THESIS

for the

DEGREE OF DOCTOR OF MEDICINE (M.D.)

presented by

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Subject

"The Sugar Content of the Blood, Spinal Fluid and Urine in Epidemic Encephalitis; its Significance, and its Application to Diagnosis."

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Introduction.

The investigations on this subject were carried out in the City of Glasgow Fever Hospital, Ruchill, during the spring and summer of 1924.

From a survey of the literature it was evident that there was considerable confusion of thought regarding the sugar content of the spinal fluid in encephalitis, and the following enquiry was undertaken to elucidate if possible its real significance. A parallel investigation was therefore made on the sugar content of the blood and urine. The presence of ketone bodies in the urine has an allied interest and this matter is touched upon. For a full appreciation of the diagnostic significance of the sugar content of the spinal fluid, it was found necessary to add brief notes on the other examinations usually made on the spinal fluid.

The epidemic of encephalitis occurring in Glasgow from March to September of this year offered ample material for experiment.

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The Arrangement of the Subject Matter.

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I A Summary of the Literature.

II. Methods of Examination Employed.

III. Experiments on the Sugar Content of the Blood and Spinal Fluid. Five Series.

IV. The Sugar and Ketone Bodies in the Urine.

V. The Application of the Results Obtained to the Diagnosis of Encephalitis with Illustrative Cases.

VI. The Physiological Interpretation of the Results.

VII. Summary of the Main Conclusions.

VIII. Bibliography.

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I. A Summary of the Literature.

The sugar content of the cerebro-spinal fluid in cases of epidemic encephalitis became of interest in 1920 when several French physicians found that it was increased above normal.(11) Typical among others, Laporte and Rouzaud(16) in a series of 12 cases, and Bourges Foerster and Marcandier(2) in a series of 6 cases found a hyperglycaemia associated with a hyperglycorraehia. This increase they considered to be a valuable aid in diagnosis. The methods of estimation employed were not stated and they accepted as the normal sugar content of the fluid Mestrezat's figure of .053%.

The following year Foster(8) in America using the Folin-Wu method, in a series of 15 cases found an increase in the sugar content of the spinal fluid but he could detect no corresponding hyperglycaemia.

Achard(1) in Paris summarizing his findings in 15 cases concluded that "in lethargic encephalitis as in many other infectious diseases we see an increase in the amount of sugar in the cerebro-spinal fluid; this elevation is not, however, constant, but when it does exist it becomes a useful aid to diagnosis, for it helps to eliminate an infectious meningitis whether meningococcal or tuberculous." He also did not find an associated hyperglycaemia.

Coope(5) using the Folin-Wu method examined eleven cases of encephalitis and found that in 9 of these the fluid sugar gave a reading over .06%; but of 69 specimens from other diseases, mainly insanities, 60 gave readings over .06%. He concluded that "the French tendency/

tendency to regard a high sugar content of the spinal fluid as in favour of lethargic encephalitis does not appear to be justified as figures quite as high occur in other nervous diseases."

Perdrau (23) in summing up the rather discrepant findings of these workers thought that it was unlikely that the sugar content of the fluid was increased at all, and he added that on only one point did there seem to be agreement, viz., that the sugar contant in lethargic encephalitis was not diminished.

Details were not given in any of these writings as to the time of the collection of the fluid or the blood.

The question revived again in 1922 when Thalhimer and Updegraff (27) in America using the Benedict method stated that the sugar content of both blood and spinal-fluid was increased in encephalitis. Most of their specimens of blood and fluid were taken together after twelve hours' starvation. They investigated the sugar content of several normal fluids and they based their conclusions on the much higher figures obtained in fluids from encephalitis.

None of these authors investigated the blood sugar curves. Schwab (26) in the course of an investigation of sugar curves in neurological cases included seven cases of encephalitis but no details are given as to the stage of the illness. Four were normal; two showed a return to the fasting level within three hours, and one was of the diabetic type.

Few references can be found regarding the sugar in the urine. The Ministry of Health's Report (23) mentioned/

mentioned two cases of encephalitis which developed glycosuria and Achard (1) quotes a case with renal glycosuria.

II. Methods of Examination Employed.

Patients were starved over-night for 12 hours and specimens of blood, spinal fluid and urine were taken in the morning.

When full blood sugar curves were made, 50 grams of glucose or its equivalent in young children, dissolved in eight ounces of water, was administered, and specimens of blood were taken usually at half hourly intervals up to 2½-3 hours. In these cases lumbar puncture was done as soon as the last specimen of the series was taken.

The blood samples were removed from a vein of the forearm by a small hypodermic syringe and a fine needle. No tourniquet was used. The upper arm was firmly grasped and the forearm massaged lightly upwards for a few seconds. This procedure occupied the minimum of time and was less dreaded especially by children than pricking the finger.

Specimens of spinal fluid were obtained by lumbar puncture. This was performed under a local anaesthetic, viz. 1 c.c. of a 5% solution of novocaine. A puncture thus made was attended by no pain and little discomfort and the patient lay quite still, thus enabling a fluid free from blood to be secured. In a few cases chloroform was administered.

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The sugar content of the blood and spinal fluid was estimated by Maclean's method (19) for blood sugar estimation. In the case of the fluid, .3 or .4 c.c. was used for examination instead of .2 c.c. in the case of the blood. The results were corrected accordingly.

A sample of urine was obtained before withdrawing specimens of blood and fluid. In cases where glucose was given a second sample was procured about 3 hours after the administration of glucose. On each sample two qualifative tests for sugar were performed.

(1) Equal parts of Benedict's qualitative solution and urine were together carefully boiled for two minutes and allowed to cool. Fehling's solution was also used for comparison.

(2) A fermentation test was performed as follows:-

The urine was acidified with a little tartaric acid, then boiled to drive off air. On cooling about 10% of fresh yeast was added and the mixture placed in a fermentation tube in the incubator for four hours.

The Rothera Test for ketone bodies was applied in each case, and was performed as follows:- One inch of urine in a test tube was mixed with an equal quantity of a saturated solution of ammonium sulphate. A few drops of 1% sodium nitroprusside freshly prepared and one inch of ammonium hydrate were then added and the whole shaken up. The development of a permanganate colour indicated a positive result.

III. Experiments on the Sugar Content of the Blood and Spinal Fluid. Five Series.

Series I.

in which 25 specimens of blood and spinal fluid mostly from cases of encephalitis were estimated for their sugar content, the specimens being taken simultaneously after 12 hours' fasting. See Table No.I.

The blood sugar content varied from .068% to .128%, the average being .095%. These figures correspond with those (.08 - .12) given by Maclean [1] as normal for the fasting level in a healthy person.

The sugar content of the spinal fluid ran from .042% to .070% and the mean was .056%.

The relationship expressed as a percentage between the sugar content of the fluid and the blood at fasting level varied from 49 to 70 and the average was 59.

Unfortunately no literature is available on the normal spinal fluid sugar estimated by Maclean's Method.

TABLE - NO.1.

TABLE NO. 1.

The Samples of Blood and Spinal Fluid were taken simultaneously after 12 hours starvation.

No.	Patient	Sex	Age	Day of illness.	Diagnosis.	Blood Sugar %	Spinal Fluid. Sugar %	Cell Count	Globulin	Fluid Sugar / Blood Sugar x 100
1	E.G.	F.	31	10	L.E.	.128	.070	10	+ (slight)	54
2	E.McP.	F	36	3	L.E.	.123	.060	30	-	49
3	M.F.	F.	12	28	L.E.	.109	.061	< 5	+	56
4	J.B.	M	36	4	L.E.	.109	.056	60	-	51
5	A.D.	M	4	-	No apparent disease.	.109	.053	< 5	-	49
6	M.McL.	F	8	12	L.E.	.108	.060	< 5	-	56
7	A.M.	F	15	15	L.E.	.106	.055	20	-	52
8	J.F.	M	48	14	L.E.	.104	.055	10	[illegible]	53
9	J.D.	M	47	27	L.E.	.100	.068	< 5	-	55
10	E.S.	F	2	-	No apparent disease.	.099	.059	< 5	-	60
11	D.K.	M	15	13	L.E.	.098	.056	< 5	-	57
12	J.A.	M	16	13	L.E.	.095	.058	20	+ slight	61
13	J.R. *	M	51	8	L.E.	.091	.060	20	+	66
14	A.S. *	F	20	17	L.E.	.089	.052	50	-	58
15	M.H.	F	7	13	L.E.	.089	.052	15	-	58
16	M.McS.	F	30	33	Cystitis	.089	.051	< 5	-	57
17	M.A.	F	25	12	L.E.	.087	.059	50	-	68
18	A.McQ.	F	8	16	L.E.	.086	.059	40	-	69
19	J.M.	M	20	5	L.E.	.085	.058	90	-	68
20	S.A.	M	2	4	L.E.	.083	.055	310	+	66
21	W.D.	M	8	12	Intestinal toxaemia.	.082	.058	< 5	-	70
22	J.McD.	M	38	4	L.E.	.081	.054	30	-	67
23	J.C.	M	25	24	L.E.	.078	.052	< 5	+	67
24	M.D.	M	14	20	L.E.	.072	.044	10	-	60
25	D.V.	M	9	29	L.E.?	.068	.042	< 5	-	62
				Average		.095	.056			59

* These cases were lumbar punctured under chloroform.

TABLE NO.1.

Experiments on the Sugar-Content of the Blood and Spinal Fluid.

Series II.

in which 6 samples of spinal fluid taken previous to spinal anaesthesia were estimated for sugar. (See Table No. II)

None of these patients could be described as strictly normal. Together with the two cases incorporated from Table I they furnished the only controls available. The figures vary from .050% to .065%, striking an average of .057% almost identical with that of .056% in series I. Unfortunately it was impossible to take simultaneous samples of blood for sugar estimation.

The absolute figures for normal spinal fluid obtained by other workers using different methods, cannot be compared with those quoted above, but the ratios between the blood and fluid sugar readings, no matter what the method used, are of value for comparison. In a series of normal individuals, Sehan and Nixon,(25) using the Myers-Bailey Method, found that the ratio between the fluid sugar and the blood sugar was on an average 56 with a minimum of 48 and a maximum of 70. This result agrees closely with the limits of 49 and 70 and the average of 59 obtained in Series I.

As the sugar ratios between the fluid and blood in encephalitis correspond with the normal ratio, and as the leval of the blood sugar in encephalitis is within normal limits, it does not therefore appear unjustifiable to conclude that the sugar content of the spinal fluid in cases of encephalitis is also within normal limits.

TABLE NO.XX

and

TABLE XXI.

TABLE NO.II.

No.	Patient.	Sex.	Age.	Diagnosis.	Spinal fluid sugar content.	Time taken after food.
1	M.B.	F	26	Uterine Fibroids	.054	12 hours
2	A.C.	M	68	Gangrene of leg	.062	8 hours
3	L.H.	F	17	Appendicitis	.061	9 hours
4	M.S.	F	35	Appendicitis	.065	9 hours
5	J.M.	M	41	Gastric ulcer	.050	7 hours
6	L.T.	F	29	Uterine fibroids	.052	10 hours
From Table I.	A.D.	M	4	No apparent disease	.053	12 hours
	E.S.	F	2	No apparent disease	.059	12 hours
				Average	.057	

TABLE NO. III. Cases of Meningitis.

No.	Patient	Sex	Age.	Day of illness.	Diagnosis.	Blood Sugar %.	Spinal fluid Sugar %.	Ratio.
1	C.L.	F	1½	13	Tuberculous..	-	.036	-
2	J.M.	M	4	15	"	.080	.035	44
	J.M.	M	4	18	"	-	.024	-
3	D.T.	F	2	10	"	.076	.032	42
4	L.M.	F.	18	18	"	-	.029	-
5	I.E.	F	4	14	"	.085	.025	29
6	J.B.	M	2	17	"	-	.019	-
7	S.A.	F	16	3	Meningococcal	.096	.014	15
8	D.S.	F	2	4	"	-	.008	-

Experiments on the Sugar Content of the Blood and Spinal Fluid.

Series III.

in which 8 cases of meningitis, tubercular and meningococcal were investigated as to the sugar content of the spinal fluid. (See Table No. iii.)

The figures range from .008% to .036%, the two lowest being the meningococcal cases. The amount of sugar thus shows an absolute decrease. The blood sugar content is not diminished and the ratio of the fluid sugar to the blood sugar varied from 15 to 44, demonstrating also a relative decrease.

Low levels of sugar are recognized to occur in infective meningitis (Coope (5)). In some cases, sugar is said to be totally absent. (Levinson.) (17)

Experiments on the Sugar Content of the Blood and Spinal Fluid.

Series IV.

in which blood sugar curves were derived from 20 cases mainly encephalitis, and an estimation made in most instances of the sugar in the spinal fluid at the close of the curve. (See Charts 1-20, Graphs 1 and 2 and Table No.IV.)

The charts are self-explanatory. The type of illness is classed as mild, moderate or severe on general constitutional grounds. It is stated whether the patient was febrile or not when the specimens were taken, and the predominating symptom is given.

According to Maclean (20) a blood sugar curve is normal if it does not rise above .18% and if it returns to its original level or nearly so, within two hours after a single dose of 50 grams of glucose. An abnormally high or prolonged curve is usually evidence of delay in the storage of sugar by the liver.

Chart 1 from a very mild case during convalescence is typically normal.

Charts 2-5 all show a delay in returning to the fasting level, signifying a slight defect in liver storage. In these cases the urine contained no sugar.

Chart 6 from a pregnant woman shows practically no rise but the urine contained a small amount of sugar indicating a mild degree of renal glycosuria.

In Charts 7-9 the fasting specimen of urine was clear but the second specimen taken after the glucose administration contained traces of sugar. The curves all show delay in regaining their base lines.

Experiments on the Sugar content of the Blood and Spinal Fluid.

Chart 10 was from a doubtful case of encephalites complicated by acute rheumatism. The curve points to a distinct defect in liver storage.

Charts 11, 12 and 13 were from severe cases of which two died. A considerable derangement of metabolism is evident. The last of these charts from a man of 59 shows a curve of the diabetic type. All these cases had definite glycosuria. In the last case the glycosuria cleared as the man recovered.

From a survey of these results, it may be concluded that a defect in liver storage is present in the acute stage of encephalitis; in the mild cases the defect is slight but it is considerable in severe cases.

Comparison was made with blood sugar curves obtained from patients with other febrile diseases.

Charts 14 and 15 were from severe cases of diphtheria.

Chart 16 was from a case of measles.

Charts 17 and 18 were from two cases of advanced pulmonary phthisis.

Charts 19 and 20 were from cases of Intestinal Toxaemia.

From a study of charts 14-20 we see that each has a prototype in the encephalitic series.

Thalhimer and Updegraff (27) adduced as one explanation for the high blood sugar readings they found in encephalitis, the possibility of a lesion in the mid-brain or near the fourth ventricle. Both these are common sites of haemorrhages and round celled

TABLE NO. IV. (derivedc from blood sugar curves in the series of charts).

The samples of blood were taken after 12 hours fasting and the samples of fluid 2-3 hours after the administration of glucose.

No.	Patient	Sex.	Age.	Day of Illness.	Diagnosis.	Blood Sugar %.	Spinal Fluid.			Fluid Blood Sugar Ratio
							Sugar %.	Cell count.	Globulin.	
1	M.B.[M]	F	54	11	L.E.(died)	.155	.092	120	+	59
2	R.C.	F	31	9	L.E.(died)	.117	.078	110	+	67
3	J.W.[M]	F	15	17	L.E.	.117	.064	60	-	55
4	M.A.	F	34	7	L.E.	.115	.062	50	-	54
5	E.M.	M	15	28	L.E.	.113	.073	30	-	65
6	J.McG.[M]	M	10	3	Intestinal Toxaemia.	.111	.074	<5	-	67
7	M.H.	F	7	12	L.E.	.111	.069	30	-	62
8	J.S.	F	13	13	L.E.	.096	.095	<5	-	57
9	R.McK.	M	11	10	L.E.? Rheumatic Fever.	.095	.083	-	-	87
10	E.C.[M]	F	20	5	L.E.	.093	.060	90	+	64
11	J.A.	M	59	9	L.E.	.087	.093	50	-	107
12	M.A.	F	24	5	L.E.	.087	.049	-	-	56
13	W.M.	M	6	5	Intestinal Toxaemia.	.085	.099	-	-	106
14	M.D.	M	15	30	L.E.	.070	.047	-	-	67
15	W.T.	M	4	9	L.E.	.067	.049	50	-	73
					Average	.100	.071			70

[M] Lumbar puncture under chloroform.

infiltration in encephalitis. Such lesions they supposed might act like the piqûre of Claude Bernard.

This explanation is theoretical and it does not seem necessary to make use of it even in the interpretation of the abnormal blood sugar curves existing in encephalitis. It is sufficient to assume that the disturbance of glycogenic function is a manifestation of the infection and toxaemia. The curves demonstrated, those from encephalitis as well as from other diseases, show great variety and no one disease appears to show a distinguishing type of curve. The uncertain influence of toxaemias and infections on the nature and constancy of the blood sugar curves, has been pointed out by Olmsted and Gay.(22) Schwab,(26) studying curves from various nervous diseases including encephalitis, concluded that "from the neurological standpoint it was impossible to attach characteristic types of curve to one type of disease."

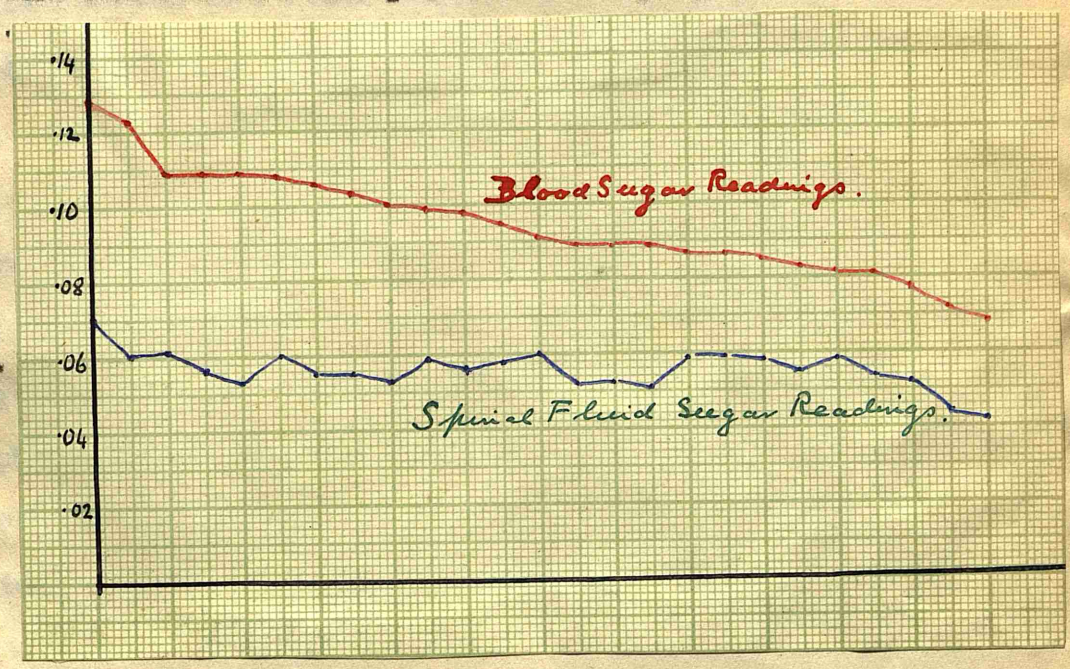
Similarly it may be concluded that there is no variety of curve peculiar to encephalitis.

From a scrutiny of Table No.IV which is derived from the blood sugar charts, it is seen that in the 15 cases in which lumbar puncture was performed at the end of the blood sugar series, the average fasting level of the blood sugar was .100% and the average level after glucose, of the spinal fluid sugar was .071%. Compared with the figures in Table No.I. the blood sugar fasting level was merely .005% higher but

TABLE OF GRAPHS.

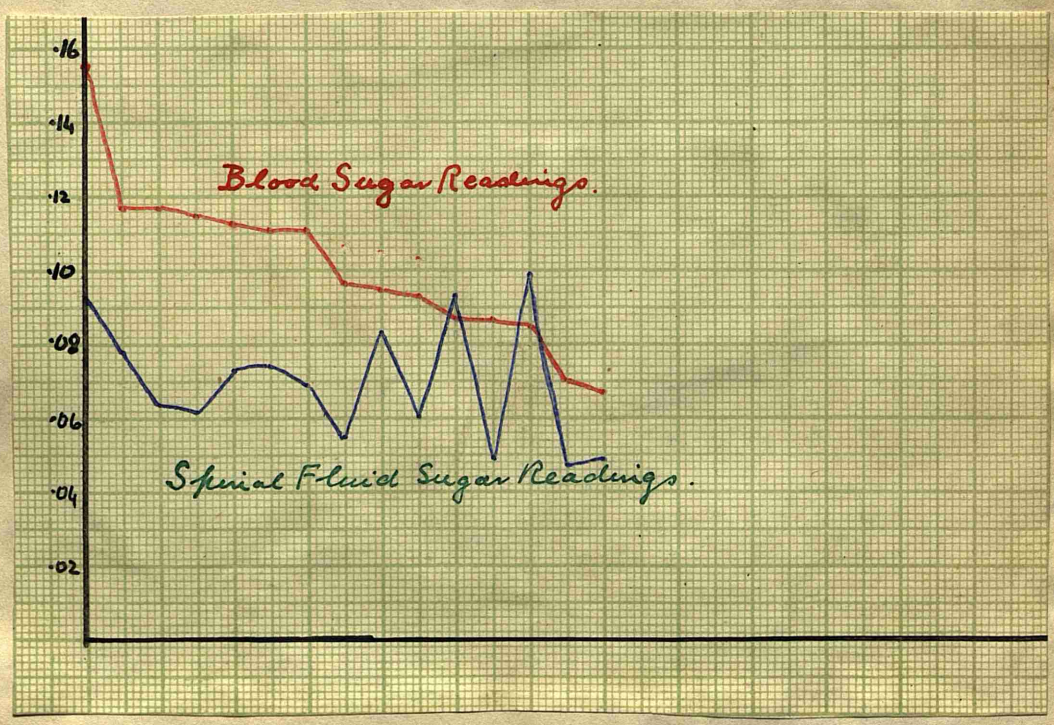
Graph No.I derived from Table No.1.*

showing the sugar content of corresponding specimens of blood and spinal fluid taken simultaneously after 12 hours fasting. The blood sugar readings are arranged in descending numerical sequence and the results are plotted as a graph.



Graph No.II derived from Table No.IV.

showing the blood sugar content at fasting level and the corresponding spinal fluid sugar content several hours after the administration of glucose.



Experiments on the Sugar Content of the Blood and Spinal Fluid.

the average spinal fluid sugar level was .015% higher. The ratio between the fluid sugar and the blood sugar was on an average 70 with a minimum of 54 and a maximum of 107; this ratio is higher than the ratio which obtained in Series I.

When the results in Tables I and IV are plotted as graphs, it is seen that in Graph No.I the fluid sugar readings are roughly parallel to the blood sugar readings. In Graph No.II that relationship is distorted. Accordingly an investigation was made to determine the effect of the ingestion of glucose on the spinal fluid sugar.

Experiments on the Sugar Content of the Blood and Spinal Fluid.

Series V

in which contemporaneous sugar estimations were made at intervals after the administration of glucose of the blood and spinal fluid in 3 cases of encephalitis (See charts 21, 22, 23. Also charts 24, 25 and 26).

Lumbar puncture was done immediately the first blood specimen was taken, and a sample of fluid was withdrawn. The lumbar puncture needle and stylette were kept in situ. Fifty grams of glucose was given. Samples of fluid were removed at half-hourly intervals by withdrawing the stylette, the first drops on each occasion being discarded. All the patients were lethargic and at first lay quiet, later they complained of being cramped in the back. When they complained the procedure was discontinued.

Chart 21. The blood sugar curve shows delay in attaining its maximum but the fall when it occurs is rapid. On plotting the spinal fluid sugar values, a gradual rise begins after the first hour. It is noteworthy that the highest reading for the spinal fluid sugar was obtained when the blood sugar had returned to fasting level. The second specimen of urine showed a slight reduction of Benedict's solution.

Chart 22 from a pregnant woman shows a case of glycosuria, perhaps renal in type. There is a rapid rise in the blood sugar and the spinal fluid sugar begins to increase after half an hour.

Chart 23. The blood sugar curve takes 2 hours to attain its maximum and the fall, as far as is shown, is equally gradual. The appearance of an increase in the

spinal fluid sugar is delayed by one hour.

Charts 24 and 25 show blood sugar curves from two cases of encephalitis; chart 26 was from a case of tuberculous meningitis. In these patients, two lumbar punctures were made, one before the exhibition of glucose, the other along with the withdrawal of the last blood specimen.

Chart 24. The blood sugar curve shows some delay in liver storage. The second reading of the spinal fluid sugar is .06% compared with the fasting level of .045%.

Chart 25. The sugar curve is abnormally high and prolonged. The first specimen of spinal fluid contained .061% of sugar; the second taken 3¼ hours later contained .094% of sugar. The woman had an enlarged thyroid gland but there was no exophthalmos.

Chart 26 was from a case of tuberculous meningitis. The low spinal fluid sugar at the onset, viz. .024% increased to .029% after 2½ hours.

In the first three cases a definite spinal fluid sugar curve is demonstrated and the other 3 charts give further evidence of its existence. This curve shows delay in starting compared with the blood sugar curve. The highest sugar readings for the spinal fluid occurred when the blood sugar curve was in the descendant. Unfortunately the decline of the fluid sugar curve could not be demonstrated as the patients became restive. The actual rise is a small one, the highest being an increase of .033% in 3¼ hours (Chart 25.) but the level attained may exceed the fasting level of the blood (Chart 23). The nature of the curve evidently bears a relation both to the height and the prolongation of the blood curve.

Experiments on the Sugar Content of the Blood and Spinal Fluid.

Discussion.

No reference to the existence of a spinal fluid sugar curve can be found in the literature, but high values for the fluid sugar are known to occur in diabetes. For instance Sehan and Nixon (25) found a spinal fluid sugar of .729% associated with a blood sugar reading of .747%. It is obvious that a fuller study of the spinal fluid sugar curve could but be made in severe cases of diabetes. Probably the rise in the fluid of normal persons would be too low to be appreciated.

It might be objected that the spinal fluid curve demonstrated is due to the fact that the fluid was taken from cases of encephalitis where a definite lesion on the vessels of the central nervous system is known to exist. But Charts 19 and 20 from cases of Intestinal Toxaemia showing quite unusually high blood sugar curves, give fluid sugar figures of .074% and .099% after the consumption of glucose. These figures are both above the average fasting level of .056% found in Table No.I where the highest fasting level found was .070%. Their fluid blood ratios are also high, viz. 67 and 106. Similarly Chart 10 from a doubtful case of encephalitis complicated by rheumatic fever, gives a fluid blood ratio of 87. It is likely that whenever there is an abnormally high or prolonged blood sugar curve, a spinal fluid sugar curve could be detected without difficulty.

Disregard of the time relationship between lumbar puncture and a meal, has evidently been responsible for the high spinal fluid sugar figures obtained from

Experiments on the Sugar content of the Blood and Spinal Fluid.

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many cases of encephalitis. The high figures also obtained by observers such as Hopkins (14) and Levinson (17) in such diverse conditions as pneumonia, nephritis, erysipelas and morphine poisoning, could similarly be accounted for, as well as the anomalous relationship between the sugar of the fluid and the blood in which the fluid sugar equalled or excelled that of the blood.

Alcohol as well as sugar passes readily into the cerebro-spinal fluid. Schottmuller (quoted by Levinson) (17) showed that after the administration of alcohol, the alcohol was found in higher concentration in the cerebro-spinal fluid than in the blood. It is probable that the estimations were made at a time when the blood alcohol wave was on the decline and the spinal fluid alcohol wave at or near its crest.

It is evident that only when specimens of fluid and blood are taken together after a period of fasting can a true ratio between them be obtained. No matter what method of sugar estimation is employed it would appear that if the ratio is less than 50 the sugar content of the fluid may be said to be decreased; if the ratio were to exceed 70, there would be grounds for claiming the existence of a "hyper-glycorrhachia."

IV. The Sugar and the Ketone Bodies in the Urine.

I. Sugar.

The urine passed after a meal from the majority of cases in the acute stage whether febrile or not, showed a certain departure from normal. On boiling together for two minutes equal parts of urine and freshly made Fehling's solution, there was an alteration in colour and translucency of the liquid. The effects obtained varied from a clear green, through an opalescent olive green, to a dirty brown turbid solution. Maclean (12) considers that the majority of such reactions are evidence of the presence of small amounts of sugar above normal. Certainly, those cases showing an abnormally high or prolonged blood sugar curve gave urines producing such phenomena. In the severe cases, Fehling's solution was more definitely reduced and the urine from such cases often caused a degree of reduction even where the sample was passed after 12 hours' starvation. (See charts.) As a patient's general condition improved and the tongue cleared, the urine lost its power of reducing Fehling and convalescents rarely had urine causing reduction. In convalescents causing reduction, a degree of reducing power was probably a normal property of the urine.

These ambiguous reactions seem to be common in all febrile disorders. They were found in the urines from patients with scarlet fever, diphtheria, measles, erysipelas and phthisis. For example, specimens of urine were obtained from two sanatoria each containing 34 patients. One sanatorium contained chiefly advanced/

advanced cases of phthisis; 28 of the 34 urines from this ward reduced Fehling's solution. The other sanatorium used as an observation-ward, where most of the patients had not tuberculosis and were up and about, provided specimens of which only 7 caused reduction.

Though this phenomenon is obviously of no diagnostic value, the disappearance of a reducing substance from a patient's urine in the course of an illness, might conceivably be of some prognostic significance.

II. Ketone Bodies (See Table No.V.)

The urine taken the day after admission of 21 out of 30 cases (70%) of encephalitis in children gave a positive Rothera reaction. In 3 cases only was the test positive during the second week. Only 9 out of 30 adult patients (18%) gave a positive reaction, often faint, on the day after admission, but in all cases this rapidly disappeared.

Ketone bodies are known to occur in the urine from certain fevers particularly scarlet and measles. In the latter connection specimens of urine taken immediately after admission to hospital from 20 patients, including four adults, in the acute stage of scarlet fever, gave strongly positive reactions in 19 cases (95%).

Apart from the specific fevers, Frew (9) showed that 60% of all cases medical and surgical admitted to a Children's Hospital had "acetonuria" on the second day/

day after admission. The acetone had usually disappeared by the fourth day. He showed that a positive Rothera reaction did not depend on the nature of the disease. He attributed the ketonuria to a temporary failure of digestion brought about by alteration in diet and he concluded that it was very common in childhood.

Although ketonuria is so frequent in children and is merely an indication of altered metabolism due to a great variety of causes, often trifling ones, the routine application of the Rothera Test gave a clue to the nature of the illness in four cases (certified encephalitis) which were admitted to hospital during the epidemic. Two of these cases are discussed in the next section.

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The Application of the Results Obtained to the Diagnosis of Encephalitis.

I. The Spinal Fluid Sugar Content.

In infective meningitis the spinal fluid sugar is decreased absolutely as well as relatively to the blood sugar, and it is within normal limits in encephalitis. It was found that a rough idea of the sugar content of the fluid could be obtained as follows:-

Boil one inch of freshly made Fehling's solution in a test-tube. Add one inch of spinal fluid and boil carefully for two minutes. Examine immediately. If against a black background the solution shows a red or brown opalescence the sugar content is not decreased. If the opalescence is greenish a decrease may be suspected. If there is no reduction even after adding drop after drop of dilute acetic acid, the amount of sugar is infinitesimal. In all instances, unless the amount of sugar is excessive, the solution should remain blue by transmitted light.

If a specimen of fluid is purulent, there is no question of encephalitis; if clear, tuberculous meningitis must first be eliminated. To appreciate fully the role of sugar estimations among other examinations of the spinal fluid, a resume of these is given. The notes are based on the examination of the spinal fluid in 126 cases, 88 of which were considered to be encephalitis. The series included 12 cases of tuberculous meningitis. Unfortunately no case of brain tumour or cerebro-spinal syphilis occurred

(25)

in the series, but from the work of Sehan and Nixon it was found that the sugar content of the fluid is apparently normal in brain tumour, cerebro-spinal syphilis, tabes dorsalis, syphilis, hemiplegia, disseminated sclerosis, neurasthenia and arterio-sclerosis - diseases which include most of those of nervous origin liable to be confused with encephalitis. In hysteria these writers found a slight increase in the sugar, but it was so small as to render it useless for diagnostic purposes. It would appear that only in the differential diagnosis between encephalitis and tuberculous meningitis, was the estimation of sugar worth while.

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Notes on the Examination of the Spinal Fluid.

A diagnosis of tuberculous meningitis was made on the findings given below which are compared with those found in the acute stage of encephalitis.

A. Suggestive.

(1). A clear fluid usually escaping under greatly increased pressure.

In encephalitis the fluid is clear but the pressure is not always increased. Only rarely is the pressure increased to the extent found in tuberculous meningitis.

(2) The formation of a pellicle on standing. This formed in from ½ - 12 hours. (18) Its absence does not exclude meningitis.

Pellicle never formed in this series of cases of encephalitis and this conforms with the literature/

The Application of the Results Obtained to the Diagnosis of Encephalitis.

literature on the subject. But in the journals of the Hospital is found the records of what was presumably a case of the meningeal type in which pellicle formation occurred. The post-mortem findings were those of encephalitis, viz. sleeve haemorrhages, round-celled perivascular infiltration and degenerated nerve cells. The meninges were infiltrated with mononuclears and plasma cells. No organisms were found.

(3) An increased cell count.

Method of counting. The fluid was examined as soon as possible after withdrawal. The test-tube containing it was shaken and a drop placed on the stage of a Thomas Zeiss haemocytometer. The number of cells in the large square was counted. This gave the cell content of 1/10 cub.mm. of fluid. The number multiplied by 10 gave the cell content per cub.mm. A series of readings was taken and an average made. The possibility of red cell contamination was controlled by centrifuging the fluid and staining the deposit with Leishmann's stain. The stained cells also enabled a differential count to be made.

In the series of tuberculous cases the counts varied from 150 to 700 per cub.mm. The cells in a healthy subject do not exceed 5 per cub.mm. (Levinson). In encephalitis, 45% of cases in the acute stage showed no increased cell count. Counts over 100 were/

were uncommon, but in one case the number reached was 340. It was found that a cell count of over 100 could readily be detected by the naked eye.

(4) The cells are usually an admixture of mononuclear and polymorphs.

In the 12 cases examined, polymorphs were present up to 65%. In one case only were mononuclears found alone.

In encephalitis, mononuclears, apart from an occasional endothelial cell and a very occasional polymorph, were the only types found.

(5) An increase of globulin.

The Nonne-Apelt Test (phase I) was employed: equal parts of spinal fluid and a concentrated solution of ammonium sulphate neutral in reaction, are mixed in a test tube. If a white precipitate occurs in 3 minutes the globulin is said to be increased. (quoted from Levinson)(17).

In Tubercular meningitis the solution was usually milky and opalescent. This contrasted with the appearance in encephalitis where the precipitate, present in 18% of the acute cases, was slight.

(6) A low sugar content.

B. Definite. The finding of the tubercle bacillus in the pellicle.

In 3 of the 12 cases, tubercle bacilli were not found till post mortem.

The following two cases illustrate the application of sugar estimations to the spinal fluid.

Case I. (see Temperature Chart No.1.)

J.M., a boy aged 4, certified Lethargic Encephalitis, was/

The Application of the Results obtained to the Diagnosis of Encephalitis.

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was admitted to hospital on the 15th day of illness. The illness began with vomiting and headache. He became drowsy and suffered from time to time from pain on the right side of his face.

On admission he complained of pain in the back of his neck. His head was slightly retracted and the neck muscles were rigid. The pupils reacted well. The abdominal reflex was depressed. Kernig's sign was indefinite. Pulmonary signs were absent. His appearance and history suggested Tubercular Meningitis. There was no tuberculosis in the family.

Lumbar Puncture after 6 hours' starvation.

Cell count 210 per cub.mm., 6% being polymorphs.

Nonne Apelt Test:- slight milkiness.

Sugar: green opalescence against a dark background on boiling with Fehling's solution.

By estimation: .035%. Blood sugar: .080%.

No pellicle formed on standing for 24 hours and no tubercle bacilli were found after centrifuging.

Comment:- In favour of meningitis were the presence of polymorphs and the low sugar content, but the reading for this .035% was not far below .042% the lowest figure in Table I. The ratio between fluid sugar and blood sugar was low, viz. 44. The absence of clot was unusual in meningitis. The cell-count and the globulin increase would conform with either disease.

Three days later the head retraction was much less evident. There was ptosis of the left eye-lid. The pupils were dilated and fixed. Continuous myoclonic movements of the muscles of the fingers and forearms were present./

present. Both cheeks showed occasional twitchings. The child's condition was very serious. The temperature had been swinging from 98°F. to 102°F.: the pulse rate had varied between 60 and 140: the respirations had crept up from 30 to 45.

Lumbar Puncture repeated after 6 hours' starvation.

Fluid clear under considerably increased pressure.

Cell count 290 per cub. mm., 2% being polymorphs.

Nonne-Apelt Test: definite milkiness.

Sugar estimation: .024%.

Again no clot formed and no Tubercle Bacilli were found.

Two days later the child was obviously going to die. He was unconscious. The respirations were 60 and the pulse rate and temperature still swinging. There was double ptosis: the left pupil remained dilated and fixed, the right being minutely contracted. The right arm and hand were rigid and held against the body in the position of tetany. The left arm made vague searching movements into the air. There was abdominal retraction and retention of urine.

Next day the boy died. At the post mortem, the gelatinous exudate at the base of the brain was found to be swarming with tubercle bacilli.

Comment: The variety of symptoms, viz. ocular palsies, myoclonic movements, rigidity etc., though not uncommon in tuberculous meningitis, made the diagnosis doubtful from the clinical point of view especially as encephalitis was rife at the time. The spinal fluid did not clot - a rare occurrence in tuberculous meningitis - and it happened that the bacilli were not found. The presence of polymorphs and the low sugar content alone made possible a sure diagnosis.

The Application of the Results Obtained to the Diagnosis of Encephalitis.

Case II. (See Temperature Chart No.2.)

R.C. a boy aged 16 on waking in the morning had intense occipital headache and pains radiating over the shoulders and down the spine. He went to work but had to abandon it. In the afternoon he found that he was unable to bend his head forward. For a few hours he was said to have had twitchings of his right foot. On the following day he was admitted to hospital certified Cerebro-Spinal Meningitis.

The boy did not look very ill. He was mentally bright and was very talkative. His temperature was 101° and his pulse rate 88. There was distinct head retraction and the neck muscles were rigid. Hie head could not be moved forward and any attempt to do so caused considerable pain. The only other definite signs apart from a lightly coated tongue, were a complete absence of the abdominal reflex and an obliteration of the naso-labial folds, but there was no definite facial paralysis. The urine gave a positive Rothera reaction and on boiling with equal parts of Fehling, the solution was green and opalescent. Clinically considered, the case might well have been an early meningitis.

Lumbar Puncture after 9 hours starvation:-

A clear fluid (under slightly increased pressure.

Cell count: 50 per cub. mm., all mononuclears.

Nonne Apelt Reaction: slight but distinct precipitate.

Sugar: Fehling's solution red against a dark background.

No pellicle formed on standing, and no organisms were found.

The Application of the Results Obtained to the Diagnosis of Encephalitis.

Comment: On account of the absence of pellicle formation and the absence of polymorphs, it was presumed that the case was not one of meningitis. The normal sugar content increased this presumption.

In 2 days the headache and rigidity of the neck disappeared. In a fortnight the abdominal reflex had returned and the face resumed its full expression. The Wassermann turned out to be negative.

Comment: The only possible diagnosis, as the case occurred during an epidemic, seemed to be encephalitis.

Conclusions: These two cases were unusual and it is rarely that an examination of the sugar content of the fluid is called for. In no single case was it the sole indication of the nature of the disease; it merely confirmed a diagnosis already suggested on other indications. Only in the differential diagnosis of encephalitis from tuberculous meningitis is a knowledge of the spinal fluid sugar of value and that value is limited.

II. The Ketone Bodies in the Urine.

The following two cases illustrate the value of the application of the Rothera Test to the urine.

Case iii. (See Temperature Chart No.3.)

J.McG. a boy aged 10 certified encephalitis was admitted to hospital on his second day of illness. The previous/

previous morning he complained of intense frontal headache and severe abdominal pain. In the afternoon he had become drowsy and at night he was delirious, attempting to get out of bed.

On admission he looked acutely ill. His lips were cyanosed and he sweated profusely: his pulse was of poor quality and he lay in a restless delirium. His tongue was thickly coated and his mouth dirty. From time to time he vomited a greenish vomit and his breath was reeking with the smell of acetone. The stools were loose, green and contained mucus. His temperature was high.

For several days his temperature remained elevated and he remained in a similar condition, drowsiness alternating with the bouts of delirium. On rousing him, he was extremely irritable and mentally confused. His eyelids were drooping and suggested a double ptosis. He occasionally had sighing respirations.

When the temperature fell he quickly improved and he was perfectly bright and normal in a week.

During his illness the urine gave a strongly positive Rothera reaction. (Gerhardt's reaction was also positive.) The ketone bodies did not disappear from his urine till his 15th day in hospital.

Lumbar puncture was done on his 3rd day of illness after taking a series of specimens for blood sugar estimation (See Chart No.19). The spinal fluid gave

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a faintly positive Rothera reaction, otherwise it showed nothing abnormal. The blood sugar curve rose in one hour from .11% to .253% and did not regain its original level after 3 hours.

On enquiry into hie previous history it was found that he was subject to bilious attacks. Three months after dismissal he reported himself to the hospital. During the interval he had apparently been quite well.

Case iv. (See Temperature Chart No.4.)

W.M., a boy aged 6, certified encephalitis: was admitted to hospital with a history of headache, vomiting and drowsiness occurring the day before.

On admission he was in a drowsy condition and on being disturbed was mentally confused. His face was flushed and his temperature elevated. He vomited occasionally and there was a heavy scent of acetone round him. His stools were loose and green but there was no mucus. His tongue was heavily coated.

For the next 5 days the vomiting and diarrhoea continued and he remained drowsy and listless. At times his respirations were prolonged and sighing. As the temperature fell the vomiting stopped, but his stool/

stools remained green for nearly 3 weeks. All this time he was mentally clear but he showed little interest in his surroundings.

Lumbar puncture on the 4th day of illness gave a fluid showing no abnormality save a faintly positive Rothera reaction. The blood sugar curve (see Chart 20) was diabetic in type rising from .085 to reach a maximum of .295 at the end of two hours. The urine contained ketone bodies for nearly four weeks. Six weeks after admission, the blood sugar curve was that of a healthy person.

His past history showed that 3 weeks before admission he had a similar but less severe attack of vomiting associated with lethargy. Three months after dismissal from hospital he had another attack of vomiting lasting several days and associated with delirium.

Comment:- The diagnosis made in such cases was Intestinal Toxaenia and ketonuria. When recounted on paper the fact that the trouble was not encephalitis seems obvious, but in practice the matter was not so simple. The association of delirium, sighing respirations, drowsiness and temperature is common to both conditions. The drooping eyelids suggested a true ptosis. During the epidemic, encephalitis in children frequently began with vomiting and diarrhoea.

On clinical grounds the diagnosis was made on the prominence of the gastro-intestinal symptoms and the obtrusive odour of acetone in the breath. It was confirmed by the very positive Rothera reaction given by/

The Application of the Results Obtained to the Diagnosis of Encephalitis.

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by the urine and by the definitely abnormal sugar curves showing marked disturbance of metabolism. Cammidge (4) reports a similar disturbance in a case of cyclical vomiting in a boy aged 11, in which the blood sugar curve showed a sudden rise to an abnormal level (.14% rise in half an hour) followed by an equally rapid fall.

The Physiological Interpretation of the Results.

Two points of physiological interest arise: first, that the spinal fluid sugar at fasting level is lower than that of the blood; second, that the spinal fluid sugar curve is a delayed curve.

A right interpretation of these facts is as difficult to-day as it was in 1914 when Cushing wrote: "As regards the cerebro-spinal fluid we stand in much the same position as did the pre-Harveian phlebotomist in regard to the circulation of the blood." The orthodox view of the circulation, formation, and absorption of the cerebro-spinal fluid may thus be stated. The fluid originates from the choroid plexuses in the ventricles by a process of secretion. Passing out of the ventricles by the foramina of Magendie and Luschka, it circulates in the subarachnoid space about the brain and cord and escapes by the arachnoid villi into the great sinuses.(3) The subarachnoid space communicates with the perivascular spaces and the fluid is thus brought into contact with the actual nerve cells. The fluid probably brings them nourishment and removes waste products.(21) As Weed(28) points out, "the fluid obtained by lumbar puncture represents not only the secretion of the choroid plexus, but also the fluid waste products of nerve cell activity poured into the subarachnoid space by way of the perivascular channels."

The foregoing figures show that the sugar content of/

of the spinal fluid is lower than that of the blood. Although we do not know the sugar content of the fluid as secreted into the ventricles - and, as Mott (21) says "This is a vital point" - it is conceivable that the fluid during its circulation loses some of its sugar to the nerve elements. This hypothesis is strengthened by the fact that the carbon dioxide content of the fluid is high. The loss of sugar resulting may partly explain the discrepancy in the sugar levels of the spinal fluid and the blood. Haan and Crefeld (10) suggest as an additional reason that some of the blood sugar is in a non-dialysable form.

The delay in the fluid sugar curve may be accounted for by the time taken in the circulation and diffusion of the fluid of increased sugar content from the ventricles to the sub arachnoid space of the lumbar region.

The above interpretation depends entirely on the truth of the choroid plexus theory of formation. This theory has been challenged by various observers. Hassin (13) brought forward evidence suggesting that the fluid originates in the tissue of the brain and spinal cord and that its function was to carry away waste products. He thought that it circulated upwards and was absorbed not only by the arachnoid villi but by the choroid plexus itself.

Again there appears to be no proof that the foramina between the ventricles and the sub-arachnoid space actually exist in the living person. (24) If they are merely post mortem artefacts, the intraventricular fluid would be shut off from the subsrachnoid fluid and might be expected to differ/

The Physiological Interpretation of the Results.

differ in its properties. There is considerable evidence of such a difference. Schmorl (quoted by Cruickshank)(6) observed that in icterus, the sub-arachnoid fluid, but not that of the ventricles, was discoloured. The latter contained bile pigment, only when there was an extensive necrosis of the epithelium covering the choroid plexus. Also in a case of diabetus mellitus, he found sugar in the subarachnoid fluid but not in the intra-ventricular fluid. Of seven cases of general paralysis each of which had given positive Wassermann results in both blood and fluid during life, he found that the spinal fluid was positive in all, but the intra-ventricular fluid was negative in six. In the seventh case where a positive Wassermann was given by the intra-ventricular fluid, the choroid plexus showed extensive degeneration.

Changes in the fluid after death may account for certain of these results. In four cases personally examined, spinal fluid and intra-ventricular fluid were withdrawn 24 hours after death, but in none was there a trace of reducing substance.

If the two fluids are not identical, the subarachnoid fluid may originate in the substance of the brain and cord, being ultimately derived from the blood; the meninges may also play a small part.(24) Bungart (quoted by Rost) resected and ligated the sub-arachnoid space in animals in two places and allowed the isolated fluid to empty itself. After twelve hours, it was again filled with fluid. Perhaps this was merely an irritative reaction.

As to the exit of the fluid it is possible that its main/

main way of escape is by diffusion into the veins of the cerebro-spinal axis and meninges. In the lumbar region the circulation of the fluid may be in the main a local one. The rarity of accidents following spinal anaesthesia, (Jonnesco's series of 2436 showed no fatalities)[15] does not favour a rapid or considerable upward circulation.

In the light of this second and somewhat heteredox theory, the two facts under consideration might be explained on the ground of a slow filtration or dialysation of the sugar from the blood into the fluid and a slow absorption from it. The last factor would permit the concentration to remain high in the spinal canal after the excess of fluid in the blood had been more rapidly removed by storage in the liver.

To sum up, until more is known of the circulation of the spinal fluid, speculation is futile, and we remain in the position of Cushing's pre-Harveian phlebotomist.

That the sugar content of the spinal fluid is diminished in meningitis is in some respects contrary to expectation. It might be imagined that the inflamed meninges and choroid plexus would be more permeable to the passage of substances into the fluid from the blood. Thalhimer and Updegraff[27] suggested that the choroid plexus in tubercular meningitis holds back the sugar from the spinal fluid just as nephritic kidneys hold back sugar from the urine. Achard[1] ascribed the small amounts of sugar to the presence of "microbes en grand nombre/

The Physiological Interpretation of the Results.

nombre qui le consomment" but Worster Drought and Kennedy (29) showed that in cerebro-spinal fever, the presence or absence of sugar were not influenced by the number of organisms present. Neither of these explanations is altogether satisfactory and a further one may be advanced.

In meningitis, there is an increase in the amount of fluid in the sub-arachnoid space; it contains increased protein and it co-agulates on standing. In many other of its physical and chemical characteristics it differs from healthy spinal fluid. It is a fluid altered and added to by the inflammation of its enclosing membranes. The dilution resulting may be an additional factor accounting for the low sugar-content. Though not strictly comparable, a specimen of pleural fluid crowded with tubercle bacilli was examined for sugar after precipitation of its proteins, and was found to contain none.

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VI. A Summary of the Main Conclusions.

1. In epidemic encephalitis the fasting level of the sugar of the blood and the spinal fluid is within normal limits.
2. The blood sugar curves are in some cases normal; in others they indicate a delay in liver storage. These curves are in no way diagnostic as similar curves are found in other conditions.
3. The fasting level of the spinal fluid sugar is lower than the fasting level of the blood sugar. In this series the average ratio was 59, with a minimum of 49 and a maximum of 70.
4. Associated with the blood-sugar curve is a spinal fluid sugar curve. This is a delayed curve. The non-recognition of this curve has been responsible for the high sugar content of the spinal fluid found by many workers in encephalitis and other conditions.
5. A specimen of spinal fluid to be estimated for its sugar content should be taken after 12 hours' fasting along with a sample of blood for similar estimation. If the sugar content of the fluid is normal, its ratio to the blood sugar should lie between 50 and 70.
6. Specimens of fluid taken at varying intervals after a meal give sugar readings which are valid only when these readings are correlated with the complete sugar curves both of the blood and the spinal fluid.
7. The determination of the sugar content of the spinal fluid is of value only in the diagnosis of an infective meningitis, and its value in this connection is chiefly confirmatory of other findings.

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A Summary of the Main Conclusions.

8. In the differential diagnosis of encephalitis in children, intestinal toxaemia is one of the conditions to be eliminated. Its recognition is assisted by the finding of a marked ketonuria and by a considerably disturbed blood sugar curve.

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TABLE NO.V.A. (Patients of ages 0-16 years.)

Name.	Age.	Day of illness admitted.	Following Day.		Week later.	
			Febrile.	Rothera.	Febrile.	Rothera.
S.A.	2	3	+	+	+	+
E.F.	11	23	-	+	-	-
F.G.	3	1	+	+	Died	-
M.H.	7	3	+	+	-	-
M.H.	7	10	+	+	-	-
S.H.	3	20	-	+	-	-
A.McC.	8	4	-	+	-	-
A.McG.	15	8	+	+	-	-
M.McL.	8	9	+	+	+	-
A.McQ.	8	8	+	+	-	-
J.S.	13	11	-	+	-	-
W.T.	4	7	-	+	-	+
J.W.	4	29	-	+	-	-
J.W.	15	14	-	-	-	-
M.F.	12	23	+	+	-	-
D.McA.	8	18	-	-	-	-
S.W.	10	7	-	+	-	-
P.C.	12	14	-	-	-	-
S.R.	9	15	-	+	-	-
E.H.	5	3	+	+	-	-
J.N.	4	5	+	+	+	-
J.S.	4	11	-	+	-	-
J.A.	16	11	-	-	-	-
M.D.	14	20	-	-	-	-
D.K.	15	21	-	-	-	-
R.McK.	11	5	+	+	+	+
D.M.	15	10	+	-	-	-
J.N.	9	20	-	-	-	-
T.P.	12	16	-	-	-	-
D.V.	9	28	-	+	-	-

TABLE NO. V.B. (Patients of ages over 16 years.)

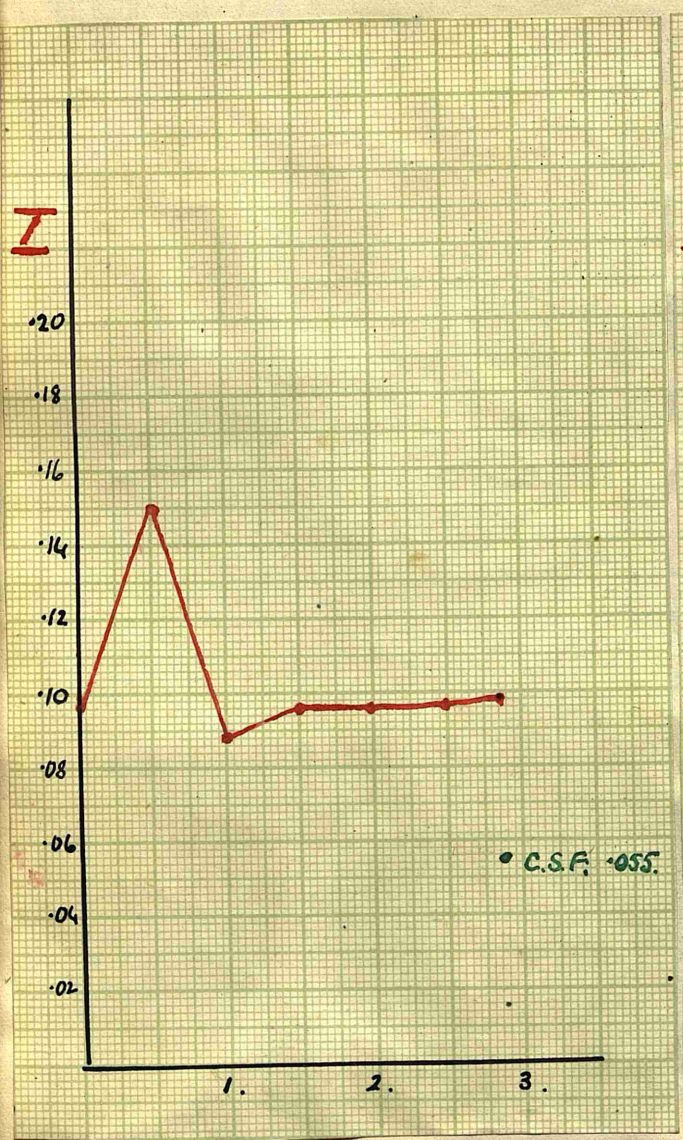
Name.	Age.	Day of illness admitted.	Following day.		Week later.	
			Febrile.	Rothera.	Febrile.	Rothera.
M.A.	34	4	-	+	-	-
M.A.	24	5	-	-	-	-
M.B.	20	3	+	-	-	-
M.B.	54	8	+	+	+	-
M.C.	23	13	+	-	+	-
R.C.	31	8	+	-	Died	
E.C.	20	4	+	-	-	-
H.D.	30	4	+	-	-	-
M.F.	26	4	+	-	+	-
M.L.	30	7	-	-	-	-
E.S.	31	7	+	-	-	-
J.G.	25	12	+	-	-	-
M.J.	41	15	+	-	+	-
S.McP.	36	4	+	+	-	-
M.M.	22	?	-	-	-	-
M.K.	45	30	-	-	-	-
M.R.	38	2	+	-	-	-
E.R.	18	5	-	-	-	-
C.R.	21	20	+	+	+	-
A.S.	20	10	-	-	-	-
J.A.	59	9	+	+	+	-
J.W.	42	7	+	+	+	-
R.C.	18	6	+	-	-	-
J.S.	28	7	+	-	-	-
J.C.	22	2	+	-	-	-
E.M.	39	5	+	-	-	-
E.McG.	42	10	+	-	+	-
J.S.	23	14	-	-	-	-
W.F.	33	7	+	-	Died	
M.C.	16	6	-	-	-	-
E.C.	20	21	+	-	+	-
J.D.	17	21	-	-	-	-
M.S.	37	6	+	-	-	-
A.L.	17	68	-	-	-	-
M.Mc.K.	33	40	-	-	-	-
E.McN.	24	4	-	-	-	-
M.T.	39	8	-	-	-	-
J.W.	24	10	+	-	Died	
J.B.	36	4	+	+	-	-
M.B.	68	4	+	-	+	-
A.C.	25	7	-	-	+	-
J.C.	24	3	+	+	-	-
S.D.	26	21	-	-	-	-
J.D.	47	49	-	-	-	-
T.F.	48	3	+	+	+	-
R.J.	34	10	-	-	-	-
M.McD.	19	5	+	-	-	-
J.McD.	38	2	+	-	+	-
J.M.	20	2	+	-	-	-
J.B.H.	28	10	+	-	+	-

TABLE OF CHARTS.

Chart 1. Encephalitis.

J.S. female. aged 13. 13th day

Mild. A-febrile. Convalescent.



Urine I and II.

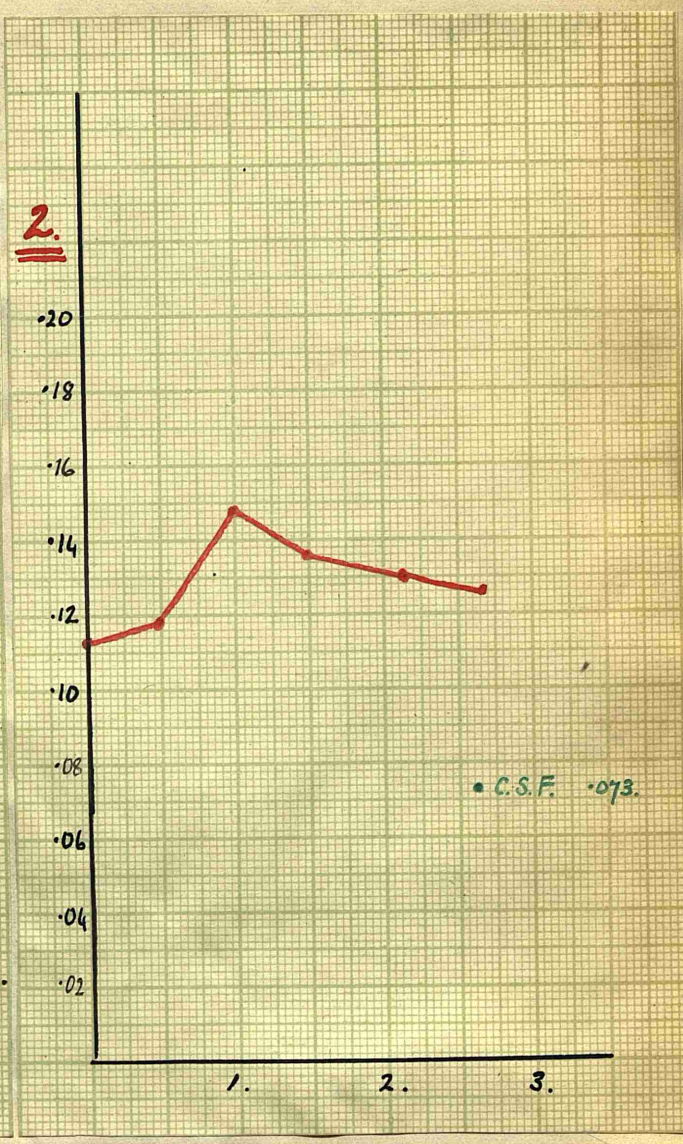
All tests for sugar negative.

Rothera: negative.

Chart 2. Encephalitis.

D.M. male. aged 15. 28th day

Mild. A-febrile. Lethargic.



Urine I and II.

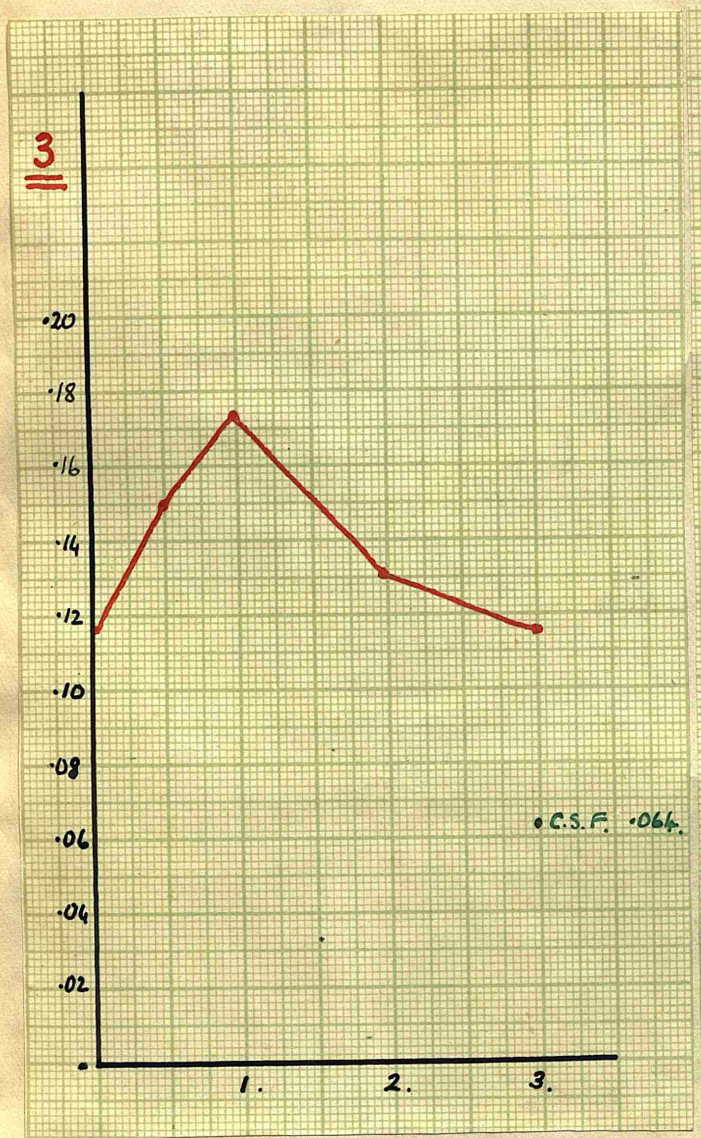
All tests for sugar negative.

Rothera: negative.

Chart 3. Encephalitis.

J.W. Female.aged 15. 17th day

Mild. A-febrile. Emotional.



Urine.

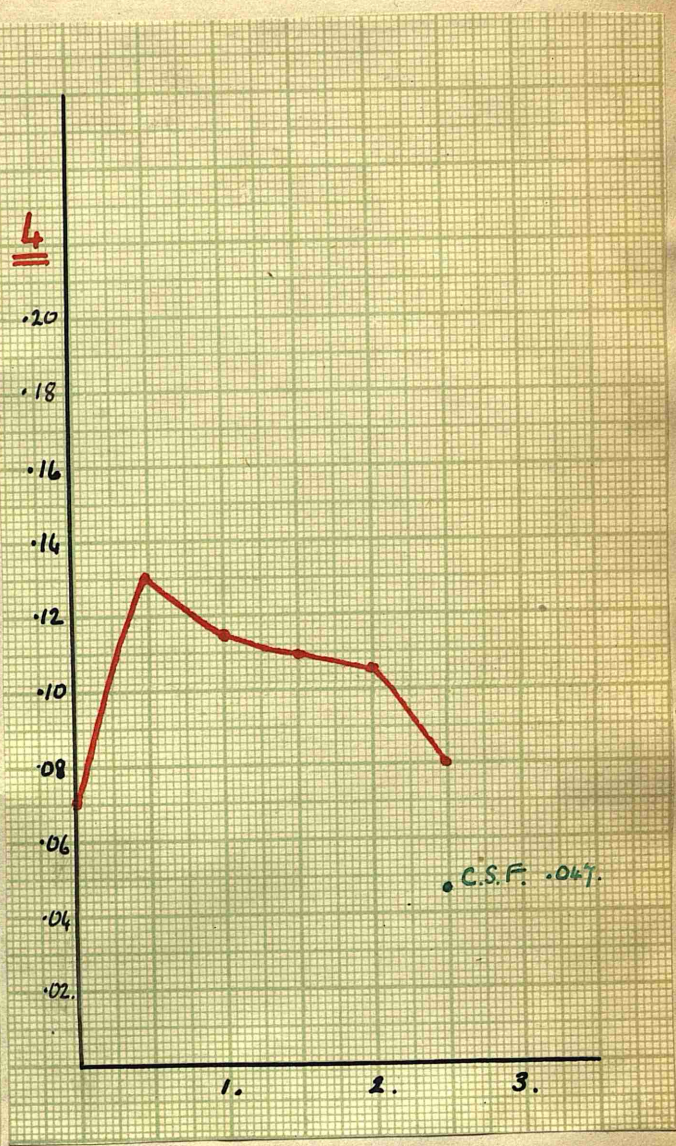
I and II all tests for sugar negative.

Rothera:negative.

Chart 4. Encephalitis.

M.D.male.aged 15.30th day.

Moderate. A-febrile.Lethargic.



Urine.

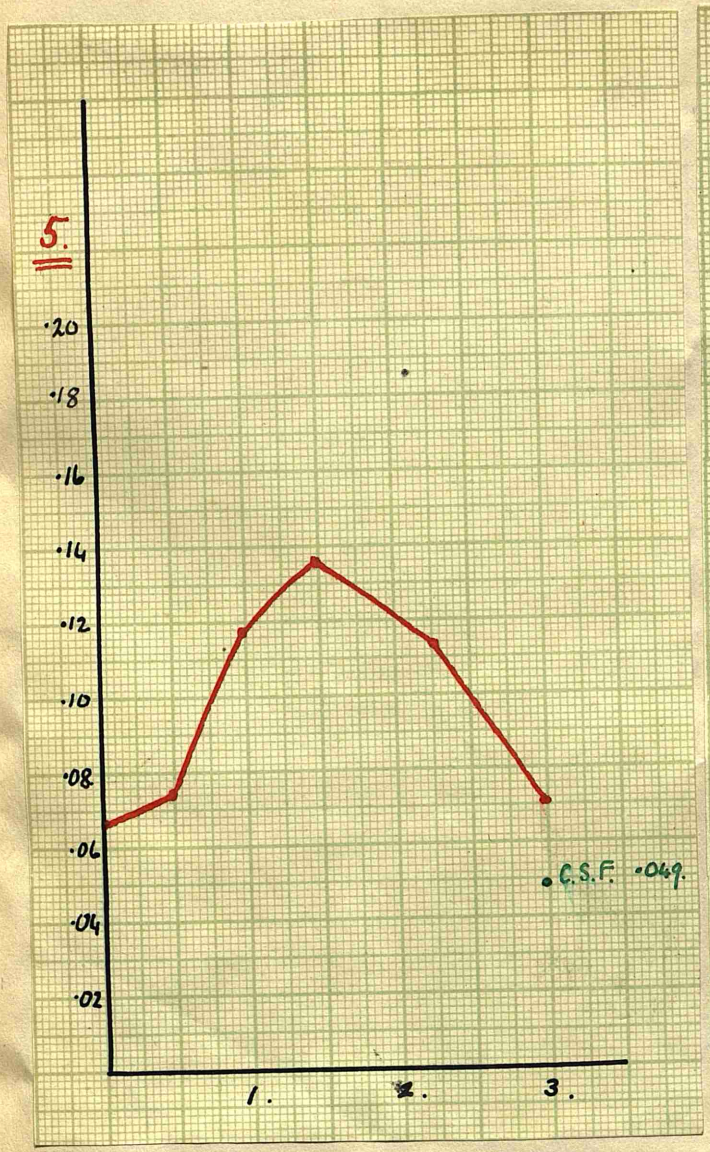
I and II all tests for sugar negative.

Rothera:negative.

Chart 5. Encephalitis.

W.T. Male. Aged 4. 9th day.

Moderate. Lethargic. Febrile.



Urine I and II all tests for sugar negative.

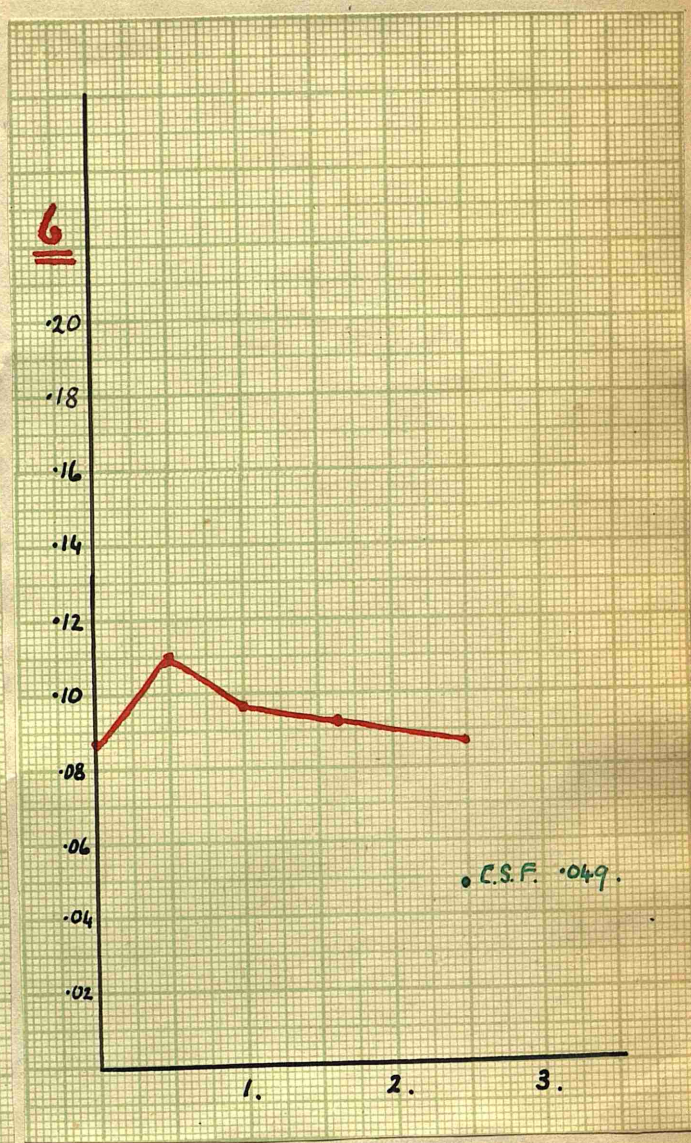
Rothera: positive.

Chart 6. Encephalitis.

Mrs. A. aged 24. 5th day.

Moderate. Febrile. Confused.

7 months pregnant.

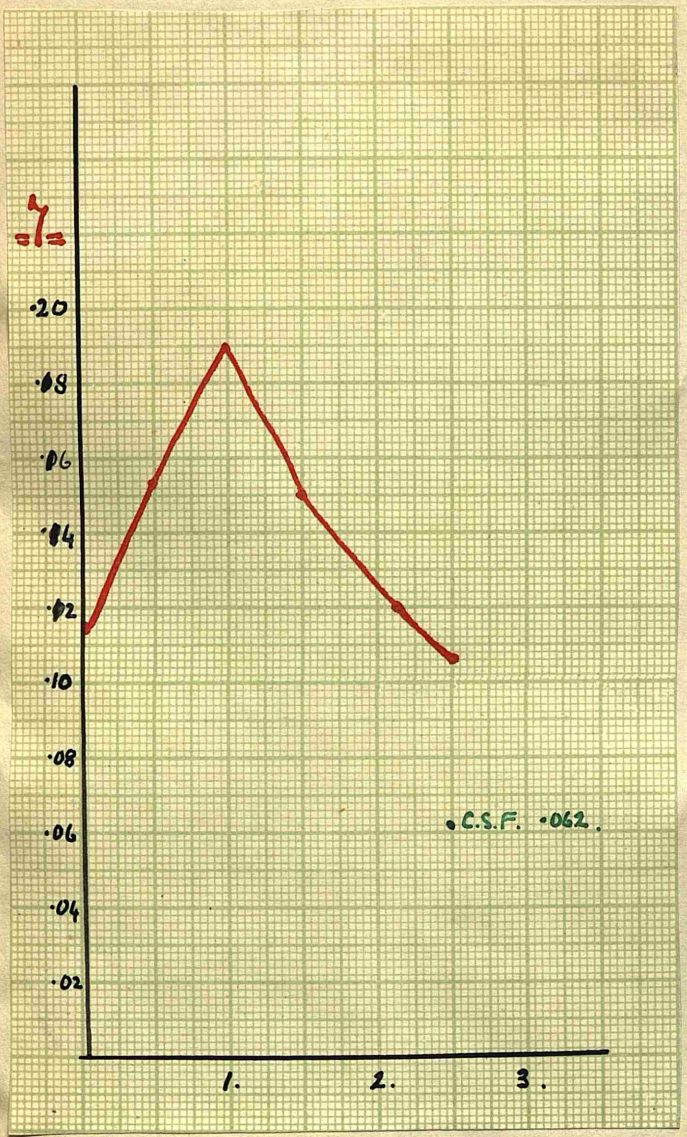


Urine I. Benedict: green, opalescent
Fermentation: few fine bubbles.
II. Benedict: green, turbid.
Fermentation: large bubble.

Chart 7. Encephalitis.

Mrs.A.aged 34.11th day.

Moderate.Febrile.Lethargic.



Urine I.

All tests for sugar negative.

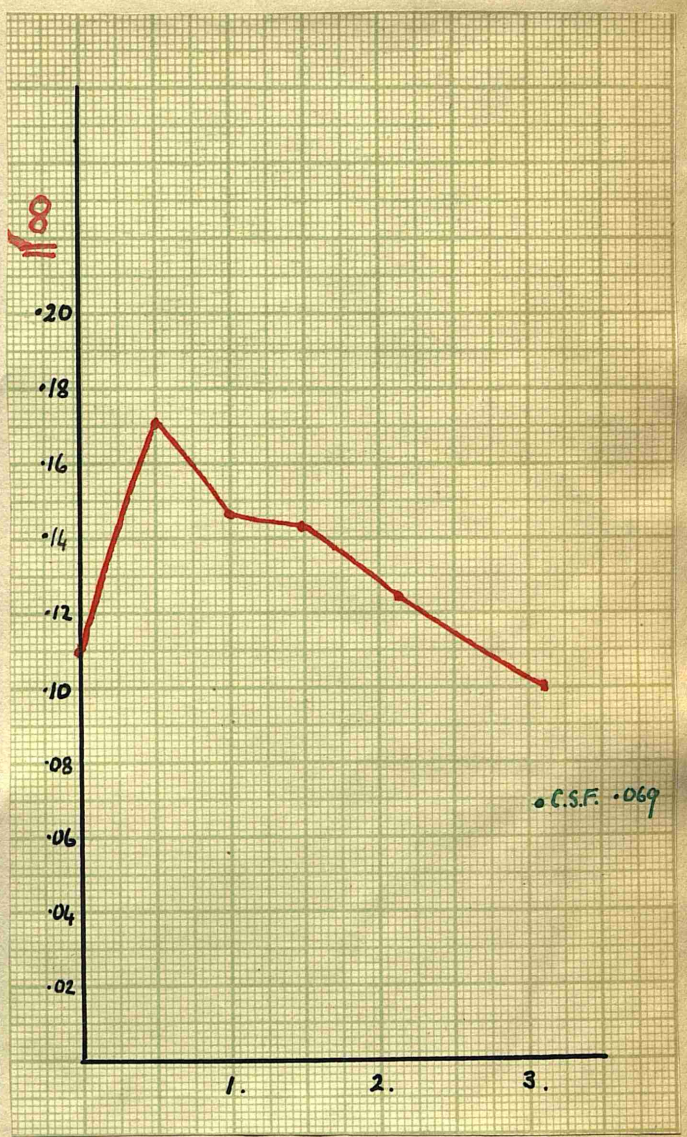
II. Benedict: clear green.
Fermentation:negative.

Rothera:negative.

Chart 8. Encephalitis.

M.H.female.aged 7.12th day.

Mild. Febrile. Squint.



Urine.

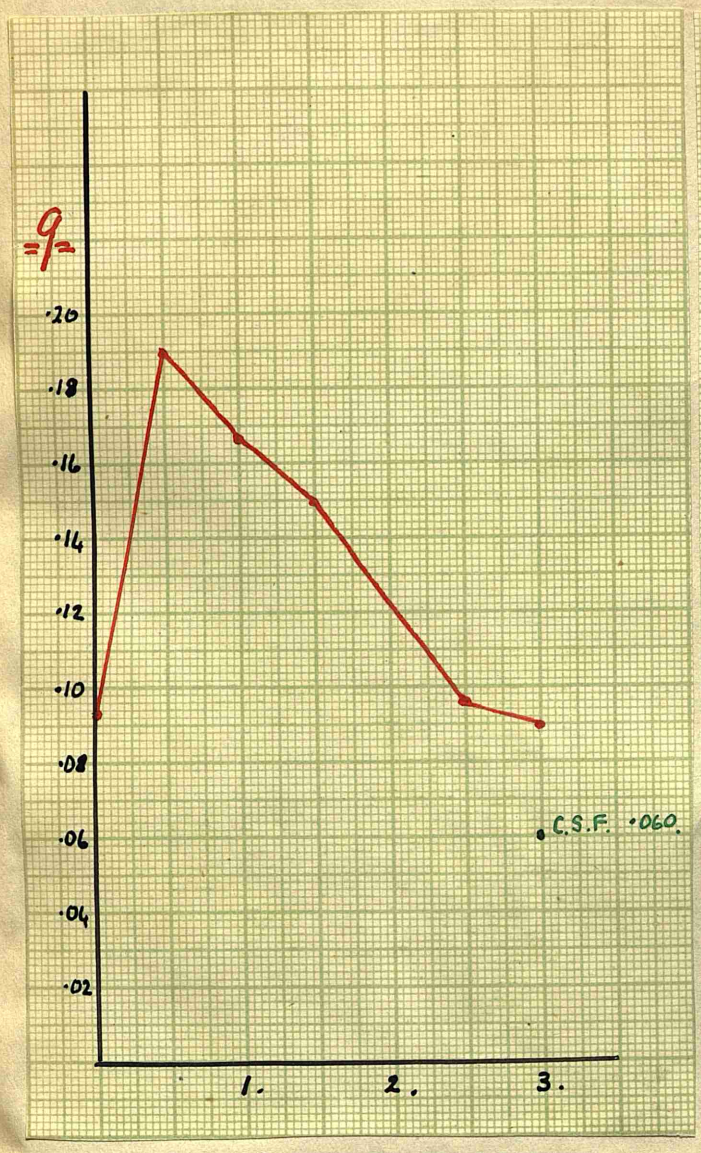
I.Benedict:clear green.
Fermentation:negative.

II.Benedict: green,turbid.
Fermentation: a few fine bubbles.

Rothera:negative.

Chart 9. Encephalitis.

E.C.(female)aged 20.5th day.
Mild. Febrile. Choreiform.



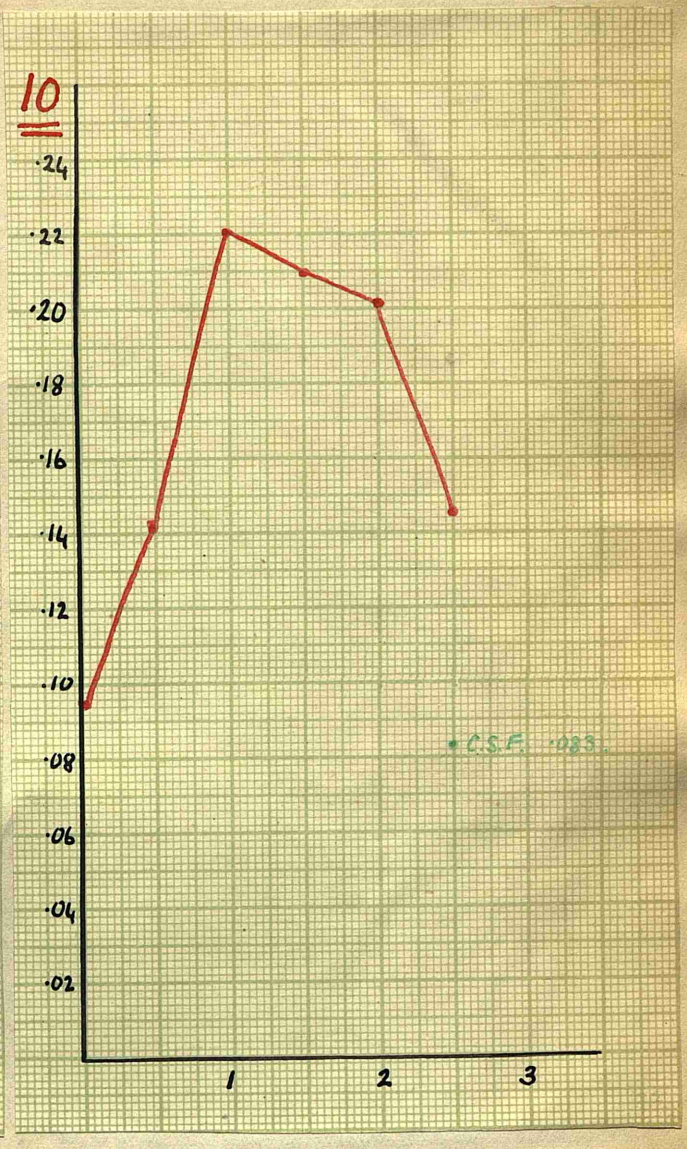
Urine:

I.Benedict: clear green.
Fermentation:negative.
II.Benedict: turbid:yellow green.
Fermentation:distinct bubble.

Rothera: positive.

Chart 10.Encephalitis.?

R.McK.(male)aged 11.10th day
Moderate: febrile: Arthritis.



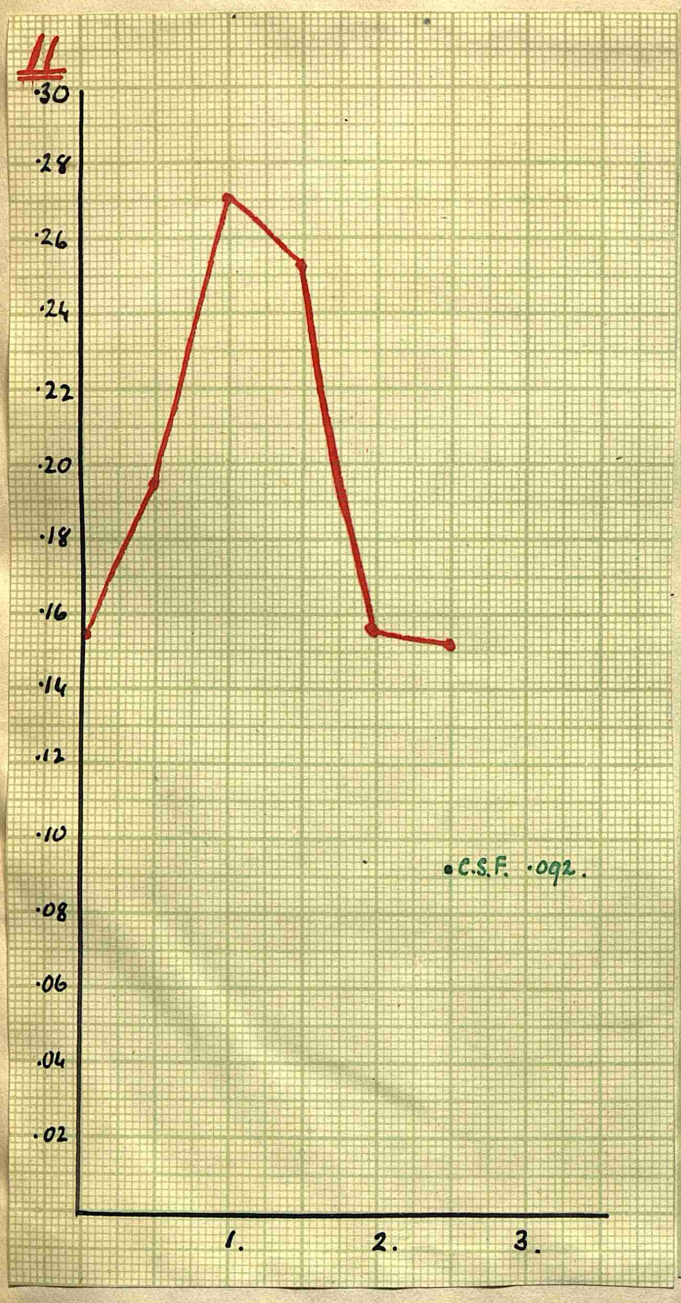
Urine:

I.Benedict:green,opalescent
Fermentation:negative.
II. Benedict:green,turbid.
Fermentation:a few fine bubbles.

Rothera:positive.

Chart 11. Encephalitis.

Mrs.B.aged 54.11th day.
Severe. Febrile. Lethargic.
Died 10 days later.



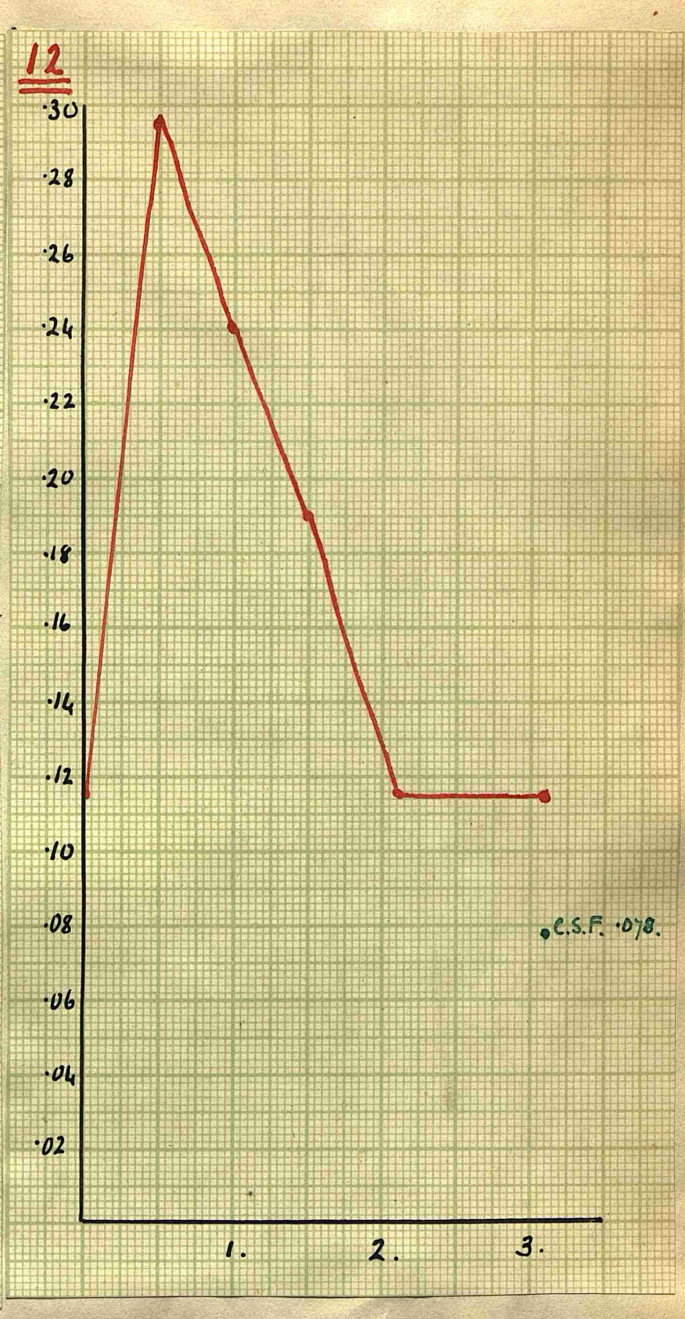
Urine.

I Benedict: green.turbid.
Fermentation: a few fine bubbles.
II.Benedict: Yellow.
Fermentation: 1½ in.in 4 hrs.

Rothera: negative.

Chart 12. Encephalitis.

R.C.female.aged 31.9th day.
Severe. Febrile. Typhoid state
Died 10 days later.



Urine.

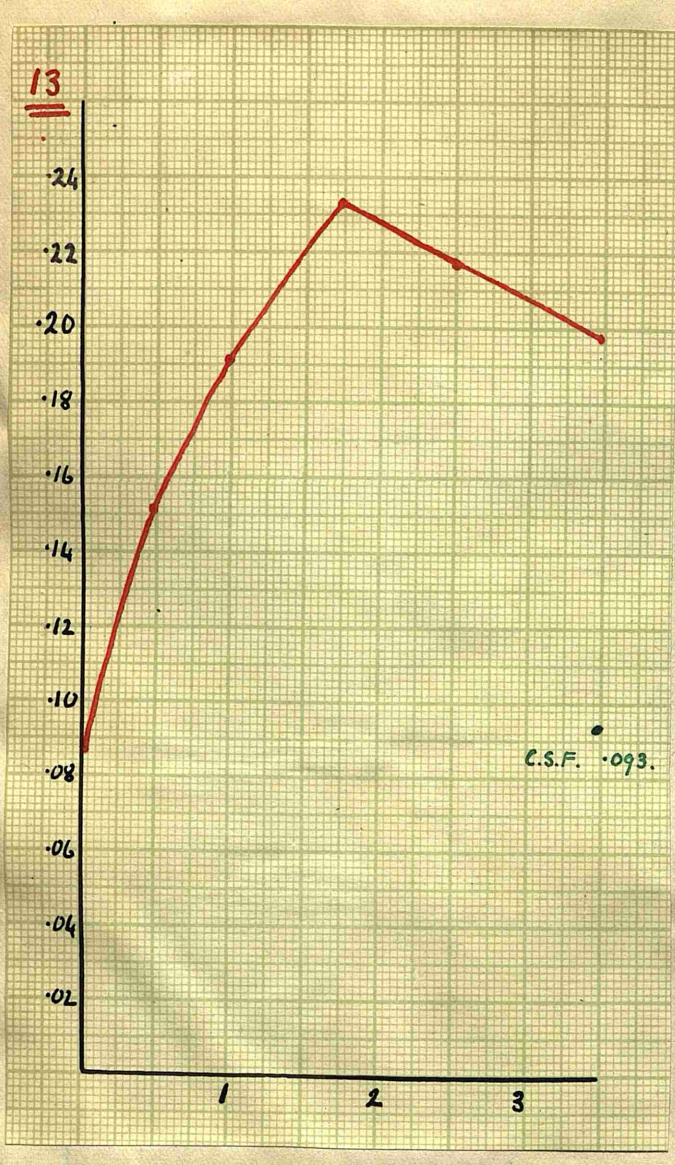
1.Benedict:clear:green.
Fermentation: negative.

II. Benedict:greenish yellow, turbid.
Fermentation: large bubble.
Rothera: negative.

Chart 13. Encephalitis.

J.A. Male. aged 59. 9th day.

Severe. Febrile. Lethargic.



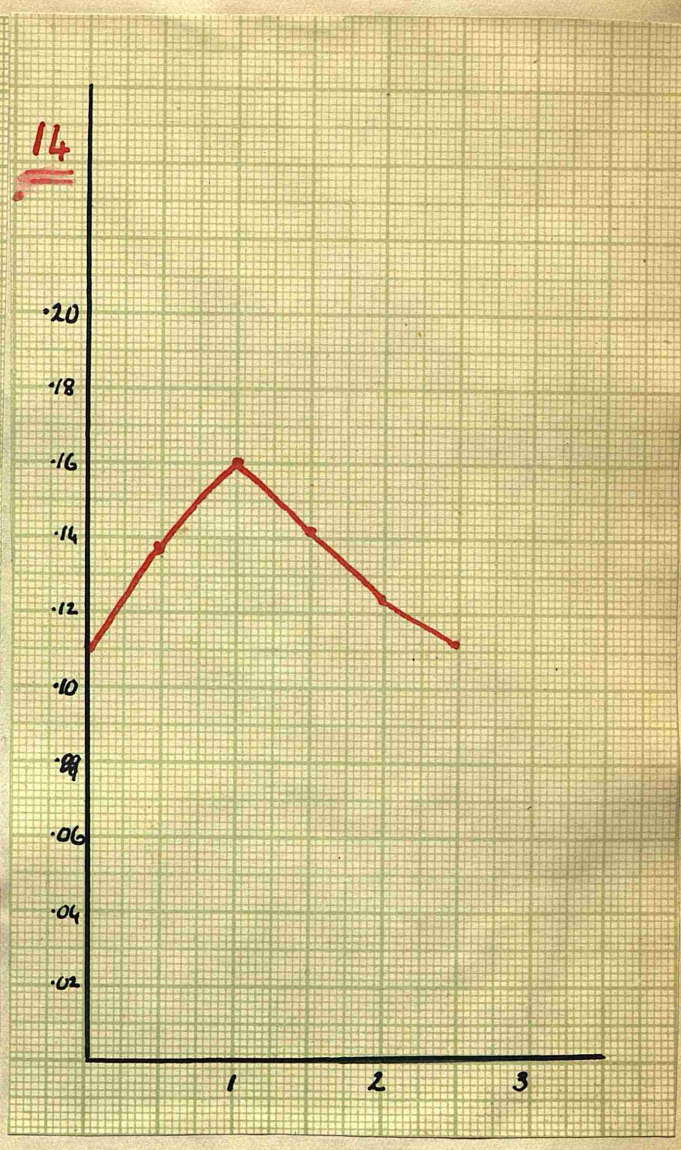
Urine:
I. Benedict: clear green.
Fermentation: negative.
II. Benedict: yellow, turbid.
Fermentation: 2 in. in 4 hours.

Rothera: positive.

Chart 14. Faucial Diphtheria.

E.M. female, aged 14. 4th day.

Severe, Febrile, Palatal paralysis

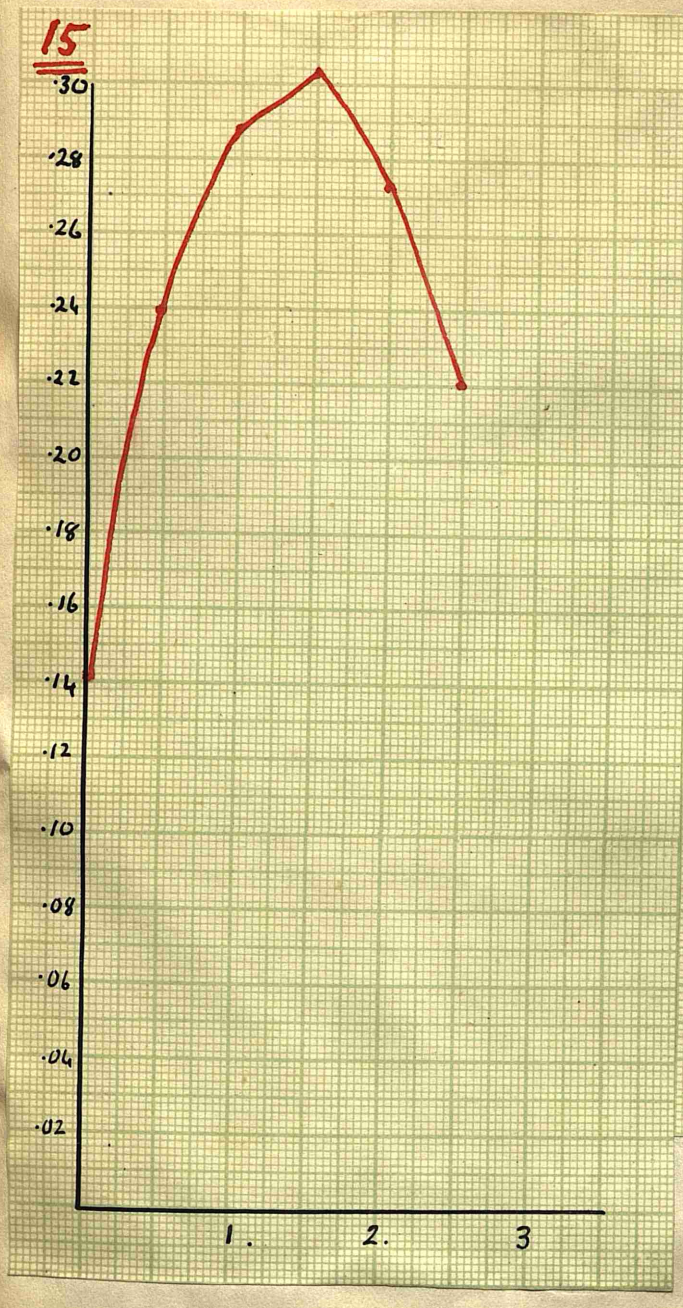


Urine:
I. Sugar free.
II. Benedict: clear green.
Fermentation: negative.

Rothera: negative.

Chart 15. Faucial Diphtheria.

M.R.(female)aged 28.5th day.
Febrile. Severe. Died 10 days later.

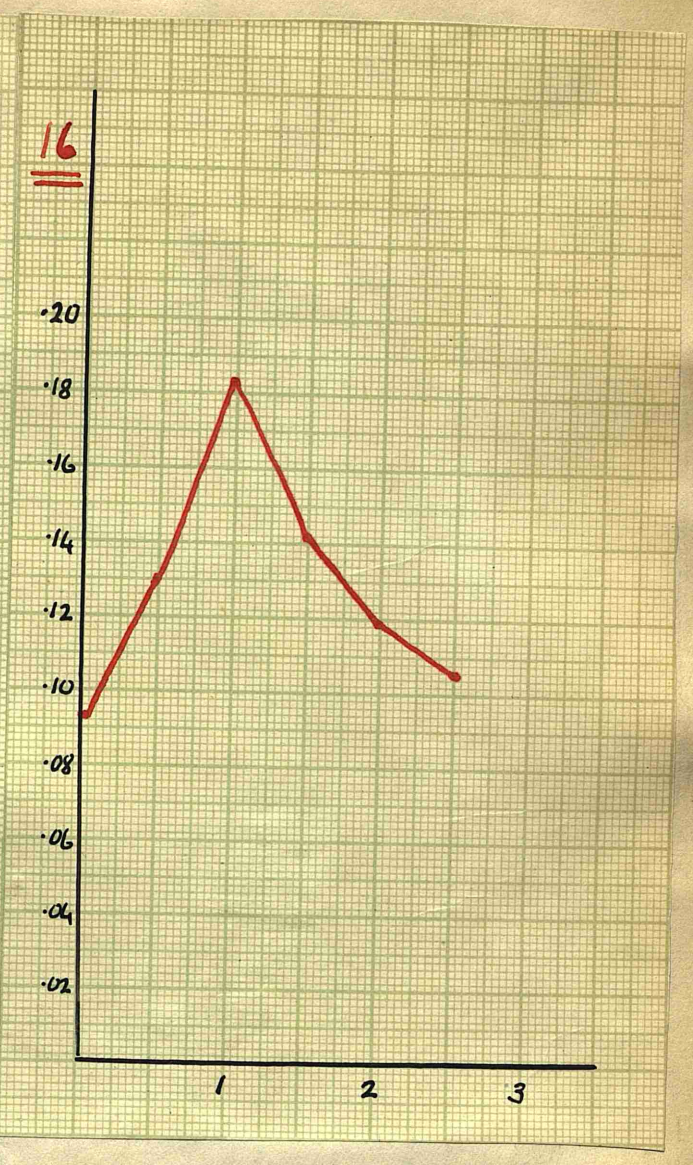


Urine.
I. Benedict: green, turbid.
Fermentation: a few fine bubbles.

II. Benedict: yellow, turbid.
Fermentation: 2 inches in 4 hours.
Rothera: positive.

Chart 16. Measles.

J.D. male, aged 23.6th day.
Febrile. Rash brilliant.

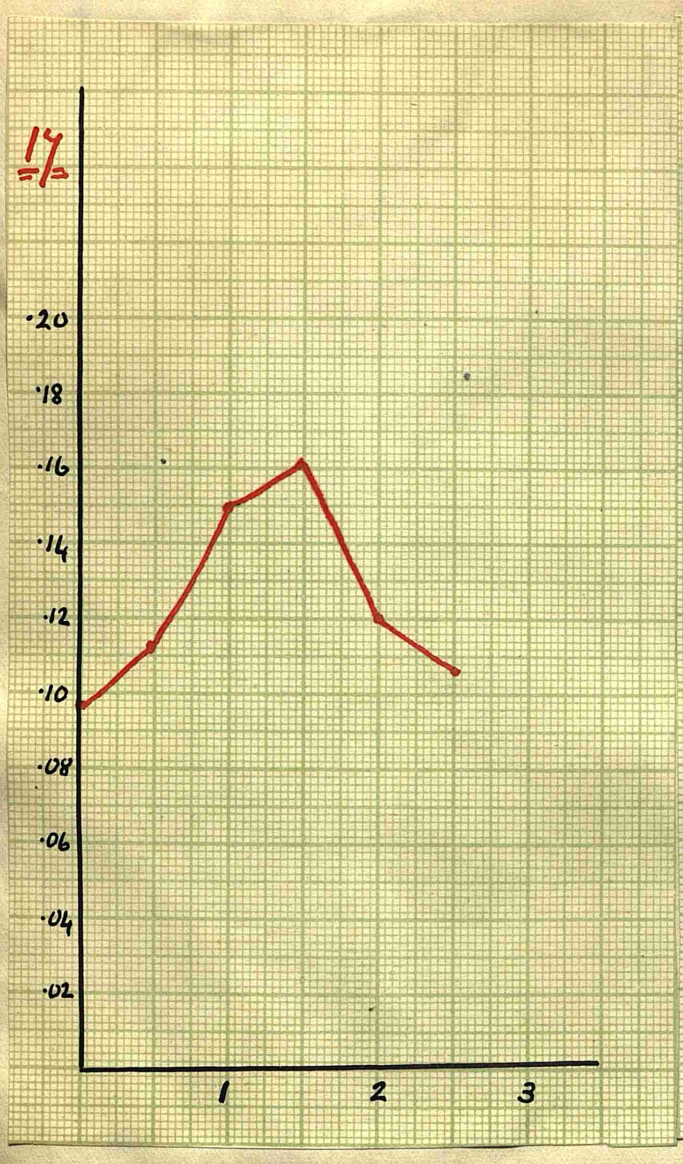


Urine.
I. Free from sugar.

II. Benedict: opalescent, green.
Fermentation: a few fine bubbles.
Rothera: positive.

Chart 17. Pulmonary Phthisis.

S.S.male.aged 36.
Febrile. Advanced. Died 3 weeks later.

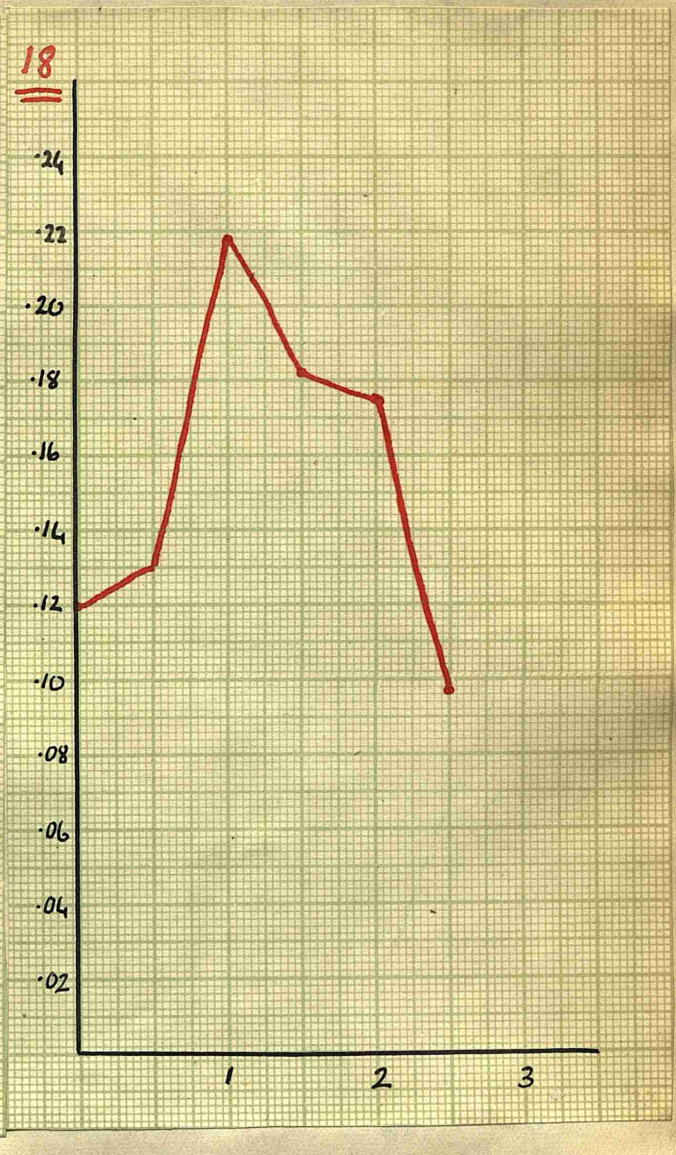


Urine.
I. Free from sugar.
II. Benedict: clear green.
Fermentative: negative.

Rothera: negative.

Chart 18. Pulmonary Phthisis.

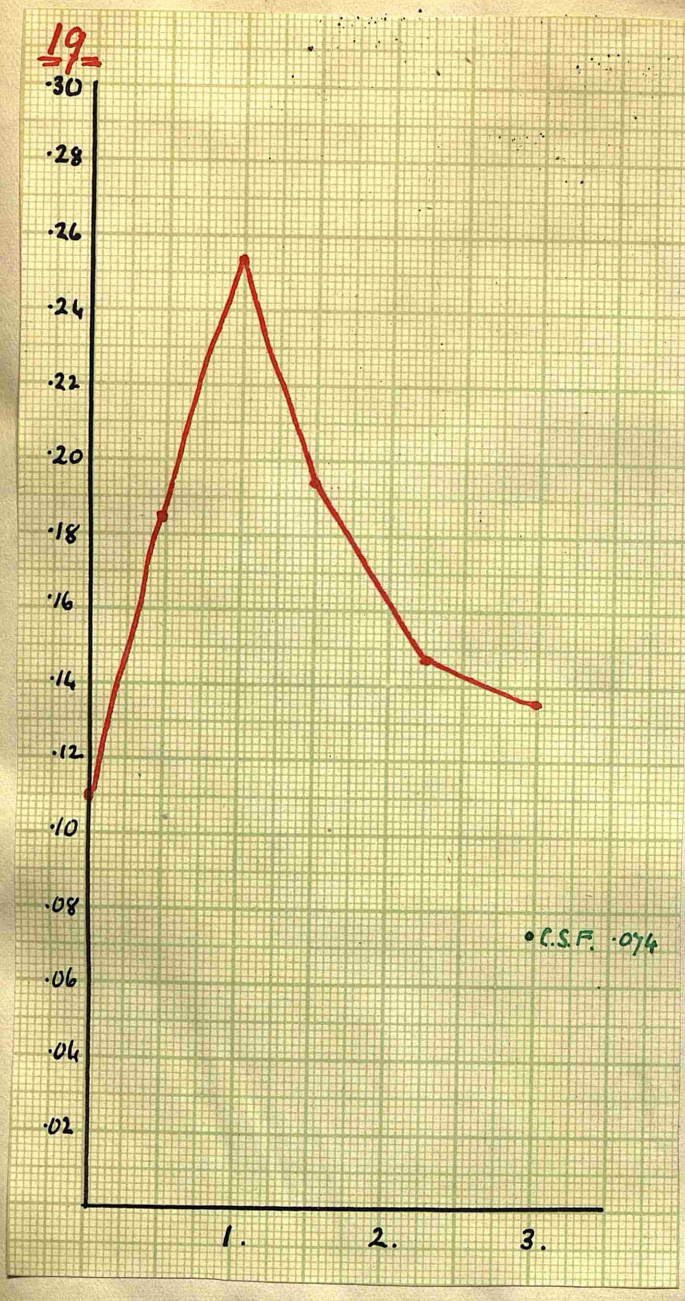
J.L.Male.aged 27.
Febrile. Advanced. Died 6 weeks later.



Urine.
I. Benedict: clear green.
Fermentation: negative
II. Benedict: green turbid.
Fermentation: a few fine bubbles.
Rothera: negative.

Chart 19. Intestinal Toxaemia.

J.McG. male, aged 10. 3rd day.
Febrile. Vomiting. Delirious.

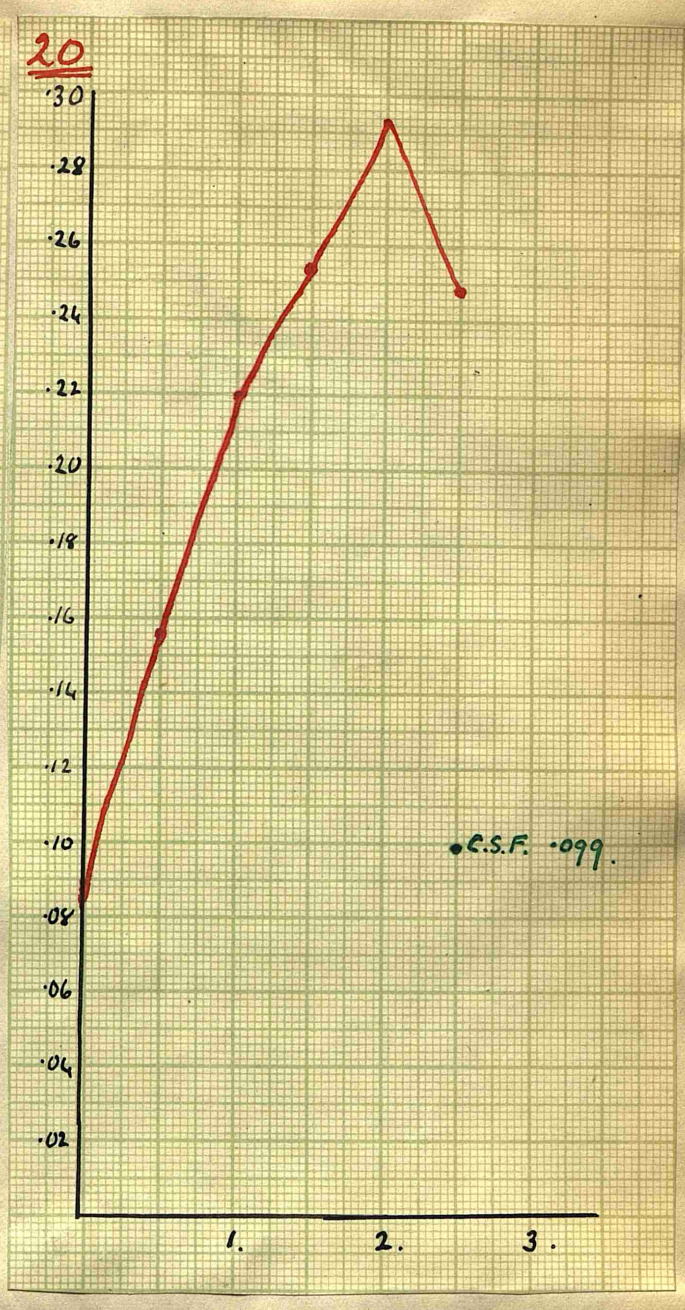


Urine:
I. Benedict: clear green.
Fermentation: negative.

II. Benedict: turbid greenish yellow.
Fermentation: large bubble.
Rothera: positive.
Gerhardt: positive.

Chart 20. Intestinal Toxaemia.

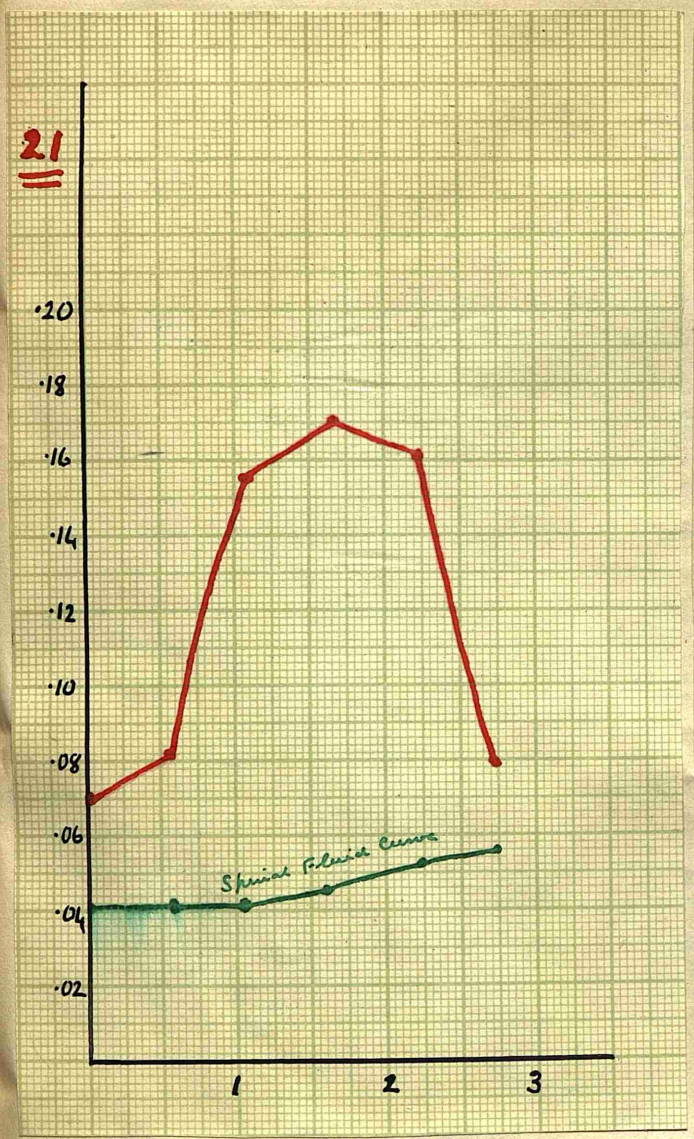
W.M. male, aged 6. 4th day.
Febrile. Vomiting. Drowsy.



Urine:
I. Benedict: green, turbid.
Fermentation: few fine bubbles.
II. Benedict: yellow.
Fermentation: 1 inch in 4 hours.
Rothera: positive.

Chart 21. Encephalitis.

H.D. female, aged 30: 5th day.
Mild. Febrile. Lethargic.



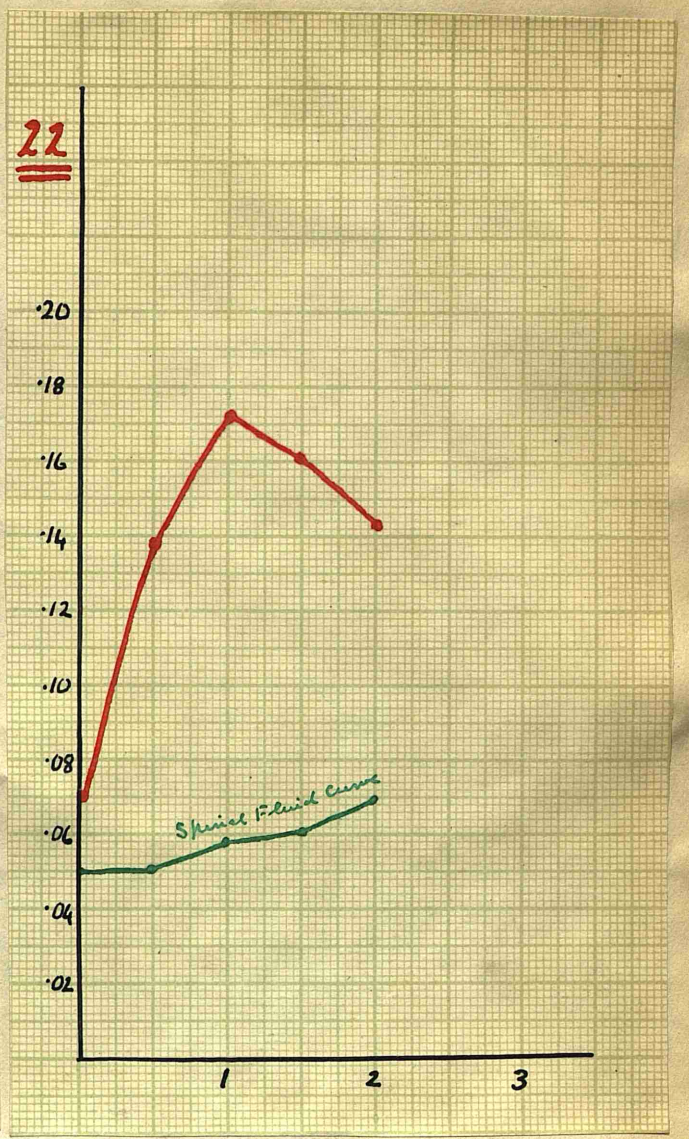
Urine.

I. All tests negative.
II. Benedict: green, opalescent.
Fermentation: negative.

Rothera: negative.

Chart 22. Encephalitis.

Mrs. I. aged 25. 15th day.
Moderate, Febrile. Lethargic.
Five months pregnant.



Urine.

I. Benedict: green turbid.
Fermentation: a few fine bubbles.
II. Benedict: yellow.
Fermentation: 3 inches i n 4 hours.
Rothera: negative.

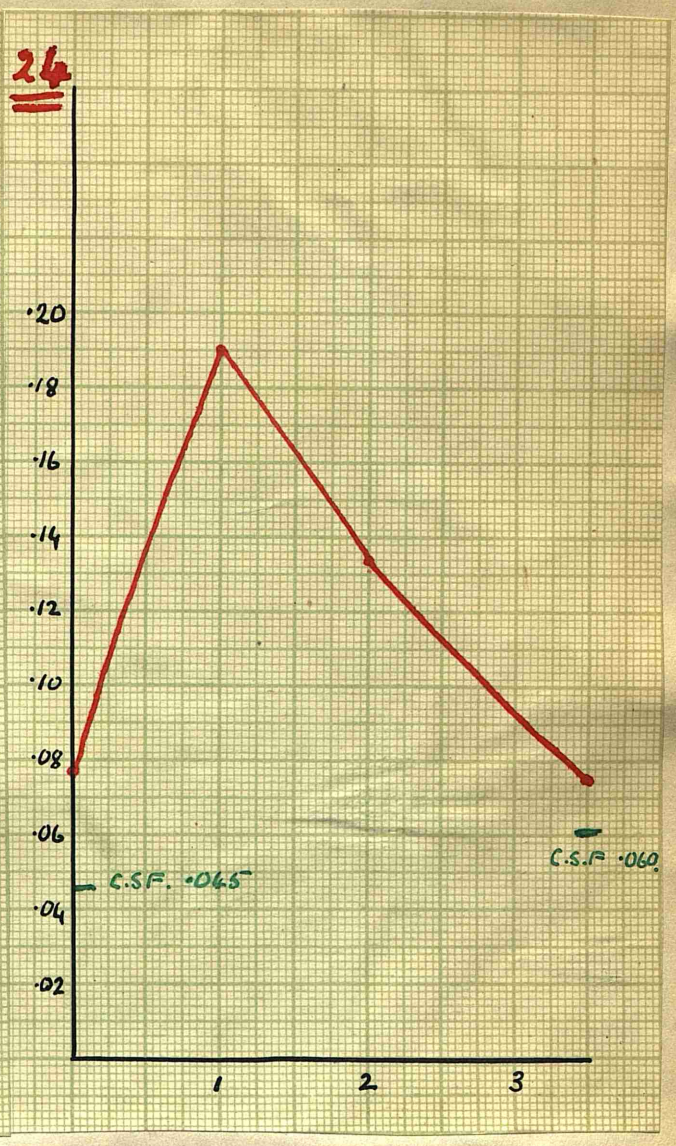
Chart 23. Encephalitis.

J.V.H. male, aged 28. 16th day.
Severe. Febrile. Lethargic.

Urine.
I. Benedict: clear green.
Fermentation: negative.
II. Benedict: greenish yellow, turbid.
Fermentation: large bubble.
Rothera: negative.

Chart 24. Encephalitis.

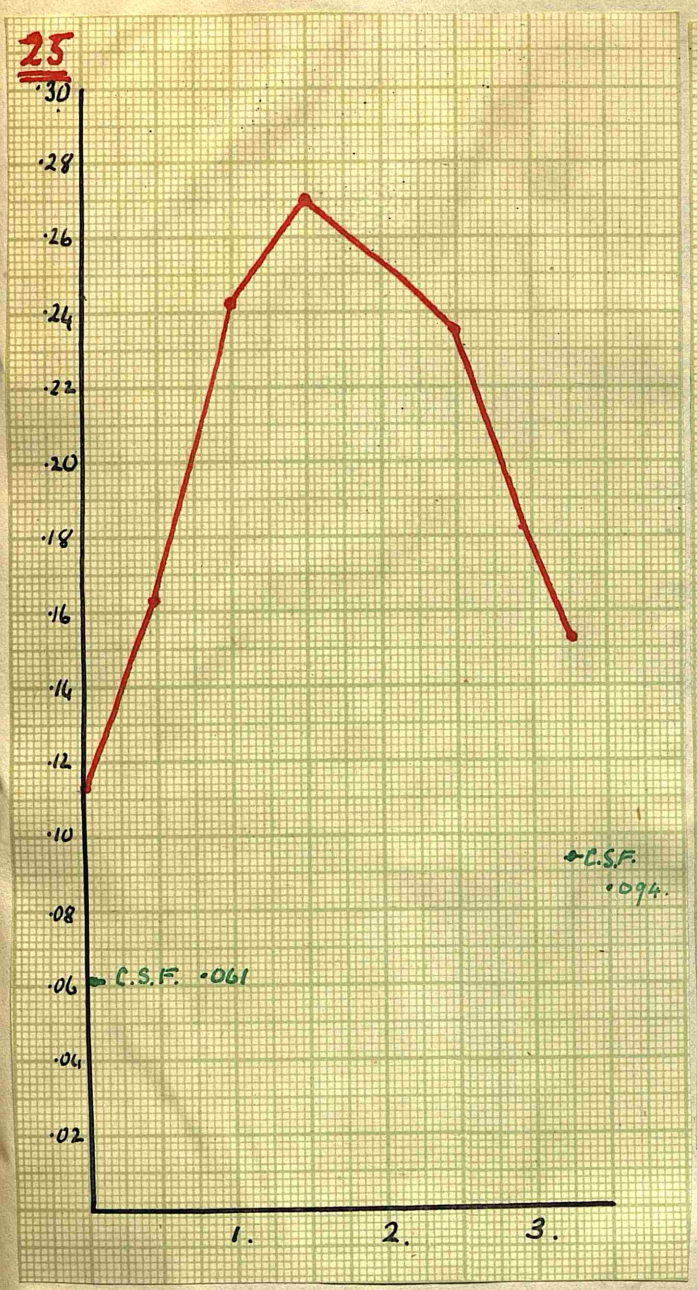
C.I. female, aged 7. 12th day..
Mild. A-febrile. Drowsy.



Urine.
I. Sugar free.
II. Benedict: green opalescent.
Fermentation: few fine bubbles.
Rothera: negative.

Chart 25. Encephalitis.

E.McN. aged 24. female. 6th day.
Severe. Febrile. Lethargic.
Enlarged thyroid gland.

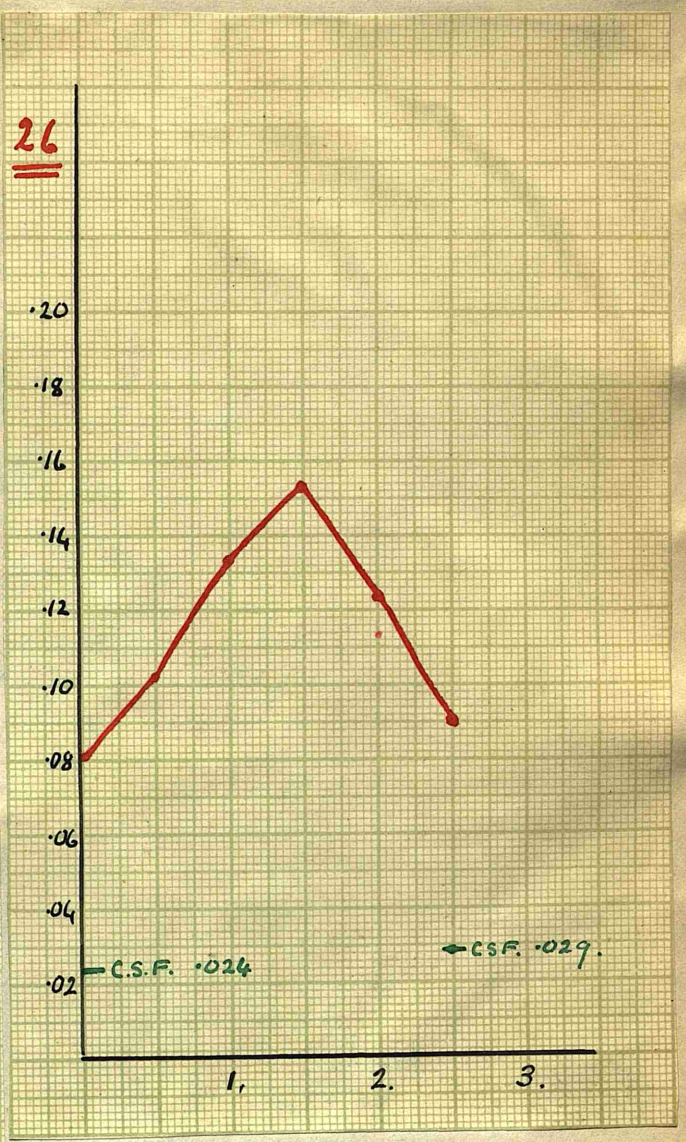


Urine.

I. Benedict: clear green.
Fermentation: negative.
II. Benedict: yellow.
Fermentation: 2 inches in 4 hours.
Rothera: negative.

Chart 26. Tuberculous Meningitis.

D.L. male. aged 5. 5th day?
Febrile. Died on 6th day.



Urine.

I. Benedict: clear green.
Fermentation: negative.
II. Benedict: green turbid.
Fermentation: few fine bubbles.

Rothera: negative.

TEMPERATURE CHARTS 1 - 4.