hold the amount of Saline that is about to be used, the quantity depending on the number of fluids to be tested; and the other beaker similarly for the Goldsol. This arrangement prevents the contamination of the stock solutions by the introduction of pipettes into them.

(2) Actual Technique of Test -

Set out the rack of test-tubes.

Using the 5 cc. pipette, put 1.8 cc. of the Saline Diluent into the first tube, and 1 cc. into each of the remaining ten tubes.

Then/

Then with the 1 cc. pipette take up .2 cc. of the spinal fluid to be examined, and put it into the first test tube, mixing the fluids thoroughly by pipetting in and out several times. This gives a 1 in 10 dilution of spinal fluid in the first tube.

Using the same pipette take up 1 cc. of this mixture from the first tube and put it into the second tube, mixing as before, thus obtaining a dilution of 1 in 20 in the second tube.

This process is repeated from tube to tube until the tenth tube, the contents of each tube thus being half of the strength of the preceding one. The final cc. from the tenth tube is thrown away.

The eleventh tube being the control receives no spinal fluid.

Then with the other 5 cc. pipette, put 5 cc. of the Goldsol into each tube. It is important that the Goldsol should be mixed thoroughly and quickly with the diluted fluid, and this can be easily managed by blowing the Goldsol into the fluid.

The rack is then set aside at room temperature for the reaction to complete itself; it is not necessary for the tubes to be stoppered in any way.
The test can be performed just as well with half the quantities mentioned above, provided the relative proportions/

proportions are unchanged. If several spinal fluids are being examined at the same time, it will be found more expeditious to put out the saline solution into all the racks before beginning to dilute the individual spinal fluids.

Similarly, time can be saved by filling a clean burette with the Goldsol and running in the necessary amount into each tube.

A separate pipette is used for each spinal fluid.

(3) Method of Reading Results -

The reaction looked-for consists in various changes in colour of the Goldsol caused by different degrees of its precipitation by the spinal fluid.

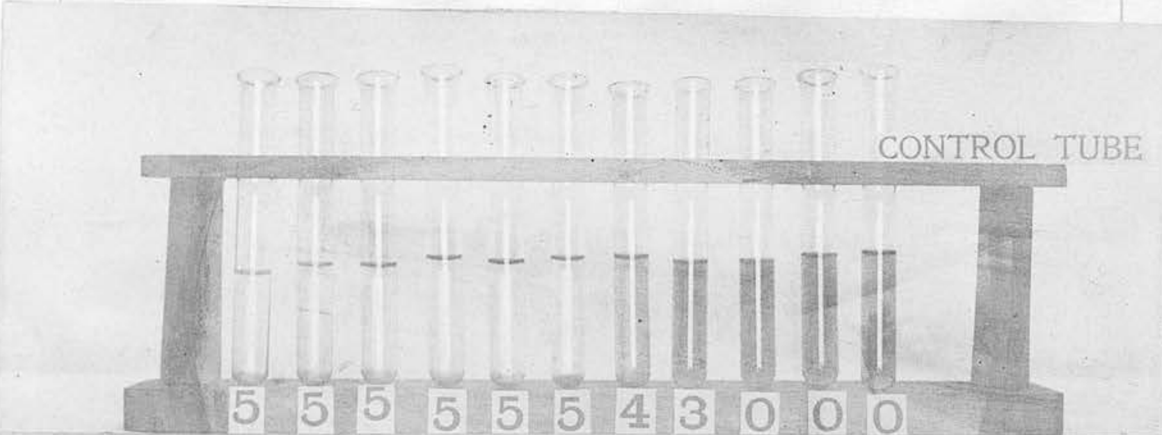
When complete precipitation occurs the Gold forms a sediment, leaving a perfectly clear and colourless supernatant fluid; this degree of reaction may be conveniently expressed by the figure 5.

With a somewhat less degree of precipitation, the fluid remains a pale blue-grey colour, designated 4.

Still less precipitation results in a fluid having a violet colour, called 3.

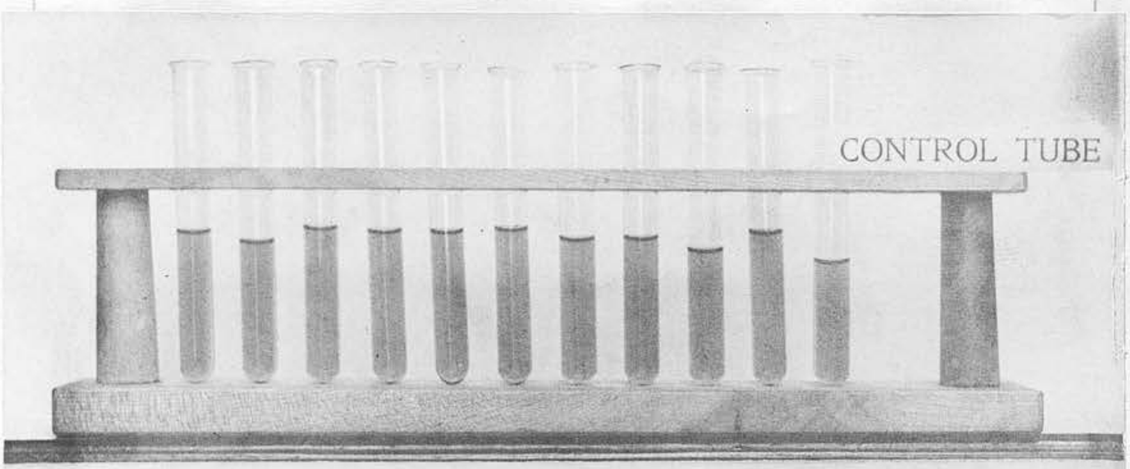
A less degree still gives a bluish-red colour, Number 2.

The figure 1 is used to represent a slight change, more in intensity than actual shade, so that the fluid looks darker and more opaque. This represents the least/



THE GOLDSOL TEST.
Typical reaction in Spinal Fluid of a General Paralytic. Note complete precipitation in first 6 tubes.

Photograph. 2



THE GOLDSOL TEST.
A negative reaction. No precipitation has occurred.

Photograph 3.

least degree of precipitation.

If there is no change in colour at all as compared with the control tube, the symbol 0 is used.

The typical reaction obtained with the fluid of a case of General Paralysis consists in a complete precipitation of the first four or five tubes, with partial precipitation of the next two or three, and no change in the remainder.

Assigning the proper number to each tube, this result would be represented numerically as -
543
55555~~310~~000 (See photograph No. 2)

A completely negative reaction would be recorded thus - 0000000000. (Photograph No.3)

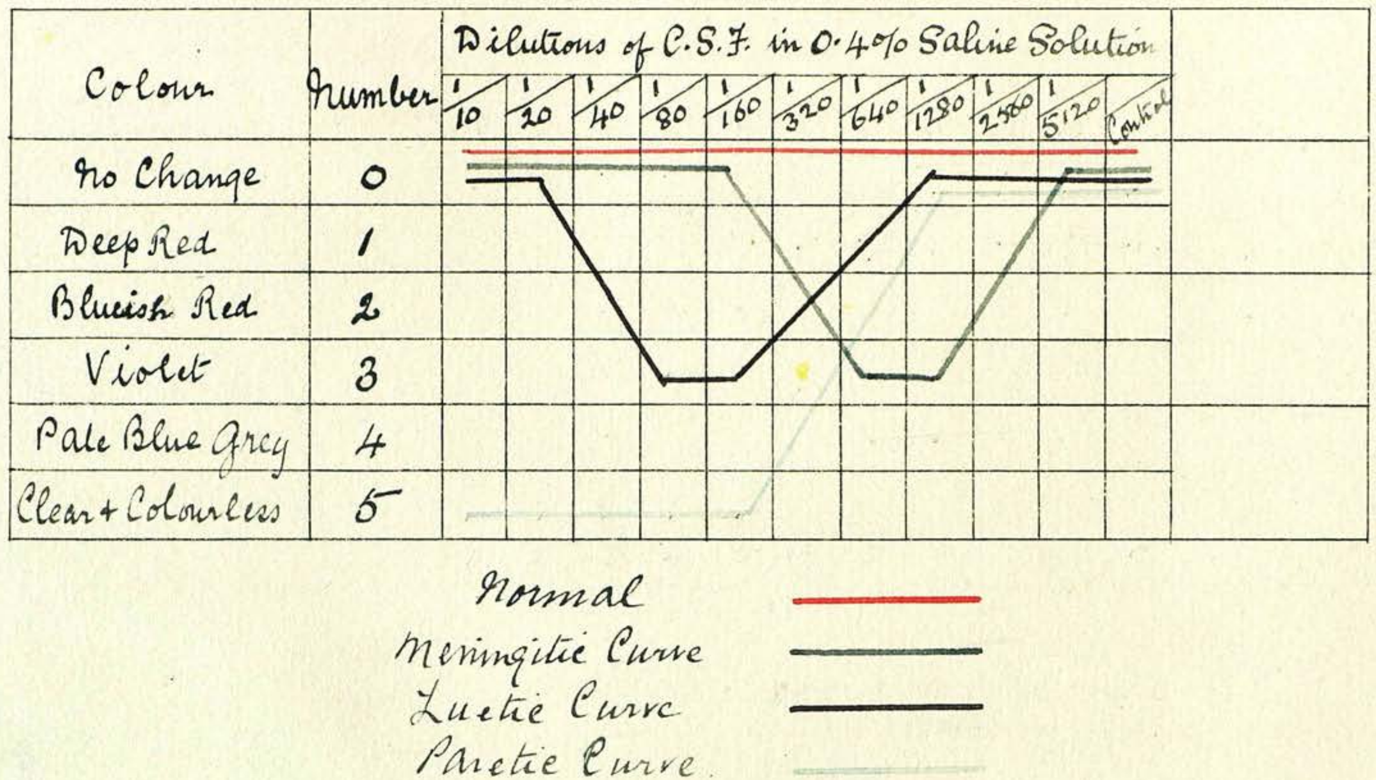
For descriptive purposes the row of tubes may be divided into three zones. Thus.-

Zone II. (tubes 3–5)

Tubes	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
Dilutions	1/10	1/20	1/40	1/80	1/180	1/320	1/640	1/1280	1/2560	1/5120
	Zone I.					Zone III.				

In General Paralysis the maximum reaction ("5") occurs in Zone I, i.e. the first five tubes.
It is claimed that in Cerebrospinal Syphilis and Tabes Dorsalis the maximum reaction occurs in Zone II, (i.e. tubes 3, 4 and 5) and should not exceed a "4" reaction, e.g. 0023311000. In Epidemic Meningitis, the/

Diagram No: 1.


Colour
Number
Dilutions of C.S.F. in 0·4% Saline Solution
1/10
1/20
1/40
1/80
1/160
1/320
1/640
1/1280
1/2560
1/5120
Control
No Change 0
Deep Red 1
Bluish Red 2
Violet 3
Pale Blue Grey 4
Clear + Colourless 5
Normal
Meningitic Curve
Luetic Curve
Paretic Curve

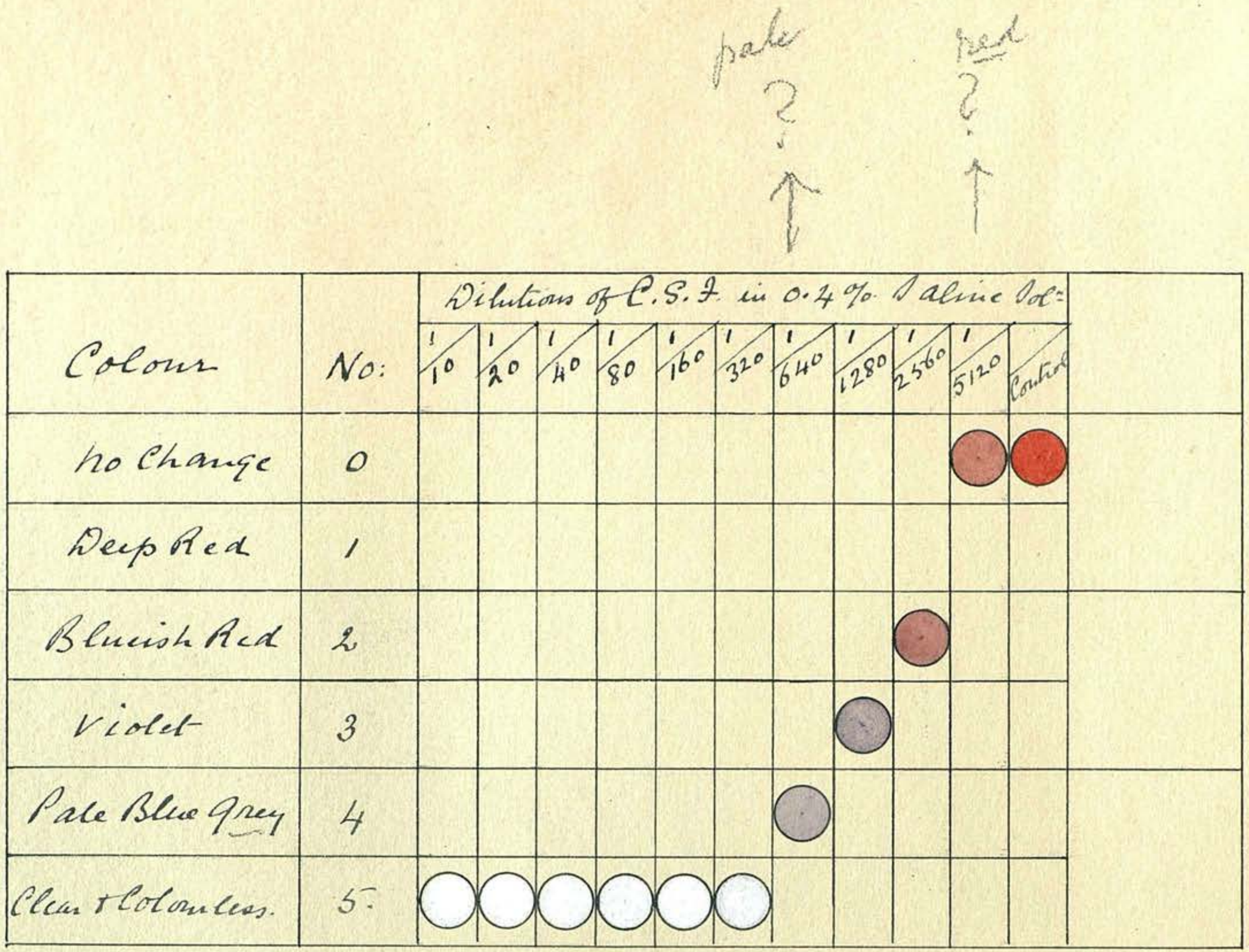
the chief reaction is said to occur in Zone III (i.e. tubes 6 to 9) e.g. 0000013310. The test is thus recommended by some authors as a means of differential diagnosis.

These results may be shown graphically as in the accompanying diagram. (No. 1.)

Thus certain "curves" become apparent, of which the "Paretic" curve is the most characteristic; the so-called "Luetic" curve I believe to be of doubtful value, as will be shown later. The Meningitic curve I have not had any experience of. A completely negative result would be indicated by a straight line. (See diagrams No. 2+3)

The reading of the results should be made ten or twelve hours after the performance of the test, so as to give time for complete precipitation to occur. Thus, it is convenient to do the test in the afternoon, and read the result next morning by daylight against a white surface, with the observer's back to the light. In this way, the colour shades may be more accurately differentiated.

With a little experience, however, it is possible, within half an hour, to predict what the outcome of the test will be; for in a positive reaction, the change/



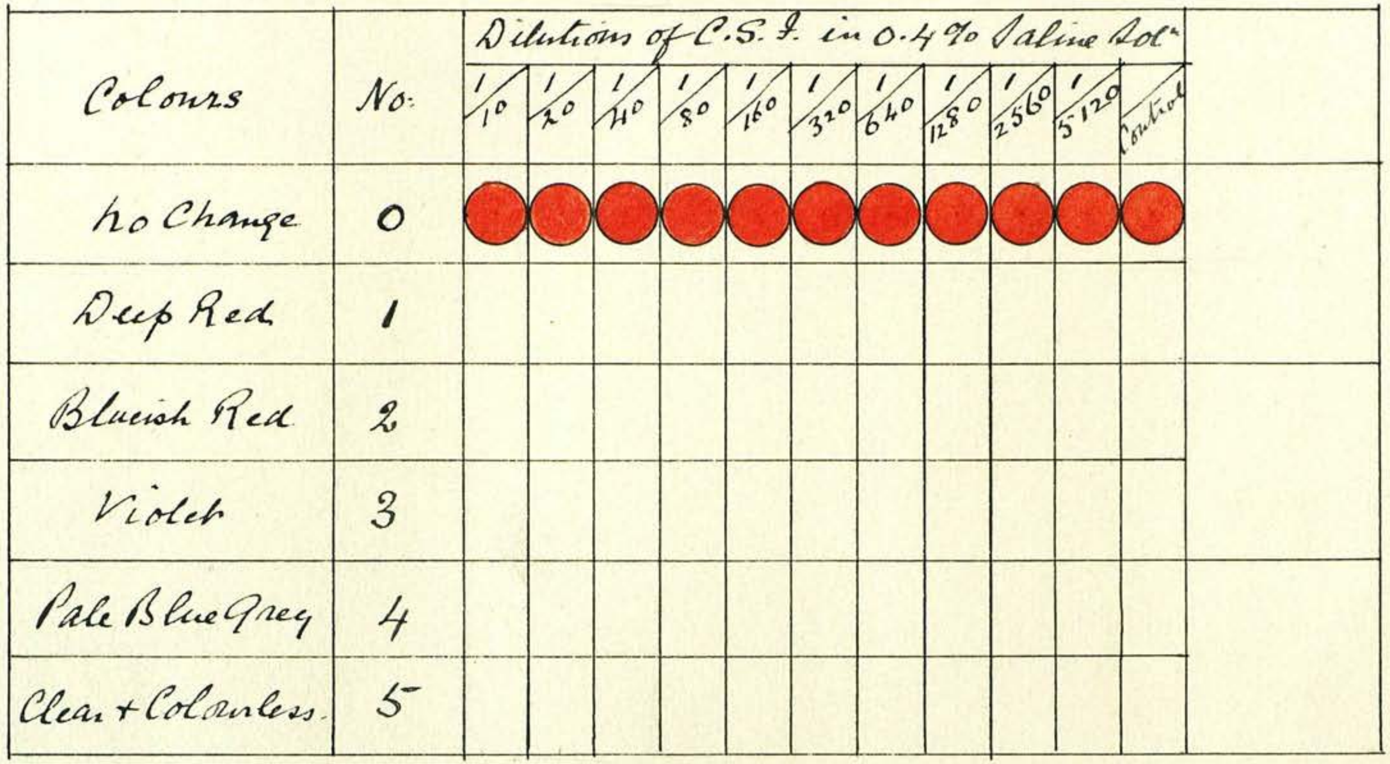
A Positive Paretic Curve. 5555554 3200

Diagram. No. 2.

change of colour begins immediately; those tubes which are going to precipitate showing a definite violet tinge which gradually fades as the gold falls, and the other tubes showing intermediate changes of colour according to the degree of precipitation. This play of colour produces a very pretty effect, and its causation will be explained later.

Furthermore, a tube which does not change in colour during the first half hour, will not change at all. As already described, the change of colour produced by a pathological fluid is gradual in the series, forming a curve with the maximum reaction at the apex; so that if a single tube shows a marked change it should be regarded with suspicion as being due to some error in technique; upon repetition, such tests are usually found to be negative. Apart from this, it is the maximum intensity of colour change, and not the quantitative amount (i.e. number of tubes) which has the diagnostic value. There is some difference of opinion on what should constitute a "positive" or "negative" reading, and some fluids give an intermediate reaction which may be labelled "doubtful", or perhaps more accurately, "transitional".

There is no dubiety about the typical "Paretic" reaction; the complete decolorisation in the first four, five or six tubes is clear cut and unmistakable, and does not occur in any other disease than 'General Paralysis'./



A Negative Reaction.

Diagram. No. 3.

Paralysis'. On the other hand, an absolutely negative reaction in which there is no change whatever in colour (0000000000) is, in my experience, rare; out of 250 examinations, only two fluids gave this result. The great majority of fluids from the insane react to the extent of "1" or "2". I therefore agree with Swalm and Mann, and Kaplan and McClellan, that little value can be placed on a 1 or 2 reaction, and that such fluids should be considered negative. A 3-reaction is doubtful; a 4-reaction is highly suspicious and a 5-reaction definitely positive. This refers to the diagnosis of General Paralysis. These slight changes of 1 or 2 degree in negative fluids may be an expression of the "Gold Number" of the particular protein in the fluid; but are more probably due to minor variations in the Goldsol; for example, over-sensitiveness in an unstable solution. At any rate they have no pathological significance. But it is interesting to note that they occur not in the strongest dilutions where one would naturally expect them, but in the intermediate dilutions of the 3rd, 4th, and 5th tubes; an explanation of this curious result will be offered later.

PREPARATION OF GOLDSOL.

1. General Principles.-

The whole value and success of the test depends upon the use of a good Goldsol, and its preparation is the only uncertain part of the procedure. The method is simple enough, but care and attention to detail is essential.

In order to obtain a solution of suitable electrolytic stability, four conditions must be observed, viz:-

(1) A dilute solution of a reducible Gold Salt in the presence of an alkali.

(2) A reducing agent.

(3) A correct temperature at which the reduction takes place, and

(4) Water, freshly distilled and of the highest purity.

2. Apparatus required.-

A Jena or other hard-glass beaker (e.g. "Duroglass")

A 5 cc. pipette for the Gold chloride solution

A 5 cc. pipette for the Alkaline solution.

A 1 cc. pipette for the Reducing Agent.

A hard-glass thermometer.

A large Bunsen burner with tripod and wire gauze with Asbestos centre.

3. Reagents necessary.-

In all cases the substances should be of the highest purity obtainable, i.e. Chemically pure.

(1) The Gold Chloride Solution - This is a 1% Solution of Gold Chloride in triply distilled water. This stock solution should be kept well stoppered in a dark glass bottle away from any bright light.

(2) The Alkaline Solution - is a 2% solution of Potassium Carbonate in triply distilled water.

(3) The Reducing Agent - is a 1 in 40 solution of Formaldehyde (40%) in triply distilled water.

The method of water distillation recommended, will be described in a later section.

4. Technique for Cleaning Glassware.

Some workers recommend boiling the beaker for thirty minutes in a soap solution; it is then brushed thoroughly under hot tap-water, and then rinsed in running water. Next it is filled with hot bichromate cleaner (Potassium Bichromate 200 grams, Sulphuric Acid Conc: 500 grms, Water up to 1500 cc.) and left standing for half an hour. When needed, the beaker is emptied, washed again for five minutes in running water, and then rinsed with ordinary distilled water and finally with trebly distilled water. The beaker is/

is now clean and ready for immediate use.

The pipettes are cleaned similarly but are not boiled. I have used this method successfully but prefer a more rapid alternative which consists in using Aqua Regia as the cleanser, followed by brushing under a running watertap and finally rinsing with the distilled waters. The pipettes should be treated in the same way. The beaker should be filled to the brim with the acid and allowed to stand for ten minutes. This does away with the boiling soap-solution and the hot Bichromate.

It is important to brush thoroughly so as to remove all acid, and to use the beaker immediately after cleaning.

5. Technique for obtaining Distilled Water.

Hard glass is recommended for the distilling apparatus, and especially for the condensing-tube, as, after repeated use, silicates tend to be dissolved out of soft glass and may adulterate the water.

The connection between the distilling flask and the condensing-tube should be a ground joint, or be made by means of a cork that has been previously boiled. Rubber connections are inadmissable.

I use a large hard-glass retort and have employed an ordinary condensing-tube with success, but would not/

not recommend the practice.

This apparatus, and the receiving-flask for the distillate, is best cleaned with Aqua Regia and water, as already described.

Ordinary distilled water is then re-distilled until a sufficient quantity has been collected; the apparatus is then rinsed out with some of this second distillate, which is then distilled again.

This triple distillate is used for making up the various reagents, and should be freshly prepared when the Goldsol is about to be made.

The two essentials are, the greatest possible cleanliness of the glassware, and the highest obtainable purity of the water; for this reason, fresh spring water is to be preferred to that which has undergone chemical purification for drinking purposes.

6. Method of Making the Goldsol.

It has been found that, for some unknown reason, no method will give absolutely uniform results. After many successful batches (and probably some relaxation of care) a solution is unexpectedly produced which is either too unsensitive or "protected", or more rarely, one which is hyper-active, reacting with unusual rapidity and exaggerated colour changes.

These failures are usually traceable to impurity of/

of the water used.

A reliable method is as follows.-

Fill the prepared beaker up to the 500 cc. mark with fresh, triply distilled water.

Heat over a large Bunsen to 60° C.

Then add rapidly 5 cc. of the 1% Gold Solution, and 5 cc. of the 2% Potassium Carbonate Solution.

Heat rapidly to 90° C.

Then turn off the flame and add drop by drop, as rapidly as possible, the Formalin Reducing Agent. About 1 cc. of this will be needed, but no fixed quantity should be employed; the secret is to keep on adding the Formalin until a deep rose-colour develops, stirring briskly with the thermometer the while. After a little experience the correct stopping-point will be recognised, and it will then be seen that the amount of Formalin Solution used varies from test to test.

In my experience the use of Oxalic Acid as a Reducing Agent has not been successful.

(7) Other Modifications of Method.

So many workers have had difficulty in pre:paring Colloidal Gold after Lange's Method, that attempts have been made to evolve a reliable technique which will give a suitable Sol of diagnostic value.

By/

By these efforts some of the governing principles have been brought to light; but every factor is not yet known; so that, although some methods are more dependable than others, none will succeed invariably.

1. Grulee & Moody - give the following directions.- "To make 500 cc. of indicator (a) take 500 cc. of freshly double-distilled water in a Jena glass beaker, and heat slowly over wire gauze; (b) when the water is approximately 60° C, add, while still heating, 5 cc. of 1% solution of Gold Chloride and then follow <u>immediately</u> with 5 cc. of 2% solution of potassium carbonate; (c) heat rapidly to boiling; (d) turn out flame as soon as steam bubbles appear, and (e) add quickly 5 cc. of 10% dilution of liquor formaldehyde; and immediately begin vigorously shaking the beaker until a change in colour occurs, which takes from ½ to 3 minutes."

2. Jaeger & Goldstein, and Flesch - use the same process except that they distil the water triply.

3. Kaplan & McClelland - direct as follows.- "In a litre Florence flask of Jena glass are poured 500 cc. of fresh double-distilled water, 5 cc. of Potassium Carbonate Solution are added and the flask placed over the flame for 1 minute, and 5 cc. of 1% Gold Chloride Solution added. The/

The heating is continued until the first bubbles appear; the flame is turned off and 5 cc. of 0.75 formaldehyde solution allowed to run in gradually. During the addition of the formalde:hyde the flask must be constantly shaken until the solution changes to a deep port-wine colour."

4. Lee & Hinton - recommend heating the water to 60° C. and then the addition of the Gold Chloride and potassium carbonate solutions. The heating is continued until the small bubbles arising throughout the fluid disappear; that is, 1 to 2 minutes of boiling. Then they add 5 cc. of 1% formalin solution and shake vigorously.

5. Swalm & Mann - advise a very similar process; thus. "In a cleansed Jena glass beaker, 500 cc. of double-distilled water is heated gradually to 60° C; then 5 cc. of 1% Gold Chloride and 5 cc. of 2% potassium carbonate are added in rapid succession. The solution is heated quickly until the first steam bubbles arise, when 5 cc. of a 1%, formaldehyde (40 %) solution are added and the beaker is shaken until a red solution tinged with yellow is obtained."

6. Miller & Levy - suggest the following.- "One litre of water is heated to 60° C. in a sterile Jena beaker. At this temperature 10 cc. each/

each of a 1% Aqueous solution of Gold Chloride and a 2% solution of Potassium Carbonate are added synchronously and thoroughly mixed at once. From this point the solution is heated as rapidly as possible by using a four or six flame Bunsen burner until a temperature of 90° C, but not exceeding 95° C, is reached. The flame is turned out and, while the contents of the beaker are briskly agitated, 10 cc. of a 1% aqueous solution of formalin are gradually added."

7. Miller, Brush, Hammers & Felton - differ from the foregoing by using Oxalic Acid. Thus.- "A beaker is filled to the litre mark with triply distilled water, and after the temperature has been <u>gradually</u> raised to about 50° C, the gas is turned on full. When the temperature has reached 60° C, 10 cc. of the 1% Gold solution and 7 cc. of the 2% potassium carbonate are added. At 80° C, the gas is turned out, and, while stirring, 5 cc. of 1% formaldehyde is slowly added, a drop at a time. If a pink colour makes its appearance before all the reducing agent has been added, stop at once, for reduction will continue to the final end-point."

They then give procedures which may be resorted to when solutions behave in an atypical manner.

8. Felton & Maxey - use the method just described with two slight variations; namely.-

"(a) In distilling the water; there is added to each litre of the first distillate 5 cc. of a saturated solution of barium hydrate. By this method the necessity of absolutely fresh first distillation is done away with.

(b) In the use of Oxalic Acid; 1 drop of a 1% solution to the litre is added at 60° C. instead of 10 drops at 85° C."

Cruickshank considers the use of Oxalic Acid both unnecessary and inconvenient, because it tends to neutralise the Pot: Carb: and to result in the formation of an Acid Sol of the hypersensitive type.

The method I have found most reliable is that described by Weston, Darling and Newcomb, and modified by Lowrey.

This has already been set forth, and it will be noticed that the modification consists only in the direction to "Stop adding the formalin when the reagent is of the proper colour." That is, no fixed amount of formalin is used. I consider this an important point.

I have not been successful with the Oxalic Acid/

Acid Method.

Sources of error have been looked for, and many suggestions made; some of them to be contradicted later.

Thus, Lee and Hinton - believe that "very rapid heating is apparently an important essential" and that the production of a good Sol" is largely dependent upon freeing the distilled water from the gases in solution."

Warwick and Nixon, on the other hand, aver that "All of the difficulties of preparation usually resulting in a protected Sol have been traceable directly to the water." And that they "found that the method of heating it was of little significance."

Accordingly they prefer fresh spring water to that which has been chemically purified.

Some workers think that an attempt to make more than 500 cc. at a time is less likely to be successful than the smaller quantity.

Lange accidentally discovered that he got better results by using an open glass beaker instead of an Erlenmayer flask, and found that this had already been noticed by others.

It would seem, therefore, that no method is absolutely reliable; that all possible sources of error are not yet known; and that it is not safe to ignore/

ignore details of technique however trivial they may appear.

Finally, experiment has shown that methods in which Phosphorus or Tannic Acid are used as reducing agents, do not produce suitable Goldsols.

STANDARD OF GOLDSOL.

Before the Sol can be used with confidence for diagnostic purposes it must fulfil certain requirements. Various criteria of suitability have been suggested, some of doubtful value. The chief test should be, that it must give a typical reaction with a known paretic spinal fluid; and that it must produce no reaction greater than a Number 1 or 2 change with a known normal fluid.

Some authors insist that the most important condition of all is, that on the day on which it is used the Sol must be neutral to 1% Alizarin Red in 50% Alcohol.

This was the conclusion drawn from certain experiments made by Miller and his colleagues. They found - that Goldsols varied greatly in reaction; that Alkaline Sols were almost entirely inert; that slightly acid Sols gave contradictory results; that strongly acid Sols gave atypical reactions; and that it was only a neutral Sol that was satisfactory.
The method they devised for testing the neutrality of the Sol consists in the use as an Indicator of a 1% solution of Alizarin Red in 50% Alcohol.
To 5 cc. of the Goldsol, two drops of this indicator are added; if a purplish-red colour results, the Sol/

Sol is Alkaline; if lemon-yellow, the Sol is Acid; if brownish-red, the Sol is neutral.

If the Sol is alkaline by this test, it may be neutralised as follows.-

10 test-tubes are set out, each containing 1 cc. of freshly distilled water.

1 cc. of N/50 HCl is put into the first tube and mixed with its contents. If 1 cc. of this mixture is withdrawn and put into the second tube, and the pro-:cess thus repeated from tube to tube, a series of dilutions will be obtained extending from a 1 in 2 dilution to 1 in 1024.

The amount of Acid in each successive tube will be 0.5 cc, 0.25 cc, 0.125 cc. and so on correspondingly, each tube having one half the amount of the preceeding one.

Then to each tube are added 2 drops of the indicator and 5 cc. of the Goldsol to be tested.

Supposing the neutral point, as shown by a brownish-red colour, is reached in the third tube of the series; then it has taken 0.125 N/50 acid to neutralise 5 cc. of the Goldsol.

If the total amount of the Goldsol to be correct-:ed is 500 cc; then.-

$$\frac{0.125 \text{ N/50 Acid} \times 500 \text{ cc.}}{5} = 12.5 \text{ cc.}$$

and/

and this is the amount of N/50 Acid which must be added to neutralise the Goldsol.

In the case of an Acid Sol, the same procedure is carried out using N/50 NaOH.

The Authors further direct - that the Acid or Alkali should be added very slowly whilst the Sol is well shaken, or some precipitation may occur; and that Sols should not be neutralised until they are at least 48 hours old.

In practice I have found this Alizarin Solution unsatisfactory as an indicator, because the colour reactions are masked by the ruby colour of the Sol itself. I have not been able to find an efficient alternative amongst the usual reagents such as Phenolphthalein.

Further, I doubt the wisdom of using such "corrected" Goldsols for diagnostic purposes. Miller and Levey believe that "it is useless to 'doctor up' a solution" which falls short of the first two requirements I have mentioned. Another suggested Criterion of suitability is the Saline test to discover whether a Sol is protected or not. According to Miller, a non-protected solution - which is the type required for the Goldsol test - is one that is completely precipitated in one hour when 5 cc. of it is mixed with 1.7 cc. of a 1% solution of Sodium Chloride./

Chloride. I have obtained contradictory results with this test, and do not consider it reliable.

On what should be the colour of a good Sol there is a great variety of opinion. Thus.- Grulee and Moody say that a good Sol "should be red with just a tinge of yellow, and a very faint shade of purple. Fluids that are purplish and murky should not be used." Kaplan and McClelland think it should be of a deep port-wine colour, with a brown shimmer or bluish tinge. They use as a standard for comparison the colour of 10 cc. of N/10 Sodium Hydroxide plus 1 cc. of a Congo Red Solution and 0.5 cc. of an Alcoholic Alizarin solution.

According to Lowrey the reagent should be dark red and have a slight blue hue at the edges. Purple, light blue, dark brown, light red, or light yellow murky fluids should not be used.

All are agreed that the Sol should be clear by transmitted light, and that by reflected light a very slight turbidity, not amounting to more than a golden shimmer, is permissible. In my experience, good Sols have a beautiful ruby red colour; but the fact is, that as long as the Sol is clear and neutral, its exact shade is of little importance.

From its appearance, however, some of its properties can be inferred. Thus:- A deep purple Sol,/

Sol, or a deep, dark red one with a purple tinge is an Alkaline Solution and is the result of an excess of Potassium Carbonate in its preparation. Such a Sol is too sensitive for use.

The orange-red solutions give the most clear-cut reactions.

So that slight degrees of turbidity and minor variations in shade are permissible provided their significance is borne in mind. But any marked departure from red in the direction of brown, purple or pink should disqualify the Sol.

If kept well stoppered in a dark place, the Sol retains its properties for a considerable period, but tends to become slightly alkaline and less sensitive. In bright light it becomes darker and may lose its reliability.

RESULTS OBTAINED.

Clinical Material - In order to test the value of the reaction I have examined 250 samples of spinal fluid.

These have been arranged in 9 groups of non-syphilitic psychoses, each group containing 15 cases; one group comprising 84 General Paralytics; one group containing 19 Miscellaneous diseases; and one group of 12 fluids obtained post-mortem.

The non-syphilitic psychoses are.-

Melancholia.

Mania.

Epileptic Insanity.

Amentia (Idiots and Imbeciles).

Dementia Praecox.

Adult Dementia.

Senile Dementia.

Confusional Insanity.

Delusional Insanity.

For control and comparison the Ross-Jones and the Wassermann Reactions were used as representing reliable tests.

A cell-count was not made because recent work by Solomon and Koefod has proved that it is of very little diagnostic or prognostic value, and that in General Paralysis it in no way parallels the other spinal fluid findings.

Group.1. MELANCHOLIA.

Case No.	Ross.Jones.	Goldsol.	Wassermann.
1	Negative	Negative:- 11222100000	Negative.
2	Negative	Negative:- 11222110000	Negative.
3	Negative	Negative:- 11222210000	Negative.
4	Negative	Negative:- 11111100000	Negative.
5	Negative	Negative:- 11111100000	Negative.
6	Negative	Negative:- 11221000000	Negative.
7	Negative	Negative:- 11100000000	Negative.
8	Negative	Negative:- 11222100000	Negative.
9	Negative	Negative:- 11122210000	Negative.
10	Negative	Negative:- 11122110000	Negative.
11	Negative	Negative:- 12222211110	Negative.
12	Negative	Negative:- 11111100000	Negative.
13	Negative	Negative:- 11111000000	Negative.
14	Negative	Negative:- 11111000000	Negative.
15	Negative	Negative:- 11111100000	Negative.

Of this group of 15 cases, all three tests are negative throughout.

The only point calling for comment is, that the Goldsol reading in every case shows a reaction to the extent of "1" or "2". This, in my opinion, is a normal reaction and has no pathological significance.

Case No:12 was suffering from Acute Phthisis at the time of puncture.

Group.2. MANIA.

Case No.	Ross. Jones.	Goldsol.	Wassermann.
1	Negative	Negative:- 11122100000	Negative.
2	Negative	Negative:- 11122111110	Negative.
3	Negative	Negative:- 11221000000	Negative.
4	Negative	Negative:- 11122211110	Negative.
5	Negative	Negative:- 11331100000	Negative.
6	Negative	Negative:- 00111000000	Negative.
7	Negative	Negative:- 11110000000	Negative.
8	Negative	Negative:- 11110000000	Negative.
9	Negative	Negative:- 00000000000	Negative.
10	Negative	Negative:- 00111000000	Negative.
11	Negative	Negative:- 11111000000	Negative.
12	Negative	Negative:- 11111000000	Negative.
13	Negative	Negative:- 11221000000	Negative.
14	Negative	Negative:- 11122100000	Negative.
15	Negative	Negative:- 11111000000	Negative.

Here again all three tests are negative throughout.

Case 5, is suspected of commencing General paralysis; his speech is suggestive. It will be noted that the Goldsol reading is pointing in the same direction whilst the other two tests are as yet negative.

Case 9, is interesting as being one of the very few Gold reactions that shows no colour-change whatever.

Group.3. Epileptic Insanity.

Case No.	Ross.Jones.	Goldsol.	Wassermann.
1	Negative	Negative:-11122100000	Negative.
2	Negative	Doubtful:-2444420 1210	Negative.
3	Negative	Doubtful:-12233221000	Negative.
4	Negative	Negative:-11111100000	Negative.
5	Negative	Negative:-12221000000	Negative.
6	Negative	Negative:-11122100000	Negative.
7	Negative	Negative:-11222100000	Negative.
8	Negative	Negative:-11221000000	Negative.
9	Negative	Negative:-11221000000	Negative.
10	Negative	Negative:-11111000000	Negative.
11	Negative	Negative:-11222222220	Negative.
12	Negative	Negative:-11122100000	Positive.
13	Negative	Negative:-11111000000	Negative.
14	Negative	Negative:-12222000000	Negative.
15	Negative	Negative:-11110000000	Negative.

Of these 15 fluids, 12 gave negative results with all three tests.

Cases 2 and 3 giving doubtful Gold reactions are both of the same type; namely, young epileptics whose fits are so frequent and severe that they have to be kept in bed; both have the facial appearance of Congenital Syphilis.

Case 12 giving a negative Gold test and a positive Wassermann is an Epileptic dement with a left hemiplegia.

Group.4. Amentia.

Case No.	Ross.Jones.	Goldsol.	Wassermann.
1	Negative	Negative:- 11110000000	Positive.
2	Negative	Negative:- 11110000000	Negative.
3	Negative	Negative:- 11221000000	Negative.
4	Negative	Negative:- 11110000000	Negative.
5	Negative	Negative:- 11110000000	Negative.
6	Negative	Negative:- 11111000000	Negative.
7	Negative	Negative:- 11222100000	Negative.
8	Negative	Negative:- 11111000000	Negative.
9	Negative	Negative:- 11111000000	Negative.
10	Positive	Negative:- 11122210000	Negative.
11	Negative	Negative:- 11110000000	Negative.
12	Negative	Negative:- 11111000000	Negative.
13	Negative	Negative:- 11111000000	Negative.
14	Negative	Negative:- 11111000000	Negative.
15	Negative	Negative:- 11111000000	Negative.

This group comprises ordinary Idiots and Imbeciles along with some that are epileptic, some Paralytic, and some morally oblique. 13 are negative throughout.

Fluid No.10 gives a positive Ross.Jones and is from an Epileptic Imbecile with hemiplegia; the Goldsol reading in this case 11122210000 would be considered by some authors as indicative of Syphilis.

Case 1 giving a positive W.R. shows no clinical evidence of Syphilis, has been epileptic from birth, and is in some ways suggestive of Dementia Praecox.

Group.5. DEMENTIA PRAECOX.

Case No.	Ross.Jones.	Goldsol.	Wassermann.
1	Negative	Negative:- 11220000000	Negative.
2	Negative	Negative:- 11122110000	Negative.
3	Negative	Negative:- 11221000000	Negative.
4	Negative	Negative:- 11122211000	Negative.
5	Negative	Negative:- 11122110000	Negative.
6	Negative	Negative:- 11221100000	Negative.
7	Negative	Negative:- 11222100000	Negative.
8	Negative	Negative:- 11122210000	Negative.
9	Negative	Negative:- 11111100000	Negative.
10	Negative	Negative:- 12210000000	Negative.
11	Negative	Negative:- 22220000000	Negative.
12	Negative	Negative:- 11221000000	Negative.
13	Negative	Negative:- 11221000000	Negative.
14	Negative	Negative:- 11222100000	Negative.
15	Negative	Negative:- 11222100000	Negative.

This group calls for no special comment.

All fluids are negative throughout and all the Gold reactions show changes to the extent of "1" or "2" degrees.

Group.6. ADULT DEMENTIA.

Case No.	Ross. Jones.	Goldsol.	Wassermann.
1	Negative	Negative:- 11122100000	Negative.
2	Negative	Negative:- 11222110000	Negative.
3	Negative	Negative:- 11111000000	Negative.
4	Negative	Negative:- 11111000000	Negative.
5	Negative	Negative:- 11221000000	Negative.
6	Negative	Negative:- 11111000000	Negative.
7	Negative	Negative:- 11222000000	Negative.
8	Negative	Negative:- 11222100000	Negative.
9	Doubtful	Negative:- 11222110000	Negative.
10	Negative	Negative:- 11222110000	Negative.
11	Negative	Negative:- 11111000000	Negative.
12	Negative	Negative:- 11111000000	Negative.
13	Negative	Negative:- 11221000000	Negative.
14	Negative	Negative:- 11221000000	Negative.
15	Negative	Negative:- 11222100000	Negative.

Case No.9 shows a doubtful Ross.Jones reaction.

The remainder are all negative throughout.

Group.7. SENILE DEMENTIA.

Case No.	Ross.Jones.	Goldsol.	Wassermann.
1	Negative	Negative:- 2222210000	Negative.
2	Negative	Negative:- 11211000000	Negative.
3	Doubtful	Negative:- 11222100000	Negative.
4	Negative	Negative:- 11111000000	Negative.
5	Negative	Negative:- 11122100000	Negative.
6	Negative	Negative:- 11111000000	Negative.
7	Negative	Negative:- 11222110000	Negative.
8	Negative	Negative:- 11221000000	Negative.
9	Negative	Negative:- 11111100000	Negative.
10	Negative	Negative:- 11111000000	Negative.
11	Negative	Negative:- 11222100000	Negative.
12	Positive	Negative:- 11221000000	Negative.
13	Negative	Negative:- 11111000000	Negative.
14	Negative	Negative:- 11211000000	Negative.
15	Negative	Negative:- 11122100000	Negative.

In this group the Goldsol and Wassermann reactions are Negative throughout.

Case,3, shows a doubtful Ross-Jones reaction and Case 12, a positive one.

Group.8. CONFUSIONAL INSANITY.

Case No.	Ross.Jones.	Goldsol.	Wassermann.
1	Negative	Negative:- 11221111100	Negative.
2	Negative	Negative:- 11221000000	Negative.
3	Negative	Negative:- 11110000000	Negative.
4	Negative	Negative:- 11111000000	Negative.
5	Negative	Negative:- 11111100000	Negative.
6	Negative	Negative:- 11000000000	Negative.
7	Negative	Negative:- 11111000000	Negative.
8	Negative	Negative:- 11111100000	Negative.
9	Negative	Negative:- 11110000000	Negative.
10	Negative	Negative:- 11222000000	Negative.
11	Negative	Negative:- 11110000000	Negative.
12	Negative	Negative:- 11221000000	Negative.
13	Negative	Negative:- 11222100000	Negative.
14	Negative	Negative:- 11111000000	Negative.
15	Negative	Negative:- 11111000000	Negative.

All these fluids are Negative throughout.

Group.9. DELUSIONAL INSANITY.

Case No.	Ross.Jones.	Goldsol.	Wassermann.
1	Negative	Negative:- 12211000000	Negative.
2	Negative	Negative:- 11111000000	Negative.
3	Negative	Negative:- 11111000000	Negative.
4	Negative	Negative:- 11221000000	Negative.
5	Negative	Negative:- 11110000000	Negative.
6	Negative	Negative:- 11111000000	Negative.
7	Negative	Negative:- 11110000000	Negative.
8	Negative	Negative:- 11111000000	Negative.
9	Negative	Negative:- 11221000000	Negative.
10	Negative	Negative:- 11111000000	Negative.
11	Negative	Negative:- 12211000000	Negative.
12	Negative	Negative:- 11221000000	Negative.
13	Negative	Negative:- 11110000000	Negative.
14	Negative	Negative:- 11111000000	Negative.
15	Negative	Negative:- 11111000000	Negative.

All these fluids are Negative throughout.

Group.10. GENERAL PARALYSIS.

Case No.	Ross.Jones.	Goldsol.	Wassermann.
1	Positive	Positive:-5555421000 0	Positive.
2	Positive	Positive:-5555555211 0	Positive.
3	Positive	Positive:-5555554321 0	Positive.
4	Positive	Positive:-5555422100 0	Positive.
5	Positive	Positive:-5555554400 0	Positive.
6	Positive	Positive:-5555432000 0	Positive.
7	Positive	Positive:-5555432000 0	Positive.
8	Positive	Positive:-5555554200 0	Positive.
9	Positive	Positive:-5555554320 0	Positive.
10	Positive	Positive:-5555432000 0	Positive.
11	Positive	Positive:-5555432100 0	Positive.
12	Positive	Positive:-5555310000 0	Positive.
13	Positive	Positive:-5555431111 0	Positive.
14	Doubtfúl	Positive:-5553210000 0	Positive.
15	Doubtful	Positive:-5543322000 0	Positive.
16	Positive	Positive:-5554332100 0	Positive.
17	Positive	Positive:-5554432100 0	Positive.
18	Positive	Positive:-5555555532 0	Positive.
19	Positive	Positive:-5555554300 0	Positive.
20	Positive	Positive:-5555533220 0	Positive.
21	Doubtful	Positive:-5555543100 0	Positive.
22	Positive	Positive:-4545543100 0	Positive.
23	Positive	Positive:-4444554420 0	Positive.
24	Positive	Positive:-5544555430 0	Positive.
25	Positive	Positive:-4445554200 0	Positive.
26	Positibe	Positive:-3444445550 0	Positive.
27	Positive	Positive:-5555554321 0	Positive.

Group.10. GENERAL PARALYSIS.

Case No.	Ross.Jones.	Goldsol.	Wassermann.
28	Negative	Positive:- 55455432000	Positive.
29	Positive	Positive:- 55555543200	Positive.
30	Positive	Positive:- 55555432100	Positive.
31	Positive	Positive:- 44545532100	Positive.
32	Positive	Positive:- 55555543100	Positive.
33	Doubtful	Positive:- 55455543210	Positive.
34	Positive	Positive:- 55555543210	Positive.
35	Positive	Positive:- 55555555430	Positive.
36	Positive	Positive:- 44445532100	Positive.
37	Positive	Positive:- 44355321000	Positive.
38	Positive	Positive:- 44345432100	Positive.
39	Positive	Positive:- 22345432100	Positive.
40	Positive	Positive:- 44445532100	Positive.
41	Positive	Positive:- 44445533210	Positive.
42	Positive	Positive:- 42224321000	Positive.
43	Positive	Positive:- 55555420000	Positive.
44	Positive	Positive:- 55555542100	Positive.
45	Positive	Positive:- 55545531000	Positive.
46	Positive	Positive:- 44553320000	Doubtful.
47	Positive	Positive:- 42234420000	Positive.
48	Doubtful	Positive:- 45521000000	Doubtful.
49	Positive	Positive:- 55555442100	Positive.
50	Positive	Positive:- 55555532100	Positive.
51	Positive	Positive:- 55555553210	Positive.
52	Doubtful	Positive:- 44555321000	Positive.
53	Positive	Positive:- 55555432100	Positive.
54	Positive	Positive:- 55455532100	Positive.

Case No.	Ross.Jones.	Goldsol.	Wassermann.
55	Positive	Positive:- 11244310000	Positive.
56	Positive	Positive:- 45445432100	Positive.
57	Positive	Positive:- 55555432100	Positive.
58	Positive	Positive:- 44344321000	Positive.
59	Positive	Positive:- 55555421000	Positive.
60	Positive	Positive:- 55543210000	Positive.
61	Doubtful	Positive:- 44321000000	Positive.
62	Doubtful	Positive:- 55554432000	Positive.
63	Positive	Positive:- 44344100000	Positive.
64	Positive	Positive:- 44455432000	Positive.
65	Positive	Positive:- 44444325410	Positive.
66	Positive	Positive:- 54344421000	Positive.
67	Positive	Positive:- 55344310000	Positive.
68	Negative	Positive:- 55544421000	Positivez
69	Positive	Positive:- 55555542100	Positive.
70	Positive	Positibe:- 44334442200	Positive.
71	Positive	Positive:- 55555543100	Positivez
72	Positive	Positive:- 55555550000	Positive.
73	Positive	Positive:- 44445510000	Positive.
74	Positive	Positive:- 45555431000	Positive.
75	Positive	Positive:- 55554430000	Positive.
76	Negative	Positive:- 55444321000	Negative.
77	Doubtful	Positive:- 44444432110	Negative.
78	Negative	Positive:- 23444300000	Negative.
79	Doubtful	Doubtful:- 33331000000	Positive.
80	Positive	Positive:- 44445532100	Positive.
81	Positive	Positive:- 55555431000	Positive.

1 2 3 4 5 6 7 8 9

2 4 10 14 29 15 21

Group. 10. GENERAL PARALYSIS&

Case No.	Ross. Jones.	Goldsol.	Wassermann.
82	Negative	Negative:-1122100000	Negative.
83	Negative	Negative:-1111000000	Doubtful.
84	Negative	Negative:-1110000000	Negative.

This group of 84 cases, is not in the order in which the fluids were examined, but is arranged to facilitate reference.

With the exception of fluid 46, which gave a doubtful W.R. and was from a clinically obvious case of General Paralysis, the first 75 instances show agreement in reacting positively to both Gold test and W.R. Of these 75, eight showed a doubtful Ross-Jones reaction; i.e. there was a slight, ill-defined haze instead of the typical clear-cut opacity at the junction of the fluids. Only two, Nos.28 & 68 gave a Negative Ross-Jones reaction; these were both clinically obvious cases of General Paralysis.

Fluid 76, is from a case of General Paralysis with grossly obvious physical symptoms; yet both Ross-Jones and Wassermann reactions are negative; not so the Gold test.

Fluid 77, is from a woman who was diagnosed a paretic three years ago, and reached the helpless bed-ridden stage. Within the last year however she has passed into a period of marked remission. Though some physical signs persist, she is up and about, occupies herself usefully and talks fairly sensibly.

Her spinal fluid gives a negative Wassermann reaction, but the "4" degrees of change in the Goldsol reading amounts to a positive result.

Cases 78 and 79 show conflicting reactions.

Fluids 80 and 81 are from Juvenile General Paralytics; the latter case is still alive, the diagnosis in the former was verified post mortem.

Fluid 82, is from a case of Chronic General Paralysis The patient was admitted twelve years ago at the age of 49. In 1911 his spinal fluid gave a positive W.R; in 1912 the reaction was weak; in 1920 it is negative. Speech defect, pupil reactions and Grandiose delusions leave little doubt of the diagnosis. What about Serum?

Fluid 83 is from a case of Dementia with slight paresis of one arm. He is suspected of being a Paralytic, but the clinical diagnosis is in doubt.

Fluid 84, is from a patient who was admitted five years ago at the age of 69, and diagnosed as a case of Senile General Paralysis. He is still alive and shows some of the signs of Dementia Paralytica.

Thus the 84 cases in this group comprise-

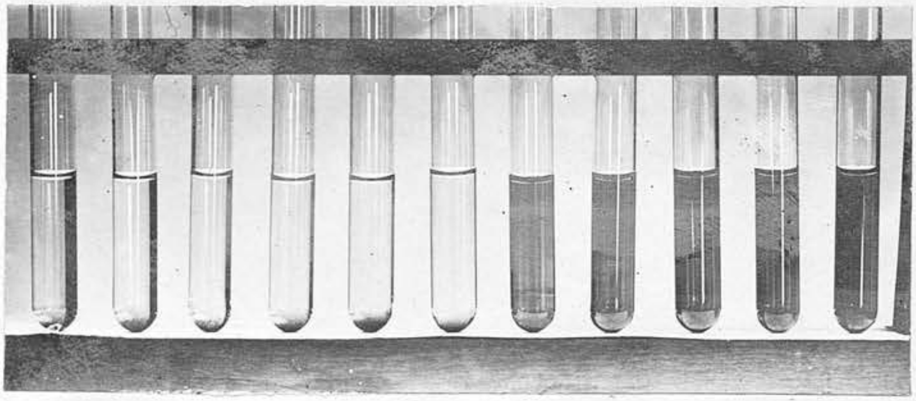
80 ordinary examples of General Paralysis;

2, Juvenile cases; 1 Senile Case; and

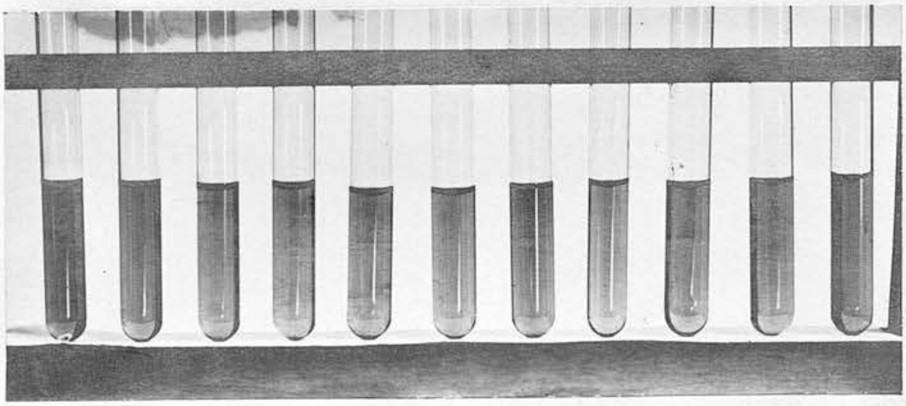
1 Chronic Case.

The relative sensitiveness of the three tests is brought out by the following table:-

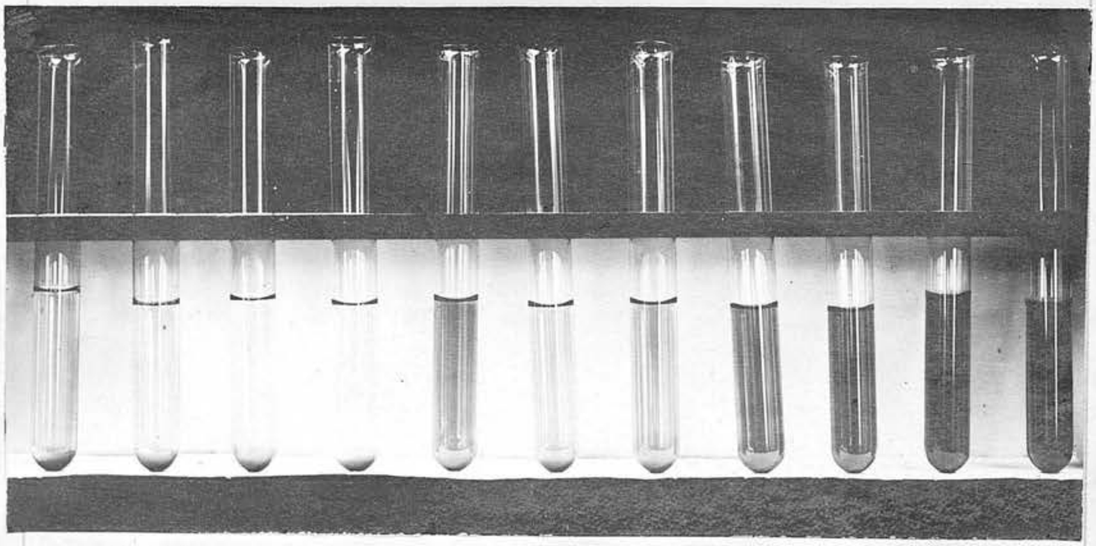
	Goldsol.	Wassermann.	Ross-Jones.
Positive:-	80	76	67
Negative:-	3	5	7
Doubtful:-	1	3	10



A typical Paretic Reaction



A Negative Reaction showing changes of "1" and "2" degrees in middle tubes



A Paretic Reaction showing an anomaly; the 5th tube is not precipitated though the 6th is

POSITIVE FINDINGS IN GENERAL PARALYSIS.

AUTHORS.	No. of Cases.	G.S.R.	W.R.	R.J.	
Cruickshank.	33	29	29	29	?
DeCrinis & Frank.	~~83~~	~~83~~	~~58~~	~~70~~	unreliable result
Eicke.	52	50	50	50	?
Eskuchen.	~~21~~	~~7~~	~~19~~	~~21~~	unreliable result
Kaplan.	52	48	47	41	
Lee & Hinton.	12	11	10	9	
Miller Brush etc.	130	122	121	116	
Miller & Levy.	49	49	49	47	
Solomon & Koefod.	16	14	16	16	
Swalm & Mann.	70	66	66	65	
Weston, Darling & Newcombe.	34	31	32	32	
Bedford.	84	80	76	67	
	~~615~~	~~583~~	~~554~~	~~542~~	
~~83~~	~~83~~	~~83~~	~~58~~	~~70~~	
	532	500	496	472	
		93.98 p.c	93.23 p.c	88.72 p.c	

R. Ed. statistics W.R. = 95%

Group.11. MISCELLANEOUS CASES.

Case No.	Diagnosis	R.J.	Goldsol	W.R.
1	Tabes Dorsalis	–	11122110000	–
2	Tabes Dorsalis	–	11111000000	–
3	Tabo-Paresis	+	22244432100	+
4	Disseminated Sclerosis	–	11112221000	–
5	Disseminated Sclerosis	–	22221000000	–
6	Old Hemiplegia	–	33333321000	–
7	Old Hemiplegia	–	33333310000	–
8	Cerebral Tumour(Gumma)	±	44222211110	–
9	Cerebral Tumour(Glioma)	–	11121100000	–
10	Cerebrospinal Syphilis	±	41222100000	+
11	Cerebrospinal Syphilis	–	11123210000	–
12	Cerebrospinal Syphilis	–	22333210000	–
13	Cerebrospinal Syphilis	–	22333211100	+
14	Cerebrospinal Syphilis	±	22333321000	–
15	Alcoholic Psychosis	–	00000000000	–
16	Alcoholic Psychosis	–	11000000000	–
17	Alcoholic Psychosis	–	11110000000	–
18	Motor Aphasia	±	11122100000	–
19	Huntington's Chorea	–	11111000000	–

In this group there are not a sufficient number of instances of any one disease to justify generalisations; but there are some points of interest.

The two cases of Tabes did not show any signs of General Paralysis, and their fluids are Negative throughout.

Swalm & Mann record that 50% of their cases of Tabes "furnished a marked luetic curve".

Warwick & Nixon state that in 74% of their cases the "Goldsol test was positive"

But the majority of Authers agree that "Tabes gives a reaction different from Paresis, fairly characteristic of Syphilis, but not in itself diagnostic of Tabes".

Case 3 is an instance of Paresis following on Tabes, and not the common type of Paresis with Tabetic symptoms.

The two cases of Dis seminated Sclerosis show Negative reactions throughout. The findings of other workers vary widely widely; thus, Moore obtained the Paretic Gold curve in 18 out of 20 clinically certain cases, whilst Kaplan saw such a curve only once in 18 cases.

The two examples of Hemiplegia following a stroke show Goldsol readings that cannot be called Negative, and that require explanation.

Cases 8 & 9 offer a contrast; in the latter the diagnosis was made post-mortem.

Of the five instances of Cerebrospinal Syphilis, all show a Goldsol reading that is suspicious.

Case No.10 was an Epileptic who died riddled with Generalised Syphilis, but showed no signs of General Paralysis.

The three Alcoholic Cases were selected because they were suggestive of General Paralysis, but the laboratory findings have disproved the suggestion.

Group.12. FLUIDS EXAMINED POST MORTEM.

Case No.	Diagnosis	R.J.	Goldsol	W.R.
A	Confusional Insanity	—	1112211000	—
B	Melancholia	+	1111221000	—
C	Secondary Dementia	+	1111122211 0	—
D	Secondary Dementia	—	1112221100 0	—
E	Delusional Insanity	—	2221111111 0	—
27	General Paralysis	+	5555310000 0	+
37	General Paralysis	+	4445532100 0	+
69	General Paralysis	+	5555554210 0	+
29	General Paralysis	+	5555554310 0	+
35	General Paralysis	+	5555555420 0	+
59	General Paralysis	+	5555531000 0	+
53	General Paralysis	+	5555532100 0	+

These fluids were obtained by puncture of the Cisterna Cerebromedullaris before Autopsy.

The first five had not been examined during life, but the last seven had; the case numbers indicate the individuals in Group 10.

The Autopsy confirmed the diagnosis in every case.

The results show, that the Gold test and W.R. are equally reliable when applied to fluids obtained soon after death.

COMPOSITE TABLE OF RESULTS.

DISEASE.	No. of cases	GOLDSOL.			WASSERMANN.			ROSS.JONES.		
		Positive.	Negative.	Doubt.	Positive.	Negative.	Doubt.	Positive.	Negative.	Doubt.
MELANCHOLIA.	15.	0	15	0	0	15	0	0	15	0
MANIA.	15	0	15	0	0	15	0	0	15	0
EPILEPSY.	15	0	13	2	1	14	0	0	15	0
AMENTIA.	15	0	15	0	1	15	0	1	13	1
DEM. PRAECOX.	15	0	15	0	0	15	0	0	15	0
ADULT DEMENTIA.	15	0	15	0	0	15	0	0	14	1
SENILE DEMENTIA.	15	0	15	0	0	15	0	1	13	1
CONFUSIONAL INSANITY.	15	0	15	0	0	15	0	0	15	0
DELUSIONAL INSANITY.	15	0	15	0	0	15	0	0	15	0
GENERAL PARALYSIS.	84	80	3	1	76	5	3	67	7	10

(5) COMPARATIVE VALUE OF THE ROSS-JONES, WASSERMANN, AND GOLDSOL TESTS AS APPLIED TO THE C.S.F.

The Ross-Jones Ammonium Sulphate test is a method of making a quantitative estimation of the globulin content. A "positive" Ross-Jones indicates that the fluid under examination contains an excess of globulin, and is therefore pathological. But the test is a "Group Reaction" - for other protein complexes besides globulin are precipitated by Ammonium Sulphate. It does not discriminate, one from the other, the various possible proteins that may be present; nor does it reveal their relationship to one another. Although it is positive in the great majority of cases of Neuro-Syphilis, it is not confined to these alone but may be found in Epilepsy and other diseases.

Further, it gives no clue to the nature of the pathological process causing it.

Yet it is of undoubted value on account of its simplicity, clear-cut results, and comparatively small margin of error.

For example, Lowrey reports that "used in 106 Syphilitic cases it was positive in 101; and used in 86 cases not diagnosed as Neurosyphilis it was positive in only 1." Analysis of my series of tests shows/

shows that out of 92 cases thought to be Syphilitic, it was negative in only 12; and of these 5 were negative to all tests. Of 135 non-luetic cases, the test was positive in only 2. The post-mortem tests are not included in this calculation.

This proves that it is sufficiently reliable to warrant its use in Neurological diagnosis.

The Wassermann Reaction is admittedly one of the most valuable signs of Syphilitic infection known to Medicine.

Unfortunately, the general utility of the test is very greatly diminished by the complexity of its highly specialised technique.

Its performance requires considerable skill and precision; its interpretation needs scientific judgment and experience.

Its ingredients are often difficult to prepare; its preliminaries are apt to be tedious.

Its literature shows the great variety of modifications which have been introduced by some, and condemned by others; in fact, there is not one of its finer details on which doubt has not been cast.

The real existence of these difficulties is evidenced by the many attempts which have been made to/

to simplify the test.

It has happened that two successive tests in the same case - and even two simultaneous reports from different sources - have contradicted each other; or, if they agree, were opposed to well-marked clinical evidence. Bayley gives a selection of seventeen such instances in which possible explanations carried no conviction.

Another source of fallacy, not sufficiently recognised, is the possibility that the cell-destruc:tion products set free by the gross brain-lesion caused by a blow on the head, might originate a positive reaction. How then shall the "General Paralytic" be differentiated from the "Progressive Dement with head injury"? The fact is, the test is quantitative and not at all qualitative, so that the recording of degrees of positiveness - for example "strongly" or "weakly", "four plus" or "three plus", are quite meaningless. Browning and Kennaway point out that there is no sharp line of demarcation between syphilitic and non-syphilitic fluids, and estimate the margin of error in border-line cases alone, as 5%, under the most favourable circumstances.
Yet in spite of all these drawbacks, it is generally accepted that a negative Wassermann reaction in the spinal/

spinal fluid is probably sufficient to exclude General Paralysis. Hence it has been chosen as a control in evaluating the Goldsol test.

When criticised in the same way as the two tests just under discussion, the superiority of the Goldsol test becomes manifest. It is more sensitive without being any less reliable because, in all probability, it is a qualitative reaction and therefore more discriminative. Thus, an analysis of eleven separate series of investigations carried out by different observers and comprising 523 cases of clinically obvious General Paralysis, shows that the Goldsol test was positive in 485, the Ross-Jones in 470 and the Wassermann in 465. In my own series, leaving out "doubtful" reactions, the figures are, 80 positive with the Goldsol Test, 76 with the Wassermann, and 67 with the Ross-Jones out of a total of 84 General Paralytics. Similarly, in Tabes Dorsalis, Lee & Hinton obtained gold reactions in 24 cases, of which 9 gave negative Wassermann reactions in both blood and spinal fluid; of these 9, two gave no other spinal test positive. These patients all had a definite Syphilitic history.

Further, in 8 cases of Syphilis, without clinical evidence of involvement of the Nervous System and with/

with negative Wassermann reactions in the spinal fluid, 4 positive Gold reactions were obtained. The blood Wassermann was also positive in these four cases.

Weston, in an article questioning the relationship of the Gold test to Syphilis, gives, in support of his argument, details of three mental cases who, during a period of two years under repeated examina:tions, always gave paretic curves with the Gold test and negative Wassermann reactions. But in a foot-note he records that one of these patients, tested while the article was in the press, had developed a positive Wassermann reaction. This would seem to indicate that the Gold test is of value in the early diagnosis of Neurosyphilis, which is the view put forward by Lange originally, and since endorsed by Kaplan and by Black and his co-workers. If this claim can be definitely established, the chances of preventing or modifying severe Neurosyphilis by early treatment will be greatly increased.

As yet there is no evidence that the test is specific for Syphilis in the sense of an immunity reaction; but it is specific for General Paralysis in so far as it is so strikingly constant and more frequent in this disease than in any other. But the specificity of the zonal reaction named "Luetic" is open to grave doubt as shown in another section.

Another/

Another great merit possessed by the Gold test is, that it is as equally well applicable to old as to fresh spinal fluid. In my experience, fluids kept eight and ten days in the ice-chest did not materially alter in their reaction. One author found that a spinal fluid was as active after a year as in the beginning.

But if the fluid has become turbid through bacterial multiplication, it is untrustworthy. The value of this is, that a sample of paretic fluid can always be kept at hand in order to test new Goldsols as they are made.

Obviously, in these circumstances, the fluid should have been received into a sterile tube and kept plugged with sterile wool in the ice-chest. The permanence of the reaction is another outstanding feature. After the first twelve or fifteen hours the tubes show little change for several days, without any special precautions being taken; they may perhaps become rather paler in tint. If the tubes are stoppered and kept in the ice-chest, the reaction may be preserved for weeks.

The general utility of any test is always determined by its simplicity and ease of application. In this respect the superiority of the Goldsol test over the Wassermann Reaction is very obvious; it takes but/

but fifteen minutes to perform, and is within the reach of any Clinician or Medical Officer.

Other features of the Test.-

Blood. Although a pure sample of spinal fluid is preferable, the presence of a small amount of blood does not render it unfit for testing. Fluids with a faint pink tinge, or which deposit a clot the size of a large pin's head on standing, are admissable. Such specimens should be allowed to sediment over-night, and the clear supernatant fluid used. I have found this preferable to separation by centrifuge. The blood may cause slight changes in colour in the higher dilutions but will not convert a negative into a positive reaction.
Gross contamination by blood is inadmissable.

Serum. The test has been applied to blood serum and the following interesting facts brought to light:- A dilution of fresh human serum corresponding to 0.08% in ordinary salt solution, when used in place of spinal fluid in the ordinary test, causes precipitation of Gold in the same way as a strongly positive paretic fluid. The Gold test is therefore not applicable to blood as a means of diagnosing General Paralysis. Human serum differs markedly/

markedly from the sera of the ox, sheep, horse, guinea-pig, rabbit, monkey and fowl, in its reaction to Goldsol; the test may accordingly come to be of use in Medico-legal cases.

The precipitating power is in the Globulin fraction of the serum, while the albumin fraction is inert. Serum left at room temperature rapidly loses its precipitating power and may become quite inactive; yet globulin prepared from such a serum is very active.

This suggests that it might be better to let blood-contaminated fluids stand for two or three days before testing them.

The experimental addition of small amounts of fresh serum to negative fluids causes a positive reaction with Gold, yet fluids mixed with appreciable amounts of fresh blood at the time of lumbar puncture do not give positive results. This agrees with the clinical finding already noted.

The Test in other Diseases. Before the Goldsol Reaction can be accepted as pathognomonic of General Paralysis, it must be applied to other forms of Neurosyphilis and to non-luetic diseases.

Warwick and Nixon examined a series of 240 miscellaneous cases comprising general Medical and Surgical patients. They found that a "3" or more reaction/

reaction occurred in only 9 instances and these were respectively - General Syphilis, Aortic Aneurism, Sciatica and Syphilis, Sciatica, Progressive Muscular Atrophy, Myelitis, Syphilitic Myelitis, Myelitis, and Alcoholic Psychosis.

Of these, 4 were Syphilitic conditions and the remaining 5 were affections of the Nervous System.

Sippy and Moody obtained negative reactions in the following conditions - Trifacial Neuralgia, Neurasthenia, Diabetes Insipidus, Polyneuritis, Brain tumour, Amoebic Dysentery (with positive W.R. in serum), Toxic oedema of brain, Epilepsy, Pernicious Anaemia, Otitis Media with Meningismus, Anterior Poliomyelitis, Cerebral Abscess, Status Lymphaticus, Acute Encephalitis, Tumour of Cord, Spinal Caries, Sinus Thrombosis, Syringomyelia, Pneumonia with Meningismus, and Uraemic Coma.

On the other hand, Moore writes that the "so-called 'paretic' gold-curve has since been obtained in a number of other conditions such as lead-poisoning, tuberculous meningitis and multiple sclerosis."

Further investigation is obviously indicated, preferably in General Hospitals where all sorts of cases are received, including incipient Nervous and Mental disease.

As/

As a Means of Measuring the efficacy of Treatment,

the Goldsol test would appear to be of little or no value. Many investigators have recorded conflicting opinions on this point. Under treatment, some paretic fluids lose their positive reaction; others remain unchanged; whilst yet others give a more intense curve of the nature of a "provocative reaction." In this respect the Gold test resembles the Wassermann Reaction, but differs from it in being the first to appear in Neurosyphilis, and the last to go under treatment, if there is any change at all.

NATURE OF THE REACTION.

Before discussing the various hypotheses that have been put forward to explain the mechanism of this reaction, it becomes necessary to consider briefly the composition of its three constituents; namely:-

The Cerebro-Spinal Fluid,

The Saline Diluent, and

The Goldsol.- referring to those properties only, which appear to have some bearing on the test.

(a) The Cerebrospinal Fluid.

The great physiological importance of the Cerebro-spinal fluid was realised by Magendie nearly one hundred years ago.

Its clinical value, however, began to be recognised only as recently as 1889, when Wynter tapped a case of tuberculous Meningitis by means of a Southey's Tube and Trocar.

In 1891 Quincke devised the operation of lumbar puncture, and, by the introduction of his needle into the dural sac, opened up a rich field of Neurological research.

Since that date the spinal fluid has been examined in a great variety of ways, and much has been learned of its pathology.

Though a small amount may be derived from the ependyma/

ependyma of the ventricles and the peri-vascular system of the nervous tissue, it is probable that the Cerebrospinal Fluid is mainly a true secretory product of the cubical cells of the Choroid Plexus. This may be the explanation of the difference in constitution which has been shown to exist between the Ventricular and the Spinal fluid, and even in the spinal fluid itself at different levels; for there is no choroid plexus in the Spinal Canal.

It has been calculated that, normally, the Cerebrospinal Fluid is renewed every four hours; its circulation, therefore, is very slow. But when drawn off by puncture, it is quickly replaced.

The total quantity of the Cerebrospinal Fluid in an adult has been put as high as 150 cc. (Contaguo) and as low as 62 cc. (Magendie). Half of it is contained in the Spinal Canal, and, of the remainder, about 25 cc. is held by the Ventricles.

After death, it disappears rapidly. This should be borne in mind when contemplating Cadaveric puncture, for in seventy-two hours there may be no fluid left.

The pressure of the fluid is chiefly dependent upon blood-pressure, respiration and the total amount of fluid present; but it is also influenced by other subsidiary factors such as muscular effort and posture.

Quincke puts the pressure so low as 40 mm. of water,/

water, whilst, at the other extreme, 200 mm. is quoted by several authorities.

The normal pressure is probably between 60 and 120 mm. of water, or 5 to 7.3 mm. of Mercury.
The withdrawal of large quantities of fluid by puncture will cause a temporary lowering of pressure.
The reaction is neutral or faintly alkaline from the presence of inorganic salts.
Zdarek gives the following analysis.-

Water		989.54
Solids		10.45
	Organic Solids	2.09
	Mineral Ash	8.35
	Albumins	0.76
	Ethereal residue	0.35
	Aqueous residue	8.22
	Sulphuric Acid (SO_3)	4.04
	Chlorine	0.24
	Carbon Dioxide	0.49
	Potassium Oxide	0.16
	Sodium Oxide	4.29
	Mineral Ash, insoluble in Water	0.16
	Glucose	0.10

The Inorganic constituents are chiefly Chlorides and Bicarbonates with traces of Phosphates, Sulphates and/

and Nitrates.

Sodium Chloride is the chief salt, being present in 0.75%.

The Organic Constituents - The identity of the protein or proteins present in the spinal fluid is in doubt. Landois regards it as Serum Albumin; Hammarsten as a mixture of Globulin and Albumose; Siemerling as Globulin only; Halliburton as being principally a nucleoprotein.

Mestrizat considers it a globulin, and denies that fibrinogen, albumoses, peptones, nucleo-albumins and mucin are present in normal fluids. For practical purposes it would seem advisable to regard the protein of normal spinal fluid as a mixture of albumin and globulin, the latter predominating in the proportion of about 3 to 1. The total quantity of protein is probably from 0.02 to 0.03%, or 0.2 to 0.3 grams per litre.

Serology - Precipitins, Agglutinins, Bacteriolysins, Toxins and Haemolysins are all absent from normal fluid.

Pathology of the Cerebrospinal Fluid.

Increased protein Content - this is a subject of great interest and importance in the diagnosis of cerebrospinal diseases.

A well marked protein increase is always pathological,/

pathological, and usually indicates an inflammatory process, either infectious or toxic.

In Acute Meningitis, for example, the increase may be tenfold.

There is evidence that in General Paralysis certain peculiar qualitative changes occur in the protein. Hence, if an exact quantitative differentiation of the various proteins could be made, it might show which particular kind is increased in disease. Such information would be not only of diagnostic value but of great theoretic interest in relation to the so-called Wassermann Antibodies.

Taking 0.25 grams of protein per 1,000 cc. fluid as the normal

Cerebrospinal Syphilis	may	show	0.3 —— 1.2
Tabes Dorsalis	"	"	0.5 —— 1.5
General Paralysis	"	"	0.3 —— 2.2

According to these figures, there may be eight times as much protein in the spinal fluid of Paralysis as in the normal. A four-fold increase is common. In the diseases just mentioned, it seems to be the globulin chiefly that is increased.

Various Nucleoproteins have been found; and the products of protein hydrolysis such as Albumoses, Peptones, Polypeptides and Amino-Acids may occur when there is an increase of spinal fluid with stasis.

On/

On the other hand, a normal protein content does not exclude organic changes in the Central Nervous System.

Neuro Syphilis - The examination of the spinal fluid is very helpful in differentiating Tabes, Paresis, and Cerebrospinal Lues.

(1) In Tabes Dorsalis - the pressure is usually raised; the protein content is slightly increased so that the globulin tests are positive in 90 to 95% of cases; the Wassermann Reaction is positive in from 21 to 60% of cases.
In about 7% there is no globulin increase, and this is usually associated with a negative W.R.

(2) In General Paralysis - The fluid changes are marked; the pressure is increased, especially in the Acute Stage. Though normal in appearance, if much protein is present fibrin flakes may form in the fluid after standing.
The protein content is increased; the globulin tests are nearly always positive, the strength of the reaction varying with the severity of the disease.
The W. R. is positive in at least 85% of cases if 0.2 cc. of fluid is used after the original method; and in 92 to 100% if larger amounts are used.

(3) In Cerebrospinal Syphilis, the fluid analysis varies with the site of infection; for example.-

(a) One third of the cases are meningeal. In these the pressure of the fluid is increased and fibrin coagula may form in it on standing. The protein content is increased sufficiently to give a positive globulin reaction in at least 50% of cases. The W.R. is positive in every case.

(b) In the "Plaut" type, which is fairly common, the fluid changes are quite similar to those in the Meningeal form, with the very important exception that the W.R. is generally negative.

(c) The Endarteritic Type is rare. It is characterised by a negative globulin test associated with a positive W.R.

Examination of the Cerebrospinal Fluid.

No Neurological examination is now considered complete unless the spinal fluid has been subjected to certain tests. Some of these, such as the quantitative estimation of the inorganic constituents, are of little clinical value on account of the wide variations that occur in diseased conditions. But other tests are of very great practical importance. Some of these have been referred to already; namely, Fehling's Test, the cell count and the pressure estimation. Those with which we are particularly concerned are three - namely.-

(1) A Test for globulin increase

(2) The Wassermann Reaction

(3) The Goldsol Reaction.

(The last named is discussed in another section.)

These three tests have been selected for comparison because they all seem to have some connection with the protein content of the Cerebrospinal fluid.

Globulin/

Globulin increase. Various methodsof protein estimation have been devised, and are associated with the names of Nonne-Apelt, Ross-Jones, Noguchi, Pandy, Kaplan, and Gordon. These are all precipitation tests, and in all the essential preliminaries are.-

(1) The spinal fluid must be free from blood so as to exclude serum proteins.

(2) Bacterial multiplication must be avoided by testing the fluid soon after withdrawal.

(3) The test-tubes should be thin-walled so as not to obscure the precipitate.

I have selected the Ross-Jones Test for my purpose because of its simplicity, reliability, delicacy and clear-cut reaction.

This test of globulin increase owes its value to the facts that it is never positive in the normal fluid and that it seldom gives a positive result except in cases of organic nervous disease. It is rarely posi:tive in any chronic affection except active syphilis or metasyphilis of the nervous system. Though it is almost invariably positive in General Paralysis, it is incorrect to say that in no other form of insanity does it give the same result. Boyd obtained a definitely positive reaction in 10 cases out of a series of 87, and in such various psychoses as Acute Mania, Melan:cholia, Dementia Praecox, and especially Epilepsy (4 cases). I can confirm this from my own observations. (See Group 4. Case 10)

A positive Ross-Jones test means that the fluid is a pathological one.

Jones believes that the protein concerned in this reaction is euglobulin, and that in General Paralysis a peculiar qualitative change takes place in this euglobulin; which change is associated with the formation of the "Anti-body" that is the active agent in the Wassermann Reaction. It is generally assumed that the reaction is due to increased protein content in the cerebrospinal fluid for the two are usually associated. But Turner found that a few fluids show:ing a positive Ross-Jones Test contained less protein than others that gave a negative reaction.
The test is not diagnostic in acute infections of the Central Nervous System or Meninges because in such cases there is often an excess of protein present whatever the nature of the infection. Nor can the test be used to differentiate between a non-syphilitic organic affection such as Multiple Sclerosis and a Syphilitic organic one like Cerebrospinal lues.
For, though never so strong in the former as in the latter, it does occur in both.

These limitations must be borne in mind in applying the test and in interpreting the results.

Technique of the Reaction. It is simply the Nissl-Nonne test modified so as to be performed in the same way as the Heller Test for albumen in urine.

By/

By means of a suitable pipette 2 cc. of a saturated solution of Ammonium Sulphate are placed in a test-tube. Then 1 cc. of spinal fluid is taken up in another pipette and allowed to flow gently down the side of the inclined tube on to the surface of the Sulphate Solution, so as to form a layer over it.

The Sulphate solution is put in first because it is the heavier.

If within three minutes a ring forms at the junction of the two fluids, the reaction is positive.

The ring should be thin, white, compact and sharply defined. It is best seen by indirect illum-:ination; that is, by looking at right-angles to the source of light, preferably against a dark background.

Later, the ring loses its definition and becomes a broad band of interwoven fibrils.

The Ammonium Sulphate Solution must be saturated in concentration and neutral in reaction. To attain this, the Salt must be chemically pure and the water distilled. Add 80 parts of Am So_4 to 100 parts of water and heat gently to boiling point. Filter whilst hot. On cooling there should be a deposit of the sulphate always present in the bottle.

The test can also be used quantitatively by making various dilutions of the spinal fluid.
Then, the greater the increase of protein, the sooner does/

does the ring appear, the denser it is, and the higher is the dilution in which it occurs.

If there is only a little spinal fluid available, the test can be just as well performed with half the quantities mentioned. It is the relative amount that is important.

In any series of comparative examinations, test-tubes of the same diameter should be employed. For the area of the fluid surfaces in contact with each other, in proportion to the amounts used, must have some influence on the rate at which the ring forms.

The actual physical conditions present at the junction of the two liquids is not known.
Jones suggests that the penetration of the Ammonium Sulphate solution by the spinal fluid occurs so gradually as to permit the formation of a layer in which the concentration is only a third; i.e. the concentration which is most favourable for the precipitation of euglobulin as distinct from other globulins. The protein molecules appear to be crowded out of the solution by the salt.

The Wassermann Reaction. A description of the technique of this test does not come within the scope of my thesis. But the features which it seems to have in common with the Ross-Jones and Goldsol tests, as regards/

regards the nature of these reactions, are relevant to my theme. Let me say at once that the true nature of the reaction cannot be said to have been determined. Bayley puts very neatly the most generally accepted hypothesis.

He says.- "This reaction is not in any sense an immunity reaction: it is neither a test for toxin nor antitoxin, but is only a remote consequence of syphilitic infection.

Probably something of the following "House-that-Jack-built" series may not be very wide of the mark - the Spirochaeta pallida produces a toxin; the toxin produces destruction of cells rich in lecethin and cholesterin; these cell-destruction products, acting as antigen, stimulate the body to produce the appro:priate antibody, and it is the presence of this antibody that we seek in the Wassermann Reaction."

The actual source of these "cell-destruction products" is not known: they may be derived from neurolysis or from leucolysis.

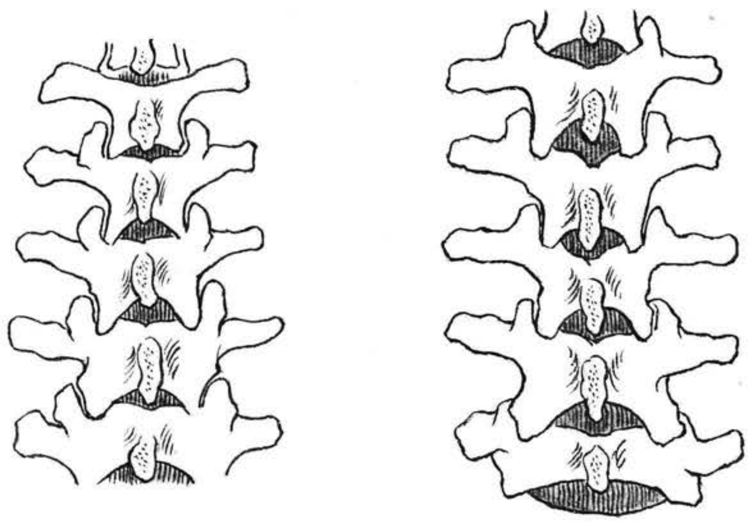
The so-called "Wassermann Antibodies" referred to have been shown to be proteids, and in fact globulins; probably englobulin. They have a great affinity for lecethin, and on their ability to produce a flocculent precipitate in lecethin emulsion, depends the well-known "Porges-Meier" reaction for Syphilis. The/

The test, therefore, would seem to depend upon the presence of an increased euglobulin content in the fluid under examination.

The reaction has been more precisely defined as an interaction of the nature of a precipitate formation, between certain hydrophil colloids, notably lecethin, and a changed form of globulin.

The test is thus both qualitative and quant-:itative. To put it in another way, - in the presence of a suitable lipoid extract, a syphilitic fluid (containing Wassermann antibodies) is capable of absorbing or fixing large amounts of complement, and this constitutes the main principle and all that is definitely known of the syphilitic reaction.

The test, therefore, is not biologically "specific" for the Spirochaeta-pallida. Practically, however, it possesses a high degree of specificity; because the peculiar reagent or antibody upon which the test depends is found in so few other diseases, and these diseases are of rare occurrence in this country.



Interarcual Spaces.

LUMBAR PUNCTURE.

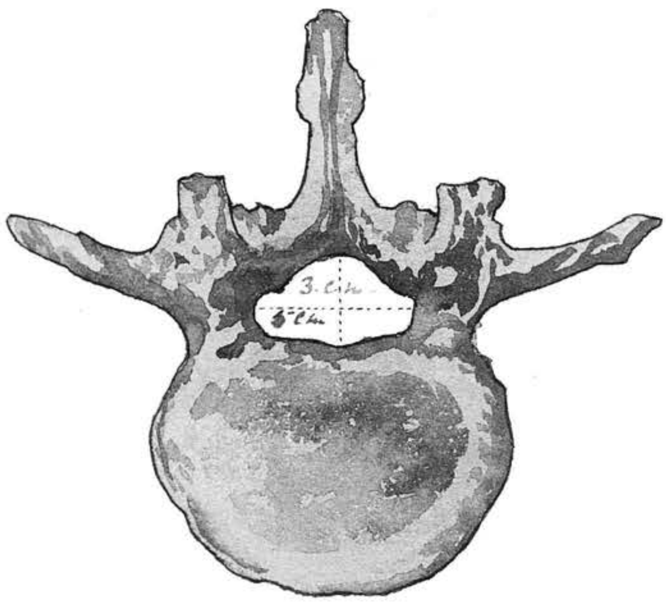
The sample of spinal fluid to be examined must be drawn off with the least possible risk and discomfort to the patient, and must be free from blood. Hence, the reliability of any test will depend in the first place upon the physician's skill in obtaining the fluid.

The technique of Lumbar Puncture, as of any other operation, is based upon the Anatomy of the part concerned - that is, on the Anatomy of the Spine and Cord in the Lumbosacral Region.

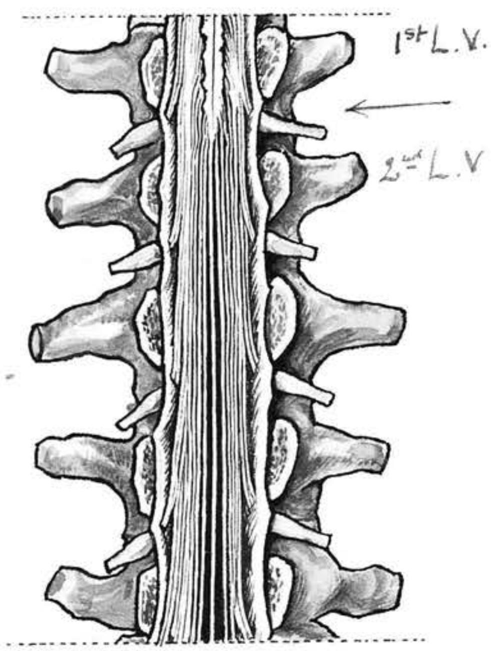
As compared with other portions of the spine, in the Lumbar Region, the intervals between the superimposed laminae are relatively large. They are arched spaces from 10 to 15 mm. in height, and, from 18 to 20 mm. across. The First, Third and Fifth interspaces are wider than the others, but all are large enough for the passage of the needle.

Also, the lumbar spinous processes are directed almost horizontally backwards. These factors, namely the large size of the interarcual spaces and the absence of overlapping of the spinous processes, facilitate access to the spinal fluid and are two of the reasons why the lumbar region is selected for puncture.

The/


3. cm

The distribution of the chief veins is of some importance as regards their liability to be punctured. The space between the dural sac and the wall of the Vertebral Canal is occupied by an irregular network of veins, the main vessels of which lie a little to either side of the middle line. This is one of the reasons for puncturing exactly in the middle line so as to avoid them; not because of any danger of serious haemorrhage, but to prevent contamination of the cerebrospinal fluid with blood. In the lumbar region the Vertebral Canal is at its largest. The expansion is greatest from the first sacral to the fourth lumbar vertebra, with a transverse diameter of 4 to 5 cm. and an Anteroposterior one of 3 cm. (See Fig.)
The Dural Sac undergoes a corresponding enlargement. The Dura Mater itself is about .4 mm. in thickness, but becomes thinner arteriorly. Its outer surface is rough, and from it anchoring strands of connective tissue radiate outwards to become attached to the walls of the vertebral canal. The spaces between the trabeculae so formed are occupied by fatty areolar tissue, small arteries and thin-walled veins. This Peridural space between the Dura and the Vertebral Canal may measure as much as 8 mm. in width.
The inner surface of the Dura is smooth and covered with a layer of endothelium. It forms the outer wall/


1st L.V.
2nd L.V

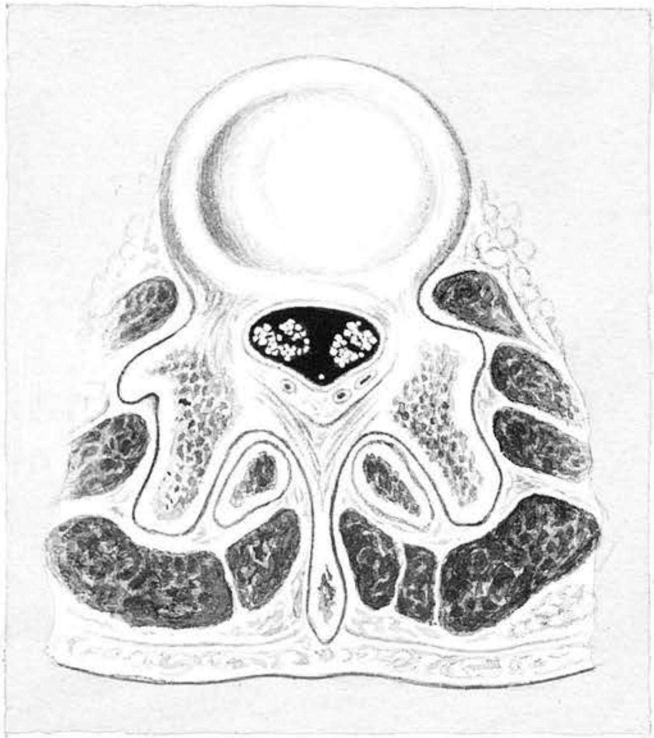
of the First Lumbar Vertebra or the disc below it usually marks its termination (See Fig. opposite).

Exceptionally, it may terminate at the Twelfth Dorsal, or even reach the Third Lumbar Vertebra.

In women and children the Cord reaches a slightly lower level than in men - a practical point worthy of note.

The last 10 mm. of the Cord is called the Conus Medullaris. This tapers into a glistening filamentous prolongation, the Filum Terminale which passes downwards among the nerve roots of the Cauda Equina, and, at the level of the Second Sacral Vertebra, reaches the lower end of the dural sac. This portion of the Filum within the dural sac is about 16 cm. ($6\frac{1}{4}$ in.) long, and consists chiefly of the fibrous tissue carrying the Anterior Spinal Artery, and Vein and surrounded by prolongations from the Pia and Arachnoid. In its upper third a little nervous tissue may be found. The Filum terminates by becoming attached to the periosteum of the Second Coccygeal Segment.

The Cauda Equina is composed of all the lumbo-sacral nerve-roots. These roots pass vertically downwards for a little distance within the dural sac before escaping through the intervertebral foramina. The disposition of the roots is of some practical importance. They are arranged in two lateral bundles with a/



a space between them measuring from 2 to 5 mm. wide; a space widest at the level of the Third Lumbar Verte:bra. (See Figs Opposite) This is an additional reason for inserting the needle exactly in the Median line so as to enter this space and thus avoid the pain and injury that might be caused by puncturing one or more nerve-roots.

The choice of Site for Lumbar Puncture, then, must be governed by (1) facility of access to the Cisterna Terminalis (2) Avoidance of the Spinal Cord, and (3) evasion of the venous plexuses and Cauda Equina. All these requirements are satisfied by the selection of the Third or Fourth Lumbar Interarcual space - preferably the Fourth Space in children and infants, because in them the Cord ends at a relatively lower level. A line drawn between the summits of the Iliac Crests usually crosses the Fourth Lumbar Space. (See Fig. p. 80) From this point the spaces are easily located by palpation.

The materials requisite for the operation are.-

(1) A low stool for the patient to sit on.

(2) Ether for cleansing the skin.

(3) Iodine - half Tinct: half Lin:- for disinfecting it.

(4) Cotton wool - for swabs and dressing.

(5) Ethyl Chloride Spray for Anaesthetising the Skin.

(6) Puncture Needle with stylet - sterilised.

(7) Test tubes, clean but not necessarily sterile, for the C.S.F.

(8)/

(8) Collodion for sealing the puncture.

(9) Gauze and Plaster Pad for further protection.

(10) Syringe for subsequent cleansing of needle - not for evacuation of fluid.

These are mentioned in the order in which they are employed.

The needle should be at least 3 inches long in the shaft. It should preferably be made of platinum - iridium which confers pliability and immunity to rust. It should be straight so as to facilitate cleansing. Its bore should not be too large or the fluid will escape too rapidly: Nor too small or it may become obstructed by clumps or cells or corpuscles. Its tip should have a short bevel, otherwise half its lumen may be within the dural sac and half without when the fluid first escapes, so that much of the fluid may spill into the epidural space and be lost. Further, a short-bevelled needle is less likely to injure the nerve-roots. The needle should also have a stout, well-fitting stylet with its tip bevelled to match the tip of the needle. This confers strength and prevents the orifice of the needle becoming blocked by a plug of skin or tissue punched out by the needle in its passage; it also prevents the needle from rusting internally when not in use, and helps to clean it.

Fancy needles with curves and stopcocks are difficult/

difficult to clean effectively and easily get out of order.

The patient may be seated for the operation, or in the left lateral position.

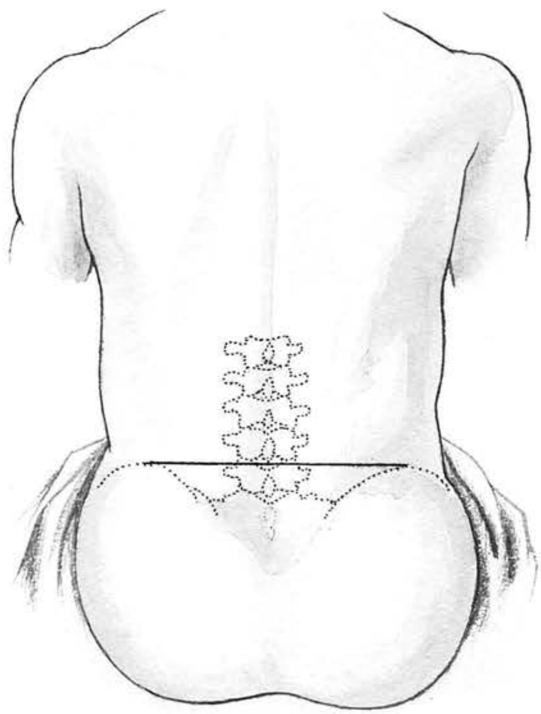
The former is not permissable if there is any reason to suspect the existence of a brain tumour, especially if it is in the Posterior Fossa of the Skull. It is claimed that the horizontal position is safer and less likely to cause headache or other cephalic disturbances.

The ill-effects of puncture are, in my opinion, more dependent upon such factors as the temperament or emotional tone of the patient, the nature of his disease, the amount of fluid removed, and improper after-care - than upon his posture during puncture.

It has been my experience that it is easier to find the fluid when the patient is seated. Hunt believes that the position of the patient during the operation in no way affects the subsequent nausea or headache, but that the latter may be decreased or even prevented by getting the patient to drink a great deal of water in the two or three hours preceeding the puncture, with the idea of assisting nature in restoring the loss of fluid.

The patient lies on his left side with his knees drawn up and his arched spine projecting over the edge of the bed.

If/



If in the sitting-posture, a low stool is required so that the patient sits with his knees well bent and leans forward to rest his elbows on his thighs.

Having located the Fourth Lumbar Spine in the way described, the Fourth Interspace can be felt as a soft spot just below it.

This area is now thoroughly scrubbed with Ether which not only removes the superficial dirt and slightly numbs the skin, but dissolves the grease and so allows the skin to freeze more readily when the Ethyl spray is turned on. The operator then cleanses his hands in the usual surgical fashion, and by palpation with his left hand determines more accurately the exact spot for puncture. This spot is then marked by indenting a cross on the skin with the finger-nail. The Iodine is now applied, and it will be found that as it dries, the cruciform mark shows up unmistakably by reason of its deeper staining and so cannot be lost. Once this spot is found and marked, the patient must not be allowed to move or the relative position of the skin and bony points will be altered.

I consider the time occupied by these preliminaries as time well-spent. For once the needle is entered in a wrong spot it is heavily handicapped in its chances of entering the Cisterna; and in his endeavours/

endeavours to persuade it to do so, the operater is liable to cause pain and much more likely to tap blood than spinal fluid.

The skin is now anaesthetised with an Ethyl Chloride spray (which will be found to work most effect:ively after it has been gently warmed.)

The needle, with its stylet "in situ", is then grasped between the thumb and index finger of the right hand, entered exactly in the middle line, and directed straight forward at right-angles to the spine.

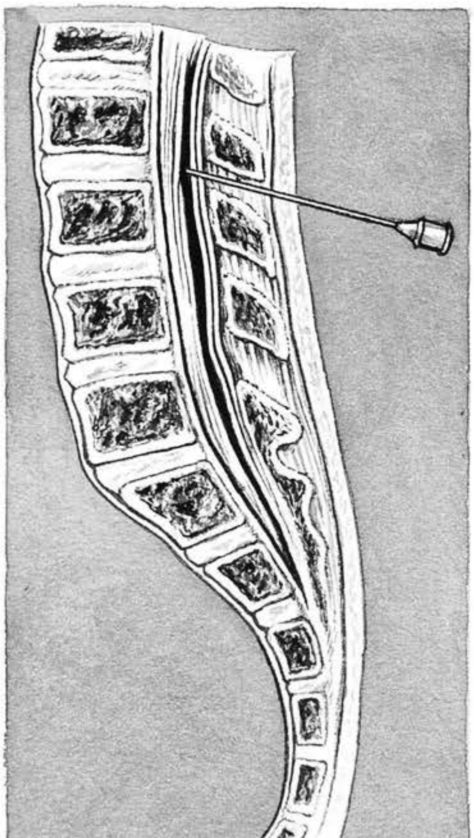
In the great majority of cases this perpendicular direction of the needle will be found the most successful.

But occasionally the needle may encounter bone; for in some 10% of cases an unciform process projects downward from the Lumbar spine and almost bridges the interspinous space. (See Fig. page 73).

If so, the needle should be withdrawn sufficiently to change its direction to obliquely upwards at an angle of 60 to 45 degrees.

In elderly persons, if flexion of the spine is difficult, the needle should be directed obliquely upwards at an angle of 60 to 45 degrees.

With regard to puncturing exactly in the middle line instead of a quarter of an inch to one side as usually advised, Lorenz states that he employed the lateral/



Structures pierced by needle.

lateral route in a large number of punctures in which "dry taps" frequently occurred; but since he has made use of the median route, failure to obtain fluid occurred in less than 2% of cases. Krönig goes so far as to say that it is only after lateral puncture that cases of nervous affliction due to injury of nerve fibres are observed.

The thickness of the Supra- and Inter-spinous ligaments and their resistance to the passage of the needle have been cited as objections to median puncture.

But the resistance of the Supraspinous Ligament is easily overcome; whilst the Interspinous Ligament, being composed of two parallel layers, is actually of assistance in holding the needle safely in the median plane and directing it into the Intervertebral space.

The structures pierced by the needle are - the Skin and Subcutaneous tissues, the Supraspinous and the Interspinous Ligaments, the Ligamenta Subflava and the Peridural Areolar Tissue, and the Dura Mater of the Cord. The distance traversed varies with the age, muscular development, and adiposity of the patient. Thus it is in

Thin subjects	from	4 to 6 cm.
Muscular "	"	6 to 8 cm.
Stout "	perhaps	10 cm.

With/

With experience it is possible to visualise the passage of the needle by the relative density of the structures through which it passes. The puncturation of the Dura may be recognised by the sense and often the sound of the needle pricking a membrane of parchment - like consistency immediately followed by a diminished resistance; and not until this sensation is felt should the stylet be withdrawn. In this way the risk of blocking of the needle or its contamination by blood "en route" is avoided.

If the skin be thoroughly frozen and the sensitive periosteum of the Vertebrae avoided, the operation will be almost painless. It is important that the passage of the needle should be painless, more especially in view of the fact that repeated examinations of spinal fluid may be necessary, not only for diagnosis but in order that the value of treatment may be correctly estimated. Otherwise, the patient on feeling pain, loses confidence. He involuntarily stiffens his back, straightens his spine in flinching away, and shifts his position; and in so doing narrows the interlaminar spaces or so diverts the needle that further attempts to reach the dural sac must be abandoned.

After such an experience the platinum needle emerges more or less bent, and instead of spinal fluid/

fluid, it is the patient's courage that oozes away.

The dural sac having been punctured, the stylet is withdrawn from the needle and a drop or two of fluid allowed to escape - this is discarded. The fluid is then collected in two portions in the test tubes provided. The contents of the second tube should be set aside for testing, as being the purer. The first portion serves to wash out the needle and is collected so that the operater can estimate the total amount of fluid removed. Five cubic centimetres is quite sufficient for Chemical, Cytological, and Serological investigations.

For the Goldsol Test 2 cc. is ample, as only .2 cc. is used for a test.

It is not advisable to remove more than 6 to 8 cc. or to lower the fluid pressure below 90 or 100 mm. of water.

The rate of escape of the fluid depends upon the pressure; but attempts to measure the pressure on the basis of drops per minute are crude and inexact. For if the patient should take a deep breath or strain in his efforts to bear pain, the fluid will spurt out in a jet. The bore of the needle, will also influence the rate of flow. If the flow is very sluggish, gently rotating the needle on its long axis sometimes improves it; but on no account should the point be moved about for fear of tapping blood and spoiling the/

the specimen. Sufficient fluid having been collected, the needle should be withdrawn rapidly, but smoothly. If there should be a little bleeding from the puncture, a moment's pressure with a swab will stay it. The spot is again touched with iodine and sealed by a small pad of wool moistened with collodion.

A fold of gauze or lint held in place by a disc of sticking plaster about the size of a crown-piece, completes the dressing.

The plaster will hold better if a few radial cuts are made round the edge.

At least twenty-four hours in bed after lumbar puncture should be the rule. There is then practically no risk to life, and greater freedom from headache and vomiting.

Few as the accidents and complications of puncture have been, they would be still fewer if the following simple precautions were observed.-

(1) The patient placed in the horizontal position.

(2) The fluid evacuated slowly.

(3) The operation stopped immediately if the patient complains of headache.

(4) The amount of fluid removed for routine examination not to exceed 5 cc.

(5) The patient kept in bed for twenty-four hours after, and longer if any symptoms appear.

Failure to obtain fluid is nearly always due to faulty/

faulty technique. In the majority of such cases the lumen of the needle is not within the dural sac, wherever else it may be.

The possibility of the plugging of the needle by tissue, clot or exudate is done away with by having the Stylet in the Needle during insertion. If no fluid appears, the needle may be rotated, or the stylet re-inserted and suddenly withdrawn for the suction effect. If this fails, another attempt in the space above may be made.

Suction by syringe should never be employed.

Lumbar Puncture is not altogether innocuous, nor to be looked upon as a trivial operation. It should be practised by those only who are acquainted with the possible risks and complications, and who have the knowledge and experience necessary to safeguard the patient.

Paralytics and Tabetics are nearly always free from subsequent ill-effects. But nervous and hysterical patients, - as well as healthy persons, often experience disagreeable symptoms for one or more days.

Excluding cases of brain tumour, in about three thousand lumbar punctures, Nonne did not observe any permanent injurious consequences. My small experience of about three hundred punctures is in agreement with this. Complaints of "slight headache" and "not/

"not feeling very well" are fairly common on the second or third day, but in only one case were the symptoms any more severe. This was a case of Dementia Praecox (No. 1.) who, though all the precautions advised were taken, began to vomit on the day after the puncture, and continued to do so intermittently for four days: but thereafter she was none the worse. Chauffard and Boidin had only three cases of vomiting in a series of 223 punctures, and no other ill-effects to speak of with the exception of slight headache.
On the other hand, Nissl met with pronounced symptoms in 48 out of a series of 112 cases - viz. headache, nausea, vomiting and even complete prostration coming on from five to twelve hours after puncture.
Of Boyd's cases, 25 out of a series of 120 suffered severely and many others to a slighter extent.

To perform the puncture in the Consulting Room - as has been done - is to court disaster.

The Complications may be divided into two groups, viz.-

(1) Those which result from damage to structures at the site of puncture - for example, Motor and Sensory disturbances in the lower extremities, pain in the back, spinal menin:gitis, etc.

(2)/

(2) Those resulting from damage to structures at a distance - that is, within the cranial cavity - causing vertigo, headache, nausea, vomiting, convulsions, and even sudden death.

Haemorrhage from puncture of an extra-dural plexus of veins is of little moment to the patient. Injury of an Arachnoid vein might conceivably have serious results, but none such are on record.

Pain at the site of puncture is trivial unless due to repeated, inexpert jabbing of the muscles, ligaments, and, especially periosteum. If the needle should prick one of the nerve-roots of the Cauda Equina, the patient will feel a sharp pain shooting down one or other leg; or a muscular spasm may be produced if the root be a motor one.

But Sensory disturbances are more frequent on account of the relative positions of the Anterior and Posterior Roots as indicated by their names and functions.

Cases are on record of subsequent paralysis not only of the Rectal and Vesical Sphincters, but of the lower extremities as well. Fortunately these are of extremely rare occurrence.

In a case of Spinal Tumour, the complications just described may be much aggravated, and paralyses are not infrequent. In all such cases the compression of/

of the Cord by the tumour is the exciting factor.

A case is on record of Suppurative Meningitis following puncture and presumably caused by it.

The Cerebral disturbances after puncture are due to vascular changes such as hyperaemia or haemorrhage; more rarely to Foraminal Hernia, i.e. the engagement of the brain-stem in the foramen magnum.
Another possible cause might be rapid hyper-secretion of the Cerebrospinal fluid causing increased intra-cranial pressure.

The more common cerebral symptoms, - headache, vomiting and vertigo, may be satisfactorily accounted for in this way. If the headache should be severe or if there be much sickness, the patient's pillows should be removed and the foot of the bed raised.
He should also be encouraged to drink plenty of fluid.

The pain may be relieved with 10 grains of Aspirin or a little Bromide. The latter also allev:iates the vomiting.

Sudden Death has occurred after lumbar puncture: some thirty-eight instances are on record, and of these, twenty-seven were cases of brain tumour.

In these fatal cases it has been noticed that the symptoms are chiefly of the Medullary type.
The train of events is probably somewhat as follows.-
The reduction of pressure in the column of fluid within the spinal canal brought about by puncture causes/

causes the descent by suction of the Tonsillae Cerebelli and their engagement in the foramen magnum, thus causing a foraminal hernia. This leads to embarrassment or paralysis of respiration by pressure on the Vital Centres in the Medulla.

In the event of impending death from such a contingency, artificial respiration must be persisted in as long as the circulation continues. An attempt may be made to replace the fluid withdrawn, or to substitute for it some sterile saline solution with the object of raising the intraspinal pressure sufficiently to reduce the hernia.

Cerebral Haemorrhage may be the cause of death in patients suffering from Aneurism or Arteriosclerosis of the Cerebral vessels, or from Uraemia. The weakened vessels, having lost the support of the cerebrospinal fluid-pressure in the perilymphatic spaces, are unable to bear the strain, and give way. The applications of lumbar puncture are twofold, namely Diagnosis and Treatment. Its value as a diagnostic measure is discussed in another section of this paper. With its use as a therapeutic agent, I am not specially concerned here.

Necessity for Lumbar Puncture.

The early involvement of the Nervous System by Syphilis is well-established, and constant evidence of this is to be found in the C.S.F. of such persons. It follows, that the possibility of diminishing the number of cases of Tabes, Cerebrospinal Lues and General Paralysis is in the hands of the physician who sees the initial lesion, and makes a routine examination of the spinal fluid.

By the time Neurological signs and symptoms have appeared, too often irreparable damage has been done.

"Cistern" Puncture in the Cadaver.

If it has not been possible to obtain a specimen of the patient's spinal fluid during life, a satisfactory sample may be procured post-mortem. Obviously, the sooner this is done the better, for absorption and reduction changes begin almost immediately.

In my experience, the Cisterna Cerebromedullaris is the best place from which to obtain fluid after death. The needle is introduced in the mid-line of the back of the neck, just above the spine of the Axis. It is directed along a plane which passes from the point of insertion, through the upper edge of the External Auditory Meatus, to the Glabella.

The average distance of insertion is 4 cm.

The Cistern is formed anteriorly by the posterior surface of the upper cervical cord and the lower part of the Medulla. Posteriorly, its Arachnoid membrane boundary lies against Dura Mater and the Occipito-Atlantoid ligament. Its depth is about 1.5 cm.

On the Cadaver this operation is easier than lumbar puncture and fluid more readily obtained at this point, especially when there is a likelihood of Meningitic adhesions having cut off the spinal from the cerebral fluid.

THE SALINE DILUENT.

The Saline Solution, which is used in making the various dilutions of the spinal fluid, is made up with doubly distilled water and contains 0.4% of Chemically pure Sodium Chloride. This particular strength is used because it has been found experimentally that by itself it causes no precipitation of the Colloidal Gold as a stronger solution would do, yet is of sufficient concentration to hold the Globulins and Nucleoproteins of the spinal fluid in solution.

Its presence is essential to the test, for pathological fluids used by themselves, or diluted with distilled water, produce no effect upon the Goldsol.

Its virtue is dependent upon its electrolytic activity.

When the salt is dissolved, the salt molecule itself is broken, so that "ions" of Sodium and of Chlorine move about in the water. Moreover, the sodium ion is found to be associated with a relatively enormous electro-positive change, and the Chlorine ion with an equal and opposite electro-negative change.

And now the saline solution has become a good conductor of electricity.

When it is remembered that the particles in a Goldsol are known to be negatively charged, the significance of the electro-positive sodium ion in the/

the mixture becomes obvious.

If there were no electrolytes, electric charges could not be carried about, and chemical reactions could not occur.

Biological phenomena are conditioned in the same way. The living body may be regarded as a framework of non-conducting material, immersed in and soaked by solutions of electrolytes.

It is the electrolytes that put life into the proteins and control metabolism just as the figure placed in front determines the value of an otherwise meaningless row of cyphers.

THE GOLDSOL.

HISTORICAL NOTE.

Colloidal Solutions of Metallic gold have been known for over two hundred years.

The "potable gold" of the Alchemists in search of the Elexir of Life was probably a Goldsol; it was a solution of gold salts in ethereal oils, which slowly reduce gold chloride with the production of gold sols.

But it was not until 1861 that the first systematic investigation of this subject was carried out by Thomas Graham, the founder of Colloidal Chemistry.

All the earliest work seems to have been confined to gold; no doubt partly on account of its Alchemistic importance, and partly because of its ready reduction.

The modern history of reduction methods begins in 1898 with Zsigmondy's re-discovery of Goldsols by the reduction of a faintly alkaline solution of Auric Chloride with Formaldehyde.

In studying dialysis Graham discovered that compounds are divisible into two main classes according as they possess or do not possess the power of passing when in solution through animal membranes or parchment paper. These two classes he called respectively "Crystalloids" and "Colloids". The former includes not only substances like salt and sugar which are/

are capable of crystallising, but compounds, such as Hydrochloric Acid, which are not known in the crystalline state.

These Crystalloids diffuse through membranes more or less rapidly and never yield Colloidal solutions by mere <u>spontaneous</u> solution in a liquid.

The other class, Colloids, is typified by gelatine and glue. These show no signs of crystallisation. They have a large molecular weight, and they pass when in quasi-solution very slowly through membranes. For example, the Crystalloid Sodium Chloride diffuses twenty-one times more rapidly than the Colloid Albumin. So that, after all, the difference between Crystalloids and Colloids is one of degree only - they are not different <u>kinds</u> of matter, but rather are different <u>states</u> of matter. As Faraday said:- "The Colloidal is in fact a dynamical state of matter, the Crystal:loidal being the statical condition. The Colloid possesses "Energia". It may be looked upon as the probable primary source of the force appearing in the phenomena of vitality."

This "Energia" we now know as "Surface Energy" of its various kinds.

"Colloid", then, is not a Chemical entity like Salt, Acid or Base, but is expressive of certain physical elements, like mechanical heterogeneity.

Sodium Chloride is a well-defined Crystalline substance,/

substance, yet a Colloidal solution of it in petroleum ether has been prepared. Even ice has been obtained in Colloidal Solution in Chloroform, so that not all Colloids are of organic origin like glue, but are obtainable even from metals which under ordinary conditions are practically insoluble in water. The word "Colloid" has thus lost some of its original significance, for the Colloidal Metals have the chief properties of Colloids but never are glue-like.
Now, the reagent used in the Goldsol Test is a Colloidal Solution of Gold, and in trying to understand its nature and mode of action, the following considerations must be borne in mind.

When a solid is brought into contact with a liquid the result depends upon the nature of both. For instance, when sugar is shaken up with water it disappears because the sugar molecules, though retaining their structure intact, have their connections with each other completely destroyed, and are uniformly dispersed through the liquid. Whereas when Salt is dissolved in water a further break-down occurs; the molecule itself is broken, and "ions" of Sodium and of Chlorine move about in the water.

Quite different from the Saccharine and Saline Solutions is the result obtained when a Colloid Substance such as Gelatine or Glue is treated with water./

water. In this case the dispersion is not molecular; the particles of gelatine or glue in it are composed of variable and rather large numbers of molecules. Such a Solution which presents an instance of very fine, but not Molecular, Subdivision is called a "Colloidal Solution" or simply a "Sol". When water is the medium of solution, the term Hydrosol is used. Thus the reagent used in this test is a hydrosol of Gold, or briefly, a "Goldsol".

Everyone is familiar with the distinction between "Solutions" and "Suspensions".

Solutions are clear; the dissolved matter does not subside and is unaffected by filtering. Suspensions, on the other hand, are turbid in aspect, and the solid can be removed by letting it settle (i.e. precipitation) or by filtration.

Colloidal Solutions occupy an intermediate position between these two.

There is thus an unbroken continuity from the coarsest-grained heterogeneity of suspensions, through the highly-dispersed state of Colloidal Solutions to the apparent homogeneity of the true solutions, and the molecular state in gases.

Now consider the effect of increasing subdivision on a suspension of finely divided Gold such as is used in the Goldsol Test. So long as the diameter of the Gold particles is much greater than/

than Mu (μ = one thousandth of a millimetre) the System will be turbid and the Gold will settle rapidly. Now it is known that the wave-length of visible light ranges between 0.4 and 0.7 μ so that if the Gold particles become much smaller than this they can no longer reflect light and the liquid loses its turbid-:ity and becomes clear. The shorter light-waves are more refracted by smaller particles than the longer, and the illumination from the particles becomes rapidly less as their size diminishes - it is a well-known theory, that the blue of the sky is due to a similar refraction of light-rays by small particles which, according to Rayleigh, may be O_2 Molecules - at the same time, with increasing subdivision of the part-:icles there will be a rapid falling off in the speed of settling. But it has been calculated that if fineness of subdivision were the only factor at work in retarding precipitation, a Gold Solution, because of the high density of its particles, would sediment at the rate of a Centimetre a month; such would be a fairly permanent solution.

But as a matter of fact Colloidal Gold Solutions have been preserved unchanged for years, and indeed do not settle at all so long as the subdivision is maintained. One of Faraday's Goldsols made in 1858 is still preserved in the Royal Institution.

Whenever/

Whenever sedimentation does occur in an unstable sol, it is preceeded by the aggregation of the part:icles into larger particles which finally attain a diameter of μ or over, and slowly subside; this change being irreversible.

There is thus an apparent contradiction between the Mathematical law (Stokes's) which calculates the rate of sedimentation as being governed by the fineness of subdivision of the particles - and the fact of the total absence of settling when the average diameter of the particles is sufficiently small.

The explanation is - Molecular Motion, or as it is sometimes called, "Brownian Movement". For under suitable conditions the Gold particles in a Sol can be seen to be in a state of great activity, jigging about in an endless dance.

It has recently been shown by Perrin that this movement is identical with that of the molecules of the containing liquid, as postulated by the Kinetic Theory. If it be assumed that the Kinetic Theory of Gases is applicable to Colloidal Solutions it follows that the Gold particles in a Sol are battered on all sides by a hail-storm of Molecular impacts from the surrounding water. If the Gold particle is very large in comparison with the molecules of water by which it is surrounded, it will be bombarded on all sides by a large number of molecules moving in all/

all possible directions, so that the blows will neutralise each other, and no movement will be per:ceptible. But as the particle becomes smaller and smaller until it is not so very much larger than the water molecules themselves, it will be hit by fewer and fewer molecules simultaneously, so that the forces acting on it will cease to be balanced, the uni-directional impacts will rapidly increase, and the particle will be driven hither and thither in a rapid sequence of zig-zag straight lines, till it begins to behave like a molecule itself and is swept along in the endless molecular movement. Thus the cause which prevents the particles in a Goldsol from settling is in no way different from the cause which prevents the Earth's atmosphere from subsiding to a snowy level a few feet deep on the surface of the planet.
Moreover, each Gold particle in a Sol ordinarily pos-esses an electric charge, which is usually negative in sign because the dispersion medium - (that is, the water) - has such a high dielectric constant that most substances suspended in it become negatively charged. The presence of this negative charge on the particles can be easily demonstrated by subjecting the Sol to Capillary Analysis by means of filter paper, or by mixing it with a known electro-positive sol, when mutual precipitation will occur.

An estimate of the charge on a single Gold particle/

particle in a Sol has been made, and is something like 2.8×10^{-2} electrostatic units. This charge can be varied and even reversed by the addition of an electro:lyte like Sodium Chloride, and may become zero at suitable concentrations.

In this condition the Sol becomes very unstable and subsidence, preceeded by the coalescence of the small particles which have thus been deprived of their charge, readily but not necessarily occurs, for the Brownian Movement may be sufficient to keep the particles in suspension.

But while the existence and stabilising influence of this electric charge is fully established, its origin and the mechanism of its action is still obscure.

If the charge is due to surface ionisation, the finer the particles, the greater will be the charge to be neutralised before precipitation can occur; and this has been found to be the case experimentally. But at any rate it may be said that the first step in the coagulation of the Sol - that is, in the precipitation of the Goldsol by the Spinal fluid of a General Paralytic - is the neutralisation of the electric charge of its particles by that of an oppositely charged electrolyte.

Further, the effect of the added fluid is produced almost exclusively on the disperse phase - i.e. the gold particles - and not on the dispersion medium/

medium (water).

It follows that a possible explanation of a positive Goldsol Reaction may be that the Spinal fluid of a General Paralytic contains an excess of Sodium Chloride or other electrolyte.

The particles in the Goldsol are known to be negatively charged; the precipitating ion is accord:ingly the positive ion (or cation) of the electro:lyte, which in the case of Common Salt would be the Sodium ion. To produce precipitation the electrolyte has to be present in a definite concentration, and the quantity depends only on the Cation.

General Properties of a Goldsol.-

It is usual to assume that the particles in a Goldsol are Solid and Spherical in shape. There are faint indications that they have the form of leaflets or little rods, but they appear in the Ultra-Micro:scope simply as brilliant, dancing points, and in reality nothing is known about their shape or colour.

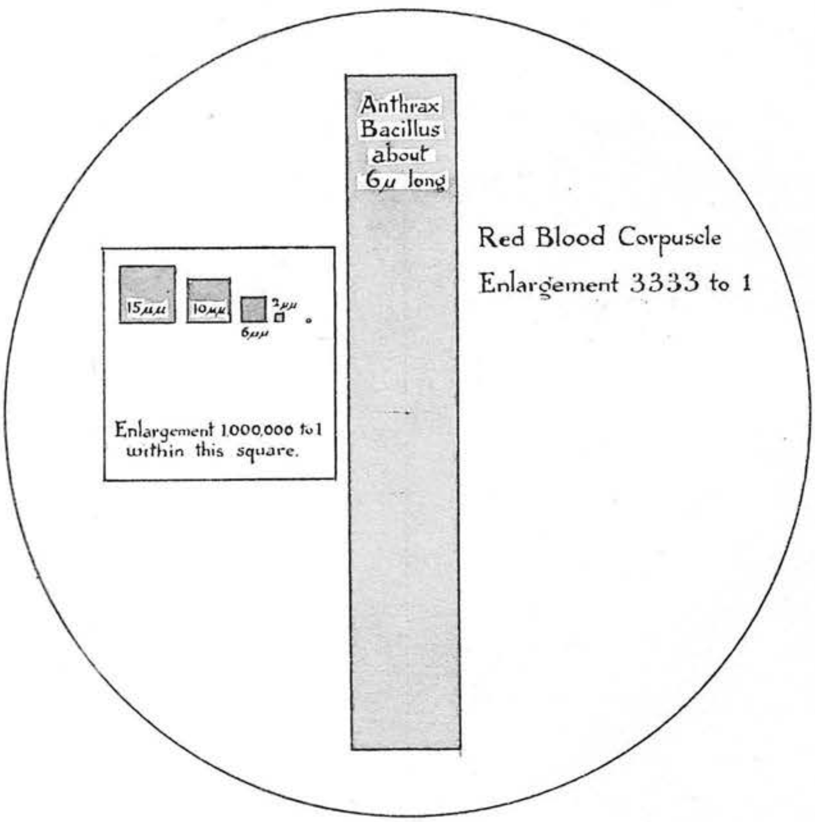
If an object is smaller than 0.4 μ, which is the smallest wave length of the visible radiations of light, ordinary Microscopic Methods of observation cease to be applicable. And since some of the particles in Colloidal Solutions are only 0.006 μ in diameter, they cannot be seen as little bodies subtending a visual angle. It is impossible to detect particles/

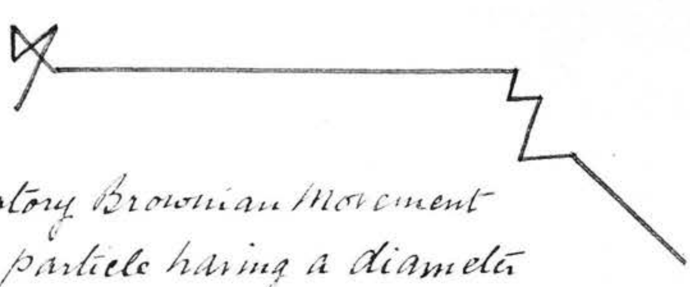
particles in a highly disperse Goldsol even with the highest Microscopic Magnification (X 2250).

But the Ultra-Microscope, employing a very intense reflected light makes the particles visible merely as glittering points on a black background. The size of the particles inspected in this way cannot be observed directly, but only inferred from a knowledge of the amount of Gold contained in a known bulk of the Sol, and the number of particles which can be counted in a given space. Nor can the colour of the particles be ascertained.

Now, if the Goldsol be examined with the Ultra-microscope it will be seen that the tiny gold particles do not float; they move, and with astonishing rapidity. The activity of a swarm of gnats dancing in a sunbeam will convey some idea of the restlessness of these lively particles. They have a continuous irregular motion in every direction through the liquid along a series of Zig-Zag straight lines. (See Diagram) p.105 This movement is able, in some cases, to overcome the influence of gravity, so that the particles become uniformly distributed through the liquid. The amplitude of the movement depends in the first instance on the size of the particles, and is inversely proportional to it. The Velocity of the particles is conditioned in the same way and has been calculated to be 100 μ per second. In fact, with/

The small, dark squares represent the relative size of the gold particles in a Sol.





The translatory Brownian Movement of a Gold particle having a diameter of about $10\mu\mu$ (enlarged 5000 times) (After Zsigmondy) with particles of very small dimensions the movements may become so violent as to assume, from all appearances, an entirely different character.

This motion gives an indication of the continuous mixing-up of the Sol which goes on hours, weeks, months and even years, if the Sol is sufficiently stable. So that Graham's statement, made in 1849 with the unconsciousness of the predestined, that the Colloidal is in fact a dynamical state of matter, is now shown to be well-founded. And yet a few drops of paretic spinal fluid, diluted to the extent of 1 in 320, strikes down these dancing particles into an inert mass of sediment. And this is what constitutes a "positive" Goldsol test.

The smallest particles which can be seen in a Goldsol show a combined movement consisting in a motion of translation by which the particle moves from 100 to 1000 times its own diameter in $\frac{1}{6}$ to $\frac{1}{8}$ of a second, and a motion of oscillation of a considerably shorter period.

Size of Particles.

The size of the particles has been calculated, but is not even approximately constant; it ranges from 0.1 μ down to about 1 $\mu\mu$ (i.e. one millionth of a millimetre) according to the method of preparation of the Sol. Thus, a Goldsol prepared with phosphorus as/

as the reducing agent gives a Sol of the highest dispersity; the size of the particles is about 1.2 to 1.5 $\mu\mu$ in diameter, and is exceedingly uniform. Even at this point the particles begin to approach in smallness the limits which have been assigned from other considerations for the diameter of molecules.

But Molecular dimensions, like Astronomical distances, correspond to nothing within human experi:ence, and are therefore unrealisable though mathematically expressable.

However, the size and form of the particles appear to have some influence on the colour of the Goldsol and its behaviour in the test. The colour of a Goldsol in transmitted light may be red, violet or blue, and occasionally yellowish-brown or brown.

According to Zsigmondy the ultramicrons of red solutions are green; those of blue solutions are yellow to reddish-brown; violet solutions contain both.

We have to deal, therefore, with green, yellow or brown ultramicrons. Both green and brown Ultramicrons may have all possible dimensions from the Amicroscopic to 120 $\mu\mu$ and over. As a general rule, however, the large particles are yellow or brown, while the very fine subdivisions are green. According to Mie's theory, particles of gold having a diameter of 40 $\mu\mu$ or under must be green.

It would seem that small brown particles are

in/

in reality conglomerates of the green; and that green ultramicrons are composed of Compact Gold, and are the result of the normal growth of Amicroscopic particles; or better, perhaps, they are tiny crystals. Analysis has shown that Rose-coloured Goldsols contain particles of an average size of 6 $\mu\mu$; bright red Sols of 15 $\mu\mu$; Violet-red Sols of 23 $\mu\mu$; and purple-red sols of 38 $\mu\mu$. That is, the more blue the colour the larger the particles. But Goldsols have been prepared in which the size of the particles could not be determined; they must therefore have been smaller than 6 $\mu\mu$.

As regards its strength; a Goldsol is very dilute because its "Saturation Concentration" or maximum ratio between dispersion medium and disperse phase lies between 0.1 and 0.2 per cent; i.e. the strength of the Gold in the Sol is from 1 in 1,000 to 1 in 500. The reason for this is, that when a Sol is formed, electrolytes are also formed and the concentration of these must be kept below a certain limit, or the Sol will precipitate. Hence it is that short of dialysis for the purpose of removing electrolytes, the most concentrated Goldsol that can be made contains only from 5 to 7.5 mgms. of gold per 100 cc.

But the chief characteristic of the Goldsol is that on the addition of varying, but always small, quant-:ities of an electrolyte - such as salt - it undergoes a/

a marked and irreversible change, the Gold being precipitated. It is on this property that the Goldsol Test is based.

The Gold particles in a Sol have a strong tendency to unite with one another; so that the preparation of the Sol may be looked upon as an interrupted condensation process.

But the precipitation may be delayed or even prevented by the protective effect of mixing the Sol with one of the more stable Colloids such as Albumen.

Instances of this curious "protection" are common; for example ink often contains a Colloid which protects the pigment and prevents it from settling.

The quantity of Colloid just necessary to protect 10 cc. of 0.0053 - 0.0058 Goldsol from precipitation by 1 cc. of a 10% solution of Sodium Chloride is called the "Gold Number" or "Gold Value" of that Colloid, and may be used as a basis of differentiation. Thus the Gold Number, or relative protecting power of egg-albumen is 0.25 as compared with 25 for potato-starch.

The question here arises, whether the normal spinal fluid contains some protective colloid which is absent from the fluid of a general paralytic.

If a strong beam of light be projected through the Goldsol, the Sol will appear turbid with a green-:ish/

greenish sheen. This is an optical property known as the Tyndall Effect and is due to the fact that the particles of the Gold reflecting the light are small as compared with the wave-lengths of light. This light is found to be polarised, thus distinguishing it from true fluorescence as seen in a solution of Quinine Sulphate which does not polarise light.
The Goldsol can be passed through filter paper without appreciable change, but Ultra-filtration through a Purkall Cell will hold up some of the particles. Animal Charcoal will separate out the Gold; this must be due to some specific attraction between the Gold and the Charcoal, and not an electrical reaction because both are negatively charged.

Faraday's Goldsol coagulates at the Boiling Point, but not Zsigmondy's.

The Absorption Spectrum of a red goldsol corres- :ponds well with that of ruby glass (which is glass containing Colloidal Gold) the maximum absorption lying near the spectral line E .

Under Kataphoresis the Gold particles, as would be expected from their electrical charge, are attracted towards the Anode.

But the most important characteristic of a Goldsol from the point of view of the Goldsol Test is its extraordinary sensitiveness to very small amounts/

amounts of chemical reagents. The degree of sensitiveness varies very greatly and depends on the method of preparation of the Sol and especially upon the nature of other substances formed in the reaction simultaneously with the Sol.

The changes brought about by these reagents, cause precipitation of the Sol, and may be directly observed. For if an "Amicron" Goldsol be examined under the Ultra-microscope, nothing will be seen as the gold particles are too small to reflect light. But if a very small quantity of Sodium Chloride is added to the Sol, the first effect is the production of "Submicrons" of Gold, i.e. slightly larger particles and these are seen as individual discs of light in active Brownian Movement. On further addition of electrolyte (Salt) the particles decrease in number, but increase in size by uniting with one another to form "Microns". Along with this the Brownian Movement becomes sluggish and, as the Micron stage passes into the Macron stage, diminishes to complete cessation: sedimentation then occurs.

The effect of the Salt is first of all to diminish the electropotential difference between the Gold and the Water; this causes the particles to unite, and the Brownian Movement becomes slower in consequence of their larger size. Complete precipitation only occurs/

occurs when the potential difference has been brought sufficiently near zero. That is, a definite concen-:tration of electrolyte is necessary; smaller or larger concentrations may produce only partial precipitation, or even none at all. The bearing of this fact upon the so-called "Syphilitic" reaction will appear later when considering the occurrence of what is called "Mutual precipitation within limits" Ostwald shows in his Handbook a photograph of a Goldsol that has undergone this condensation process.

Another peculiarity of the Goldsol is that the manner of adding the reagent has a marked effect on precipitation. When the reagent is added slowly or a little at a time, a much larger amount is necessary for complete precipitation; the Sol appears to become "Acclimatised" or tolerant because the particles have all been equally affected by the electrical charges; whereas precipitation is due to inequality and irreg-:ular distribution of electric changes.

This explains the necessity of immediately and thoroughly mixing the Goldsol with the diluted Spinal fluid when performing the Goldsol test.

It has been established, then, that precipitation is a consequence of removing a definite electric charge from the Gold particles by means of ions of opposite charge, and these ions are carried down with the/

the precipitate in electrically equivalent amounts. There is thus a balance between two opposing influences; a suspending or stabilising effect due to the ion of the same sign as the Sol, and a labilising or precipi:tating effect due to the ion of opposite sign.

But the stability of a Goldsol may be dependent upon the presence in the Sol of small quantities of other substances, usually substances related to, or derived from, the Colloid itself. Thus the Sol formed by the reduction of Auric Chloride contains Chlorine, for after precipitation, Chlorine is found in the liquid.

This explains the necessity for Chemical clean:liness of the vessels and the utmost purity of the water used in preparing the Goldsol.

Highly disperse Goldsols are very sensitive to electrolytes, but the sensitiveness does not seem to depend entirely on the minuteness of the particles. For as Zsigmondy points out, Goldsols which have been protected by the addition of a small amount of albumen are rendered very stable thereby; yet in them the particles must have increased their size and mass by adsorbing the albumen and therefore approximating to a suspensoid. This ought to render them more easily precipitable instead of less so.

In seeking for a possible explanation of the Goldsol Test, the only hypothesis in accordance with the/

the known facts would seem to be, that in a positive reaction if the Gold Ultramicrons come sufficiently close together, the attraction of the particles for one another is great enough to cause an irreversible union. And this is what actually occurs during Ultra-filtration or Centrifugalisation.

All influences, therefore, that render it easier for the particles to come within this "Critical Distance" (at which they will unite) tend to make the Sol more precipitable.

For example -

1. The average distance of the particles from one another. The stability of a Goldsol is increased by dilution and decreased by evaporation.

2. The electric charge on the particles. In all cases when the particles are discharged of their electri-:city, precipitation occurs, This is chiefly caused by electrolytes, but may also be brought about by X-rays, ultra-violet rays, certain dye-stuffs such as Fuchsin, Bismark Brown, etc., and by a number of fine crystalline precipitates such as Calcium Carbonate and Barium Sulphate.

3. The viscosity of the medium - which in the case of the Test is diminished by the addition of the Saline diluent.

4. The union of the metal ultra-microns with pro-
:tective colloids.

An allied phenomenon is the mutual precipitation of Sols without the addition of any electrolyte. It has been found that a positive Sol will precipitate a negative sol, while Sols of the same electric sign will not do so. The precipitate contains both Colloids. Thus, if a constant amount of a negative Sol is added to a varying amount of a positive Sol it is found that very small amounts cause no visible change, more causes partial or complete precipitation, larger amounts give less precipitate, and at last no pre-:cipitate forms. The region of complete precipitation is fairly narrow, while with large excess of either Sol no precipitation occurs at all. Now this experi-ment is closely analagous to what is done in perform-:ing the Goldsol test when 5 cc. of a negative Sol (the Goldsol) is added to varying dilutions of Spinal fluid. The experiment obviously shows that there is an amount of one Sol which is equivalent to a given amount of the other. But it is not a Chemical equiv-:alence, nor is the precipitate, which must contain both colloids in practically constant proportions, to be regarded as a Chemical Compound in spite of its constant composition. In these Colloidal reactions the physical (i.e. electrical) and chemical changes are two aspects of one and the same phenomenon; they are/

are never in opposition, nor mutually exclusive.

The equivalence, then, is electrical, the maximum precipitation occurring when the positive charge on the one Sol exactly equals and neutralises the negative charge on the other. This is in agreement with what has already been described regarding the precipitation of Sols by electrolytes, and the maximum of instability at the isoelectric point. The optimum precipitation may not correspond exactly to electrical equivalence for the number of particles required and their size (i.e. the electric charge and the dispersity) as well as the relative concentrations of the two Sols, must affect the precipitate, as also does the rate at which they are mixed. In accordance with this, the compos-:ition of the precipitate is not quite constant. It always contains both Colloids, but so does the remain-:ing Sol, unless complete precipitation has occurred. This distinguishes it from an ordinary Chemical re-:action.

The essential feature, then, of the mutual pre-:cipitation caused by the action of a negative Sol on a positive Sol is that excess of either Sol protects, while precipitation only occurs in a middle zone which is usually narrow.

This I believe to be the explanation of the slight reaction given by most negative spinal fluids to/

to the Goldsol test and an exaggeration of which con-
:stitutes the so-called "Syphilitic" Reaction.

At first sight it would seem anomalous that a stronger reaction should be obtained in the middle tubes of a series of dilutions since these tubes con-
:tain less spinal fluid than the first few tubes; the first tube, for example, is a dilution of 1 in 10, whilst the fifth is a dilution of 1 in 160.

But if the mixture of the spinal fluid and the Goldsol be looked upon as a mixing of a positive and a negative Sol, then the explanation surely must be that "excess of either Sol protects, while precip-
:itation only occurs in a middle zone which is usually narrow."

This precipitation occurs only within certain fixed limits, because the electric charges on the particles must be completely neutralised before the maximum precipitation can be obtained. If one or other of the two Colloids is present in large excess, the oppositely charged particles will unite, but only those unions which are exactly neutral will be precipitated; that is, only partial precipitation occurs. Further, many ultra-microns will not be neutralised because the substance in the smaller quantity is completely adsorbed by the one present in excess, and the aggregates thus formed will have the/

the same charge as the colloid present in the larger amount. Thus, at the beginning of the series of tubes where the C.S.F. is in relative excess, and at the end of the series where the Goldsol is in rel-:ative excess, protection has occurred so that pre-cipitation is prevented. Whereas, at the intermediate concentrations in the middle zone of the series, where there is no marked excess of either constituent, slight mutual precipitation occurs; on either side of it are stable sols, but of opposite electric charge.

This inhibition of precipitation closely re-:sembles the phenomenon observed in the "Precipitin Reaction" where an excess of the antigenic protein will prevent precipitation.

Agglutination is a similar process, for agglutinins carry positive electric charges whilst bacteria are negative.

These two reactions have in common with the precipitation of Colloid Solution the fact that pre-:cipitation is accompanied by and dependent upon an aggregation of their particles as a result of electro-:lytic action. The only difference is that they are specific reactions.

Other instances of such complex mixtures of interacting Colloids occur in the coagulation of blood, and the varied phenomena of haemolysins, immunity/

immunity and anaphylaxis, not to mention the Wasser-
:mann Reaction.

Zunz has pointed out that the electric charge on the particles cannot be the only factor involved. For if so, Goldsols and Mastic sols should react in the same manner as they are both negative. Whereas the fact is, that hetero-albumoses precipitate mastic turbidities but have a protective action on Goldsols.

The action must be attributed to some specific properties that have not yet been clearly explained.

The complexity of the problem now becomes mani-
:fest. In delving into it one finds that the deeper one excavates, the greater is the surface to work at, and the larger the hole one finds oneself in.

The display of colours in the Goldsol Reaction is a characteristic property of all pure, red-goldsol.

This change to blue is caused by the union of two or more particles that diffract green. The com-
:plex thus formed diffracts only brown light-waves.

According to Zsigmondy it is impossible to ex-
:plain this colour change on the ground of an increase in size alone, because it occurs regardless of whether anicrons or submicrons units. In the first of these cases, the complex may still remain Amicroscopic and have a mass several hundred times smaller than that of a large red particle, yet these tiny particles diffract/

diffract brown and the liquid appears blue.

It seems necessary to assume that the particles unite to form a somewhat loose, flocculent mass, and do not melt into one another as drops of liquid do. For if the latter were the case the colour would be the same for all particles of the same substance having like dimensions. But actually there is no relation between size and colour unless the growth has been normal.

In trying to prepare a red Goldsol, it sometimes happens that when the process is complete, the Sol has a very strong blue tinge. This blue colour may be attributed to three possible causes. Namely:-

1. The reduction of the Gold may be incomplete and Colloidal Gold-oxide formed instead of Colloidal Gold. Further reduction, perhaps at higher temperatures, might cause the blue to change to red.

2. The reduction may be complete and the blue colour attributable to the flocculent union of small particles as just described; or perhaps to irreg-:ular growth so that instead of flakes or needles, perhaps husk-shaped, submicroscopic bodies are formed.

3. The liquid may contain large massive gold particles which, according to Mie's Theory, would account for the blue colour.

(2) HYPOTHESES CONCERNING THE NATURE OF THE REACTION.

It may be stated at the outset, that the Mechanism of the Goldsol test is not yet fully understood, and is probably of a very complex nature.

Some of the factors influencing precipitation are known, and have already been described. But the nature of the substance which initiates the sequence of changes in the Goldsol resulting in complete sedimentation is not known.

Lange suggested that the reaction might be due to certain qualitative changes in the fluid's porteins rather than to their quantitative increase. And this is supported by the fact that some fluids which give a typical "paretic" gold curve, show no excess of globulin by the Ross-Jones test; four instances of this occur in my series; viz: Nos. 28, 68, 76, and 78 in Group 10. Conversely, a fluid giving a positive Ross-Jones reaction may be negative with the Goldsol test; illustrations of this also occur among my cases, viz: Nos. B + C in Group 12; No.12 in Group 7; and No.10 in Group 4.
Further, Globulin collected from large amounts of negative fluids and concentrated in saline solution causes/

causes little or no precipitation of gold.

This disposes of Felton's plausible suggestion that the reaction is caused by a change in the relative proportions of the albumin and globulin fractions; that is, a change of ratio implying a quantitative increase of globulin without any quali-:tative change in its nature.

And yet, the various types of Goldsol reaction can be reproduced artificially by using suitable mixtures of globulin and albumin, the former causing precipitation and the latter conferring protection.

Zaloziecki regards the test as a form of immunity reaction; it is probable that all the serum reactions are colloidal phenomena.

Jaeger and Goldstein think it may be a physical effect of an electric nature.

Eskuchen holds that a pathological increase of albumin is the cause; this is difficult to accept in view of its known protective power.

McDonagh's hypothesis is that there is an in-:crease of electrolytes in luetic spinal fluid, and that these are adsorbed by the lipoid protein part-:icles, these combined electrolytes being the active bodies. He thus brings it into line with his view of the Wassermann test which he regards as a purely physical reaction. But the fact is, that the chief electrolyte/

electrolyte in the spinal fluid is Sodium Chloride, and I have not been able to find any record that its per:centage is increased in paretic fluids.

Weston's experiments seemed to have established the following facts; namely, (a) that the gold precipitating substance is not present in normal fluid; (b) that it is dialysable through thimbles impermeable to albumin, and that another substance, resembling globulin in that it is precipitated by a saturated solution of Ammonium Sulphate, is also thus dialysable; whereas the Wassermann reacting substance is not dialysable and therefore cannot be the cause of the gold precipitation; (c) that it is destroyed by heat and therefore is not peptone; (d) that the Salts and the Copper-reducing substance of the spinal fluid are not responsible.

Recent experiments by Cruickshank have contra:dicted some of these findings. Using a Celloidin Capsule, he subjected paretic fluids to dialysis for so long as seventy-two hours without finding any trace of Gold reducing substance in the dialysate, whereas the fluid within the thimble retained its activity almost unimpaired. Weston probably used a parchment dialyser and the fact of his recording that another substance, resembling globulin in its response to Ammonium/

Ammonium Sulphate, was also dialysable, gives rise to the suspicion that the thimbles he used were permeable to globulin; this would vitiate the experi:ment.

The significance of this result is that the Gold-reducing substance is present in Colloidal form. Now, it is known that the Wassermann-reacting substance resides in the globulin fraction of the protein of the paretic spinal fluid; that is, in Colloidal form. To investigate this similarity, Cruickshank precipi:tated the globulin from paretic fluids, washed it free from albumin, and found that it was very active in reducing gold and in giving a positive Wassermann reaction.

The same experiment performed with the globulin from negative spinal fluids gave no Gold reduction and no Wassermann reaction. Further, when paretic spinal fluids which gave anomalous reactions with the Gold test were examined in the same way, the Globulin when isolated gave typical paretic reactions, and it became evident that it was the presence of albumin that was interfering with the reduction; in fact, acting as a protective colloid. For Cruickshank was not only able to convert a positive paretic fluid into a negative one, but could make it react in any zone at will by the addition of suitable proportions of human/

human serum-albumin.

This shows the danger of regarding a so-called "Luetic" zone reaction as diagnostic of Neuro-Syphilis, especially when one bears in mind the difficulty, almost impossibility, of excluding traces of blood-contamination during lumbar puncture. Experimentally, $\frac{1}{2}$ cc. of a 1 in 300,000 dilution of fresh human serum, normal and not syphilitic, will cause this "luetic" reaction when added to a normal fluid.

This argument does not apply to paretic fluids, for curiously enough, considerable amounts of blood do not mask the paretic reaction. This strongly supports the hypothesis that the Gold reduction is due to some qualitative change in the globulin of the paretic fluid and not merely to an alteration in quantitative proportions.

Further than this, my earlier suggestion that the luetic reaction is merely an exaggeration of the "normal" reaction and that it is in fact an example of a colloidal phenomenon known as "Mutual precipita-:tion within limits", gains added support.

The explanation offered by Cruickshank that the "Meningeal" reaction is due to contamination of the spinal fluid with blood-serum caused by leakage of plasma through Meninges damaged by inflammatory change,/

changes, seems reasonable enough; and it is supported by the fact that this type occurs in a variety of diseases dependent on Meningeal irritation.

It seems hardly possible that the factors so far discussed do not exert a considerable influence on the reaction, but there are other features that require explanation. If Albumin is the protecting agent, how is it that when a spinal fluid is deprived of its albumin by boiling and subsequent filtration, the protective effect of the fluid is not lessened and may even be increased?

The explanation I offer is purely hypothetical, but, right or wrong, it is of value so long as it tends to further investigation.

It seems to me that there is some change in the electrolytic constitution of a paretic fluid. On this assumption the problem just stated can be ex:plained by saying that the fluid after removal of albumin gains in protecting power because the pre:cipitating electrolytes have been removed along with the albumin to which they were adsorbed in a colloidal union.

Cruickshank seeks to exclude electrolytes as the cause on the grounds (a) that they are present in such small amounts, and (b) that they would need to be attached/

attached to the globulin fraction in such a way as not to be freed by dialysis.

The first objection is met by the established fact that it requires only minute traces of electro:lytes to bring about colloidal phenomena.

As regards the second, it is no more unreasonable to assume that the electrolytes are adsorbed by the proteins in an undialysable combination, than it is to assume that the Gold-reducing substance resides in the globulin fraction because it does not dialyse out.

Now, it has been shown by Bayliss that if the suspensoid particles of a colloidal protein are given a positive or a negative charge by traces of acid or alkali, the precipitating effect of electrolytes comes into play, and the Anion or Cation respectively becomes prepotent according to Hardy's Rule.

Further, the Salts of proteins are electrolytically dissociated in solution; the sodium salt of globulin, for example, partially dissolves into sodium and a large organic ion which has the properties of the colloidal state. The hydrochloride dissociates into Chlorine and a large, colloidal, organic cation.

Thus by direct chemical means we can obtain the same protein with a negative or a positive charge; and these colloidal ions are very ready to form aggregates. It follows, that in an acid spinal fluid,/

fluid, the particles forming the internal phase - that is, the protein particles - will have a positive charge; and the converse holds true for an alkaline fluid.

This can be proved experimentally; for the addition of small amounts of acid to paretic fluids increases the zone of precipitation, while the addition of alkali diminishes it. It has already been noted that Acid Goldsols precipitate with negative fluids, and that Alkaline Sols are inert with positive fluids. This is simply another aspect of the same phenomenon.

At this point it becomes obvious why it is necessary to make a Goldsol neutral for diagnostic purposes.

In preparing the Sol, the reduction of the Gold Chloride by the formaldehyde is accompanied by the liberation of free acid; if this is insufficiently neutralised by shortage of potassium carbonate in the Alkaline Solution, or rendered too alkaline by excess of carbonate, the corresponding type of Sol will result in each case.

From all this there emerges the conclusion that in performing the Goldsol Test, we are mixing a negatively charged colloidal solution (the Goldsol) with a positively charged colloidal solution (the paretic spinal fluid) in the presence of electrolytes (the/

(the Saline Diluent) and obtaining a precipitate; and further, that this result can be reversed by altering the Chemical reaction of either colloidal solution.

It seems to me, therefore, that the change which has occurred in the paretic fluid is that it has acquired an Acid reaction and thereby developed a positive electric charge on the globulin particles.

In other words, I venture the opinion that the Goldsol Test is nothing more or less than a rough but easy method of demonstrating changes in the Hydrogen - ion concentration of the spinal fluid.

Levinson has shown that such changes do occur in the Meningitides, but the biological phenomena initiating them are yet to seek.

SUMMARY AND CONCLUSIONS.

(1) Of other workers.

In reviewing the work of other investigators it becomes evident that the advantages claimed for the test fall into two groups. Viz:- those merits upon which most are agreed; and those upon which there is conflict of opinion. Taking the latter group first, there appears to be doubt whether the Gold test is more sensitive than the Ross-Jones or Wassermann reactions; whether it is more reliable; whether it is able to differentiate between General Paralysis and Cerebrospinal Syphilis; whether the "luetic" and "Meningitic" curves are of any diagnostic value; whether the test is of use in Congenital Syphilis, and whether it is the first of the three to appear in Neurosyphilis and, accordingly, the best for early diagnosis; whether the reactions in Tabes Dorsalis and in Multiple Sclerosis are characteristic; and whether it is of any value in judging the efficacy of treatment. Allthese have been affirmed and denied. Extravagant claims can ony discredit the test. The fact is, that no single reaction is infallible or pathognomonic.

A diagnosis cannot by centrifuged, precipitated, or extracted from a spinal fluid, but on weighing the evidence for and against, it would appear to be established—

1. That the most marked reactions and typical curves are obtained only in cases of General Paralysis, Tabo-Paresis and Juvenile Paresis.

2. That normal fluids give Negative reactions.
3. That the test is helpful in the diagnosis of Acute Poliomyelitis.
4. That it might prove to be of much more value in the diagnosis of Congenital Syphilis than any other tests hitherto employed.
5. That it is more sensitive (and accordingly appears earlier) than the other tests.
6. That it is the most valuable of all confirmatory evidence.

Cause of conflicting results-

Apart from the use of unsuitable Goldsols and errors in technique, the lack of any standard of "positiveness" is obvious to anyone studying the numerical readings as being the cause of the contradictory findings. There is no difficulty with the clear-cut Paretic curve; but many workers record changes of "1" and "2" degree, when occurring in the second and third zones, as positive; whilst others regard such fluids as Negative. This must inevitably lead to confusion, and even with correct reading ,fallacy of interpretation may occur through forgetfulness of the Serological Rule that whilst a positive reaction is not found in a normal fluid, a negative result may be obtained in Neurosyphilis.

(2) Personal experience-

With care and attention to details of technique, there is no real difficulty in preparing a good

Goldsol; the key note to success is purity.

Of 135 cases of non-luetic Psychosis, not a single one gave a positive Goldsol reaction; of 84 cases of General Paralysis, 80 showed a positive curve, 3 were negative, and 1 doubtful.

Of 5 cases of Cerebrospinal Syphilis, all showed an abnormal reaction to the test.

There is some evidence in support of the claim that the test is of value in the early diagnosis of Neurosyphilis.

The "Paretic" Curve is of real diagnostic value. The so-called "Syphilitic" Curve is not characteristic. Goldsol readings of the type 1111000000 and 1122000000 are so frequently obtained with spinal fluids otherwise normal, that they cannot be regarded as having any pathological significance-especially in the absence of any clinical evidence of Syphilis.

The Goldsol test is more sensitive than the Wassermann reaction, and quite as reliable.

Its simplicity minimises chances of error, and its performance occupies but a few minutes.

It uses only two or three drops of Spinal fluid.

Its nature is in doubt, but from experimental evidence the inference is drawn that the reaction is merely a test of the Hydrogen-ion Concentration of the Spinal fluid.

Further testing of the Goldsol reaction in General Hospitals is called for if the test is to be established as a diagnostic method; but any expectation of obtaining an infallible and characteristic laboratory process is unreasonable.

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