THE VALUE OF ROUTINE EXAMINATION OF THE CEREBROSPINAL FLUID: REPORT ON THE EXAMINATION OF 3,200 FLUIDS.*

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THE examination of the cerebrospinal fluid is such a valuable aid to the diagnosis of nervous and mental diseases that it naturally forms a prominent feature of the work done in the laboratory of any mental hospital. A complete examination of the fluid is made in practically every case admitted to this hospital, and I have in this article analysed the results of examination of 3,200 fluids carried out in our laboratory during the last ten years.

In 2,400 normal specimens the fluid was clear and colourless, and there was no coagulum. The reaction was alkaline.

The protein content ranged between $\cdot 02$ and $\cdot 035$ per cent.: that of the chlorides between $\cdot 72$ and $\cdot 75$ per cent., the average being $\cdot 74$ per cent. Fremont-Smith and Dailey¹ also regard the normal chloride content as from $\cdot 72$ to $\cdot 75$ per cent. The average cell-count was $\cdot 4$ cells per c.mm., and ranged between 0 and 2.6 cells per c.mm., the cells consisting of large and small lymphocytes. The sugar content ranged between $\cdot 062$ and $\cdot 089$ per cent., the average being $\cdot 077$ per cent.

Lange's gold sol test was constantly negative, as were also the colloidal gamboge test, the Wassermann reaction, and the Meinicke reaction.

I found no polymorphonuclear leucocytes in normal fluids, and this coincides with the results obtained by most recent workers. Fontecilla and Sepulveda², however, consider that normally cerebrospinal fluid contains 5 per cent. of polymorphonuclear leucocytes. Leredde, Rubinstein and Dronet³ consider the number of cells in the normal fluid to range between $\cdot 5$ and 1 per c.mm., and Levinson's⁴ figures are 4 to 6 per c.mm., all the cells being small lymphocytes. Greenfield⁵ gives $\cdot 3$ cells per c.mm. as the normal finding.

Stowe⁶, in an analysis of 556 normal fluids, found the average sugar content to be about $\cdot 075$ per cent. Greenfield⁵ gives the normal range as $\cdot 050$ to $\cdot 075$ per cent., while Levinson's⁴ figures are $\cdot 064$ to $\cdot 09$ per cent. Alpers, Campbell and Prentiss⁷ give the normal range as $\cdot 053$ to $\cdot 084$ per cent.

In dementia præcox, mania, melancholia, secondary dementia, acute confusional insanity, senile dementia and epilepsy, the fluid was found to be normal. Lochelongue⁸ reported the fluid to be normal in epilepsy.

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GENERAL PARALYSIS OF THE INSANE.—In 555 fluids examined before the commencement of treatment the following results were obtained.

The fluids were clear and invariably under tension. The protein content was constantly raised, and ranged between .04 and .06 per cent. The average sugar content was .067 per cent., and ranged between .055 and .116 per cent. The chloride content ranged between .72 and .75 per cent.

A normal cell-count was found in 2.7 per cent. of cases, and the remainder showed a pleocytosis of varying degrees; in 66.6 per cent. it was between 2.7 and 50 cells per c.mm.; in 14 per cent. between 51 and 100 cells per c.mm.; in 14 per cent. between 101 and 200 cells per c.mm., and 2.7 per cent. gave a count over 200.

Small lymphocytes were the predominating cells; and the remainder consisted of large lymphocytes, 10 to 25 per cent.; 2 to 3 per cent. of polymorphonuclear leucocytes, and usually 2 to 5 per cent. of plasma-cells.

The Wassermann reaction of the fluid was positive in every case, and in only one case was the Wassermann reaction of the blood negative.

The Meinicke reaction was also positive in every case.

With Lange's gold sol test 95 per cent. of cases gave a so-called 'paretic' response such as 5554321000, 5554432110, or 4443211000. A better term than 'paretic' response or curve, for reasons which will be advanced later, is a 'zone 1' curve. The remaining cases gave a 'luetic' or 'zone 2' curve, such as 0014320000 and 1354321000.

The colloidal gamboge reaction showed a complete precipitation in the first three or more tubes in 95 per cent. of cases, typical readings being 222220 and 222210. A 'zone 2' curve, 111000, was present in 5 per cent. of cases.

The Braun Husler test was positive in 100 per cent.

JUVENILE GENERAL PARESIS.—The results coincided with those obtained in the acquired type.

The above results all refer to fluids withdrawn before the commencement of treatment by malaria or tryparsamide. Examination of the fluid following treatment by malaria, 235 cases of general paralysis having been so treated by us, revealed an improvement in all but three cases, but in no case was there a complete return to normal. The most common change was a decrease in the cell-count—this occurred in 90 per cent. of cases.

Protein content was lower than before treatment in 50 per cent.

The Wassermann reaction was found to be negative in 15 per cent. after treatment, while another 15 per cent. showed a diminution in the intensity of the reaction.

The colloidal gold curve showed an improvement in 30 per cent. of cases, and in 7.5 per cent. a 'zone 1' curve was changed to a 'zone 2' curve.

In 7 per cent. there was a combined improvement in protein, cell-count, Wassermann reaction and colloidal gold curve.

Excluding the gold sol, there was a combined improvement as regards protein, cell-count, and Wassermann reaction in 15 per cent.

The serological improvement or otherwise was found to bear no constant relation to the mental state of the patients. Some of the patients who showed very little serological improvement have been discharged recovered, while some cases with marked serological changes have exhibited little or no mental improvement.

TABES DORSALIS.—The fluid was clear and under tension and the cell-count was much the same as in general paralysis, as was also the type of cell present, but plasma-cells were rarely found. Protein was also increased in this disease. The average sugar content was .07 per cent., while the chlorides were normal.

In 90 per cent. of the cases the colloidal gold test gave readings such as 0244310000, 0022100000, and 0012211000—typical luetic curves—no change occurring in the first one or two tubes and the maximum colour reaction in the fourth or fifth. Ten per cent. gave readings of 5555421000—typical paretic curves.

The colloidal gamboge test in 90 per cent. of cases gave readings of 111000.

The Wassermann reaction was positive in 85 per cent. of cases.

In one case the only abnormality in the fluid was a slight pleocytosis, while in another a positive Wassermann reaction represented the only change.

CEREBROSPINAL SYPHILIS.—The fluid was clear and under tension. The cell-count was mostly between 10 and 50 cells per c.mm., and consisted mainly of lymphocytes. Plasma-cells were never found in this disease. The protein content was increased to much the same extent as in tabes. The chloride content was normal, and sugar also showed little variation from the normal.

The Wassermann reaction was positive in 90 per cent. of cases. The colloidal gold curve was most frequently 0244310000 or 1344210000; but no fewer than 35 per cent. gave a 'zone 1' curve. In one case the fluid was completely normal.

Therefore, although general paralysis and tabes dorsalis are both types of parenchymatous syphilis, the results of examination of the fluid in tabes, it will be seen, approximated more to those found in the meningovascular type than to those found in general paralysis. In these two diseases the Wassermann reaction was generally weaker than in the last-named.

The term 'paretic curve' is a misnomer, because it is by no means pathognomonic of paresis. The Lange reaction is not constantly a 'paretic curve' in paresis, and a paretic curve is obtained in many cases which have the characteristic symptomatology of meningovascular syphilis and tabes dorsalis, with no symptoms of true paresis. It would, I think, be more satisfactory to use the term 'zone 1' curve instead of 'paretic' curve, and 'zone 2' curve instead of 'luetic' curve. Solomon⁹ states that the presence of 'paretic' curves in almost 50 per cent. of cases of cerebrospinal syphilis shows that the presence of such curves does not differentiate cerebrospinal syphilis from paresis. They occur in multiple sclerosis, tabes, brain tumour, etc. Practically

identical conclusions have been reached by other workers in this field, notably Kafka¹⁰ and Weigeldt¹¹.

It will be seen that, from the above results, it is impossible to differentiate between general paralysis, tabes dorsalis and cerebrospinal syphilis by means of the colloidal gold reaction. It has been held by various workers that malaria does not change a 'zone 1' curve to a 'zone 2' curve, but we have found this to occur in 7.5 per cent. of our cases treated by malaria.

POST-ENCEPHALITIS LETHARGICA.—In 22 fluids examined it was found to be clear in colour and under slight tension.

Fourteen fluids were completely normal. Four cases showed a weak luetic curve and of these, two had a sugar content of .104 per cent. and .102 per cent. respectively. In the latter case the cell-count was 295 per c.mm., and this was the only case which showed an increase in the protein content.

Four other cases showed a pleocytosis of 10, 12, 20 and 28 respectively. The sugar content, excepting the two cases above mentioned, ranged between .062 and .080 per cent.

The Wassermann reaction was normal in every case. Therefore, no constant findings occurred in this disease, and examination of the fluid is of little help as an aid to diagnosis in postencephalitic psychosis.

ACUTE MENINGITIS (meningococcal or pyogenic).—Twelve fluids were examined, and the colour varied from a grayish-white to a yellowish-green hue. In the initial stages it was turbid, but soon assumed the typical purulent appearance. Xanthochromia was present in some cases. Pressure was increased in all but one; it usually ranged between 300 and 900 c.mm. of water.

In every case there was a marked increase of protein.

The sugar content was reduced in every case, and the quantity present depended on the state of the disease. With the progress of the disease the sugar steadily diminished in every case; .018 per cent. was the average reading at the height of the affection.

Chlorides were slightly reduced, the average being .66 per cent.

All cases showed a marked pleocytosis, and in one it was as high as 7752 cells per c.mm. The differential count was 87.5 per cent. polymorphonuclear leucocytes, and 12.5 per cent. lymphocytes.

The colloidal gold reaction gave the typical meningitic curve, the greatest change in colour occurring in tubes 7, 8, 9 and 10. Slight variations occurred, but the most typical curve was 0000112342.

As the disease advances, the colloidal gold curve is more displaced to the right into the weaker concentrations, and if improvement occurs the curve is gradually displaced to the left into the stronger concentrations.

The following Table shows the changes which took place in the curve with the advancement of the disease in a fatal case. The gamboge reaction is given for comparison :—

			<i>Colloidal Gold.</i>	<i>Colloidal Gamboge.</i>
1st Puncture	...	...	0011221000	112000
2nd ,,	...	...	0000132210	012220
3rd ,,	...	...	0000112342	001220
4th ,,	...	...	0000012332	001220

TUBERCULAR MENINGITIS.—Ten fluids were examined, which were usually clear or slightly turbid. The average pressure was lower than in acute meningitis.

Protein was increased, but not to the same extent as in the acute type.

Cells were constantly increased and ranged between 200 and 1000 cells per c.mm. In most cases small lymphocytes predominated, but in one case polymorphonuclear leucocytes were in the majority. This may have been due to a mixed infection. Sugar was always diminished at the height of the disease, but in one case was normal in the initial stages.

Chlorides were constantly reduced, more so than in acute meningitis, the average being .63 per cent. at the height of the disease. One case gave a reading of .52 per cent., and such a low reading is considered to be pathognomonic of this condition.

The colloidal gold curve was in the meningitis zone, but slightly weaker than with acute meningitis, the usual curve being 0000123100.

CEREBRAL ABSCESS.—In four fluids out of five examined the fluid was clear; in the fifth it was slightly yellow.

Protein was increased.

The average sugar content was .066 per cent.

The chloride content was normal, except in one fluid, which gave a reading of .69 per cent.

The cell-count ranged between 6 and 756 cells per c.mm., but in only one case was it over 100. In all except the fluid with a count of 756, lymphocytes were the predominant type of cell. In the case mentioned polymorphs constituted 93 per cent., large lymphocytes 3 per cent., and small lymphocytes 3 per cent.

The colloidal gold curve varied from 0012100000 (practically normal) to a very weak meningitic curve.

TUBERCULAR COMPRESSION PARAPLEGIA.—The seven fluids examined showed the typical Froin's syndrome, which it is unnecessary to give in detail. In addition, the readings in the colloidal gold and gamboge tests were respectively:—

<i>Colloidal Gold.</i>	<i>Gamboge.</i>
1111221000	011220
1334455455	111220
0000111340	000120
5432100000	210000
0000111000	001100
0000112321	002210
0000011232	001110

DISSEMINATED SCLEROSIS.—Nine fluids from five cases were examined. The fluid was clear and the pressure normal in every case. One case had a cell-count of 15, but the others showed no pleocytosis. Sugar was normal except in one case, which gave a reading of .124 per cent. Chlorides were normal.

The colloidal gold findings in four cases were 0122100000, 0012210000, 5444321000, 3320000000, while the fifth was completely normal.

CEREBRAL HÆMORRHAGE.—Six fluids were examined, of which three were slightly yellow, two yellow, one red and evenly mixed with blood. Protein was invariably increased. Sugar was slightly increased. A moderate pleocytosis was present in every case. The colloidal gold and gamboge in three cases gave respective curves as follows :—

<i>Colloidal Gold.</i>	<i>Colloidal Gamboge.</i>
1112220000	210000
0001210000	011100
0012210000	022220

OLD HEMIPLEGIA.—Nine fluids were examined and showed in every case a slight increase of protein. The average cell-count was 8.3, and the usual colloidal gold curve was 0022100000.

HERPES ZOSTER.—In 20 cases examined the most common abnormality was a mononuclear lymphocytosis, accompanied by a slight excess of protein, and this was present in 17 cases. In two of these the cell-count was over 50. One fluid was normal, while two showed excess of protein, without any accompanying pleocytosis. On further examination of each fluid about a month after the attack, it was found in three cases that there was a diminution but not a disappearance of the pleocytosis.

DIABETES MELLITUS.—The sugar content in five fluids was constantly increased, and ranged between .256 and .568 per cent. Diacetic acid and acetone were present in one fluid, and this was in a case of impending coma—otherwise the fluids were normal. There was no increase of cells, and no change in the colloidal gold reaction. The increase in the fluid sugar was parallel with that of the blood.

CEREBRAL TUMOUR.—Twelve fluids from six cases were examined. The fluid presented the following characteristics :—

(1) It was usually clear and colourless, but in two fluids was slightly xanthochromic, and the pressure was constantly raised.

(2) The cell-count was normal in two instances, in eight it ranged between 3 and 12.6 per c.mm., and in the other two the counts were 28 and 41 cells respectively. The cells consisted of large and small lymphocytes.

(3) Protein was increased in every case.

(4) Chlorides were normal.

(5) The sugar content was within normal limits in 10 fluids ; in two it was slightly raised.

(6) Two fluids showed no change in the colloidal gold, one gave a 'zone 1' curve, two showed a very slight change in tubes 4 and 5, and the remainder gave a meningitic curve 0000123100.

(7) The Wassermann reaction was negative.

Lange¹² in a report on a series of fluids from cases of cerebral tumour obtained the following results :—

(1) A typical gold curve with colour changes occurring in the dilutions above 1:80.

(2) A moderate increase of protein.

(3) Almost invariably a yellow coloration of the spinal fluid.

Mourez¹³ analysed the fluids from eight cases of brain tumour and concluded that the most important findings in the spinal fluid were an increase in total protein with a low cell-count, and a characteristic gold curve. He also stated that xanthochromia when present was a most important sign.

Spurling and Maddock¹⁴ have stated that the picture presented by the fluid in brain tumour is marked by a low cell-count, a high total protein value, a characteristic gold curve 0000123100, and no significant variation in the sugar content.

HUNTINGTON'S CHOREA.—Three fluids were normal, and Eskuschen¹⁵ reported no characteristic changes in his examinations.

VON RECKLINGHAUSEN'S DISEASE.—The only abnormality in two cases was a slight pleocytosis, accompanied by a slight increase of protein. In another case the fluid was entirely negative.

JAUNDICE.—The fluid in two out of eight cases was yellow in colour, and the discoloration was due to urobilin.

PELLAGRA.—Three cases were examined, of which two were normal, and the other gave a cell-count of 34.

INFANTILE CEREBRAL PARESIS.—The five fluids examined were normal.

PERIPHERAL NEURITIS.—Four fluids were normal.

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