THESIS.

AN INVESTIGATION INTO POST-ENCEPHALITIC PARKINSONISM

BY

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FOREWORD.

The layout of this thesis is given in the forewword so that the continuity may be as complete as possible.

Firstly ,there is a general introduction giving the history of the disease Encephalitis Lethargica. This chapter traces the disease from the acute epidemics to the chronic stages of the disease with special refereh̄ce to Post-encephalitic Parkinsonism and is rounded off by the bibliography relating to it.

Secondly there is a brief chapter on the sedimentation rate of the red blood corpuscles which was one of the tests used in the investigation. This chapter is also followed by its own bibliography

Thirdly there is a chapter on the examination of the cerebro-spinal fluid which was the other line of investigation. The bibliography also follows this chapter.

Fourthly, before going on to the actual case results, a resume of the scope of the investigation is given. Again the bibliography follows its relevant chapter.

Fifthly the case results are given one page being allotted to each case. The sedimentation rates being given graphically and the cerebro-spinal fluid results in tabular form.

Sixthly the results of a control series of cerebro-spinal fluid is given in tabular form. Again this is followed by a bibliography.

The case results are then summarised with relevant bibliographies appended and the thesis completed by a chapter giving the conclusions drawn from these summaries.

GENERAL INTRODUCTION.

During the Great War of 1914/1918 it was inevitable, with the unnatural living conditions, that infections of all types should become more prevalent. Of these infections probably the most important was influenza with its attendant disease Encephalitis Lethargica.

This thesis deals with the Post-encephalitic Syndrome of Parkinsonism.

In the month of April, 1917, in Vienna, Von Economo[1] described cases of a new disease with the signs and symptoms of a diffuse brain infection. Then Netter[2], the French neurologist, described similar cases in a military base hospital in France.

From this sporadic beginning the disease took on an epidemic form and finally became pandemic, spreading to all corners of the earth in a short space of time.

Although described by Von Economo and Netter as a new disease there is historical evidence that a disease with similar characteristics had been chronicaled several times as will be seen from the following history.

In 1580[3] there is record of a serious epidemic affecting the whole of Europe which was described as " Morbus epidemicus per totam fere Europa Schlafkrankheit dictus", non tam letalis nisi accidents alio morbo". Again in London from 1673 to 1675 there was an epidemic of a disease which Sydenham describes as "febris comatosa", this disease was often associated with singultus .

The next record of a disease characterised by somnolence and nerve symptoms is by Albrech of Hildesheim in 1695. This was an isolated case described by him under the title of " de febre lethargica in strabismo utriusque oculi desinente" which would agree with the modern somnolent ophthalmoplegic form of the disease.

The next mention of febrile disease with somnolence was at Tubingen in 1712 but there is dubiety about the occurrence of somnolent states in this disease.

From 1723 to 1727 an epidemic occurred in London described as "febris soporosa et apoplectica". Then in 1763 Lepecq de la Cloture described a " coma somnolentum" occurring during an influenza epidemic in Rouen, and again from 1780 to 1782 there was an influenza epidemic with marked cerebral manifestations. From 1830 to 1833 there was an influenza epidemic in Paris characterised by somnolence.

The previously mentioned diseases characterised by fever, somnolence and other cerebral manifestations are only put forward hypothetically as being Encephalitis Lathargica, but in 1846 there was described by Dubinni the electric chorea in Northern Italy which is generally recognised as having been myoclonic encephalitis. Again from 1889 to 1890 there was an epidemic of influenza in Italy and from 1890 to 1891 the disease called "Nona"[4] was seen in Italy: this had many of the characteristics of Encephalitis Lethargica.

The first name associated with the modern epidemic of Encephalitis Lethargica is that of Constantin Von Economo of Vienna. In the winter of 1916/1917 there came to the Vienna Psychiatric Clinic many cases which could not be classified under any definite heading but all of which showed lethargy combined with ocular paralyses which led him to associate it with the disease "Nona" which had occurred in Northern Italy in the nineties of the previous century. This knowledge of "Nona" was derived from the fact that he had spent his youth in Southern Austria where tales of this disease were still prevalent.

Although Von Economo was the first to classify this disease as Encephalitis Lethargica, Cruchet in France, claimed to have seen cases in the winter of 1915/1916 and Urechia of Roumania described similar cases but did not associate them with any recorded disease. More cases continued to be described but it was not till after the influenza epidemic of 1918 that Encephalitis Lethargica assumed a pandemic form instead of localised epidemics.

After the pandemic stage of the disease had passed off localised epidemics again made their appearance, three of such being, at Sheffield in 1924,[5,& 6] at St. Louis in America during 1933[7,&8.], and in Japan. At present, the disease in the acute form is only seen in sporadic cases, but with the advent of world-wide hostilities and the possibility of similar conditions to those of the War of 1914/1918, there is the fear of sporadic cases of Encephalitis Lethargica becoming localised epidemics or even pandemic.

During the epidemic and pandemic stages of Encephalitis Lethargica it it was first thought to be an acute inflammatory disease which subsided by resolution in the recovering cases, but as time passed and the after effects became more obvious, there were two schools of thought as to the cause of the after effects.

The first school of thought stated that these after effects were due to consequent degeneration following damage done in the acute stage and labelled the after effects sequellae. In 1924, discussing these sequallae, Ivy Mackenzie[9] stated that in his opinion, there was no active inflammation but changes bore a resemblance to inflammation in the basal nuclei of the brain. Abro in Beaumont's text book of medicine[10] refers to chronic cases, but says they are due to the previous destruction of nerve cells. The Ministry of Health,[11] in a memorandum published in 1929, described the after effects as sequallae and not as chronic infective processes.

The second school of thought favours the theory of a still active infection in a chronic stage. From the literature this has a greater following, and the proof of this can be grouped under three headings:- clinical, pathological and epidemiological.

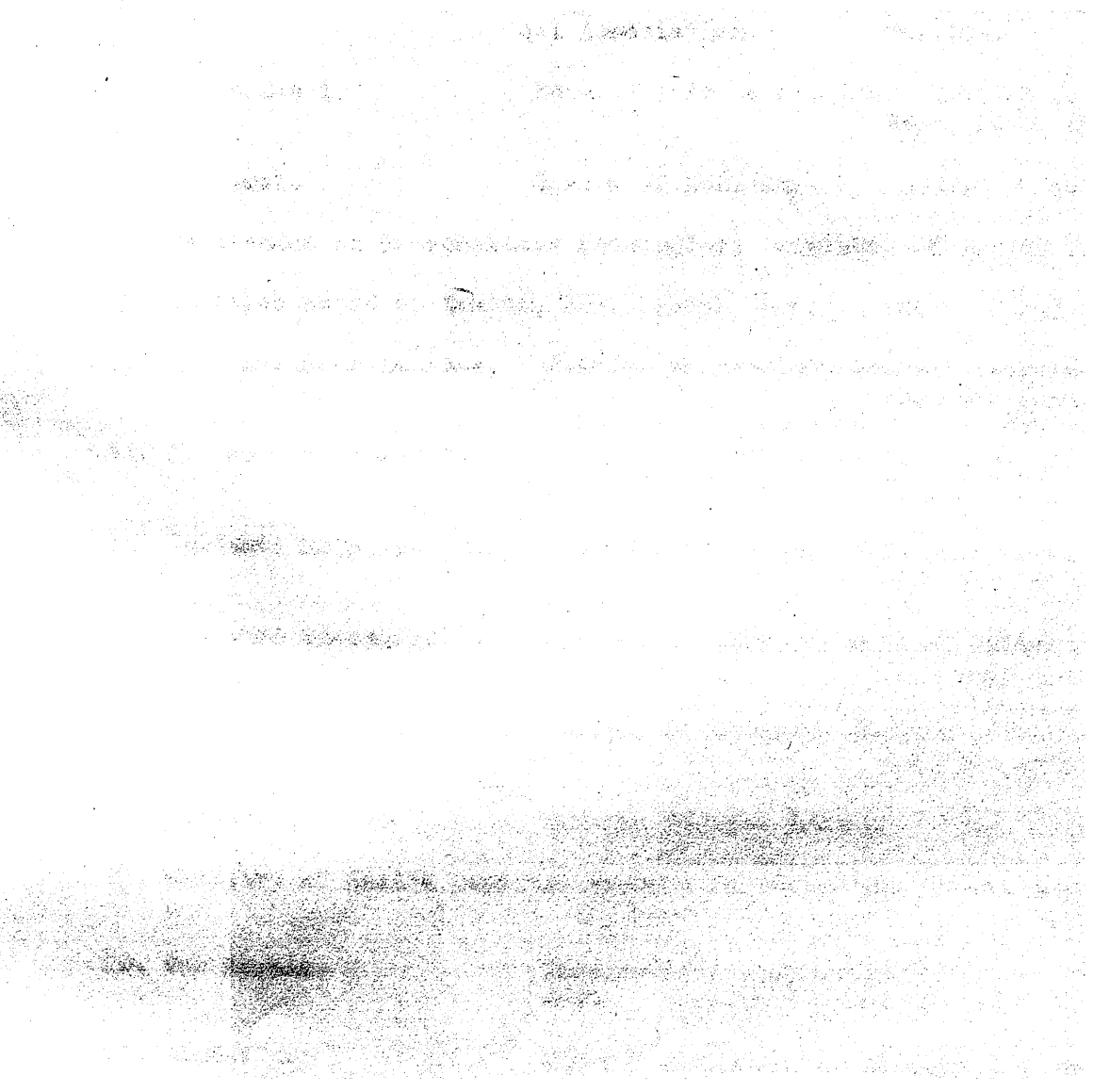
On the clinical side Von Economo,[12 to 19] Wimmer,[20] Hall,[21] McNalty,[22] Duncan,[23] Grossman,[24] and Freeman[25] support the view that the infection is still active, but in a chronic state.[26] In addition, several of the observers[27, 28] liken chronic Encephalitis Lethargica to General Paresis of the Insane, which is a definitely proven chronic infective Encephalitis due to the presence of the Spirochaeta Pallida in the brain tissue.[29] Also, one observer finds a similarity between chronic Encephalitis Lethargica, General Paresis and Disseminated Sclerosis, which is a chronic Encephalitis characterised by recurrences of activity.

Pathologically, many[30, 31] are found to support the chronic infective theory; these include Muir,[32] McAlpine,[33] Vegni,[34] Carmichael,[35] Freeman, Hunt & Cornwall,[36] Reynolds & Slater.[37] Their findings are all based on histopathology and are the results of post-mortem examinations on Post-Encephalitic cases at varying intervals of time from the first attack.

The epidemiological evidence is scarcer than either the clinical or pathological, but Freeman[38] writing in the Journal of the American Medical Association, quotes seven cases of probable contagion of Encephalitis Lethargica from patients suffering from post-Encephalitic Parkinsonism. Steifler suggests that acute exacerbations of a chronic case of Encephalitis Lethargica may be a source of new infections.

From these paragraphs the evidence would seem to point to the persistence of Encephalitis Lethargica as a chronic infection, and this paper is based on work done with thirty such cases of post-Encephalitic Parkinsonism over a period of six months, in an effort to prove that the infection was still in existence in these cases. The investigation was directed, firstly to the sedimentation

/sedimentation rate of the red blood corpuscles and to an examination of the cerebro-spinal fluid. In the cerebro-spinal fluids, special attention was paid to the albumen-globulin ratio. Before proceeding to the actual investigation, it was found necessary to study the literature on the sedimentation rate of the red blood corpuscles and to practical methods of analysing cerebro-spinal fluids; thus the following notes on the history and application of the red blood corpuscle sedimentation rate to infective processes and the importance of the albumen-globulin ratio in the cerebro-spinal fluid of cases of nervous disease became essentially a part of the investigation.



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THE SEDIMENTATION RATE OF THE RED BLOOD CORPUSCLES.

A definition of the sedimentation rate of the red blood corpuscles is difficult to give but that given by Panton[1] is concise " a non specific test for the presence of an active infection".

Although the clinical application of the test in its present form is comparatively recent sedimentation has a long history with its beginnings in the writings of Hippocrates and Aristoteles, whc held that the four fundamentals of life were Air, Water, Fire and Earth. These in varying proportions composed all things living and dead. Similarly in the human body there were four fluids intimately mixed forming the contents of the blood vessels and the body fluids. The Air corresponds to the blood, Water to phlegm, Fire to yellow bile and the Earth to black bile. These fluids were known as the Humours.

This theory of four Humours was supported by venesection which was the only method of blood examination then known. The shed blood,after standing, differentiated itself into several layers, the dark coloured lower portion of the blood clot represented the black bile, the red portion represented in the upper part of the clot was the blood proper while the yellow bile was the serum expressed from the clot. Finally, in pathological bloods the phlegm collected as a whitish layer above the blood clot and was called the "Febria" content. Thus this whitish layer was taken as an evidence of the presence of fever.

In therapeutic venesection it was customary to measure the amount of phlegm in the shed blood and to base the prognosis on the amount present. The presence of phlegm in the blood of patients who were ill led to it (the phlegm) being regarded as the causal agent of disease. Thus in the Grecian theory of medicine phlegm was held to be the most important causal factor in disease. Galen gave the name "Buffy Coat" to this layer of phlegm.

Until the advent of Paracelsus in the sixteenth century this theory held sway. He stated that the increase of phlegm was the result and not the causal factor of the illness but his theory did not replace the old one. In the seventeenth century Harvey's discovery of the blood circulation in 1628 and Malpighi's discovery of the capillaries and red blood corpuscles also helped to undermine the old theory but did not completely replace it.

Sydenham (1624/1689) believed that "inflammation of the blood" was the basis of disease and the two signs of this were fever and the formation of a "buffy

/buffy coat" in the venesected blood. Boerhaave (1668/1738) spread this theory on the Continent of Europe. John Hunter (1728/1793) thought that the "buffy coat" was in the nature of a preventative reaction while still considering the blood to be the source of all diseases.

Priory (1794/1879), a French physician, again brought the "buffy coat" into prominence and considered that there was an increase of it in the blood and that it was also deposited at the site of disease by the blood.

The final stronghold of this humoral pathology was in Vienna under Rokitansky but its downfall was brought by Virchow (1821-1902) the founder of cellular pathology. Since the "buffy coat" was one of the central features of the old humoral pathology it was investigated in the new reactionary method and thus began the modern conception of the "buffy coat".

The first name in this modern conception of the "buffy coat" is that of Biernacki[2] who in 1894 published a work which showed the relationship of the "buffy coat" to the sinking velocity of red blood corpuscles in shed blood treated with an anticoagulant. His interest in this phenomen continued and in 1897 he published another paper[3] in which he applied the phenomen to clinical practice and published findings in many diseases including pneumonia, tuberculosis, rheumatic arthritis and anaemia. Again in 1906 he published a further paper[4] giving a simpler technique. In these last two publications he advocates that the clinical application of the test be used as a prognostic guide.

Inspired by Biernacki's work to correlate the sinking velocity of the red blood corpuscles with the clinical condition Marcano[5] recorded his findings in many diseases and also the fact that the sinking velocity of the red blood corpuscles was increased in women during menstruation. Holobut[6], while investigating blood changes in relation to the blood pressure, included the sinking velocity of the red blood corpuscles as part of a complete blood examination.

Continuing the clinical investigation of the "Biernacki phenomenon" Fahreus[7] in 1921 published a review and gave the name "suspension stability" to the phenomemon. He published a series of cases with the results of tests in pregnant women and found that the "suspension stability" was decreased in their blood, that is, the corpuscles of the shed blood sank faster than those of non pregnant women. In the same year Westergren[8] published his

/his method and the findings in pulmonary tuberculosis: he concluded that the "suspension stability" was decreased in pulmonary tuberculosis and that this test gave an indication of activity even if no pyrexia was present. Since these results were published the "suspension stability" of the red blood corpuscles has become a routine test in the investigation of chronic disease where there is little pyrexial reaction.

In the post-Encephalitic syndrome of Parkinsonism there is little pyrexial reaction and so the "suspension stability" of the red blood corpuscles was used as a more delicate means of detection for evidence of activity.

9 & 10

The original Westergren technique for determining "suspension stability" was used. This is more familiarly known as the " Sedimentation Rate" of the red blood corpuscles

DESCRIPTION OF METHOD.

The apparatus required is :-

1. Westergren sedimentation tubes of a diameter 2.5 mm. and graduated from above downwards in millimetres from 0 to 200.
2. Westergren syringe. This has two markings on the barrel, one at 0.4 cc. and the other at 2.0 cc. This is used to dilute the blood with the anti-coagulant which is 3.8% sodium citrate solution in sterile water.
3. Sterile sodium citrate solution 3.8% in water.
4. Wooden stand to hold the Westergren tube vertical with a spring clip at the top and a flat rubber pad at the base.

TECHNIQUE.

The syringe is filled to the 0.4 cc. mark with sterile sodium citrate solution and venous blood drawn up to the 2.0cc mark, carefully avoiding the introduction of air bubbles. A slack tourniquet is used to congest the veins. The mixture of blood and citrate is then transferred to a small test tube and carefully marked.

Within an hour this blood is drawn up into one of the Westergren tubes to the mark 200 and fixed in the stand with the tip on the rubber pad. Readings of the clear fluid column which appears with the settling of the corpuscles are taken at the end of one and two hours from the time of setting up the tube in the stand.

To ensure uniformity of results and to make the accuracy as great as

/as possible the following precautions were taken:-

1. Tubes were set up within an hour of withdrawing the blood.

2. Specimens were all taken at the same time of day, in the forenoon mid-way between meals.

3. Any specimen showing haemolysis or agglutination were discarded.

4. The stand, with tubes in place, was always set up on the same bench in the laboratory out of direct sunlight.

5. The tubes were exactly perpendicular.

These precautions were taken in view of the considerable differences exerted by apparently trivial factors as is mentioned in the literature. 11 to 15.

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THE EXAMINATION OF THE CEREBRO-SPINAL FLUID.

On consulting the standard monographs regarding the cerebro-spinal fluid in chronic Encephalitis Lethargica there appear to be very few abnormalities constantly present, so it was decided to concentrate the investigation on the protein content with special reference to the Albumen-globulin ratio. Other tests performed were the Lange Colloidal Gold Reaction, a Cell count and the Pandy Test. As a matter of routine all fluids on first examination had a Wassermann test performed.

1.2.3. 4 & 5

Realising that the examination of a single fluid in each case was not sufficient it was decided to examine a spinal fluid from each case every month over a period of six months. In actual practice, however, this was difficult to carry out and the cases had to be grouped into three classes.

1. Those patients who were in institutions and permission was obtainable to procure a fluid every month.

2. Those patients where permission for withdrawal of a single fluid was obtainable.but where a series was impossible.

3. Those patients where it was impossible to obtain permission for withdrawal of fluid and in those investigation was confined to the sedimentation rate of red blood corpuscles.

In addition to the foregoing difficulties there were technical difficulties in the withdrawal of cerebro-spinal fluid because of the rigidity presented by patients with Parkinsonism; another difficulty met with was the accidental contamination of the spinal fluid with blood from one of the thecal vessels. These are not mentioned to explain the gaps in the series but were found to be very real in actual practice.

The cell count, the Pandy test and the Lange colloidal gold curve were done as described by Merritt and Fremont Smith, the technique being uniform throughout all examinations. A comparatively new method for determining the protein content and the albumen-globulin ratio was used and since this entailed much reading a history of protein estimation in cerebro-spinal fluid is given followed by a detailed description of the method used.

Three main methods for estimating the protein content of cerebro-spinal fluid are in use:-

1. The simplest and least accurate being the precipitation of the protein in a specially graduated centrifuge tube and measuring the deposit after centrifuging for a fixed time at a fixed speed.

The scale on the centrifuge tube is previously determined by calculating a protein precipitate by the Kjeldhal method and from several of these estimations the tube is graduated. Advocates of this method are Young and Bennett[6] who used acetic acid, alcohol and heat to precipitate the protein; Christleib and Myers[7] used Tsuchiaya's method of precipitating the protein with phosphotungstic acid, hydrochloric acid and heat.

2. The second method of estimating the protein content of cerebro-spinal fluid is by the use of a turbidimeter. The proteins are put into a colloidal state by means of sulphosalicylic acid and comparing the degree of turbidity with that of a known protein solution. The names associated with this method are Denis and Ayer[9], Daly and Fremont Smith[10], and Hempel and Geise[11] who used alcohols to produce the turbidity. A similar turbidimetric method using different reagents to produce the colloidal suspension is reported by Exton and Rose[12].

3. The third method of estimating the protein content of cerebro-spinal fluid depends on the estimating of the tyrosine content as compared with the tyrosine content of a known solution by means of a colour indicator and a colorimeter. The technique was evolved from Wu's[13 & 21] method of estimating the plasma proteins. The first adaptation was described byHewitt, in this the indicator was the phenol reagent of Folin and Denis[15 & 16]. A further advance was made by Johnston and Gibson[17] who used the Folin-Ciocalteu[18] reagent in place of the phenol reagent used by Hewitt.

In this paper the method used is an adaptation of that of Johnston and Gibson. The main differences from their method being that 20% trichloracetic acid was used instead of 3%, ammonium sulphate was used instead of sodium sulphate for the fractionation into albumen and globulin and the time allowed for the colour reaction to develope was increased to twenty minutes instead of the ten minutes recommended. This last difference was judged necessary because of the slow developement of the colour reaction.

DESCRIPTION OF METHOD.

In this the total protein was estimated, then the albumen content and finally by subtraction the globulin content was found.

A. Total Protein.

Take 2 ml. cerebro-spinal fluid into a clean,dry, tapered 15 ml. centrifuge tube.

Add 2 ml. 20% trichloracetic acid.

Close with rubber stopper and invert several times, allow to stand overnight.

Immerse in boiling water bath for 1 minute.

Cool by standing in cold water.

Centrifuge for half-an-hour.

Pour off the supernatant fluid and remove final traces of liquid with a piece of clean, washed gauze.

Add 0.25 ml. of 10% sodium hydroxide and place in a boiling water bath for ten minutes.

Add 3.75 ml. of distilled water and 0.5 ml. of Folin-Ciocalteu colour reagent.

Add 1.5 ml. saturated sodium carbonate solution.

Mix contents of tube by closing with the thumb and inverting several times.

Do not use a rubber bung as this might affect the colour.

Leave fot twanty minutes before comparing with the standard solution in the colorimeter.

B. Albumen.

Take 2.5 ml. cerebro-spinal fluid in a clean, dry, tapered 15 ml. centrifuge tube.

Add 2.5 ml. saturated solution of ammonium sulphate.

Close with a rubber stopper and invert several times, allow to stand overnight.

Centrifuge for half-an-hour.

Decant the supernatant fluid and pipette 4 ml. of the decanted fluid to another clean, dry 15 ml. centrifuge tube.

Add 4 ml. 20% trichloracetic acid.

Put in boiling water bath for 1 minute.

Centrifuge for half-an-hour.

Pour off the supernatant fluid.

Add 0.25 ml. of 10% sodium hydroxide solution.

Place in boiling water bath for 10 minutes.

Add 0.5 ml. of Folin-Ciocalteu colour reagent.

Add 1.5 ml. of saturated sodium carbonate solution.

Mix contents by inverting several times with thumb over the end.

Leave for twenty minutes till colour developes.

C. Standard Tyrosine Solutions.

Into three test tubes pipette respectively 0.5 ml., 1.0 ml., and 2.0 ml. of an 0.02% solution of tyrosine in $\frac{N}{10}$ hydrochloric acid.

Make the volume up to 8 ml. by adding respectively 7.5 ml., 7.0 ml., and 6.0 ml. of distilled water.

Add to each test tube 1 ml. of Folin-Ciocalteu reagent and 3 ml. of saturated sodium carbonate solution.

Mix all tubes thoroughly.

Leave for twenty minutes till the colour developes.

Although described as three separate pieces of work it will be seen that the first two operations, A and B., coincide from the point where the centrifuge tubes are put into the boiling water bath for 1 minute and that the preparation of the tyrosine standards, operation C., coincide from the addition of the Folin-Ciocalteu colour reagent. Thus all three operations can be combined to have the colour reagent added to the final solution at the same time, and so allowing the colorimetric readings to be done consecutively.

Several technical points cropped up in doing this series of fluids. The first of these being at the point when treating the protein precipitate with the hot sodium hydroxide the whole of the precipitate must be dissolved; if this does not happen the specimen must be discarded and half the amount of cerebro-spinal fluid used making up the required volume with distilled water. In the present series only a few required to be done in this way where the protein content was high. The second point being the use of clean, washed gauze to remove final drops of fluid after decanting, this is necessary as filter paper absorbs protein.[19] The final point is the mixing of the tubes after the colour indicator has been added where the thumb is used to close the tube instead of a rubber stopper as this discolours the solution.

The calculations are based on the tyrosine equivalents given by Johnston and Gibson,[20] namely :-

1 mgm. tyrosine is equivalent to 11.1 mgm. albumen.

1 mgm. tyrosine is equivalent to 11.4 mgm. total protein.

It was found that the standard tyrosine solution containing 1 ml. of an 0.02 % solution of tyrosine in $\frac{N}{10}$ hydrochloric acid made up to 8 ml. with distilled water was the best to use. The depth of solution in the colorimeter cup being 10 mm..

CALCULATION.

Percentage strength of tyrosine solution is 0.02%.

100 cc. tyrosine solution contain 0.02 gms. tyrosine.

1 cc. solution contain 0.0002 gms. tyrosine.

Concentration is 0.0002 gms. in 8 cc. solution.

Percentage strength in 8 cc. solution is $\left(\frac{0.0002 \times 100}{8}\right)\%$

$= 0.0025\%$.

When the colours match in the colorimeter

$S \times X = U \times Y$.

Where S is depth of standard solution.

X is concentration of standard solution.

U is depth of unknown solution.

Y is concentration of unknown solution.

The standard is at 10 mm. depth.

$S \times X = 0.0025 \times 10$

$= 0.025\ \%$

$U \times Y = 0.025\ \%$

$Y = \frac{(0.025)}{(U)}\ \%$ concentration of unknown.

1 cc. of unknown contain $\frac{(0.025)}{(100\ U)}$ gms.

$= \frac{0.00025}{U}$ gms.

$= \frac{0.25}{U}$ mg.

4 cc. of unknown solution contain $\frac{(0.25 \times 4)}{(U)}$ mgm. tyrosine.

2 cc. of unknown (i.e. original C.S.F.) contain

$\frac{(0.25 \times 4)}{(U)}$ mgm. tyrosine.

$= \frac{1}{U}$ mgm. tyrosine.

100 cc. of original C.S.F. contain $\frac{50}{U}$ mgm. tyrosine.

but 1 mgm. tyrosine is equivalent to 11.4 mgm. total protein.

$\frac{50}{U}$ mgm. tyrosine is equivalent to $\frac{11.4 \times 50}{U}$ mgm. total protein.

$= \frac{570}{U}$ mgm. total protein.

Similarly for albumen the value is $\frac{555}{U}$ where 1 mgm. tyrosine is equivalent

/equivalent to 11.1 mgm. albumen. Therefore the result of these calculations is in milligrammes of total protein or albumen per 100 cc. The globulin content is obtained by simple subtraction of albumen content from that of total protein content.

Thus from these two estimations there was found:-

1. Total protein in mgm. per 100 cc. of cerebro-spinal fluid.
2. Albumen content in mgm. per 100 cc. of cerebro-spinal fluid.
3. Globulin content in mgm. per 100 cc. of cerebro-spinal fluid.
4. The albumen-globulin ratio of the specimen of cerebro-spinal fluid examined.

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SCOPE OF PRESENT INVESTIGATION.

The blood and cerebro-spinal fluid of thirty (30) cases of Post-Encephalitic Parkinsonism was investigated in an attempt to determine whether or not the infection was active.

In the blood the hourly and two-hourly sedimentation rates were found by the Westergren method. This was done weekly over a period of six months. As discussed in the chapter on sedimentation rates this was taken as the most sensitive test for the activity of an infective process.[1]

In the cerebro-spinal fluid the following tests were carried out:-

1. The total protein content.
2. The albumen content.
3. The globulin content.
4. The albumen-globulin ratio.
5. The cell count.
6. The Pandy test.
7. The Lange colloidal gold curve.

It was attempted in each case to obtain a cerebro-spinal fluid for examination each month for a period of six months.

These investigations on the blood and cerebro-spinal fluid were carried out over the same period of six months. Owing to the difficulties mentioned in paragraphs 2 and 3 of the chapter on the examination of the cerebro-spinal fluid the cases finally resolved themselves into four groups:-

A. Cases where the blood examinations were made weekly over the six months and also cerebro-spinal fluid was examined monthly.

B. Cases where the blood examinations were made weekly over the six months but where only one or two cerebro-spinal fluids were obtained.

C. Cases where the blood examinations were made weekly over the six months but no cerebro-spinal fluids were obtained.

D. Cases who died of intercurrent disease during the investigation.

In category A. there were twelve (12) cases, in category B. there were ten (10) cases, in category C. six (6) cases and in category D. two (2) cases.

The easiest way to present all the results for one case on one page was by making a graphic representation of the sedimentation rate with the number of weeks plotted horizontally and the sedimentation rates vertically. The hourly sedimentation rate plotted in black ink, two-hourly rate in green ink; while two red horizontal lines indicated the normal average reading for the

/the hourly and two-hourly readings.

To correlate the cerebro-spinal fluid results with the graph of the sedimentation rates a table of these was drawn below the graph with an arrow indicating the week in which it had been taken.

Below this combined representation of the case results was printed a few sentences correlating the results and noting any outstanding abnormality.

CONTROL SERIES.

No control series of blood sedimentation rates was considered necessary as all the standard references[2] gave findings which are universally recognised as being those of normal health.

With the cerebro-spinal fluid the reverse was found as even the monographs did not give results of any great number of cases of Post-Encephalitic Parkinsonism. Therefore a control series had to be found and the best source for this was found to be Schizophrenic patients[3.4.&5.] as all the references consulted agreed that the cerebro-spinal fluids of such cases was normal. Twenty-two(22) such cases had a cerebro-spinal fluid examined to provide a control series.

All the cases, both of Parkinsonism and the control series, had a Wassermann Reaction done on the blood and cerebro-spinal fluid as a routine measure.

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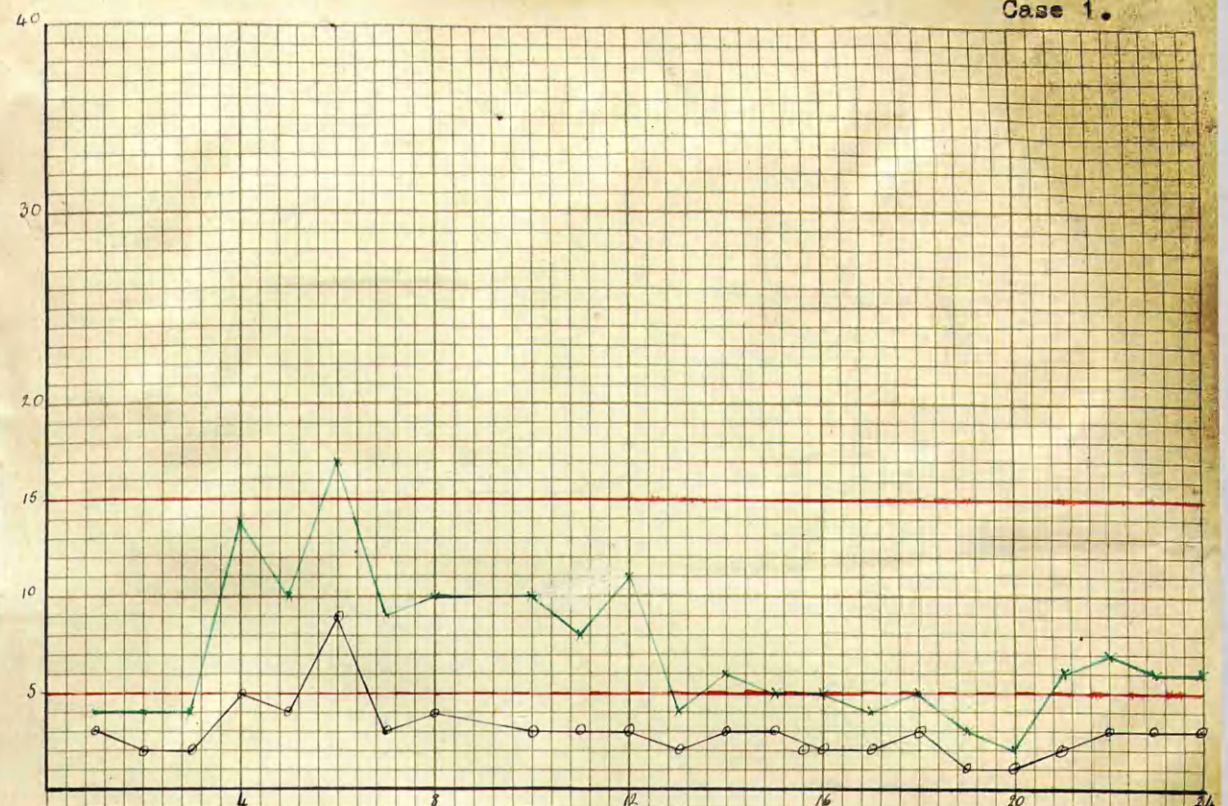
Case 1.



	A	B	C	D	E	F	G
Protein	50	26	29			43·9	46·0
Albumin	34	18	24	Slight opalescence	Slight opalescence	32·8	33·2
Globulin	16	8	5			11	12·7
Ratio	21/1	23/1	47/1			3·0/1	2·6/1
Cells	R.B.C	Nil	1			R.B.C	Nil
Pandy	Negative	Negative	Negative			Positive	Neg.
Lange	0 0 0 0 0 0 0 0 0	1 1 2 2 1 0 0 0	1 1 1 1 1 0 0 0 0 0			1 1 0 0 0 0 0	0 1 1 0 0 0 0 0 0

Sedimentation Graph.

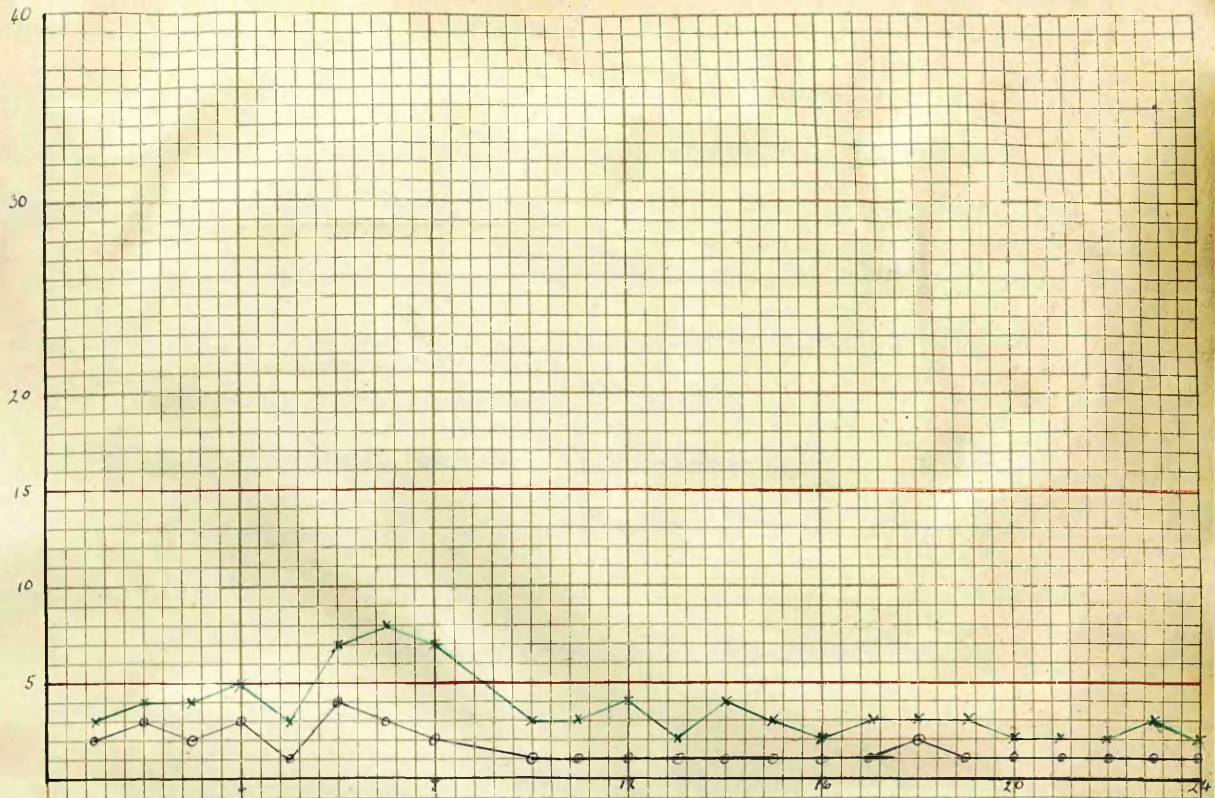
This graph over the whole period of six months was within normal limits, (indicated by the horizontal red lines, except for the sixth week where both the hourly and two-hourly readings were slightly greater than normal. During this week there was a coryzal infection.

Cerebro-Spinal Fluid results.

Here five complete results were obtained in addition to two specimens which contained frank blood.

The evaluation of these results is not attempted here, with the small space available, but is consolidated in the pages following the case results. This applies to all the cases where cerebro-spinal results are quoted.

Case 2.



	A	B	C	D	E	F	G
Protein	37			35	34	36·1	36·3
Albumin	28			28	22·5	27	23·8
Globulin	9			7	11·5	9·1	12·5
Ratio	3·0/1			4·0/1	1·9/1	3·0/1	1·9/1
Cells	5	RBC.	2	Nil	Nil	1	Nil
Pandy	Negative	Negative	Negative	Negative	Negative	Negative	Neg.
Lange	0 0 0 0 0 0 0 0	1 2 3 3 2 1 0 0	1 1 1 0 0 0 0 0	0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	0 0 1 1 0 0 0 0

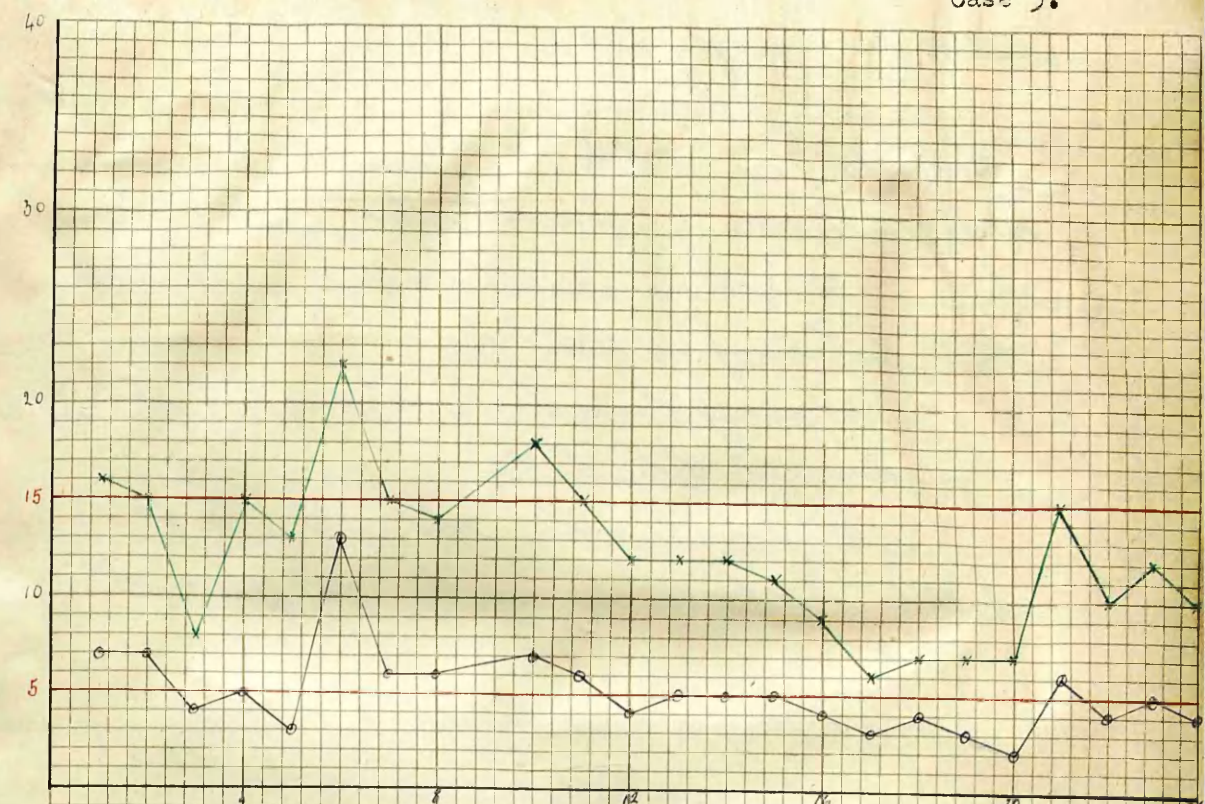
Sedimentation Graph.

In all aspects this graph gave a completely normal picture, over the whole period of six months.

Cerebro-spinal fluid results.

Five complete results were obtained and two specimens which had sufficient fluid only for a cell-count and Pandy test and Lange colloidal gold curve.

Case 3.



	A	B	C	D	E	F	G
Protein	40	44		46		42.2	35.7
Albumin	31	31		33		30.3	25.3
Globulin	9	13		13		11.9	10.5
Ratio	3.5/1	2.4/1		2.5/1		2.5/1	2.4/1
Cells	4	1	3	Nil	Nil	1	4
Pandy	Trace	Trace	Negative	Negative	Negative	Negative	Neg
Lange	0 0 1 1 1 1 0 0	1 2 2 3 3 2 1 0	1 1 2 2 2 1 0 0	0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0

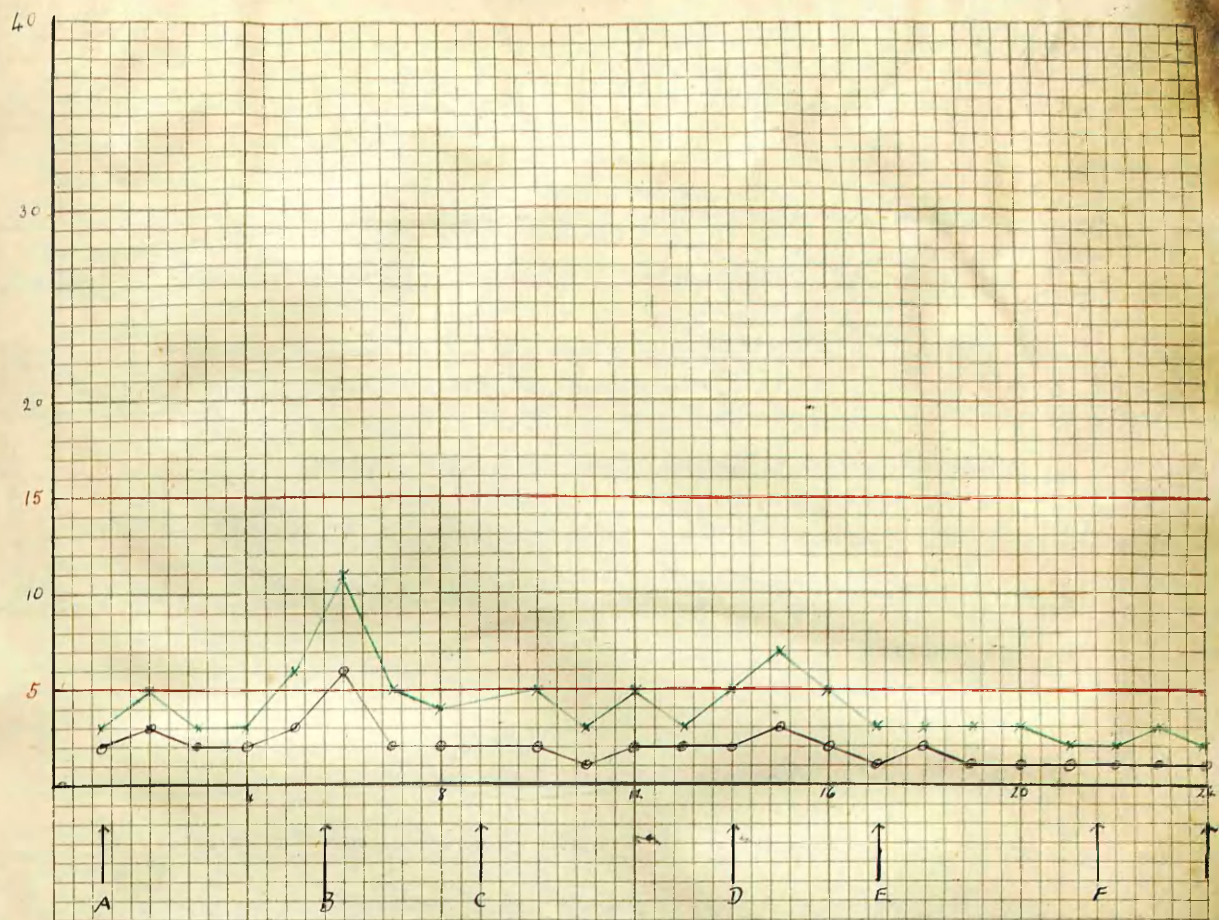
Sedimentation Graph.

This graph showed high readings over the first three months, a chronic bronchitis was present and showed some activity during this period.

Cerebro-spinal fluid results.

Five complete results were obtained and two specimens which had sufficient fluid only for a cell count, Pandy test and Lange colloidal gold curve.

Case 4.



	A	B	C	D	E	F	G
Protein	43	36		31	31·6	29·5	30·4
Albumin	26	24		22	25·3	23·1	23·8
Globulin	17	12		9	6·2	6·3	6·8
Ratio	1·5/1	1·9/1		2·4/1	4·1/1	3·7/1	3·5/1
Cells	6	2	4	Nil	2	Nil	1
Pandy	Neg	Trace	Neg	Neg	Neg	Neg	Neg.
Lange	0 0 0 0 0 0 0	0 0 1 2 2 1 0	1 1 1 0 0 0 0	0 0 0 0 0 0 0	0 0 0 0 0 0 0	0 0 0 0 0 0 0	0 0 0 0 0 0 0

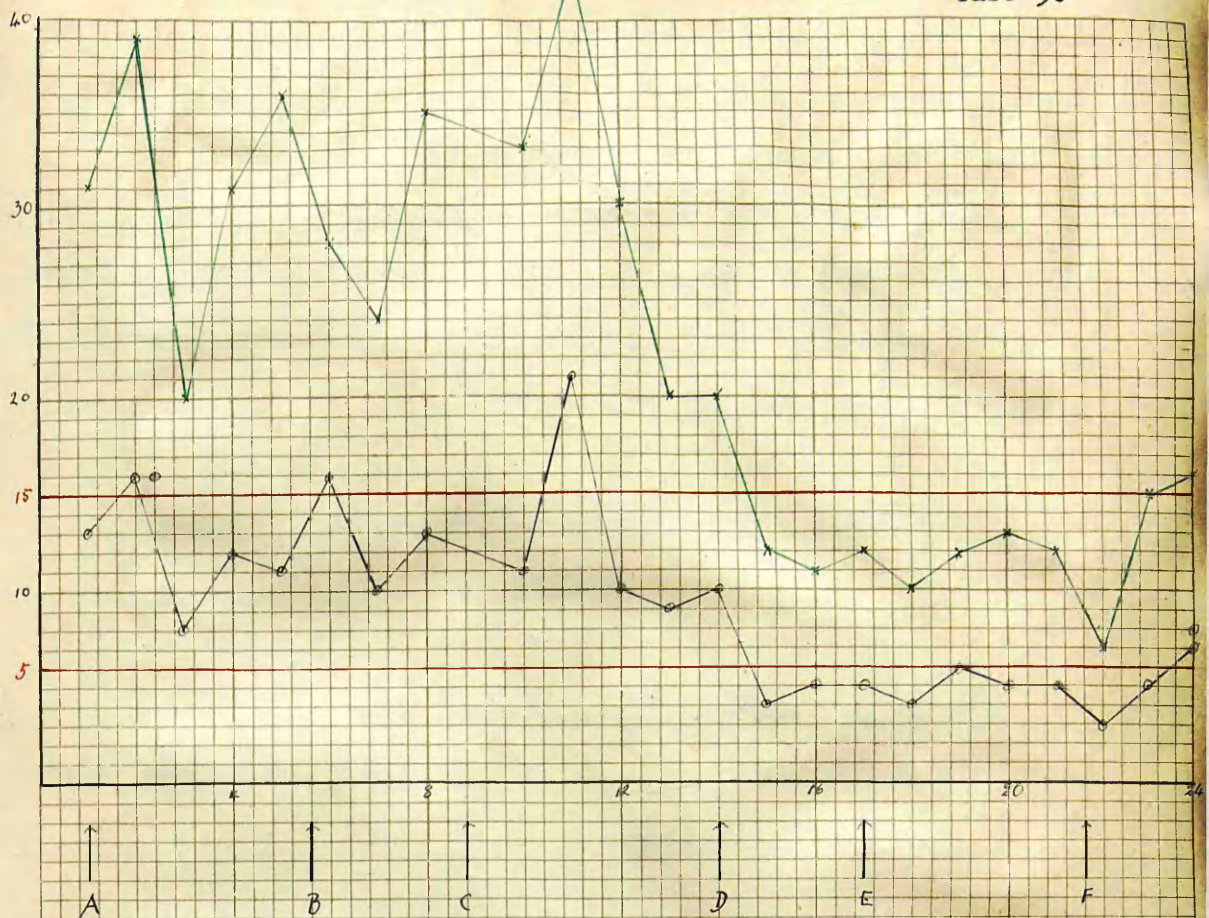
Sedimentation Graph.

In all aspects this graph gave a completely normal picture over the whole period of six months.

Cerebro-spinal fluid results.

Six complete results were obtained and one specimen which had sufficient fluid only for a cell count, Pandy Test and Lange colloidal gold curve.

Case 5.



	A	B	C	D	E	F	G
Protein	77	55	79	59	43	65·5	53·3
Albumen	58	49	59	40	38	48·3	40·5
Globulin	19	6	20	19	4·6	17·2	12·8
Ratio	3·0/1	8·6/1	3·0/1	2·1/1	8·3/1	2·8/1	3·2/1
Cells	1	3	2	Nil	Nil	Nil	1
Fandy	?+	+	Positive	Negative	Negative	Positive	Neg
Lange	0 0 1 2 2 2 1 0	0 1 1 1 3 3 3 2 1	1 1 1 2 2 2 1 0 0	0 0 0 1 1 1 0 0 0	0 0 0 0 0 0 0 0 0	0 0 1 1 1 0 0 0	0 0 1 0 0 0 0 0

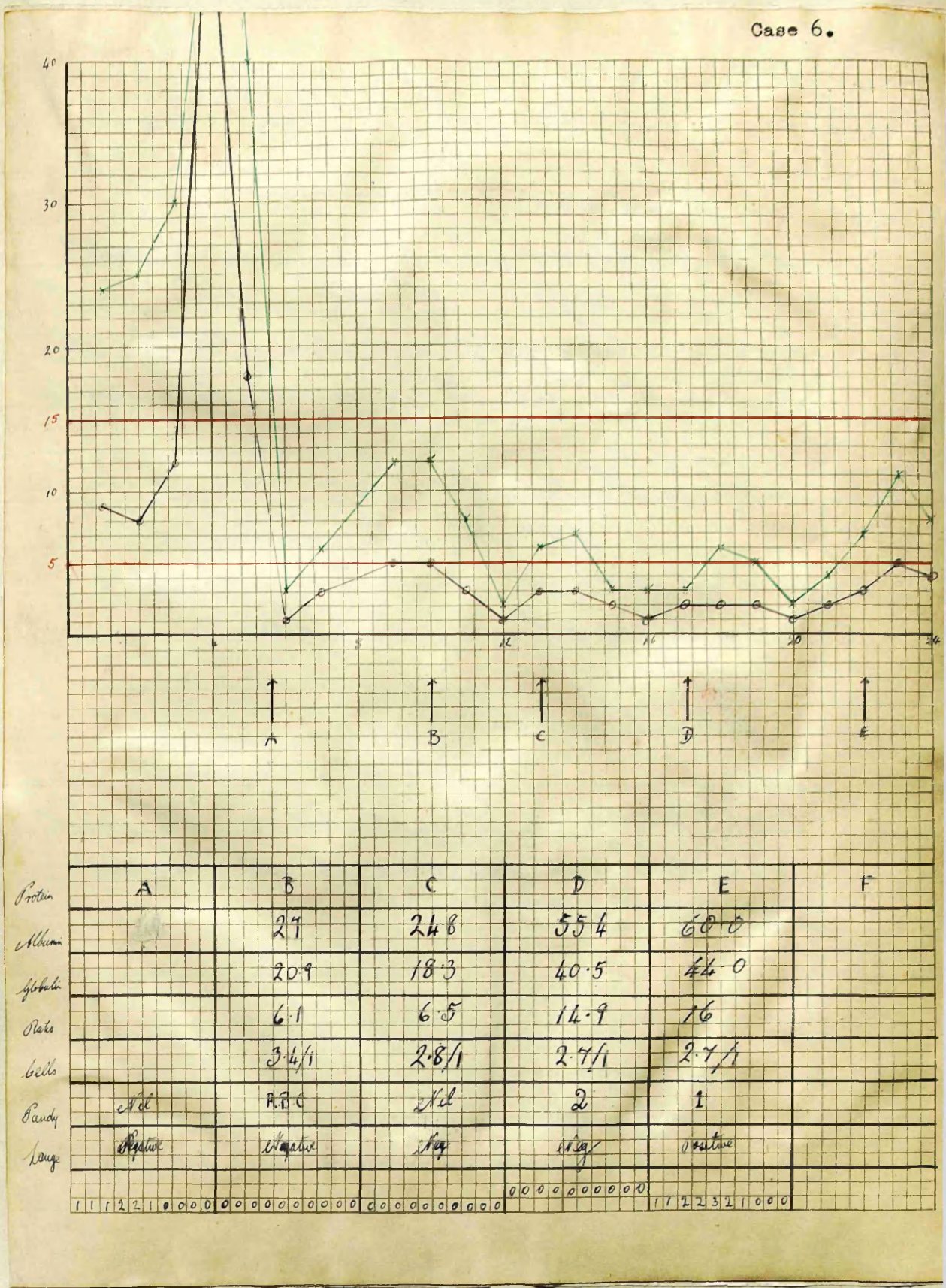
Sedimentation Graph.

This graph showed high readings over the first three and a half months, a pyelitis was present and also increased hilar markings in an X-ray plate of the chest.

Cerebro-spinal fluid results.

Seven complete results were obtained.

Case 6.



	A	B	C	D	E	F
Protein		27	24·8	55·4	60·0	
Albumin		20·9	18·3	40·5	44·0	
Globulin		6·1	6·5	14·9	16	
Cells		3·4/1	2·8/1	2·7/1	2·7/1	
Pandy	Nil	R.D.C	Nil	2	1	
Lange	Negative	Negative	Neg	Neg	Positive	

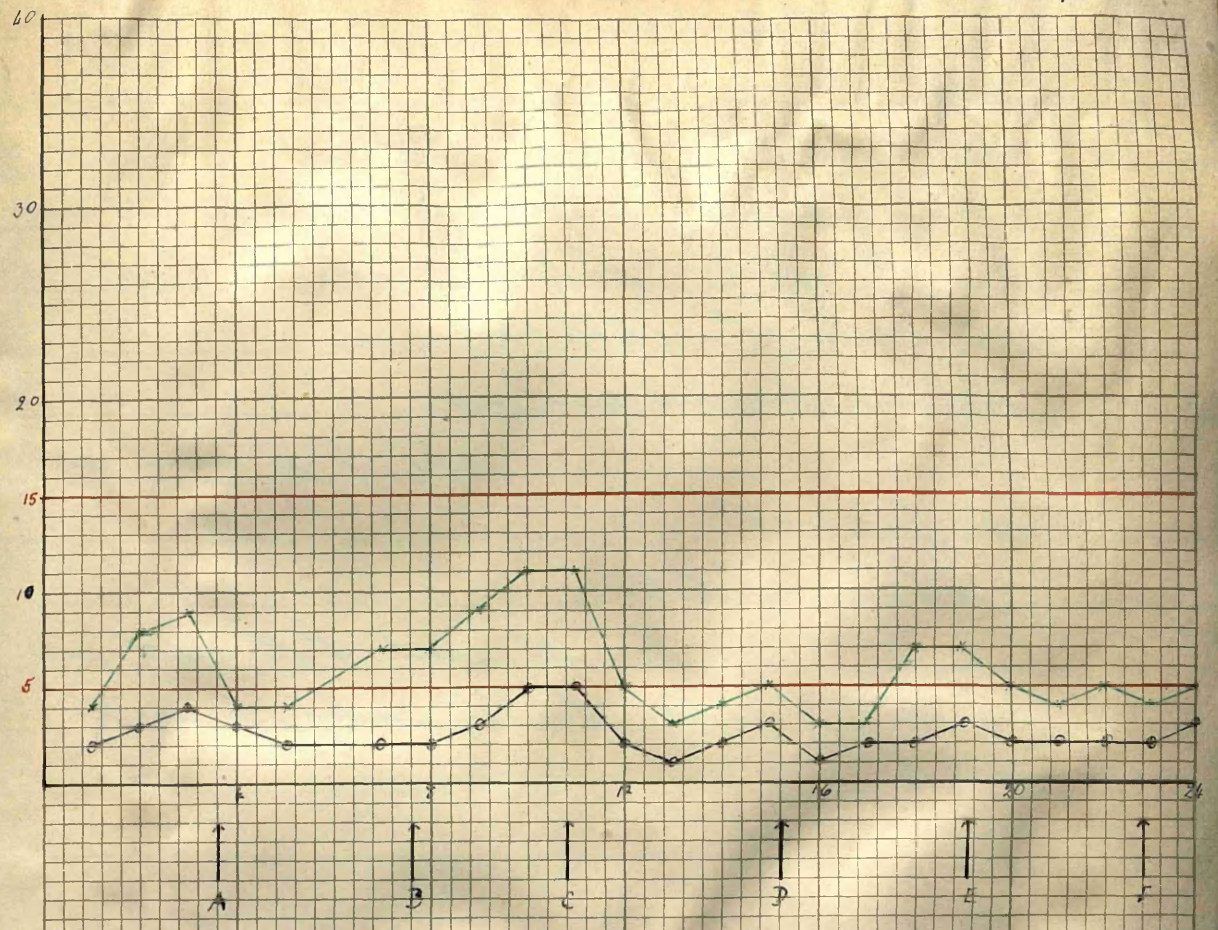
Sedimentation Graph.

This graph showed high readings over the first six weeks, a coryza followed by an acute bronchitis was present during this period.

Cerebro-spinal fluid results.

Four complete results were obtained and one specimen which had sufficient fluid only for a cell count, Pandy test and Lange colloidal gold curve.

Case 7.



	A	B	C	D	E	F	G
Urine.	39		38·8	40·4	41·6	39·0	
Fibrin	30		27·8	30·8	31·1	30·8	
Globin	9		11	9·6	9·1	8·2	
Ratio	33/1		25/1	32/1	32/1	37/1	
Casts	+		ditto	R.B.C.	ditto	2	
Bacilli	Negative		ditto	ditto	ditto	Negative	
Fungi							

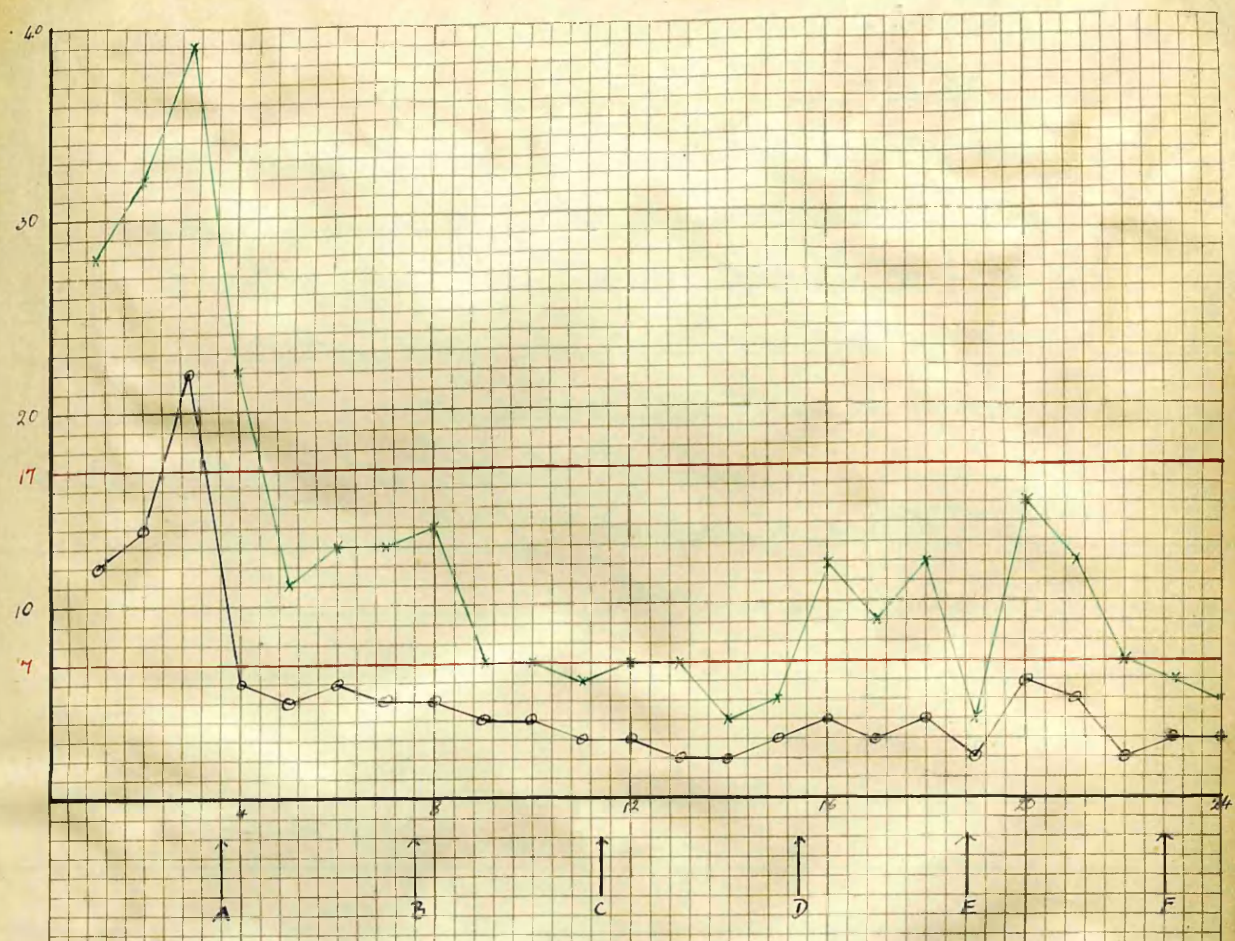
<u>Sedimentation Graph</u>.

In all aspects this graph gave a completely normal picture over the whole period of six months.

<u>Cerebro-spinal fluid results</u>.

Five complete results were obtained in addition to one specimen which contained frank blood.

Case 3.



	A	B	C	D	E	F	G
Protein	39	35	35·9	37	40·4		
Albumin	29	26	28·8	26·8	28·6		
Globulin	10	9	7·1	10·2	12·1		
Ratio	2·9/1	2·8/1	4·0/1	2·6/1	2·4/1		
Cells	23 c.	2	nil	nil	1.		
Pandy	Positive	Negative	Negative	Negative	Neg		
Range	2 2 3 3 3 1 1 0	1 1 1 1 0 0 0 0	0 0 0 0 0 0 0 0	0 0 1 2 2 1 0 0	0 0 0 0 0 0 0 0		

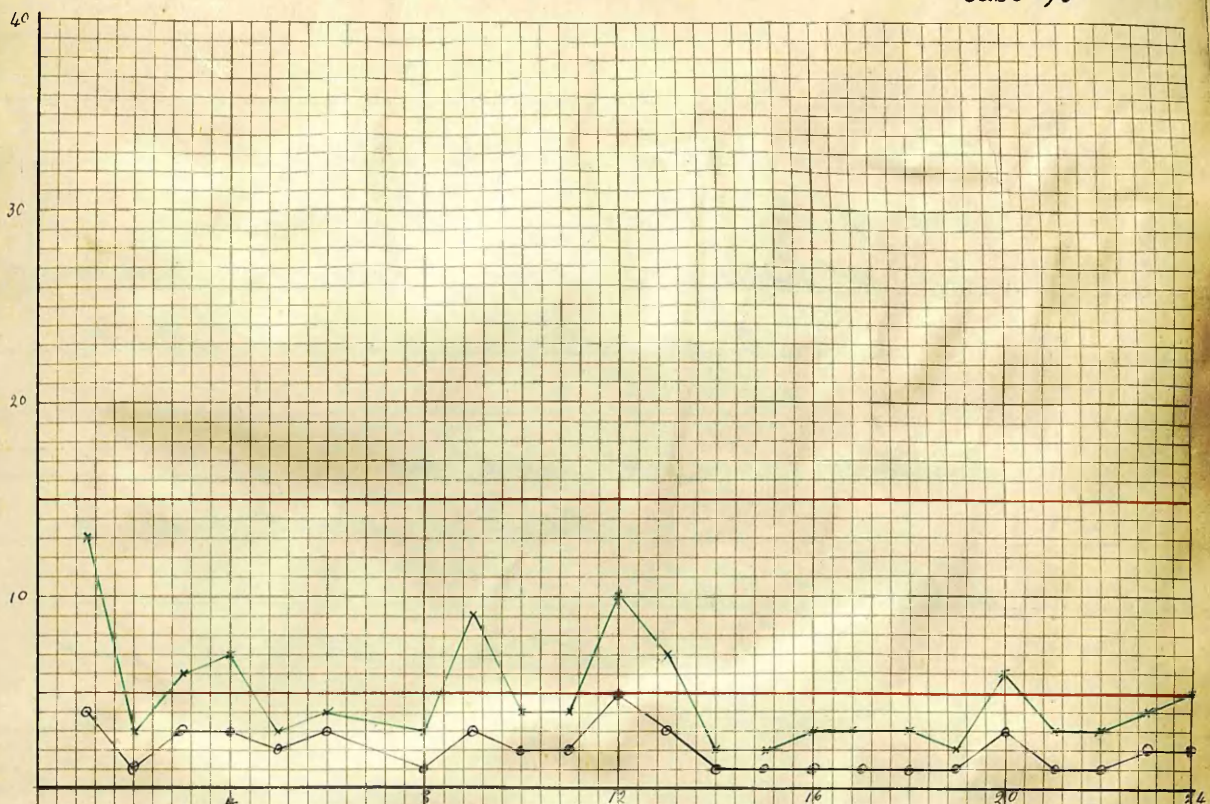
Sedimentation Graph.

This graph showed high readings over the first four weeks, an acute bronchitis was present over this period.

Cerebro-spinal fluid results.

Five complete results were obtained in addition to one specimen which contained frank blood.

Case 9.



	A	B	C	D	E	F
Protein	24		42.5	23.8	24	24.8
Albumin	18		31	18	18.6	19.5
Globulin	6		11.5	5.8	5.4	5.3
Ratio	2.7/1		2.7/1	3.0/1	3.5/1	3.7/1
Cells	7		1	R.B.C.	2	1.
Pandy	+Negative		+Negative	+Negative	+Negative	+Neg.
Fungi	1 1 1 1 1 0 0 0		0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0

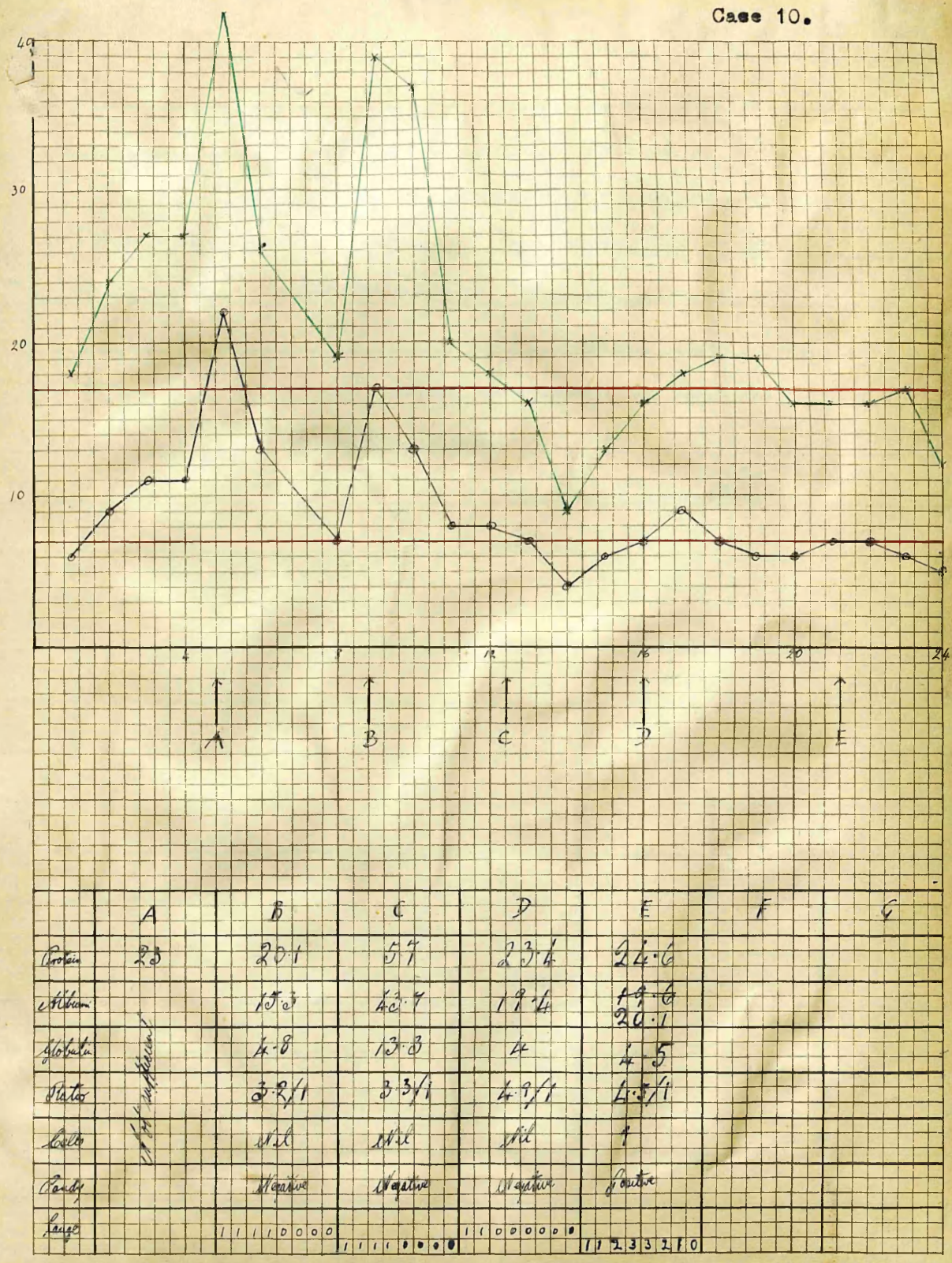
Sedimentation Graph.

In all aspects this graph gave a completely normal picture over the whole period of six months.

Cerebro-spinal fluid results.

Five complete results were obtained in addition to one specimen which contained frank blood.

Case 10.



	A	B	C	D	E	F	G
Protein	23	20·1	57	23·4	24·6		
Albumin		15·3	42·7	18·4	~~19·6~~ 20·1		
Globulin		4·8	13·3	4	4·5		
Ratio		3·2/1	3·3/1	4·2/1	4·5/1		
Cells		Nil	Nil	Nil	1		
Pandy		Negative	Negative	Negative	Positive		
Lange		1 1 1 1 0 0 0 0	1 1 1 1 0 0 0 0	1 1 0 0 0 0 0 0	1 1 2 3 3 2 1 0		

Urine sediment

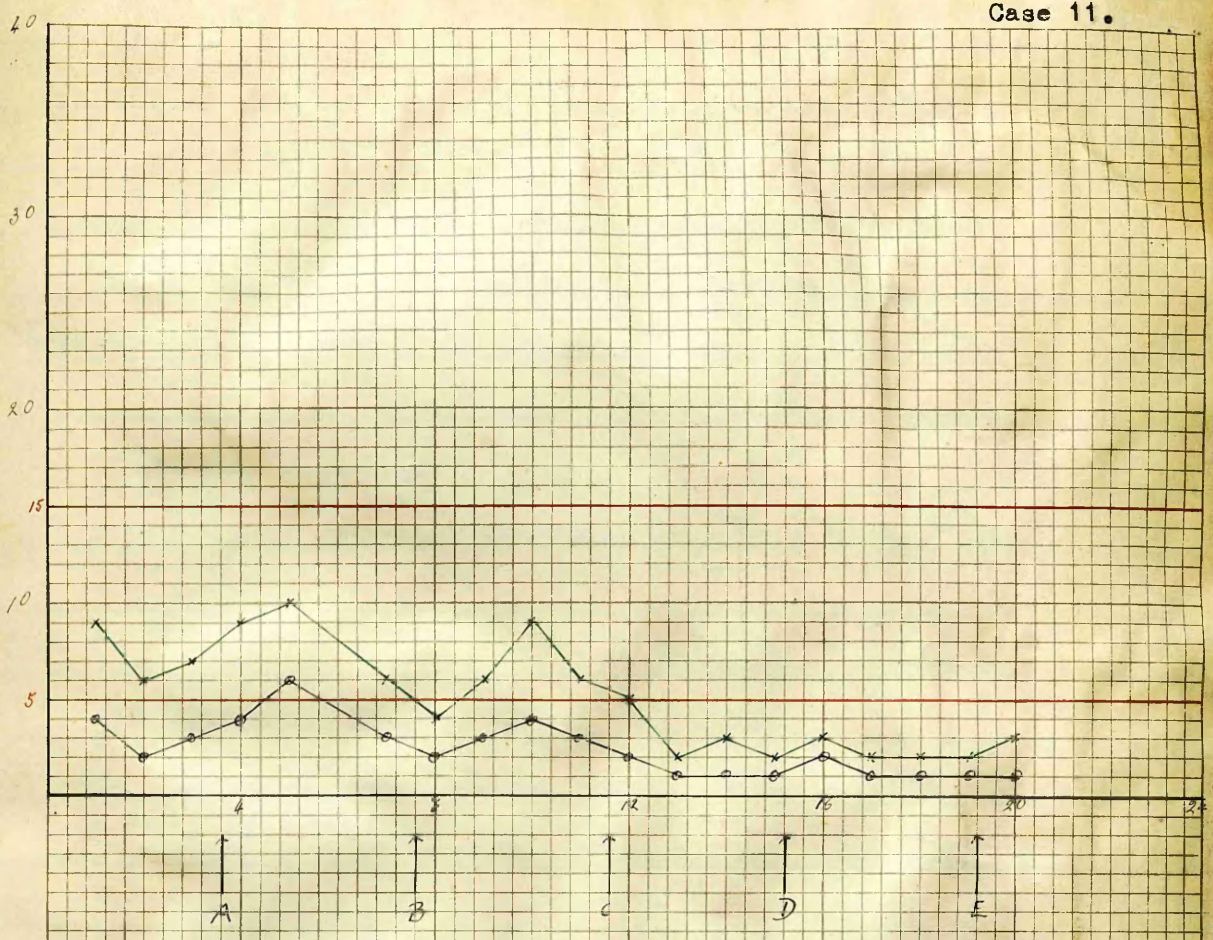
Sedimentation Graph.

This graph showed high readings over the whole period of six months, a chronic bronchitis complicated by moderately acute exacerbations was present.

Cerebro-spinal fluid results.

Four complete results were obtained.

Case 11.



	A	B	C	D	E
Protein	32	29	29·4		28·6
Albumin	23	22	23		23·3
Globulin	9	7	6·4		5·3
Ratio	2·3/1	3/1	3·5/1		4·4/1
Cells	1	Nil	Nil		1
Sandy	Negative	Negative	Negative		Neg
Benge	1 1 1 1 1 0 0 0 0 0	1 1 1 1 1 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0		0 0 0 0 0 0 0 0 0 0

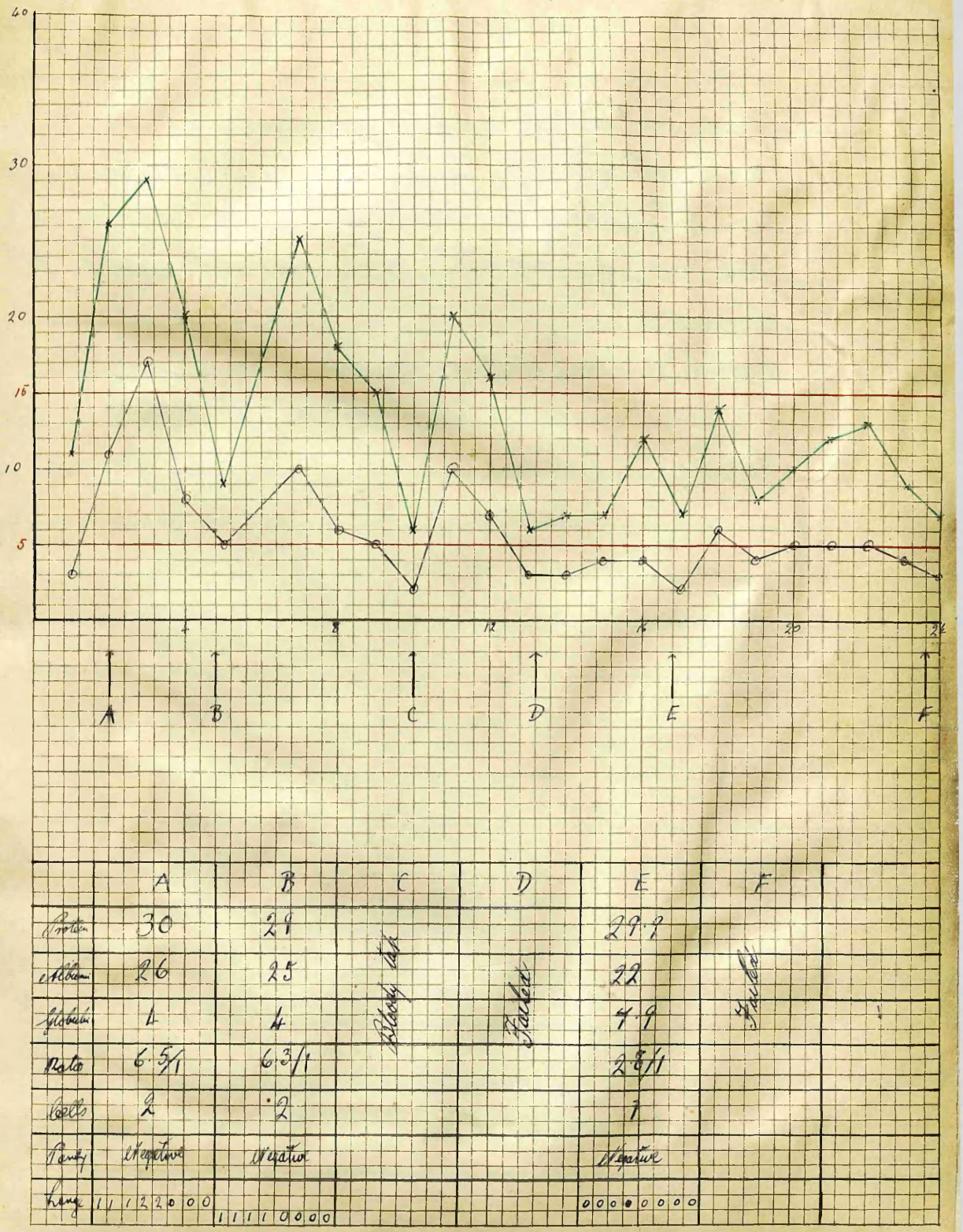
Sedimentation Graph.

In all aspects this graph gave a completely normal picture over a period of five months.

Cerebro-spinal fluid results.

Four complete results were obtained in addition to one specimen which contained frank blood.

Case 12.



	A	B	C	D	E	F
Protein	30	28			29·2	
Albumen	26	25	Bloody tap	Faulty	22	Faulty
Globulin	4	4			4·9	
Ratio	6·5/1	6·3/1			2·8/1	
Cells	2	·2			7	
Pandy	Negative	Negative			Negative	
Fehling	1 1 1 2 2 0 0 0	1 1 1 1 0 0 0 0			0 0 0 • 0 0 0 0	

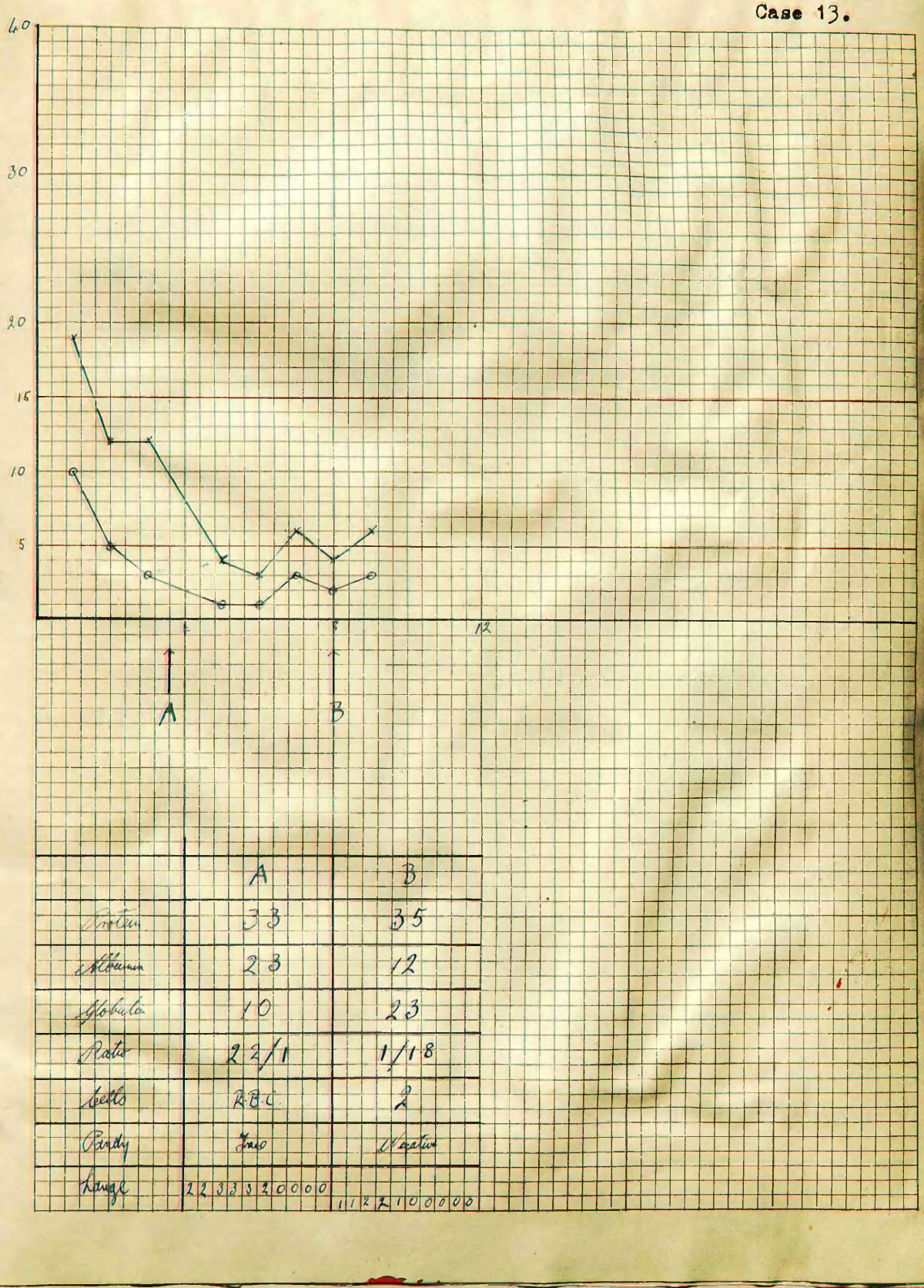
Sedimentation Graph.

This graph showed high readings over the first three months, a chronic bronchitis with acute exacerbations was present.

Cerebro-spinal fluid results.

Three complete results were obtained in addition to one specimen which contained frank blood.

Case 13.



	A	B
Proteins	33	35
Albumen	23	12
Globulin	10	23
Ratio	2 2/1	1/1·8
Cells	R.B.C.	2
Pandy	Trace	Negative
Lange	2 2 3 3 3 2 0 0 0 0	1 1 2 2 1 0 0 0 0 0

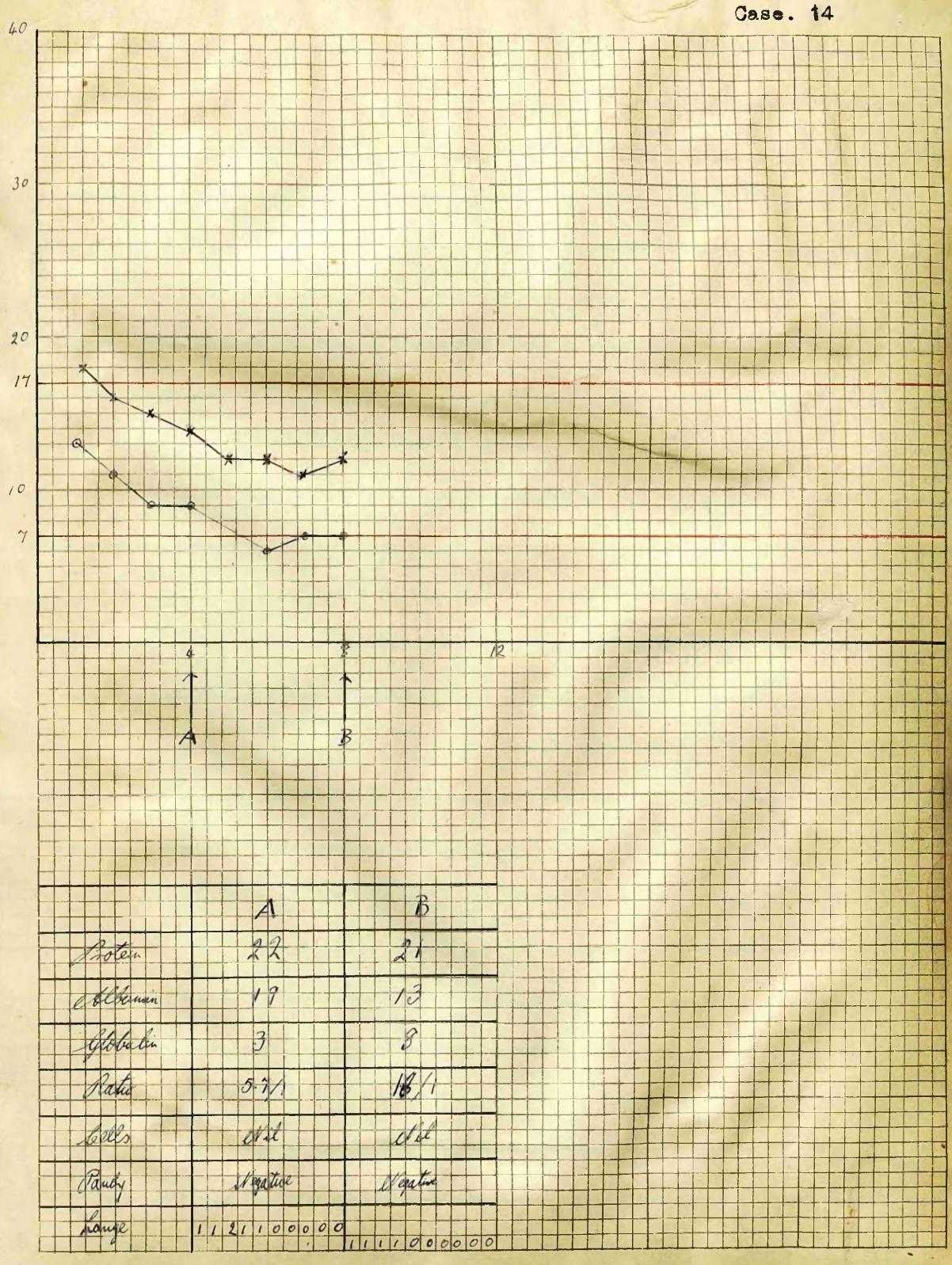
Sedimentation Graph.

The sedimentation rate was taken over only a period of two months, as an acute respiratory infection culminating in broncho-pneumonia and death developed.

Cerebro-spinal fluid results.

Two complete results were obtained.

Case. 14



	A	B
Protein	22	21
Albumen	19	13
Globulin	3	8
Ratio	5.7/1	1.6/1
Cells	Nil	Nil
Pandy	Negative	Negative
Lange	1 1 2 1 0 0 0 0 0	1 1 1 1 0 0 0 0 0 0

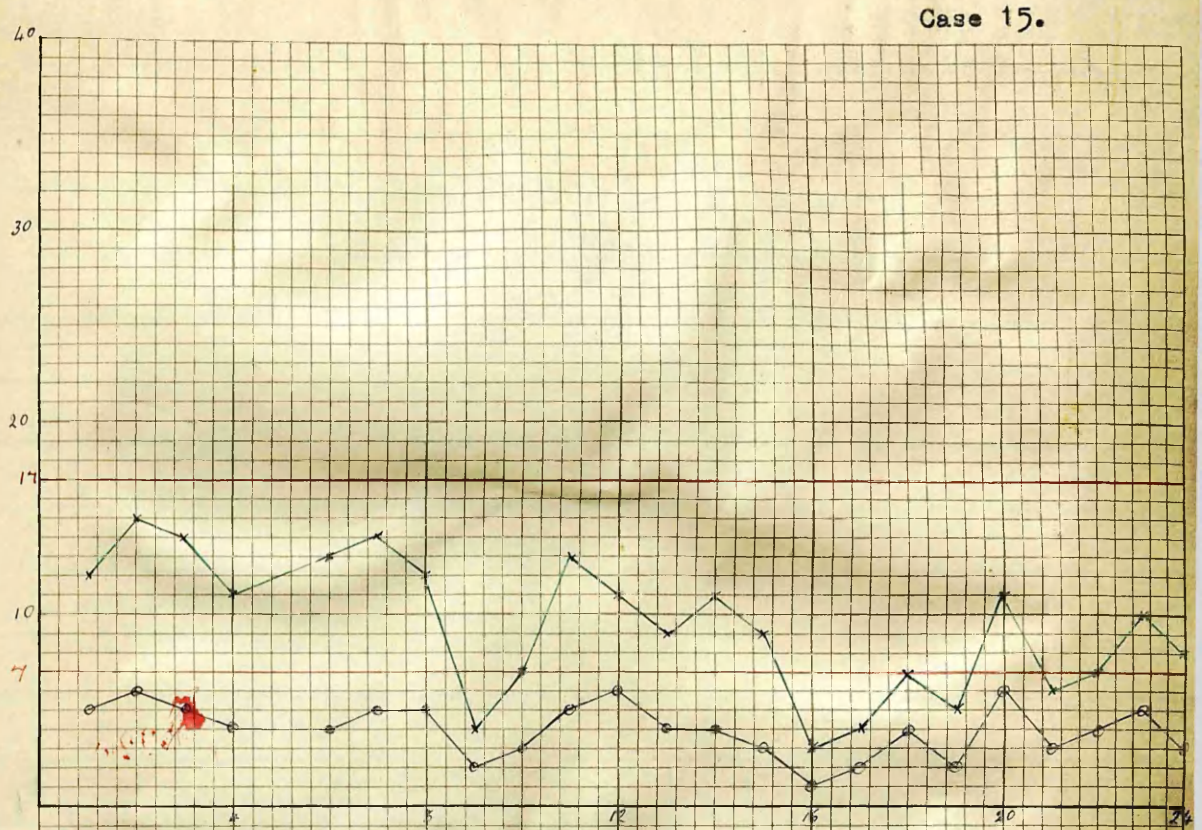
Sedimentation Graph.

The sedimentation rate was taken only over a period of two months as an acute respiratory infection, culminating in broncho-pneumonia and death developed.

Cerebro-spinal fluid results.

Two complete results were obtained.

Case 15.



	A	B
Protein	35	36
Albumin	29	24
Globulin	6	12
Ratio	52/1	2·0/1
Cells	Nil	Nil
Cavdy	Negative	Negative
Range.	1 1 1 1 1 0 0 0 0 0	1 1 2 2 1 0 0 0 0 0

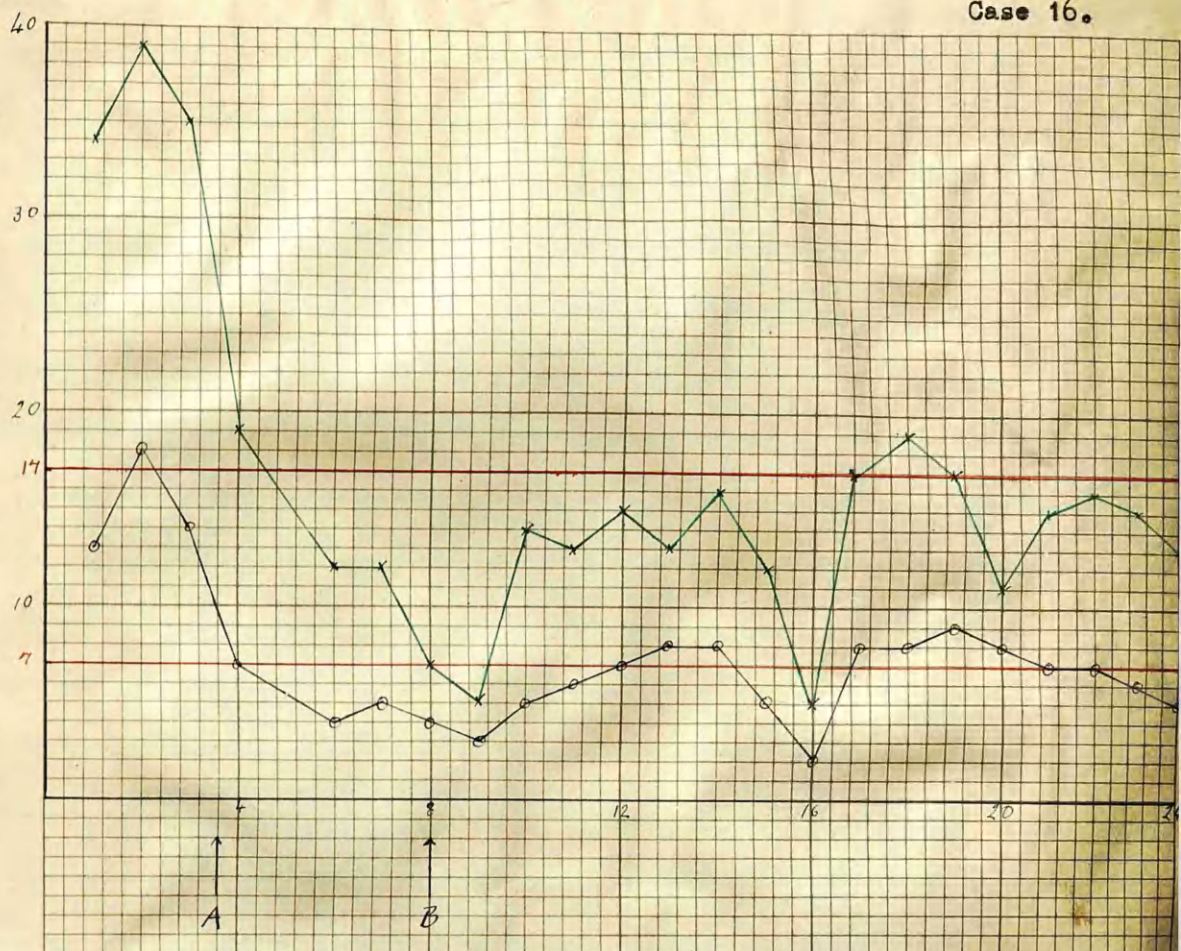
Sedimentation Graph.

In all aspects this graph gave a completely normal picture over the whole period of six months.

Cerebro-spinal fluid results.

Two complete results were obtained.

Case 16.



	A	B
Protein	38	41
Albumen	29	29
Globulin	9	12
Ratio	33/1	25/1
Cells	Nil	R.B.C
Pandy	Trace	Negative
Lange	1 2 2 3 2 0 0 0 0 0	1 2 2 2 1 0 0 0 0 0

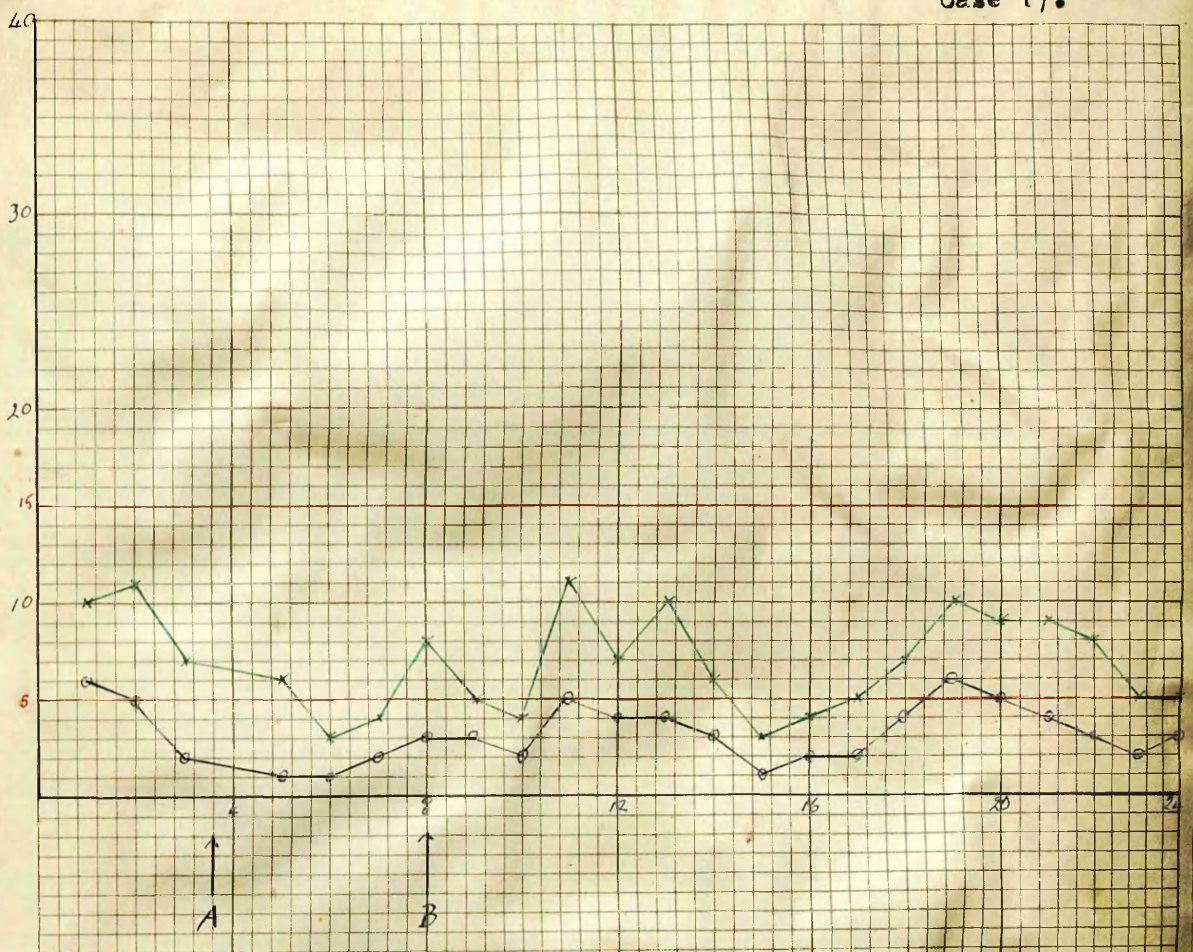
Sedimentation Graph.

This graph showed high readings practically over the whole period of six months as a chronic bronchitis was present complicated by an acute exacerbation during the first month.

Cerebro-spinal fluid results.

Two complete readings were obtained.

Case 17.



	A	B
Protein	38	48
Albumin	30	26
Globulin	8	16
Ratio	38/1	1·6/1
Cells	2	Nil
Candy	Trace	Negative
Lange	1 1 2 2 1 0 0 0 0 0	0 1 1 1 0 0 0 0 0 0

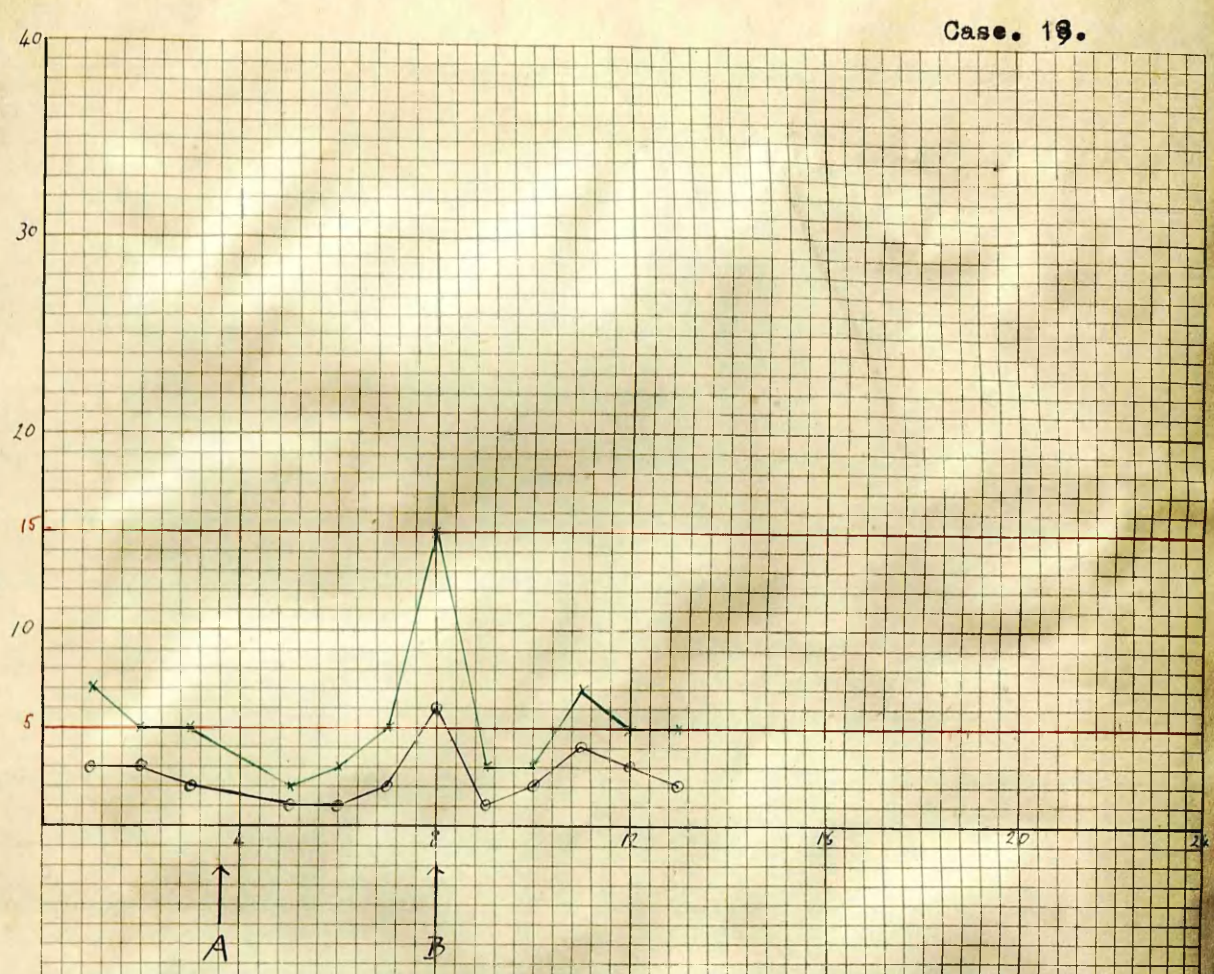
Sedimentation Graph.

In all aspects this graph gave a completely normal picture over the whole period of six months.

Cerebro-spinal fluid results.

Two complete results were obtained.

Case. 19.



	A	B
Protein	36	31
Albumin	30	24
Globulin	6	7
Ratio	5/1	3.4/1
Cells	Nil	3
Pandy	Trace	Negative
Sugar	1 1 1 1 1 0 0 0 0 0	1 1 2 1 1 0 0 0 0 0

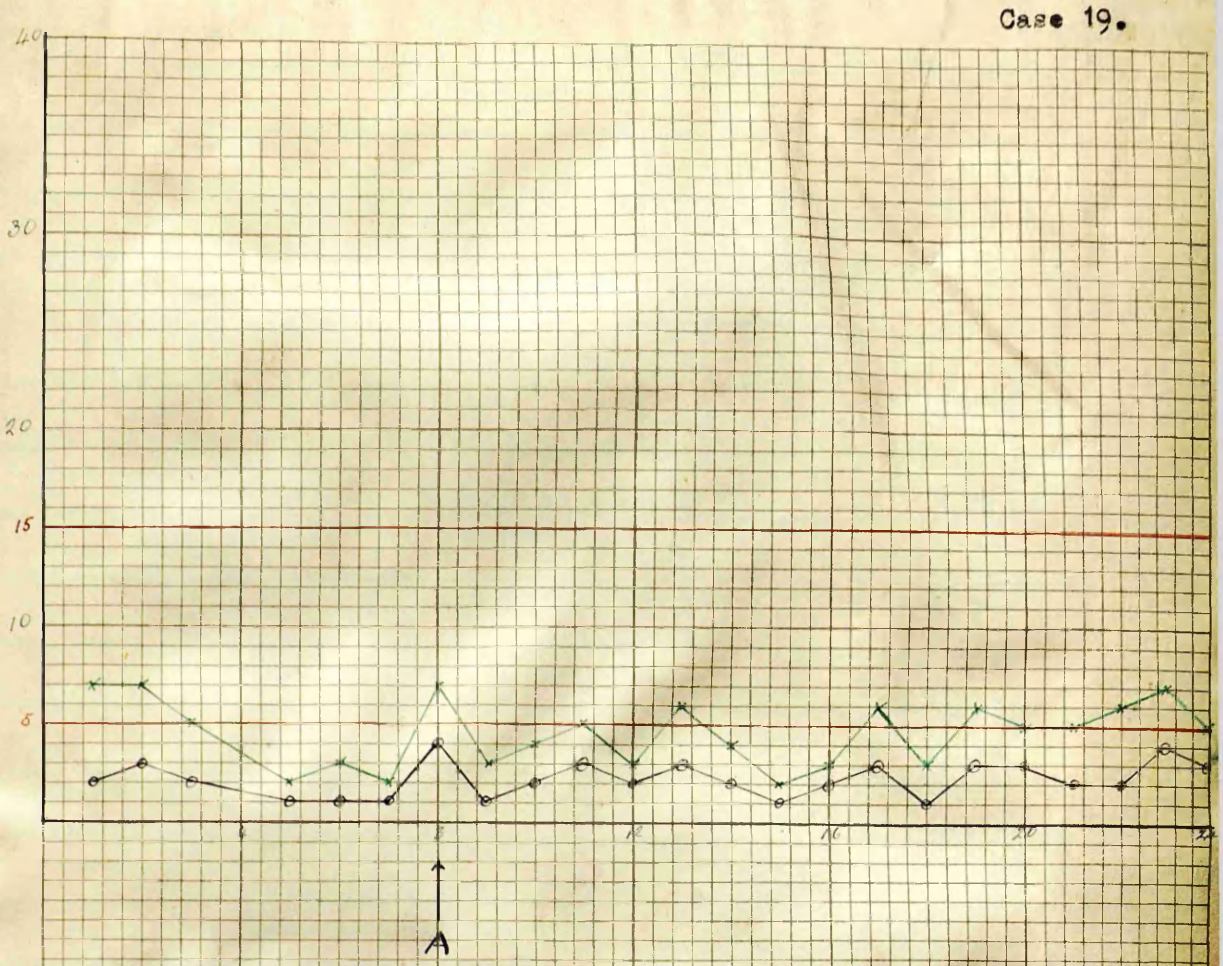
Sedimentation Graph.

In all aspects this graph gave a completely normal picture over the whole period of three months.

Cerebro-spinal fluid results.

Two complete results were obtained.

Case 19.



	A
Protein	31
Albumin	27
Globulin	4
Ratio	4/0/1
Cells	Nil
Pandy	Negative
Range	0 1 1 2 1 0 0 0 0 0

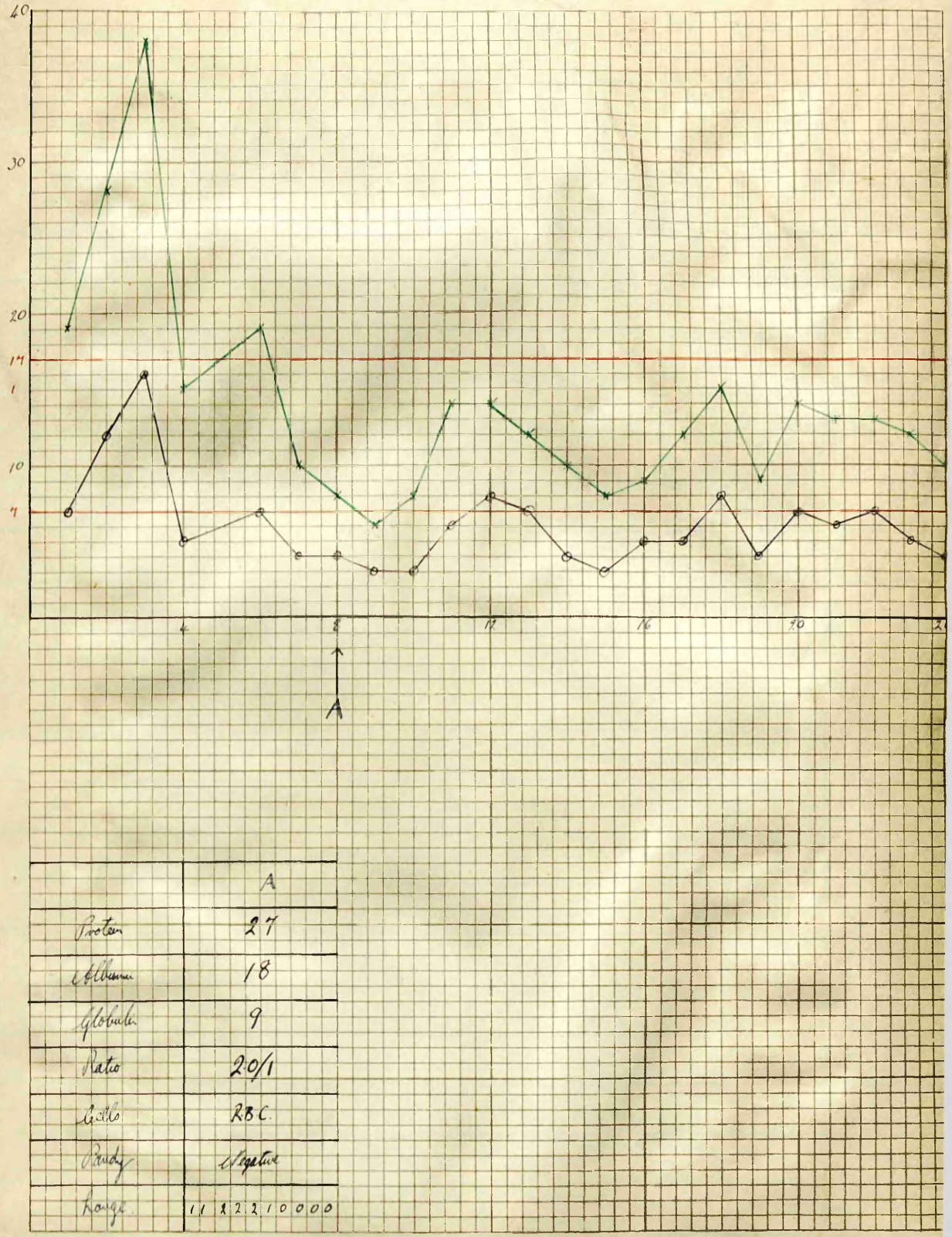
Sedimentation Graph.

In all aspects this graph gave a completely normal picture over the whole period of six months.

Cerebro-spinal fluid results.

One complete result was obtained.

Case 20.



	A
Protein	27
Albumin	18
Globulin	9
Ratio	2.0/1
Cells	RBC.
Pandy	Negative
Lange	1 1 2 2 1 0 0 0 0

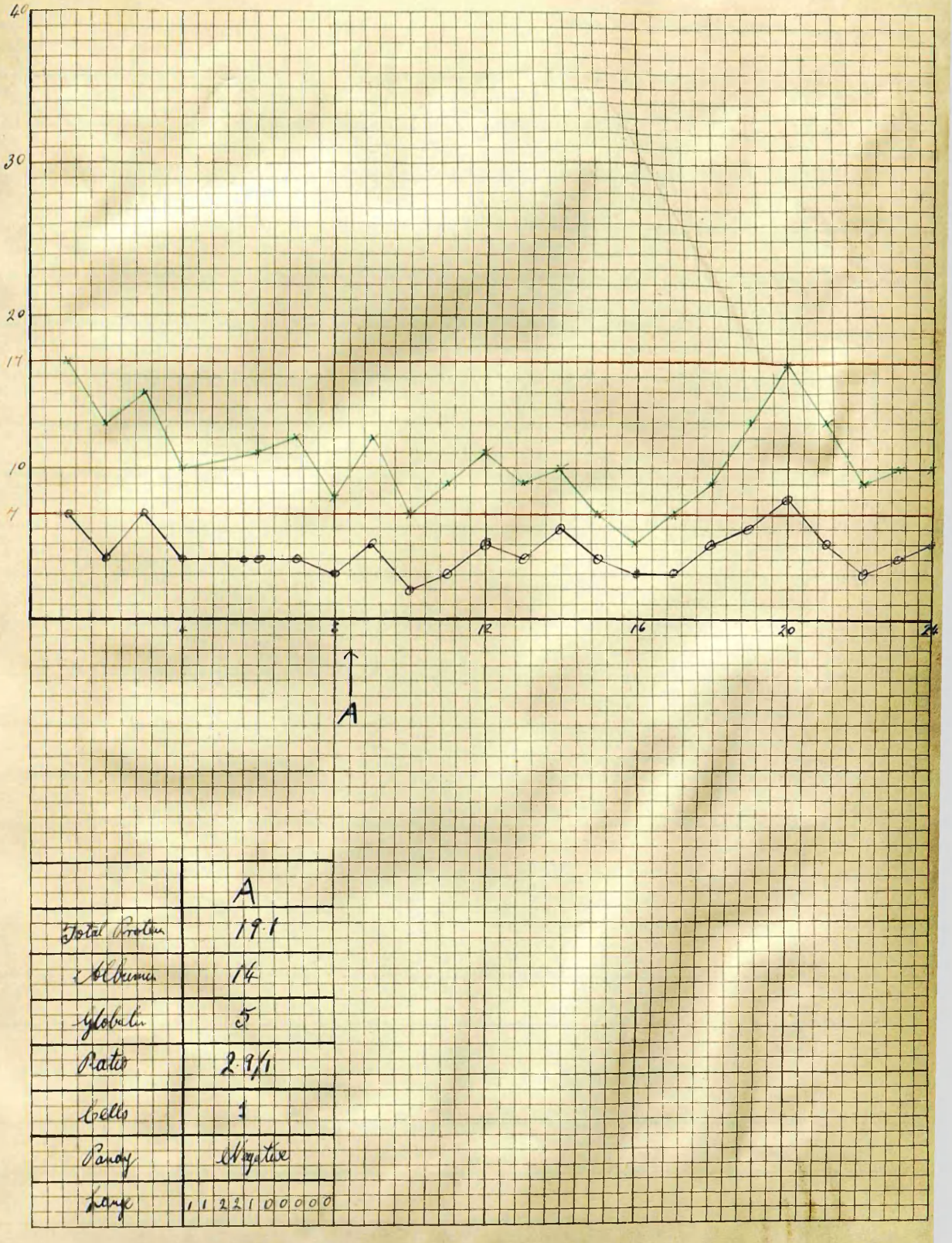
Sedimentation Graph.

This graph showed a high reading over the first two months as a bronchitis was present.

Cerebro-spinal fluid results.

One complete result was obtained.

Case 21.



	A
Total Protein	19.1
Albumin	14
Globulin	5
Ratio	2.9/1
Cells	1
Pandy	Negative
Lange	1 1 2 2 1 0 0 0 0 0

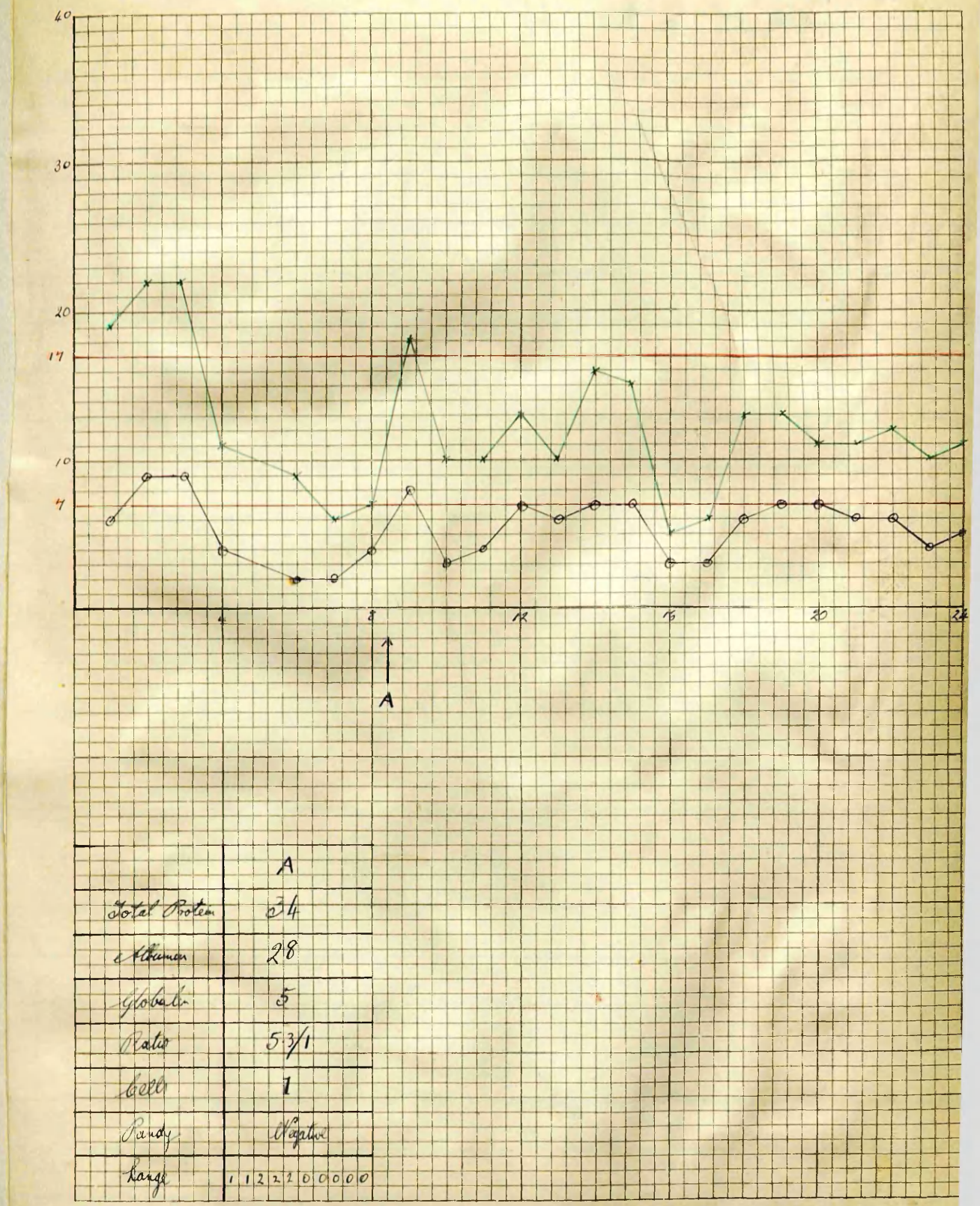
Sedimentation Graph.

In all aspects this graph gave a completely normal picture over the whole period of six months.

Cerebro-spinal fluid results.

One complete result was obtained.

Case 22.



	A
Total Protein	34
Albumen	28
Globulin	5
Ratio	5 3/1
Cell	1
Pandy	Negative
Lange	1 1 2 2 1 0 0 0 0 0

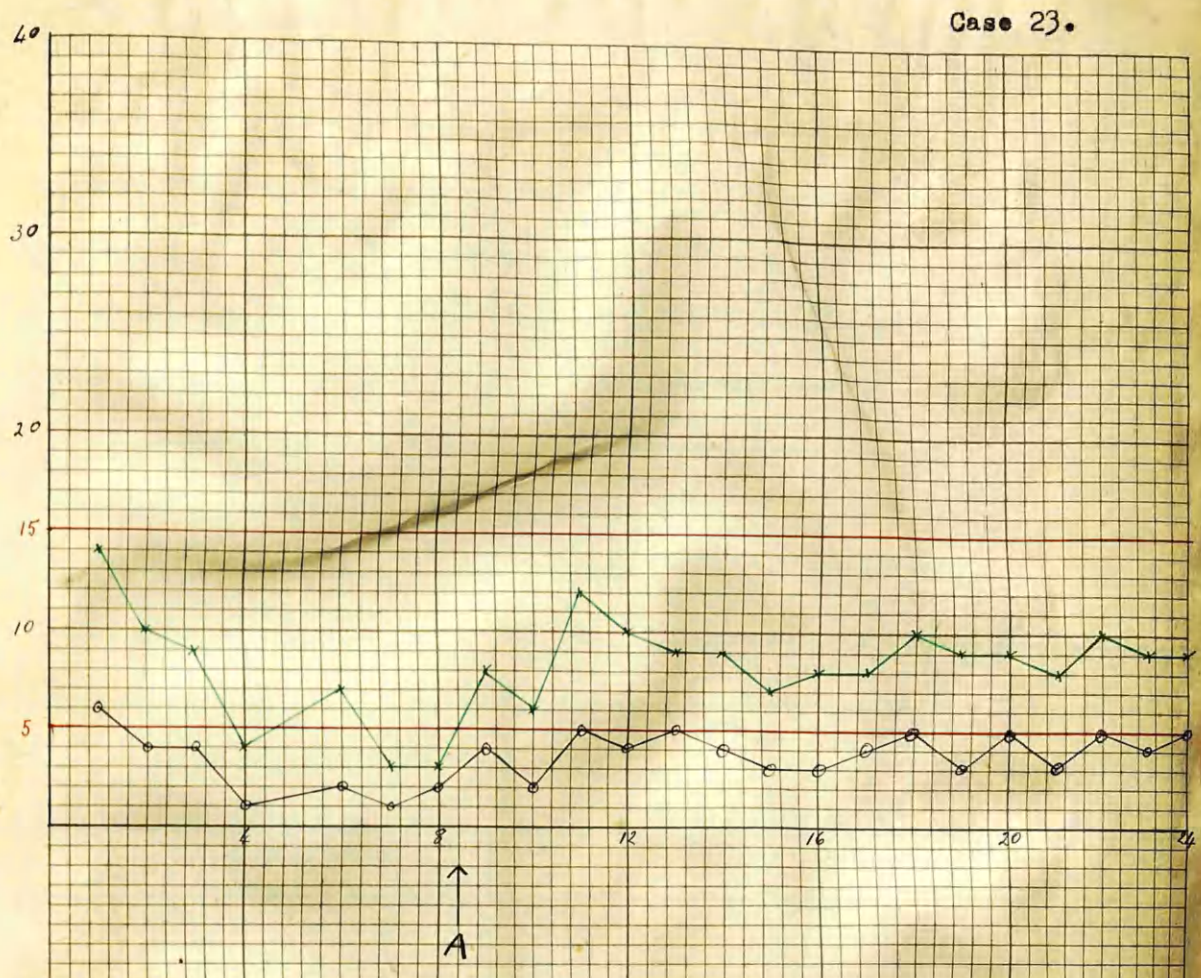
Sedimentation Graph.

This graph showed high readings over the first month, a chronic bronchitis was present.

Cerebro-spinal fluid results.

One complete result was obtained.

Case 23.



	A
Total Protein	49
Albumin	36
Globulin	13
Ratio	2·8/1
Cells	1
Pandy	Negative
Lange	0 1 1 1 0 0 0 0 0 0

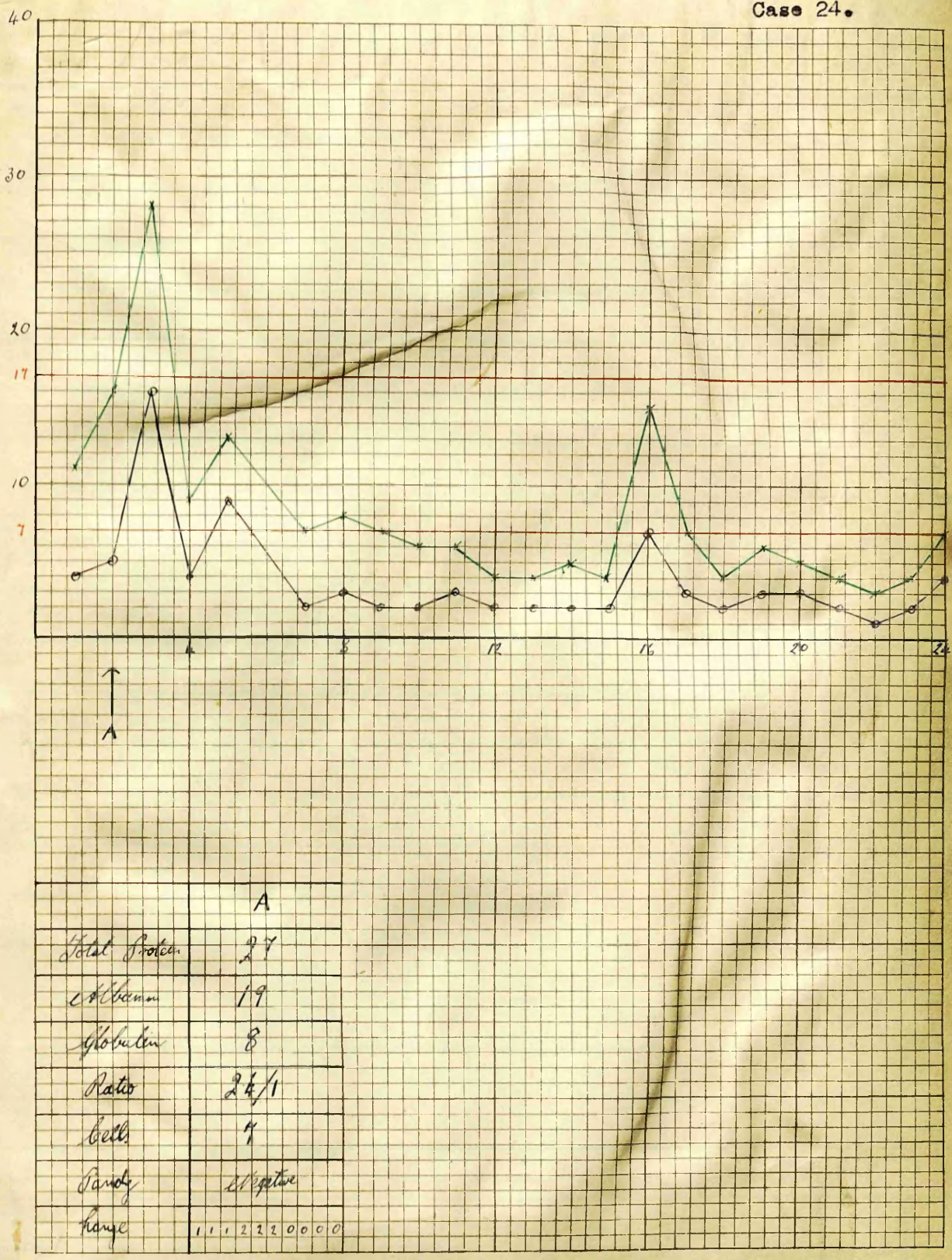
Sedimentation Graph.

In all aspects this graph gave a completely normal picture over the whole period of six months.

Cerebro-spinal fluid results.

One complete result was obtained.

Case 24.



	A
Total Protein	27
Albumen	19
Globulin	8
Ratio	24/1
Cells	7
Pandy	Negative
Range	1 1 1 2 2 2 0 0 0

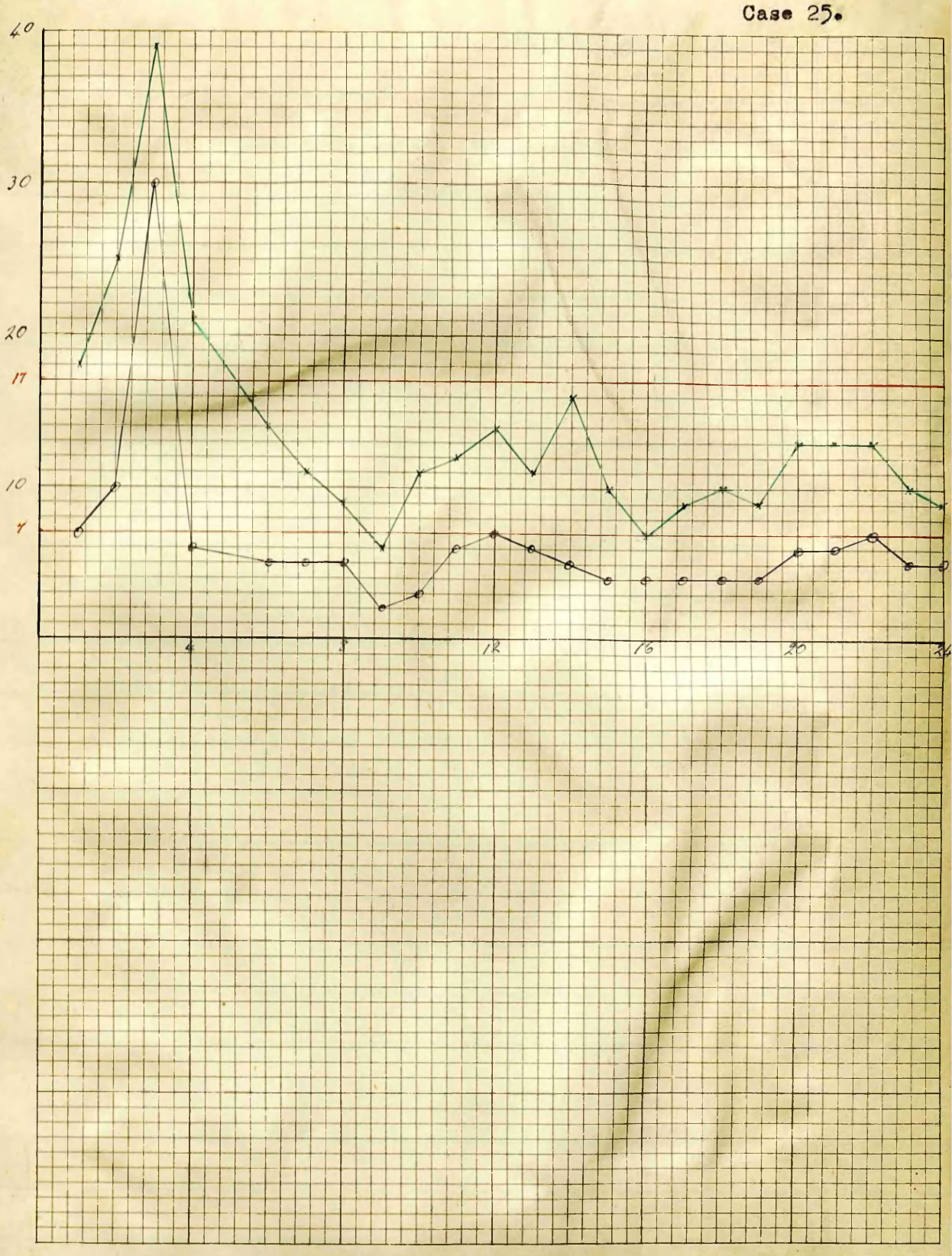
Sedimentation Graph.

This graph showed high readings over the first month, an acute bronchitis was present.

Cerebro-spinal fluid results.

One complete result was obtained.

Case 25.



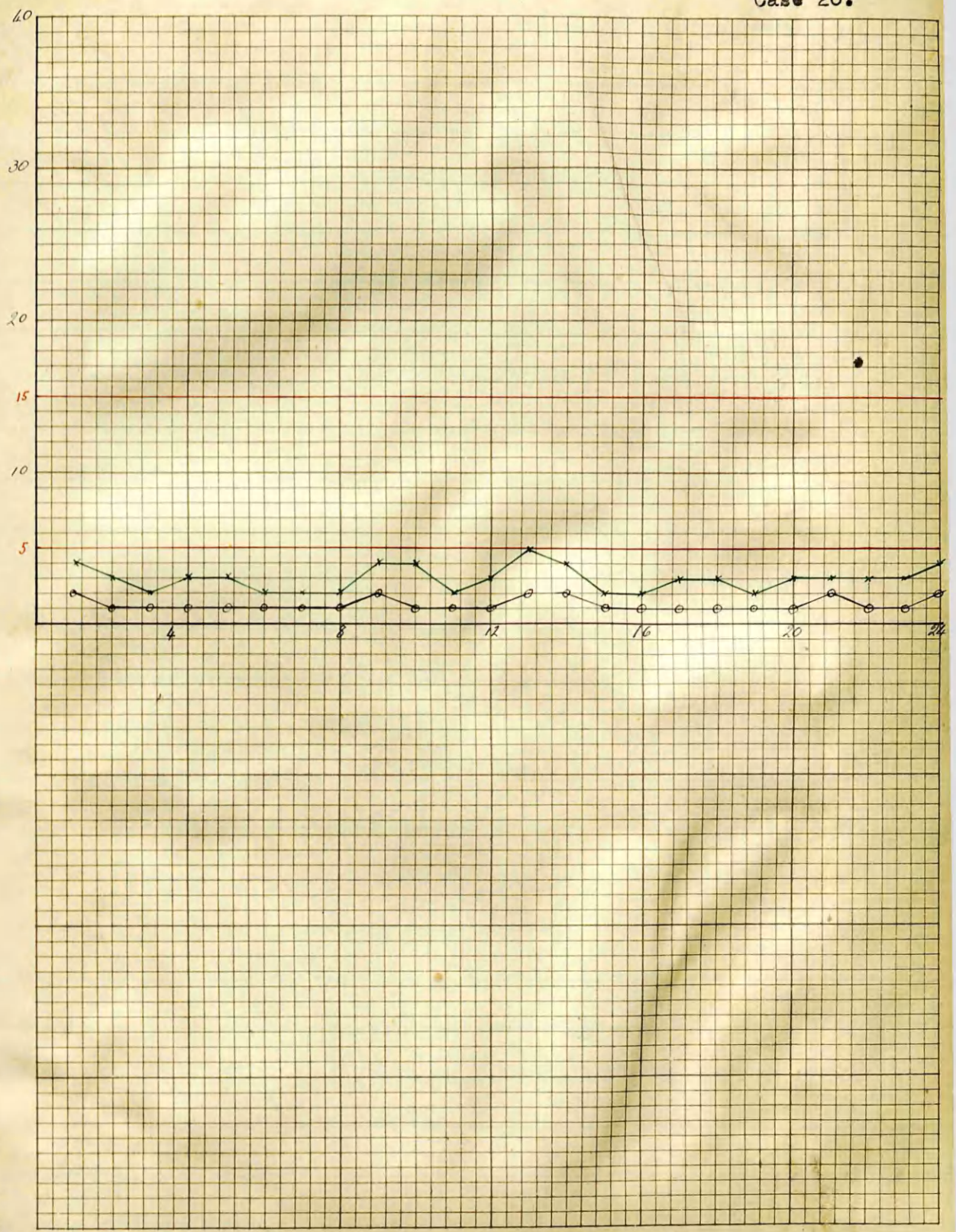
Sedimentation Graph.

This graph showed high readings over the first month, an acute bronchitis was present.

Cerebro-spinal fluid results.

Cases 25 to 30 had no serebro-spinal fluid examinations carried out.

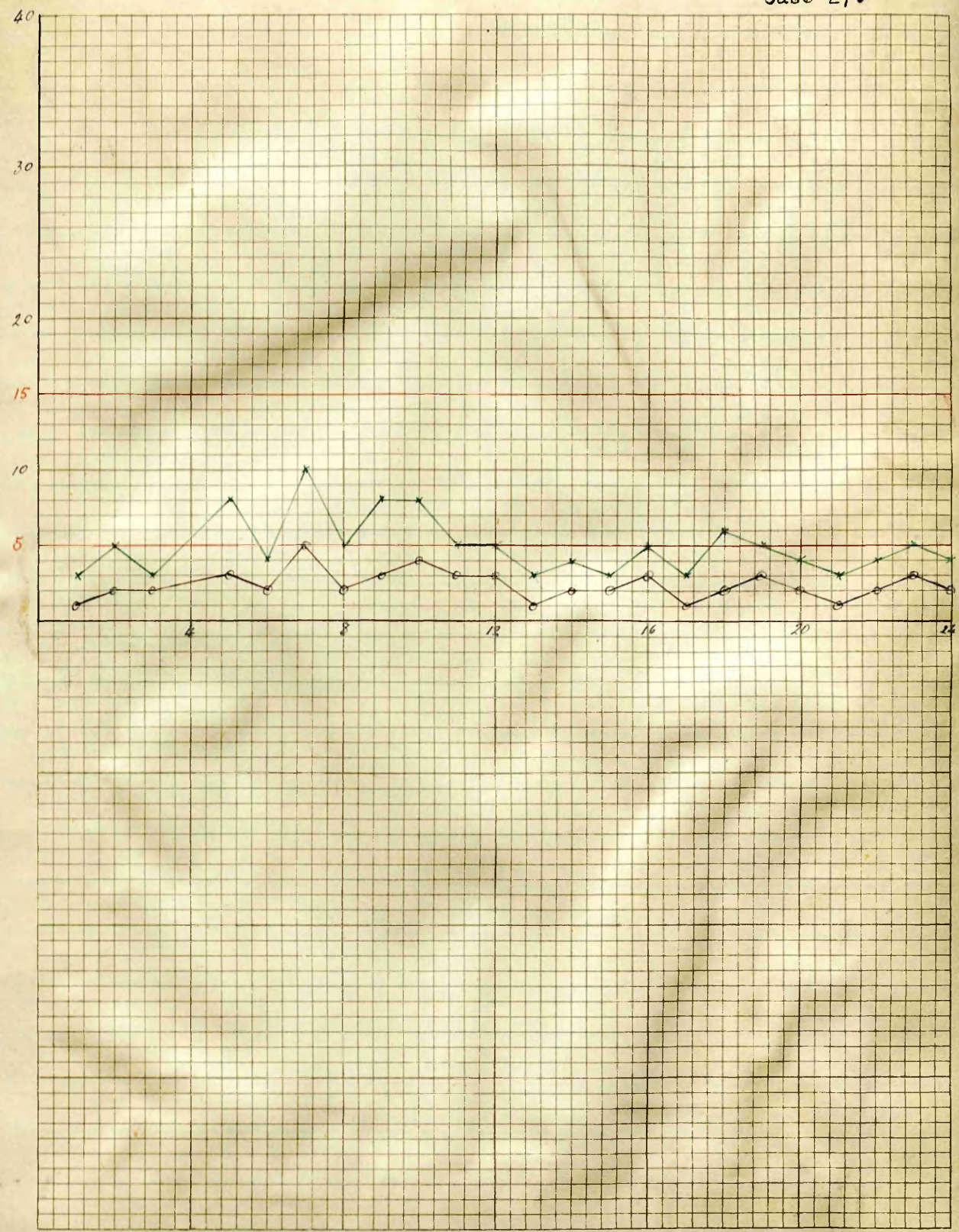
Case 26.



Sedimentation Graph.

In all aspects this graph gave a completely normal picture over the whole period of six months.

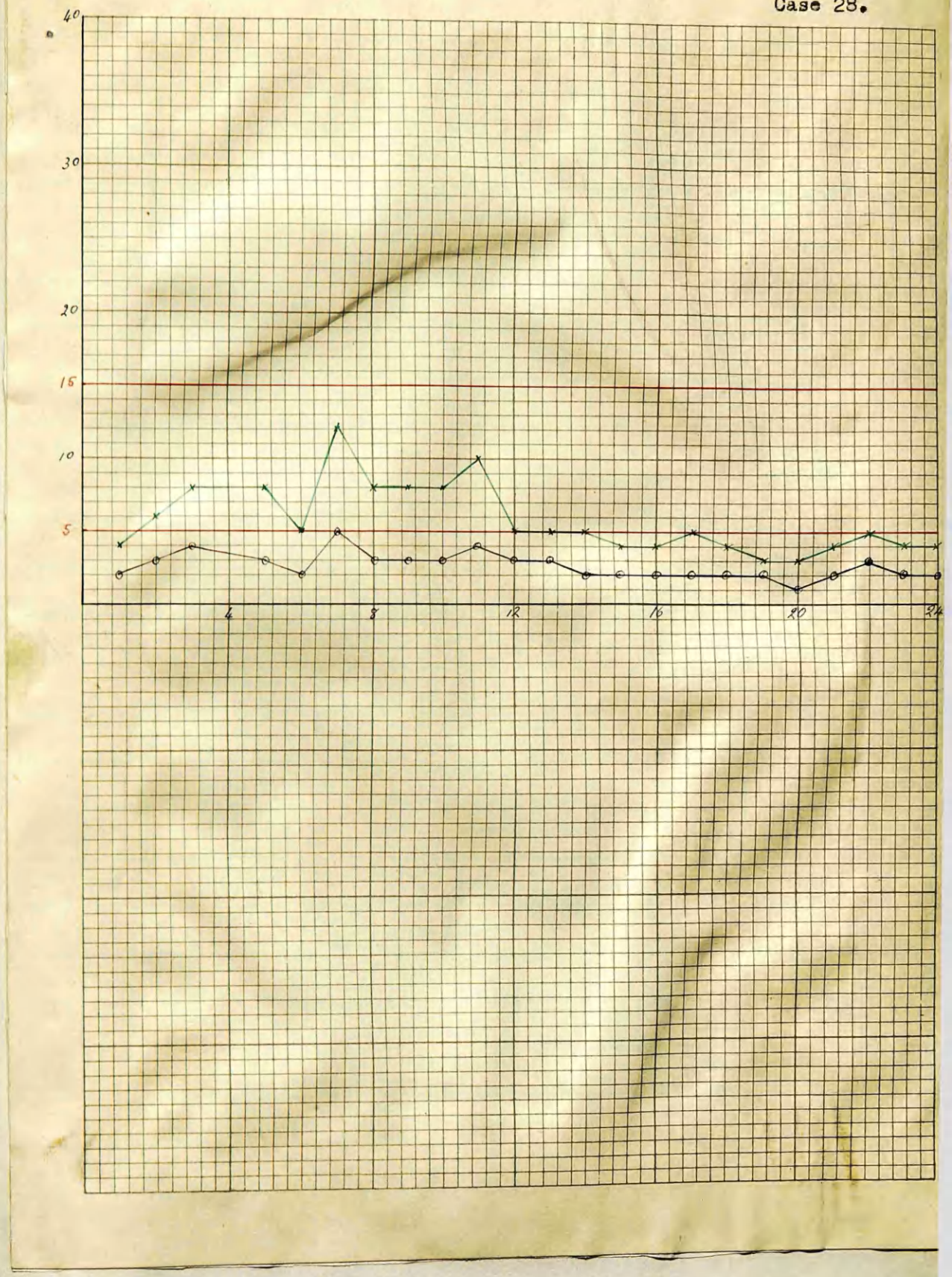
Case 27.



Sedimentation Graph.

In all aspects this graph gave a completely normal picture over the whole period of six months.

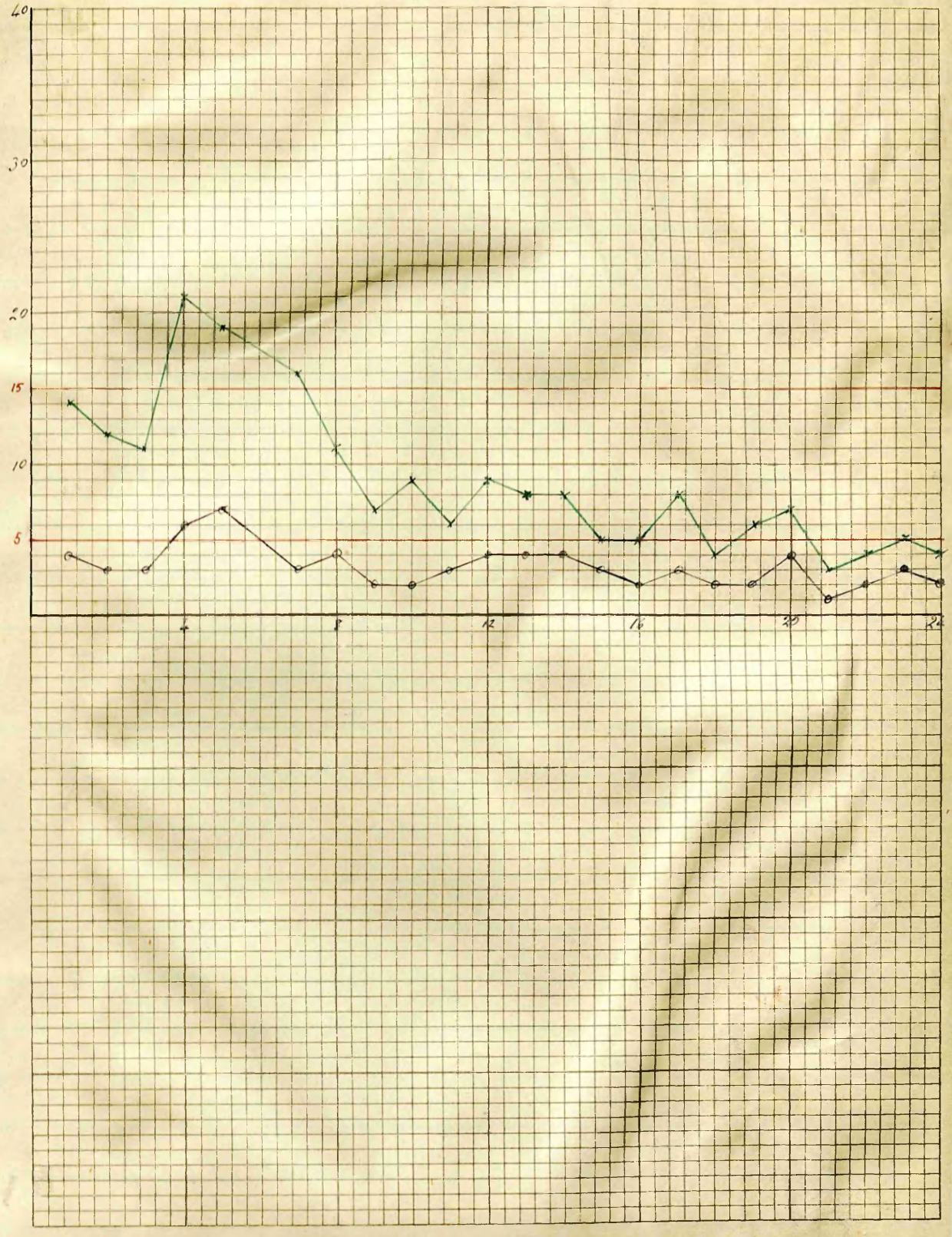
Case 28.



Sedimentation Graph.

In all aspects this graph gave a completely normal picture over the whole period of six months.

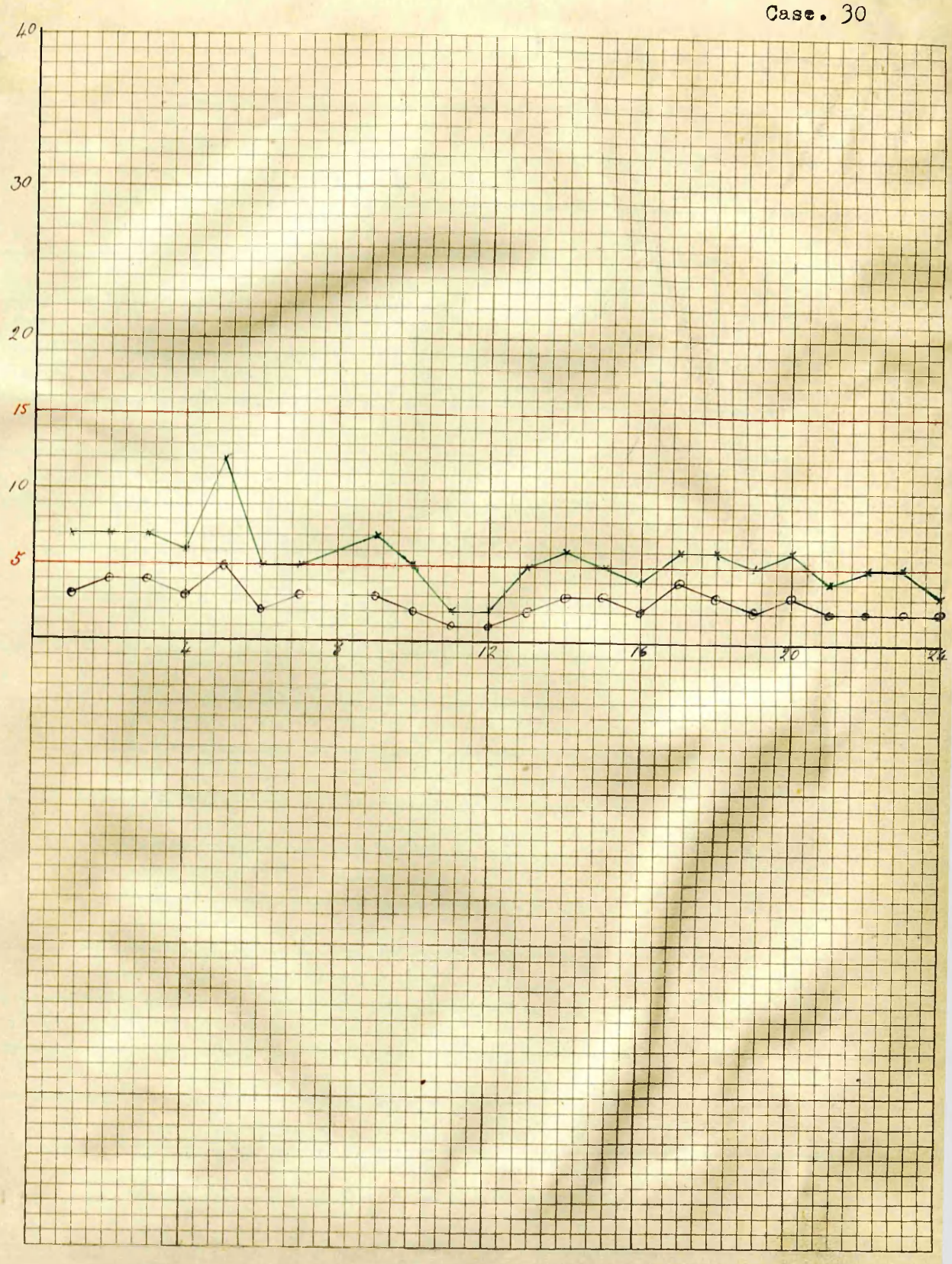
Case 29.



Sedimentation Graph.

This graph showed high readings in the second month, a coryza with bronchitis was present.

Case. 30



Sedimentation Graph.

In all aspects this graph gave a completely normal picture over the whole period of six months.

CONTROL SERIES OF CEREBRO-SPINAL FLUIDS TAKEN FROM CASES OF SCHIZOPHRENIA.

For the control series of cerebro-spinal fluids twenty-two (22) cases of Schizophrenia were chosen. This was necessary as fluids from normal people were unobtainable. In the references consulted the cerebro-spinal fluid was considered to be normal in cases of Schizophrenia, the defect in them being regarded as purely functional.[1.2. & 3.]

The results are arranged in similar tables to those used for the cases of Post-Encephalitic Parkinsonism.

	Case 1.	Case 2.
Total Protein.	34.08	52.48
Albumen.	28.16	38.16
Globulin.	5.92	14.32
Albumen-globulin ratio.	4.8/1	2.7/1
Cell count.	R.B.C.	1.
Pandy Test.	Neg.	Neg.
Lange colloidal gold curve.	0000000000	1112210000

	Case 3.	Case 4.
Total Protein.	37.67	32.90
Albumen.	29.70	23.90
Globulin.	7.97	9.00
Albumen-globulin ratio.	3.7/1	2.7/1
Cell count.	1	R.B.C.
Pandy Test.	Neg.	Trace.
Lange colloidal gold curve.	0011100000	0112211000

	Case 5.	Case 6.
Total Protein.	46.70	25.60
Albumen.	30.30	19.20
Globulin.	16.40	6.40
Albumen-globulin Ratio.	1.8/1	3.0/1
Cell count.	1	4
Pandy Test.	Neg.	Neg.
Lange colloidal gold curve.	0001210000	1122100000

	Case 7.	Case 8.
Total Protein.	24.50	26.90
Albumen.	19.20	23.30
Globulin.	5.30	3.60
Albumen-globulin ratio.	3.6/1	6.5/1
Cell count.	R.B.C.	6
Pandy Test.	Neg.	Neg.
Lange colloidal gold curve.	1112220000	1122100000

	Case 9.	Case 10.
Total Protein.	33.80	41.70
Albumen.	27.50	28.50
Globulin.	6.30	13.20
Albumen-globulin ratio.	4.4/1	2.2/1
Cell count.	10	R.B.C.
Pandy Test.	Neg.	Neg.
Lange colloidal gold curve.	1122210000	1111100000

	Case 11.	Case 12.
Total Protein.	30.70	34.40
Albumen.	22.30	27.20
Globulin.	8.40	7.20
Albumen-globulin ratio.	2.7/1	3.8/1
Cell count.	0	0
Pandy Test.	Neg.	Neg.
Lange colloidal gold curve.	1111000000	1111000000

	Case 13.	Case 14.
Total Protein.	42.20	33.80
Albumen.	31.00	25.50
Globulin.	11.20	8.30
Albumen-globulin ratio.	2.8/1	3.1/1
Cell count.	0	0
Pandy Test.	Neg.	Neg.
Lange colloidal gold curve.	1111100000	1111000000

	Case 15.	Case 16.
Total Protein.	35.00	31.00
Albumen.	26.00	23.00
Globulin.	9.00	8.00
Albumen-globulin ratio.	3.0/1	2.9/1
Cell count.	0	0
Pandy Test.	Neg.	Neg.
Lange colloidal gold curve.	0000000000	1110000000

	Case 17.	Case 18.
Total Protein.	29.00	89.00
Albumen.	21.00	71.00
Globulin.	8.00	18.00
Albumen-globulin ratio.	2.8/1	4.0/1
Cell count.	0	R.B.C.
Pandy Test.	Neg.	Neg.
Lange colloidal gold curve.	0001110000	1111222000

	Case 19.	Case 20.
Total Protein.	33.00	33.00
Albumen.	27.00	26.00
Globulin.	6.00	7.00
Albumen-globulin ratio.	4.5/1	3.8/1
Cell count.	1	0
Pandy Test.	Neg.	Neg.
Lange colloidal gold curve.	0001110000	0001100000

	Case 21.	Case 22.
Total Protein.	27.00	42.00
Albumen.	22.00	36.00
Globulin.	5.00	6.00
Albumen-globulin ratio.	4.4/1	6.0/1
Cell count.	0	1
Pandy Test.	Neg.	Neg.
Lange colloidal gold curve.	0000000000	0000000000

BIBLIOGRAPHY.

1. Craig & Beaton. Psychological Medicine. 4th. Ed. 1926. p.p.124.

2. Merritt & Fremont Smith. The Cerebro-spinal Fluid. 1st. Ed. 1937. p.p. 188.

3. Greenfield & Carmichael. The Cerebro-spinal Fluid in Clinical Diagnosis. 1st. Ed. 1925. p.p. 198.

SUMMARY OF SEDIMENTATION RATE GRAPHS.

Only four references to the sedimentation rate of the red blood corpuscles in cases of Post-Encephalitic Parkinsonism were found. The first was by Lorenz[1] writing in the Deutsche Medizinische Wochenschrift, but these cases were in an acute stage and the findings are not comparable with those in the present work. The second, by Paulian and Tomovici[2], found decreased sedimentation rates in Post-Encephalitic Parkinsonism. The third, by Lorenz and Berger[3], found increased rates in some cases and normal in others. Finally, Hachez[4], who found similar results to Lorenz and Berger.

These references give very little indication as to what the findings in a large series of sedimentation rates in cases of Post-Encephalitic Parkinsonism would be and the summarising of results was undertaken with an open mind.

A scrutiny of the results indicated a method whereby the graphs could be divided into three types, namely:-

1. Graphs which in all aspects gave a completely normal picture over the whole period of six months. This group comprised thirteen (13) cases.

To this group was added the cases where the period was less than six months but where the graph was in all aspects completely normal over the period investigated. This group comprised four cases.

Thus group one contained seventeen (17) cases.

2. Graphs which gave increased sedimentation rates over varying periods of time during the six months but where an active intercurrent infection was present. This group comprised thirteen (13) cases. These intercurrent infections were mainly respiratory in type, varying from a simple coryza to an acute bronchitis, in one case a pyelitis was present in a female case. This high incidence of intercurrent infection in a relatively small series of cases is explained by the fact that they were in an advanced state of Parkinsonism and, with the exception of a very few cases, were bed-ridden. Another factor contributing to respiratory infection was the rigidity of the whole skeletal system, including the chest, presented by these cases. The six month period during which all cases were investigated began in January and so respiratory infections were more common during the early part of the period. Many of the cases showed a chronic bronchitis as they had been bed-ridden for many years and had had a respiratory infection each winter. The two cases which died did so from Broncho-pneumonia which is the commonest terminal event in the life of a case of Post-Encephalitic Parkinsonism.

3. This group theoretically contains those cases where a disturbance of sedimentation rate existed in the absence of an active intercurrent infection. No such cases were observed.

From the above three paragraphs it will be seen that, in this series of thirty (30) cases of Post-Encephalitic Parkinsonism the blood sedimentation rate was normal except in those cases where an active intercurrent infection was present. In each such case the infection was sufficient to explain the increased blood sedimentation rate.

For interest, a survey at one institution, which admitted cases of Post-Encephalitic Parkinsonism, to determine the cause of death, was carried out. Out of twenty (20) cases eight were classed as dying from Broncho-pneumonia, nine gave no other cause of death than Post-Encephalitic Parkinsonism, while three cases died from cardiac failure.

BIBLIOGRAPHY.

1. Lorenz H.F. — Sedimentation Rate in Encephalitis. Deutsche Medizinische Wochenschrift. Vol. 50 1924. p.p. 752/753.

2. Paulian & Tomovici. — Sedimentation Tests in Post-Encephalitic Parkinsonism. Journal of the American Medical Association. Vol. 81 p.p. 2067.

3. Lorenz & Berger. — Sedimentation Tests in Epidemic Encephalitis. Journal of the American Medical Association. Vol. 83 p.p. 158.

4. Hachez E. — Sedimentation Rate in Encephalitis Lethargica. Deutsche Medizinische Wochenschrift. No. 7 1923. p.p. 217.

SUMMARY OF TOTAL PROTEIN CONTENT RESULTS.

For purposes of analysing the total protein content of the cerebro-spinal fluids examined two standards were used, namely, the average of the control series results and the normal figures as given by Merritt & Fremont Smith.[1] These results were :-

1. Control series; average total protein content - 34.90 mgm. per 100 cc. C.S.F.
2. Average normal total protein content - 45.00 mgm. per 100 cc. C.S.F.

Since these two results agree Merritt and Fremont Smith's classification was followed as under :-

A. Normal. - 45 mgm. per 100 c.c. C.S.F. or less.

B. Slightly increased. - 45/75 mgm. per 100 c.c. C.S.F.

C. Moderately increased. - 75/100 mgm. per 100 c.c. C.S.F.

D. Greatly increased. - 100/500 mgm. per 100 c.c. C.S.F.

E. Very greatly increased. - 500/3,500 mgm. per 100 c.c. C.S.F.

The cases were divided into five groups as above. Any result showing red blood corpuscles (R.B.C.) in the cell count was not considered.

Group A. Those cases in which all cerebro-spinal fluids were normal. Those cases numbered nineteen (19).

Group B. Those cases in which one or more specimen cerebro-spinal fluid showed results from 45 to 75 mgm. per 100 c.c. C.S.F. Those cases numbered four (4).

Group C. Those cases in which one or more specimen cerebro-spinal fluid showed results from 75 to 100 mgm. per 100 c.c. C.S.F. Those cases numbered one (1).

Groups D. & E. contained no cases.

From those results only five (5) cases showed an abnormal picture in the total protein content. Those cases were Case 1, 3, 6, 23, and case 5. In none of those cases was the increase of total protein content very marked.

BIBLIOGRAPHY.

1. Merritt & Fremont Smith. The Cerebro-spinal Fluid. 1st. Edit. 1937. p.p.30.

SUMMARY OF ALBUMEN CONTENT RESULTS.

For purposes of analysing results of the albumen content of the cerebro-spinal fluid specimens, one standard was used; this was the average albumen content of the control series which was twenty seven (27) mgm. per 100 cc. C.S.F.

This divided the cases into two groups, those above and those below the average of control series.

Group 1. Those cases in which the albumen content was less than that of the average of the control series. This group contained nine (9) cases.

Group 2. Those cases in which the albumen content of one or more cerebro-spinal fluids was greater than the average of the control series. This group contained fifteen (15) cases.

Any result showing red blood cells (R.B.C.) in the cell count was not considered.

From those results fifteen cases (15) showed an abnormal picture in the albumen content as compared with the control series average result. The highest result in the control series, having ignored the results which showed red blood cells (R.B.C.), was 36 mgm. per 100 cc. C.S.F. Taking this figure as the upper limit of abnormality group 2. resolved itself into a further two categories as under:-

A. Those results within the highest normal figure in the control series. Those numbered twelve (12) cases.

B. Those results above the highest normal figure in the control series. Those numbered three (3) cases.

From those results only three cases showed a definitely abnormal picture in the albumen content of the cerebro-spinal fluid. Those cases were Case 5, 6 and case 7.

SUMMARY OF GLOBULIN CONTENT RESULTS.

For the purposes of analysing results of the globulin content one standard was used; this was the average globulin content of the control series, which was 7.65 mgm. per 100 cc. C.S.F.

This divided the cases into two groups, those above and those below the average of the control series.

Group 1. Those cases in which the globulin was less than that of the average of the control series. This group contained four (4) cases.

Group 2. Those cases in which the globulin content of one or more cerebro-spinal fluids was graater than the average of the control series. This group contained twenty (20) cases.

Any result showing red blood cells (R.B.C.) in the cell count was not considered. This reduced group 2. to nineteen (19) cases.

The highest globulin content in the control series was 16.40 mgm. per 100 cc. C.S.F.. Taking this result as the upper limit of normality group 2. was further subdivided into a further two categories.

A. Those cases in which the results of globulin content were within this upper limit of normality. Those cases numbered sixteen (16).

B. Those cases in which one or more cerebro-spinal fluids showed higher globulin content than the highest globulin content of the control series. Those cases numbered three (3).

From those results only three cases showed an abnormal picture in the globulin content of the cerebro-spinal fluid. Those cases were Case 4, 5 and case 13.

SUMMARY OF ALBUMEN-GLOBULIN RATIO RESULTS.

For purposes of analysing results of the albumen-globulin ratio one standard was used; this was the average albumen-globulin ratio of the control series, which was 3.59/1.

This divided the cases into two groups, those above and those below the average of the control series.

Group 1. Those cases which the albumen-globulin ratio was less than that of the average of the control series. This group contained eight (8) cases.

Group 2. Those cases in which the albumen-globulin ratio of one or more cerebro-spinal fluids was greater than the average of the control series. This group contained sixteen (16) cases.

Any result showing red blood cells (R.B.C.) in the cell count was not considered.

The highest albumen-globulin ratio in the control series was 6.5/1. Taking this result as the upper limit of normality, group 2 was further subdivided and those results above this figure retained as being abnormal.

A. Those cases in which results of albumen-globulin ratio were within this upper limit of normality. Those cases numbered fourteen (14).

B. Those cases in which one or more cerebro-spinal fluids showed a higher albumen-globulin ratio than the highest albumen-globulin ratio of the control series. Those cases numbered two (2).

From those results only two cases showed an abnormal picture in the albumen-globulin ratio of the cerebro-spinal fluid. Those cases were Case 5 and case 19.

SUMMARY OF CELL COUNT RESULTS.

For purposes of analysing the cell count of the cerebro-spinal fluids in this series of cases, the basis was partly the results found in the control series and partly the findings given in the standard monographs. From those sources the cases were divided into three groups.

Group 1. Those cases in which the cell counts were between 0 and 5 cells per c. m.m.

Group 2. Those cases in which one or more cerebro-spinal fluids showed a cell count between 5 and 10 cells per cu. m.m.

Group 3. Those cases in which one or more cerebro-spinal fluids showed a count of over 10 cells per cu. m.m.

Group 1. contained twenty-one (21) cases.

Group 2. contained three (3) cases.

Group 3. contained no cases.

Any result which showed red blood cells (R.B.C.) in the cell count was not considered.

In the control series the highest cell count was 10 cells per cu.m.m. Taking this as the upper limit of normality none of the cases under investigation was abnormal in respect of the cell count. This agrees with Merritt & Fremont Smith[1] who consider 5 to 10 cells per cu.m.m. suspicious and over 10 cells as pathognomonic of an active lesion of the brain or meninges. Levinson[2] agrees also with those standards.

As judged by the cell count none of the series of the cases showed evidence of an active lesion of the brain.

BIBLIOGRAPHY.

1. Merritt & Fremont Smith. The Cerebro-spinal Fluid. 1st. Edit. 1937. p.p.57.

2. Levinson. The Cerebro-spinal Fluid. 3rd. Edit. 1929. p.p.136.

SUMMARY OF PANDY TEST RESULTS.

For the purposes of analysing the Pandy test results two group of cases were formed.

Group 1. NEGATIVE.

(a) Cases which showed negative Pandy tests throughout all cerebro-spinal fluids examined.

(b) Cases which showed "trace". Those were taken as negative.

Group 2. POSITIVE.

(a) Cases which showed one or more positive Pandy tests in the series observed and not showing red blood cells (R.B.C.) in the cell count.

(b) Cases which showed one or more positive Pandy tests in the series observed but which showed red blood cells (R.B.C.) in the cell count.

Group 1. (a). contained fourteen (14) cases.

Group 1.(b). contained five (5) cases.

Group 2. (a). contained three (3) cases.

Group 2. (b). contained two (2) cases.

One case, namely Case 5, fell into Groups 1 (b) and 2 (a).

Those cases which showed a positive Pandy test and the presence of red blood corpuscles in the cell count were not considered.

From these results nineteen (19) cases gave a negative finding and three cases gave a positive finding with the Pandy test. Thus three cases only out of this series showed evidence of activity in respect of the Pandy test. Those cases were Case 5, 6 and case 10.

SUMMARY OF LANGE COLLOIDAL GOLD CURVE RESULTS.

For purposes of analysing the results of the Lange colloidal gold reaction in this series of cases, four groups were formed.

Group 1. Those cases in which all the cerebro-spinal fluids showed no change, this is represented by a series of ciphers:- 0000000000.

Group 2. Those cases in which one or more fluids showed a colour reaction of a red colour. This colour reaction being represented by the figure 1:- 0011100000.

Group 3. Those cases in which one or more fluids showed a colour reaction of a lilac colour. This colour reaction being represented by the figure 2 :- 0022000000.

Group 4. Those cases in which one or more fluids showed a colour reaction of a blue colour. This colour reaction being represented by the figure 3 :- 1123100000.

Group 1 contained no cases.

Group 2 contained three (3) cases.

Group 3 contained twelve (12) cases.

Group 4 contained nine (9) cases.

Any results which showed red blood cells (R.B.C.) in the cell count was not considered. This reduced group 4 to six (6) cases.

From the standard references consulted changes in the colloidal gold test up to, and including, the lilac colour were considered as normal. Thus only group 4, which contained six (6) cases showed a pathological change. The control series showed no greater change than a lilac colour.

Thus only six cases showed evidence of activity as judged by the Lange colloidal gold test. Those cases were Case 3, 5, 6, 7, 10 and case 16.

BIBLIOGRAPHY.

1. Merritt & Fremont Smith. The Cerebro-spinal Fluid. 1st.Edit. 1937. p.p. 92.

2. Greenfield & Carmichael. The Cerebro-spinal Fluid.in Clinical Diagnosis. 1st. Edit. 1925. p.p.242.

3. Merritt & Fremont Smith. The Cerebro-spinal Fluid. 1st. Edit. 1937. p.p. 64 & p.p.270.

CONCLUSIONS.

This thesis consists of an investigation into thirty cases of Post-Encephalitic Parkinsomism with a view to determine whether or not the infective process was still active.

The investigation was divided into two parts:-

1. The sedimentation rate of the red blood corpuscles was done weekly in each case over a period of six months with the exception of a few cases where a lesser period of time was involved.
2. An examination of the cerebro-spinal fluid was made monthly over the same period of six months. Again several cases showed an incomplete series.

SEDIMENTATION RATES.

From the summary of sedimentation rate graphs already given no abnormal readings were found to be directly due to the Post-Encephalitic state alone. Where abnormal readings were found there was also present an active intercurrent infection generally of the respiratory type.

CEREBRO-SPINAL FLUID FINDINGS.

These results were difficult to summarise and tabular form was adopted to present them.

	Total Protein.	Albumen.	Globulin.	Albumen-globulin Ratio.	Cell Count.	Pandy Test.	Lange colloidal gold curve.
Case 5.	Pos.	Pos.	Pos.	Pos.	Neg.	Pos.	Pos.
Case 6.	Pos.	Pos.	Neg.	Neg.	Neg.	Pos.	Pos.
Case 10.	Neg.	Pos.	Neg.	Neg.	Neg.	Pos.	Pos.
Case 3.	Pos.	Neg.	Neg.	Neg.	Neg.	Neg.	Pos.
Case 1.	Pos.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Case 4.	Neg.	Neg.	Pos.	Neg.	Neg.	Neg.	Neg.
Case 7.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Pos.
Case 13.	Neg.	Neg.	Pos.	Neg.	Neg.	Neg.	Neg.
Case 16.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Pos.
Case 19.	Neg.	Neg.	Neg.	Pos.	Neg.	Neg.	Neg.
Case 23.	Pos.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.

Pos. (Positive) in the table indicates an abnormal finding.

Neg. (Negative) in the table indicates a normal finding.

Analysing the cases given in the table it will be seen that only two (2) cases show a preponderance of abnormal findings. The other cases show scattered positive findings which are difficult to interpret.

No case shows abnormal findings in all the tests applied to the cerebro-spinal fluid. Twenty-four (24) cases in all had cerebro-spinal fluids investigated, of those eleven (11) cases show abnormality in one or more of the tests applied to the cerebro-spinal fluid. Only two (2) of those cases show a preponderance of abnormal findings which could be interpreted as evidence of a still active brain lesion; those cases were Case 5 and case 6.

From those results it will be seen that there is insufficient evidence to prove that the infective process is still active in this series of cases of Post-Encephalitic Parkinsonism as judged by the cerebro-spinal fluid findings.

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