FURTHER NOTES ON EXAMINATION OF CEREBRO-SPINAL FLUID BY ULTRA-VIOLET LIGHT.

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IN a previous paper* I described some observations on the absorption of ultra-violet light by cerebrospinal fluid. In the course of these observations it was noticed that there was a certain amount of general absorption of the light waves varying with different fluids and that the most striking of these results occurred in cases of tuberculous meningitis.

These results were obtained with a primitive apparatus and were rightly criticised on the ground of insufficient standardisation; so a further series of observations has been made during the past year to standardise results as far as is possible under the conditions in which the work has had to be carried out, conditions hampered by my own lack of training in research work and the unavoidable spasmodic nature of the observations.

My previous observations were made with a copper arc since I found the tungsten arc very expensive to work with, as the metal burned away so quickly; but Mr. Clarke, of the Physics Department of the Sheffield University, to whom I am indebted for very valuable assistance, suggested that the tungsten spectrum was a much more reliable band to work with and that most of the recent observation on ultra-violet light had been done with this spectrum, and I therefore decided to use this metal for the next series. I modified the apparatus so that instead of using a direct current to energise the copper rods, I adapted an old X-ray 32-inch induction coil with a condenser of .005 microfarad capacity in parallel with the spark. This apparatus, taking a primary current of 25 amps. at 250 volts, produced a fat spark across the tungsten rods when the latter were separated by a gap of 3 millimetres, which gap was used throughout the experiments. The rest of the apparatus, which was set up on a home-made optical bench, consisted of a Hilgar spectrometer of low dispersion, a quartz lens to focus the rays and a suitable screen to hold the quartz cell containing the spinal fluid. These cells were made of two plane parallel faces of quartz 4.5 cm. in diameter cemented to sections of glass tubing.

Observations were first carried out to determine the best results from a photographic point of view and it was found these were given by an exposure of

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* See this JOURNAL, October 1929, vol. x, p. 97.

5 seconds, using Wellington panchromatic plates, which were afterwards developed by time and temperature method, using standard rytol.

One question raised by the previous paper was the effect on the spectrogram of varying thicknesses of fluid and a preliminary series of observations was made to ascertain what such difference might be. Cells of .25, .5 and 1 cm. were made and it was found that unless the fluid was very turbid spectrograms taken through these varying thicknesses of fluid showed remarkably little difference; after a number of tests a cell with a depth of .5 cm. was chosen as the standard and all spectrograms were taken through this thickness of fluid, unless otherwise stated.

Fig. 1 shows the general lay-out of the apparatus.

FIG. 1.

Fig. 2 shows the normal spectrogram of tungsten produced under the above conditions. It is, of course, sparking in air which itself absorbs a certain amount of the ultra-violet waves and an attempt was made to obtain an *in vacuo* spectrum.

FIG. 2.

Fig. 3 shows such an attempt. So far as I could see there was no difference between the two, and the added difficulty was such that I did not consider it necessary to carry out any further *in vacuo* observations, particularly as absorption in the fluids concerned was found well before the end of the spectrum

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taken in air. (It will be noted that the last spectrum is one of copper and not tungsten.)

FIG. 3.

Fig. 4 shows the spectrogram of spinal fluid photographed through thicknesses of .25, .5 and 1 cm. respectively, as mentioned above, and it will be seen that the difference is quite a small one.

FIG. 4.

Fig. 5 is the spectrum of tungsten with some of the more easily identified wave-lengths marked. It will be noticed that these wave-lengths vary in value from 4348 a.u. somewhere near the blue of the visible spectrum, to 2256 a.u. well down in the ultra-violet band.

FIG. 5.

With this rather long preface I will now very briefly describe the findings in the second series of observations that have been made, and I would like to quote the last paragraph of my previous paper : " The conditions I have cited give spectrograms which appear more or less constant in type but on what they depend at present I cannot say. I am quite sure they do not depend on the number of cells present in the fluids nor do the variations in the protein constituents appear to bear any fixed relationship. The only definite statement possible is that absorption seems to take place in toxi-infective conditions and varies directly with the severity of this process ; the nearer a fatal termination the more complete the absorption."

It is, of course, perfectly clear that changes such as I am describing in one tissue (spinal fluid) cannot carry a diagnostic label ; our labels are too gross for such minuteness. For instance the label 'general paralysis' conveys to our minds a more or less definite clinical picture ; but the picture is really a moving one inasmuch as we envisage a series of events occurring in time, whereas an examination such as we are making can only be the results of certain metabolic accidents at a given moment of time and such results as I have obtained must vary at different stages within the range of one disease-process.

FIG. 6.

It is manifestly absurd to think, for instance, that every case of general paralysis must give the so-called paretic gold curve in the Lange test since the factors on which this test depends are probably only progressively developed. The results I have obtained spectrographically, if they have any value at all, can only suggest that certain tendencies are at work and can never have the same evidential value for a given instant as say, an X-ray picture of a fractured bone.

With this fact clearly stated I may be allowed to use the clinical labels for convenience and confine myself to the results I have obtained in cases of meningitis.

Fig. 6 shows the amount of absorption by normal spinal fluid, this fluid having been obtained from a perfectly healthy volunteer from the Labour Exchange, and it will be observed that absorption only begins at a wave length of 2397 μ .

Fig. 7 gives the characteristic spectrogram from a case of tuberculous meningitis. It can be seen that a very considerable amount of ultra-violet light is absorbed, the absorption commencing about a wave-length value of 3051 a.u. I will quote the pathological report on this particular fluid :—

Clear fluid containing a 'spider' clot.

Leucocytes ... .. 80 per c.mm.

Protein increased.

Chlorides ... .. .75 per cent.

Gold test 001223342

Autopsy (two days later). Many tubercles on vertex of the brain ; much basal exudate. Miliary tubercles in spleen and lungs.

FIG. 7.

I wish to draw attention to the number of cells, 80 per c.mm., the increased protein and the gold curve, which I believe is called the meningitic curve and which in my experience is rather a rare type.

Fig. 8 is also from a case of tuberculous meningitis, and fig 9. as well.

FIG. 8.

FIG. 9.

This type of spectrogram is very striking, and it is evident that such a large amount of absorption must depend on some change in the chemical or physical constituents of the fluid.

The obvious suggestion that increase in the cell count might account for it was investigated, but fig. 10, which is from a case of general paralysis in which the cell count was almost identical with the last and yet in which the absorption is quite different, shows that such a hypothesis is untenable. Nor can the absorption be wholly dependent on increase in the amount of protein since in both the fluids depicted the protein is equally increased.

FIG. 10.

The Lange test in these two fluids gave very strikingly different results and the last case gave the most marked paretic curve I have seen. However, I will return to this point later. Meanwhile I have depicted a summary of these two cases, as they both represent 'type' spectrograms and pathological findings in the fluid in the next figure (fig. 11).

FIG. 11.

To return to the consideration of tuberculous fluids. I found that the spectrograms I obtained last year using a copper arc were corroborated in this second series of observations and I was beginning to feel that a spectrogram

might be of some diagnostic significance, at any rate in cases of suspected tuberculous meningitis. Then in November last (1929) I examined the fluid from a case which had been admitted as a suspected tuberculous meningitis and obtained a spectrogram which did not agree with my previous cases. This particular spectrogram is shown in fig. 12.

It will be seen that absorption begins about the same place as in the other tuberculous cases, though as a matter of fact it is really a little further along the band, the actual wave-length value being 2937 a.u. But instead of the usual absence of any further lines, in this spectrogram there are to be seen a number of lines further along actually in the region of 2702 a.u. to 2440 a.u. From this I suspected that the case was probably not one of tuberculous meningitis. The clinical history lent some colour to this suspicion, since after a very short illness, a few days only, the patient developed a bilateral choked disc, headache and vomiting, with some slight paresis of a left hemiplegic type. The pathological report on the spinal fluid was also not without ambiguity, for

FIG. 12.

although the cells were increased to 520 per c.mm. with a 90 per cent. mononuclear count the chloride content was not diminished, which I have come to look upon as unusual in tuberculous meningitis.

After a few days' observation therefore, with an increase in the swelling of the optic discs, in view of the absence of 'diminished chloride' content, a suspicion of cerebral tumour was raised and as there was a definite though slight left-sided paresis, it was considered justifiable to carry out a right-sided temporal decompression. Although there was a slight improvement in the general condition for a day or so the patient quickly began to lose ground and died ten days after admission. At the autopsy the original diagnosis was proved to be correct, there being "some miliary tubercles scattered over the base of the brain and the vertex of the cerebellum."

There was no doubt as to the diagnosis and I was disconcerted at finding my previously conceived view of the definiteness of the spectrogram in this condition upset; but since this observation I have seen two other cases of tuberculous meningitis established by autopsy in which the spectrogram has been similar to the last, as is seen in the next two figures (figs. 13 and 14).

In fig. 13 absorption commences at 2937 and then a few lines are seen about 2764 to 2440, almost identical with the last plate.

FIG. 13.

In fig. 14 absorption commences at 3051, the usual place for tuberculous meningitis, and then after a long interval a few lines are to be made out about 2702 a.u.

FIG. 14.

Although I was disconcerted at these readings there could be no shirking them : and though I did my best to make them fit in with my previous results the discrepancy was too obvious, so I had to accept them and realise that my ideas on the fixity of type of the spectrogram in tuberculous meningitis were wrong.

The next setback to these ideas occurred a few weeks after taking the last spectrogram, when I admitted an emergency case to the Nursery Ward with an outside diagnosis of purpura. Two days after admission it was clear that some meningitis was present and a lumbar puncture was done, giving exit to a turbid fluid on which the pathologist reported as follows :—

Turbid fluid.

Red cells 0.

Leucocytes 132,000	Polymorphs	85 per cent.
	Lymphocytes	13 per cent.
	Endothelial cells	2 per cent.

Protein much increased.

Globulin test positive.

Chlorides	.. .. .	75 per cent.

Although no organisms were found in direct films a pure growth of meningococci was obtained and a diagnosis of cerebrospinal fever definitely established.

Fig. 15 shows the spectrogram obtained in this case.

FIG. 15.

It will be seen that this is very similar to those of the last three cases of tuberculous meningitis. Absorption begins about the same place, viz., 2937, and then after a short interval there are further lines to be seen from 2702 to 2440 a.u.

I will complete this short series of cases by one more. It was that of a child of five admitted moribund one evening suffering from meningitis following otitis media. A cistern puncture was done as part of an attempt to flush out the subarachnoid spaces with saline and serum, and the spinal fluid obtained was reported on as follows:—

Turbid fluid, clotting spontaneously.

Leucocytes 2,180 per c.mm.	Poly.	..	75 per cent.
	Lymph.	..	25 per cent.

Protein much increased.

Globulin test positive.

Chlorides	..	..	..	..	..	..	67 per cent.

Gold	..	..	..	..	..	..	0112222110

Hæmolytic streptococci isolated from fluid.

The child died 24 hours after admission.

Fig. 16 shows the spectrogram obtained in this case.

FIG. 16.

This fluid was so purulent that it is very difficult to make out where absorption really commences, but careful measurement shows it to be about 3951, i.e., the region at which absorption usually begins in tuberculous meningitis.

I thought it might be worth while to centrifuge this fluid which I did at high speed for ten minutes and on re-examining the centrifuged fluid I obtained the spectrogram shown in fig. 17, which will be seen to be almost identical with the atypical spectrograms from tuberculous meningitis.

On reconsidering this group of cases of meningitis I had to admit that my previous view of the spectrogram of tuberculous disease was too narrow and in trying to find some common factor I took into consideration the length of time elapsing between examination of the spinal fluid and death or other termination of the case, since my conclusion previously was that "the nearer a fatal termination the more complete is the absorption."

FIG. 17.

It appears just possible that there is some relationship between this interval and the type of spectrogram obtained, the details of this small series from this point of view being as follows :—

T.B. Cases absorbing beyond	3051	death within 3 days.
Strep. Case absorbing beyond	3051	death within 1 day.
T.B. Cases with partial absorption	2937	death within 10 days.
C.S. Fever with partial absorption	2937	non-fatal.

Thus the cases of delayed fatal tuberculous meningitis show a few lines in the spectrum a little further along, as does also the fluid from the non-fatal case of cerebrospinal fever and also as does the centrifuged fluid from the case of streptococcal meningitis. I am therefore tempted to suggest that in cases of meningitis there is a 'type' spectrogram in which absorption begins at about 3051, is more or less complete for a short distance and then shows a few more lines about 2764 to 2440; if there be any tendency to improvement then this interval from 3051 to 2764 tends to fill up with lines, whereas if, as is usual, the case progresses to a fatal termination not only does this interval never show any line but those about 2764 disappear, so that total absorption occurs from 3051.

It might thus appear that the spectrogram has some prognostic value according as the interval between 3051 and 2764 tends to widen or fill up in a series of fluid examinations. Fig. 18 shows this interval actually in the process of so filling up. This spectrogram is from the case of cerebrospinal fever 14 days after the first one was taken.

FIG. 18.

CONCLUSIONS.

To conclude, first of all I feel that formerly I stressed too much the individuality of the spectrogram in any of the conditions I examined; and, secondly, I would modify my previous opinion by saying that in cases of meningitis of any type there appears to be a certain selective absorption with an interval between wave-lengths of 3051 and 2764 and that variation from this type depends on the natural history of the individual case.

I have tried to depict this view in fig. 19 in which the middle band represents the 'type' spectrogram whilst the upper and lower represent the variants of it.

FIG. 19.—Diagrammatic representation of spectrograms in meningitis.

Whether the above conclusions are warranted or not will remain for more extended observations but I am inclined to offer a speculation that the absorption depends on some physical factor in the fluid which is at present undetermined.

When one looks at the perfectly clear fluid from a late case of tuberculous meningitis and an equally clear fluid from a case of tabes or general paralysis and in both finds a pleocytosis, an increased protein content, and an identical salt content and yet with spectrograms very different in their appearance,

the conclusion seems fairly legitimate—either our means of chemical investigation are too gross to detect the minute differences in composition on which the spectrograms are dependent or, what is more likely, the differences depend on factors other than chemical.

If the reader will refer to the two first figures and their epitome in fig. 11, he will see the only difference in their pathological reports lay in the Lange gold test.

Lange's test almost certainly depends on an altered electrical state in colloid particles in the mixture of spinal fluid and gold chloride, and the so-called 'curves' obtained in various clinical conditions may not be much more specific than the spectrograms I have shown. I think it not unlikely that both phenomena depend on similar though, of course, not identical variations in the surface charges of particles of colloid.