

# THESIS

## EPIDEMIC CEREBRO-SPINAL MENINGITIS

With an account  
of twenty-five cases  
personally observed  
in the Leith Epidemic  
of 1907, and an inquiry  
into the spread of the  
disease

by

JOHN D. COMRIE

M.A., B.Sc., M.B., Ch.B..

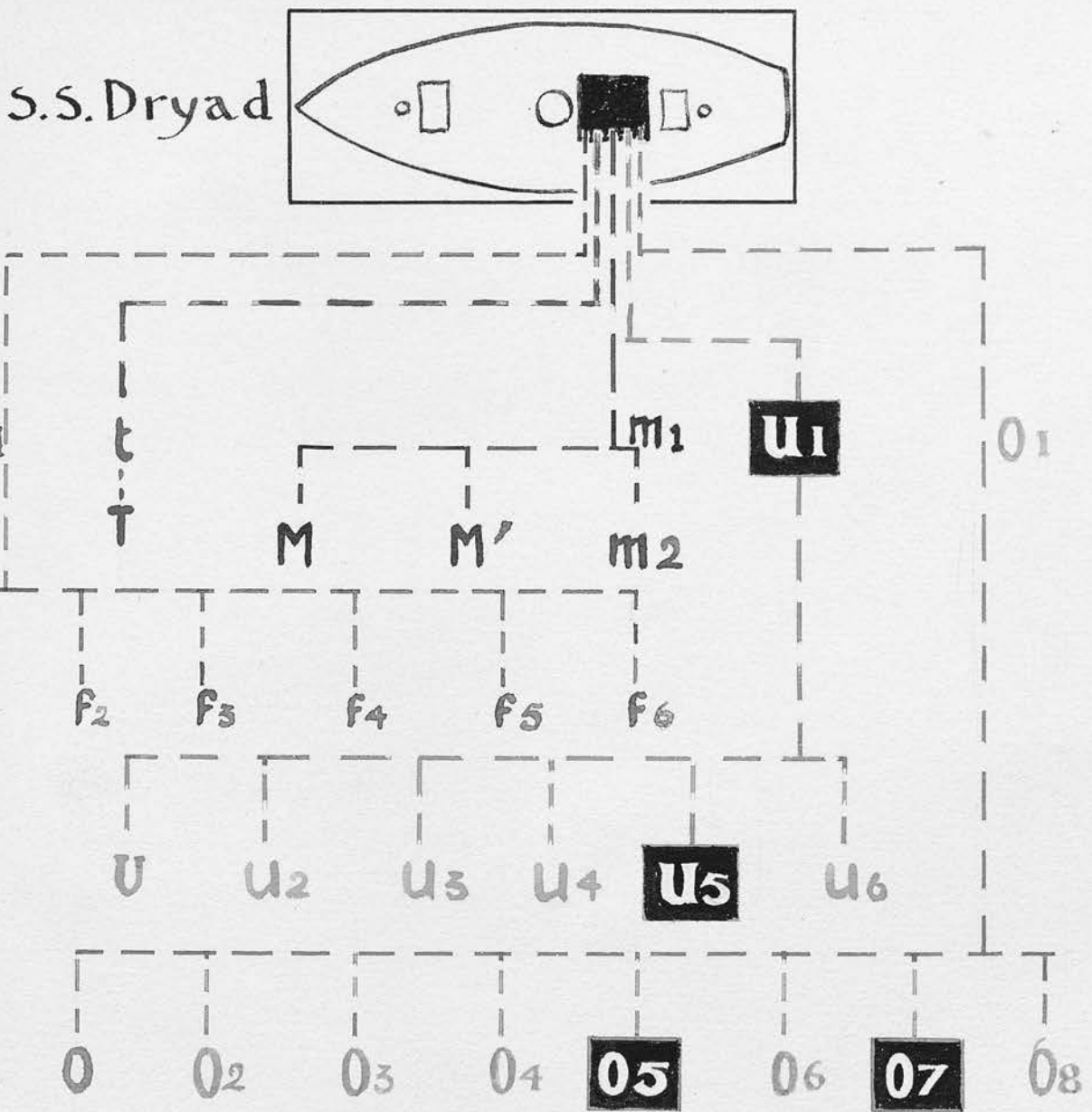


Diagram showing the relation of five affected families to the infected ship s. s. Dryad at Leith. The five fathers are indicated as F<sub>1</sub>, T, M<sub>1</sub>, U<sub>1</sub>, O<sub>1</sub>, and the cases of meningitis in their families as F, T, M, M', U, O. The letters surrounded by squares, U<sub>1</sub>, U<sub>5</sub>, O<sub>5</sub>, O<sub>7</sub>, indicate individuals in whose naso-pharynx the meningococcus was found; in the others it was sought for, but not discovered.  
(See p. 19.)

## EPIDEMIC CEREBRO-SPINAL MENINGITIS.

The present thesis has in view to give a resumé of Cerebro-spinal fever with a short account of the epidemic in 1907 at Leith and of a number of cases which came under the writer's personal observation at that time, together with some original work done by him as a small contribution to the question of the manner in which the disease spreads.

### History of Outbreaks of the Disease

Hirsch traces this disease back to the beginning of the nineteenth century (before which time it was probably confounded with typhus fever) and finds that during the past century it has appeared in a series of severe outbreaks becoming sporadic in the intervals. These outbreaks he divides into four distinct periods.

The first of these periods extended from 1805 to 1830 and while the outbreaks in Europe were comparatively limited, appearing at Genoa (1805), at Grenoble and Paris (1814), Metz (1815), Genoa (1815), and in the North of England (1830), on the other hand in the United States there was a widespread epidemic in the Western States, Kentucky and Ohio (1808), and in the New England States (1814-16).

The second period of the disease lasted from 1837 to 1850. Beginning apparently separately in the S.W. and S.E. of France, it spread especially and with

disastrous effect among the garrisons of that country until about 1842 when it subsided. From 1846 to 1850 another series of garrison epidemics took place in the Eastern part of France and at Paris and Orleans. In Algiers also there was a severe epidemic (1840-1847) but the central parts of France were not much affected at any time. In the latter part of this period the disease spread to other countries; thus Italy and Sicily suffered from 1840 to 1845, Denmark and Iceland 1845-1848, and some of the towns of Ireland (especially as a workhouse epidemic) in 1846. Towards the end of the period it again appeared in the United States particularly in the Western and Southern States and in Pennsylvania (1848) and New Orleans (1850).

The third period from 1854 to 1874 saw the Northern countries of Europe chiefly affected. The disease broke out first at Gothenburg in 1854 and spread north through Sweden in the following year causing outbreaks of a very fatal character in this country until 1858. In 1861 Portugal was affected. In 1863 the disease broke out in Silesia, and spread widely throughout Prussia, Pomerania, Saxony and the other States of Northern Germany. Later in 1864 it attacked South Germany beginning in this year at Erlangen and Nürnberg and spreading throughout Bavaria, Baden and Hesse. After 1866 the outbreaks began to die down in Germany. Russia was severely affected in various

parts such as the Crimea in 1867 and 1868. Ireland again had an epidemic at Dublin in 1866 and 1867, while there were a few small outbreaks in England of no great importance. The United States for a third time suffered severely. Beginning in North Carolina and New York State (1856 to 1857) it spread widely among the troops during the war of the Rebellion in 1861 to 1863 and was afterwards distributed practically over the whole extent of the States forming an important cause of the general mortality until 1874.

The fourth period from 1876 to the present is one of comparative quiescence except towards its close. It has been characterised by curiously limited but severe and fatal outbreaks. In England, cases occurred in the Midlands, at Oxford and Birmingham (1876); in 1877 and 1878 there was an outbreak in Dundee; and in 1878 several cases appeared in Dublin. Dublin was again visited by a more serious epidemic in 1885 when fifty-two deaths occurred, chiefly among the well-to-do classes. Other cases occurred at Galston near Kilmarnock in 1884, at Aberdeen in 1885, and near Faversham in 1886. In 1890 a widespread outbreak occurred among the villages of Norfolk and Suffolk, and ten years later, in 1900, there was yet another outbreak at Dublin. In 1905 the disease appeared in the United States again beginning with a severe epidemic in New York, and in the succeeding three years various

seaport towns of Britain, e.g. Belfast, Glasgow, Leith, were seriously affected. In the following pages an account will be given of the epidemic which lasted throughout 1907 in Edinburgh and Leith so far as it concerns the latter town.

#### Bacteriology of the Disease.

Notwithstanding that the disease has been known since 1805 it was not till 1887 that Weichselbaum described the organism to which he gave the name of the Diplococcus intracellularis meningitidis and which subsequent observers have confirmed as the cause of the malady. The first communication of Weichselbaum dealt with eight cases of cerebro-spinal fever, in two of which the pneumococcus seems to have been present, while in the remaining six the organism under present discussion was first described. He gave to it the name of 'intracellularis' because it was chiefly found in the cells of the exudate, described it as a diplococcus in which each member of the pair was flattened by their mutual apposition, which did not retain Gram's stain, and which he was able to cultivate on various media, such as agar, blood serum, and bouillon. Growth took place at 37° C. but not at 20°C. Cultures were found to retain their vitality only for about six days and therefore sub-culture on fresh medium was recommended every second day. Weichselbaum found that the

organism was pathogenic to certain animals, such as mice, guinea-pigs, rabbits, and dogs. Intraperitoneal and intrapleural inoculations proved fatal in mice and guinea-pigs, while in three dogs Weichselbaum was able by intradural injection to produce a lepto- and pachymeningitis. At a later period Betten~~er~~Court and França attempted without success to infect monkeys both by injection and by rubbing the nasal mucous membrane with cultures of the organism, though at a later date this was achieved by Flexner and others.

After its first description by Weichselbaum this organism was a good deal confused with the pneumo-coccus. Thus in 1890 Netter in a paper upon the pneumococcus expressed the opinion that this organism was especially the cause of epidemic cerebro-spinal meningitis. Four years later Flexner and Barker reporting upon an epidemic of meningitis, which had broken out in the district of Georges Creek in 1893 and affected some 200 cases, came to the conclusion that at least in a few of these cases that they had examined, the pneumo-coccus was responsible for the disease. They were of opinion that the poor health of the community living in this district, which was a very insanitary one, was largely responsible for the outbreak.

Again in 1895 Jaeger describing the occurrence of some cases in the German army, noted differences between the organism he found and that described by

Weichselbaum. The chief points of variation were firstly, that the organism sometimes occurred in chains, secondly, that in culture it was Gram-positive, and thirdly, that it was sometimes capsulated. In 1896 Heubner followed Jaeger with regard to confirming the Gram-positive character and produced a typical meningitis in a goat by means of one of these organisms.

The question was greatly discussed in the next few years, some observers siding with Jaeger as to the Gram-positive appearance, others with Weichselbaum, e.g. Kiefer (1896), Kister (1896), Kischensky (1896), Franz (1897), while some described organisms that took up an intermediate position and were sometimes Gram-positive, sometimes Gram-negative. The question had been complicated before the discovery of Weichselbaum's Meningo-coccus by the records of several observers, e.g. Foa and Bordoni-Uffreduzzi (1886, 1888) who showed that the pneumo-coccus might be the cause of both primary and secondary meningitis. Bonome in 1890 described a "streptococcus meningitidis" which was however soon recognised to be simply a variety of the pneumo-coccus. The same fate for some years overtook the diplococcus meningitidis, and it was not till 1902 that the literature dealing with the two organisms was reviewed under separate headings in Baumgarten's Jahresbericht.

In 1898 Councilman, Mallory, and Wright reported upon an outbreak of the disease in Boston, and from

35 cases examined found the diplococcus meningitidis in all but four. They found the pneumococcus seven times associated with the meningo-coccus and this in part explained the variety in staining power which earlier observers had noticed. Streptococci and staphylococci were also occasionally seen but these were attributed to terminal infections. They found the organism feebly pathogenic to animals but produced typical meningitis by intraspinal injection in a goat.

Also in 1898 an important contribution was made to our knowledge of the subject by Still who pursued researches into the cause of posterior basic meningitis, a disease occurring among infants below two years of age in the earlier months of the year. This disease had been described by Gee and Barlow twenty years before, and Still was now able to demonstrate and cultivate the causative organism which he found to be similar to, but slightly different from, the meningo-coccus described by Weichselbaum. These posterior basal meningitis cases are, as a rule, more prolonged and slower in development than the epidemic cases, though some of the latter extend to many weeks. The organism described by Still is also more resistant and possesses greater viability than that of Weichselbaum, growing too in more opaque colonies upon culture media. In this type of disease the inflammation limits itself to the posterior part of the base of the brain as the

primary seat of inflammation in the majority of cases, and spreads thence in a varying degree down the cord, upwards into the ventricles and forwards over the base to the optic commissure and tips of the temporo-sphenoidal lobes. At an early stage the exudate, though circumscribed, is purulent; and, while it may be absorbed later on, it leaves adhesions. These adhesions may obliterate the fourth ventricle and foramen of Magendie and so bring on hydrocephalus. On the cord all stages and degrees of purulent lepto-meningitis are met. Sometimes it is covered throughout by a sheet of purulent, gelatinous exudate and the roots of the cauda equina may be matted together by a similar material. Sometimes this occurs in patches, and sometimes absorption has taken place so that only adhesions between the dura and pia mater are left. These appearances are just those that we have observed in some of the long-standing cases of epidemic cerebro-spinal meningitis that came to post mortem examination in the Leith epidemic. Clinical observations by Koplik support the view that the so-called posterior basic meningitis is simply an attenuated form of epidemic cerebro-spinal meningitis, while various transition stages in the characters of the organism have been described, as will be stated later. These two types of the disease are now generally regarded as simple varieties of one malady, both as concerns their

clinical features and their cause. This may be summed up as in a recent pronouncement upon the subject by Koplik that "cases of posterior basic meningitis of the type described by Gee, Barlow, Lees, and Still may occur in epidemics and are due to the same essential cause as the form of the disease in older children and adults. In fact it would appear that in the majority of children attacked by cerebro-spinal meningitis below the age of two years, both in epidemics and sporadic instances, the disease takes the form described by these authors". It may therefore be regarded as established that so-called "posterior basic meningitis" is simply one variety of acute cerebro-spinal meningitis and that its organism is a variety of the diplococcus of Weichselbaum which, as will be stated later, presents at times considerable divergences from type as regards cultural and staining characters.

In 1901 and 1903 Albrecht and Ghon placed the meningo-coccus upon a firm basis, confirming Weichselbaum's original observations; and in the same year Jaeger published a monograph "Die Cerebro-Spinalmeningitis als Heereseruche" in which he to a large extent departed from his previous position, abandoning, as the result of studying more cases, the ideas that the organism has a capsule and that it occurs in long chains.

In 1903 Betten Court and França found during an epidemic in Portugal that an overwhelmingly large proportion of the cases were due to the meningococcus; (270 cases due to this organism and 3 cases to others).

In 1905 von Lingelsheim in reporting upon a widespread epidemic in Germany found the organism consistently Gram-negative.

In 1907 Flexner produced important experimental results from his study of the organism. Injections of cultures of the meningococcus into the spinal canal of apes produced death in 15 to 40 hours, with punctiform haemorrhages on the surface of the brain and cord in the earlier cases and leucocytic infiltration along the vessels in the later ones. He further discovered the important and curious fact that meningococci were to be found in these cases in leucocytes of the nasal mucous membrane. It thus appeared that the cocci might pass or be carried from brain to nose presumably by way of the lymphatics, and this affords a prima facie probability to the fact which we shall discuss later that they may, in persons who become affected by the disease, pass in the reverse direction from nose to brain and so produce their pathogenic effects. Flexner found that animals which recover after experimental infection with this disease mostly do so within three or four days of the onset. He also has elaborated a serum which will be discussed later.

*Stuart Macdonald*

In the same year Macdonald studied the organism as it occurred in the Edinburgh epidemic of the time and found it to conform to most of the characters which Weichselbaum had previously described; yet in three instances he found a Gram-positive reaction and in one a development of short chains out of fifty strains of the meningococcus.

Although the opinion of Jaeger and Heubner had been mainly abandoned as the result of Albrecht and Ghon's work, we still find that Lehmann and Neumann in 1907 isolated strains of the meningococcus which, although originally Gram-negative, after repeated culture became Gram-positive, thus substantiating observations recorded by Lepierre in 1903, Kob in 1905, Castellani in 1905, Weyl in 1905, and Vansteenbergh and Grysez in 1906.

In 1908 Ritchie and Shennan, as the result of studying the organism in 27 cases, found the meningococcus consistently Gram-negative, although after being grown in fluid media the strain was somewhat less resistant than those grown on solid media.

With regard to the frequency with which the meningococcus has been found as the cause of the disease in recent epidemics, Faber in 1900 found it in 87 per cent of cases, Cochez and Lemaire in 1902 in 88 per cent, Schottmüller in 1905 in 87.7 per cent, von Lingelsheim in 1906 in 64.6 per cent, Ritchie and Shennan in 85.7 per cent.

Methods of Culture and Study of the Meningococcus  
adopted.

The culture media employed by Weichselbaum have been already alluded to. In 1907 Gordon, reporting to the Local Government Board on the micrococcus of Epidemic Cerebro-Spinal Meningitis and its identification, proposed certain media and methods and these were in the main followed in our investigations.

Whether in the investigation of swabs from the naso-pharynx or of lumbar puncture fluid, the original growth was made upon sloped tubes or plates of blood-agar or ascitic-fluid agar or ovarian-fluid agar (in the latter cases 1 of the ascitic or ovarian fluid to about 4 of agar). On the second or third day of incubation at 37° any organisms resembling the meningococcus were subcultured upon fresh tubes of blood-agar or ascitic agar. After a series of three or four subcultures had thus been made in the case of organisms from the naso-pharynx, the desired organism was usually obtained pure. These media were found more convenient than the nasagar medium recommended by Gordon, and as they gave equally good or better growths were used instead. It should be observed here that in making cultures at post-mortem examinations disappointment was several times experienced in getting a growth from the thick gelatinous exudate, organisms being much more frequently found in a viable state in the thin sero-

purulent material around the nervous system.

Identification of Colonies:- At the end of 24 hours' growth upon ascitic fluid agar at 37° C. the colonies of the meningococcus appear as round colourless translucent discs of 1 to 2 mm. breadth. The surface is moist and glistening and the edges thin and regular. On examination through a lens the centre of the colony is found to be rather thicker than the edge and to have a finely granular appearance and faintly yellowish or brownish colour. The colonies are readily broken up when touched with the platinum needle and do not dislodge 'en masse' like those of some of the saprophytic nasal diplococci of a hardier more tenacious growth which can be pushed about over the surface of the medium.

At the end of 48 hours the colonies are larger being 4 or 5 mm. in diameter and somewhat more opaque in appearance at the central part. Under the lens the centre is found slightly yellowish or brownish in colour and granular in appearance, while the spreading and somewhat wavy edge is still quite transparent. The colonies never become distinctly yellow to the naked eye like some of the saprophytic diplococci. Radiating streaks are often visible.

At the end of 72 hours the growth has become almost stationary though the centres of the colonies may have become somewhat thicker and darker. The edge

is also more distinct and forms a kind of halo round the central less translucent part. In the condensation water a fine pellicle develops and later ~~the~~ drop of water becomes turbid.

Vitality:- In several instances subculture was found to be impossible from a culture of a week old, and though some observers have obtained growths after the lapse of three months, we failed in any case to propagate the meningococcus from a tube after six weeks' growth. It seems as if the degree of inspissation of the medium were an important point in this connection, for cultures in the case of which evaporation was prevented seemed to retain their vitality longer than in tubes not so protected.

Reaction to Carbohydrates:- The method of testing the growth in sugar-containing media which we adopted for routine examination was to add to a tube containing sterilized bouillon one fourth of its bulk of ascitic fluid and one per cent of sterile sugar and litmus. The tubes so prepared were tested by 24 hours' incubation at 37° C. before use.

The sugars which have been tested by other observers, e.g. von Lingelsheim (1906), Gordon (1907), Goodwin and von Sholly (1906), ~~Symmers~~ Symmers (1907), and Ritchie and Shennan (1908) are glucose, laevulose, galactose, saccharose, maltose, lactose, dulcite, mannite, raffinose, dextrin, and inulin.

Generally speaking the meningococcus fails to ferment any of these except glucose and maltose with occasionally galactose and dextrin. In fermenting glucose and maltose it differs from the micrococcus catarrhalis which is negative for both of these sugars; while it is differentiated from the closely similar diplococcus gonorrhoeae by the fact that the latter is positive with galactose and negative with maltose. As the question of the presence of the gonococcus did not enter into our investigations on the naso-pharynx, and as the behaviour towards glucose forms a sufficient differentiation from the micrococcus catarrhalis, we confined our observations so far as carbohydrate reaction is concerned to the action upon glucose of the organisms that were isolated.

Reaction to Gram's Stain:- Notwithstanding the discrepancy of opinion which we have mentioned as occurring in the past in regard to the behaviour of the organism to Gram's Stain, and despite the fact that in old cultures we twice found that occasional organisms retained the stain while it was discharged generally from the film, we nevertheless accepted the meningococcus as being negative to Gram's stain. We therefore excluded as being other organisms those which retained the stain.

Agglutination Tests:- We saw a considerable amount of work done by Jehle at the Anna Kinder Spital

in Vienna upon the use of antimeningococcal serum in recognizing the meningococcus by its agglutination. In his hands its use appeared to be moderately successful but we decided not to continue its use in view of the doubts cast upon the value of the method by Gordon (1907), Dunham (1906), and Goodwin and von Sholly (1906). Ritchie and Shennan (1908) also using nine strains of known meningococci in combination with two sera prepared from patients and one commercial serum found a great degree of variability, some strains reacting while others failed to do so.

We therefore depended for the recognition of the meningococcus upon the appearances of the colonies to the eye and under the lens, the morphological characters of the organism, its behaviour towards Gram's stain, and the result of its growth upon glucose-litmus media.

Investigations upon the Mode of Spread of  
Epidemic Cerebro-Spinal Meningitis.

The idea of carrying out an investigation upon the subject of meningococcus carriers was suggested by reading papers of Ludwig Jehle upon the epidemiology of the disease in Silesia and the Rhine coal districts. He concluded that cerebro-spinal fever is not like other infectious diseases in its mode of spreading and that children may be largely excluded as infection bearers. On the other hand he pointed out that miners make good carriers of infection, as they frequently suffer from chronic rhinitis and pharyngitis and are in the habit of constantly hawking and spitting and frequently use the same tools and drinking vessels in the mines. On the return of the miner to his home the children might become affected by kissing, or using the same drinking vessels as the father, or, in the case of very young children, by crawling about on the floor on which the miner had expectorated.

Our own researches were the first upon the subject in this country, and, while the subject is still in a doubtful state as regards the paths by which the organism reaches the meninges, we believe that, as one of the chief means of spread from person to person, the occurrence of the meningococcus carrier is now regarded as of the first importance. The investigation of this subject was done in conjunction with Dr. J. S.

Fraser, the bacteriological part being entirely the work of the present writer.

We <sup>a</sup>examined the naso-pharynx in 13 cases of the disease and in 69 persons coming into intimate contact with these cases. The meningococcus was present in 2 of the 13 cases (15 per cent), and in 10 of the 69 contacts (14 per cent). Of these 69 contacts, 15 were fathers of cases, the remaining 54 including mothers, brothers, sisters and other persons who had all been in intimate contact with the cases. Five of the persons in whose naso-pharynx we found the meningococcus were among the 15 fathers, the other 5 fell into the group of 54 contacts. Thus while we found the organism in 33 per cent of the fathers of cases, among other contacts having apparently quite as close intercourse with the patients we discovered it only in 9 per cent. The fathers appear therefore especially prone to have the meningococcus in the naso-pharynx although they do not themselves contract the disease.

The method of obtaining the secretion from the naso-pharynx was by means of a long platinum loop sterilized immediately before introduction. By the help of a forehead mirror and sterilized nasal speculum this was introduced into the naso-pharynx, and the greatest care was taken in withdrawing it to avoid touching the vestibule of the nose. The secretion was immediately smeared over the surface of sloped blood-agar or

ascitic agar tubes which were in all cases placed in the incubator within one hour. The resulting growth was examined in the manner described above.

Inquiring into the employments of the various fathers we found that 5 of the 15 examined were engaged in overhauling a ship (S.S. Dryad) at the docks, and on exposing Petri dishes containing Ascitic agar in various parts of the ship below decks, we found the meningococcus in the air of the engine-room. The relation of this ship to 5 of the affected families is shown by the diagram.

We found Gram-negative diplococci in the naso-pharynx of several other fathers of cases but were unable to isolate them so as to apply the tests for verification as the meningococcus.

We examined the naso-pharynx also in 23 controls, who had no connection with the disease and failed to find the meningococcus in any of them.

A summary of the results is presented in Table I which gives the cases and the number of contacts with each, indicates in how many of the cases the diagnosis was confirmed by lumbar puncture and examination of the cerebro-spinal fluid for the meningococcus, and in the last column gives the results of the search for the meningococcus in the naso-pharynx.



Corroborative Evidence as to the Importance  
of Meningococcus Carriers.

Various other observers, since the time when the writer's researches were published, have produced corroborative evidence on the importance of the naso-pharynx as a lurking place of the meningococci.

Thus Bochalli investigating the contacts with cases that occurred in barracks found numerous persons who carried the coccus in the naso-pharynx without themselves suffering from the disease. Similarly von Lingelsheim found this organism both in the sick and in those around them, and Selter, out of 26 persons coming into contact with cases, found the coccus in no less than 8 carriers.

As to the length of time that the meningococcus may remain in the naso-pharynx, Ghon was able to recover them after a period of five months. Selter found the organisms in the naso-pharynx of a mother and daughter affected by a prolonged form of cerebro-spinal meningitis four months after the onset of the disease. In the case of persons actually suffering from the disease however, the experience of Flexner in apes experimentally infected in the central nervous system and showing in the nasal cavities meningococci which had passed outwards, must be borne in mind.

The fact that small houses are those from which cases of the disease are chiefly drawn while it might

support other theories equally well, is in complete accord with the idea of infection from the air passages of one person to those of another. Thus in Leith the crowded nature of the houses of the patients is shown by the following table:-

Number of 1-roomed houses involved	15
" " 2 " " "	44
" " 3 " " "	11
" " 4 " " "	3
" " 5 " " "	2
" " 6 " " "	1

During the 1907 epidemic several villages in Lanarkshire were affected and the following two instances are quoted by Lewis Thomson as corroborative of infection by carriers:-

"A boy S. sickened on February 21st and died after four days' illness. The parents visited the house of a relative in a neighbouring village four miles away on March 3rd. On the following day the baby in this house sickened and died on the 6th. This was the first case in the village and Mrs S. had been fondling the child a good deal."

"A baby sickened on February 24th and was removed to hospital on March 2nd and an aunt who had helped to nurse him returned to her home in another village. She was intimate with a family living a few doors away. In this family a baby, whom she often

fondled, sickened on April 4th. This again was the first case in the village."

Many other cases such as these might be cited from the literature of the subject, e.g. by Bruns, Vincent et Bellot, etc..

Method of Entrance of Meningococcus into  
the Nervous System.

Comparative Ages of Brain and Cord Lesions:- In support of the theory that the meningococcus makes its way from the alimentary system, by which it enters the body, into the lymphatics of the trunk and so into the cord, and subsequently to the brain, the fact is generally adduced that the lesion of the cord is older than that of the brain. While it is impossible to draw any decided inference from the examination of fifteen cases, we would point to the fact that in two of the cases (V & XIII) recorded on page            and page            the changes in the brain were obviously earlier than those present in the cord. While therefore it may be that some cases are characterised by a primary infection of the cord, there is at least prima facie evidence that in others the brain is first affected.

It should be stated that some clinical facts have been adduced in favour of the theory that infection is carried by the food and enters the central nervous system by way of the cord. Fowler and Stuart Macdonald, in supporting this theory, found their argument mainly on the following statements.

1. The cord lesion is of longer standing than and therefore antecedent to the brain lesion.
2. The abolition of the abdominal reflex at an early age suggests spinal involvement.

3. The retention of the mental faculties is in many cases characteristic thus freeing the brain of early involvement.

4. Breast fed infants were not in their series of cases affected.

With regard to the first contention, we have found, as already stated, that it is not always the case. The abdominal reflex is notoriously slight and difficult to elicit and when the sensibility is dulled and all the superficial reflexes diminished as they are in this disease, it might readily occur that the abdominal reflex is abolished or so slight as to escape notice without the necessity of supposing any special involvement of that part of the cord with which it is connected. With regard to the mental faculties, they are often retained long after the headache and other symptoms have shown that the head is affected, and on the other hand, the first sign of the disease is, in many of the 25 clinical cases quoted later, unconsciousness, showing that the brain is affected from the first.

Lymphatic Connections of Brain and Nose:- Schwalbe, Kay and Retzius have shown that the lymphatics of the nose can be infected from the cranial cavity; and the work of Flexner already mentioned proves that organisms pass along these channels. The writer succeeded readily at post mortem examinations in making a mixture of jelly and methylene blue pass under pressure from the submucous tissue high up in the nose through the

ethmoid plate and appear in the cranial cavity. The possibility of the passage of organisms from nose to sub-dural space by the lymphatics must therefore be admitted.

Another point at which the nasal and cranial cavities come closely into relation with one another is through the posterior wall of the sphenoidal sinuses formed by the basisphenoid. On turning to the literature on this subject it appeared that practically no research had been done with regard to discover<sup>er</sup>ing to what extent the mucous membrane of these sinuses is inflamed or otherwise rendered suitable for the passage of organisms in the average person. Accordingly the writer undertook the preparation of microscope sections from 50 cases of sphenoidal sinus mucous membrane obtained post mortem, in the microscopic examination of which he has to acknowledge the valuable co-operation of Dr. J.S. Fraser, Assistant Surgeon of the Ear, Nose and Throat Department, Royal Infirmary. We found the presence, on one or both sides, of slight catarrhal changes in the mucosa in 17 cases (34 per cent) and of a marked inflammatory condition in 3 cases. The mucous membrane of these sinuses is therefore in a fit state in one third of all persons to become infected by such an organism as the meningococcus which may from it invade the cranial cavity and set up meningitis.

The following table gives the results of our examination in detail:-

Results of Microscopic Examination of Sphenoidal CellMucous Membrane.

Case	Age	Cause of Death	Right Sphenoidal Sinus	Left Sphenoidal Sinus
1. J.K., m.	71	Gangrene of leg.	Normal	Normal; goblet cells +.
2. J.T., f.	40	Aortic and mitral disease.	Normal	Normal; goblet cells +.
3. J.C., f.	45	Pneumonia	Normal	Great oedema of submucosa; cells of mucous membrane mostly goblet cells; superficial layer lost in places; very little small cell infiltration.
4. W.L., m	68	Cirrhotic kidney. OEdema of brain.	Great loss of superficial cells; small-cell infiltration of submucosa and mucous membrane; vessels distended; basement membrane thick and eroded.	Characters similar; great oedema.
5. J.M., m.	33	Miliary tuberculosis.	Normal.	Normal.
6. C.B., m.	31	Tuberculous meningitis.	Normal.	Normal; mucous glands in submucosa numerous.
7. M.H., f.	73	Cerebral haemorrhage.	Normal.	Normal.
8. J.M., m.	15	Accident.	Normal.	Normal; numerous mucous glands.
9. J.S., m.	70	Atheroma of cerebral vessels.	Normal.	Normal; numerous mucous glands.
10. T.R., m.	52	Cerebral haemorrhage.	Normal.	Normal.

Case	Age	Cause of Death	Right Sphenoidal Sinus	Left Sphenoidal Sinus
11. E.C., f.	65	Cancer of stomach.	Normal.	Normal; goblet cells+.
12. R.N., m.	60	Ulcerative endocarditis.	Normal; mucous glands numerous.	Normal; mucous glands numerous.
13. A.R., f.	13	Acute tuberculous broncho-pneumonia.	Normal; mucous glands numerous.	Normal; mucous glands numerous.
14. J.T., f.	42	Spleno-medullary leukaemia.	Normal; goblet cells+.	Oedema of submucosa; much small-celled infiltration around glands; goblet cells+.
15. J.F., m.	60	Cardiac failure.	Normal.	Normal; numerous mucous glands.
16. M.S., f.	9	Burns; endocarditis.	Slight small-celled infiltration; oedema; mucous glands numerous.	Oedema of submucosa; small-celled infiltration; congestion and haemorrhages.
17. A.R., m.	37	Chronic Bright's disease; uraemia.	Normal.	Normal.
18. J.P., m.	70	Acute lobar pneumonia.	Slight oedema of submucosa; mucous membrane quite healthy.	Normal.
19. R.M., f.	49	Scirrhus of breast.	Oedema, congestion, infiltration with leucocytes; basement membrane thickened; mucous membrane ragged.	Oedema; congestion; infiltration of mucous membrane with thickened basement membrane.

Case	Age	Cause of Death	Right Sphenoidal Sinus	Left Sphenoidal Sinus
20.W.F.,m.	9	Accident.	Papillae in mucous membrane; mucous glands numerous; normal.	General haemorrhage in submucosa, due to fracture. Normal.
21.A.J.,m.	23	Acute meningitis.	Normal.	Normal.
22.M.S.,f.	39	General tuberculosis.	Normal.	Normal.
23.P.M.,m.	74	Fracture of skull.	Normal.	Normal.
24.I.W.,f.	35	Fracture of skull.	Normal.	Normal; much haemorrhage into submucosa.
25.J.G.,f.	48	Nephritis.	Normal.	Normal.
26.A.C.,f.	50	Malignant disease of ovary.	Slight oedema of submucosa.	Slight oedema and congestion of submucosa; many goblet cells; catarrh.
27.J.S.,m.	55	Cancer of liver.	Normal.	Normal.
28.R.L.,m.	45	Bronchopneumonia.	Oedema of submucosa marked; mucous membrane healthy.	Oedema of submucosa marked; mucous membrane healthy.
29.M.S.,f.	37	Lobar pneumonia.	Oedema of submucosa and dilatation of vessels marked; goblet cells +; mucous glands in submucosa.	Excessive oedema of submucosa, with many haemorrhages; very great goblet cell formation.
30.F.M.,m.	54	Bronchopneumonia.	Much oedema of submucosa; goblet cells+.	Some oedema of submucosa; goblet cells much+.
31.J.G.,m.	40	Acute gastroenteritis.	Normal.	Normal; some haemorrhage in submucosa.
32.J.K.,m.	68	Heart failure.	Some small celled infiltration into submucosa; mucous glands present; goblet cells+.	Normal; goblet cells+.

27d.

Case	Age	Cause of Death	Right Sphenoidal Sinus	Left Sphenoidal Sinus.
33.J.S.,m.	50	Diabetes, broncho-pneumonia.	Normal; mucous glands present.	Normal.
34.M.H.,f.	46	Heart failure.	Normal.	Superficial epithelium generally healthy, but desquamated in places; great oedema of submucosa and dense small cell infiltration.
35.W.T.,m.	36	Acute encephalitis with oedema of brain.	Desquamation of superficial epithelium; great oedema of submucosa; dilatation of blood spaces; mucous glands present.	Similar to right.
36.A.L.,m.	42	Meningitis.	Normal.	Normal.
37.J.D.,m.	37	Cerebral haemorrhage.	Oedema of submucosa.	Oedema of submucosa; goblet cells+; mucous glands present.
38.M.J.,f.	34	Exophthalmic goitre; pericarditis.	Normal.	Normal; goblet cells+.
39.J.K.,m.	44	Cerebral softening; pneumonia.	Normal.	Slight oedema of submucosa; goblet cells considerably+
40.J.D.,m.	37	Chronic Bright's disease.	Submucosa shows small-cell infiltration. Cavity contained mucus.	Cavity contained a cyst; goblet cells+.

Case	Age	Cause of Death	Right Sphenoidal Sinus	Left Sphenoidal Sinus
41. A.M., m.	50	Meningitis; ulcerative endocarditis.	Goblet cells+; oedema of submucosa; blood-vessels engorged and great amount of erectile tissue.	Goblet cells+; much erectile tissue.
42. R.R., m.	34	Abscess of brain.	Normal.	Normal.
43. J.S., f.	40	Mania; oedema of brain.	Normal; mucous glands numerous.	Submucosa a little thickened and vessels dilated; mucous glands numerous.
44. R.C., m.	54	Purulent leptomeningitis.	Normal.	Normal.
45. J.H., m.	61	Acute congestion of kidneys; oedema of brain.	Mucous membrane healthy; some oedema of submucosa.	Mucous membrane healthy; some oedema and dilatation of vessels in submucosa.
46. M.G., f.	39	Acute nephritis.	Normal; goblet cells+.	Normal; goblet cells+.
47. M.R., f.	19	Tuberculous meningitis.	Desquamation of superficial epithelium in places; great oedema of submucosa and much erectile tissue.	Similar to right; also erectile tissue and glands present.
48. T.S., m.	49	Aortic stenosis.	Normal.	Normal; glands and erectile tissue in submucosa.
49. J.G., m.	35	Acute pericarditis.	Normal.	Normal; goblet cells+; erectile tissue and glands.
50. W.T., m.	36	Not known.	Normal; erectile tissue.	Normal; erectile tissue.

Experimental Inoculation of Animals.

A series of rabbits were treated with various bacteria including streptococci, pneumococci, and meningococci. An emulsion of the bacteria derived from a two days' growth upon agar was in some cases wiped upon, in others inoculated into the submucous tissue of the nose. In the case of the pneumococcus a strain of low virulence and another strain which had been rendered highly virulent by passage through three rabbits were tried. Our results were, however, inconclusive. In some cases no result occurred, in others a local inflammation, while in two only was a meningitis set up. The last mentioned result was produced in the two rabbits by the virulent strain of pneumococci, but as the animals developed pericarditis in one case and peritonitis in the other and as the pneumococcus was recovered from the blood, the meningitis must be regarded simply as part of a general infection not dependent upon the site of inoculation being situated in the nose. It must be remembered however that we were here dealing with a healthy mucous membrane and not with the catarrhal nasal cavities so often found in the subjects of cerebro-spinal meningitis.

Morbid Anatomy and Histology of Cerebro-Spinal  
Meningitis based upon 15 post-mortems per-  
sonally performed.

External Appearances:- In cases which terminated very speedily there has been as a rule no emaciation and on the contrary the children have appeared to be well nourished and well developed. Cases which were prolonged in a state of semi-consciousness showed extreme wasting. In about 60% of all the cases the purpuric or haemorrhagic rash was a prominent feature distributed generally on the chest, front of thighs and front of arms, less commonly and more sparsely on the abdomen and back.

Naso-Oro-Pharyngeal Cavities:- Marked nasal catarrh was a prominent feature in many of the cases, and the mouth was in some of the advanced cases very foul, though this was no doubt a late infection. Several attempts were made to isolate the meningococcus, both in the later stages of life and after death, but even if it was still present this was not found possible owing to the presence of other quickly growing organisms. With regard to the possibility that the meningococcus should pass from the nasal cavity where we found it present in 2 out of 13 early cases of the disease examined during life we performed certain researches already mentioned.

Thorax and Abdomen:- In no case was any large amount

of fluid either serous or purulent found in the pleural or pericardial cavities, nor was there any peritonitis.

Heart:- In most cases the heart muscle was soft, flabby, and pale, and the ventricles were dilated somewhat. None of the cases showed endocarditis, and we failed in several cases in which it was attempted to obtain any growth of meningococci from the blood.

Lungs:- The surface in many cases showed minute haemorrhages immediately under the pleura. There was usually a considerable amount of muco-purulent exudation in the bronchial tubes and the lung tissue was congested and oedematous. A definite bronchopneumonia was present in about half the cases due probably to inspiration of food &c.

Stomach and Intestines:- The whole alimentary canal was in general healthy but in a few cases there was some acute congestion of the small intestine. The condition of the mesenteric glands is noted below.

Liver:- Beyond cloudy swelling which was always present and in some cases fatty change there was nothing to note.

Spleen:- This organ was constantly somewhat increased in size and softened showing some enlargement of the Malpighian bodies; the softening was however not extreme in any cases as in general septic condi-

tions.

Kidneys:- There was generally fairly well-marked cloudy swelling and congestion of a mild degree, but no haemorrhagic nephritis such as described by Councilman. The ureters and bladder were healthy in all cases.

Lymphatic Glands:- A striking feature in some of the cases was the enlargement of lymphatic glands. The mesenteric glands were found enlarged, firm and hyperaemic in a number of cases (about 25%); in some of the cases however the enlargement was due to an old standing tuberculous lesion with typical tubercle-formation and caseous and calcareous deposits in several of the glands. A similar condition of enlargement and hyperaemia in the glands, generally associated with tuberculous changes in some of their number, has been repeatedly observed by the writer in the mesenteric glands of children belonging to the same class as those most affected in this epidemic but not suffering from meningitis, and it is doubtful whether this condition of the glands should be regarded as anything more than a coincidence in cases of cerebro-spinal fever. In several of the children who died of cerebro-spinal fever the cervical glands were also found enlarged and showed a condition very similar to that of the mesenteric glands.

Brain:- The scalp, skull and dura-mater showed no

special change except occasionally hyperaemia of the last mentioned. The appearances of the brain varied considerably according to the length of time the case had lasted; but, generally speaking, the brain presented the following characters:-

The surface of the brain was greatly congested and there was a sero-purulent or fibrino-purulent exudation in the depressions of the surface. This was most evident from the optic commissure back over the crura pons and medulla, and in the sulci on the lateral aspect for some distance in front of and behind the fissure of Rolando. The exudate also sometimes extended over the upper and under surfaces of the cerebellum. In no case was much exudate present in the longitudinal fissure. Several cases showed a condition which is often stated to be characteristic of pneumococcal meningitis, but which in these cases was associated with an early death due to the meningococcus, viz: a special collection of pus on the sides and vertex of the brain with a much smaller amount or none at all in the region of the base. To attempt any naked eye distinction between cases due to the pneumococcus and those caused by the meningococcus is, in the writer's opinion, quite fallacious. The exudate was, except in the earliest cases, of a thick, tenacious, gelatinous character and could only with some difficulty be detached from

the surface to which it adhered.

In two very acute cases dying within twelve hours there was intense congestion of the upper part of the brain with a considerable amount of slightly turbid fluid under the dura and arachnoid. The cord was in a similar state, and from the fluid around both brain and cord the meningococcus was readily obtained in films. It did not appear as if the inflammation were of an older date in the spinal canal than it was within the cranium. The writer did not in any of these cases meet with the experience which has been stated by others that the inflammatory changes may be still absent or only slightly marked on the brain although well developed on the cord. On the other hand, in Case V and Case XIII the very reverse occurred.

In four cases dying about the end of the first week the exudate was well marked, in the sites mentioned above, and formed in some cases a uniform greenish-yellow, gelatinous cap spread over all the convolutions of the sides and upper surface of the cerebrum. In this exudate the meningococcus was readily obtained. The ventricles often contained a large quantity of turbid fluid and were considerably dilated. It was very common to find the purulent exudate collected thickly round the 7th and 8th nerves and passing out into the internal auditory

meatus.

In several cases which lasted from two to four weeks there was a considerable amount of organisation visible in the form of whitish patches and strands of fibrous tissue both on the vertex and more particularly in the region of the interpeduncular space.

In still older cases plaques of white fibrous tissue were met with on the pia mater.

Spinal Cord:- The Pia and Arachnoid membrane covering this was also very densely infiltrated as a rule with fibrino-purulent material. In the earliest cases the cord like the brain was acutely congested and bathed in turbid serous fluid. In most cases the fibrino-purulent exudate was almost uniformly distributed over the cord being thickest on the posterior surface, and around the posterior nerve roots.

In the long-standing-cases, very little exudate was found but the dura and arachnoid membranes were adherent and in places firmly matted together by strands of fibrous tissue.

Internal Ear:- In one case of permanent deafness, the 8th nerve was found infiltrated by polymorphonuclear leucocytes and lymphocytes which penetrated along it into the internal ear and were found in masses in the various parts of this cavity.

Microscopic Examination:- The lymphatic glands in a case of simple, non-tuberculous enlargement, were

hyperaemic and showed hyperplasia in the cortical part with dilatation of the lymph sinuses and active proliferation of the endothelial cells lining the spaces. The brain in an early case showed much infiltration of the perivascular spaces with polymorphonuclear leucocytes and a large admixture of lymphocytes, and a similar appearance was noted on section of the cord. Among and within the polymorphonuclear leucocytes were numerous diplococci in various stages of degeneration.

The brain tissue showed minute haemorrhages in some places and in others thrombi in the small vessels with areas of softening. In the superficial exudate, among the polymorphonuclear leucocytes and lymphocytes were seen the peculiar cells described by Councilman, in diameter several times that of ordinary leucocytes, having a large vesicular nucleus, and apparently actively phagocytic for leucocytes and blood-corpuscles. These are probably derived from the endothelial cells of the lymph spaces. The cells of the neuroglia appeared to be increased in numbers.

	Age	Vomiting	Headache	General pains	Unconsciousness	Temperature 12 hours after admission	Kernig's Sign	Knee Jerks
Case 1	5	Present	Present	Present	-	103°	Present	+
2	4	Present	-	-	-	103.5°	Present	Present
3	9	Present	Present	Present	Present	101.5°	Present	+
4	2	Present	-	-	Present	100°	Present	Present
5	37	Present	Present	-	Present	102°	?	+
6	7	Present	Present	-	Present	99°	Present	Present
7	2	Present	Present	Present	Present	101.5°	Present	+
8	27	Present	Present	-	Present	100°	Present	+
9	45	-	-	-	Present	98°	Present	Present
10	4	-	Present	-	Present	100°	Present	Present
11	14	Present	Present	-	-	98.5°	Present	Active
12	5	Present	Present	-	Present	100.5°	Marked	Present
13	2	Present	Present	-	Present	99°	Present	Present
14	6	-	-	-	Partial	102.5°	Absent	Present
15	16	Present	Present	-	Partial	98.5°	Present	Present
16	27	Present	-	Present	-	99°	Absent	Present
17	8	Present	Present	Present	Delirious	101.5°	Marked	Present
18	2	Present	-	Present	Partial	99.5°	Present	Active
19	12	Present	-	Present	Partial	105°	Present	Present
20	4	Present	Present	-	-	100°	Present	Present
21	34	-	Present	Present	-	102°	Absent	Present
22	56	Present	Present	-	-	99.5°	Present	Present
23	1	-	-	-	Present	101°	Present	Present
24	3	Present	Present	-	-	100°	Marked	Present
25	10	Present	Present	Present	-	102°	Marked	Active

	Plantar Reflex in first week	Head Retraction	L.P.	Duration be- fore admission	Duration of Disease	Ocular Paralysis	Deafness	Eruption
	Extensor	Marked	+	1 day	153 days	Present	None	None
	?	Spasmodic	+	4 hours	1 day	Present	None	Present
	Flexion	Present	+	1 day	4 days	None	None	Present
	Flexion	Absent	+	3 days	4 days	None	None	Present
	Flexion	Absent	+	1 day	2 days	Pupils unequal	None	Present
	Flexion	Absent	?	14 days	30 days	None	None	None
	Flexion	Absent	+	1 day	3 days	None	None	Present
	Flexion	Slight	+	1 day	22 days	Present	None	Present
	Flexion	Absent	+	1 day	18 days	None	None	Present
	Extensor at times	Present	+	1 day	56 days	None	Present	None Recovery
	Flexion	Absent	+	1 day	60 days	None	None	?
	?	Present	+	2 days	3 days	None	None	Present
	Flexion	Present	+	1 day	1 day	None	None	None
	Flexion	Absent	+	7 days	36 days	None	None	Present
	Flexion	Absent	+	3 days	44 days	None	None	Present
	Flexion	Slight	+	4 days	80 days	None	None	None
	Flexion	Marked	+	14 days	97 days	None	None	None Recovery
	Flexion	Marked	+	1 day	1 day	None	None	None
	Flexion	Absent	+	3 days	4 days	None	None	Present
	Flexion	Absent	+	1 day	11 days	None	None	Present
	Flexion	Absent	+	2 days	28 days	None	None	None Recovery
	Flexion	Absent	?	4 weeks	40 days	None	None	Present
	?	Absent	+	1 day	3 days	None	None	Present
	Flexion	Marked	+	3 days	7 days	None iritis	None	Present
	?	Very marked	+	1 day	2 days	None	None	Present

CASE I.

A. J. aged 5 years.

Admitted:- 30/1/06.

Complaint:- Pain in stomach and head and vomiting lasting 1 day.

History:- On the day before admission she went back to bed and vomited frequently during the day and following night. On the morning of admission to hospital she became blue and collapsed, complaining also of pains in the head and stomach.

State on admission:- Child unconscious, crying out when moved, lips cyanosed and face very pale.

Pulse 160 per minute. Child lies curled up in bed and refuses to extend legs. Head not retracted. Kernig's sign well marked. Knee jerks increased. Plantar reflexes, slight extensor response. Pupils slightly contracted and equal.

2/12/06. Child quite incapable of attention when spoken to but cries frequently with a shrill piercing note. She sleeps only for a few minutes at a time, then wakens tossing about and grinding her teeth. Quieted considerably by 5 grain dose of Chloral Hydrate.

4/12/06. Marked head retraction. Internal strabismus of both eyes. Pulse varies from 140 to 160. Lumbar puncture obtains a large quantity of turbid fluid which spurts out under considerable tension.

Name *Amiel Wilson*

Age *3 Years*

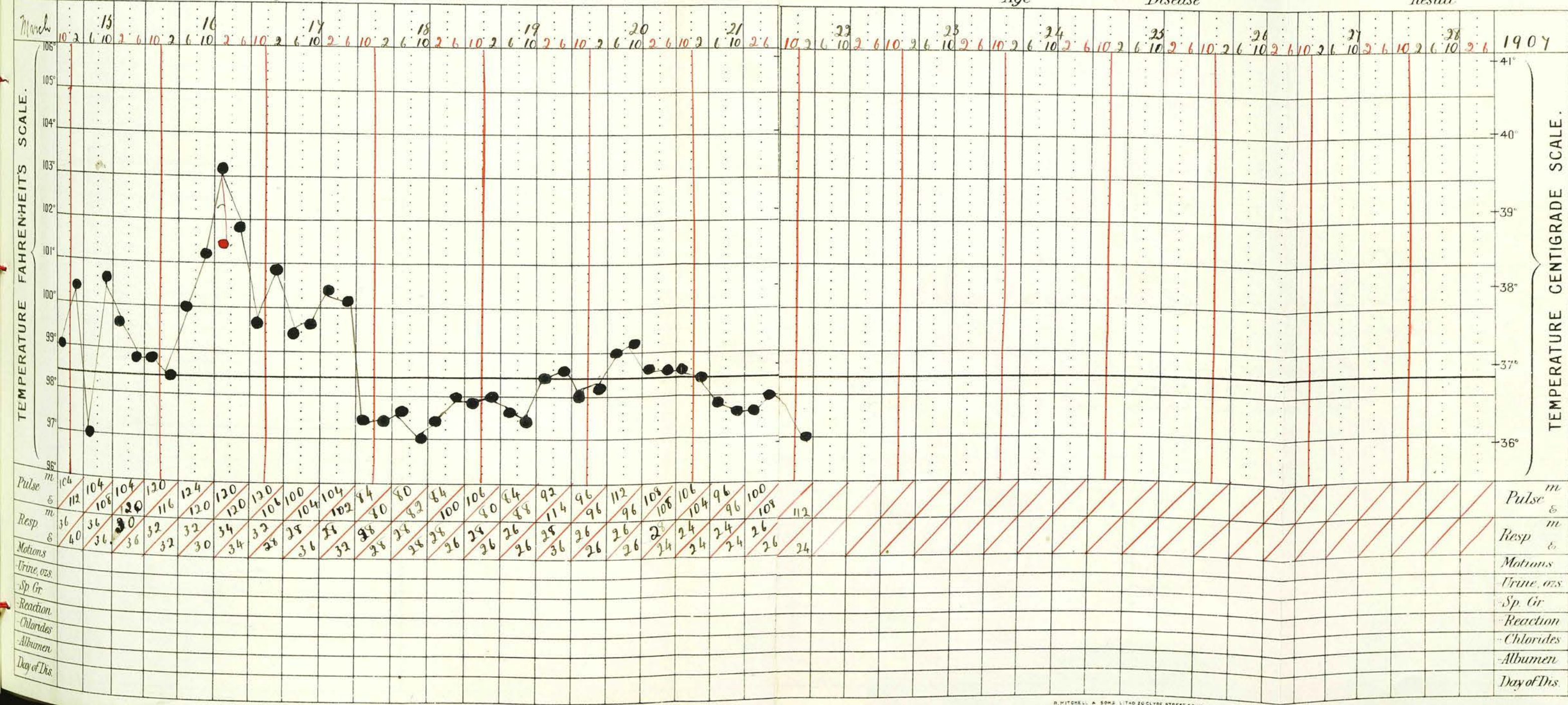
Disease

Result

Age

Disease

Result



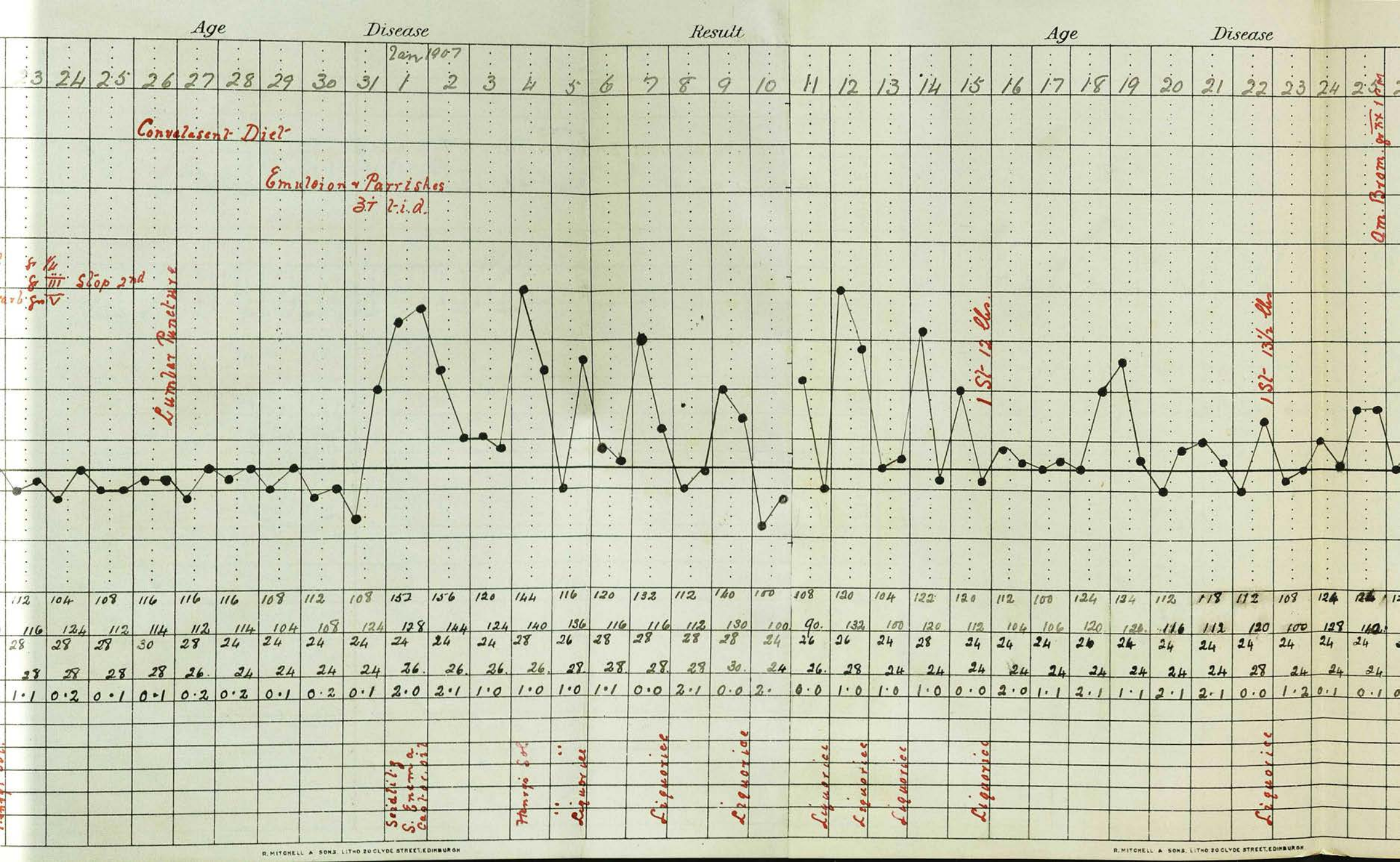
*Complications*

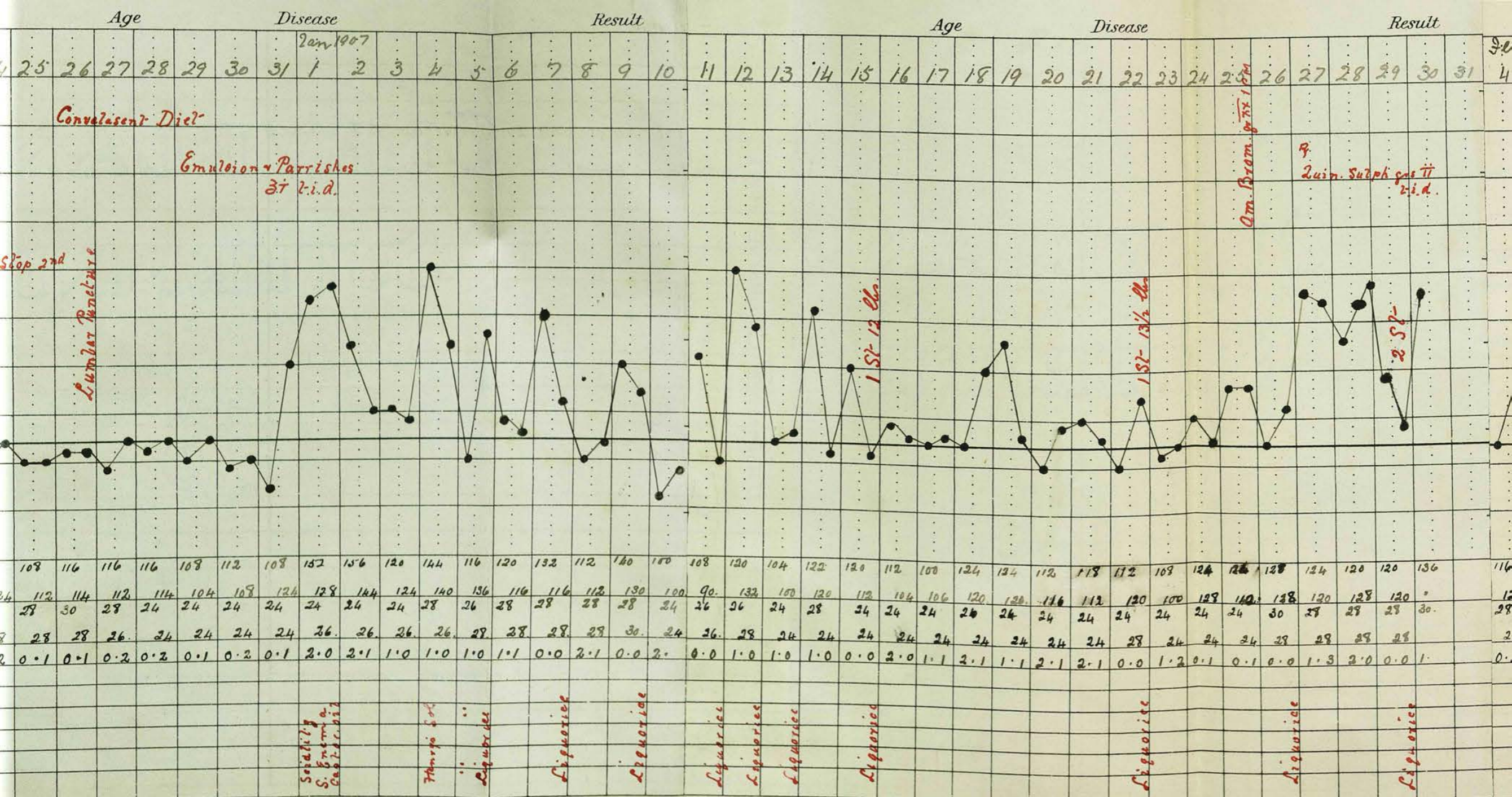
*Occasional Notes and Prescriptions (To be copied into the General Report)*

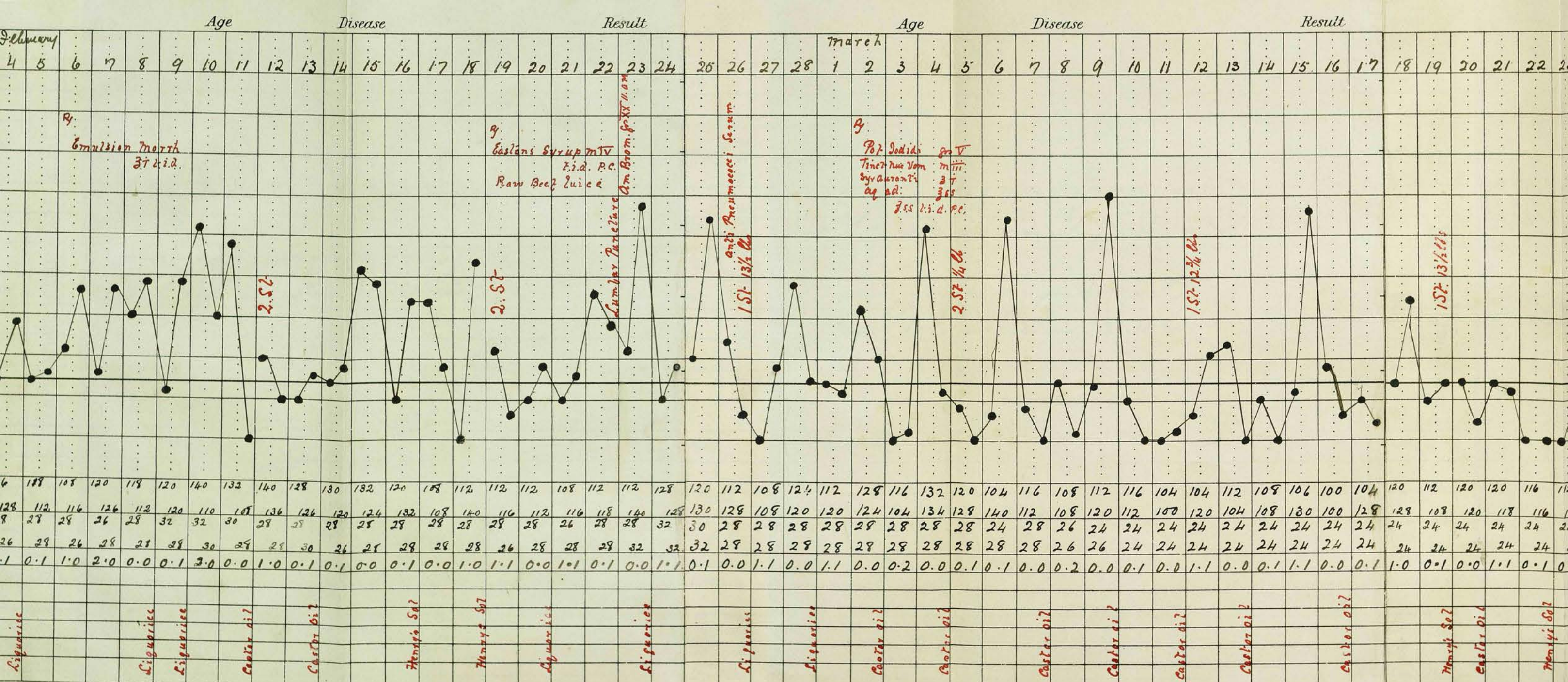
*Complications*

*Occasional Notes and Prescriptions (To be copied into the General Report)*











When centrifuged and examined it is found to contain chiefly large lymphocytes with a great number of diplococci giving the reactions of Weichselbaum's Diplococcus. Intracellular meningitidis except that the reaction to Gram's stain is doubtful. Some hours after the lumbar puncture the child seemed to be much easier and the temperature fell from  $103^{\circ}$  to  $101^{\circ}$ .

9/12/06. Child lies awake but quite unintelligent. Cries out when touched. Internal strabismus of right eye very marked.

11/12/06. Parotitis with swelling of eyelid and general oedema of right side of face.

14/12/06. Abscess of parotid burst through right external auditory meatus with discharge of greenish pus.

20/12/06. The abscess has practically ceased to discharge pus.

28/12/06. Temperature has been normal for six days. General condition better. Child speaks and sometimes sings to herself, but will not answer questions and seems to be quite deaf. Leucocytes in blood 14,000 per c.m.m.

7/1/07. Child has been getting a rise of temperature once every 24 hours. She is quite intelligent and asks for everything she wants, but is still deaf.

No perforation of either tympanic membrane.

16/1/07. Lumbar puncture shews clear fluid in which no organisms are to be found.

20/1/07. Child greatly frightened with delusions.

22/2/07. Lumbar puncture gives slightly opaque fluid from which there is no growth on blood agar.

2/4/07. An attack of headache, vomiting and high temperature.

7/4/07. Lumbar puncture; 50 c.c. of opaque fluid drawn off under great pressure; many polymorphs; no organisms.

11/4/07. Child has had headache and delusions again.

2/5/07. The condition of the patient remained practically unchanged although she had become progressively more emaciated during all the earlier part of this year. She died on this date. The body greatly emaciated.

3/5/07. Post Mortem Examination:- On opening up of skull and dura mater the cerebral convolutions were found to be greatly flattened and the blood vessels somewhat congested. There was a very large amount of turbid cerebro-spinal fluid collected in and almost entirely limited to the posterior fossa. The posterior and under surface of the cerebellum was found to be somewhat adherent to the dura. On removing the brain there was on this part of the

cerebellum a marked depression filled up by a thick layer of yellow pus partially organized. This pus extended in the arachnoid around the medulla and under surface of the pons to as far forwards as the anterior perforated space. The roots of all the cranial nerves were surrounded by pus especially the 7th and 8th and the pus passed into the internal auditory meatus on both sides. The pus did not extend up on to the cerebrum nor to the upper surface of the cerebellum.

The spinal cord was soft, the pia arachnoid whitish and thickened and there was a small quantity of pus along the whole length of the cord.

N.B. This case in the distribution of the exudate corresponded to a case of posterior basic meningitis.

#### CASE II.

G.C. Aged 4.

Complaint:- Vomiting for a few hours past.

Admitted:- 28/12/06.

History:- Last evening patient felt vaguely ill, but slept well during the night; to-day she has been in bed all day, vomiting, and shortly before admission she had a sort of convulsion with general

rigidity and jerking of the limbs.

State on admission:- Child is very pale with lips blue and is quite unconscious. Pulse very feeble, breathing rapid; pupils normal. Convulsive seizures similar to that mentioned above come on every few minutes and between these the child seems to sleep. On the back, lower part of abdomen and face are numerous small bright red or brownish spots which do not disappear on pressure. Temperature  $103.5^{\circ}$ ; Pulse 170; Respirations 60. Lumbar puncture yields a turbid fluid under high pressure in which are great numbers of polymorphonuclear leucocytes and cocci arranged in fours which retain the stain by Gram's method.

29/12/06. Child quite unconscious. Internal strabismus of both eyes marked. Pupils widely dilated especially right. Kernig's sign present. Knee jerks present. Plantar reflex doubtful. Child died at 10.30 p.m.

29/12/06. Post Mortem Examination:- Body well nourished but limbs much distorted by rickets. Great general anasarca.

Brain: The dura mater was very thick and firmly adherent over the occiput. The Pia Arachnoid greatly congested on under surface of cerebellum, much sero-purulent material along the vessels

and in the interpeduncular space. The lateral ventricles were considerably distended by similar fluid.

Spinal cord showed a great infiltration of the pia-arachnoid with sero-purulent fluid especially on the posterior aspect and around the nerve roots.

Thymus large extending down to the 4th costal cartilage.

Heart and lungs healthy.

Kidneys and liver healthy.

Spleen large weighing 20 ounces.

Culture made from the brain on agar after 24 hours showed yellowish white tenacious growths resembling staphylococcus, which upon further were found to consist of a coccus tending to adhere in fours and Gram-negative in its staining reactions.

### CASE III.

H.D. Aged 9 years.

Admitted:- 11/1/1907.

Complaint:- Pain in back and head with vomiting, lasting one day.

History:- Child went to school feeling quite well at

9.30. At 12.30 she had a shivering attack and went to bed. Almost at once she began to complain of pain in her back, later in her head and by 11 p.m. she was quite unconscious. She was very restless all night and occasionally got rigid all over. On the morning of following day she roused a little and drank some milk which however she vomited at once.

State on admission:- Child is quite unconscious, but screams occasionally when touched. Head slightly retracted. Pupils unequal. No ocular paralysis or spasm. Kernig's sign present; knee jerks very active. Plantar reflex flexion. There is a haemorrhagic rash all over the body; some of the spots being bright red and others brownish; it is especially evident on the neck and eyelids. Temperature 101.5; Pulse 148; Respirations 32.

Lumbar Puncture yields about 15 c.c. of very turbid fluid at very high tension; films of this show numbers of polymorphonuclear leucocytes within which the diplococcus intracellularis meningitidis is very common

N.B. These cocci are rather small but in a culture upon blood agar they become very much larger.

14/1/07. Child is much weaker. Rash still very marked.

15/1/07. Death.

Post Mortem Examination:- Whole body covered with dark petechial spots especially over the front of the thighs, chest and upper arms.

Skull cap much adherent to dura along coronal and sagittal sutures. Dura is very thick for a child, especially in the frontal and occipital regions.

Brain: There is a considerable amount of pus along the larger vessels and the large veins are greatly distended. The base of the brain shows similar collections of pus in the sulci and a considerable amount of blood stained cerebrospinal fluid in the interpeduncular space. There is a little pus on the upper surface of the cerebellum. On section the basal ganglia are somewhat congested and there is distension of the lateral ventricles.

Spinal cord. The veins in the spinal canal are very much congested as also are the small vessels in the dura. A peculiar and offensive odour emanates from the spinal canal. The cord is covered by a thin layer of yellow pus. The diplococcus intracellularis meningitidis was recovered in culture on blood agar from the pus both of the cord and of the brain.

Name *David Glover*

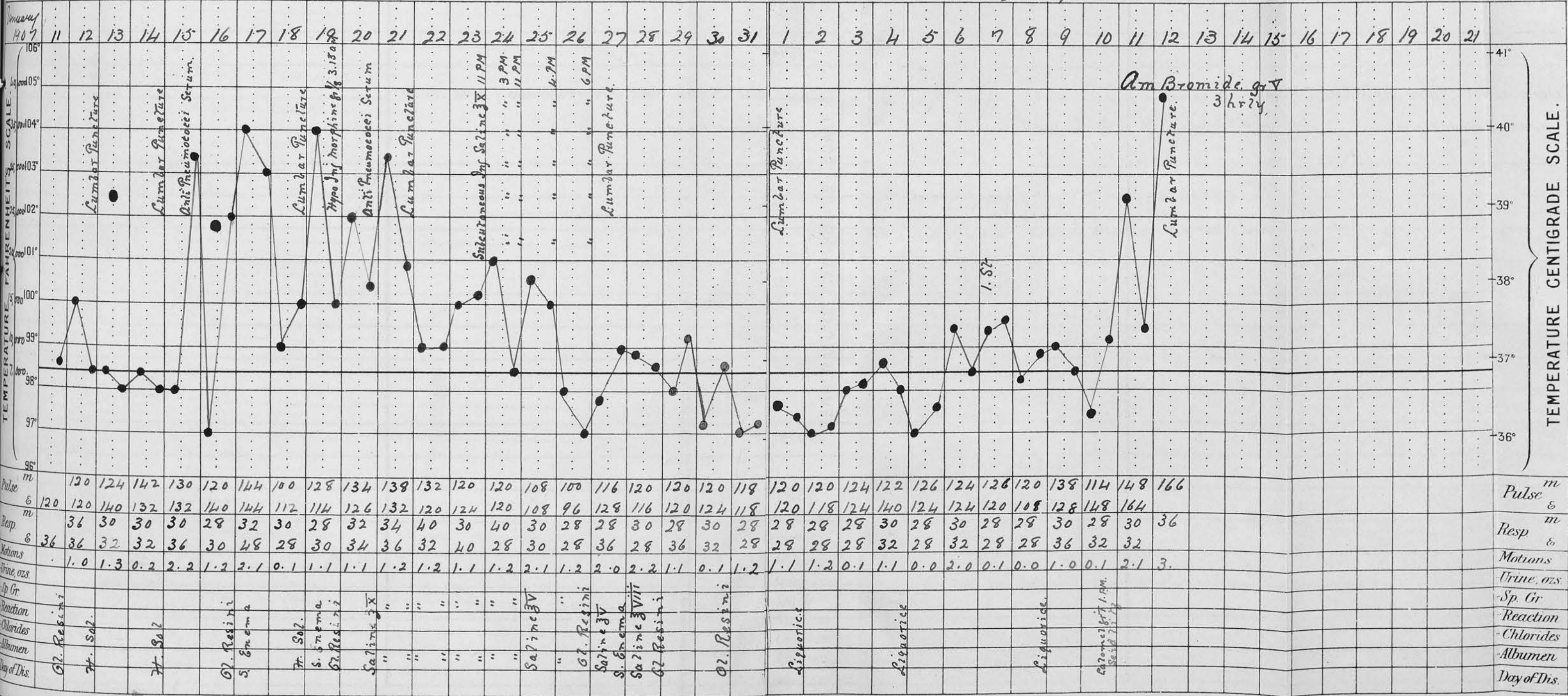
Age *2 years* Disease

Result

Name *David Glover*

Age *2 years* Disease

Result

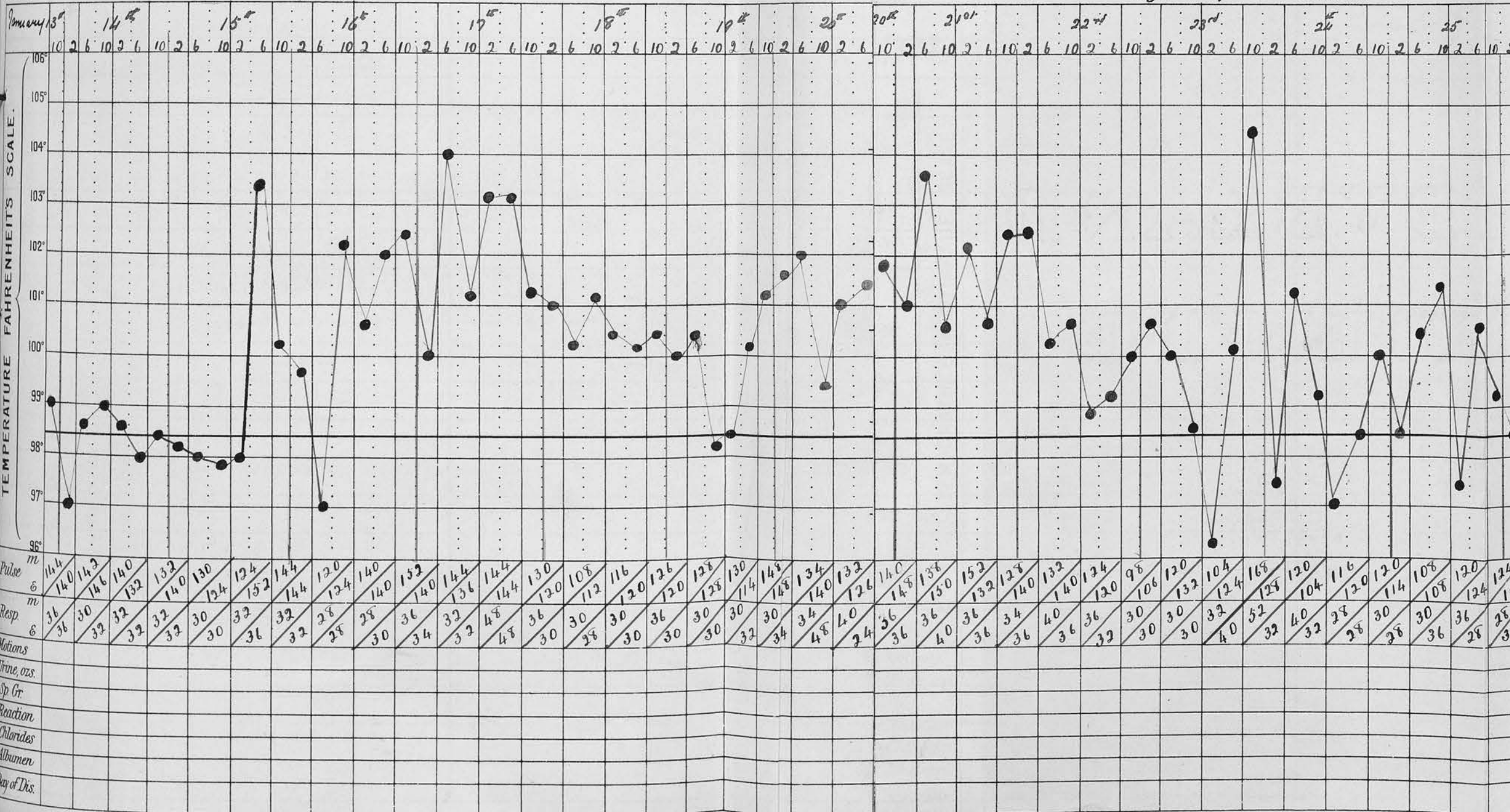


Name *David Glover.*

Age *2 Years.* Disease

Result *and Glover*

Age *2 Years* Disease





C A S E IV.

D.G. aged 2 years.

Admitted:- 11/1/1907.

Complaint:- Unconsciousness for two days.

History:- On the 8th inst. he would not take his dinner but lay down to sleep. Since then he has slept on except that when disturbed he rouses up sufficiently to cry out. Since 9th inst. he has vomited up everything he took to drink.

State on admission:- The child lies in a semi-comatose state but can be roused up sufficiently to swallow fluid food. No head retraction; Kernig's sign present; knee jerks present; plantar reflex flexion. Pupils contracted. No ocular paralysis. Leucocytes in blood 28,000. Temperature 100; Pulse 120; Respirations 36. Lumbar puncture gives about 15 c.c. of very turbid fluid, in which are very many polymorphonuclear leucocytes containing numbers of the diplococcus intracellularis meningitidis.

13/1/07. Purpuric spots on neck, abdomen, and back.

14/1/07. Lumbar Puncture; about 15 c.c. of fluid drawn off in which the same diplococcus is abundantly present. Patient's condition improved after the lumbar puncture.

17/1/07. Child remains very drowsy all the time but does not seem to have much pain.

4/2/07. Child is in the same condition and getting

thinner.

9/2/07. Child vomits everything he takes and cannot retain nutrient enemata. He is very much wasted. Unconsciousness has passed off, no spasm of any muscles, no head retraction. Reflexes deep and superficial are all very difficult to elicit.

12/2/07. Died.

13/2/07. Post Mortem Examination:- Brain: The dura is very much adherent to the skull in the neighbourhood of the sutures. There is a considerable amount of thin, turbid, serous fluid underneath the dura about the base of the brain and in the spinal canal, and the ventricles are greatly distended by similar material. Here and there along the lines of the great vessels is a thickening of the arachnoid apparently due to organization of a previous exudate. In the interpeduncular space and on the undersurface of the cerebellum is a mass of thick greenish-yellow pus of the consistence of clotted cream, extending out laterally on to the petrous bones and surrounding the 7th and 8th nerves. Anteriorly it extends forwards to the optic chiasma. The whole brain is very soft. The middle ears are not affected, the right being somewhat catarrhal only, the left dry.

Spinal cord: In the middle and lower dorsal regions there is a considerable amount of reddish

gelatinous material in which run many congested new formed vessels lying outside the dura. The dura in the lower dorsal and lumbar regions is firmly adherent to the posterior common ligament of the vertebrae, and is greatly thickened. On slitting it up one finds the cord covered with thick pus, similar to that on the base of the brain, especially in the lumbar region and on the posterior aspect of the cord.

Heart pale and cloudy.

Lungs pale but no sign of pneumonia or bronchitis.

Stomach and intestines healthy.

Liver, slight fatty change, and some minute metastatic abscesses.

Spleen, large, dark, and shows numerous minute white areas the size of millet seeds apparently metastatic abscesses.

#### CASE V.

R.H. aged 37.

Admitted:- 27/1/1907.

Complaint:- Headache and vomiting for one day with a cough for several days before.

History:- Patient had felt shivery for several days, but on morning of admission he vomited for the first

time after breakfast. Subsequently he was very drowsy and heavy till about 2 p.m. he became unconscious.

State on admission:- He is very restless and groans constantly but gets quite violent when touched or moved. No head retraction. Kernig's sign not definitely present. Knee jerks exaggerated. Pupils markedly unequal, right being dilated, left contracted. No spots on body. Leucocytes 29,000. Temperature 102°. Pulse 100. Respirations 32.

Lumbar Puncture. Only a few drops of very thick purulent fluid obtained, in which polymorphonuclear leucocytes are abundant containing the diplococcus intracellularis meningitidis.

29/1/07. Patient died.

30/1/07. Post Mortem Examination:- Much mottling about the sides, hips, and shoulders with spots ranging in size up to  $\frac{1}{4}$  inch in diameter. Nutrition and muscularity very good.

Brain: Dura a little adherent posteriorly and along the longitudinal sinus. Subarachnoid space contains a great quantity of pus especially along the lines of the larger vessels. In the interpeduncular space and on posterior surface of cerebellum and between its lobes are large collections of pus. There is a much softened area on the upper part of the left parietal lobe and also in the left lateral lobe of the cerebellum.

The arteries of the brain are somewhat atheromatous. On section the ventricles are a little distended with slightly turbid fluid, and the white matter is somewhat oedematous.

Spinal cord: The dura is adherent by old fibrous bands to the posterior common ligament of the vertebrae throughout its whole extent. Under the dura is a large quantity of yellowish turbid fluid. The cord and nerves appear to be healthy.

Pus from fluid round cord and pus on brain showed when examined numerous diplococci which gave the characteristic reactions of the meningococcus.

#### CASE VI.

B.M. aged  $7\frac{1}{2}$  years.

Admitted:- 21/1/07.

Complaint:- Headache and vomiting for a fortnight.

History:- For a fortnight she had vomited all she took to eat and has slept most of the day as well as at night. She has had no motion of the bowels for a week. She has also had much headache holding her hand to her head even in sleep, and waking up crying with pain. The social surroundings in this as in many of the other cases are very poor and dirty.

State on admission:- Child lies in a semi-comatose condition with eyes half closed not complaining unless disturbed but resenting any movement. When asked she complains of pain in the forehead. Pupils are contracted and equal, but the child objects to light. No head retraction, no rigidity of neck muscles. Kernig's sign present to a slight degree. Knee jerks present but not exaggerated. Plantar reflex flexion. Temperature 99; Pulse 108; Respirations 26.

22/1/07. Lumbar puncture gives perfectly clear fluid under slightly raised tension; there is no deposit when it is centrifuged and it contains no organisms.

23/1/07. Kernig's sign more distinct. Marked photophobia.

26/1/07. Lumbar puncture; fluid slightly turbid, tension slightly increased; contains numerous polymorphonuclear leucocytes but no organisms found.

4/2/07. Condition has varied a good deal from day to day, the child being at times free from pain and talking voluntarily. She is now quite comatose and greatly emaciated. Breathing occasionally of the Cheyne Stokes type.

6/2/07. Breathing Cheyne Stokes type all day. Died 10 p.m.

No Post Mortem Examination allowed.

CASE VII.

D.M. aged 2½ years.

Admitted 2/2/07.

Complaint:- Unconsciousness, pain in head, vomiting lasting one day. Also cough.

History:- Patient was quite well when he went to bed last night, but about 1 a.m. this morning he woke up and vomited. He vomited everything he took to drink in the morning, was very ill all forenoon and about 4 p.m. he became unconscious. He has been coughing since he took ill, and cries out when he is touched. At 8 p.m. had a fit.

State on admission:- Child is very much exhausted with blue lips, cold hands and feeble pulse. There are a few purpuric spots on the neck and on the left side of abdomen. Breathing very laboured, almost Cheyne Stokes in character. Kernig's sign present. Knee jerks increased. Plantar reflex flexion. Temperature 101.5. Pulse 130. Respirations 54.

Lumbar Puncture:- About 18 c.c. of very turbid fluid was withdrawn; contains many leucocytes; Also a growth of the diplococcus intracellularis meningitidis obtained.

3/2/07. Patient gradually sank and died.

4/2/07. Post Mortem Examination:- Skin shows numbers of purpuric spots especially over front of legs and thighs and inner side of the arms.

Brain: Dura thick. Under the arachnoid is a

great amount of pus along the lines of the large vessels and scattered here and there over the cerebellum. It is particularly plentiful in the interpeduncular space and along the Sylvian fissure. The whole brain is very soft.

Spinal cord: Spinal dura is much congested and beneath it is a large amount of turbid fluid. The posterior part of dura is much thickened over an area corresponding to the last six dorsal nerves as if from a previous meningitis. There is no infiltration of the nerves with pus.

The pus from the spinal cord on culture shows a diplococcus Gram-negative, glucose fermenting, &c. which is considerably larger than that obtained direct during life by lumbar puncture. The blood of heart failed to produce any growth on blood agar or ascitic-fluid-agar.

On subculture the organism from the cord which originally was found to be Gram-negative became Gram-positive in its staining reaction as well as being larger than it was in films obtained during the patient's life.

Heart: Healthy.

Right lung: Congested greatly at base posteriorly with some flakes of fibrin on the surface produced apparently by an impending pneumonia. Left lung similar.

Liver: cloudy swelling.

Kidneys apparently healthy.

Spleen shows enlarged Malpighian bodies.

Stomach and intestines, &c. healthy.

### CASE VIII.

J.G. Aged 27 years.

Admitted:- 18/2/07.

Complaint:- Headache and vomiting for one day.

History:- Patient had a rigor early yesterday morning, followed by headache lasting all day and he vomited in the evening. Vomiting continued during the night and by 1 a.m. he became unconscious.

State on admission:- Patient regained consciousness about 10 a.m. but remained very drowsy, and complained of headache. Kernig's sign present. Knee jerks increased; plantar reflex flexion. No ocular paralysis, &c. present. Temperature 100; Pulse 84; Respirations 28.

Lumbar Puncture:- 25 c.c. of very turbid fluid withdrawn; it shows many polymorphonuclear leucocytes in a few of which is seen a Gram-negative diplococcus.

19/2/07. Patient has slight head retraction and internal squinting of right eye; purpuric spots are

appearing on the back.

Lumbar puncture done again and 20 c.c. of turbid fluid removed under high tension. The diplococcus intracellularis meningitidis present in very great numbers.

Patient sent to Pilton Hospital for Infectious Diseases.

11/3/07. Patient sank into a comatose state, became very much emaciated and died on this date.

#### CASE IX.

M.S. Aged 45 years.

Admitted:- 16/2/1907.

Complaint:- Unconsciousness for some hours.

History:- Patient went to bed apparently in good health, but in the morning was found unconscious.

State on admission:- She lies on her side with legs drawn up and turned away from the light and objects very much to being touched. She is incapable of being roused to answer questions though irritable when interfered with. Pupils are equal and moderately contracted; no ocular paralysis; Kernig's sign present; knee jerks active; plantar response flexion. Breath has a foul odour and patient is occasionally sick. A few purpuric spots on the back.

Conjunctivae greatly injected. Temperature 98.  
Pulse 84. Respirations 28.

Lumbar Puncture:- Fluid turbid and flowed out under high pressure; it contains a great number of polymorphonuclear leucocytes many of which contain the diplococcus intracellularis meningitidis.

17/2/07. Patient sent to Pilton Hospital for Infectious Diseases.

6/3/07. Patient, after a period of several days' complete unconsciousness and restlessness during which she was only able to take a little fluid nutriment, died on this date.

#### CASE X.

A.W. Aged  $4\frac{1}{2}$  years.

Admitted:- 14/3/1907.

Complaint:- Headache, drowsiness and rigidity for 24 hours.

History:- Patient was at school in ordinary health and took a good tea about 5 p.m. At 6 p.m. she complained of a sore head and asked to be put to bed. She slept quietly until 3 a.m. when she woke, was very thirsty and complained greatly of her head. From that time she was restless, appeared drowsy but was restless and talkative in her sleep.

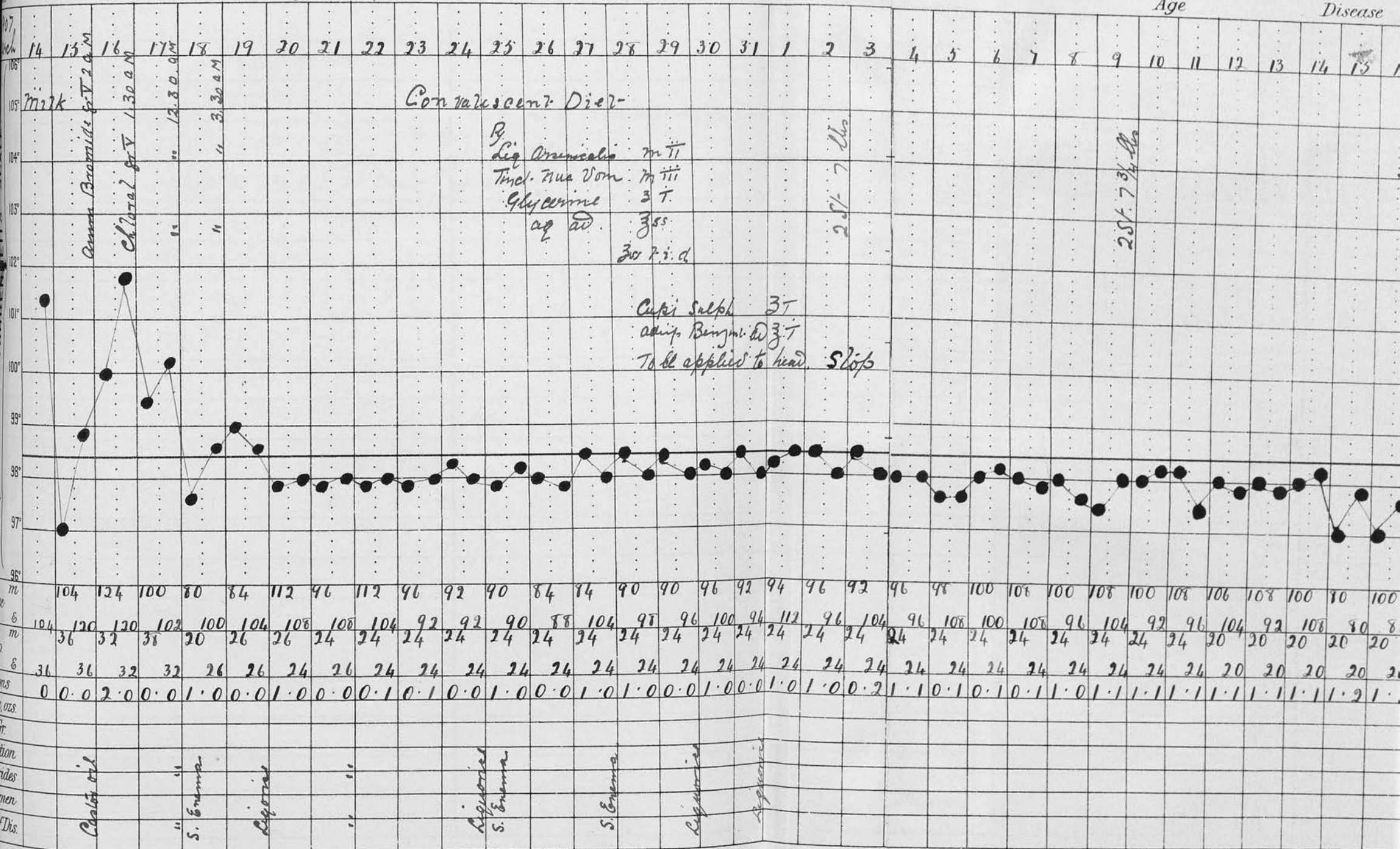
Amie Wilson

Age 5 Years Disease

Result

Age

Disease



Result										Age					Disease					Result												
16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	1907		
2 St 7 lbs										2 St 7 lbs					2 St 6 1/2 lbs																	
										Emulsion of Peppermint 3i. t.i.d. P.C.																						
2 St 7 1/2 lbs										2 St 7 lbs																						
TEMPERATURE CENTIGRADE SCALE.																																
00	88	84	72	88	88	80	88	84	88	88	88	84	88	84	80	100	88	90	84	88	88	88	84	100	88					Pulse		
80	80	96	84	116	116	100	80	88	88	88	80	80	80	80	104	108	100	88	88	88	104	88	104	88					&			
0	20	20	20	20	20	20	20	28	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	Resp			
20	20	20	20	20	20	20	20	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	&			
1	1	0	1	1	1	0	1	1	2	0	1	0	1	2	0	1	0	1	0	1	1	0	0	1	0	1	2	0	2	0	1	Motions
Urine, ozs.																																
Sp. Gr																																
Reaction																																
Chlorides																																
Albumen																																
Day of Dis.																																

Throughout the forenoon she was quite conscious when roused but drowsy and feverish. About 7.30 p.m. she began to moan loudly, became quite unconscious, tossed about in bed, and was somewhat blue about the lips. She has not vomited at all.

State on admission:- The child was semi-conscious with rigidity to some extent in all the limbs. The head is distinctly retracted and the muscles of the neck markedly rigid. All movement is much resented and the child moans when touched but will not speak. Kernig's sign is well marked. Knee-jerks present. Plantar reflex flexion. Pupils equal moderately dilated, react to light. No rash. No lung symptoms. Temperature 100, Pulse 104, Respirations 36.

Lumbar Puncture:- A turbid fluid is obtained under moderate tension; there is a great number of polymorphonuclear leucocytes in the fluid but no organisms are obtained either in film or on culture.

15/3/07. The child has become unconscious again at intervals, and spoken to the nurse once or twice. She puts out her tongue and does similar simple acts when told to do so. She has vomited twice and between the lucid periods lies in a semi-comatose state with the head strongly retracted. There are a few purpuric spots on the abdomen.

16/3/07. The child was very noisy through the night. Quite conscious in the morning, though Kernig's sign

and head retraction are still very well-marked.

Lumbar Puncture:- Fluid is turbid and under very high tension. A few diplococci are seen in films and on culture on blood-serum there is a distinct growth of the diplococcus intracellularis meningitidis.

17/3/07. Child is better to-day, quite conscious, rigidity of neck less marked, Kernig's sign still present. Since yesterday she has apparently become completely deaf.

18/3/07. The general condition is more satisfactory. The night was spent more quietly. The patient is now quite conscious, the rigidity of the neck muscles is less, Kernig's sign is hardly to be made out. The deafness continues as before.

22/3/07. Kernig's sign has quite disappeared. There is no pain. Temperature normal. The child takes food well. The muscles of the back, neck and legs have to a great extent lost their power and the child is rather flabby. She cannot sit up in bed without leaning to one side or other and resting on her hand. When a little push is given to the body the head falls back with a jerk and it is only after a few seconds that the child holds up its head again. When trying to stand the child falls towards one or other side and when attempting to walk she has to be firmly balanced by holding on to two hands. In attempting to step out the foot sometimes cannot be

moved forward but simply moves a little to one side. There is no paralysis of any one muscle or group of muscles, but this diminished power of movement seems to be largely a failure of co-ordination.

Reflexes:- Knee jerks exaggerated; very slight ankle clonus on both sides; plantar reflex is doubtful but there seems to be a slight extensor response at times on both sides.

25/3/07. Improvement maintained.

2/4/07. Child can walk a little better and the muscles are not so flabby. The head and neck muscles are more under control. The deafness is still absolute.

11/4/07. Child can walk better and the muscles are improved in tone. The powers of co-ordination and equilibration in walking are the most noticeable defect as the feet are often not pushed forward when the child attempts to walk, but to one or other side. The temperature is now constantly normal.

9/5/07. Patient has improved very much in power of walking and went out to-day. She is fairly well, but the deafness remains.

C A S E XI.

E.W. Aged 14 years.

Admitted:- 20/3/07.

Complaint:- Headache and vomiting for 24 hours previously.

History:- Patient went to bed in her usual health on 18/3/07, but on waking had a good deal of headache and felt sick and giddy. She rose but went back to bed. Once or twice during the day she vomited.

State on admission:- Patient tosses about in bed crying with the pain in her head. She is able to speak coherently though at times she is delirious. Kernig's sign present. Knee jerks somewhat active. Plantar reflex flexion. Temperature 98.5°; Pulse 128; Respirations 28.

Lumbar puncture yields cerebro-spinal fluid markedly turbid and under high tension; in it are numerous polymorphonuclear leucocytes and large numbers of the diplococcus intracellularis meningitidis.

21/3/07. Patient was removed one day after admission to Pilton Hospital for Infectious Diseases.

9/5/07. Patient died.

C A S E XII.

E.C. Aged 5 years.

Admitted:- 25/3/07.

Complaint:- Headache and vomiting for two days.

State on admission:- Patient is in a comatose state paying no attention to anything around him. Head

somewhat retracted and neck muscles stiff. Kernig's sign marked. Knee jerks present. Plantar reflex cannot be elicited. Some faint purpuric spots on arms and abdomen. Temperature 100.5°; Pulse 118; Respirations 44.

Lumbar Puncture. Yielded a large quantity of very thick fluid in which polymorphonuclear leucocytes were present in great numbers and the diplococcus intracellularis meningitidis was also found.

Patient was sent to Pilton Hospital for Infectious Diseases and died 26/3/07.

### C A S E XIII.

J.S. Aged 2 years.

Admitted:- 30/3/07.

Complaint:- Headache, vomiting, unconsciousness lasting for one day.

State on admission:- Patient is comatose, head retracted; Kernig's sign present; Knee jerks present; plantar reflex flexion. Temperature 99°.

Lumbar Puncture gives a turbid fluid under considerable pressure in which are copious polymorphonuclear leucocytes and numerous diplococci intracellularis meningitidis.

Death on same day.

Post Mortem Examination:- Body well nourished. There is a well marked purpuric rash under the chin and on abdomen and thighs.

**Brain:** The dura is greatly adherent to the vertex of the brain especially over the right temporal and parietal regions. The vessels in the sulci are greatly engorged and the convolutions markedly flattened. Around the vessels on the vertex, in both lateral regions, and on the upper surface of the cerebellum is a collection of greenish yellow sero-pus. There is a little of the same material at the base but not so much as on the vertex.

**Spinal cord:** There is a very little fluid on the surface of the cord with here and there small yellowish spots of pus and a generally turbid appearance of the arachnoid. The cord itself is extremely soft and almost diffluent.

**Heart:** The large vessels and the heart itself contain frothy blood and gas. No organism was obtained to account for this appearance.

**Lungs:** both somewhat congested.

**Liver:** shows marked cloudy swelling.

**Spleen** large firm and shows extremely well-marked Malpighian bodies.

**Kidneys** show marked cloudy swelling.

**Mesenteric glands** are markedly enlarged and hyperaemic; and the Peyer's patches in the intestine stand out prominently and are congested.

C A S E XIV.

M.W. Aged 6 years.

Admitted:- 8/4/07.

Complaint:- Sleepiness and swelling of abdomen for the past week.

History:- The child did not complain of anything but had been found asleep several times on the floor at school, during the previous week. She had had no vomiting. At about the age of 1 year she had been treated for rickets but generally was quite healthy.

State on admission:- The child is very drowsy but quite intelligent when roused, says she has no pain. The abdomen is swollen and tense and slightly tender on pressure. There is a purpuric rash on both sides of abdomen and a few spots on the thighs. Temperature 102.5°; Pulse 132 per minute; Respirations 32. No headache. No head retraction. Pupils equal and react to light but sluggishly. No Kernig's sign. Knee jerks present; plantar reflex normal.

Over the chest there are a few scattered crepitations.

Abdomen is distended partly by ascitic fluid, as evidenced by its dulness varying with the patient's position, partly by inflation of the intestines.

Blood Count: Haemoglobin 70%; Red Blood Corpuscles 3,500,000; White Blood Corpuscles 12,000.

There is a slight relative increase in the large lymphocytes.

- 12/4/07. Child still very drowsy.
- 16/4/07. Widal's Reaction performed, - negative.
- 20/4/07. Child more lively. Abdomen still considerably swollen; Spleen tender.
- 3/5/07. White blood corpuscles 15,000. The temperature is to a great extent intermittent often rising to 103° and falling below normal within 12 hours. Lumbar Puncture performed; turbid fluid escaped under considerable pressure, and in it were large numbers of polymorphonuclear leucocytes containing the diplococcus intracellularis meningitidis.
- 6/5/07. Patient died in Pilton Hospital.

C A S E XV.

M.F. Aged 16.

Admitted:- 24/4/07.

Complaint:- Headache and vomiting for past three days.

History:- For the past three days she has been feeling ill with severe and increasing headache.

State on admission:- Patient is in a very lethargic state becoming at times quite unconscious at other times being still capable of rousing. Kernig's sign present; Knee jerks present; Plantar response

flexion. Temperature normal. Pulse 100 per minute.  
Respirations 20.

25/4/07. Lumber Puncture gives turbid fluid under considerable pressure in which polymorphonuclear leucocytes are present in great numbers containing the diplococcus intracellularis meningitidis.  
Some red spots of small size on arms chest and thighs.

26/4/07. Patient was removed to Pilton Infectious Diseases Hospital where she lived for 40 days dying on 4/6/07.

C A S E XVI.

H.G. Aged 27 years.

Admitted:- 26/4/07.

Complaint:- Pains all over body for past 4 days.

History:- Four days ago patient began to vomit after coming home from work, and complained of pain in the back of the neck. Since then the pains have spread all over the body being worse on movement. He has had no fits nor unconsciousness but has been rather drowsy.

State on admission:- Patient lies still in bed quite conscious and complains of pain when he is touched. Some rigidity of neck muscles. Kernig's sign is not present. Knee jerks normal. Plantar reflex

flexion. Temperature 99°; Pulse 76 per minute;  
Respirations 28.

27/4/07. Lumbar Puncture performed, and, as the fluid was turbid and contained the diplococcus intracellularis meningitidis the case was sent to Pilton Infectious Diseases Hospital where patient died 11/7/07.

C A S E . . . X V I I .

E.W. Aged 8½ years.

Admitted: - 6/5/07.

Complaint: - Headache and vomiting for 2 weeks.

History: - A fortnight ago patient rose in the morning with severe headache and vomited shortly afterwards. She went to school but in the afternoon came home complaining of severe headache, went to bed and has not been up since. The headache has been severe all along and there have been pains in the back, abdomen and limbs. She sleeps only by snatches, has seemed very feverish some nights and been delirious.

State on admission: - Patient lies moaning constantly but quietly. The head is markedly retracted. Pupils contracted. Kernig's sign is well marked. Knee jerks present. Plantar reflex flexion. No rash. The child resents any movement but answers

intelligently when roused; though as a rule she lies in a semi-comatose condition. Temperature 101.5°; Pulse 168; Respirations 24. Urine 20 ozs. per diem, no abnormal constituent.

Lumbar Puncture yields a turbid fluid under considerable pressure; polymorphonuclear leucocytes are present in great abundance and many contain the diplococcus intracellularis meningitidis.

7/5/07. Patient sent to Pilton Hospital for Infectious Diseases.

28/7/07. Patient after remaining in Hospital for 82 days, - during which time her temperature fluctuated between normal and 102° and the headache gradually passed off, - was dismissed cured on 28th July 1907.

### C A S E XVIII.

H.R. Aged 2 years.

Admitted:- 30/5/07.

Complaint:- Vomiting and pain on movement, lasting one day.

History:- On the day before admission patient began to be sick and to complain of pain in the legs. He took to bed and cried whenever he was touched or moved. Within a few hours he became lethargic and next day semi-unconscious.

State on admission:- Patient is almost quite unconscious but cries out when moved. The head is retracted strongly; Kernig's sign is present; Knee jerks active; plantar reflex flexion. Pupils contracted. Temperature 99.5°; Pulse 104; Respirations 52.

Lumbar Puncture gave a little turbid fluid in which polymorphonuclear leucocytes were present in great numbers and the diplococcus intracellularis meningitidis was found both inside and outside of the latter.

Patient died the same day.

### C A S E . . . X I X .

W.P. Aged 12 years.

Admitted:- 29/7/1907.

Complaint:- Pain in the back and vomiting for the past 3 days.

History:- Patient was staying with friends in the country where he had been for about a fortnight when he suddenly took ill and vomited. He was sent home next day.

State on admission:- Patient lies on his back staring up to the ceiling in a semi-conscious condition. He cries out when touched. There is no head retraction and no rigidity of the neck muscles.

There are large purplish blotches over the front of the abdomen. Kernig's sign present; Knee jerks moderate; Plantar reflex flexion; pupils contracted. Temperature 105; Pulse 144; Respirations 36.

Lumbar Puncture gave a good flow of turbid fluid containing many polymorphonuclear leucocytes and numbers of the diplococcus intracellularis meningitidis.

2/8/07. Sent to Pilton Hospital for Infectious Diseases; where he died next day.

C A S E XX.

T.D. Aged 4 years.

Admitted:- 9/10/07.

Complaint:- Pain in the head and vomiting lasting one day.

History:- Two days ago patient got a wetting on the way home from school; next morning he began to vomit soon after wakening, and kept on doing so till the afternoon. He then began to complain of severe headache, at first frontal then on the top, and to-day at the sides. The vomiting began again in the evening and continued most of the night.

state on Examination:- Patient does not complain of very great pain nor cry out; there is no retraction of the head though some stiffness and pain are elicited when an attempt is made to bend the head forwards. There is no unconsciousness nor even drowsiness. Kernig's sign is present; Knee jerks normal; Plantar reflex flexion. Pupils contracted, equal. Temperature 100; Pulse 120; Respirations 22.

Lumbar Puncture:- produces a little turbid fluid not under high pressure in which the diplococcus intracellularis meningitidis is plentifully present.

10/10/07. Patient sent to the Pilton Hospital for Infectious Diseases.

19/10/07. The symptoms became gradually more pronounced, blotches appeared on the arms legs and back, unconsciousness set in, and patient died on this day.

### C A S E XXI.

A.D. Aged 34 years.

Admitted:- 21/10/1907.

Complaint:- Pain in head and back lasting 2 days.

History:- Patient was in gaol for 3 days and on coming out he went to a lodging house and lay down

complaining of great headache and backache and a desire to sleep.

State on admission:- The patient seemed to be seriously ill, being cold, shivering and stiff. No head retraction; Kernig's sign not to be elicited; knee jerks normal, Plantar reflex flexion; Pupils react well; no abnormality of eye muscles. Temperature 102; Pulse 66; Respirations 24.

Lumbar Puncture gave a slightly turbid fluid under increased tension; polymorphonuclear leucocytes were found in the deposit and large numbers of the diplococcus intracellularis meningitidis.

22/10/07. Sent to Pilton Hospital for Infectious Diseases.

16/11/07. He gradually lost the headache, the temperature returned to normal, and the pain subsided. On this day he was dismissed cured.

### C A S E XXII.

M.B. Aged 56 years.

Admitted:- 5/12/07.

Complaint:- Vomiting and weakness lasting about 4 weeks.

History:- About a month ago patient began to vomit after her food; she had no pain but the food seemed to come up at once after she took it. She has had

a very little pain in the head also, and has been getting progressively weaker.

State on admission:- Patient is somewhat worn and senile for her age; habits fairly good as to alcohol. She has an enlarged and hypertrophied heart with a systolic murmur and accentuated second sound as heard in the aortic area. She complains of some headache and feels sick constantly even when she is not vomiting. There is no special stiffening of the muscles of the neck or back, but she is at times very restless. The legs are stiff (Kernig's sign present); knee jerks normal, plantar reflex flexion. Temperature 99.5; Pulse 116; Respirations 24.

Red Blood Corpuscles 1,500,000; Haemoglobin 75%; White Corpuscles 15,000.

12/12/07. Patient has been spitting up a good deal of frothy material, streaked with blood. Her sickness is less marked and she has been vomiting for the past three days chiefly a short time after food.

15/12/07. Patient has sunk somewhat in general condition but no fresh symptoms have developed.

17/12/07. Patient became yesterday very sick again several times. She had, however, a fairly good night with very little sickness, till 5 a.m. She then began to shiver and became speedily much collapsed. About 8 a.m. she had another shivering

attack, her temperature began to rise and she sank into unconsciousness. She died without returning to consciousness but without any rigidity or convulsion during the forenoon.

Post Mortem Examination:- Numerous petechial haemorrhages are scattered over the surface of the body and limbs.

Skull shows considerable old adhesion to dura and dura to brain.

Brain: The vessels of the brain are greatly congested and there is a large amount of thick, gelatinous pus on the under surface of the cerebellum and round the pons and medulla. The ventricles are distended by turbid thin serous fluid and the choroid plexus oedematous. There is no suppuration from the ear or nose.

Spinal Cord: There is a considerable quantity of thick yellow gelatinous pus on the posterior surface of the cord throughout its whole extent not extending down the nerve roots.

Films of the pus showed diplococci which did not retain Gram's stain but no culture was obtained.

Heart: Old standing endocarditis of the mitral and tricuspid valves with incompetence is present; heart muscle soft and infiltrated by fat.

Lungs: Both are oedematous and have much mucopurulent secretion in the bronchial tubes.

Liver shows fatty change and gives a marked Prussian blue reaction.

Spleen slightly enlarged.

Kidneys show cloudy swelling.

C A S E XXIII.

T.A. Aged  $1\frac{1}{2}$  years.

Admitted: 18/2/08.

Complaint: A convulsion lasting about two hours.

History: Patient has had whooping cough for the past six weeks and had been greatly reduced by his illness. This morning the child took a fit about 9 a.m.; the eyes were fixed and staring and he moaned a great deal. The arms were limp but the legs were rigid and twitching. The twitching passed off in a few minutes and the child lay still in a state of semi-unconsciousness with the eyes wide open.

State on admission: Patient is quite unconscious and very much cyanosed. There is now no twitching, but the legs are somewhat stiff. No head retraction; Kernig's sign present; knee jerks present. Pupils moderately dilated. No ocular or other paralyses. Some purpuric spots on legs and arms. Temperature  $101^{\circ}$ ; Pulse 132; Respirations 32.

Lumbar puncture gives a turbid fluid that issues un-

der considerable pressure. It contains the diplococcus intracellularis meningitidis in large numbers. 19/2/08. Child sent to Pilton Hospital for Infectious Diseases. Remained unconscious and in otherwise unchanged condition there for the next two days when he died 21/2/08.

C A S E XXIV.

W.M. Aged 3 years.

Admitted: 19/6/08.

Complaint: Headache above right eye, vomiting for past 3 days.

History: Five days ago patient had a severe fall and two days afterwards began to vomit; three days after he began to suffer pain over the right eye. He continued to vomit and occasionally to cry with pain.

State on admission: Patient lies in bed on his right side with the head markedly retracted and the knees drawn up. The left eye shows marked iritis and the patient's sight seems to be very defective, though he understands everything said to him. He resents any attempt to bring the head forward, and cries out in a sharp shrill peevish manner when moved. Kernig's sign is well marked; knee jerks active; plantar reflex flexion. Pupils contracted and equal; no abnormal position nor movements of the eyes.

Some blotches on arms and chest. Temperature 100;  
Pulse 140; Respirations 36.

20/6/08. Head retraction much more marked, and opisthotonos present.

Lumbar puncture gave two test tubes full of a very turbid fluid, which was crowded with leucocytes and contained quantities of diplococcus intracellularis meningitidis, some of them being within and some on the margins of the cells.

23/6/08. Sent to Pilton Hospital for Infectious Diseases.

Died three days later.

C A S E XXV.

A. B. Aged 10.

Complaint: Vomiting, headache, and pains all over the body lasting one day.

History: Patient was in perfect health on the preceding day and attended school.

State on admission: The boy was in a semi-comatose state, the extremities very cold and the lips cyanosed. The legs were firmly flexed at hip and knee, the arms folded across the chest and the fingers clenched. Temperature 102°. Head retraction was greatly marked, and the rigidity of the neck and

back muscles was so great that, when the head was raised from the pillow, the whole body moved with it. Any movement such as this caused great pain which made the patient cry out. Knee jerks active; Plantar reflex could not be properly elicited. The chest and front of abdomen showed numerous small purpuric spots.

Lumbar puncture gave a turbid fluid under high tension containing copious numbers of leucocytes and the diplococcus intracellularis meningitidis.

Patient died on the day after the onset of the disease.

Symptoms of Cerebro Spinal Meningitis with Special  
reference to twenty-five Cases observed in the  
Leith Epidemic.

Types. Several types of cerebro spinal meningitis are to be recognised differing chiefly with regard to the tendency of the cases in their early stages.

The malignant or fulminating form is one in which the symptoms appear suddenly, quickly attain a maximum and result in death within a few hours. Four of these cases were observed in the Leith epidemic or about 16 per cent of the total. Or, after the disease has commenced in the ordinary way to be described later, the patient passes into a condition resembling shock with small pulse, sighing respiration, and total abolition of reflexes, a condition probably due to sudden distension of the ventricles with exuded fluid.

The abortive type is one of which examples are found in every epidemic. The illness begins with headache, vomiting, fever, neck rigidity, and it may be, convulsions, in the ordinary way. But the patient, after a few days' illness, may either recover completely or with some permanent effect of the disease such as deafness.

The ordinary type includes cases which last from one to four weeks and either die or within that period commence to recover.

Chronic cases are those which last for two or more months with symptoms like those of the acute form and

then either recover with various complications or die of exhaustion. This type includes most of the cases of posterior basic meningitis described by Gee and Barlow.

Onset:- There is very seldom a history of gradual onset but the patients are struck down within a few hours by the disease, having been as a rule in a state of previously excellent health.

As will be seen from the tabular statement of symptoms, headache, general pains through the body and limbs, drowsiness passing into unconsciousness and vomiting were among the most common early signs. The position usually taken up by the patient in bed is to lie on the side with the knees drawn up, the head retracted, the arms flexed and the hands placed under the chin. Generally speaking the patient lies still with occasional cries and slight movements, but sometimes there is great restlessness till complete unconsciousness supervenes.

Temperature:- There is nothing characteristic about the temperature curve, but three charts are given as examples of a case which ran an acute course, of a chronic case with remissions, and of one that recovered. Even in the severest cases the temperature may be only a little elevated and it is seldom higher than  $102^{\circ}$ . In our 25 cases the average temperature taken twelve hours after admission to hospital was  $100.6^{\circ}$ . In occasional cases the temperature may rise at some

period of the day to  $105^{\circ}$  or  $106^{\circ}$  and may intermit once or twice in every twenty-four hours. These are cases of very serious prognosis, but the condition of rise and fall round the normal may persist for weeks. In most cases the temperature remits a little every morning but persists at a slightly elevated level. In other cases there are occasional remissions almost to normal prolonged for several days; the patient seems to be recovering; but at the end of a few days or a week the temperature mounts again to its original level and the symptoms return as before. This is shown for example in the chart of the case of Annie Jones from 22nd to 30th November 1906.

Pulse:- The heart beat is rapid and commonly irregular in time and in force. Thus the pulse differs in the two important respects of rapidity and irregularity from the pulse of tuberculous meningitis in which it is regular but characteristically slow. The average pulse rate in our cases twelve hours after admission was 118, and in most of the cases it was somewhat over 100.

Respiration:- The breathing is somewhat more rapid than usual in consequence both of the pneumonia which is a frequent accompaniment and the rise in temperature. The average respiration rate in our cases was 33. An important feature to note is that the normal 1 to 4 ratio of respiration to pulse is greatly increased, a fact which often obscures the diagnosis between this

condition and pneumonia.

Eruption:- The eruption appears to vary in frequency and in character in different epidemics. In the Leith epidemic a roseolar or mulberry coloured rash was very frequently present and 60 per cent of our cases showed it. The rash consisted of small spots of congestion which sometimes faded on pressure, sometimes were unchanged. In cases that died these spots were found on microscopic examination to consist of intensely dilated vessels lying in the subcutaneous tissue with occasional minute haemorrhages. The spots were most frequent on the front of the arms, thighs, and chest, less numerous on the abdomen, face, and back. Sometimes the eruption begins with a widespread erythema which in a few hours fades and leaves the petechiae. Herpes in some epidemics is very common, but was seen only in one of our cases. These herpetic eruptions do not seem to have anything characteristic as to site, appearance, or organismal contents, but occur on the lips, nose, or other parts of the body.

Blood:- In all cases leucocytosis is found consisting of increase in the polynuclear corpuscles. The count is in general much above that found in a case of pneumonia, a disease with which cerebro-spinal meningitis is rather apt to be confounded in the early stages. In the chronic form however the leucocyte count may again drop and thus forms no safe guide to a

diagnosis between chronic cerebro-spinal and tuberculous meningitis. The same is true in the diagnosis of the posterior basic cases in young children. The leucocyte count in general is higher the thicker and more turbid the cerebro-spinal fluid; and it may in purulent cases rise to 60,000 per c.m.m. or even over this figure. It cannot be said that the count is a safe guide in prognosis; for, in cases that recover it may touch nearly the figure mentioned above. Generally speaking however, 25,000 per c.m.m. appears to be a favourable number.

The following table shows the blood counts in ten cases occurring during the Leith Epidemic:-

Case	White Corpuscle Count per c.m.m.	Polymorph per cent	Lymphocyte per cent	Large Mono- nuclear per cent	Eosinophile per cent
3	53,000	83	17	-	-
4	15,000	88	11	1	-
6	21,000	74	23	3	-
7	20,000	75	18.5	5	1.5
8	18,000	82	13.5	4.5	-
10	16,000	88	12	-	-
11	39,000	97	2	.5	-
12	16,000	84	10.5	4	1.5
17	34,000	83	11	6	-
19	32,000	86	8.5	5.5	-

Urine:- In many cases albumin is present in the urine to a moderate degree. In others there may be blood due doubtless to the haemorrhagic nephritis described by Councilman, though this was not present in any of our cases.

Kernig's Sign:- This forms, like lumbar puncture, one

of the most important diagnostic signs of the disease in differentiating it from such a condition as pneumonia. Kernig first published his results in 1884 having observed frequently that in patients, proved post mortem to be cases of meningitis, there was during life an inability to bring the leg into a position of complete extension when the thigh was placed at an angle of ninety degrees with the body. It may be absent in those very severe and sudden forms of malignant meningitis in which the reflexes are all abolished, and it may also be absent during the first day or two in an attack of ordinary severity. In those cases which recover, it gradually diminishes and finally disappears as convalescence is established. Also in young infants its presence does not mean so much as in older people because in the former there is always a greater amount of muscular tonicity which becomes readily increased upon any slight illness with increased temperature. It was present in 84 per cent of our cases.

Head Retraction and Neck Rigidity:- Rigidity of the neck is an important early sign of cerebro-spinal meningitis. As a rule there is present along with it a certain degree of opisthotonos, and it appears with or before the Kernig's sign. In the posterior basic forms of infants the rigidity and opisthotonos often reach an extreme degree. The rigidity of the neck not only causes difficulty in bending forward the head, but

any attempt to do so causes pain and often sets up an appreciable degree of mydriasis due doubtless to irritation of the cervical nerve roots. Head retraction and neck rigidity were present at an early stage in 48 per cent of our cases, and, in all the cases, came on at a later stage in the disease.

Mental State:- Generally speaking intense headache is present at the beginning (68 per cent of our cases) passing on soon to a state of stupor in which the headache is dulled. Along with or instead of headache, pains in the body or limbs were present in 36 per cent of cases, and were due doubtless to irritation or infiltration of the posterior nerve roots. Along with the state of stupor there is sometimes noted a condition of irritability in which the patient starts at the least sound, and resists any attempt to disturb him or change his posture. Unconsciousness supervened during the first two days of the disease in 64 per cent of our cases, and was generally accompanied by delirium which in most cases was of a mild type, but in a few was noisy. During the remissions of temperature which, as we have mentioned, occurred in several cases there was usually an improvement as regarded the unconsciousness and delirium, the patient waking up although the symptoms such as Kernig's sign, head retraction, and rigidity persisted. In favourable cases, which later recovered, one of the first signs of improvement was usually disappearance of the delirium. In the unfavourable cases the patient became successively

stuporose and comatose prior to the fatal termination; or if recovery took place there was always noted some mental enfeeblement.

Convulsions:- At the onset convulsions were frequently noted though they were not so common as simple dulness with intense headache. When they occur one may presumably infer that they are due either to distension of the lateral ventricles of the brain with fluid, or to a considerable rise of pressure in the fluid of the subdural or subarachnoid space. They occurred at a later stage in some cases which were progressing moderately well, and were probably caused by adhesions between medulla and cerebellum causing interference with the foramen of *Magendie*. Several cases in which convulsions supervened were markedly improved both as regards the convulsions and the general symptoms after the performance of lumbar puncture. Frequently the temperature came down to normal, the patient became less restless and it seemed as if recovery were about to ensue, though the condition returned to its previous state within two or three days at most.

Reflexes:- The superficial reflexes became dulled and more difficult to elicit from the first. The condition of the abdominal reflex has been already referred to and the importance which some authorities attribute to its early enfeeblement as regards the diagnosis of the site of primary involvement of the nervous system has been commented on. The plantar

reflex was found to be variable and its character too inconstant to be of any use for purposes of diagnosis. In general the response to stroking the sole was by flexion of a feeble type, though in two cases an extensor response was obtained at an early stage in the disease. Koplik gives the frequency of an extensor response at 16 per cent of cases of cerebro-spinal meningitis.

The deep reflexes as a rule are present in the earlier stages and disappear as the symptoms become more severe or when at a later period a chronic case becomes moribund. There is, however, nothing characteristic about them. The knee-jerks were present at the commencement in all the cases and in about one-third appeared to be more active than usual.

The readiness with which the pupil dilates has been commented upon above. The irritation of the medulla at an early stage is shown by the fact that vomiting forms an initial symptom in 80 per cent of the cases.

The *tâche cérébral* is very readily elicited in almost every case both at the beginning and during the course of the disease, but it is present not only in other forms of meningitis but even in several other conditions of childhood where high temperature and toxæmia affect the nervous system, so that its diagnostic value is not high.

Nerve Affections:- In those cases where the fundus oculi could be examined no change was noted in the

optic papilla. In this respect epidemic cerebro-spinal meningitis differs very greatly from meningitis of the tuberculous type. We have not seen any case of blindness, though in some epidemics this is stated to be a common sequel. Nor in making post mortem examinations on fatal cases have we met with an example in which infiltration of the optic nerve by extension of the pus upon the base had taken place. In one of our cases, where death occurred on the 7th day, iritis was present in the later stages, but whether this was due to the diplococcus meningitidis could not be ascertained. Keratitis is said to come on as a result of infiltration of the fifth nerve, and various forms of strabismus ensue from affections of the different nerves to the eye muscles, although in the serious condition of the patients these are difficult to make out. Nystagmus due probably to some intracranial affection of these nerves ~~was~~ however very common in young children. Similarly in regard to photophobia, so much irritability is expressed upon the mere attempt to open the eye-lids that it is impossible to say how much of this is due to resentment against the entrance of light.

The auditory nerve is more commonly affected and seems specially liable to be infiltrated with pus continued outwards from the collection on the base of the brain. Otitis media is also common and we observed it in varying degrees up to complete filling

of the middle ear and its accessory cavities with gelatinous, purulent material in several cases. Many patients who recover show permanent deafness as in case X, and from examination of cases that die this appears to be due to extensive infiltration of the inner ear along the sheath of the auditory nerve. Even some mild attacks may be followed by this complication, and the proportion of deafness in cases that recover is given by various writers in figures approaching 60 per cent of recoveries. In our series there was one case of absolute deafness in three recoveries.

The seventh nerve is also frequently affected but the resulting paresis or paralysis is not so absolute as in the case of the eighth nerve and recovery from it may take place with convalescence.

Joint Complications are noted in some epidemics more than in others and vary greatly in severity. Osler has described two cases in which the hands, wrists, elbows, knees, hip and various other joints were affected, the skin became red, swollen, and diffusely erythematous for several inches above and below the affected joints. In one of these cases the meningococcus was isolated both from one of the joints and from the blood. Various other observers have had similar cases but none of ours showed any joint affection.

Lumbar Puncture:- In all the cases of which the notes are given on pp. 37 to 77 with the exception of two, the diagnosis was confirmed by lumbar puncture. Of these two, case VI., which failed to give meningococci in the spinal fluid, may possibly have been one of tuberculous meningitis, though diagnosed as and presenting other characteristic symptoms of epidemic cerebro-spinal meningitis, while the diagnosis of case XXII., as one of the latter disease, was confirmed by post-mortem examination.

The operation was performed in the usual manner, through the fourth lumbar interval, the fluid received in a sterile centrifuge tube, and the corpuscles in it counted either by centrifuging when the fluid was thin and examining the sediment in the tube, or by using a white-corpuscle haemocytometer pipette and counting-stage without centrifugalization or dilution of the fluid. The fluid in general was under considerable pressure and spurted out when the needle penetrated to the subarachnoid space, but in cases where the exudate was thick it often came drop by drop as mentioned under the individual cases above. The amount obtained varied from about 5 c.c. to 50 c.c.

In films the meningococcus was always quite readily obtained at all stages of the disease. In the earlier stages the diplococci lay both inside and outside of the cells, but later on as the cells became more numerous the tendency was to find fewer and fewer organisms extra

cellular. The cells present were chiefly polymorphs with some of the large mononuclear cells mentioned above in describing the morbid anatomy of the condition. The number of cells present was frequently as high as between 200 and 300 per cubic millimeter. In one case where lumbar puncture was performed after several weeks' illness the predominating cells were mononuclear.

There does not appear to be any definite relation between the characters of this fluid and the course of the disease. In two cases where recovery took place the fluid was thick, turbid, under high pressure and contained large numbers of the diplococcus from the first. In another case of recovery the fluid was at first serous and contained very few organisms.

Also between the characters of the fluid and the symptoms such as head retraction and Kernig's sign there is very little connection. It must be remembered, however, that the pressure of the fluid withdrawn from the spinal canal may be quite different from that around or still more within the cavities of the brain. Many of the cases show matting around the foramen magnum, and in a large proportion the cerebellum is so much adherent to the upper surface of the medulla that the pressure within the brain has led to great dilatation of the ventricles. This may take place without any increase of the intraspinal tension.

It must be observed that many patients in whom the spinal fluid escaped under high pressure were greatly

relieved from symptoms of pressure and cerebral irritation after a quantity of excess cerebro-spinal fluid had been withdrawn. The guide to the amount best suited for withdrawal in order to give relief was the apparent pressure, the fluid being allowed to run off till it came in drops.

Age and Mortality:- While epidemic cerebro-spinal meningitis is mainly a disease of infancy and childhood, it is very fatal among those adults whom it happens to attack. There were 86 cases in the Leith Epidemic available to us for statistical purposes, and the mortality among these at different age periods is shown on Table III. The period between birth and one year of age is generally stated to be that in which the greatest number of deaths take place; and, while our cases in this period were few in number, they all died. The greatest incidence of the disease took place in the periods from 1 to 5 years and from 5 to 10 years, the numbers being almost equal. In these two periods the percentages of deaths were respectively 64 and 69. Between 10 and 15 years of age the percentage of deaths was 57. As the age rose into adult life, however, the death rate increased, being in the period from 15 to 25, as high as 81 per cent and after 25 years reaching 90 per cent. of those affected. The general percentage of deaths at all ages was 72, with 62 deaths and 24 recoveries out of the 86 cases observed.

T A B L E III.

AGE, DISTRIBUTION AND MORTALITY

Age	Number of Cases	Number of Deaths	Percentage of Deaths	Number of Recoveries
Under 1 year	3	3	100	0
1 - 5 years	28	18	64	10
5 -10 "	26	18	69	8
10-15 "	7	4	57	3
15-25 "	11	9	81	2
25-60 "	11	10	90	1
over 60 "	0	0	0	0
TOTALS	86	62	72	24

Differential Diagnosis.

Some of the most important positive characters of the disease serve to mark it out sharply enough during the prevalence of an epidemic. The chief points are the abrupt onset of illness, the neck rigidity, the vomiting, the headache, and later the unconsciousness or delirium. Later, the appearance of the eruption, the presence of Kernig's sign, and the head retraction serve more definitely to recognize the disease, the diagnosis of which is established by lumbar puncture.

The diseases most liable to be taken for cerebro-spinal meningitis are other forms of meningitis, pneumonia, and typhoid fever.

Of the other forms of meningitis, the tuberculous variety is the most important. This begins in a more prolonged and insidious fashion than cerebro-spinal fever, the headache, vomiting, and head retraction becoming gradually more marked over a period of several weeks as a general rule. The hollowing of the abdomen, frequently found in tuberculous meningitis, and the slow pulse, that usually characterizes it, are in marked contrast to the fulness of the abdomen and rapid pulse that generally obtain in cerebro-spinal fever. The ophthalmoscope and lumbar puncture form, however, the most useful aids to diagnosis. The discovery of tubercles in the choroid, where they may be found in a large number of the cases affected by tuberculous meningitis, forms a positive diagnostic sign of this disease, and the characteristic eruption, if it has appear-

ed, does the same for cerebro-spinal fever. The fluid obtained by lumbar puncture affords, except in very chronic cases of cerebro-spinal fever, a safe guide; for in tuberculous meningitis it is clear, the cells it contains are not very numerous and are all lymphocytes, while the tubercle bacillus can in many cases be discovered. With regard to the other forms of acute meningitis, such as that due to the pneumococcus, the therapeutic importance of a precise diagnosis is not of paramount importance, but the causative organism can be readily discovered from examination of the fluid obtained by lumbar puncture. In the case of secondary meningitis due to some local cause like a suppurating ear or wound, the history and the characters of the lumbar puncture fluid again form an effective aid.

With regard to the diagnosis from pneumonia, in the Leith cases, difficulty was experienced in several instances. This is particularly apt to occur when we have to deal with the symptom-complex, to which Dupré has given the name of "meningism", a term describing the presence of such symptoms as convulsions, twitching, strabismus, and head retraction, due simply to the toxæmic condition, induced by the severity of the lung disease; This condition may come on suddenly, rendering it thus all the more liable to be mistaken for cerebro-spinal meningitis. The diagnosis is cleared up on the one hand by the appearance and discovery of physical signs in the lung, or on the other by the result of lumbar puncture and finding of the meningococcus.

Typhoid fever is a diagnosis sometimes made in a case of cerebro-spinal meningitis, in which the early signs have not been well marked and which is passing into the chronic state. Case XXII., being admitted to Hospital after 4 weeks' illness, was thus diagnosed and treated, and the correct diagnosis was only fully established post-mortem. Widal's Test is an important deciding point, as also is the Diazo Reaction which is usually given in advanced cases of typhoid fever, and which we failed to find in any case of cerebro-spinal meningitis.

Influenza may occasion doubt by simulating a mild attack of meningitis, but in this case the absence of Kernig's sign and the negative result of lumbar puncture have both been found of the greatest value in eliminating this cause of fallacy.

It may be mentioned here that a precipito-reaction for cerebro-spinal meningitis has been devised by Vincent, and has of late been recommended by other writers, but its value does not seem to be greater than that of the agglutination method which is discussed above.

T R E A T M E N T.

The prophylactic treatment of epidemic cerebro-spinal meningitis, while not difficult as regards the individual, forms a serious problem for public health authorities during an epidemic. Compulsory notification is generally regarded as a necessity, so that the health authority may at the earliest possible moment be able to take steps to control contacts and surroundings.

In the Leith epidemic, Robertson not only made a thorough disinfection of the houses where cases occurred, and especially of their floors, mainly by the use of the formalin spray, but he isolated all the contacts for a short period and took this opportunity to disinfect their nasal and pharyngeal mucous membrane. In the case of the Leith epidemic, chlorine water was the disinfectant employed for the nasal douche and throat gargle, while in other localities peroxide of hydrogen, pyocyanase, and even normal saline solution have been used. Special attention was directed in this epidemic to the persons whom the writer's examination showed to be "carriers" and in all epidemics it is a valuable measure if possible to examine a swab from the nose of all suspects, and when a "carrier" is found to isolate him and subject him to special treatment by nasal douches and the like.

As regards curative treatment, the onset of the disease is so sudden, its course so severe, and the morbid anatomical lesions so extensive and so intense, that there does not seem at first sight much ground to

hope for usefulness in any curative method of treatment.

So far as the management and nursing of a case are concerned, the ordinary principles of expectant treatment must simply be followed. The diet should consist of nourishing fluids and semi-solids given at the outset in large quantity to counteract the wasting, which forms one of the main features in a late chronic case of this disease. Sedatives are a prime necessity to relieve the pain in the head, diminish the head retraction, and check the vomiting. Many persons recommend morphia for this purpose, but in the Leith cases it was found that chloral was far better tolerated and relieved the pressing symptoms excellently. Morphia was found to bring on coma in some patients, who previously had been progressing moderately well, and in any case its use was not followed by benefit to the pain beyond a short period immediately following its administration. Chloral, however, given in 5 grain doses at regular intervals was found to be most beneficial in allaying pain, quieting restlessness, and to some extent diminishing the rigidity and head retraction. Ice-bags, although their application to the head and spine has been recommended, were not found to be of much value in diminishing headache, and the cold seemed to be ill-borne by most patients and to increase the spasm of the neck and back muscles. On the other hand hot applications afforded great relief. The same thing has been the experience of various other writers, who have found that pain, spasm, and sleeplessness are all quieted by the

hot pack or hot bath. Ker goes further and recommends the routine treatment of cerebro-spinal fever patients by three baths daily in which the patient is immersed for twenty minutes in water as hot as can be borne. The result is some hours freedom from pain and often a quiet sleep.

The therapeutic value of the withdrawal of cerebro-spinal fluid by lumbar puncture has been already mentioned and the reasons have been discussed which sometimes prevent it from being of benefit. In the majority of cases, however, it is of considerable use in diminishing pain, rigidity, and spasm, especially when there is a considerable excess of fluid under pressure. The results of Flexner's experimental work on apes and his discovery that the meningococcus speedily dies and disintegrates in the presence of normal saline solution have led some to try irrigation of the spinal canal with this fluid, after lumbar puncture. This form of treatment, however, did not seem in the Leith cases any more than in those quoted by other writers to have any permanent effect on the course of the disease. The use of various antiseptics for direct attack upon the meningococcus in the spinal canal has also been suggested. In several cases observed by the writer, a one per cent. solution of lysol was employed in this way, but no benefit appeared to follow its use, and in at least one case, where death took place immediately after its injection, the fatal issue appeared to have been hastened. Collargol has also been recommended for the same pur-

pose, but with similar want of effect. In one case where the writer made a post mortem examination some three days after its use, the spinal cord was found to show in its entire length a brown deposit of silver which penetrated along the perivascular spaces deep into its substance. This certainly showed the widely diffusive power of the collargol, but made one doubt whether in the event of recovery from the disease such metallic deposits might not be harmful in other respects.

The most modern type of treatment is that by antimeningococcal Serum. Of such sera several have been introduced by Kolle, Jochmann, Ruppell, Dopter and others. As the writer's experience is confined to the use of Flexner's serum and as the most satisfactory statistics are available regarding its employment it alone will be shortly considered. As showing the fallacy liable to attend the use of novel modes of treatment it may be mentioned that Elder and Ievers in publishing details of three cases from the Leith epidemic declared that decided benefit had followed the injection of an anti-pneumococci serum, although these cases were found by the writer to be due to the meningococcus. It is fitting, therefore, that the evidence for the value of treatment by serum should be carefully weighed. There is a general consensus of opinion that the serum of Flexner and Jobling is possessed of powerful bactericidal and antitoxic action, and that its systematic use early in cases of this disease has been productive of a diminished death rate. The serum is injected at the present day directly into the spinal

canal, the cerebro-spinal fluid having previously been allowed to escape. About 30 c.c. of serum for an adult and 15 c.c. for an infant is the amount recommended; the injection is made slowly, the serum having been previously warmed to body temperature; and the serum replaces in part the fluid previously withdrawn. This procedure is repeated daily for three or four days. Generally the injection is followed by some relief of pain and lowering of temperature, but in a few patients the reverse is the experience. In a proportion of cases after several such injections the disease ends by a kind of crisis instead of the usual lysis. Flexner found that this result was brought about in between 25 and 30 per cent. of his cases and regarded it as a very favourable sign.

The general result from using this serum systematically is that the mortality of the disease is said to have fallen from the 70 or 80 per cent., which is the rule among cases treated without it, to about 30 per cent. It was found, for example, by Gardner Robb that in the Belfast epidemic this reduction occurred among cases treated by the serum, while in cases treated otherwise the old figure persisted. Dunn, Holt, Marsh and Williams, Ker, and others have published similar results. On the other hand, some writers such as Netter have entered protests against the use of serum. The question is obviously one upon which generalization from a few cases is quite unsafe and the most valuable and extensive statistics are those collected by Flexner. From these

it appears that among 712 cases treated by the serum and collected from over the United States there were 488 recoveries and 224 deaths, giving a mortality reduced to 31.4 per cent. The sole corrections made upon the results received by Flexner were that only those cases were included in which the diagnosis had been verified by bacteriological examination, and in which life had lasted for at least 24 hours after the injection of the serum. When these results are grouped into classes corresponding to the period of the illness at which injection took place, the value of early use of the serum is still more clearly brought out. Thus of patients injected between the first and third day of the disease, 180 recovered and 61 or 25.3 per cent. died. Of patients injected between the fourth and seventh days 179 recovered and 69 or 27.8 per cent. died. While among 129 patients who did not receive the serum till seven days or more had elapsed, 129 recovered and 94 or 42.1 per cent. died. Thus even after several days of illness the serum seems to possess decided power against the disease, though its beneficial action is specially exerted in the earliest stage.

C O N C L U S I O N S .

1. Epidemic Cerebro-Spinal Meningitis has occurred since it was first recognized over a century ago in a cyclic manner as a series of outbreaks, between which it is endemic in a sporadic form. (pp. 1-4 and p. 7).

2. The micrococcus first described by Weichselbaum in 1887 is the cause of most cases; though, in every epidemic, cases due to other organisms occur, e.g., cases due to the pneumococcus. The diplococcus intracellularis meningitidis is still found to correspond in the main to Weichselbaum's original description, though the writer, as well as many other observers, has met with divergences in staining reaction, size, and viability. (pp. 4-11).

3. The most satisfactory methods for the recognition of the organism were found by the writer to be (1) The power of rapid growth for a day on ascitic-fluid-agar at 37° C; and failure to grow at 20° C.; (2) The appearance of the Colonies to the unaided eye and through the lens; (3) The morphology of the organism; (4) Its behaviour towards Gram's stain; (5) The result of its growth upon glucose - and maltose - containing media. (pp. 12-16).

4. As the result of an original investigation, the writer found that the meningococcus is frequently present in the nose or naso-pharynx of persons who come in contact with but do not themselves suffer from the disease (pp. 17-20). This has been since corroborated by various other observers and is now generally accepted (pp. 21-23).

5. The path by which the organism enters the central nervous system from the naso-pharynx is still doubtful, Although there is evidence that in some cases it enters by the alimentary canal and first affects the cord, there is a stronger probability that in most cases it passes directly in through the roof of the nose and primarily sets up disease in the brain (pp.24-25; see also Conclusions 6 and 8 ).
6. As the result of an original histological investigation the writer has shown that the sphenoidal-cell mucous membrane presents catarrhal changes in 37 per cent. of all persons, thus rendering it permeable for the passage of organisms to the base of the brain. (pp. 26, 27a-27e). This supports conclusion 5.
7. In rodents the writer was able to produce meningitis by nasal infection, but it was shown that distribution took place through the blood-stream. (p. 28).
8. Post-mortem examination of 15 cases by the writer goes to support conclusion 5. (pp. 29-35).
9. Clinical observation of 25 cases gives the general characters of the Leith Epidemic; a tabular statement of the more important features is given on p. 36, a resume of cases on pp. 37-76, and a critique on pp. 77-88).
10. The case mortality of this disease was 72 per cent. in the Leith Epidemic (pp. 90, 91); and has been reduced where Flexner's serum has been used to about 30 per cent. (pp 97-99).
11. The other diseases from which diagnosis was dif-

ficult in the Leith Epidemic were tuberculous meningitis, pneumonia, and typhoid fever. (pp 91-93).

12. The most effective means of treatment are:-

(1) Prophylactic by nasal disinfection according to the above research; (2) Expectant by Chloral, hot baths, and lumbar puncture; and (3) Curative by Flexner and Jobling's Anti-meningococcic serum. (pp 94-99 ).

References.

- Albrecht und Ghon .. Wien. Klin. Wochenschr.  
1901. xiv. S. 984; Centralbl.  
f. Bakter. u. Parasitenkunde,  
Jena 1903. Ab. 1. XXXIII. S. 496.
- Bettencourt et Franca .. Zeitschr. f. Hyg. u. Infectionskr.  
Jena. 1904, x/vi. S. 463.
- Bochalli .. Zeitschr. f. Hyg. u. Infectionskr.  
1908. /xi. 454.
- Bonome .. Beitr. z. path. Anat. u. Phys.  
Jena 1890. Bd VIII. 377.
- Bordoni Uffreduzzi .. Centralbr. f. Hyg. u. Parasitenk.  
1890. viii. 188, 670.
- Bruns .. Klin. Jahrbuch Bd. 17.
- Carpenter .. Contractures following Epidemic  
Cerebro Spinal Meningitis. Arch.  
Pediatr. N.Y. 1908 xxv. 844.
- Castellani .. Lancet. London 1905 ii. 353.
- Cocher et Lemaire .. Arch. gén. de Méd. Paris 1902  
vii. 574, 667.
- Colin .. Berl. Klin. Wochenschr. 1909  
x/vi. 53.
- Comrie and Fraser .. Edinburgh Med. Jour. Nov. 1910.
- Cosmettatos .. Annal. d'ocul. Paris 1908 cxl. 276.
- Councilman, Mallory and Wright. Am. Jour. Med. Sci.

- 1898 . cxv . 251 .
- Dunham  
Dunn  
Elder and Tevers  
Faber  
Foa e Bordoni-Uffreduzzi  
Hepper  
Hepper and Barker  
Hepper and Tobling  
Fraser and Comrie  
Fowler  
Frons  
Gee and Barlow  
Ghon
- Tour. of Infectious Dis. Feb. 1906.  
Trans. Am. Pediatr. Soc. N. Y. 1908  
xx . 26 . ; Internat. Clin. 1908. iv 250.  
Med. Chir. Trans. Edin. 1907 xxvi 110.  
Zeitschr. f. Hyg. u. Infektionskr.  
1900 xxxiv 253 .
- Deut. Med. Wochenschr. 1886 xii 249  
Zeitschr. f. Hyg. 1888. iv. 67.  
Brit. Med. Jour. 1906. ii. 1023.  
Jour. Exper. Med. N. Y. 1907. ix. 105.  
do 1907 ix. 142 . Jour.  
Am. Med. Assoc. 30<sup>th</sup> Oct. 1909.  
Am. Jour. Med. Sci. cviii 1894.  
Trans. Assoc. Am. Physicians, Phil.  
1908. xxiii. 76.  
Scot. Med. and Surg. Jour.  
1907. xxi. 18.  
Review of Neur. and Psych.  
Edinburgh. 1907. p. 257.  
Wiener Klin. Wochenschr. 1907  
No. 15.  
St. Bartholomew's Hosp. Reports  
1878. xiv  
Wien. Kl. Wochenschr 1907. xx. 1277.

Ghon

Bericht über die XIV Internat.  
Kongr. für Hyg. u. Demographie  
in Berlin. II. 94.

Goodwin and von Sholley Jour. Infect. Dis. Chicago.

1906. No 2. p. 21.; Ann. Rep.  
Board of Health, City of New  
York 1906, II. 653.

Gordon

Report to the L.G.B. on the  
Micrococcus of Epidemic Cerebro  
Spinal Meningitis and its  
Identification. London Feb. 18. 1907.

Heubner

Deut. Med. Wochenschr. 1896.

XXII, 423; Jahrb. f. Kinderheilk.  
u. Phys. Erziehung 1896 XLIII, 1;  
and 1902 LVI, 359.

Hirsch

Handbuch der geog. u. histor.  
Path. Bd. III.

Holt

N.Y. State Jour. of Med. 1909. IX. 239.

Jaeger

Zeitschr. f. Hyg. u. Infektionskr.

1895. XIX. 351; Deut. Med.  
Wochenschr 1899. XXV. 472;

"Die Cerebrospinalmeningitis als  
Aereseuche". Berlin 1901; Med  
Klin. Wien. 1905. I. 990.

Tschle.

Wiener kl. Wochenschr. 1906. 25.

- Lehle Muench. med. wochenschr.  
 1906. No. 29; Wiener Klin.  
 wochenschr. 1907. No. 1..
- Toehmann Deut. med. wochenschr. 1906.  
<sup>ii</sup>  
 xxxii . 788.
- Ker "Infectious Diseases" 1909 London SIS.
- Kiefer Berl. klin. wochenschr 1896 xxxiii. 628.
- Kischensky Centralbl. f. allg. Path. u. Path.  
 Anat 1906 vii 401.
- Kister Centralbl. f. Bakter. u. Parasitenk  
 1896. Ab 1. xx. 148.
- Kob Charité Ann. Berlin. 1905 xix. 252.
- Kollé u. Wassermann Klin. Jahrbuch. 1906 xv. 507.
- Koplik System of Medicine by Osler  
 and McCrae. Vol II London  
 1907, p. 496; and p. 524.
- Leperre Jour. de Physiol. et de path.  
 gén. Paris 1903, v. 527.
- Liebermeister Muench. med. wochenschr.  
 1909. Ivi. 914.
- von Lingelsheim Klin. Jahrbuch 1906. xv 373.
- von Lingelsheim u. Leuchs Klin. Jahrbuch. 1906 xv. 489.
- Macdonald Rev. of Neur and Psych. 1907  
 593, 686.
- Marsh and Williams Liverpool Med. Chir. Jour 1909  
 xxxix. 270.

Netter

Archiv. gén. de médecine 1887  
clx. 28. Archiv. de  
méd. expérimentale 1890. ii  
Bull. et Memoires Soc. Méd.  
des hôp. de Paris 1909. 3s. xxvi  
1013 and 1909 3s. xxviii.

Robertson

Brit. Med. Jour. July 27. 1907.

Robb, G.

Pub. Res. Def. Soc. London 1909. 168.

Schottmüller

Muench. med. Wochenschr. 1905.  
Bd. liii. 1617.

Schwalbe, Kay and Petrus. Quoted by Poirer on the  
Lymphatics, tr. of C. H. Lees.  
London Constable 1903.

Selter

Klin. Jahrbuch. Jena 1908-09. xx. 469.

Still

Jour. Path. and Bact. 1898. v. 147.

Shennan and Ritchie Jour. Path. and Bact. April 1908.  
456.

Symmers and Wilson Brit. Med. Jour. 1907. i. 1477.

Thomson, L.

Journal of Preventive Medicine  
1909. xvii. 75.

Vansteenberghe et Jory. Ann. de l'Inst. Pasteur.  
Paris. 1906. xx. 69.

Vincent

Bull. Acad. de Méd. Paris 3s.  
1909. lxi. 326. ; and Bull.  
et mem Soc. Méd. des Hôp. de

Paris, 1909. 3s. XXVI. 1229.

Vincent et Bellot Bull. et mémoires Soc. méd. des  
Hôp. de Paris. 1909. 3s. XXVIII. 1824.

Weichselbaum Fortschritte der Med., Berlin  
1887. V. 573, 620.; Wien.  
Klin. Wochenschr., 1888. I  
573, 595, 620, 659.; Centralbl.  
f. Bakter. u. Parasitenk.

1903, Ab. I. XXXIII. 570.

Weyl

Jahrb. f. Kinderh. u. phys.

Erziehung. Berl. 1905. Ixi. 385.