THE CEREBROSPINAL FLUID IN 230 CASES OF GENERAL PARALYSIS AFTER MALARIAL TREATMENT.

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AMONG modern methods of diagnosis of late syphilis of the nervous system, examination of the cerebrospinal fluid has proved of very great value. At this hospital special interest has centred round cases of general paralysis, and recently the problem of changes before and after treatment with malarial inoculation has been investigated. This has been done by a number of other writers, but we have been specially favoured in this study by the fact that malarial treatment was first started in England at Whittingham Mental Hospital in July, 1922. The records therefore extend over a period of nine years and include a series of 230 cases treated and examined during that period. In addition I have been able to collect cerebrospinal fluid for examination from 14 patients who were discharged as recovered and who are now living at their own homes. More patients living at home might have been induced to allow lumbar puncture, but minor after-effects were sometimes complained of and on one occasion a patient collapsed merely from the pin-prick in the skin. These 14 cases, however, are of value in that the patients had been discharged for varying periods of time; they form a sufficient basis on which to formulate reasonably definite views. The purpose of this article is to ascertain the results in the cerebrospinal fluid after malarial treatment of general paralysis among three distinct classes of patients:

1. Patients not recovered and now dead.
2. Patients not recovered and now living in hospital.
3. Patients recovered and now living at home.

The changes which occur in the cerebrospinal fluid and the tests applied are too well known to require detailed description here. They may however be briefly mentioned with special reference to the tests carried out on the cases investigated in this hospital. Cell counts are increased. The Ross-Jones and Pandey tests show an increase of globulin. The Wassermann test of the cerebrospinal fluid is positive, and the Lange colloidal gold reaction gives a zone I curve. In addition to these tests the colloidal gamboge reaction has been carried out in the cerebrospinal fluid and an experience of

three to four thousand examinations in this hospital shows it to be as reliable as the colloidal gold test. All tests were performed in the hospital laboratory with the exception of the Wassermann which was done in Manchester University laboratory.

GENERAL RESULTS

A detailed presentation of 230 cerebrospinal fluid examinations with changes recorded after treatment is a difficult task on account of the large numbers involved, but it is possible to give the general findings after careful consideration. The first point is that in nearly all cases examined within one or two months after treatment with malaria, the cerebrospinal fluid shows a decrease in the cell count, very often in a marked degree. The diminution in the cells present remains even when no other improvement in the laboratory examinations can be found at later times. This finding is not without significance and suggests that the pathological condition of the brain and meninges producing the increased number of cells in the fluid has been arrested, even at such an early time after treatment. To begin with, this is the only change found from that of the typical cerebrospinal fluid of the general paralytic. As years go on, however, further changes appear. There is a gradual return of the fluid to a normal condition after treatment with malaria. This statement is correct for the majority of cases, but a small number, even after five or six years, still yield to laboratory examination findings of general paralysis.

Discussing each test individually one finds that the Pandy and Ross-Jones tests for increased globulin both gradually return to normal and so give a negative result. The Wassermann test of the fluid proves more resistant to change than any of the other laboratory tests, and even after all other findings are negative, a positive Wassermann may still be recorded. The Wassermann, however, also shows a gradual return to negative, but several years elapse in most cases before this change appears. The colloidal gold test and the colloidal gamboge test show changes which are more or less similar. In a certain number of cases they change to a zone II curve and if taken a year or so later this zone II curve may be found to have disappeared and a negative response may be found. Most of the other cases, after a year or more, give a curve which is only slightly changed from the normal or negative reaction. Thus it may be said that in examining a large number of fluids after treatment with malaria, there is, over a period of several years, a gradual return to negative reactions in many; that many more show a diminution in the pathological findings; and that only a small number still give all the reactions of general paralysis several years after treatment.

No attempt can be made to differentiate between the changes in the recorded cases and in those which have not improved mentally. It appears

from the examinations that there is no appreciably quicker improvement in the fluid among those who fare well than among those who do not.

Again, as regards the period of time for a positive reaction to become negative or nearly negative no definite duration can be fixed. Some may do so in one year while others take two, three, four or more years. The average period of time would appear to be about two to three years.

The findings in the 14 who had fluid withdrawn at their own homes and who were in a satisfactory mental condition after treatment are as follows:

	Ross-Jones test	Pandy test	Cell count	Wassermann reaction	Colloidal gold reaction	Colloidal gamboge reaction
1	neg.	neg.	1.6	+	0011000000	100000
2	neg.	neg.	6.0	doubtful	0121000000	100000
3	+	+	16.6	+	0122000000	200000
4	neg.	neg.	2.6	neg.	0011000000	000000
5	+	+	2.6	+	0011000000	000000
6	+	+	2.3	+++	0122000000	100000
7	neg.	neg.	0.6	neg.	0011000000	000000
8	neg.	neg.	0.6	neg.	0011000000	000000
9	neg.	neg.	0.3	+++	0011000000	000000
10	+	+	3.0	neg.	5554210000	210000
11	+	+	4.0	neg.	5543200000	221000
12	+	+	2.0	doubtful	0022100000	221000
13	+	+	5.0	+++	5554320000	221000
14	+	+	5.3	weak +	1122000000	100000

In most of these cases the approach to a normal finding is definite, and some are completely negative.

It has been my experience throughout to find that mental improvement precedes marked improvement in the spinal fluid, but that an approach to a normal fluid gradually makes its appearance. This progress to normality is found to an equal degree in the patients who still remain in hospital and whose mental state shows no improvement. It thus appears that following treatment of general paralysis with malaria, there is, in the majority of patients, a diminution of pathological changes as found by laboratory tests, and that over a period of several years there is a gradual return to a normal fluid. This improvement in the fluid is therefore no index to the mental improvement in the patient. Patients who remain demented may after the lapse of several years give a negative finding in the fluid.

These findings seem to be of definite help in assessing the value of malarial treatment and indicate that such treatment has the power of bringing about a return to normal conditions in the central nervous system.

As further confirmation of this return to normality, whereas before treatment with malaria the presence of spirochaetes in the brain was of frequent occurrence in general paralytics, we can no longer demonstrate the organisms of syphilis in the brain employing the same methods as formerly. Thus both from the point of view of mental improvement and also of the laboratory findings, malarial treatment can be advocated as of definite value in general paralysis and the earlier such treatment is given the better the results will be.

CONCLUSIONS.

1. The cerebrospinal fluid improves in patients suffering from general paralysis after treatment with malaria and may become normal. This improvement usually takes several years to occur.
2. The improvement in the fluid occurs in patients who have improved mentally and also in those who do not improve.