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L U M B A R P U N C T U R E

Its Present Position; with Special Reference
to the Results of its Performance
in Children.

Being a Thesis for the Degree of M.D.,
University of Edinburgh.

by

G. STIRLING LANDON,

M.B., Ch.B.

April, 1909.



LUMBAR PUNCTURE.

Its Present Position; with Special Reference
to the Results of its Performance
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The following remarks are based partly upon an experience of lumbar puncture in some 50 cases of meningitis and allied conditions, with other cases of hydrocephalus, meningism and acute anterior poliomyelitis, occurring during a six months' appointment as House Physician at the Queen's Hospital for Children, London: also upon references to the subject of lumbar puncture in the literature.

With reference to the above cases, I am responsible for the examination of the fluids and for most of the post-mortem reports, as well as for such clinical notes as may be included.

INTRODUCTION.

To Quincke of Kiel is generally attributed the first publication of the results of puncture of the spinal membranes for the removal of cerebro-spinal fluid which he performed in 1890, for the relief of hydrocephalus, his monograph on the subject appearing the next year. But Essex Wynter of London published his results of lumbar puncture performed for the relief of pressure, in the Lancet in 1890.

Though failing in the object for which it was introduced, it has since proved of immense value in diagnosis, largely due to the numerous observations of Widal, Sicard, Ravant, Babinski, Furbinger, Stadelmann and others. Osler says "during the past ten years no single measure of greater value in diagnosis has been introduced."

Therapeutically it has been used to relieve intra-cranial pressure by single or repeated tapping, and even by continuous drainage (Quincke). In septic conditions the removal of bacteria or their toxins is said to be of benefit, in addition to relieving co-existing intra-cranial pressure. It is also performed preparatory to the injection of serums, drugs or analgesic solutions into the spinal canal.

It is, however, in diagnosis that it is of most value. The pressure, amount, naked eye appearances of the fluid; its chemistry, including alterations in albumin, sugar, choline, urea and salts; its physical changes, as its freezing point, specific gravity and even electrical conductivity; while of most importance probably are its cytology, both cell-content and cell-type, and bacteriology, with which are associated its toxicity and opsonic and agglutinative properties. Some of these are hardly within the scope of ordinary clinical investigation or application.

ANATOMY AND PHYSIOLOGY OF THE CEREBROSPINAL FLUID.

There is but one serous cavity in the body which in the normal state contains a considerable amount of fluid - the cerebro-spinal cavity. The central nervous system is surrounded by this fluid - the cerebro-spinal fluid. The dura in the skull is closely attached to the bone; while in the vertebral canal it forms a hollow tube separated from the bone by the periosteum and connective tissue, in which lie the extradural venous plexuses. In the skull, the dura and arachnoid are separated by the subdural space: in the cord they are practically adherent. Though very rarely, subdural pus in the cranial cavity has gravitated down the spinal canal separating the dura and arachnoid.(Quincke).

Subdural serous effusions apparently do not occur. Secretion into the ventricles and subarachnoid spaces predominates, hence the arachnoid becomes tense and separates from the pia and is pushed against the dura. Thus in lumbar puncture the needle on piercing the dura enters the subarachnoid space. The delicate pia-arachnoid covering the brain and spinal cord is composed of two membranes (leptomeninges) united by a loose connective tissue forming an open meshwork - the subarachnoid spaces - being more loose and roomy in the sulci than on the convolutions.

The greater part of the cerebro-spinal fluid is found in these subarachnoid spaces: "the physiologic, water-seeking, connective tissue" (Henle), whose meshes in brain and spinal cord freely communicate with each other. In certain places, as on the under surface of the brain, the subarachnoid spaces are especially large and loosely attached, forming the "cisternae", where pathological accumulations of fluid are especially liable to collect.

The cerebro-spinal cavity consists of firm tissue, forming the central nervous system; blood; and cerebro-spinal fluid. The two latter are most liable to alteration. The cerebro-spinal fluid serves mainly as compensation for the other two, and adapts itself to variations in volume of the other two. When this is decreased it increases as meningeal oedema or ventricular dropsy (hydrops ex vacuo): less common is its decrease in neoplasms, etc. Here the presence of a tumour, or even of blood clot, seems to set up increased secretion: the tumour also may, by pressure on the outlets, impede the escape of the fluid; or by pressure on the veins of Galen cause increased venous transudation. Secreted chiefly from the ependyma covering the choroid plexuses in the ventricles, also from the epithelium lining the central canal of the cord and receiving matter from the

lymphatics of the central nervous system and transudation from the blood capillaries, the cerebro-spinal fluid passes along the ventricles and through the foramina of Key & Retzius and of Majendie, into the subarachnoid spaces, and along the veins of Galen and into the spinal canal.

From the subarachnoid spaces it emerges by the villi of the arachnoid to the venous sinuses and along the subdural space and sheath of the dura, along the issuing nerve roots and through the ethmoid to the nasal mucous membrane (Flexner).

The pressure in the cerebro-spinal cavity depends upon the mass of tissue (central nervous system + pathologic products); upon blood pressure; and upon the amount of cerebro-spinal fluid present. By their combined action pressure is exerted on the cerebro-spinal cavity, so that its walls are distended and elastic: this we may call "elastic pressure". Owing to the free intercommunication of the subarachnoid spaces, this pressure is equal throughout the cerebro-spinal cavity; so increased pressure in the skull is transmitted after a time to the spinal sac.

In man the only place we can estimate this pressure is in the lumbar portion of the spinal sac. The pressure in this region is affected by the

position of the patient, whether horizontal or upright; so that in the latter position, to the "elastic" pressure we must add hydrostatic pressure; the sum of which gives the pressure of the cerebro-spinal fluid, which is greater, therefore, in the upright than in the horizontal position. The spinal cord ends in the adult at the top of the 2nd lumbar vertebra: in children, at the top of the 3rd lumbar vertebra up to the end of the first year: at the level of the 2nd lumbar vertebra by the end of the third year; but once in a child of four years, at the level of the 4th lumbar vertebra (Quincke). From the level of the 2nd lumbar vertebra down to the level of the 2nd or 3rd sacral vertebra we have the arachnoid sac containing only the roots of the cauda equina bathed in the cerebro-spinal fluid.

We have, therefore, a cul-de-sac, which we can tap with a needle without injuring any vital structure. It is reached through the spaces between the laminae of the vertebrae.

THE SITE OF THE PUNCTURE:

There is some difference of opinion as to which is the best space to enter by. Quincke advises the third space, but says the 4th and 5th, and in adults the 2nd space, may also be used; and that with re-

peated punctures it is advisable to vary the point of insertion. Purves Stewart prefers the 4th space. D'Este Emery prefers the third space. Sahli and Kronig think sometimes the space between the 5th lumbar and 1st sacrae vertebra should be chosen, this being the lowest point and cells tend to gravitate to the lowest part of the conical sac. To identify the 4th lumbar vertebra, draw a line connecting the highest points of the iliac crests, and it will cut the tip of the 4th vertebral spine.

I have found in children the third, fourth and fifth spaces can be used quite well, differing in different cases: sometimes one gets no fluid or only a little blood-stained fluid, when copious fluid may escape from the one above or below. This is sometimes due to the theca being pushed in front of the needle.

METHOD OF PERFORMING LUMBAR PUNCTURE:

The actual method of performing lumbar puncture varies slightly, with different workers. Some prefer the patient in the sitting posture, the head low between the knees and the spine thus strongly curved. This is convenient in cases of tabes, or general paralysis, where the operation is only for diagnostic purposes and only a small quantity of fluid is

removed. In children and in those who are ill, the horizontal position, lying at the edge of the bed with head and knees as nearly approximated as possible, is probably more appropriate. Most authorities say the patient should lie on the left side. I have found the right side quite as convenient in children. Whatever the position, the patient should lie down for 24 to 48 hours after the operation to avoid unpleasant symptoms, apt otherwise to follow, such as headache, giddiness or vomiting.

But I understand lumbar puncture is performed in the out-patient Department at Westminster Hospital as a routine diagnosis for tabes and general paralysis, and syphilis of the central nervous system.

The patient being in position, one may use a local or general anaesthetic. Some recommend Ethyl Chloride locally, but this renders the insertion of the needle more difficult from its hardening of the skin, while the after thawing is probably as painful as the needle would be without it. I think either a general anaesthetic should be used or none at all in bad cases, as meningitis; while in other cases, holding a piece of ice in antiseptic gauze pressed against the skin will, as a rule, sufficiently deaden sensation, without hardening the skin. Small children can be held while the needle is

inserted, when as a rule they remain quiet, but in adults and bigger children there is a risk of their struggling and, in straightening the spine, of breaking the needle.

The needle should be of small calibre to prevent too rapid escape of the fluid. Platinum iridium needles are an advantage in that they can be sterilized in a flame and are not likely to break. But I have found that when the operation is often done, it is difficult to keep the point of the needle sharp, and it may be rendered temporarily useless by blunting it against the bone if misdirected. Various authorities mention special needles and various lengths. The depth to be traversed by the needle before fluid is reached, varies from two to four cm. in children to four to seven cm. or even up to ten cm. in adults (Quincke, Heiman, etc.). Purves Stewart recommends a needle about three inches in length. Heiman uses Quincke's needle with a movable guard which he can set at will to prevent the needle piercing to a greater depth than desired; this prevents wounding the dura on the far side of the spinal canal. The needle should be fitted with a stilette to prevent blocking of its lumen. Emery uses a curved needle bearing a socket into which a handle fits to facilitate its insertion.

The skin having been prepared and the needle and tubes sterilized - preferably by dry heat - the needle is inserted as follows: Having chosen the interspace - usually the 3rd or 4th - the needle is pushed straight in, about half an inch below and to one side of the tip of the 3rd or 4th lumbar spine; when deep in the tissues incline the point slightly up and inward, when it should pass between the laminae. Here we meet the tough ligamentum subflavum and when through that it is in the spinal canal. I have only seen Quincke mention the point of inserting the needle deeply before slanting it, and I am sure it is a practical point; for otherwise one may run along the outside of the laminae for quite a distance, vainly waiting for the resistance offered by the ligamentum subflavum - which is an important "landmark". Quincke recommends, where possible, to enter in the median line immediately below the spine of the vertebra above; since they overlap in the adult, this can only be possible if the spine is well curved: in children this is quite a feasible route, in fact, in them the needle usually enters without difficulty. Having entered the canal and pierced the theca fluid should appear. It may not, because the theca has been pushed before, and not pierced by, the needle. I have found sometimes if the needle be twisted round

on its own axis something seems to give way and the fluid appear; otherwise one must explore another interspace - endeavouring to reach the theca in the median line. The needle may become blocked by blood clot or tissue encountered en route or by flocculi in purulent fluid - these may be cleared by using the stilette, or it may be kept in the needle during insertion.

Instead of fluid, blood may appear - usually from wounding the venous plexus lying external to the dura: this may only be very transitory, though it contaminates the needle and the specimen of fluid. If profuse, it is better to clean the needle and try another space.

I have found very slight and only momentary suction with a sterile syringe will sometimes clear the needle of blood and allow clear fluid to pass.

Otherwise a syringe should not be used: all observers seem to be agreed that suction should be avoided. On the appearance of fluid, the first few drops should be allowed to escape, lest it be contaminated by blood or other matter which has entered the needle en route. Then it should be collected directly into previously sterilised centrifuge tubes and some be allowed to fall directly into the culture medium. These tubes should then be covered

with sterile rubber caps and examined as soon as possible.

Owing, however, to the danger involved in unduly diminishing the intracranial pressure, by too great or too rapid a removal of fluid, many observers use a manometer attached to the needle.

Sahli uses a mercury manometer. Quincke and at the John Hopkins Hospital (Peyton Rous) the pressure is measured in terms of the height of the fluid itself. When the fluid appears the manometer is attached. This consists of a thick glass tubing of fine bore (1.5 to 2 mm.); some 10 to 15 cm. long, attached to rubber tubing of fine bore and 20 to 40 cm. long. This tubing is attached to the needle by a conical metal cap fitting into the needle, as does the end of a syringe. The fluid enters the tube and the glass tube is held vertical till the column of fluid is stationary - the patient being relaxed and quiet - this is measured off along a straight rule. This height measured from the point of insertion is noted, then the tube lowered and the fluid allowed to run out. By raising the tube from time to time we can estimate the alteration in pressure.

Quincke gives the range of normal pressure as between 40 and 130 mm. water, which is about same

for spinal fluid whose specific gravity is low (1.007 - 1.010), and states that the pressure should not be allowed to fall below normal - i.e. it must equal 100 mm. of water: others give 50 mm. as the limit. The zero of the scale should be at the level of the point of insertion of the needle.

Peyton Rous says only gross differences in pressure are of any significance and with the above manometer gives the normal range at between 50 and 300 mm. of the fluid. For diagnostic purposes it is only necessary to remove about 1 to $1\frac{1}{2}$ drachms of the fluid. Kronig uses his own modification of Quincke's manometer using capillary tubes by which he can measure the pressure with escape of less fluid than is required with Quincke's instrument. After the operation, the needle being removed, firm pressure should be applied while a collodion dressing is applied and the patient should then keep his bed for 24 to 48 hours.

Of course if the patient be tapped in the upright position we have hydrostatic added to elastic pressure and in obtaining fluid post mortem it is better to have the spine vertical and even to use a syringe. But unless performed immediately after death, such investigations are not of much value: terminal infections are apt to vitiate the results, and organisms tend rapidly to die out in the spinal cord.

DANGERS OF LUMBAR PUNCTURE AND PRECAUTIONS:

It is often stated that lumbar puncture can be done without risk; there have, however, been several fatal results reported. I have performed the operation a good many times in children, in various conditions, and have seen no bad results, even when a large amount of fluid has been removed; except perhaps in so-called "hydrocephaloid" cases, occurring in diarrhoea, where the loss of even a small amount of fluid seems to aggravate rather than to relieve.

The chief source of danger is in a too rapid reduction of intracranial pressure, or in reducing it below normal.

These may be prevented by using a manometer, and not allowing the pressure to fall rapidly, or below normal, and by not withdrawing too much at a time. There are some special precautions necessary. A comparison of the amount evacuated and the corresponding fall in pressure is important, for if a rapid or marked fall occur with a loss of only a very little fluid, it points to insufficient communication between the cranial and spinal cavities, so that we are merely draining the spinal canal. We may also suspect this when with repeated punctures we get marked differences of pressure, without amelioration of the other signs or symptoms.

Withdrawal of fluid under these circumstances may be followed by complete occlusion of the foramen magnum by the brain itself which is pushed down by intra-cranial pressure, so that the "tonsils are seen at either side of the medulla, where with the neighbouring convolutions of the cerebellum, which are elongated and in shape more or less like a cone, they occlude the foramen magnum like a conical plug" (Quincke).

I have seen such a case in post-basilar meningitis with hydrocephalus: the last attempt at lumbar puncture was a failure, and at the post-mortem I noted the adhesions round the foramen magnum and that the brain seemed to be pushed down into the foramen as described above. I did not see Quincke's description till later. He calls it "automatic closure" by the brain itself. Such an occlusion, if sudden, is apt to be followed by collapse and death from allowing pressure on the medulla.

A similar catastrophe may follow removal of only a little fluid in tumours below the tentorium, as in tumours of the cerebellum and even of the occipital lobe (Schlesinger, Cushing). Therefore, if a tumour of the posterior cavity be suspected, lumbar puncture should be cautiously performed, and if the pressure fall rapidly this should confirm the diagnosis.

A rapid or marked diminution of intracranial pressure may be the cause of haemorrhage into a tumour, as in Schlesinger's case, where fatal haemorrhage occurred into a glioma; or it may lead to rupture of some vessel weakened by atheromatous or other changes; or may cause rupture of a thin-walled cerebral abscess; or lead to the diffusion of an otherwise localised septic meningitis (Stadelmann).

Haemorrhage is generally from the extradural venous plexus and does not appear to be harmful; but Woolff records a case where haemorrhage was copious and was followed by symptoms of irritation of the cord - pain in back and later in chest, neck and head, lasting several days, from which he concluded the haemorrhage was from an intradural vessel. Gumprecht records a similar case causing pressure symptoms from blood clot in the spinal canal. Such symptoms might possibly result from pushing the needle too far and wounding the anterior venous plexus.

Herpes of the buttock has been recorded as following after ordinary lumbar puncture, the fluid being normal at the operation (Achard). It is said the needle may penetrate between the bodies of the vertebrae and so wound the vena cava (Peyton Rous).

I have seen the needle penetrate for a considerable portion of its length, but this has been because it has run up outside the vertebrae.

Pain in the leg, sharp and shooting down, may be experienced at the time, when no general anaesthetic is used: this is due to the needle touching one of the roots of the cauda equina and is of no importance.

I have drawn attention to the advisability of the recumbent position being maintained after the operation, to avoid unpleasant symptoms which may follow. Headache or giddiness is sometimes severe - generally after the removal of a considerable amount of fluid. The amount of fluid to be withdrawn at a time varies with the individual case, the pressure and its alteration and other symptoms, and not upon the quantity discharged. It might seem that the more the fluid spurts the more it should be drained, but this is not true, though in subacute and chronic cases of meningitis and in acute serous meningitis a good deal can be withdrawn with advantage. But "draining to the full in meningitis" is not safe (Peyton Rous).

As mentioned above, the pressure should be watched from time to time as the chief danger lies in its too rapid reduction. Special care must also

be observed in the case of tumours and cerebral abscess in only withdrawing a little at a time.

Babinski & Chailous, in recording a series of cases in which lumbar puncture was performed for relief of optic neuritis, recommend gradual evacuation drop by drop, not more than 8 - 10 cc. at a time and say "the amount removed should be in inverse proportion to the severity of the symptoms of compression".

Buchanan in recommending repeated lumbar puncture in tubercular meningitis says not more than 20 cc. to be withdrawn at a time.

Canby Robinson mentions removing 3 to 60 cc. with an average of 19 cc. in 19 cases of tubercular meningitis, and an average of 19.5 cc. in 20 cases of epidemic cerebro-spinal meningitis.

Several speakers, at a discussion in Paris on the role of lumbar puncture in injuries to the skull, testified to its value diagnostically and therapeutically, and all insisted on only a small amount being removed at a time, lest the bulb be exposed to pressure. Several writers have apparently allowed - in meningitis - the fluid to escape till it begins to drop.

This, I am afraid, was often my rule in many of my cases of meningitis, of which I had about 45

cases of various kinds. In one case of Posterior basic meningitis of about eight weeks' history, my predecessor removed $2\frac{1}{4}$ oz. and I, nine days later, evacuated $2\frac{1}{2}$ oz. "with immediate but only temporary relief". In some cases of acute anterior poliomyelitis, meningism, and even in a case of possible concealed hydrocephalus, seven or eight years after meningitis, I have removed quite three drachms without any ill effect and generally with apparent relief; and quite 4 oz. from a case of chronic hydrocephalus. Buzzard and Batten apparently do not apprehend danger from lumbar puncture in meningitis.

Continued Lumbar Drainage:

Quincke has tried continuous drainage from the lumbar sac in cases of persistently recurring high pressure, allowing the fluid to dissipate into the surrounding tissues. For this purpose he uses a special lancet with which he slits up the dura; pressure of the escaping fluid soon stops the haemorrhage. He says he has never seen serious consequences from this method and that drainage may continue for several days, sometimes an oedematous swelling forming over the site of the puncture. Once I unintentionally obtained a continuous drainage in a case of tubercular meningitis in an infant

a boggy swelling forming for a day or two over the site of puncture, but it did not seem to affect the case.

Quincke also quotes Lenhartz & Sahli as obtaining continuous drainage by means of a needle or canula left in the canal, but objects because it cannot be long continued from risk of infection and difficulty of retaining the instrument in position.

It would seem advisable in most cases to use a needle of fine calibre to ensure gradual evacuation, for danger lies apparently in its too rapid withdrawal. If using a manometer the rate of flow can be readily adjusted by raising or lowering the glass tube. More care is called for in acute than chronic cases, for "in acute cases there is moderate increase of pressure with severe symptoms, while in chronic cases markedly increased pressure with slight pressure symptoms". In chronic cases I have found it safe to let the fluid escape till it reaches its normal rate - that is, until it begins to drop instead of running. I have never been able to determine what influence free removal has upon re-accumulation, as it must take some time for equilibrium to be reached, between the fluid left in the cranial cavity after lumbar puncture and its subsequent dissipation throughout the cerebro-spinal

cavity. It is often not advisable to empty an over-distended secreting sac lest it be stimulated to over-secretion, and this may be equally true in the case of cerebro-spinal fluid.

It is, however, in cases of tumour that most care is necessary, lest rapid diminution of pressure occur, followed by pressure on the medulla, or giving way of a weakened vessel in it, or in its vicinity, and in abscess lest having a thin wall it burst and so set up a septic meningitis.

Having obtained the fluid, its examination should follow as soon as possible, for the cells undergo changes and become difficult to identify (Peyton Rous); the organisms increase and may be affected by contamination, or may die out.

THE COLLECTION OF THE FLUID FOR EXAMINATION:

The technique I have adopted has been as follows: The needles centrifuge tubes and rubber caps I have boiled myself; the centrifuge tubes should be sterilized preferably by dry heat, as if boiled in ordinary water crystals may collect, deposited from the water, which interfere with microscopic examination. To obviate this I boiled the tubes with a plug of sterilized wool in the end. The fluid was caught directly in the tubes, one being allowed to

stand lest a coagulum should form, the other being centrifuged for five, or ten, or twenty minutes - less if evidently purulent - the clear fluid kept to examine for sugar and albumin; the deposit - often invisible to the naked eye - removed with a sterilized capillary pipette and spread on a slide and allowed to dry; or if a culture was required, a sterile looped platinum wire was used to collect the deposit, the remainder being collected and spread on slides. Sterilized rubber caps were kept on the tubes before, during and after centrifuging.

As a rule the cultures were taken and slides made soon, often directly, after being collected; if delayed the fluid was kept at or slightly below body temperature.

THE CEREBRO-SPINAL FLUID.

Normal cerebro-spinal fluid is clear, transparent, of low specific gravity (1007-1010), slightly alkaline, containing some salts, e.g. chlorides, a trace of serum-globulin and albumose; no albumin or fibrinogen. Trace of choline; - a reducing agent

supposed to be a sugar - "reducing Fehling's solution and depositing glucosazone crystals" (P. Stewart). No cells beyond an occasional lymphocyte and endothelial cell - no polymorph leucocytes, and sterile.

The above is based upon Halliburton's description and other authorities apparently agree in their findings. Some find no cells at all in normal fluid. Changes may be found affecting its chemical properties, affecting the proteid content, sugar, choline, urea and chlorides: alteration in its physical properties - its freezing point and specific gravity: the amount, pressure and naked eye appearances: its cytology, both of cell-content and cell-type: its bacteriology, opsonic and agglutinative powers.

The pressure of the cerebro-spinal fluid depends upon the elastic pressure described above, and, if not in the horizontal position, the hydrostatic pressure must be added. The pressure exerted by the cerebro-spinal fluid depends on its amount, which is influenced by the rate of secretion and the patency of its outlets; both of which factors are centred principally in the cranial cavity.

Causes of increased intracranial pressure:

High intracranial - and usually lumbar - pressure may be due to Increase in amount of tissue present - as tumours: inflammatory swelling: effusions of blood or blood clot; serous or purulent exudates which may be of inflammatory origin, or secondary to the inflammation: or irritation set up by the pressure of tumours, blood clot or depressed fractures: or increased transudation from pressure on veins of Galen: or blocking of outlets by pressure of tumours or of the fluid itself: or by adhesions: or by blocking of the foramen magnum by pushing down of the brain which sets up a vicious circle, for the outlet is stopped, and the increased pressure causes increased secretion.

Lumbar pressure is generally in proportion to the clinical symptom of brain pressure provided the communication between brain and spinal cord is patent. "Generally in acute diseases there is moderate increase in pressure with severe clinical symptoms; in chronic diseases markedly increased pressure may exist, with slight pressure symptoms: and in the latter there is also frequently a gradual compensation of the brain" (Quincke).

Causes of low lumbar pressure:

Low lumbar pressure with an existing high intracranial pressure undoubtedly occurs. After eliminating blocking of needle and not entering the canal, it may be due to closure of the communication between brain and cord, by adhesions or pushing down of the brain into the foramen magnum, or to the pressure of very little fluid, the presence of a tumour accounting for the pressure symptoms. With all those we may obtain very scanty fluid - only what is contained in the spinal canal, accompanied by a rapid diminution in the lumbar pressure without relieving the cranial pressure, which now may allow pressure on the medulla and death. It is said that if a tumour of the posterior cranial fossa be suspected, it is confirmed if on lumbar puncture we find a very rapid fall in pressure, or when with repeated tappings the pressure shows marked differences in height, the cerebral symptoms remaining the same (Quincke). For these cases trephining or puncture of the brain is indicated.

Clinical estimation of state of pressure:

The pressure of the fluid may be measured with a manometer, but many observers (Buzzard, Emery, etc) apparently are content to judge by experience, being guided by its rate of flow from the needle. Normally this should be drop by drop, but is increased by crying, coughing or straining. Eve claims to have proved by means of his apparatus for measuring the pressure that the rate of flow is not a true gauge of the state of the pressure. This is especially true of the first few drops. The viscosity may also affect the rate of flow, especially with a fine bore needle. There may be all stages from the normal rate of dropping to a vigorous spurting.

Peyton Rous holds that "only gross differences of pressure are of much significance."

Relation of increased pressure to increased amount of fluid.

The increase of pressure is roughly proportioned to the amount of fluid; with high pressure the fluid is usually increased, but not necessarily so, as in some tumours. There may be intense hydrocephalus and yet scanty flow of fluid at low pressure, especially when the communication between brain and spinal cord is not free.

Both pressure and amount are usually increased in the same conditions - tumours, meningitis, inflammatory conditions causing increased secretion of fluid, hydrocephalus whether congenital or post-meningitis, uremia or angio-neurotic hydrocephalus (Quincke), while fluid may be increased without rise of pressure in the hydrocephaloid state, seen in infantile diarrhoea, and in hydrops ex vacuo where the cerebro-spinal fluid increases to compensate for diminution in brain substance (Osler).

Conditions in which amount of fluid is increased:

In an analysis of 32 cases of meningitis in which the diagnosis was beyond doubt, I found the amount of lumbar fluid increased in 18; in five out of 16 cases of tubercular meningitis; in seven out of eight cases of septic meningitis; in six out of eight cases of post-basilar meningitis. On three occasions only a few drops were obtained, while the brain was found enormously distended; in one case, after twice failing to obtain more than a few drops of fluid, I tapped the lateral ventricle through the anterior fontanelle and removed a large quantity of fluid. I do not think any of these "dry taps" were due to failure to enter the spinal theca. Some were undoubtedly due to adhesions at the base; and

one case was due to adhesions and the "automatic closure" of the foramen magnum by the soft brain, which was pushed into it like a plug.

In the same 32 cases of meningitis pressure was noted as increased in 17; in seven out of 16 cases of tubercular meningitis; in five out of eight of septic cases, and in five out of eight cases of post-basic meningitis. But these are somewhat arbitrary findings. Sometimes it begins with a rush and continues in a steady stream for a considerable time; in others it nearly stops, increasing with a slight movement of the needle, while it may begin gently and increase, or run reluctantly for a considerable time, yet being more than normal. In several cases of meningism, or that pseudo-meningitic condition, not infrequently seen in children at the onset of acute illness - especially pneumonia and the specific fevers - I have seen the fluid at fairly high-pressure and certainly increased. And of four cases of acute anterior poliomyelitis, the lumbar fluid spurted in one was increased in another and normal or very slightly increased in the other two.

The most marked increase in pressure and in amount I have found has been in post-basic and in serous meningitis, but in these the fluid is often clear and watery and so flows readily through the needle.

Naked eye appearances:

The fluid normally is clear like water; it may, however, be opalescent, turbid - either white or yellowish - or so thick as to deposit a thick layer of pus cells. It may be stained with blood giving it a yellowish to a bright red colour; or it may be tinged yellow in jaundice.

It may be quite clear even when held up and looked through and yet contain leucocytes; generally turbidity is due to the presence of leucocytes, from a faint opalescence with a slight lymphocytosis, to a thick yellow due to a purulent meningitis, with copious polymorph cells. As a rule, on standing, a clear or almost clear fluid remains clear or shows a slight deposit at the bottom of the tube after a long time: but in tubercular meningitis generally, a fine cobweb-like coagulum forms, floating lightly in the fluid and apparently suspended from the top. Canby Robinson, in 12 out of 19 cases of tubercular meningitis, found the fluid almost quite clear with a slight opalescence and in it this fine cobweb-like coagulum. In a case of acute poliomyelitis in which there was marked lymphocytosis, I obtained a fine coagulum differing from the true tubercular coagulum in adhering to the sides of the tube. The coagulum in septic meningitis also adheres to the

sides of the tubes in flakes, rather than in a veil-like piece; these are quite different when one attempts to tease them out on a slide; the tubercular coagulum is elastic and pliable; the others break up into little pieces, and are quite different under the microscope - being opaque and granular. I have found this coagulum in every case of tubercular meningitis, since I heard of its importance, and in every case have found tubercle bacilli in it, that is, in 10 successive cases. Of the 32 cases of meningitis, the fluid was clear in five and turbid in 27; in the tubercular cases clear in two, turbid in 14. If not absolutely clear, like water, I have called it turbid. Some of these were just opalescent. Of eight septic cases one was clear and two others gave clear fluid until the final tapping: seven gave turbid fluid, two of these being turbid only in the final tapping. Of eight post-basic cases two were clear and six turbid effusions. Two post-basic cases gave an almost clear, transparent, syrupy fluid of a deep yellow colour - with a few leucocytes: this was very scanty and difficult to obtain, and as there was marked distension of the brain present, I concluded the connection between brain and cord was blocked, and that the cellular elements had been disintegrated. In my cases of "meningism" the fluid was clear: in serous

meningitis it is clear, as in two of my cases: in hydrocephalus clear as a rule - but this depends on how long after the acute inflammatory condition from which it arose, and on the presence or absence of leucocytosis: in one of my cases it was clear on most occasions, but a fine, almost glistening turbidity was present on two occasions, when I found some cells which would not stain, were of no definite form and seemed devoid of structure; as if they were the "ghost" forms of some degenerated cells. In 47 cases of tubercular meningitis Forbes found the "fluid clear in most cases". The presence of blood entirely alters the appearance. Here we must, when possible, distinguish between recent haemorrhage due to the operation and blood or blood-pigment which was present in the fluid before.

Significance of the presence of blood in lumbar puncture:

Blood in lumbar puncture may be due to the needle injuring the extra dural plexus, in which case it will be dark, copious and coagulate quickly; or it may be copious at first and then rapidly be diluted by the escaping spinal fluid, or it may only be sufficient to tinge the fluid.

Blood may also be due to previously existing

cerebral or spinal haemorrhage: this may be due to trauma as when complicating a fractured skull, or rupture of a vessel. If the haemorrhage be outside the arachnoid, then blood cells will not be found in the lumbar fluid: if the haemorrhage be into the subarachnoid space or if the arachnoid be injured along with a subdural haemorrhage, or if it be into the ventricles, then blood cells may be found, if quite recent; otherwise only the haemoglobin and perhaps debris of the red corpuscles will be found.

An extradural or subdural haemorrhage may also result in a yellowish red lumbar fluid due to diffusion of haemoglobin pigment (Quincke).

In the case of a recent subarachnoid haemorrhage or spinal haemorrhage due to the operation of lumbar puncture the red cells should sink to the bottom on centrifuging, leaving the clear, supernatant spinal fluid. If, however, the haemorrhage be two days old the supernatant fluid will be yellow, owing to laking of the corpuscles and diffusion of the pigment (Emery): in such cases, the haemoglobin derivatives may be recognised with the spectroscope (Peyton Rous). In the case of a recent haemorrhage complicating meningitis (tuberculous) the spinal fluid may be uniformly red, and on standing a clot form containing a mixture of red cells and leucocytes,

with a yellowish fluid above; whereas in simple subarachnoid haemorrhage the spinal fluid does not tend to coagulate, and only contains such white cells as are due to the haemorrhage (Warrington). So that if the spinal fluid show blood contamination which persists in spite of moving the needle, or changing to the space above, it may be due to haemorrhage complicating a meningitis, when it will coagulate on standing, having a yellowish fluid above, and a coagulum containing blood cells and leucocytes due to the meningitis. It may be due to a subarachnoid haemorrhage, when, if recent, the red cells will sink on centrifuging leaving a clear fluid; or, if two days old, will give the debris of red cells and fluid tinged with pigment.

An extradural (rarely) or subdural haemorrhage may also tinge the spinal fluid by diffusion of pigment, but no red cells will be present. Hence blood in the spinal fluid may help to distinguish between cerebral haemorrhage and thrombosis, as in the latter the fluid will be normal, or between coma of various kinds and cerebral haemorrhage due to rupture of a vessel or fractured skull, etc. (P. Stewart, Quincke, Chauffard, Emery, etc.). In the case of cerebral injuries lumbar puncture sometimes affords relief.

In my experience small contaminations by blood are frequent and often not discernible by the naked eye. In one case there was extensive haemorrhage into the ventricles and two small haemorrhages into the substance of the brain in the course of a meningitis. The first tapping was quite clear, and contained some pale cells with a very few doubtful lymphocytes, not more than normal in number. These cells, I suppose, were altered, decolourised blood cells, but the fluid was not coloured. I could make nothing of the fluid for diagnosis. Immediately after death I drew off a blood-stained fluid with copious organisms, and leucocytes in fair number, but as it was drawn off with a syringe and post mortem the blood contamination was expected, from probable local injury.

In another case, an infant with eczema, suddenly developing convulsions and retraction and dying in a few hours; lumbar fluid was in excess and showed blood contamination, but not more than I have often obtained in cases with no sign of haemorrhage post mortem. In this instance, there was a subdural haemorrhage on either side of the longitudinal sinus between the dura and the brain, and haemorrhages under the membranes.

In four cases of acute anterior poliomyelitis

there was noticeable blood contamination, in one or two cases visible at the time of puncture and persisting in spite of changing the position of the needle. In one case blood was present in more than one tapping though absent from the last.

The determination of the source of a blood contamination in spinal puncture has always appeared to me a difficult matter: "Instances occur in which it is impossible to state whether the blood depends on a previous intracranial or intraspinal haemorrhage, or on injury done in lumbar puncture" (Peyton Rous).

Peyton Rous gives a method for determining in a case of marked blood contamination whether there is a leucocytosis of the spinal fluid, on the basis of the relation of the red and white cells in the blood and in the contaminated fluid. The red cells must be intact and countable.

Chemistry of the Cerebro-spinal fluid, and alterations and their significance:

Of the chemical constituents of the cerebro-spinal fluid the protein content is the most important clinically.

Albumin:

Normally a trace of serum globulin is present, while in pathological states this may be increased and serum albumin be present. Clinically the combination of the two - the total protein content - is alone of significance (Peyton Rous).

In my cases, I have adopted the boiling test with acetic acid, which in normal fluid should give merely a "faint haze" (Emery). Sometimes I have been unable to detect any appreciable difference between the boiled and unboiled portions of the tube. Peyton Rous describes a modified Esbach's tube which can be used to compare different fluids. He gives $\frac{1}{2}$ gm. per litre (by scale) as normal; $\frac{3}{4}$ to 2 gm. in ordinary tuberculous meningitis, while in purulent meningitis the albumen may so clog the tube as to prevent a reading.

Albumen is usually increased in acute inflammatory conditions, as in acute meningitis, also in general paralysis of the insane, but not in tabes (Stewart). In general paralysis it has been found (Stewart) that if the globulin, coagulated by boiling the lumbar fluid, be precipitated by adding saturated solution of magnesium sulphate and then filtered, the filtrate on being boiled will again yield an albuminous precipitate. Normal fluid on second boiling remains clear.

Protein increase and cell increase usually go hand in hand (Peyton Rous), but the relation of the amount of albumen to the number of cells is not a constant one (Buzzard). In my cases the albumen did not seem to be of any help in diagnosis; as a rule, it was only increased in those cases where the diagnosis was scarcely in doubt. Of 29 cases of meningitis it was appreciably increased in 15; and in some of these it varied considerably in different tapplings. Of 13 cases of tubercular meningitis it was increased in seven, but rarely to any large extent, even in those cases where polymorphs were present. Of eight cases of septic meningitis it was recorded increased in three, not at all or very slightly increased in five. But some of these records were made in the earlier stages. In eight post-basic cases it was increased in five. I found the greatest increase in the septic and post-basic cases.

It was very slightly increased in my four cases of acute anterior poliomyelitis; not at all in my cases of meningism, serous meningitis and hydrocephalus.

Quincke says it may be marked in acute serous meningitis and slightly increased in chronic hydrocephalus and markedly in "hydrocephalus" due to

venous stasis, and in cases of brain tumour; which is, I imagine, the same thing, since hydrocephalus from venous stasis is most often due to pressure by a tumour.

Oppenheim suggests an increase in the albumen may be in favour of a diagnosis of cerebral tumour, as opposed to hydrocephalus in which he says it is normal.

Like nearly every individual test in the spinal fluid, a negative result is of little or no value, while the positive results are of greater or less value, as they confirm one another and the clinical evidence.

Sugar:

The substance which reduces Fehling's solution is said to be a sugar and to produce glucosazone crystals (Stewart) and to be present normally in sufficient amount (about .06 per cent) to vigorously reduce Fehling's solution, while being absent in meningitis. Emery regards it as a very important test for meningitis in which he says he has found it absent in all but one of 100 cases, though he has since found it in reduced amount in several cases of tubercular meningitis.

Stewart says it is almost always absent in meningitis, tuberculous or septic, and reduced in paresis, tabes and chronic meningitis.

It is said to be increased in diabetes (Buz-zard), to be variable in cerebral tumours and present in chronic hydrocephalus (Quincke).

In my cases I omitted this test as a rule: it was reduced in a case of serous (?) meningitis, and present in four cases of anterior poliomyelitis, but I think reduced. Quincke regards this test as of very uncertain diagnostic importance.

Choline:

Another substance found normally in the cerebro-spinal fluid (and in the blood) in mere traces is choline, a derivative of lecithin. Halliburton & Mott described an increase in the blood and cerebro-spinal fluid in katabolic processes in the central nervous system and held that its presence in appreciable amount was proof of the existence of organic nervous disease, as in general paralysis. Halliburton endorses this in his Oliver-Sharpey lectures (April 1907) regarding it as definite use in the differential diagnosis of organic from functional nervous disease. He there mentions an improved test for choline which is crystallised out as a cholin-platinum salt.

P. Stewart quotes Hebb as using this test at the Westminster Hospital in the diagnosis of cerebral haemorrhage, syringomyelia, disseminated sclerosis, etc.

Aldren Turner quotes Donath and Wilson as having found cholin in cerebro-spinal fluid of epileptics, the former finding it in 19 out of 22 cases. Halliburton questions Donath's methods and results, doubting its increase in epilepsy. It is believed by some to be responsible for the fits, as it has been described, especially in general paralysis, with epileptiform attacks: others suggest it is a result of the fits. Buzzard and Allen, after experimenting, found it only produced convulsions when injected into the blood in excessive amount.

Buzzard says while it is undoubtedly increased in all katabolic diseases of the nervous system it is rarely necessary to seek for it in order to distinguish between functional and organic disease.

The process of isolating the platinum salt is too complicated for ordinary clinical work.

Urea: Chlorides:

Other substances found normally in cerebro-spinal fluid are urea (.035 to .04 per cent) and chlorides (.7%). These may be increased in uremia, the

urea to .4 per cent, the chlorides to 1. per cent (Emery). Thus in diagnosis of a person found unconscious, lumbar puncture may reveal blood-stained fluid in fractured skull or cerebral haemorrhage; clear fluid in thrombosis; clear fluid with increase in urea and chlorides and lowered freezing point in uremia.

Physical characters of cerebro-spinal fluid:

Specific Gravity:

The specific gravity of the cerebro-spinal fluid given normally as about 1004 to 1007 (Halliburton) has no special significance clinically owing to the difficulty in measuring it.

Freezing Point:

The freezing point of cerebro-spinal fluid has been studied by Widal, Sicard & Ravant, who have recorded its lowering in meningitis, etc. Emery has found the freezing point lowered in renal inadequacy, being about -0.56°C . in the normal fluid of a healthy person, and regards this test, with the condition of urea and chlorides, as "the simplest test of the functional capacity of the kidney".

Permeability of the meninges:

Some investigators have studied the permeability of the meninges toward certain substances in various conditions. Sicard never saw iodine and methylene-blue pass into the normal cerebro-spinal fluid, when ingested or injected subcutaneously. According to Widal the same condition holds in tabes, paralysis and meningococcal meningitis, while in tuberculous meningitis iodine does pass from the blood into the cerebro-spinal fluid. But these results do not appear to have been constant or to have any real diagnostic value (Gubb).

Some drugs injected into the spinal theca seem to act much quicker and in smaller doses than when injected subcutaneously, e.g. strychnine and morphine (Sicard); but these results seem to have been obtained in animals.

Opsonic and agglutinative properties:

The cerebro-spinal fluid of both healthy persons and patients with cerebro-spinal meningitis was found in all cases to have a lower opsonic and agglutinative power than the blood serum: the cerebro-spinal fluid being therefore a "locus minimae resistentiae". (Mackenzie & Martin: Houston & Rankin).

Cytology:

From the clinical standpoint the two most important characters of the cerebro-spinal fluid are its cytology and its bacteriology. These should always be investigated, for it has often been found that cells may be present in an apparently perfectly clear fluid, and that bacteria may be obtained in a fluid free from leucocytosis, either in films or in culture.

The fluid should be examined as soon as possible after collecting it, "for at room temperature the cells degenerate rapidly and in the course of six hours will often be unrecognisable, if they have not disappeared" (Peyton Rous). In cyto-diagnosis we note the cell-number and cell-type.

The usual method adopted is that of Widal, Sicard and Ravant. The fluid is centrifuged for a time which varies with the nature of the fluid up to 10 or 20 minutes.

Unless a deposit was quite apparent I generally centrifuged for 5 to 10 minutes. The supernatant fluid being poured off and kept for chemical examination, the tube is inverted and the last drop stirred in the bottom of the tube is taken up in a capillary pipette and carefully blown out upon a slide. There may not be any visible deposit: it may be yellowish

like a drop of pus. In the former case one film was made from one centrifuge tube; the remnants of the deposit, to which a drop of the clear fluid may be added for the purpose, being perhaps used to make a subsidiary film to be stained differently. All the tubes and pipettes were washed out with acid solution, methylated spirit and sterilized after and before each investigation, to prevent any contamination. When the deposit after centrifuging was obvious, then often two or three films were made from it, and stained differently. This I know is inexact, but accurate enough for purposes of comparison. Some observers examine one slide wet and unstained, allowing some aqueous methyl violet solution to run in at one end of slide.

Buzzard deems these films as sufficient for deciding whether there is a leucocytosis or not and considers cell counts unnecessary unless it should be proved that more delicate differential counts are of value.

Peyton Rous, Purves Stewart, Emery and others prefer the more accurate method, as used in blood counts. Emery uses Thoma Zeiss haemocytometer without the diluting fluid. The two other observers use a modification of that instrument designed by Fuchs and Rosenthal; Rous preferring to dilute the

fluid with aqueous solution of methyl violet (4 parts to 996 parts spinal fluid), omitting the acetic acid which destroys the erythrocytes; whose presence may enable us to discount some white cells, which may be due to blood contamination.

The disadvantages of this method are the time required, the lack of a permanent record and its failure to give bacteriological information.

The film allows one to make a permanent record for future reference or comparison; the bacteria present are stained as well as the cells; and according to Stewart, the more accurate counting only endorses the results obtained by means of films, so that he uses both methods in order to have a permanent record. I have found that in the films the various cells are often so unequally distributed that it is necessary to examine various parts of the slide before deciding on the relative proportions of the various cells, and the number of the organisms.

The stain used will depend more or less upon the choice of the observer. I have used Jenner most; others prefer Leishman. Carbol. Thionin also makes very clear slides, especially when the cells are not much disintegrated.

Using a counting chamber, normal cerebro-spinal fluid is found to contain very few cells - often

none. P. Stewart gives one to two lymphocytes and an occasional endothelial cell per cubic m.m.: Peyton Rous gives one to seven lymphocytes per cubic m.m.: while in a stained film with a magnification of 400 diameter, not more than two or three lymphocytes should show in a field. (Stewart).

Normally only lymphocytes, in the scanty amount stated, should be found, or an occasional endothelial cell. Any polymorphs are pathological, but we must be careful to exclude white cells due to blood contamination: also red cells which may take on a blue stain and be mistaken for lymphocytes (Emerson).

In practice three types of spinal leucocytosis occur: lymphocytosis due to the small mononuclear cell; polymorph leucocytosis due to the polynuclear leucocyte; and a combination of these. Other cells may be found, large mononuclears; endothelial cells often closely resembling the large mononuclear (Emery) and sometimes seen dividing - "active" endothelial cells; eosinophiles generally due to blood contamination; cancer cells; while phagocyte cells containing drops of myelin or erythrocytes may be found in cases of focal haemorrhage or softening (Buzzard). I thought I had obtained cells of this nature in a case of hydrocephalus. Red blood cells may also be found intact or in various stages of degeneration

in cases of cerebral haemorrhage, whether constitutional or traumatic.

I once found what I took to be two or three nucleated red cells in the spinal fluid of a case of post-basilar meningitis - aet 8 months - not I think due to the meningococcus; blood films did not show any. If leucocytosis exists, we note the amount, the type of cell, and, if more than one type, that which predominates. The condition of the cells, whether showing histolysis or not, for a type of effusion has been described, especially in France, wherein the cells are "intact", showing unaltered contour of cell and of nucleus and unaltered protoplasm, whereas in most effusions, particularly when septic, the cells show considerable breaking down and are often difficult to stain; this applies chiefly to the polymorphs. Precise cell formulae are of little value; only that part of the cell formula is important, which expresses the relationship between the polymorph and lymphocyte (Peyton Rous). Roughly we may say - in health there are never more than single figures per cubic mm. on an average one or two, and those lymphocytes.

In aseptic meningitis as in syphilis, tabes, general paralysis, etc. from 50 to 200 lymphocytes per cubic mm. In tubercular meningitis lymphocytes

are the rule, in larger numbers, from 200 to 2000 per cubic mm.: while in microbic (non-tubercular) meningitis, e.g. meningococcal, pneumococcal, etc. the fluid may be so thick with cells as to render it uncountable, polymorphs being the rule.

Significance of polymorph leucocytosis:

With regard to the significance of a polymorph leucocytosis different views are held.

Buzzard suggests it is the expression of a phagocytosis called forth by the presence of organisms, or that it may be due to a chemical agent. He apparently believes that while a polymorph leucocytosis is the rule in a well-established non-tubercular microbial meningitis, yet in its earlier stages a lymphocytosis may exist, being the expression of an irritation of the meninges, "as seen in the lymphocytosis of herpes zoster, spinal paralysis and epidemic parotitis". In other words, that the first effect of microbial invasion is an irritation, with an accompanying lymphocytosis; while, when well-established, phagocytosis is set up with a corresponding polymorph type predominating: then, as the invasion is overcome and the organism overpowered, phagocytosis being no longer actively required, the lymphocytes again become predominant.

Many observers have recorded this change of type from polymorph to mononuclear, as the acute stage gives way to the subacute and chronic, and hold that the appearance of lymphocytes is of good omen in microbic meningitis (Emery, P. Stewart, Quincke, and others). I have found a small lymphocytosis to precede, by some days, the polymorph type in a case of pneumococcal meningitis, which seems to support Buzzard's suggestion. Ross also associates polymorphs with microbial infection and explains the occasional presence of polymorphs in tubercular meningitis to a mixed infection; in support of which he quotes some cases. This question of a mixed infection altering the type of cell is interesting, and I hope to refer to it again when speaking of tubercular meningitis, merely saying here that I have seen a diplococcus in the polymorph cells in a case of undoubted tubercular meningitis, and have obtained cocci in culture from lumbar fluid in that and at least one other case in which there was a mixed leucocytosis. Bernard has recorded a case of tubercular meningitis with at first lymphocytes in excess of polymorphs; four days later the polymorphs were found in excess - "this change coinciding with a secondary infection by pyogenic organisms".

Graham Forbes appears to read a polymorph

leucocytosis as indicating the acuteness or intensity of the process. He explains the presence of polymorphs in two cases of tubercular meningitis as occurring in cases with chronic tubercular focus, the meningitis being a terminal infection ending acutely.

My first case of mixed leucocytosis in tubercular meningitis was of this nature, having a large focus in one lung, but I am not sure there was not as well a mixed infection. It was not clinically an acute meningitis. He also has found polymorphs superseded by lymphocytes in meningococcal meningitis when becoming chronic or convalescent. Purves Stewart regards the polymorph as the symbol of an acute process; the lymphocyte as that of chronicity. He mentions the production of a polymorph leucocytosis experimentally in monkeys by injecting intraspinally sterile salt solution, or sterile emulsion of coloured particles. This would seem to dispose of Buzzard's theory that an irritant produces a lymphocytosis. He refers to the transitory occurrence of polymorphs in the pyrexial attacks of general paralysis, and attributes the presence of polymorphs in tubercular meningitis to such cases being "acutely advancing".

In microbial meningitis, he finds the polymorph as the type cell, with some large monomorphs as well,

as the acute stage passes, the polymorphs diminishing to be replaced by lymphocytes.

Peyton Rous says: "Polymorph cells speak for an acute process, mononuclear cells for chronicity."

He also records finding a polymorph leucocytosis the result of irritation caused by a previous lumbar puncture - a fact that should be remembered where repeated punctures are performed at short intervals, since it may account for an alteration in the type of a subsequent tapping. This would seem to support Purves Stewart's experiment with irritant injections in monkeys.

I have not found any such production of polymorphs, which I could certainly attribute to a previous puncture. In a case of hydrocephalus a sequel to post-basis meningitis of recent history, the first tapping gave a few lymphocytes, no definite polymorphs; next day it was repeated and a large polymorph leucocytosis was found containing both many degenerate polymorphs and many apparently "intact" forms with well preserved contour, which latter may have been due to the puncture of the preceding day. He was tapped at intervals of a week two or three times afterward, but never showed a polymorph type again.

Quincke, Redlich & Schuster all hold the polymorph to be characteristic of an acute, and the lymphocyte of a chronic inflammation.

Klopstock & Kowarsky state that : "polynuclear leucocytes seem to prevail in the earlier stages of tubercular meningitis", and that in non-tubercular meningitis the nature of the fluid varies with the intensity of the process, even when the cause is the same. Their statement as to tubercular meningitis and its cytology is at variance with any other account I have found. Widal found polymorphs in the later stages of tubercular meningitis.

Widal, Sicard & Ravant, and Abadie have reported polymorphs as typical of acute microbic infections, as opposed to tubercular meningitis, in which though polymorphs occur lymphocytosis is the rule.

Zambelli holds that the type of cell is not sufficient for a diagnosis, but practically endorses the findings of the last mentioned observers.

Marcon-Mutzner records a case with post-basic symptoms, polymorph leucocytosis and tubercular meningitis found post-mortem.

The bulk of opinion, it seems, is in favour of regarding the polymorph as indicating an acute process, and especially an acute microbic infection, other than of tubercular origin.

At a Meeting of the Académie de Médecine of Paris, April 30th, 1907, Widal & Philibert reported the existence of sterile puriform effusions - meningeal and pleural - in which the cells are "intact" - in a state of perfect preservation - the contour of both cell and nucleus being clear, as distinguished from the polynuclear cells in a septic effusion, where, owing to phagocytosis, being more or less damaged, they show more or less degenerative change; this difference being so distinct as to permit of a diagnosis being made from their appearance alone; the prognosis being also much better where "intact" cells are found, even with severe symptoms. They quote a case with severe meningitic symptoms which they attribute to influenza. Lumbar fluid gave puriform fluid, large amount, high pressure, with large excess of polymorphs and some lymphocytes. Films, cultures and inoculation experiments attested to its being sterile. All the cells were "intact". Symptoms were relieved by the withdrawal of fluid. Three days later the lumbar fluid gave mostly lymphocytes, the cells being still "intact". Recovery ensued 19 days after admission. They compare these cases to the lymphocytosis of acute syphilitic disease of the nervous system "where spirochaetes have never been found", and to the

polynucleosis consequent on the injection of sterile cocaine solution, non-isotonic with the cerebro-spinal fluid.

They also claim to have noticed it in cases where a distant focus of infection has acted indirectly on the meninges - from a distance as it were - causing irritation by toxins.

At the Societe Med. des Hopitaux in Paris, July, 1907: Rist stated he had observed intact polynuclear leucocytosis in children with otitis media, the pus-like lumbar fluid being sterile in culture, films and inoculations, and the cells of the "intact" variety. In one or two fatal cases he found a localised patch of septic meningitis, and suggested that while the bacteria were confined to a localized area, the toxins being diffused set up inflammation at a distance. These observations received confirmation in a case reported to the same Society by Massary and Weil, not long after.

A man was admitted with severe meningitic symptoms - Kernig's and Babinski's signs being present - which were relieved by the escape of copious flow of pus from one ear. Lumbar fluid on several occasions gave a purulent fluid with intact polymorphs, and sterile in films, culture and inoculations. As improvement took place lymphocytes replaced the

polymorphs. This aseptic meningeal reaction in septic otitis media they explain by Rist's suggestion, which seems to agree also with that of Widal, that a localised zone of infection can, by means of toxins, set up inflammation at a distance.

I might here refer to two cases of otitis media with cerebral symptoms and with polymorph leucocytosis in lumbar fluid, which recovered, reported by Ballance and Wilkinson. In Ballance's case there was a temporo-sphenoidal abscess. There is no mention of the actual cytology in Wilkinson's case. It would be interesting to know if in these and similar cases, which recover, the cells in the turbid lumbar fluid are of the intact variety. Caussade and Willette report a case of uremic coma, treated by venesection and lumbar puncture, the latter revealing a puriform effusion under high pressure, with polymorphs amounting to 90%, the cells being "intact" and the fluid sterile. Five days later the lumbar fluid was free from cells. They attribute the puriform fluid to congestion of the meningeal vessels caused by the poisons retained in uremia with diapedesis of cells from them from chemiotaxis.

Chauffard has reported a similar case, in which he attributed the puriform fluid to the action of retained nitrogenous substances acting as toxins,

and to diapedesis of leucocytes from vessels congested by the convulsions. The polymorphs, being the most mobile cells, predominating.

Beattie & Dickson say that "sterile pus" is so, because of death of the organisms, but that it may be formed without organismal agency, by chemical substances having a positive chemiotactic attraction for polymorph leucocytes.

In endeavouring to account for the presence of a particular type of cell in different cases, the behaviour of the polymorph and lymphocyte as seen in the phenomenon of inflammation may be studied. The polymorph is active in acute inflammation, its function being to remove the irritant, be it organic, as in bacteria, or inorganic, as in colouring matter; or it may be attracted by various substances organic and inorganic, as in the production of sterile pus (chemiotaxis).

These properties will explain polymorph leucocytosis in microbial infections and in the experiments of P. Stewart in injecting salt solution or colouring matter into the spinal canal of monkeys; also the formation of aseptic puriform effusions above. The lymphocyte takes little part in the acute stage of inflammation, but in chronic conditions, and in cases where cell reaction is delayed,

as in that produced by the tubercle bacillus, or where toxins have been acting over a long period, they may be predominant (Beattie & Dickson).

"The polymorph cells are especially active where bacteria are present. But some bacteria, notably those of typhoid and tubercle, are chiefly dealt with by mononuclear cells, and in these diseases, the polymorph plays but a small part."

(Greenfield & Lyon). There being thus a selective action as it were on the part of some bacteria for certain types of leucocytes, can we explain the presence of lymphocytes in herpes zoster, parotitis and acute poliomyelitis by some similar chemiotactic selective action instead of by meningeal irritation.

I have not had any cases giving an effusion of intact polymorph cells. They are usually "intact" when due to blood contamination, if examined without delay. There is considerable difference in the state of preservation seen in the polymorphs in different cases; and I find a note, made with regard to the polymorphs in the lumbar fluid of a basal septic meningitis, secondary to pneumococcal otitis media, in which there were only a few extra-cellular diplococci, that "the cells were remarkably well preserved". He died four days later.

Significance of Spinal Lymphocytosis:

A lymphocytosis occurs in a greater variety of conditions than does the polymorph leucocytosis. It is the accepted type of a tubercular meningeal effusion, as it is in pleural effusions of the same origin, Emerson, however, claiming it to be a more reliable test in pleural than in meningeal effusion. Forbes found a lymphocytosis in 42 out of 47 cases of tubercular meningitis, being of slight degree in 11 cases. He found polymorphs present in two cases.

It is also diagnostic of syphilitic disease of the central nervous system - syphilitic hemiplegia (Niedner), facial palsy (Milian), gummatous meningitis; and in such cases of active syphilitic disease the degree of lymphocytosis is influenced by anti-syphilitic treatment, the lymphocytes being reduced by it.

But it is in the "parasyphilitic" diseases - tabes and general paralysis - that it has been so widely investigated.

According to Fuchs and Rosenthal, who summarized numerous investigations made, over 90 per cent of the cases of syphilitic and parasyphilitic nervous affections exhibit, during their acute stages, an increase in the cell-content of the cerebro-spinal fluid, while in those diseases not depending

on syphilis, but 6 per cent shewed a cell increase; the mononuclear being always the prevailing cell, and generally the only one. (Peyton Rous).

Widal, Sicard & Ravant found marked lymphocytosis in 36 out of 37 cases of tabes: Babinski and Nageotte in 25 out of 26 cases: P. Stewart found an average of 125.4 cells per cubic mm. in 15 cases, the highest being 477 per cubic mm. It may be marked when clinical proof is wanting; it may also be absent when clinical evidence is present (Stewart, Erb.)

In general paralysis Siemerling found it marked in 37 out of 38 cases; and Sicard in all of 17 cases. P. Stewart found in a series of 12 cases an average of 131 cells per cubic mm. the highest being 295 per cubic mm. The lymphocytes are most numerous in tubercular meningitis, then in tabes and paresis.

In these diseases anti-syphilitic treatment does not influence the number of cells.

Stewart says syphilis not implicating the central nervous system does not cause a lymphocytosis, or in only negligible amount, the average number in five secondary cases being 2.7; in tertiary cases with even active lesions - ulcers, rupia, etc. - being even less.

But it has been stated to be present in cases of secondary syphilis not involving the central nervous system (Schuster) and as being present in headache of secondary syphilis (Peyton Rous). In disseminated sclerosis lymphocytes have been described (Emery), Carriere finding them in all of three cases, while Sicard in only two out of seven cases.

The value of a lymphocytosis in many of the above cases lies in the fact that it is not to be found in those diseases with which they may be confused.

In idiopathic epilepsy P. Stewart says they are absent, thus allowing of a diagnosis between that disease and general paralysis with epileptiform convulsions, in which they are found. Merzbacher found them in six cases out of 12, four of these being traumatic epilepsy, and only a very small quantity in the other two. Vorkastner found lymphocytes in scanty number after an epileptic fit.

Cortical tumours, and even deep-seated cerebral tumours (Emery, Stewart) may produce a lymphocytosis (75 in a field); while its presence in herpes zoster is recorded by many observers (Buzzard, Stewart, Peyton Rous, Redlich). In epidemic parotitis (mumps) it is recorded (Peyton Rous), and Chauffard and Boidin describe two cases with meningeal

symptoms in mumps in which the lymphocytosis came and went with the meningeal symptoms. It has been described by Chauffard in a case of localised spinal meningitis (zonular meningitis), which reads, in a measure, not unlike a case of "girdle pains" in tabes; and by Picard in a case of localised spinal (cervical) meningitis occurring in mumps.

In acute anterior poliomyelitis a lymphocytosis is mentioned by Buzzard. In all four cases examined by me I found appreciable lymphocytosis marked in two cases; one case being admitted as tubercular meningitis, which the result of lumbar puncture seemed to corroborate, though the coagulum differed from that obtained in tubercular fluid.

Hebb has found "marked lymphocytosis" in several cases of lymphatic leukemia and in a case of chloroma. It is recorded also in chronic alcoholism (Emery, Redlich) and in a case dying from fractured skull (Turton); also in some forms of meningitis, or cases with meningeal symptoms, occurring in typhoid fever in children (Rocaz and Carles). Numerous observers have noted that as an acute microbial meningitis becomes chronic or enters upon recovery, the polymorphs - the predominant cell at the height of the disease - may be replaced by mononuclear cells (Emery, Forbes, Stewart, Peyton

Rous, Canby Robinson and others). Thus, "smears from a case of epidemic cerebro-spinal meningitis of three or four weeks standing often coincide cytologically with those from a recent case of tubercular meningitis. Even in tubercular meningitis the polymorphs may predominate, though the total cell-content is generally less than in meningitis due to other organisms" (Peyton Rous). This difference in total cell-content I do not think sufficient to determine a diagnosis. The appearance of mononuclear cells in septic effusions is of good omen. They seem to finish off the attack, in which it would appear that they resemble their behaviour in the later stages of the phenomenon of inflammation.

I have found a small increase of lymphocytes - hardly sufficient to call a definite lymphocytosis - in two or three cases which, presenting symptoms of meningeal irritation, have developed into pneumonia. These cases of meningism will be referred to later. One case which showed marked retraction and a small but appreciable increase in lymphocytes on two occasions, had a small pharyngeal abscess. It completely recovered. Another case showing a small but definite lymphocytosis and persistent tremulousness, did not develop anything definite, and was

discharged well. This seems to be either an abortive meningitis, or "meningism" (with a small non-located pneumonia) which I think is probably the same thing.

Cancer cells in spinal fluid:

Cancer of the central nervous system has been diagnosed by the discovery of cancer cells in the cerebro-spinal fluid obtained by lumbar puncture (P. Stewart). A case of hemiplegia with cancer cells in lumbar fluid showed a cancerous tumour involving the internal capsule, with cells identical with those found in the spinal fluid (Widal and Abraim).

Stadelmann has reported a case of gastric cancer with cerebral symptoms, in which cancer cells were found in lumbar fluid, and carcinomatous meningitis found post mortem. He suggests the cerebral symptoms seen in gastric cancer may often be due to cerebral cancer not to toxæmia or functional causes.

Krönig has reported a similar case.

Yeast cells in spinal fluid:

Yeast cells have also been reported as found in spinal fluid, in two cases of blastomycosis of the brain, related by Benda at the Verein für innere medizin, Berlin, June 1907. In each case the cells

were found post mortem in the meninges and in the cortex.

A syphilitic meningitis, with lymphocytosis containing 5% eosinophiles in the last two of three lumbar punctures, is reported by Mosmy and Harvier. There was no eosinophilia of the blood. They state the eosinophiles were of local origin and traceable as being derived from the lymphocytes.

Bacteriology of the Cerebro-Spinal Fluid:

The bacteriology of the cerebro-spinal fluid has been carefully studied by many observers in recent years largely owing to the epidemics of cerebro-spinal meningitis which have been prevalent in different parts of the country.

In the search for the meningococcus and in the efforts made to particularise its characteristics, several other cocci have been isolated, which closely resemble it both in appearance and habits, as well as in the symptoms they produce, while other organisms have been found, differing from it in appearance, yet capable of causing, if not epidemics, at any rate sporadic cases, with symptoms of a

cerebro-spinal distribution, closely resembling it.

There are, therefore, organisms met with in the cerebro-spinal fluid which may simulate the meningococcus in appearance and in effect, or which may occur along with it. Sometimes these may represent merely a terminal infection, the meningococcus - which is said to be easily killed - having died out (Kolle).

The effective bacteriological examination of the lumbar fluid presents some difficulties. There are so many loop-holes for the introduction of contamination, during its collection and transit, even if it be not centrifuged, that it should be collected and examined by an experienced bacteriologist.

To prevent changes taking place before it is examined, the laboratory should be situated at least near the place whence it is obtained, especially if the fluid is to be examined cytologically as well as bacteriologically; while the tests required to differentiate the various organisms are such as to call for the resources of a well-appointed laboratory, as well as an experienced investigator.

It is, therefore, with some diffidence that I venture on this portion of my subject, more especially with regard to my own investigations. The opportunities afforded me of bacteriological examination - whether as regards laboratory equipment or

advice - were distinctly rudimentary, while the time available for it was very limited.

I have already described the method of obtaining the fluid so that the risk of contamination should be as slight as possible. The fluid may be allowed to drop directly on to the culture medium and it is advisable to use at least 5 to 20 c.c. for this purpose (Hewlett) owing to the difficulty frequently experienced of obtaining a growth. "It is well-known that in many undoubted cases it is impossible to demonstrate the specific coccus (meningococcus) by cultural methods" (Symmers, Weichselbaum) in which case the opsonic and agglutinative properties of the fluid may give important information. Langdon Brown also records a case with diplococci found in films of spinal fluid which could not be cultivated.

So it does not necessarily follow that a fluid sterile in culture is really sterile, and may help to explain the difficulty experienced in finding a causative organism in acute anterior poliomyelitis and Landry's paralysis, in which several organisms have been recorded as found, yet not as yet substantiated. Redlich and others state that organisms responsible for spinal disease tend to die out quickly and so may not be obtainable toward the end of a disease, or post-mortem.

Organisms found in cerebro-spinal fluid:

The various organisms found in meningitis are given in an oft-quoted table by Osler, in which he gives the meningococcus, epidemic and sporadic, and the pneumococcus as causes of primary meningitis, secondary meningitis being attributed to the pneumococcus, various pyogenic cocci and the bacilli of tubercle, anthrax, typhoid, influenza, diphtheria and others.

In Weichselbaum's Standard Article on cerebro-spinal meningitis published in 1903, he gives the meningococcus and the pneumococcus as the most frequent organisms responsible for primary meningitis "either of which may be present in inflammatory conditions of the nasal cavities, accessory sinuses or tympanic cavity". He apparently insists that the mere presence of infective organisms in the meninges is not of itself sufficient to determine a meningitis, that predisposing causes must also be at work. This is important for I have seen a few cocci, in at least one case, in films obtained with all aseptic precautions and examined immediately after obtaining the fluid, and which gave rise to no symptoms, nor to any change in the cytology of the fluid, though in one case a very few polymorphs were present.* He also mentions that the pneumococcus may assume

* See Fig.13.

in meningitis atypical forms, appearing in long chains in films or cultures, being in some cases so atypical as to be described by some observers as a different organism.* It is much less liable to produce a chronic condition than is the meningococcus and is generally extra-cellular. Other organisms mentioned by him as found in meningitis are - streptococcus, staphylococcus, and the bacillus of influenza, pneumonia (Friedländer's), typhoid, plague, glanders and the bacillus coli communis.

Numerous observations have confirmed the view that the meningococcus and pneumococcus are the organisms most frequently found in primary meningitis, the former accounting for by far the larger majority, and being probably the real causal agent in epidemics.

Symmers found in the epidemic of cerebro-spinal fever in Belfast that the chief organisms obtained were - meningococci, and occasionally pneumococcus, streptococcus, bacillus typhosus, bacillus enteritidis of Gaertner and bacillus anthracis.

At the discussion on cerebro-spinal meningitis at the British Medical Association Meeting in 1908, a fairly long list of organisms isolated from the lumbar fluid or cerebral meninges were reported,

* Brit. Med. Journ. Vol. I., 1907, p.378.

both in epidemic and sporadic cases. Those reported by Symmers I have quoted.

A new organism - a gram-negative bacillus often growing in leptothrix form originally described by Stuart McDonald was referred to by Ker and Ritchie.

A gram-positive bacillus associated with a gram-negative bacillus, probably belonging to the coli-typhoid group, its identity not being known, was mentioned by James Ritchie.

Arkwright described four stains of gram-negative cocci which in films might easily be mistaken for meningococci, but differing culturally therefrom; two of these stains showing pleomorphism.

Two cases of gonococcal meningitis were described by W. T. Ritchie.

Wilson described a gram-negative coccus resembling micrococcus catarrhalis in some points and being pleomorphic, also seven cases of gram-positive cocci of the streptococcus faecalis group.⁽¹⁾

I have attempted to collect some of the various gram-negative and gram-positive cocci described by various observers as found in cases of meningitis.

Gram-negative cocci found in the cerebro-spinal fluid:

Weichselbaum in 1887 described the diplococcus

(1) Lancet, Vol. II. 1908, p.472.

intra-cellularis meningitidis (meningococcus) as resembling the gonococcus in shape (bean-shaped or reniform), not in chains, gram negative, nor growing at 20°C. forming a viscid growth and often confluent, requiring frequent subculture, and easily killed by drying.

Jaegar in 1895 described a diplococcus of similar characters, but showing tendency to become gram-positive in cultures. Councilman Mallory and Wright in 1898 confirmed the findings of Weichselbaum as seen in cocci isolated in an epidemic of cerebrospinal meningitis in Massachusetts.

Still, in 1898, cultivated the meningococcus in several cases of post-basis, or sporadic cerebrospinal meningitis, finding it agreed with Weichselbaum's organism, but was longer lived in culture and grew more readily on artificial media.

Albrecht and Ghon appear to have proved that Jaegar's coccus having a tendency to take on a gram-positive phase, was a contamination and that he had two cocci, the gram-positive one being the contamination. They confirmed Weichselbaum's description.

Dunn and Gordon, in 1905, in an epidemic simulating influenza and due to *m. catarrhalis* found in the lumbar fluid of a case with meningeal symptoms,

a gram-negative coccus apparently *M. catarrhalis*.

Barker, (1908), also has reported *M. catarrhalis* in lumbar fluid in case of otitis media with meningitis.

Arkwright in 1907 described a coccus isolated from the lumbar fluid in a case of meningitis, resembling *M. catarrhalis* morphologically, but differing in cultural and emulsifying characteristics. He thought it resembled the *M. cinereus* of V. Lingelsheim.

Wilson of Belfast in 1908 described a gram-negative coccus, isolated from the lumbar fluid in a case of fulminant epidemic cerebro-spinal meningitis. This was of the *M. catarrhalis* class, but differing in its tendency to grow in chains, growing well on Couradi-Drigalski medium; it was pathogenic to mice.⁽¹⁾

Wilson also described⁽²⁾ some gram-negative cocci resembling meningococcus in appearance, differing in - growing on Couradi-Drigalski medium in diplococcal form; tending to form chains and not tetrads; tending to assume a bacillary form on both solid and fluid media; not producing acid in any of the sugars; grows well on agar at 20°C; stains uniformly not showing degenerate and feebly staining forms.

(1) Lancet, Vol. I., 1908, p.1687.

(2) Lancet, Vol. II. 1908, p.1796.

Lastly, of the gram negative cocci, we come to the gonococcus, which was responsible for two cases of meningitis seen by W. T. Ritchie.

A typical meningococcus is reniform with flattened opposed surfaces, showing in culture isolated spherical forms - more numerous in an old culture - and many degenerated feebly staining forms.

In culture it does not form chains, but tends to form tetrads. It does not grow on the Couradi-Drigalski medium. In ascitic litmus bouillon it produces acid in glucose, and maltose, not in galactose (Symmers). Arkwright and Gordon say it produces acid in galactose. It shows no growth below a temperature of 25°C.

Gram-positive cocci found in the cerebro-spinal fluid:

Gram-positive cocci have also been found in lumbar fluid. Wilson and Darling describe a pleomorphic gram-positive diplococcus in a sporadic case of cerebro-spinal meningitis. The cocci were mostly spherical, some flattened on opposing surfaces like meningococci, forming acid in galactose, growing well on Couradi-Drigalski medium and assuming thereon a bacillary form. This organism appears to belong to the streptococcus faecalis group and to be identical with the micrococcus rheumaticus.

At the British Medical Association Meeting in 1908, Wilson reported having found gram-positive diplococci in seven cases of cerebro-spinal meningitis; some of these cocci belonging to the streptococcus faecalis group.

Thus two pleomorphic diplococci have been described - one gram-negative, growing on Couradi-Drigalski medium in diplococcal form, assuming bacillary form on agar or in both, especially in old cultures (Wilson, Arkwright); the other gram-positive, growing on Couradi-Drigalski in bacillary form (Wilson and Darling).

In one of my cases I obtained apparently such a pleomorphic organism. In examining an old culture of the diplococcus originally obtained, for means of comparison, I found to my surprise bacilli, but not knowing of this pleomorphism I supposed it to be a contamination and destroyed it.

The diplococcus Crassus resembles the meningococcus, but is partly gram-positive, partly gram-negative (Arkwright); according to Hewlett it is gram-positive.

It is supposed by V. Lingelsheim to be the "meningococcus" of Jaegar (which he described as being in culture both gram-positive and negative) and is believed by some to often occur with the true

meningococcus as a mixed infection and to perhaps be responsible for some of the symptoms (Westenhoeffer, V. Lingelsheim).

Various kinds of staphylococcus and streptococcus have been described, more often as mixed infections or secondary to septic foci in ear, scalp and elsewhere. They may be intra-cellular (Wright & Archibald) and may appear to be in pairs, thus resembling diplococci.

Gram-positive diplococci isolated from lumbar fluid growing on agar and forming tetrads have been described (McWeeny); also a gram-positive diplococcus growing in chains, obtained from the pus in meninges of a case supposed to have typhoid fever. Widal test was positive. Lumbar puncture twice failed to give any fluid. The Lister Institute reported ⁽¹⁾ bacillus typhosus and meningococcus were absent, but this gram-positive diplococcus in chains which was non-pathogenic to a rabbit.

In one of my cases of supposed post-basic meningitis, I obtained both gram-positive and gram-negative cocci in culture from the lumbar fluid, and in films from pus in the ventricle post-mortem.* Some of these were intra-cellular, and in several films appear to show some diplococci which give up the gram stain, but more which persistently retain it.

(1) Brit. Med. Jour. Vol. I. 1907, p.374.

* See Figs 22 and 23.

Stuart McDonald, in his description of his leptothrix forms, found in lumbar fluid, says in the first case were some elongated diplococci (gram-negative) which he is "convinced were merely stages in the development of the longer thread forms". This would make a third pleomorphic organism described in spinal fluid.

Stuart McDonald described the occurrence of both gram-positive and gram-negative meningococci in cultures from organisms which were purely gram-negative when fresh from the spinal fluid, and details experiments in support of this gram-variability of some strains of the meningococcus, as evidenced in cultures.

Shennan and Ritchie deny this gram-variability, attributing the appearance of gram-positive cocci to contamination or to faulty staining.

Houston and Rankin suggest this should be decided by testing the opsonic and agglutinative properties of the strain of diplococcus in question.

In the differentiation of the various cocci which may be found, either in the cerebro-spinal fluid, or in those positions where the meningococcus may be looked for, with reference to the etiology of meningitis and the route of infection, various tests are in use, the most important being - their

behaviour with Gram's differential stain; their growth or not on the Couradi-Drigalski medium; their fermentation characters, as judged by the presence or absence of acid formation, when grown in ascitic litmus bouillon containing various carbohydrates; growth on ascitic agar at 20°C. and their morphology and their opsonic and agglutinative properties.

With regard to the identity or not of the diplococcus found in post-basic meningitis or sporadic cerebro-spinal meningitis, with that found in epidemic cerebro-spinal meningitis: between Still's organism and that of Weichselbaum: some difference of opinion exists. Some hold they are the same organism in different degrees of virulence, cases clinically identical with the sporadic form occurring during epidemics of cerebro-spinal meningitis (Koplik); while post-basic meningitis may occur in epidemics; and clinically the one disease merges into the other if studied at different ages (Langmead). Houston and Rankin claim they shew distinct differences in opsonic and agglutinative properties, while being practically identical culturally and morphologically. Eve and Clement find differences, cultural, agglutinative and phagocytic as well as clinical. Culturally, the sporadic organism grows

more freely on agar, has greater vitality, and while the primary cultures may be alike, in subculture the sporadic organism is more abundant, often confluent, more opaque, "iridescent" and sticky. Phagocytic - the sporadic organism is more extra-cellular and in the blood of a patient, in that of a normal person or in the cerebro-spinal fluid, it shows little or no tendency to be engulfed by the polymorphs; so that for diagnostic purposes it is only necessary to observe whether phagocytosis and agglutination are conspicuously present or absent. I would merely remark that these observations of Eve and Clements appear to have been made on a very restricted number of cases: for out of seven cases of posterior basic meningitis examined by Wilson⁽¹⁾ six were identical with the meningococcus of epidemic cerebro-spinal meningitis in morphology; four were identical culturally; two differed from it in their production of acid in sugars; while one differed from it in the fermentation test and also in showing good growth on Couradi-Drigalski medium. All these seven were found by Houston & Rankin to differ from the epidemic meningococcus in opsonic and agglutinative properties.

(1) Lancet, Vol. I., 1908, p.1796.

It would seem, therefore, that the condition understood as posterior basic meningitis may be due to other organisms than the diplococcus of Still, or that it occurs in different strains.

In one of my cases, clinically diagnosed as that disease, I obtained only a few drops of lumbar fluid with no cocci in the films made from it, culture of the spinal fluid giving only a staphylococcus. From the pus exuding from the fourth ventricle post-mortem I obtained films showing distinct and numerous gram-positive diplococci,* both intra and extra-cellular, and some gram-negative diplococci; culture seemed to confirm this, giving both a whitish and yellowish coloured culture and latterly a staphylococcus. The gram-positive nature of the cocci seemed undoubted, and was the same when using Weigert's modification of Gram's method. I was unable to make use of the fermentation tests, but in one case where I obtained a culture of gram-negative diplococci morphologically resembling the meningococcus from a case of tubercular meningitis with polymorph leucocytosis, I was able to apply this test with four of the principal sugars (thanks to the kindness of Dr J. L. Bunch) in none of which did it produce acid, while it grew on the Couradi-Drigalski medium. In one other case of post-basic meningitis, similar

* See Figs 22 and 23.

to that mentioned above and identical with it clinically, I obtained gram-positive diplococci in culture from fluid taken from the lateral ventricle during life, no cocci being visible in the films from the fluid. I left the Hospital before the child's death, and the films sent me were not very satisfactory, especially the one stained by Gram's method; there are in it what resemble gram-positive cocci, very few and very doubtful. A few diplococci, intra and extra-cellular, are visible in two of the other films. No culture was taken post-mortem. In each of these cases, the post-mortem revealed a condition of basal meningitis resembling the condition seen in "posterior basic meningitis".

Arkwright thinks that some strains of true meningococci may not give typical reaction with the sugar (fermentation) test and yet be genuine.

Poynton & Holmes have reported the isolation of the diplococcus rheumaticus from the cerebrospinal fluid and from the pia mater, post-mortem, in three cases of chorea of rheumatic type in 1906. This organism, according to Wilson, is a streptococcus faecalis and allied or identical with the gram-positive diplococcus he isolated from a case of cerebrospinal meningitis.

Is it possible that the same organism, or an

allied strain, may in one case be capable of producing by its presence, or by its toxins, the symptoms clinically recognisable as chorea; while in another case, whether due to a greater virulence, a more suitable soil, or a combination of these, it may give rise to an active, even fulminant meningitis? If so, then the difference in the results due to the diplococcus of Still and the more active meningococcus of Weichselbaum might be similarly explained.

Marsh has recorded a case of staphylococcal meningitis with recovery. Lumbar puncture gave a turbid fluid, with polymorph leucocytosis, which reduced Fehling's Solution, and contained staphylococcus pyogenus aureus. It was clinically a very chronic type of case.

I have had one staphylococcal meningitis - a terminal infection in a septicaemia from a neglected periostitis. I obtained pure culture of staphylococcus from vegetations on heart valves and from the meninges.

My cases also included a streptococcal meningitis in an infant of nine months, with very indefinite symptoms, lumbar fluid being turbid, in excess, and under increased pressure: albumen increased; marked leucocytosis, in which mononuclears

largely predominated. Numerous chains of streptococci were visible, some cocci being visible in the cells, both of the spinal fluid and in the meningeal pus.* A pure culture of streptococcus was obtained from the spinal fluid, and the meninges (post-mortem) also streptococci in smears from the spleen.

Under the heading of "Pseudo-epidemic meningitis" Baginsky draws attention to a disease resembling epidemic cerebro-spinal meningitis, but differing from it in its bacteriology and in its more rapid and favourable course. The causal organism as found in lumbar fluid may be - pneumococcus, diplococcus Crassus, streptococcus or staphylococcus.

In one case the lumbar fluid contained cocci, a few of which were intra-cellular, but no growth could be obtained in culture. One case, "probably due to micrococcus flavus" ended fatally. The others ended in complete and rapid recovery.

W. T. Ritchie has recorded two cases of gonococcal meningitis, the lumbar fluid being turbid, full of polymorphs, with scanty intra and extra-cellular gram-negative diplococci, exactly like meningococci. No growth was obtained, the identity of the organism being established by agglutination and inoculation tests; as also by the ferment-

* See Fig.7

tation tests with sugars, in which the gonococcus forms acid in glucose and galactose, but not with maltose or dextrin.

A leptothrix, occurring in the cerebro-spinal fluid of cases of acute meningitis, has been described by Stuart McDonald, also by Ker, in cases sent to the Edinburgh Fever Hospital as cerebro-spinal meningitis and by James Ritchie, in one of whose cases it seems to have caused a general pyaemic condition (Scott Carmichael & Ritchie). Stuart McDonald in culture obtained a growth which consisting at first of elongated diplococci, showed in films a few days later a "tangled mass of sinuous filaments", and says he was "convinced these diplococci were merely stages in the development of the longer thread forms", which are gram-negative and extracellular. These leptothrix forms seem to have been accompanied in some cases by other organisms, by a coccus resembling the diplococcus Crassus, and by the true meningococcus. Whether it is the causal organism, or whether it reinforces the meningococcus, or other organism remains to be proven.

TUBERCULAR MENINGITIS:

Next to the meningococcus the tubercle bacillus is the most frequent cause of meningitis. Tubercular meningitis is generally considered to be secondary to some pre-existing focus in the body - most frequently a caseous bronchial or mediastinal gland. Shennan in his investigation into the focus of origin found it was in a large majority of cases a caseous lymphatic gland; more often mediastinal than abdominal.

The fluid obtained by lumbar puncture is generally clear or very slightly opalescent. Canby Robinson found it "almost perfectly clear" with a slight opalescence" in 12 out of 19 cases, and slightly turbid in four cases. Klopstock and Kowarsky find it clear in most cases, but occasionally opalescent and Graham Forbes the same; the more acute the case the more cloudy the fluid. In my cases it was clear in two and turbid in 14, but this "turbidity" includes slight opalescence.

In my cases the albumen was slightly increased in seven out of 13 cases.

Forbes found slight trace in 18, marked trace in 12.

When describing the method of examining the fluid, I advised, if possible, leaving some fluid

to stand to see if a coagulum should form in it. This should always be done if tubercular meningitis be suspected.

In nearly all cases a fine veil-like coagulum like a spider's web, forms in the fluid, apparently suspended from the surface of the fluid and reaching to the bottom. The coagulum forming in other effusions differs in appearance, being usually flaky, thicker and adherent to the sides of the tube. Canby Robinson found this coagulum in all but one of his cases; I have found it in all of my cases since I learnt to look for it - in 10 successive cases.

This clot may form in a few hours; it is not necessary to wait for 48 hours, nor have I ever found it necessary to cool it artificially, as some advise. It should be removed, teased out on a slide, dried and stained in the usual method. It is best removed with a pipette; if a platinum wire be used it adheres firmly to it. The strands forming the coagulum are elastic and easily spread out. There is also sometimes a little coagulum of the nature of that found in other effusions; this is brittle and opaque, nor have I ever found any tubercle bacilli in it. Under the microscope the blue-stained coagulum is searched for the tubercle

bacillus. This method is a saving of time, as well as very sure, for it is quite easy to follow the stained coagulum, and as a rule to find the tubercle bacilli,* against the blue background with a high power, the oil immersion lens being used to conform it. I have found the tubercle bacillus in every case of tubercular meningitis since I used this method - that is, in 10 cases - and before that in films made from the centrifuged deposit, in four cases. In only one fluid did I fail to find the bacillus; that was in the first tapping; in the next tapping a few days later I found it. They vary considerably in the numbers in which they may be found. I have found clumps of 15 to 30 bacilli in more than one case; in others only two or three after careful search. Bernstein adds the centrifuged deposit to the coagulum when spread on the slide. He was successful in 38 out of 40 cases. Canby Robinson reports finding the bacillus in 17 out of 19 cases; and Forbes in 25 out of 31 cases, by means of this method.

The advantage of finding the bacillus is great, as it settles the diagnosis. In two of my cases the clinical picture was typical of post-basilar meningitis** Retraction and opisthotonus being extreme; but the bacillus was demonstrated on several occasions

* See Figs. 16 and 19

** See Photograph and Figs 14, 15 and 16.

in fluid withdrawn for the relief of symptoms.

As an alternative to staining the coagulum for the bacillus, Wall states that "if the albumen be precipitated by adding an equal volume of a 5 per cent phenol solution and the deposit stained, the bacillus may be occasionally demonstrated."

The predominant cell in tubercular meningitis is the mononuclear.* This is also true of the primary effusions met with in tubercular disease affecting the pleura and peritoneum. Emerson believes the lymphocyte a more constant finding in pleural than in cerebro-spinal effusion due to the tubercle bacillus.

On one occasion I had three tubercular effusions under examination - pleural, peritoneal, cerebro-spinal - all from different children, all full of lymphocytes. The lymphocytes were most typical in the pleural effusion. All three were examined in the same way, slightly modified; the bacillus being found in the stained coagulum in the pleural and in the spinal effusions. The child with meningitis died, the others left Hospital.

Sometimes the lymphocytosis in tubercular meningitis is marked; at others slight; in some absent. In others there may be an admixture of polymorphs, even exceeding the lymphocytes.** There may be some

* See Fig. 10.

** See Figs 15, 17, and 18.

fibrin visible in the film, which is unlikely in most of the other diseases wherein the lymphocyte is found.

I have found no cytological evidence of the nature of the disease in three cases, all with definite general miliary tuberculosis found post-mortem; one having well-marked tubercular meningitis, the others having evidence of early meningitis without definite tubercles visible to the naked eye. In these two latter cases, a very few lymphocytes were visible after lengthy centrifuging, but hardly sufficient for a diagnosis, for I have seen as many or more in cases of so-called "pseudomeningitis" or "meningism" which have entirely cleared up. One of these was tapped more than once with the same negative result. The first mentioned case gave a perfectly clear fluid, with no cells visible in it. It was an infant of seven months, admitted as marasmus with pneumonia; the fontanelle was not bulging and the retraction, which developed after admission, was attributed to "cerebral pneumonia" or more probably to a hydrocephaloid condition. The lumbar fluid was quite clear and watery; albumen not increased; no cells; increased in amount, not in pressure; all quite in keeping with the original diagnosis. At the autopsy there was well-

marked early tubercular meningitis, with a few definite tubercles, and tubercular consolidation of one lung and abundant miliary tubercles elsewhere. All these three cases belonged to a period prior to my adopting the method of looking for and staining the coagulum.

Of 16 cases in which there was no doubt of the existence of tubercular meningitis (all showing definite meningeal tubercles at autopsy, except one, where typical tubercle of the choroid was present, a post-mortem being refused), a pure lymphocytosis of the spinal fluid was found in seven; no cells in one case; mixed polymorphs and lymphocytes in eight. In four of these, lymphocytes were in excess; in two the polymorphs predominated, while in two cases, the proportion of these two types differed during the progress of the case; in one the polymorphs were in excess at first, the lymphocytes towards the end;* while in the other the reverse was the case, there being practically a pure lymphocytosis at the beginning.** This latter case was in hospital 16 days with intense retraction and opiothotonus and a good deal of convulsive movement. The total history of the illness was about six weeks. Post-mortem the brain was so soft, it fell out like "batter" and was studded with tubercles; there was no pus.

* See Fig. 18.

** See Figs 14 and 15.

There was general miliary tubercle throughout.

In the former case I found one or two cells with cocci in them in the first tapping; and, as the polymorphs were in excess, I at first thought it was a meningococcal meningitis; next tapping the polymorphs were not so evident and tubercle bacilli were found in the coagulum; while cultures on agar gave one or two discrete colonies, growing easily in subculture on agar, consisting of bean-shaped diplococci, in pairs and tetrads, staining fairly uniformly, and gram-negative. They showed also good growth on Couradi-Drigalski medium. The polymorphs were present in large numbers towards the end in the other case; and culture of the fluid gave no growth.

Mixed infection in tubercular meningitis:

This question of mixed infection in tubercular meningitis being accountable for the change in the type of cell in the effusion is of interest.

Significance of polymorphs in tubercular meningitis:

As mentioned above, Graham Forbes found two cases with polymorphs present in excess, which he explains as indicating an acute exacerbation of a long-standing tuberculous infection. Stewart has

found polymorphs "in cases of acutely advancing tuberculous meningitis". Klopstock and Kowarsky state "a polymorph leucocytosis seems to prevail in the early stages"; a statement I have been unable to find elsewhere. Emery says polymorphs occasionally occur, but are never numerous. Widal and others, while recognising their presence, yet apparently consider the lymphocyte to be the rule. Peyton Rous says polymorphs appear if a tubercular meningitis take an acute form, but that the total cell content is less than in other forms of bacterial meningitis. This may be true and the polymorph leucocytosis may be due to pure tubercular meningitis of an acute form, or to mixed infection complicating a tuberculous meningitis, and it may be that the total cell-content is greater in the latter instance; but I doubt if it is a distinction of much diagnostic value. Cases of tuberculous meningitis with mixed infection have been recorded by Ross, Oppenheim, Warrington and Heubner. Ross mentions a case which he says he could multiply, where a polymorph leucocytosis of the spinal fluid was found and tuberculous meningitis post-mortem; but explains the presence of the polymorphs by having isolated the staphylococcus albus from this fluid obtained during life. I would venture to point out that Gordon has

found this is the organism most likely to be found as a contamination in lumbar puncture, through contamination from the skin. Ross does not mention the presence of pus in the meninges, and I do not think this case at all convincing, in support of his belief that polymorphs in tubercular meningitis are generally, if not always, due to mixed infection.

Marcon-Mutzner quotes a case dying with symptoms of post-basic meningitis, in whose lumbar fluid a pure polymorph leucocytosis was found and yet tubercular meningitis post-mortem. This much reads very like my case, already quoted, in which polymorph leucocytosis was found in the later tapplings and such marked retraction and opisthotonus as to closely resemble a posterior basic meningitis. But Mutzner found "a purulent muff 1 cm. thick beneath the chiasma, the pons and the bulb"; on the fact of this distribution Ross suggests it was a septic infection.

Oppenheimer contents himself with stating the fact that the meningococcus has been found once in tubercular meningitis.

Heubner has described 14 cases of tubercular meningitis, two of which were associated with meningococci, both organisms being found, the meningococcus being regarded as a secondary infection.

Warrington says lymphocytes are the rule in tubercular meningitis, a large number of polymorphs usually indicating the existence of a secondary septic meningitis, secondary to septic focus elsewhere; quoting among his cases an otorrhoea and purulent epiphysitis, as the foci of secondary infection.

Quincke says the fluid may be perfectly clear, "in rare cases purulent, for example, in mixed infections with meningococci or pneumococci."

To the eight cases with mixed leucocytosis occurring among my series of 16, may be added one in which I found one tubercle bacillus in a film from the fluid. This child was removed from hospital after being in less than 24 hours and died two days later after an illness of five days. Lumbar puncture on the second day of the illness, gave scanty fluid with many polymorphs and lymphocytes*. After much search I found what I thought to be one definite and two very doubtful tubercle bacilli. No culture was taken. This certainly was an acute case. I have not included it in my series as one tubercle bacillus is a diagnosis open to criticism.

Of the other eight cases proof of the nature of the disease was found post-mortem, save two cases; in one several bacilli were found in the smears from the lumbar fluid; in the other definite typical

* See Fig.9

tubercle of the choroid and tubercular dactylitis were present.

I have tried to divide them into acute and chronic, but hardly know on what to base this difference. Duration of illness is so uncertain, as one must depend on the history; degree of leucocytosis is, I believe, unreliable, and amount of albumen a very erratic factor. I propose, therefore, to take duration of illness as my guide. Of the more acute cases, four in number, the duration of illness was 14 days or under, averaging 13 days; of the less acute cases, four in number, the average was over $4\frac{1}{2}$ weeks.

I have tabulated the 16 cases of tubercular meningitis, Tables 1 and 2 containing those having a noticeable amount of polymorph cells present. Tables 3 and 4 contain those in which a practically pure lymphocytosis existed. The duration in the more acute of these cases with pure lymphocytosis, averaged about 14 days; in the more chronic cases the average was about three weeks, perhaps more, the histories being very indefinite in these.

TABLE TO SHOW COMPARISON BETWEEN CASES OF TUBERCULAR MENINGITIS WITH POLYMORPH AND WITH LYMPHOCYTE LEUCOCYTOSIS.

Name	Age	Duration	Albumen	Cytology with reference to relative proportions of Polymorph and Lymphocyte cells.	Presence of tubercle bacilli.	Organism seen in film.	Organism found in cultures.		
<u>A. Cases with Polymorph Leucocytosis:</u>									
<u>Table 1. Acute:</u>									
1.	W.	8 mos.	11 days	+ +	L. predom. P. appear in second tapping.	T.B. in coag.	None	A gram - neg. diplococcus.	
2.	F.	1 yr. 5 mos.	13 days	+ +	L. predom. especially in second tapping.	T.B. in coag. very numerous	None	A gram - neg. diplococcus.	
3.	C.	5 yr. 3 mos.	14 days	Slight +	L. slightly predominate	T.B. in film.	None	Culture, no growth.	
4.	G.	2 yr. 2 mos.	14 days	Slight +	Polym. predom. at first Lymp. slightly predominate later.	T.B. in coag.	Several intra-cellular cocci.	gram - negative diplococcus.	
<u>Table 2. Less Acute:</u>									
5.	Y.	5 yr.	3 weeks	Slight +	Polym. predominate	T.B. in fluid	No definite cocci.	Mixed growth.	
6.	E.	1 yr.	4½ weeks	+	Polym. predominate	Not looked for.	Doubtful pneumo-cocci	Mixed growth, chiefly gram-positive cocci.	
x	7.	O.	3 yr. 7 mos.	5 weeks	+	Lymp. slightly predom.	T.B. in fluid	Doubtful intra-cellular cocci.	No culture taken.
*	8.	L.	1 yr. 4 mos.	6 weeks	+	Lymp. predominate at first. Polym. predominate later.	T.B. in coag. very numerous	No cocci	Culture, no growth.
<u>B. Cases without Polymorph Leucocytosis:</u>									
<u>Table 3. Acute:</u>									
* 9.	A.	6 mos.	(?) 10 days.	Slight +	Large pure lymphocytosis	T.B. in coag.	No cocci	Culture, no growth.	
10.	S.	1 yr. 6 mos.	14 days	+ +	Large lymphocytosis, hardly any polymorphs.	T.B. in coag.	No cocci	No culture taken.	

	Name	Age	Duration	Albumen	Cytology with reference to relative proportions of Polymorph and Lymphocyte cells.	Presence of tubercle bacilli.	Organism seen in film.	Organism found in cultures.
<u>Table 3. Acute: (Cont.)</u>								
	11.	Ch.	2½ yrs.	15 days	Slight +	Pure Lymphocytosis	T.B. in coag.	No cocci No culture taken
	12.	Cr.	5 yrs.	16 days	+ +	Pure lymphocytosis	T.B. in coag.	No cocci Culture, no growth.
<u>Table 4. Less Acute:</u>								
§	13.	M.	1 yr.3 mos.	18 days ++	Slight +	Large pure lymphocytosis	Not looked for	No cocci No culture taken
	14.	Ft.	3 mos.	3 weeks	+ +	Large pure lymphocytosis	T.B. in coag.	No cocci No culture taken
	15.	D.	7 mos.	? ?	not +	No cells at all	Not looked for	No cocci No culture taken
	16.	P.	1 yr.4 mos.	3 weeks	not +	Large pure lymphocytosis	T.B. in coag.	No.cocci No culture taken

X Case with choroidal tubercle, "obsolescent" tubercle, and recent, acute tubercles. No optic neuritis.

* Case simulating post-basic meningitis; very marked retraction and opisthotonus.

✱ Case simulating post-basic meningitis on admission.

§ Case with choroidal tubercle; no optic neuritis; tubercular dactylitis present.

N.B. Temperatures have not been included as several cases were only in hospital for two or three days; besides mixed infection would probably cause a raised temperature.

In comparing the two first tables, it will be seen that polymorphs were in excess of lymphocytes in one only of the acuter cases and then only in the earlier tapping, while they predominated in two of the less acute cases and in the latter tapplings of a third. So as far as my results go, relative preponderance of polymorphs does not mean acuteness. This is especially evident if we allow that the cases in table 3 were as acute as these in Tables I and 2; clinically I should say they were quite as acute, if not more so than those in Table 1. Of the eight cases with polymorphs, cultures were made in seven, which gave no growth (on agar or nasgar) in two; a growth of a gram-negative bean-shaped diplococcus in three; a mixed growth, mostly of an elongated gram-positive diplococcus, very like the pneumococcus, and tending to die out early, in one (E); while in the last, the culture was taken from a specimen which had been standing for sometime and seemed to consist of a mixed growth, chiefly of a gram-negative organism, with a few diplococci, which resembled the pneumococcus (Y).

The circumstances which led to my investigating this part of my subject were as follows.

Case 5 (Y) was one where there was a large focus in the lung, the meningitis apparently being a

terminal infection. The lung gave rise to no symptoms and was not appreciated during life. It was an exceedingly mild case clinically, with no definite symptoms till four or five days before death and yet there was this large mixed leucocytosis of the spinal fluid. I was not present at the post-mortem but no pus was found. Smears from the lymph at the base gave numerous tubercle bacilli and here and there a doubtful degenerated diplococcus.

Not long after, cases 3 and 6 (C. and E.) were admitted, whose spinal fluids resembled that of Y.

I then carefully re-examined the films from Y. and found one or two doubtful pneumococci in them, also in E. which I thought probably a septic meningitis.* At post-mortem it was a typical tuberculous meningitis, as was Y. I was at a loss to account for the polymorphs, as acuteness did not seem to fit the case, except perhaps with C. Culture of the fluid obtained from E. seems to corroborate the suspicions aroused by the findings in the films. Culture of Y's fluid was less convincing; culture of C's fluid gave no growth.

So I determined to examine my future cases more carefully, and to avoid any risk of contamination if possible, I now began the strict aseptic routine I

* See Fig.17.

have described, and soon after, learning of the method of looking for the bacillus in the coagulum, I kept a tube separate for that purpose. Up to this I had found the bacillus in ordinary films specially stained for it, in the case of Y, C and O. No culture was taken of O's fluid, but on re-examining the films I found some very doubtful intra-cellular diplococci. The four remaining cases (W. F. G. L.) with the exception of L. gave in culture a gram-negative bean-shaped diplococcus, while in the smears from the centrifuged deposit, intracellular cocci were seen in G. (which at first I took to be a case of posterior-basis meningitis)* This last piece of evidence seemed to me the most important, as cocci in films, and especially in cells, could not be due to contamination introduced during lumbar puncture, carefully performed. The cultures were made on agar and masgar, and gave usually one or two small, circular, colonies, with smooth margin, not tending to enlarge, of a greyish or bluish colour. When subcultured they grew well on agar, tending to become slightly yellowish, confluent and moist. They appeared to consist of diplococci, mostly in pairs or tetrads, not in chains, gram-negative, though in some there seemed to be larger, more spherical, cocci, which seemed loath to give up the gram stain.

* See Fig.18.

The culture of F. I was able to try with several sugars, though it was then of old standing and I think contaminated; no acid was produced in any of them and it grew well on Conradi-Drigalski medium, retaining its diplococcal form. The original culture in this case and a sub-culture were seen by a pathologist of some experience who agreed they were exactly like the meningococcus. The culture of W. seemed to consist of smaller cocci than the others and they grew on Conradi-Drigalski, retaining its diplococcal form.

The culture of G's fluid (in which intra-cellular cocci were seen in film) gave a similar discrete greyish white colony, consisting of diplococci similar to the others, but not arranged so much in tetrads, and also growing on Conradi-Drigalski medium.

The last fluid, that of L., gave no growth nor were any cocci seen in the films.

Of those cases in which a practically pure lymphocytosis was found, no growth resulted in the two cases in which a culture was taken. No culture was made from the remaining six cases.

Hence of the eight cases with polymorph leucocytosis, putting aside two (Y. and E.) in which there was considerable possibility of contamination of the fluid, no growth resulted in culture from two, nor

was suspicion of the presence of cocci aroused by an examination of the films; no culture was attempted in one, in which subsequent scrutiny of the films suggested the presence (doubtful) of intra-cellular cocci; while the remaining three (W.F.G.) gave a culture of a diplococcus, which was believed to have been seen in several cells in the films made from the centrifuged lumbar fluid in one case.

In no case was pus found in the brain, nor were cocci carefully sought for in the ventricular fluid except in case G. where a few extra- and intra-cellular diplococci were found in the fluid removed from the ventricles post-mortem.

These remarks are, I know, very incomplete, but I was unable to devote the time, or employ the methods which an adequate investigation of the subject requires. Still I consider the polymorphs not necessarily a sign of acuteness, nor do I feel they of necessity indicate a mixed infection; for cocci may not be seen in smears in a case even of meningococcal meningitis, though there be a well-marked spinal leucocytosis, and failure to obtain in culture from spinal fluid an organism which is known to be the causal agent of a meningitis and which has been seen in smears has been repeatedly recorded (Eichhorst, Langdon Brown and others).

Mixed infection in meningitis generally:

There are numerous instances on record of mixed infection in meningitis. Horder believes mixed infections of the meninges to be uncommon, and those found post-mortem he attributes to post-mortem or terminal infections, except when secondary to ear disease (None of the cases in my series of tubercular meningitis had otorrhoea except G. the one with intracellular cocci seen in films; he had had otorrhoea for about six months), and quotes a case of mixed infection by influenza bacillus and pneumococcus. Mixed infections of the patient he believes to be common, such as meningococcal meningitis and influenzal pneumonia. Several observers have recorded the frequent association of meningococcal (epidemic) meningitis and pneumonia due to the pneumococcus (V. Leyden, West, Immermann). Other cases of mixed infection in meningitis are - "In epidemic cerebro-spinal meningitis, streptococcus, staphylococcus, pneumococcus and influenza bacillus have all been found associated with the meningococcus" (Eichhorst); meningococcus with pneumococcus (Hislop); bacillus typhosus and *M. catarrhalis* (Gordon); Meningococcus and the diplococcus *Crassus* (V. Lingelsheim, Arkwright, Westenhoeffer). Two kinds of gram-negative cocci morphologically alike, but differing culturally

(Wilson); leptothrix associated with diplococcus Crassus (?), meningococcus and with the pneumococcus in different cases (S. McDonald); leptothrix with pneumococcus (James Ritchie).

Besides mixed infection with the tubercle bacillus already mentioned. One may repeat here Kolle's observation that in some cases - particularly in epidemic cerebro-spinal meningitis - organisms may be found which are secondary infections, not causal of the meningitis, the causal organism of which has died out.

On the other hand we may not find the organism or even a leucocytosis until late in the disease,* more especially with the pneumococcus (Batten); or it may disappear comparatively early - at any rate, some time prior to death - in the case of the meningococcus; as in three cases of mine, in two of which only clear fluid was obtained, probably due to early closing of the foramen of Magendie.

Meningitis without naked eye evidence:

An interesting point in connection with a negative result in the examination of the spinal fluid in tubercular meningitis, and indeed in other forms of meningitis, is the occurrence of a real meningitis with absence of naked eye evidence, as found post-

* See Figs. 1 and 2.

mortem. I have mentioned one case of tubercular meningitis with normal fluid, and yet well defined early meningitis post-mortem. I have had two cases of tubercular meningitis without tubercles; one very acute and fulminant, with general miliary tuberculosis, optic neuritis, convulsions, early meningitis and yet no tubercles visible to the naked eye; though three of us searched for them, including the pathologist to the Hospital. This case died within a few hours of the onset of meningitic symptoms. The other was not acute, there was head-retraction and indefinite signs in the lungs. It was a beautiful case of wide-spread miliary tubercle, even including the pericardium and kidney. But though early evidence of meningitis, no visible tubercles. The fluid in this case was normal - not enough lymphocytes (twice tapped) to call a lymphocytosis. In the former case there was some blood contamination and a very few lymphocytes. As tubercle was not suspected a coagulum was not looked for. Two or three cases were admitted with convulsions, and dying within 24 hours, one showed lymphocytosis, another only marked blood contamination and a few cells, which were, at any rate in part, due to the contamination; in the third lumbar puncture was not performed. Of these I hope to speak later. As there were no signs of

miliary tubercle elsewhere I should not like to have suggested any of them to have been tubercular meningitis, but for the following cases recorded by others. Siredey and Tinel, and Delille (at the Société Méd. des Hôpitaux of Paris) stated that tuberculous disease may exist without visible tubercle, especially in tubercle of the central nervous system, all the clinical signs of tuberculous meningitis existing and yet no tubercles. In a case quoted only congestion of the meninges with milky thickening was visible to the naked eye; but tubercle bacilli and leucocyte infiltration were found microscopically, grouped especially round the blood vessels, lumbar puncture showing lymphocytosis and a few polymorphs.

Wilson & Miller quote two cases of tubercular disease of the central nervous system; one they summarise as tuberculous meningitis and myelitis. No naked eye evidence of tubercle, but cell infiltration with a few accompanying tubercle bacilli found. Lumbar puncture was not performed. The other case showed a caseous bronchial gland with many tubercle bacilli. Microscopically, cellular infiltration of cord and meninges with tubercle bacilli; some early meningitis visible in meninges; no tubercles visible anywhere.

So here are three cases recorded with no visible signs anywhere of miliary tubercle, microscopic examination being necessary.

Unfortunately the central nervous system was not examined microscopically in my cases, nor were cultures taken.

Wilson (Belfast) has recorded a case of streptococcal meningitis in which no pus was present, the cocci being obtained in culture from the spinal fluid, and post-mortem from the meningeal exudate.

Ballance also mentions how fatal meningitis may supervene in otitis media with no pus formation, due to fulminant malignant meningitis.

Langdon Brown has also recorded a case dying with cerebral symptoms and post-mortem no naked eye evidence of septic meningitis, though the meninges were teeming with pneumococci.

As to the value of lumbar puncture in the diagnosis of tubercular meningitis, there can be little doubt, as the various results given above testify. A lymphocytosis in a child, or where meningitis is suspected, especially if marked, and if corroborated by the formation of the typical veil-like coagulum, is strongly suggestive. In fact, to quote Canby Robinson "It is fair to say that when clear, slightly opalescent fluid in which a veil-like clot forms

in a few hours, is obtained comparatively early in the disease in a case with meningeal symptoms, that in all probability it is a case of tubercular meningitis. The finding of the bacillus is the sure and final test" and I think I have adduced evidence to show its discovery is not such a difficult and lucky chance, as it has been under the old method of searching films.

Even the methods of adding a sterile fleece were of little avail. Lenhartz who tried it had but one success in seven cases.

I might mention that in one case I found several tubercle bacilli in fluid which I had left in the incubator for a few days, in ordinary smears stained for the bacillus. I have since seen it stated (by Quincke) that Langer has used this method, which he calls "using the fluid itself for culture"; after four or five days in the incubator he has been able to demonstrate bacilli, which he could not do in the fresh specimen.

There is also the inoculation test with guinea pigs.

Recovery in tubercular Meningitis:

As regards treatment, it has been usually regarded as hopeless to expect recovery - the only

hope lying in the chance of a mistaken diagnosis. For as a rule - in all my cases - tubercular meningitis has been only a part of a general infection. But in at least two of my cases - one following directly after a severe fall on the head, with previous good health - the post-mortem findings showed that the meninges were far more affected than the rest of the body; the changes - naked eye - being slight elsewhere. Why should not trephining give a chance of recovery in such a case, if done early, as it seems to do in tubercular peritonitis?

In one of my cases (M.M.) in which symptoms pointed rather more to a tumour perhaps than to meningitis, the fluid on every occasion showed a high pure lymphocytosis.* It was before I learnt to examine the coagulum, but in a film I found what I thought to be one or two tubercle bacilli, one of my colleagues being more emphatic as regards its identity than myself. There was also double otorrhoea. Operation was performed lest an abscess were present; none was found, but a lot of clear fluid escaped; the symptoms improved, and she recovered from what seemed a hopeless condition. The meninges at operation seemed healthy - what was seen of them. The intense papillitis did not get better for some days after the operation, and the lymphocytosis persisted. Could this have been a

* See Figs.12 and 13.

tubercular tumour, the symptoms perchance being due to localised softening or haemorrhage, and relieved by trephining? or a tubercular meningitis improved by operation, as a tubercular peritonitis is by laparotomy? or one of the forms of non-septic meningitis met with in association with otitis media and resolving after removal of the focus of irritation? (radical mastoid operation was performed at same time as dura and brain were examined in this case); or was the lymphocytosis due to syphilis which was relieved by trephining?(antisyphilitic treatment was not used); or what Oppenheim calls localised tubercular meningo-eucephalitis? Recovery in tubercular meningitis has been recorded by several observers, chiefly on the continent.

Osler does not seem hopeful: "I have never seen a case which I regarded as tuberculous recover, nor have I seen post-mortem evidence of past disease of that nature. Cases of recovery have been reported by reliable authorities, but they are extremely rare and there is always a reasonable doubt as to the correctness of the diagnosis."

Yet he quotes Furbinger as removing 60 c.c. lumbar fluid in which tubercle bacilli were found, followed by relief of symptoms and recovery in a man.

Also Wallis Ord and Waterhouse as treating a case of tubercular meningitis with trephining and drainage with recovery.

Whitla believes she has seen one recovery but says " it may be regarded as universally fatal".

Emery says "at least one case has been cured by repeated punctures, acting by relieving high tension and removing toxins."

Quincke contents himself by saying "I will merely mention that Freyhan, Henkel and Gross proved that the disease does not always terminate fatally."

Cornet says "The termination of general military tuberculosis is death as a rule. Now and then a transition to a more chronic form occurs, and exceptionally recovery takes place. Since Freyhan and Henkel's observations, the cure of a bacteriologically determined meningitis must be admitted."

Reabold reports a case of tubercular meningitis with cure after repeated lumbar puncture. Symptoms were severe; tubercle bacilli being found in the spinal fluid and by inoculation of guinea pigs. Lumbar puncture was performed daily for nine days, then at intervals for three weeks.

Buchanan showed, at the Liverpool Medical Institution, a child as a case of recovery from tubercular meningitis. Illness lasted four weeks, coma

eight days; classical symptoms of tubercular meningitis; lumbar fluid showed lymphocytosis; no tubercle bacilli; no cocci found; Calmette reaction positive. He attributes recovery to injection of tuberculin, improvement following immediately after the first dose (1/4000th mg.), combined with lumbar puncture. He advises not more than 20 c.c. of fluid to be removed at a time. Here the diagnosis rests on Calmette's reaction and the spinal lymphocytosis, neither being conclusive.

Freyhan quotes a case of recovery from tubercular meningitis after repeated lumbar puncture.

Oppenheim states he has seen several cases of what he calls localised tubercular meningo-encephalitis which recovered. These he thinks may remain localised and become quiescent through cicatrisation, and mentions one or two cases seen post-mortem years after, in support of this contention. These cases may closely simulate cerebral tumour; operation and excision has been successfully performed in France, while Mayer saw such a case in which operation lit up an extensive tubercular infection with fatal result.

The case of mine quoted above as recovering after operation despite grave symptoms and lymphocytosis of spinal fluid may have been a case of this sort.

As regards the assistance to be obtained from Calmette's ophthalmic reaction, I can say nothing from experience. I never used it, other methods seeming more reliable; moreover, it is accompanied by a definite negative reaction (Eyre and others) and so may prejudice the case. The reaction is not to be relied on, and generally not obtainable, during the last week of life (Eyre). I have repeatedly seen it set up a troublesome rhinorrhoea, or conjunctivitis, or both.

Nathan Raw gives a good illustration of the difficulties that may be experienced in correctly applying the data obtained by lumbar puncture, in diagnosing between acute tuberculous meningitis and acute meningitis of other origin. He quotes two cases, both having polymorphs and lymphocytes in the spinal fluid. The symptoms in each were very similar and both were supposed to be acute cerebro-spinal meningitis; at that time epidemia. Meningococci were obtained in the fluid of one; no organism in that of the other, in which ample evidence of a tuberculous meningitis was vouchsafed post-mortem. I gather from the account given that tubercle bacilli were not looked for in the coagulum.

I have also seen two cases of tuberculous meningitis, which clinically were typical examples of ordinary posterior-basic meningitis, in each case diagnosed by lumbar puncture.

PNEUMOCOCCAL MENINGITIS:

Among the acute inflammations of the cerebro-spinal meninges, pneumococcal meningitis comes third in order of frequency. It may occur in epidemic form like pneumonia (Osler). At one time epidemics of meningitis really due to the meningococcus were attributed to the pneumococcus (Weichselbaum); this being partly due to cases of primary pneumococcal meningitis occurring in epidemics of cerebro-spinal meningitis, partly because the pneumococcus in meningitis tends to occur in atypical form and so was confused with the meningococcus (Weichselbaum).

The pneumococcus has long been known to be a cause of primary meningitis, cases being described by Weichselbaum in 1887 (Arkwright), who says the meningococcus and diplococcus pneumoniae are the two most frequent causes of primary meningitis.

As regards its diagnosis in lumbar puncture, there are several instances quoted where the lumbar

fluid has given no clue to the existing meningitis, which is in keeping with the clinical picture of the group of pyogenic meningitis, as these cases may show no clinical symptoms beyond some drowsiness, right up till the end; and I have seen two cases of pneumococcal meningitis, in which the absence of symptoms was so marked, that in the one case an experienced specialist in nervous diseases did not think meningitis existed, until nearly the end; while in the other, I could not find sufficient evidence to justify my wish to repeat the operation of lumbar puncture, which had given absolutely negative results four days before death.

Herringham quotes six cases of pneumonia ending fatally, in which well-marked pneumococcal meningitis was found post-mortem, of which only one gave any definite meningeal symptoms during life beyond some drowsiness which occurs in pneumonia quite apart from meningitis. Tooth records a case of pneumonia in which marked pneumococcal meningitis was found post-mortem and yet no meningitis was even suspected during life.

Failure to obtain any help from an examination of the lumbar fluid in cases of pneumococcal meningitis has been recorded by Ashby, the fluid being clear with no cocci, while there was intense head

retraction, and post-mortem, intense suppurative meningitis.

I have found the fluid negative in two cases, perhaps a third. In my two cases, quoted as having no definite clinical meningeal symptoms, one (Hg)*developed symptoms the day before death, when the fluid contained polymorphs and pneumococci, while in previous tapplings only a few lymphocytes were found. I suspected a septic meningitis because of an otorrhoea which had stopped; the lack of definite symptoms; the fluid obtained in lumbar puncture was a little increased and also the cells in it. The child then developed signs of consolidation of one upper lobe; as there was lymphocytosis of the spinal fluid, it might have been a case of tubercular meningitis. It was not till within 12 hours of death that the spinal fluid gave a correct indication of the existing condition. At post-mortem there was a dense collection of pus all over the vertex and sides in which pneumococci were found in smears and culture. The possibility of an abscess which had ruptured with consequent diffuse septic meningitis was entertained, but there was no evidence of this. In the other case (Gd) the fluid was normal except some increase in amount. Post-mortem four days later, there was marked meningitis, with copious

* See Figs 1 and 2.

yellow rather greenish effusion filling up the sulci, and swarming with pneumococci as obtained in smears and culture. This case had a localised patch of inspissated empyema and pyopericardium, and yet was sitting up, with no grave symptom - save an excusable irritability - until 12 hours of its death. The third case (C.J.) in which repeated negative lumbar puncture was performed, was a case of primary empyema - pneumococcal - in which severe meningeal symptoms had existed before admission, but which increased, with intense head retraction and irritability and restlessness; all of which were from time to time markedly relieved by withdrawal of large quantities of spinal fluid. This fluid was quite normal as regards sugar, and albumen, and no increase of cells were seen, only lymphocytes being obtained with difficulty. The fluid got less, the symptoms worse. A post-mortem was refused. Was it a serous meningitis? or septic meningitis, with closure of the cranio-spinal communication? The ophthalmoscopic examinations were persistently negative, only some doubtful haziness of the discs being noted; though optic neuritis may have been kept in check by the repeated lumbar puncture.

These cases quoted so far, have all been meningitis secondary to pneumonia, empyema or other

existing focus. The picture in primary pneumococcal meningitis is, I think, a different one. Here the clinical symptoms are marked and the lumbar fluid full of information. I can speak of two cases from experience and refer to one similar to these.

My two primary cases were quite well till they met with an accident. The one, a baby of eight months, fell off a high bed on to its head; cerebral symptoms set in that night, with recurrent fits, for which it was admitted, and it died on the third day of the disease, after being in hospital some 12 hours. The lumbar fluid* showed a very large polymorph leucocytosis with copious extra-cellular diplococci, found in smear and culture to be pneumococcus; a thick layer of pus covered the vertex at the post-mortem done that day. The other was a boy of nearly eight years who was knocked down and dazed by a collision with a bicycle, and fell off a wall on to his head next day. The following evening - having been quite well in the interval - he became drowsy. He was admitted for headache and fits on the fourth day and died a few hours after. He had a severe convulsion soon after admission, which was cut short by performing lumbar puncture, after which he was markedly easier; the fits recurred a few hours later, while I was at out-patients and he died before

* See Fig.3.

I could reach him. Here the lumbar fluid* was full of polymorphs and extra-cellular pneumococci, also some intra-cellular cocci taken to be pneumococci, which were obtained in culture from the spinal fluid, as also from the meningeal pus post-mortem.

Smears from the blood showed a high degree of polymorph leucocytosis and apparently cocci in the blood, in a few instances situated in the polymorph cells.

A similar case of primary pneumococcal meningitis, with positive evidence obtained from the lumbar puncture, was recorded in the Lancet.⁽¹⁾ In this case, as in my two cases, the ears were healthy.

There were three other cases in my series of pneumococcal meningitis (seven in all), one of which was almost a duplicate of the one with empyema, pyopericardium and normal lumbar fluid; this case was twice tapped with negative result; it also had a localised empyema. Of the other two, one was a basal pneumococcal meningitis, secondary to long existing mastoid disease, in which lumbar puncture gave a clue to the diagnosis, showing a large polymorph leucocytosis and extra-cellular pneumococci - not in large number. The remaining case I shall refer to again, as a case shewing the latency of

(1) Lancet, Vol. I., 1908, p.1694.

* See Fig.4 and 5.

pneumococcal infection, in which the spinal fluid was full of polymorphs and pneumococci.*

It is evident that lumbar puncture may give definite evidence or none at all. Out of seven cases, the lumbar fluid showed lymphocytes in one; clear fluid in two, if not three; an intense polymorph leucocytosis in four.

Forbes mentions eight cases of pneumococcal meningitis, with polymorph leucocytosis in three, scanty lymphocytes in two and normal fluid in two, though pneumococcal meningitis was found in these post-mortem. He also obtained pneumococci in culture in one case of tubercular meningitis. I also had one doubtful case of a similar mixed infection, mentioned under tubercular meningitis.

With reference to the occurrence of meningitis as a complication of pneumonia, it is apparently more frequent in America than on the Continent or in England. Osler says it is a "not uncommon complication", and is quoted by Babcock, and by West, as finding it in eight out of 105 cases. West had none in 200 cases of pneumonia. Hector MacKenzie found one case in ten years at St. Thomas' Hospital. Babcock says it is a more common complication in some epidemics than in others, and quotes Sello as having five in 750 cases; Aufrecht 10 in 1500 cases,

* See Fig.6.

and an epidemic at Basle, where there were three in 230 cases. Von Leyden says it is a very rare, and very fatal complication or sequel of pneumonia.

Hector MacKenzie mentions that complications, due to pneumonia, may occur at a long interval after the primary lesion: "it having been shown (Tizzoni and Panichi) that the pneumococcus may remain in the circulatory blood for days, weeks and even months". This may explain some cases of apparent primary pneumococcal meningitis. I have mentioned one case which I think is an illustration of this point. It was a boy, aet 2 years, who had been operated on for pneumococcal empyema a year before; he was admitted with indefinite signs in the chest. A radiograph suggested fluid, which we had already failed to find with the needle. The signs got better, but never disappeared, and he was sent out as probably tubercular. In ten days he returned with urgent symptoms and signs of pulmonary mischief, and then developed meningeal symptoms. Tubercular meningitis was diagnosed, lumbar puncture proving this to be wrong, by giving a large polymorph leucocytosis in which pneumococci were abundant.* A dense layer of greenish pus full of pneumococci covered the vertex at the autopsy performed the same day that he died. There was pus in one middle ear. He had never had

* See Fig. 6.

any ear symptoms or otorrhoea. The lungs showed no sign of pneumonic consolidation. The pleurae pericardium and all the thoracic contents were densely adherent; there was no pus in the chest; the lungs showing marked fibrosis. Was all this the sequel to the empyema over twelve months previously?

With regard to the frequency with which pneumococcal meningitis occurs, out of 50 cases of meningitis which I have seen during about seven months at a Children's Hospital, seven of these were pneumococcal, two being primary, no other lesion being found.

Forbes during four years at the Ormond Street Children's Hospital (1904-1907 inclusive) found pneumococcal meningitis nine times out of 142 cases in which lumbar puncture was performed.

Eyre during the same four years (1904-1907 inclusive) at Gay's Hospital, out of 168 cases (other than pneumonia) due to the pneumococcus, found pneumococcal meningitis 14 times, eight of these occurring in 1907.

He also quotes Turner (1907) as finding 17 cases to be pneumococcal, out of 70 cases of meningitis, occurring among native miners on the Rand (S. Africa).

Previous to this Wolff (1897) analysing the results of various workers, found that the pneumococcus was regarded as the causal agent in over 40 per cent of the total cases of meningitis.

Negroes are very much more susceptible to the pneumococcus than the white man, succumbing more easily to its infections (Osler, Eyre).

As in tubercular meningitis, so pneumococcal meningitis may exist without definite macroscopical evidence, as seen in Langdon Brown's case, where no naked eye meningitis was visible, yet the subarachnoid space was found to be teeming with pneumococci.

Recovery from pneumococcal meningitis, even when the organism has been found in the lumbar fluid has been recorded (Achard and Grenet; Concetti - two cases). It would seem that, like tuberculous meningitis, it is part of a general infection, for the coccus is repeatedly recovered from the spleen, as in three of my cases, and was seen in the blood in one of my cases. This would seem to be in keeping with the view that there is always some bacteraemia in pneumonia (Hadsworth, Banti, Prochaska, Rosenow) "even in mild cases of pneumonia" (Eyre).

Pneumococcal meningitis may, it seems, take on a chronic course, assuming a sero-fibrinous form (MacKenzie, Tooth).

I have quoted a case (M.M.) where double otorrhoea existed, and spinal lymphocytosis which recovered after radical mastoid operation and trephining, and which was strongly suspected of being cerebral tubercle or cerebral abscess. While convalescent and waiting to go out, I examined her spinal fluid to see if any change had occurred. This was 24 days after the operation. There was less fluid, but no diminution in the marked lymphocytosis; a few polymorphs were present - not seen before - and several(?) pneumococci extra-cellular.* Now I have on more than one occasion noticed these apparent diplococci resembling pneumococci,** and giving rise to no symptoms. This may be an example of the existence of organisms in the meninges, without necessarily producing a meningitis, as stated by Weichselbaum just as they are frequently found in the buccal cavity. I found what I took to be pneumococci in the pus from the ears, at the time of the operation. The swelling of the optic disc had not apparently quite gone down at the time of this last lumbar puncture. She was, however, apparently quite well, and her eye-sight unimpaired. I understand she has not had any further cerebral trouble (it is nearly a year since she left) having been seen at Hospital recently. A sister has since been under treatment for surgical tuberculosis.

* See Fig.13.

** See Fig.17.

Commandeur in a paper on suppurative meningitis occurring in pregnancy and its differentiation from eclampsia attaches great importance to the value of lumbar puncture. He states that it is only very rarely a complication of puerperal infection and that it is most often due to the pneumococcus.

MENINGITIS DUE TO PNEUMOBACILLUS:

The bacillus pneumoniae of Friedlander is mentioned as being found in meningitis by Weichselbaum and Oppenheim. But I have not been able to find mention of a definite case. One of my cases appears to have been an infection due to that organism.

H.P., aet 2 months, was admitted June 9th, 1908 for "difficulty in breathing". Some bronchitis was present, and signs suggesting asthma, expiration being noticeably prolonged. After about a fortnight with indefinite signs and symptoms, it developed head retraction, which got more pronounced and was accompanied by opisthotonus. The fontanelle being depressed, no definite signs of consolidation could be found, and the question of tubercular meningitis arose, but as it also had developed severe diarrhoea a few days before the cerebral symptoms appeared the cerebral symptoms might have been due to it ("hydro-

cephaloid"). Lumbar puncture gave a slight excess of clear watery fluid, at no increased pressure; albumen very slightly increased; a few doubtful leucocytes and some degenerated cells of no definite shape or structure. Fundi were normal, no tubercles visible. This withdrawal of fluid did not seem to confer any benefit. Two days later he began fitting, with definite squint, increased retraction and fontanelle still depressed, and died. The temperature had been normal or subnormal till the diarrhoea set in; it then rose slightly, rising higher till reaching 104° on day of lumbar puncture, after which it fell to 101° where it remained till death.

On further examination of the films from the above lumbar puncture, I found two very doubtful, degenerated, faintly staining polymorphs, no definite lymphocytes, and other cells apparently laked red blood corpuscles. The lumbar fluid was not cultured. Immediately after death, I performed lumbar puncture with sterilized syringe and needle and easily obtained a blood-stained yellowish turbid fluid which showed in smears numerous organisms which I at first took to be pneumococci, but which on more careful examination proved to be bacilli.* There were a few polymorph cells, but not a large leucocytosis, most of the cells present being lymphocytes and red blood

* See Fig.8.

corpuscles. It was not like a septic exudate and as apparently there was so large a blood contamination I did not take a culture, before making the films. These organisms proved to be gram-negative. At the autopsy, less than 24 hours later, I was present, and, expecting a septic meningitis, was surprised to find an absence of pus. The notes read: "Brain much congested all over surface; few nodules in Sylvian fissure (? tubercular); Large haemorrhage into lateral ventricle; pleurae nil; lungs - normal, some purulent discharge from bronchial tubes; liver fatty; spleen congested; no evidence of tubercle anywhere."

The meninges showed early meningitis - in the congestion and increased effusion noticeable in the sulci. These nodules were too opaque for tubercular tubercles; there were only three or four present, situated near the under surface in the Sylvian Fissures. I took careful smears and cultures of these; they were scarcely as large as the head of an ordinary pin.

Both smears and cultures proved them to be the same as the organism obtained from the spinal fluid. I then sent one of the films from the spinal fluid and cultures to my friend, Dr Milne, late Assistant in the Pathology Department, Edinburgh University.

I am much indebted to him for a careful examination of these, which, after several tests, he assured me he thought was "in every way a typical pneumobacillus, although it was mixed with a staphylococcus albus". He described it as "a bacillus, non-motile, gram-negative invariably, non-sporing. Two mice injected died in 24 hours. On potato it produced a white growth, and slightly coagulated milk".

The immediate cause of death was, probably, an extensive bilateral haemorrhage into the lateral ventricles; more pronounced on one side, and one or two small haemorrhages into the substance of the brain, as seen after the organ had been hardened. These probably accounted for the blood in the spinal fluid and for the cells seen in the first lumbar puncture.

Emerson has mentioned the fact that erythrocytes may take on the blue stain with Methylene-blue and be mistaken for lymphocytes. They may also become laked, and their significance be missed as in this case. The blood contamination in the second lumbar puncture might quite well have been due to local injury, it having been performed post-mortem, and with suction. This is the only definite case of meningitis due to the pneumobacillus that I have been able to find.

Arkwright has described an oval bacillus gram-negative obtained in lumbar fluid from a child of four months old. The fluid was clear, with a few leucocytes, mostly polymorphs, and a few streptococci; culture gave a gram-negative oval bacillus which liquefied gelatine. Post-mortem, no microscopic meningitis. (1)

MENINGITIS DUE TO DIPHTHERIA BACILLUS:

Cerebro-spinal meningitis due to the diphtheria bacillus has been recorded by Nash in a case of endocarditis with meningitis. The spinal fluid was obtained by lumbar puncture post-mortem, and was found to contain definite diphtheria bacillus of slight virulence both in culture and inoculation tests. The brain showed hyperaemia and some petechiae.

Morrell and Wolf report a case in which the diphtheria bacillus was isolated from the cerebro-spinal fluid during life and from the meninges at autopsy.

MENINGITIS DUE TO INFLUENZA BACILLUS:

Cases of meningitis occurring in Influenza have been frequent. Cases where the Pfeiffer's Bacillus

(1) Journal Hygiene, Vol.VII., 1907.

has been isolated from the cerebro-spinal fluid, or from the meninges are not so common. In most cases it has been accompanied by other organisms. Dubois and Weichselbaum have given instances.

Saundby, in an article on Cerebral Influenza, shows how all stages from congestion only to purulent meningitis may be met with.

Ortner mentions several cases of influenzal meningitis and gives references.

Pfuhl, Fraenkel and Hegerstedt have all found the bacillus in purulent meningitis. In one case lumbar puncture gave a fluid containing many polymorphs, and pure cultures of the influenza bacillus were obtained from it.

In this country, Douglas records a case wherein Pfeiffer's bacillus was obtained during life from the lumbar fluid in pure culture and from the meninges post-mortem. The lumbar fluid was yellowish, containing much albumen and many polymorphs. There was a considerable collection of pus over base and vertex of brain and along the spinal cord.

Dudgeon and Adams record a case of pyaemia, multiple arthritis and meningitis due to Pfeiffer's bacillus. Lumbar puncture only gave a few drops of turbid fluid from which a pure culture of the bacillus was obtained. The bacillus was also

isolated from the pus in elbow and hip and from the spleen. The brain showed purulent meningitis.

MENINGITIS DUE TO TYPHOID BACILLUS:

The bacillus typhosus has also been isolated from the cerebro-spinal fluid obtained by lumbar puncture.

Two cases have been reported, in which meningitis due to the bacillus typhosus has been found with no other discoverable lesion; no intestinal lesions.

In Lavenson's case Widal's reaction was negative at first, then positive; lumbar puncture gave bacilli, which proved in culture to be bacillus typhosus. Death occurred a week later, when pus was found over convexity of brain, yellow turbid fluid in ventricle, the bacillus typhosus being obtained from it. This case developed meningeal symptoms with rigidity, Kernig's sign and delirium - after nursing her brother with typhoid fever. At the autopsy there were no intestinal lesions, nor was the spleen enlarged.

Henry and Rosenberger also record a case of typhoid meningitis without definite intestinal lesions, beyond some enteritis. Lumbar puncture twice performed gave a turbid fluid, depositing pus cells

on standing; the bacillus typhosus being isolated from the spinal fluid and from the blood and from the pus obtained from the brain and spinal cord post-mortem. "The meningitis appears to have been a primary lesion due to the typhoid bacillus."

Epidemic cerebro-spinal fever and typhoid fever with meningeal symptoms may closely resemble each other (Curschmann) and each may give a positive Widal reaction.

Milligan reports such a case in which bacillus typhosus was isolated from the lumbar fluid obtained post-mortem in pure culture.

Gordon, at the end of his report on the meningococcus mentions an outbreak of typhoid fever in Norfolk in 1905, which clinically suggested epidemic cerebro-spinal meningitis. Swabs from the nasopharynx showed *M. catarrhalis*, while the lumbar fluid was clear and sterile. Examination of three fatal cases gave proof of its being typhoid fever, which was confirmed by the agglutination tests applied to others. A sample of blood from the cranial cavity of one case in culture gave bacillus typhosus in large numbers, and also a few colonies of what resembled *M. catarrhalis*.

A case has also been reported of typhoid fever complicated by cerebral injury, for which operation

was performed, it being found that a linear fracture of skull existed with extra-dural blood clot, and haematoma of scalp, all being septic, the bacillus typhosus being found in the pus in the haematoma and in the extra-dural clot. Lumbar puncture was negative; no increased pressure; negative in smears and sterile in culture - this was three days before operation. Blood count gave leucocytes 5000. Widal reaction positive; Diazo reaction positive; Kernig's sign present both sides; knee jerks absent. Some cervical rigidity was also present. Recovery ensued. There had been some injury to head a month before and again more recently. ⁽¹⁾

Rocaz and Carles, in a paper on meningitis occurring in typhoid fever in children, mention lumbar puncture as revealing purulent fluid with bacillus typhosus, alone or mixed with other cocci; transparent clear fluid containing bacillus typhosus which they state represents infected meninges; or clear fluid with lymphocytes, which they take to denote irritation of meninges by toxins; and clear fluid free from leucocytes, normal save in amount which is increased, denoting hypersecretion, probably due to irritation by toxins. They recommend lumbar puncture as a therapeutic measure in all these cases.

(1)"Annals of Surgery", January 1908.

It would appear that the meningococcus, the pneumococcus and the bacillus typhosus may all be found in the spinal fluid associated with a primary meningitis. To these may be added various gram-negative and gram-positive cocci, resembling the meningococcus, and a new organism - the leptothrix - described by Stuart McDonald.

Organisms found in the lumbar fluid associated with a meningitis of secondary origin are numerous, and include:- the Bacilli of Diphtheria, Influenza, Typhoid and Pneumonia (Friedlander), Anthrax, the Bacillus Enteritidis of Gaertner; and especially the Tubercle Bacillus; the Gonococcus, Staphylococcus, Streptococcus, Pneumococcus, Micrococcus Rheumaticus and Streptothrix of actinomycosis; and perhaps the leptothrix mentioned above.

These organisms may be causal of the meningitis in the cases where they exist in the spinal fluid; or they may be terminal, or secondary infections only.

Meningitis due to these organisms may exist without their being found by lumbar puncture in films or in culture, or even rendering the lumbar fluid abnormal.

Many of them may set up a leucocytosis of the lumbar fluid resembling epidemic cerebro-spinal

meningitis, and, since most organismal forms of meningitis are cerebro-spinal in distribution, they may all cause symptoms simulating the epidemic meningococcal meningitis, especially when they occur during such an epidemic.

The cytology of the cerebro-spinal fluid is not the same in the case of all these organisms - notably in tubercle and syphilis, which usually give a lymphocyte type of effusion.

A mixed infection of the meninges may occur and may be accountable for abnormal types of effusion.

It is possible (Weichselbaum) that organisms may be present in the meninges without causing an inflammation.

Meningitis may result from microbic invasion ending fatally and leaving no naked eye evidence, the microscope being necessary to reveal the actual pathological condition.

A leucocytosis of the cerebro-spinal fluid has been described, resembling that due to septic organisms, but in which no organism can be found by any method, and which has, therefore, been termed a "sterile puriform effusion". These cases are said to be distinguished by the "intact" condition of the cells.

In all cases where the existence of a microbial meningitis is suspected, the lumbar fluid should be cultured, no matter how normal it may appear, 5 to 20 c.c. being used for this purpose (Hewlett).

The trypanosome of Sleeping Sickness has also been found in the fluid obtained by lumbar puncture (Castellani and Bruce; Broden and Rodhain).

LUMBAR PUNCTURE IN VARIOUS CONDITIONS:

Lumbar puncture has been tried in various conditions, some of which are associated with diseases of the brain, of the cord, or conditions simulating these.

MENINGISM OR PSEUDOMENINGITIS:

Meningism or pseudomeningitis - to which I have already referred - is an interesting condition met with chiefly in children, in the early stages of the specific fevers, and especially in apical pneumonia. It is barely mentioned in the text-books and is apparently considered to be a purely functional and transient condition, and beyond its liability to simulate a true meningitis of no importance.

Tylecote in a long paper has tried to put it upon a more scientific basis and offers the following definition of meningism. "A functional condition caused by the selective action on the meninges and cerebral cortex of the toxins circulating in the blood in various diseases". Similar symptoms, more severe and persistent, are seen in other cases, where post-mortem no naked eye evidences of meningitis are discernible. He divides cases with such similar symptoms into organic and functional. For instance, otitis media, or erysipelas of scalp, may set up meningitis by direct extension of the hyperaemia; this he calls organic; or meningitic symptoms may arise from the action of toxins circulating in the blood - this he would put in the functional group.

Similarly mumps may be accompanied by a definite, even fatal meningitis - an organic illustration; or, as is more often the case, be accompanied at its outset by a transient cerebral irritation - or meningism - which he would call functional.

Meningeal symptoms simulating organic meningitis are frequently seen in children with specific fevers, especially scarlet fever, diphtheria, influenza, typhoid, mumps, and in pneumonia, especially if apical; while a practically similar condition is seen accompanying otitis media.

The question is, are these functional, or are they merely early stages of what may progress, till they ultimately develop into unmistakably definite meningitis?

Dupre in 1894 gave the name "meningism", others "pseudo-meningitis", to these symptoms.

Clinically it is distinguished by occurring at the onset of one of the above diseases; often before definite physical signs are present; marked head retraction; restlessness and irritability and perhaps twitchings; absence of the changes in pulse and temperature seen in true - that is well-established - meningitis. Lumbar puncture gives relief; the fluid being increased, but otherwise normal. Kernig's sign is absent.

Now Thomson says Kernig's sign may be present in this condition, while it may be present in other conditions than meningitis, as well as absent in many cases of undoubted meningitis. Lumbar puncture does not by any means always give an abnormal fluid in true meningitis, especially if early in the case. It often gives temporary relief in hopeless cases of meningitis. Cases of true meningitis are said to recover sometimes, partly as the result of lumbar puncture. Moreover, we can trace all stages in some diseases between a mere serous condition of the

meningeal exudate - sterile and devoid of leucocytes - to a definite purulent condition, as has been done by Rocaz & Carles in typhoid fever and Saundby and others in cerebral Influenza. The condition would appear to be closely allied to serous meningitis, or some forms of that condition, as that seen in otitis media (Ballance).

The grounds for calling it functional are that it often completely and quickly clears up; it may be unaccompanied by naked eye changes post-mortem; and that definite changes are not seen in the lumbar fluid. Several cases have been recorded above under tuberculous meningitis, where various kinds of meningitis have existed without naked eye evidence, even when there has been a fatal termination.

Is it not justifiable to suggest that many of these cases are early or abortive cases of what might have proved definite meningitis?

With regard to meningeal symptoms in pneumonia, Jean and Cardamatis appear to hold that meningism and meningitis differ pathologically only in the degree of the intenseness of the infection - in other words, they do not regard it as a merely functional condition.

Nobecourt and Voisin apparently hold much the same opinion, attributing the symptoms to varying

conditions as regards virulence and number of the germs and their toxins and the condition of the soil.

Buzzard quotes these same authors, as interpreting their investigation of the spinal fluid in cases of pulmonary disease in children, as frequently showing a condition of congestion and oedema of the meninges to be present, and as suggesting that in these diseases, raised fluid tension may account for some of the cerebral symptoms.*

Jacobi also believed that hyperaemia and some oedema may be the cause of cerebral symptoms in pneumonia.

But cases which have died with fulminant meningitis may only show hyperaemia and slight increase of fluid, which appear to be the first stages in a bacterial meningitis.

Oppenheim, speaking of this condition of "pseudomeningitis", says: "The symptoms are similar to meningitis, but terminate in recovery, or, at autopsy, negative a purulent meningitis and show either no alteration or only oedema, hyperaemia or a serous exudate. In some cases a toxic cerebral disease was probably the cause; in others the course was too foudroyant to allow of a purulent stage being reached, while in others it was a serous meningitis."

* See case described postea p.207.

I have performed lumbar puncture in several children who presented marked meningeal symptoms, with no definite physical signs: several of these proved to be pneumonia; one (A) had otorrhoea, appeared very septic, had early changes in the optic discs and was said to be typhoid eventually, as the cerebral symptoms soon disappeared. But the Widal reaction was negative. Another (B) never developed anything definite and went out apparently well; one (C) proved to have a small pharyngeal abscess - though the marked retraction persisted for some time.

All these gave clear, watery fluid, nearly always in appreciably increased amount, sometimes even spurting at first; occasionally the albumen seemed very slightly increased; very rarely could any cells be seen. There was a slight lymphocytosis in cases B. and C. quoted above. They nearly always seemed better, less irritable and slept after it. I have also obtained similar fluid from cases which have proved to be septic or tubercular meningitis.

There is also a condition met with in acute diarrhoea, simulating meningitis - "pseudo-hydrocephalus" (or hydrocephaloid condition) - which is said to be distinguishable from meningitis by the depressed fontanelle; but I have found a slightly depressed fontanelle in two cases of meningitis - one

tubercular. Lumbar puncture in these cases is a fatal mistake; the condition is due to want of fluid. These cases may show some slight milkiness of the membranes at autopsy. I have seen it in two cases; one I lumbar punctured as the fontanelle was not appreciably depressed and the diarrhoea had stopped and the symptoms were equivocal. The fluid was normal and came very readily. It is a condition of "arterial anaemia of the brain" (Ashby).

Serous meningitis is in some of its forms closely allied to this condition of meningism - I refer to such conditions as cerebral influenza, cerebral rheumatism, the so-called serous meningitis sometimes met with in otitis media.

Here, also, we get distinct meningeal symptoms, and a spinal fluid that is normal or only increased in amount.

Ballance in speaking of lumbar puncture in otitis media notes that we may have cerebral symptoms and various kinds of spinal fluid. It may be purulent; it may be clear and form a coagulum on standing - these indicate the presence of actual meningitis; but if the cerebral symptoms are due to meningitis serosa benigna, we find a clear fluid, increased in amount and pressure, containing no cells and its removal followed by an amelioration of the symptoms

which may occur without its removal. If the mastoid be operated on the symptoms may now entirely clear up; otherwise, if the septic focus be left, it may develop into a septic meningitis. Oppenheim says much the same.

Saundby, in an exhaustive article on Cerebral Influenza, shows how one may find gradually increasing conditions, beginning with mere congestion, no naked eye meningitis; then early macroscopic meningitis merging into purulent meningitis. Does not this explain why "some recover despite severe meningeal symptoms?" because the process has been arrested in an early stage.

Moorhead, on the same subject, records a case with cerebral symptoms and clear fluid obtained by lumbar puncture and sterile.

Rocaz and Carles in recording the value of lumbar puncture in meningitis occurring in typhoid fever in children, say that lumbar puncture may reveal clear fluid, perhaps issuing in a jet under high pressure, with no cells in it, denoting hypersecretion and probably irritation by toxins; or again clear fluid with abundant cells, generally lymphocytes, denoting meningeal irritation by toxins; or transparent or turbid fluid with the bacillus typhosus present in it; or even purulent fluid. In all these cases they hold that lumbar puncture does good.

Hoppe writing upon cerebral rheumatism believes the symptoms are due to toxins and says one may find a serous meningitis. I have not found any account of lumbar puncture performed in this condition.

It would seem as if there were some similarity between this condition of meningism and idiopathic pleurisy and hysteria. The unaccountable appearance of fluid in the chest - apparently giving rise to no symptoms and mysteriously disappearing - has now a more definite place in medicine and is generally associated with tubercle; while what has been regarded as functional, and so put down to hysteria, has too often proved to be a cerebral tumour, or disseminated sclerosis.

The increased fluid in these cases, the occasional suspicion of an increase in the lymphocytes and the amount of albumen, all suggest some slight change in the meningeal exudate, quite compatible with the views I have recorded - of hyperaemia, slight oedema, and increased secretion due to the hyperemia or to irritation by toxins. This, it would seem, is the first change. If now the organism arrive, the soil is prepared, and all is ready for a still further stage in the process, so that we may get a definite purulent meningitis - arising as a later stage of what we call meningism.

This is well seen in otitis media where on removing the septic focus or where the pus has found its own exit through the perforated tympanum, the cerebral symptoms clear up, the irritant focus having been removed.

I am inclined to think there may be a gradual transition from meningism with its hyperemia to serous meningitis, with its increased, still serous, exudate, to meningitis, without naked eye pus, but microscopic evidence of bacteria, till finally we arrive at an evident purulent meningitis; the course taken depending on the organism, its virulence and numbers and upon the soil.

On the other hand, the infection may be so virulent, or the resistance so feeble, or both these conditions prevailing, that a foudroyant meningitis may be the result; or rather a fulminant infection, since there is hardly time for more than an early meningitis to develop, still less pus. Rocaz and Carles maintain the cerebro-spinal fluid is a bad culture medium for bacteria. This may account in part for purulent meningitis not being more frequent than it is.

It must be remembered, however, that absence of visible meningeal changes does not negative the existence of bacteria in the exudate, as in Langdon

Brown's case of "cerebral pneumonia" which at autopsy showed no naked eye appearances to explain the symptoms, through microscopical examination proved the meninges to be teeming with pneumococci.

HYDROCEPHALUS:

Hydrocephalus may be acute or chronic. The ordinary chronic form may be congenital or acquired, probably it is generally due to some previous meningitis, which may have missed detection, and which has caused the occlusion of the foramina of Key & Retzins or of Magendie (Hildesheim). I have had one such case, and several where it was known to follow after meningitis, while in one there was a condition probably of concealed hydrocephalus and some mental deterioration in a girl of eight who had had apparently posterior basic meningitis in infancy.

Chronic hydrocephalus may give normal fluid in large amounts, if the foramen of Magendie is patent; or it may show some degenerated cells or cells containing droplets of myelin. I never found anything that could be called diagnostic in the fluids I examined, though I did once or twice find some debris of apparently degenerated cells, in fluid otherwise normal, save in its increased amount.

I have already, when discussing the significance of the presence of polymorphs in spinal fluid, mentioned a case of hydrocephalus admitted about a month after acute meningitis. In this case the meningitis had been missed and it had been treated for vomiting. The fluid in this case contained some lymphocytes and on one occasion a large number of polymorphs. It was an early stage in the transition from acute to chronic hydrocephalus. While in the case of some eight years standing; there was increased amount, no increase in albumin, clear watery fluid, which when centrifuged gave "no cells but some apparent cellular debris". Another case of some four months standing gave as much as three and four ounces of clear, watery fluid, with no increase in albumin, and once some pale degenerated cells, with no definite structure, some of them looking as if they contained the remains of other cells or droplets of myelin; sometimes a few lymphocytes or endothelial cells were visible.

Acute hydrocephalus has been applied to that variety of acute tuberculous meningitis accompanied with marked ventricular effusion (Turner).

ACUTE SEROUS MENINGITIS:

Oppenheim has described a primary idiopathic hydrocephalus, the acute serous meningitis of Quincke, to which is allied the acute transitory serous exudation which Quincke has called angio-neurotic hydrocephalus. *

Acute serous meningitis is apparently a simple serous inflammation of the intracerebral pia - an ependymitis - (Quincke). At first it was supposed to be non-parasitic, resembling idiopathic pleural effusion; but as Quincke remarks, the organism may not be discovered though present.

Some of these cases become subacute and show exacerbations after long intervals (Osler, Quincke, Oppenheim). They are often remarkably benefitted by lumbar puncture, either a simple puncture or repeated; optic neuritis and the ordinary symptoms of meningitis may be present; or it may exactly simulate cerebral tumour, but there is little or no pyrexia. The tendency is to complete recovery, and probably many cases of cured tubercular meningitis, or of cerebral tumour were really this disease. Redlich says "What stamps this serous meningitis characteristically, however, is its curability, either spontaneously or after lumbar puncture; its pathology still requires elucidation". The exudate is normal

save increased in amount, with no cells. If the albumin is increased it is probably a form of hydrocephalus due to stasis, from pressure effect of tumours or the hypersecretion caused by the presence of tumours or blood clot. (Quincke, Oppenheim).

Angio-neurotic hydrocephalus is a very transient form of acute serous exudate, which Quincke likens to angio-neurotic oedema of other parts. This acute and transitory condition is eminently benefitted by lumbar puncture, giving a normal but increased fluid.

Lumbar puncture in serous meningitis may throw some light on the condition of things, for high pressure indicates existing hypersecretion, and large amount of fluid suggests dilatation of the cerebrospinal cavity, which means cure is yet some way off; though it may occur spontaneously after a considerable period, or show an intermittency, with exacerbations at long intervals. The significance of increased albumen content has been already mentioned.

Conditions in which serous exudate is increased:

Increased serous transudation into the subarachnoid spaces and into the ventricles occurs in sinus thrombosis and compression of the superior vena cava and temporarily in epileptic attacks, causing increased lumbar pressure (Quincke, Nolke, Braunstein).

Increased serous fluid is also found in lead colic and uremia in which the pressure may or may not be raised, and in chlorosis - where it may be due to sinus thrombosis (Lenhartz, Hawthorne) - and in syphilis where we may have a serous meningitis. In all these we may obtain a normal fluid with or without an increase of pressure, and with sometimes marked amelioration of the symptoms.

Harris reports a case of serous meningitis, with severe symptoms optic neuritis, with recovery after trephining and incision of dura with escape of serous fluid.

I have had one such case. A girl, aet 1 year, 8 months, who was shown at the Children's Society in London, as a case of recovery from encephalitis.⁽¹⁾ She had symptoms of meningitis, with marked optic neuritis, some squint and screaming fits; also that extraordinary voracious appetite seen in cerebral cases, which are not unconscious. This child improved markedly after lumbar puncture, the fluid on two occasions spurted, was quite normal and contained no cells, and was sterile in culture. I saw this child some two and a half months later and kept her in Hospital for a few days, to re-examine her spinal fluid. It again spurted; there was no increase in albumen, it was quite clear and contained no cells. It was then a different child - bright, happy and

(1) Lancet, Vol. I., 1908, p.1213.

apparently quite well. It had lost its insatiable appetite and only very rarely indulged in apparently causeless screaming fits. The optic discs appeared normal.

I have recently heard of a similar case in a Cottage Hospital here. It was supposed to be a miraculous recovery from tubercular meningitis; lumbar puncture was not performed.

I have already referred to a case (C.J.) under pneumococcal meningitis. It was admitted for meningitis and was found to have an empyema which was operated upon and found to be pneumococcal. The boy had severe meningeal symptoms, but the fluid, though increased, was normal, unless the sugar were reduced - it was present - no cells, no increase of albumen was found, nor definite ophthalmoscopic changes. Lumbar puncture always gave temporary relief. A post-mortem was refused. Was this a serous meningitis complicating empyema, or pneumococcal meningitis with clear spinal fluid, perhaps due to some closure of the connection between the brain and cord?

Localised serous spinal meningitis:

A localised serous spinal meningitis has been recorded with recovery after laminectomy (Mendel, Adler), and after lumbar puncture (De Montet) which

showed a mixture of a few polymorph and lymphocyte cells, and sterile in culture.

Krause has described eight cases presenting the symptoms of tumour of the spinal cord. He found localised collections of fluid in the spinal arachnoid, after escape of which recovery was complete. He ascribes these collections to inflammatory adhesions, proving the existence of what he calls "meningitis serosa spinalis".

I have already referred to a lymphocytosis of the spinal fluid found in zonular meningitis or localised spinal meningitis described by Chauffard, which to me suggests the girdle pains and lymphocytosis of tabes.

Also a case of localised cervical spinal meningitis with spinal lymphocytosis, occurring in a case of mumps (Picard).

LUMBAR PUNCTURE IN CEREBRAL TUMOUR:

In cerebral tumour and cerebral abscess lumbar puncture does not convey much information and is, moreover, fraught with danger: in the case of abscess lest it be thin-walled and burst as a result of lowered intracranial pressure; in the case of the tumour lest it be in the posterior fossa and cause pressure

on the medulla, as the result of a sudden diminution of intracranial pressure; or lest haemorrhage occur from vessels weakened by the neoplasm. These dangers have been referred to early in this paper.

In tumours, as a rule, the lumbar fluid shows only some increased pressure or amount, the result of hypersecretion, or of increased venous transudation, owing to its pressing on the veins of Galen; or to impeding the escape of the cerebro-spinal fluid, by pressure on the outlets of the subarachnoid spaces.

Stewart says lymphocytes may occur even in deeply seated tumours, and mentions a deep-seated glioma causing a lymphocytosis amounting to 75 cells in a single field.

Acute serous meningitis may often closely simulate a cerebral tumour (Oppenheim, Redlich, Quincke).

There may be slight increase in the albumen which may distinguish between tumour and hydrocephalus (Oppenheim). The albumen is more often increased when the fluid is due to venous stasis and transudation. The effects of a tumour vary with its position; consequently the findings in lumbar puncture also vary with the position of the tumour.

Lumbar puncture in cerebral abscess:

Cerebral abscess acts mechanically, like a

tumour. Lumbar puncture can only reveal increased pressure, if that is present.

Forbes records two cases of cerebral abscess of the temporo-sphenoidal lobe, showing a few degenerated cells in once case; a "faint haze" of albumen and a few leucocytes in the other; both fluids being sterile and abscess found in both cases; also three cases of cerebellar tumour - "probably tubercular" - giving a few lymphocytes, sterile in culture.

Langdon Brown has recorded a case of cerebral abscess of the frontal lobe, the lumbar fluid being light yellow containing a few lymphocytes and sterile in culture, the abscess pus giving pure culture of streptococcus. (1)

If there is a localised meningitis associated with the abscess, we may then get the fluid altered as in meningitis.

If the abscess be rapidly forming, without a capsule, with surrounding inflamed and softening brain substance, we may get some leucocytosis of the fluid.

Maiella of Naples has studied the cyto-diagnosis of cerebral abscess, cerebral compression and meningitis (septic) in dogs by lumbar puncture. He believes all forms of acute meningitis give rise to polymorph leucocytosis. Cerebral abscess caused no

(1) St. Bart's Hosp. Journal, June 1907.

change if deep; slight polymorph leucocytosis if near surface; marked polymorph leucocytosis if cortical encephalitis were present. A very acute staphylococcal meningitis might give rise to only a slight excess of cells, if death occurred in two or three days; if life prolonged to a week, a large leucocytosis, mainly polymorph, resulted. Cerebral compression appears to cause increase of fluid, with some polymorphs present the first two or three days, these passing off in less than a week, leaving a normal fluid.

An extra-dural abscess will not give a septic lumbar fluid ⁽¹⁾ just as extra-dural haemorrhage will not give blood cells in the spinal fluid as long as the arachnoid remains intact.

Lumbar Puncture in otitis media with intracranial complications:

The study of the results of lumbar puncture in otitis media is full of interest. The intracranial complications are so important, so difficult to diagnose and often so latent that any aid to diagnosis is welcome.

The chief complications are meningitis - serous and purulent; abscess - extra-dural and cerebral; and sinus thrombosis.

(1) Annals of Surgery, January 1908.

Lumbar puncture may help in diagnosis; it may do harm. It may do harm by causing the diffusion of a localised purulent meningitis, or causing the rupture of a thin-walled abscess.

It may do good by removing fluid in acute serous meningitis and so relieving tension (Ballance); it may by removing fluid, remove also bacteria and their toxins and so prevent a fatal issue (Barker).

I have already shown that a normal lumbar puncture does not negative an active septic meningitis; also that there is little or no help to be obtained from the results of lumbar puncture in diagnosing cerebral abscess.

In cerebral abscess, lateral sinus thrombosis and serous meningitis, we generally obtain clear normal fluid, increased in pressure and amount, but not always (Chavasse & Mahu).

Ballance says the lumbar fluid may be turbid with a polymorph leucocytosis, or clear, forming a coagulum on standing; these denote meningitis - almost certainly septic.

Or the fluid may be clear, serous, devoid of cells, increased in amount and tension, and followed by relief of symptoms. This he calls meningitis serosa benigna; if the septic mastoid be left this may develop into a purulent meningitis.

On the other hand, we may get a serous effusion in fulminant septic meningitis -meningitis serosa maligna - where resistance has not been sufficient to cause pus formation. Maiella found this also in experimenting with dogs.

As a rule, clear normal fluid, increased in tension and in amount, is taken to indicate serous meningitis, the prognosis being good.

Harvey Cushing recommends when this fluid is found, whether on trephining or by lumbar puncture, not to be too persistent in looking for an abscess, the removal of the fluid being often followed by relief of symptoms.

Ballance quotes a case of otitis media with cerebral symptoms, in which he found by lumbar puncture, abundant polymorph cells: operation revealed temporo-sphenoidal abscess and rapid recovery.

Wilkinson quotes a case with marked cerebral symptoms pointing to an abscess; lumbar puncture revealed a turbid fluid; radical mastoid with exploration of dura revealed no meningitis, the patient recovering rapidly.

I referred to these cases before when speaking of the aseptic puriform effusions of various French observers who believe that an aseptic puriform cerebro-spinal fluid may be caused by the toxins of a

localised septic focus acting at a distance from that focus.

Barker records two cases of otitis media with cerebral symptoms; in one case due to septic meningitis in temporal region; in both purulent lumbar fluid was obtained, containing *M. catarrhalis* in one; and a bipolar-staining red, which could not be cultured, in the other. These were operated on and lumbar puncture done repeatedly, the organisms becoming less numerous and finally disappearing from the fluid, which remained full of polymorphs for some time though sterile. Towards the end the lymphocytes became more numerous, though occasionally a temporary increase of the polymorphs occurred, without bacteria being obtained. A third case of acute streptococcal infection died.

Potts records a case of mastoid disease with very severe cerebral symptoms which cleared up entirely on performing the radical mastoid operation. Some of these cases may be cases of extra-dural abscess, which is drained by the operation on the mastoid.

I have only had one case of otitis with complications. This was a boy who had been operated on for mastoid disease in 1902, 1905 and March 1908, without a complete cure. Cerebral symptoms set in April 22nd, 1908 - vomiting, drowsiness, temperature 104

and severe headache. I performed lumbar puncture in the afternoon of April 25th, and found a large polymorph leucocytosis and a few extra-cellular pneumo-cocci. The fluid was turbid, in excess, but not much increase in pressure. The polymorphs seemed unusually well-preserved and the lymphocytes numerous. Cultures showed similar gram-positive diplococci. That evening the dura was exposed and found apparently healthy; the brain was explored for an abscess and none found. I suggested a basal meningitis. I was not permitted to repeat the lumbar puncture and the boy died April 29th. At the post-mortem, a basal septic meningitis was reported, with diplococci resembling the pneumococcus.

In otitis media with cerebral symptoms, lumbar puncture may give clear serous fluid in a variety of conditions: cerebral abscess, sinus thrombosis and meningitis - generally non-bacterial, but sometimes even when septic. Turbid fluid with leucocytes may be due to septic meningitis, or even to abscess, without meningitis (Ballance, Massary, Weil). Even when due to septic meningitis recovery might ensue, especially if the septic focus be removed and the meninges and spinal arachnoid be drained (Ballance, Oppenheim, Barker, Curtis).

Lumbar puncture may reveal a serous fluid, increased in amount, sometimes in pressure, generally devoid of cells, in various cerebral conditions - meningism, acute serous meningitis and angio-neurotic hydrocephalus (Quincke), chronic hydrocephalus, sinus thrombosis, compression of superior vena cava and temporarily during epileptic attacks: cerebral tumour - where there may be some increase in albumen and some lymphocytes, especially if cortical: intracranial blood clot - where the fluid may be tinged by pigment, which may be defined with the spectroscope: cerebral abscess, non-purulent serous meningitis associated with otitis media: chlorosis, uraemia and lead poisoning.

Lumbar Puncture in Cerebral Injury:

There are cases on record to show that lumbar puncture is of use both in diagnosis and treatment in cases of cerebral injury. Cases found unconscious often prove difficult to diagnose at first. Lumbar puncture has in some cases helped to elucidate the problem.

Fractured skull has been diagnosed by the discovery of blood in the spinal fluid, which is also present in traumatic laceration of the brain itself (Ballance); and in ordinary cerebral haemorrhage

when it may help to distinguish from cerebral thrombosis (Purves Stewart). Cathcart has reported a case where lumbar puncture led him to operate in a case of cerebral injury with haemorrhage; the clot removed and the bleeding stopped, recovery ensued. Spick found polymorph leucocytosis in a case of cranial injury with haemorrhage in which he trephined and removed a clot, lumbar puncture being continued for some days. This polymorph leucocytosis agrees with Maiella's experiments with dogs, where he found there was a polymorph leucocytosis for the first few days of cerebral compression.

Chauffard distinguishes between meningeal haemorrhage, due to haemorrhage from a damaged meningeal arteriole with pressure on the subjacent brain - where he says the prognosis is good - and cerebro-meningeal haemorrhage, where a cerebral haemorrhage finds its way into the subarachnoid space, and so colours the spinal fluid. Lumbar puncture in these cases gives fluid under pressure, of a pink colour, containing a large number of red blood corpuscles and a few white cells. He distinguishes between cerebral haemorrhage and softening of the brain, by finding pink coloured lumbar fluid in the former. Similarly between cerebral haemorrhage and uremia, in both of which albuminuria may be present.

Cerebral syphilis, cerebral haemorrhage and uremic coma all may have albuminuria present: lymphocytosis will point to the first, pink fluid with red cells the second. Similarly diabetic coma and cerebral haemorrhage may show some glycosuria. He quotes a case where this was present, disappearing in a few hours, after removal of pink stained lumbar fluid.

At a discussion on this subject at the Société de Chirurgie of Paris (1906) Quénu, Potherat and Ferrier all spoke of the value of lumbar puncture in the diagnosis of cerebral injury, especially fractured skull and of its benefit.

Rochard questioned the presence of blood in lumbar fluid as being diagnostic of fractured skull, as he had found it in cases proving to be only "cerebral commotion".

It would seem that the identification of blood in the spinal fluid is of diagnostic value, but it is not easy to be sure it is not due to the operation itself. The methods of distinguishing the source of the blood were discussed earlier in this thesis.

It is necessary to be most careful to remove only small quantities of fluid at a time, especially soon after an injury or haemorrhage, lest it be re-started.

Quinke states that the presence of a haemorrhage sets up increased secretion of cerebro-spinal fluid from cerebral irritation, causing increased intracranial pressure which lumbar puncture relieves.

Lumbar puncture in Uremia:

In uremia several cases have been recorded where lumbar puncture has had a good effect. The fluid may be increased in amount and sometimes in pressure. Emery states it shows marked changes in its urea percentage, freezing point and percentage of chlorides which allow of a very reliable test of the functional capacity of the kidneys.

In uremia the urea may be raised from .035 or .04 per cent at normal, to .4 per cent: the freezing point from $-.56^{\circ}\text{C}$. is lowered appreciably: the chlorides from .7 per cent, being raised to as much as 1 per cent.

The description of an aseptic puriform effusion in uremia has been already described (Caussade and Willette; Chauffard).

Lumbar Puncture in Epilepsy:

In epilepsy there may be lymphocytosis. Merzbacker found lymphocytosis in six out of 12 cases; four of these were traumatic epilepsy and the

lymphocytosis very slight in the other two. Vorkastner has found a slight lymphocytosis after an attack.

Purves Stewart regards the presence of lymphocytosis as diagnostic of general paralysis with epileptiform attacks, from ordinary epilepsy.

Donath reports finding chölin increased in epileptics. Halliburton, however, questions Donath's results.

Richenol and Castin report a very severe case of status epilepticus in which lumbar puncture was done five times; tension being very high, the fluid showing no special features, temporary relief following its removal.

Lumbar puncture in Landry's paralysis:

In Landry's paralysis various organisms have been cultivated from the spinal fluid (P. Stewart). Buzzard is quoted by Osler and Warrington as finding a gram-negative tetracoccus in the spinal fluid in this disease.

Lumbar Puncture in acute anterior poliomyelitis:

In acute anterior poliomyelitis "various organisms have been found by various observers in the spinal fluid, but so far no single organism can be

regarded as specific" (P. Stewart). In seven cases out of 26 in which lumbar puncture was performed in a recent Australian epidemic, cultures of cocci in pairs and tetrads were obtained, giving a pale yellow growth and non-pathogenic to rabbits and guinea-pigs. Smears showed extra-cellular cocci, generally as diplococci, and staining feebly. These results are stated to be analogous with those obtained by Geirswold in the Norwegian epidemics. ⁽¹⁾

I have performed lumbar puncture in four cases of this disease. Two of these cases "J.A. and "L.W." were admitted as cases of meningitis, which they closely simulated.* "J.A." got much better but died of respiratory paralysis apparently. "L.W." was regarded as tubercular meningitis for some days and her fluid carefully examined for tubercle bacilli - in vain! "A" was lumbar punctured about the fifth day of his illness.** His legs and intercostals were affected; there was no suspicion of meningitis.

"K" I examined about the 21st day of his illness. There was a remarkable similarity in all these cases. The fluid was increased in all except J.A.; it actually spurted in "K" and it was increased more in the last tapping done on "L.W." than on the others (there was an interval of three weeks between the first and last). There was a distinct lymphocytosis in all;

(1) Lancet, Vol. I. 1909, p.999.

* See Page 207.

** See Fig.11.

most marked in "L.W." and "A" in which it resembled films from tubercular meningitis. They all reduced Fehling's solution. Albumen was not increased; culture of fluid from "L.W." was sterile on nasgar, agar and Couradi-Drigalski medium.

Culture from "K" gave a strong growth, on nasgar, and on Conradi-Drigalski medium, of a gram-negative bacillus staining irregularly, giving a bipolar appearance. I sent this culture for further examination and identification, but it arrived too late, and as I was leaving the Hospital I could not keep the culture.

These cases are too few for any deductions to be drawn from them. Cultures were not taken from "J.A." and "A".

Buzzard also mentions the occurrence of lymphocytosis in acute anterior poliomyelitis.

Lumbar puncture in pregnancy:

In pregnancy lumbar puncture may be used to diagnose between eclampsia and meningitis. Meningitis is rare as a complication of puerperal infection; in pregnancy it is generally pneumococcal (Commandeur). The same symptoms, as seen in meningitis, may be met with in eclampsia. In eclampsia the spinal fluid is usually clear and transparent;

it may be tinged yellow by biliary pigment and occasionally blood-stained.

In meningitis it is usually turbid, with leucocytosis and containing the causal organism.

Lumbar puncture in sleeping sickness:

In sleeping sickness the trypanosome has been found in the lumbar fluid (Castellani and Bruce).

Broden and Rodhain have published results of examination of 145 cases of sleeping sickness in the Belgian Congo.

They have examined the spinal fluid cytologically and chemically. In the early stage no change is found. When the disease is more advanced - "the stage of definite establishment" - there is marked lymphocytosis with occasional vacuolated cells; the albumen is increased, the sugar normal. Trypanosomes are only present in the advanced stage and then not constant.

In the terminal stage occasionally myelocytes are present. Thus lumbar puncture is of no use in early diagnosis, the blood or lymphatic glands being better for that purpose. The action of atoxyl on the disease is well seen in the condition of the spinal fluid. They recommend treatment to be continued till the fluid is normal clinically and cytologically.

The state of the spinal fluid is an index of the stage to which the disease has progressed. If the changes are marked the disease is well advanced.

Cysticercus of brain diagnosed by lumbar puncture:

Cysticercus of the brain has been diagnosed by lumbar puncture through the discharge of a cysticercus (Hartmann).

Lumbar puncture in tetanus:

In tetanus lumbar puncture has been performed as a rule prior to injecting serum or drugs.

Norman Henry, in recording results of injections of magnesium sulphate, mentions that the fluid obtained by lumbar puncture prior to the injection in two cases was negative as to microscopical examination, and sterile in cultures.

Therapeutics of Lumbar Puncture:

The therapeutics of lumbar puncture is disappointing as compared with its value in diagnosis.

In increased intra-cranial pressure:

Most favourable results are occasionally observed, but very often in those cases where spontaneous improvement sometimes occurs: in these cases it may have just turned the tide in favour of recovery.

Cerebral tumours:

Originally introduced for the relief of increased intra-cranial pressure, it is still employed for this purpose. In tumours causing hydrocephalus, it may relieve some of the pressure symptoms as headache and optic neuritis, but trephining is more efficacious and lasting (Risien Runell, Marcus Gunn, Donald Armour). Its place in such cases is merely palliative, to relieve urgent conditions. Cases have been reported when it has kept symptoms in check over a long period (Newton Pitt, Stewart).

I have already drawn attention to risks present in withdrawing much fluid in this condition. Schlesinger gives the following as contra-indicating lumbar puncture in cerebral tumour - marked vascularity of tumour; if pressure is low at the beginning or rapidly falls; if marked respiratory or circulatory embarrassment occurs.

Cerebral injuries:

In cerebral injuries - with fracture of skull

and haemorrhage, or laceration of the brain with haemorrhage or "cerebral irritation" or traumatic meningitis - lumbar puncture may confer considerable benefit by removing blood which acts as an irritant; by removing increased fluid and so relieving pressure. Terrier says it markedly relieves pain (Quenu, Potherat, Terrier, Quincke, Stewart, Chauffard, Spick, Ballance).

All authorities agree that only small quantities of fluid should be removed at a time; the operation to be repeated at intervals as necessary.

Rawling and Kellock, in a paper before the Medical Society of London, regard lumbar puncture as useless in the treatment of cerebral injuries. Rawling advocates the "decompression" operation of Harvey Cushing, using the temperature as his danger signal. He says: "the presence of blood in the lumbar fluid suggests the presence of intra-dural haemorrhage, nothing more. I have never seen the slightest benefit result from that mode of treatment".

Schlesinger reports relief of symptoms by repeated lumbar puncture in acute haemorrhagic meningo-encephalitis.

Cerebral haemorrhage:

In cerebral haemorrhage Chauffard apparently removes about 10 to 15 c.c. lumbar fluid every two or

three days, keeping the patient at rest with ice to the head.

Langdon Brown and Leonard Williams have shown that in this condition the blood pressure is high, due to a vaso-motor impulse and is unnecessary in order to overcome the increased intra-cranial pressure which results from the haemorrhage acting as an irritant, and which impedes circulation of blood in the medulla. Up to a certain point reduction of blood pressure may do good, by lessening the bleeding but if beyond that point, the blood supply to the medulla will fail and death ensue. This increased intra-cranial pressure is partly caused by increased serous exudate. Removal of a small amount of lumbar fluid may do good by removing some of the increased cerebro-spinal fluid and the blood, which acts as an irritant. We must, however, not reduce the intracranial pressure appreciably, lest the haemorrhage be restarted.

Serous meningitis:

In acute and subacute serous meningitis, and that very transient form of sudden serous exudation which Quincke calls angio-neurotic hydrocephalus, the result of removing a large amount of clear, normal fluid by lumbar puncture is often most marked (Quincke Oppenheim, Redlich) as seen in one case I have quoted from my series.

Harris has seen similar result from trephining.

Quincke also advises mercurial treatment, the lumbar puncture being repeated as required.

Meningism:

A similar improvement is seen in cases of so-called "meningism", serous meningitis - non-bacterial - accompanying otitis media, cerebral abscess, cerebral influenza and a form of serous effusions seen in syphilis which may be transitory, chlorosis, lead poisoning, uremia, eclampsia and other allied states where there is an increase in the intra-cranial pressure due to the presence of increased serous fluid.

Its use in meningism has been already mentioned and cases quoted. Improvement, or at any rate temporary relief of symptoms of cerebral irritation has frequently followed the removal of an apparent excess of cerebrospinal fluid and I have seen no harm from it. It is possible, as Rocaz and Carles state, by removing the fluid and toxins we tend to forestall the development of a purulent condition. When performed in otitis media or cerebral abscess, the major operation should always be done to remove the septic focus.

Hydrocephalus:

In chronic hydrocephalus lumbar puncture is not

of much use.

In acute hydrocephalus which is generally acute serous meningitis, or an early stage of a meningococcal meningitis, removal of fluid tends to prevent distension of the cerebro-spinal cavity. If this once occurs, the brain being inelastic and confined in bony unyielding walls, there is not that tendency to improvement after removal of fluid as is seen when the pleura is tapped; here the lungs expand and tend to obliterate the pleural cavity. So to be of use lumbar puncture must be performed early and repeatedly to prevent distension; once dilated, the brain cavities tend to remain dilated, and to oversecrete.

In long-standing hydrocephalus where parts of the brain substance have undergone atrophy - by prolonged pressure - and in cases where secretion is continuous and profuse, lumbar puncture is generally only of transient benefit.

In very young children, however, we may be able by relieving over-distension, to allow of more development of the brain substance (Quincke).

In cases of concealed hydrocephalus it may afford a transient relief, and, as Quincke says, allow of greater development than can occur if the high pressure is constant.

Harris has reported a case where intermittent hydrocephalus was due to a loose fibroma occasionally plugging the foramen of Mouroué in the lateral ventricle. In this case leeches were used to relieve the intracranial pressure.

Such intermittent attacks of increased intracranial pressure also occur in serous meningitis and are markedly relieved by lumbar puncture (Oppenheim).

Cantley reports a case of hydrocephalus after posterior-basic meningitis for a time much improved by repeated lumbar puncture.

I have seen two such cases which were temporarily relieved, but which left the Hospital in statu quo.

In optic neuritis:

In optic neuritis due to cerebral tumour trephining is the more lasting and efficient remedy, though while waiting for operative measures, lumbar puncture will often relieve urgent needs.

Babinski and Chaillous report on the results of lumbar puncture in eight cases of optic neuritis of intra-cranial origin with success in nearly all. They recommend this procedure in optic neuritis due to traumatic or inflammatory intracranial effusion. In intracranial tumour they regard it as only palliative. They advise the patient to be in the horizontal position, the fluid to be gradually evacuated

drop by drop, not over 8-10 c.c. at a time; the recumbent position to be maintained for several days after the operation.

Koenig points out that optic neuritis may be peripheral, with infiltration limited to the nerve ending, and not due to a cerebral lesion, but to toxins. In these cases lumbar puncture will be of no avail, and he suggests tapping the anterior chamber of the eye by means of a sclerotomy.

Ocular neuritis (where the optic nerve and the external ocular nerves are involved) occurring in lead encephalopathy is said to be improved by the withdrawal of some two drachms of spinal fluid, repeated if, and as, symptoms of raised pressure return (J. L. Gibson).

In uremia:

Benefit resulting from lumbar puncture in uremia has been reported by McVail and Peabody, Chauffard and others.

Wilson from an experience of lumbar puncture in ten cases of uremia advises its use, especially in cases where tension is high and oedema absent.

Ortner recommends its use as it relieves, even if only temporarily, the coma, cramp and headache.

Lépine records two cases where it did no good.

Cushing and Bordley record a case where it did no good, yet trephining did, relieving the optic neuritis, but death ensued. Quincke says it sometimes affords relief, and several observers have stated that it relieves the uremic convulsions.

In eclampsia:

In eclampsia lumbar puncture has been found of benefit by Helme, Cooper, Audebert & Fournier and Commandeur.

In Meniere's Disease and in tinnitus:

Lumbar puncture may relieve obstinate aural vertigo and tinnitus (Harris, Stewart). Babinski claims to have had good results in 21 out of 32 cases. There is usually headache and nausea for several days after the operation. If no reaction then no therapeutic result follows. If symptoms recur the operation is repeated, to remove fluid which has re-collected. He removes usually 4 to 5 c.c. at a time and the recumbent position is maintained after the operation.

This reaction he mentions does not sound like the relief of tension. It reminds one of a case of tetany in which Eve used lumbar puncture; 1 ounce of clear, normal lumbar fluid was removed; next day the child was more rigid and thereafter improvement

set in, being rapid and complete, the case having been obstinate before. Eve suggests the removal of normal fluid induced a condition of hyperaemia, so improving the nutrition of the nervous tissues; a sort of Bier's hyperemic treatment.

It is possible some such result occurred in Babinski's cases, and in other conditions where fluid is removed.

In Status Epilepticus:

In a bad case of status epilepticus transient relief, from apparent reduction of increased pressure, has been recorded by Richenol and Castin.

Chipault saw improvement in two cases of epilepsy after lumbar puncture.

In Localised Spinal Meningitis:

Several cases of localised spinal meningitis are said to have been relieved with subsequent recovery and after tapping of the fluid, which was pressing on the cord. (Mendel, De Montet, Krause, Chauffard, Picard).

In Meningitis:

There are several cases of meningitis of various kinds which are said to owe their recovery to repeated lumbar punctures; even tuberculous meningitis. Epidemic cerebro-spinal is believed by many to be relieved by removal of fluid.

. That it affords marked relief in many forms of meningitis there is no doubt. I have repeatedly performed the operation at night when I knew the case was beyond recovery, but also knew it would afford the child relief; quite apart from any scientific interest in the matter. I have seen a child cry and object to the preliminary handling, and then when the needle had been inserted go off to sleep, not only in tuberculous meningitis; but in posterior basic cases, septic meningitis and in some cases of meningism. I have not seen consciousness restored in an unconscious child, but this may be more likely to occur in older patients (Stewart). I am doubtful of the wisdom of withdrawing much at a time; little and often would be, I think, better, and it should be begun early. As stated early in this thesis, an acute increase of pressure causes urgent symptoms. If the pressure increases gradually the symptoms may not be marked until pressure has become so great, or has existed so long, as to cause dilatation or other effects which earlier removal of fluid might have avoided. The removal of a large amount might quite possibly be followed by a rapid re-secretion which slower methods might have obviated.

In meningitis removal of fluid relieves pressure; removal of bacteria and toxins dilutes the fluid, and

assists the *vix medicatrix naturae* in getting the upper hand.

In addition we may assume the offensive and attack the organism by means of antiseptics injected after removal of fluid.

The fluid may also be used to obtain vaccines from.

Whether a useful hyperemia is ever induced as mentioned above, is doubtful, for there is already hyperemia and congestion.

Cases of vaccines prepared from the spinal fluid and their successful employment in meningococcal meningitis have been reported by Hector MacKenzie, and Rundle and Williams.

Ker quotes Radman who successfully inoculated two cases of epidemic cerebro-spinal meningitis with their own purulent spinal fluid. Ker also tried it without success; but in practically hopeless cases.

Cases where lumbar puncture with antiseptic injections have been used are recorded by Franca with lysol in 1 per cent solution in streptococcal meningitis, with success; also in meningococcal cases during an epidemic in Lisbon. He injects 6 c.c. of 1 per cent lysol solution; another 3 c.c. in three days time.

Widal and Ramond have successfully used collargol

(5 c.c. of 1 per cent solution). Laurens has used repeated lumbar puncture and intra-venous injection of collargol (4 c.c. of 1 per cent solution) followed by injections of 5 c.c. into the spinal canal. The case quoted was septic meningitis, associated with otitis media and due to an "enterococcus".

It has been suggested (Ballance, L. Hill) to drain the meninges by operation, to perform lumbar puncture and to irrigate the meninges, in septic meningitis. Quincke says irrigation of the spinal meninges is of no practical value, and Halstead is quoted by Osler as employing it unsuccessfully.

Barker advocates repeated lumbar puncture and removal of the septic focus, in septic meningitis with otitis media.

Where the connection between the brain and spinal cord is occluded lumbar puncture can be of no use; in such conditions trephining is the only course; as in a case recorded by Boswell, where lumbar puncture was of no avail in a case of cerebro-spinal meningitis, which quickly recovered after trephining.

Buchanan claims a recovery from tuberculous meningitis after repeated lumbar puncture and injection of tuberculin (1/4000th mg. repeated in three weeks); but no tubercle bacilli were found. Calmette's reaction was positive.

In meningococcal meningitis, especially the epidemic form, much work has been done in attempting to find a serum to reduce the mortality in this disease. Some of these have been used subcutaneously, but the best method is to use them intra-spinally, as in the employment of the antiseptic solutions just referred to above. Some spinal fluid is withdrawn, and some workers even irrigate with normal isotonic saline, then the serum is injected. The latest work on this subject has been done by Flexner, and his serum was used with promising results in Belfast and Edinburgh. (1)

In tetanus also, anti-tetanic serum is best injected intra-spinally (Stewart, Jacob). Magnesium sulphate solution has also been recommended in tetanus used intra-spinally (Meltzer, Blake, Franke, Norman Henry).

In Sleeping Sickness:

Broden and Rodhain regard the condition of the spinal fluid as important in sleeping sickness, as indicating the state of the case. If well advanced the fluid shows cytological and chemical changes - chiefly consisting of a lymphocytosis and increase in albumen. If far advanced myelocytes may be present.

(1) Brit. Med. Journ. Vol.II., 1908, p.1334.

The trypanosome may or may not be present.

The reaction to the treatment by atoxyl is also well seen in the changes produced in the fluid. Treatment should be continued until the fluid is normal cytologically and chemically.

In pruritis:

Thibierge and Ravant report having found lumbar puncture extremely efficacious in pruritis.

In Spinal Analgesia:

Lumbar puncture also forms part of the process of inducing spinal analgesia, fluid being withdrawn before the anaesthetic solution is injected; but I do not propose to discuss that method of treatment in this thesis.

Continuous Lumbar Drainage:

Quincke has tried continuous drainage of the spinal arachnoid in various conditions, especially where the fluid persistently re-accumulates, as in hydrocephalus. His method is to slit the dura and allow the fluid to drain into the surrounding tissues. He suggests it is deserving of further trial.

Lenhartz and Sahli have endeavoured to attain the same end by leaving a needle or canula in situ, after performing lumbar puncture, but the drawbacks to this method are sepsis and the difficulty in retaining the instrument in position.

The material from which a practical experience of the applications of lumbar puncture was derived was comprised in a series of 67 cases, which were admitted to the Queen's Hospital for Children, London, during the months of January to August, 1908.

These cases have already been referred to, from time to time, and some have been described. I propose to apply the principles detailed above, with a view to illustrating the possibilities and limitations of the operation of lumbar puncture, and to mention some points of interest.

These 67 cases were made up as follows:-

Meningitis, 51 cases, including 23 cases tubercular;
 10 cases posterior basic; 1, perhaps 2, acute serous meningitis; 7, perhaps 8, pneumococcal; 1 each due to pneumo-bacillus, streptococcus, staphylococcus; and seven cases not definitely diagnosed.

Acute Poliomyelitis, 4 cases.

Hydrocephalus, 4 cases.

Meningism, 6 cases; and "hydrocephaloid" 2 cases.

Of the 23 cases of tubercular meningitis, only 16 have been included in the analyses referred to above, there being no doubt as to the accuracy of the diagnosis in these. Of the rest, lumbar puncture

was not done in three, not examined in one. Only one tubercle bacillus was found in the fluid of another (a polymorph leucocytosis), no post-mortem being obtained.

In two cases the lumbar fluid was negative - in one of these, on two occasions - while post-mortem there were wide-spread miliary tubercles, the brain showing early meningitis, but no visible tubercles. In one of the cases included in the analyses, the lumbar fluid gave no indication of the condition of the meninges - being quite normal microscopically - while the brain showed well-marked, if early, tubercular meningitis, with visible tubercles.

Of the 23 cases tubercle bacilli were not expected in some, and were not looked for in nine.

It was found in all of the 14 cases in which it was searched for; in all of ten cases in which the coagulum, forming on standing, was examined, and in films made from the centrifuged deposit in four.

The diagnosis by the finding of the tubercle bacillus in films from the centrifuged deposit is not, I think, so reliable and certainly not so satisfactory, as when the coagulum is examined.

Of 19 cases in which the cerebro-spinal fluid was examined, a practically pure lymphocytosis was

present in nine, a polymorph leucocytosis in eight, while no definite microscopical changes were discoverable in two.

The average age in the whole 23 cases was about 2 years, $7\frac{1}{2}$ months; seven being under 1 year, and 14 under 2 years; the oldest being 5 years 3 months, the youngest 3 months.

The average duration of the process was about 18 days, varying from five days to six weeks, but this can only be a very rough estimate, being largely dependent on the statements of mothers, or more often of other relatives or friends who bring the child for admission.

Several of the cases were only admitted at the close of the disease - for some two or three days.

The temperature is indefinite and would seem to be influenced more by the general condition, than by that of the meninges. It can only be at all satisfactorily studied in cases which have been in Hospital several days.

There is generally some irregular temperature, often raised when convulsions are active, showing a terminal rise in most cases, which may reach as high as 105° or 106° , or only to 101° or 102° . Less often there is a terminal fall, the pulse and respiration not sharing in this false improvement. The average

radius seems to lie between subnormal and 101° or 102° . There was a low range of pyrexia in five, being hardly above normal in three cases. Yet two of these ran a rapid course, one showing a pure lymphocytosis, the other a polymorph leucocytosis at the end. Whether the temperature is influenced more by the tubercular process elsewhere than in the meninges, or by the amount of encephalitis present, it would be difficult to say.

Tooth records a case where the temperature rarely rose above normal, during more than three weeks, while under observation, and post-mortem definite tubercular meningitis was found, with no visible tubercle elsewhere.

A mixed infection would probably cause a raised temperature. In the eight cases with polymorph leucocytosis, the average pyrexia was about the same as in those having a lymphocytosis, but they showed the actually highest temperatures, especially in the terminal rises.

This might be adduced as further evidence of a mixed infection, in these cases with mixed spinal leucocytosis, but the temperatures in meningococcal cases, as judged by my ten cases, generally show a low reading.

Of the 23 cases, squint was noted at some time in seventeen, and facial paralysis in three. This was generally an early phenomenon and frequently passed off. There was a modified hemiplegia in one case.

Optic neuritis in varying degrees was noted in six; in one of these it was of the choked disc variety, more characteristic of a tumour. None was seen post-mortem. Choroid tubercles were seen in two cases. In one of these there was a large "obsolescent" tubercle, with several recent typical satellites, the obsolescent tubercle showing a large amount of black pigment. Cases of this nature are described in a well-illustrated article by Carpenter and Stephenson.⁽¹⁾ Optic neuritis was not present in the two cases showing choroidal tubercles.

There was a definite history of cerebral injury in two cases. The children were quite well prior to the injury, and in them the disease ran a rapid course (13 and 14 days) and at post-mortem the meningeal condition was apparently more advanced than the changes elsewhere.

We see that the opportunities for diagnosis offered by lumbar puncture in tubercular meningitis are considerable. The association of the almost clear

(1) Reports of the Society for the Study of Disease in Children, Vol. I. (1900-1901).

fluid with its typical coagulum and a child with meningitic symptoms is strong presumptive evidence which in most cases can be strengthened by a cytological examination of the fluid and rendered certain by the searching of the coagulum, after proper staining, for the bacillus itself.

As marked examples of this, I would refer to two cases which when admitted were typical of posterior basic meningitis; marked retraction, opisthotonus and turbid spinal fluid, all pointing to that condition, one of them also being under one year of age.

Examination of the fluid gave a typical coagulum and numerous bacilli were found in the stained coagulum.* Such cases, with post-basic symptoms appearing early, are liable to cause errors in diagnosis.**

With regard to treatment, I have elsewhere referred to reported successes, attributed to lumbar puncture, with or without tuberculin injections.

I have found no mention of any intra-spinal injections being tried in this condition. I would venture to suggest that early trephining combined with early lumbar puncture, might save some lives. The cause of death is said to be generally attributed to toxæmia, from the fact that the meningeal is only part of a general tuberculous infection.

* See Figs. 14, 15 and 16.

** See also case "L.W." page 163 = acute polio-myelitis with lymphocytosis simulating tubercular meningitis.

Cases have been quoted where only the brain apparently was affected (Tooth). I have seen at least two cases where the meningeal infection was much in advance of the changes seen elsewhere. I have quoted one case at length (M.M.) where the fluid was very suggestive of a tubercular meningeal condition, and in which I had thought tubercle bacilli were present, and which recovered from an apparently hopeless state after trephining; in which it bears a resemblance to many cases of tubercular peritonitis which have recovered after laparotomy, with only the removal of more or less effusion.

It would seem, therefore, that early operation might in some cases find an early condition and cause its arrest; for, as Whitla observes: In the operation for tubercular peritonitis, the only constant factor is the anaesthetic, and he suggests this itself may have a beneficial effect. In which connection, one may refer to Darling's results in studying the effect of a general anaesthetic on the blood. He found a distinct leucocytosis to result from general anaesthesia, averaging an increase of 8000 and as much as 14,000; while Da Costa and Kalteyer found a rise of 5000 after ether, and after chloroform a similar effect, but of longer duration.

The only result of performing lumbar puncture in

tubercular meningitis that I have seen, has been to markedly alleviate the symptoms of irritation; where much crying out or convulsive movement is present; the removal of fluid is generally followed by instant relief - lasting 12 to 24 hours or even longer.

It has on one or two occasions appeared to relieve the optic neuritis. The more completely ossified the skull, the more beneficial is its performance. It would seem as if the causal organism in meningitis is to be found earlier in the disease in tuberculous and meningococcal meningitis than in other forms. This may be because these are chiefly basal in position, or it may be explained by the view that these diseases arise in the cord and ascend to the base of the brain and descend to lower cord.

In tubercular meningitis this view is held by Professor Greenfield (Beattie & Dickson) and Strumpell (Oppenheim), the infection reaching the cervical cord by lymphatics. It is remarkable how many of these cases arise from a caseous mediastinal gland. In one of my cases there was a caseous upper mediastinal gland - well-marked cerebral tubercle and very slight evidence elsewhere, and copious tubercle bacilli in the spinal fluid. Flexner found during his experiments on monkeys, that the meningococcus when injected into the spinal canal soon produced a

basal meningitis and could be traced into the nasal mucosa; where it penetrated from the subarachnoid spaces along the lymphatic spaces enclosing the olfactory nerves. This may account for the reported discovery of meningococci in the nasal cavities of those suffering from cerebro-spinal meningitis: though some of these have undoubtedly been due to confusion between the meningococcus and other gram-negative cocci (Arkwright, Gordon).

The cases of posterior basic meningitis, ten in number, were all under one year of age, except one of two years and one of 13 months. This is clinically a useful differentiation from cases of tubercular meningitis, which are more often over 12 months old.

Lumbar puncture may frequently give clear fluid with no leucocytosis; either in the later stages of the disease, when convalescence is approaching; or earlier, when the communication is closed at the base of the brain.

I found clear fluid with no leucocytosis in two cases. A lymphocytosis may also be found in the later stages, replacing the polymorphs which are the rule in the earlier stages.

In one case there was herpes labialis and a purpuric eruption on the trunk and neck, a well-

marked polymorph leucocytosis with copious intra- and extra-cellular diplococci. The contractures in this case were very marked, affecting chiefly the flexors, so that the hands were clenched and turned inward, and flexed on forearm, the thumbs being outside.

Clinically, vomiting was a constant and persistent feature; still, loss of weight in several cases was not marked till near the end, as they seem to take their food well; comparing well with cases of tubercular meningitis in that respect.

There was no optic neuritis, but marked pallor of the disc, to an extent suggesting atrophy, in three. Some appeared to be blind. These cases seem to be quieter, less inclined to convulsive movement than in tuberculous or septic meningitis.

The temperature was generally low.

In three or four cases lumbar puncture only gave a few drops of fluid, though hydrocephalus was present. One of these I tapped through the anterior fontanelle; while it prolonged life and gave temporary relief, it did no ultimate good.

All my cases died, and beyond temporarily relieving the rigidity and the pulse and respiration, lumbar puncture did not appear to alter the progress of the case.

It would appear that other diplococci than the meningococcus may cause a post-basic meningitis, as I have found gram-positive diplococci in two cases. Out of the ten cases, a typical polymorph leucocytosis of the spinal fluid, with typical intra-cellular diplococci, was found in six. In two more there was a polymorph leucocytosis, but no cocci seen. In two the fluid was clear, with no cells seen in it.

The ten cases of septic meningitis included seven of pneumococcal origin; of which two were primary and followed after an injury to the head while in good health; with no aural affection, nor any lesion elsewhere at post-mortem. Two were associated with purulent middle ear disease, one having a long-standing otorrhoea, the other no symptom of ear mischief at all.

One was a surgical case, meningitis complicating mastoid disease, which had been operated on several times.

Two were secondary to a small patch of inspissated empyema, one of these also showing pyopericardium. These two cases are of interest, as they are very difficult to diagnose. The physical signs may suggest fluid, but the needle will show nothing. One

case was supposed to be tubercular. The other I explored twice, the needle each time passing through the patch. The child gave no definite symptoms and indefinite signs; it was sitting up a day before death; and the lumbar puncture four days before death was quite normal, save for some increase in amount. The lung itself was apparently normal; the patch of empyema was about the size of a crown-piece. In the first case it was no larger than a penny.

Of these seven cases due to the pneumococcus, lumbar puncture was performed in six. It was quite negative in one; gave a small lymphocytosis in three tappings out of four in another, and was definite and conclusive in three cases and in the fourth tapping of the case mentioned above, giving a large polymorph leucocytosis teeming with pneumococci. The other case - the surgical case with mastoid disease - the pneumococci were few, but the polymorph leucocytosis was very large and characteristic.

In none of these cases did removal of fluid appear to postpone the fatal termination; it relieved urgent symptoms only.

It would seem that in primary meningitis the symptoms are more marked, and definite changes in the spinal fluid found earlier, than in secondary cases, where the clinical symptoms and spinal fluid may be very misleading.

The case of meningitis due to the pneumo-bacillus I have fully described elsewhere.

The case of streptococcal meningitis was associated with a small septic periostitis at lower end of the tibia. The child showed no definite symptoms on admission, but appeared not to notice anyone. It developed convulsions about 5 a.m. and was relieved by lumbar puncture, dying a few hours later. The fluid obtained was typical, containing a large polymorph leucocytosis and teeming with streptococci showing typical chains.* Streptococci were also obtained from the subperiosteal pus.

The case of staphylococcal meningitis was secondary to septic periostitis of the femur, with septic endocarditis. Lumbar puncture was not performed as she was moribund on admission, only living a few hours. Staphylococci were obtained from the subperiosteal pus, the meninges, the spleen and the fleshy vegetations on the heart valves.

Lumbar puncture is not so effective in diagnosis in the early stages in these pyogenic forms of meningitis as in tubercular meningitis. When well-established, the aspect of the fluid is typical, and is very similar to that seen in post-bacillary meningitis, the type of organism being the differential factor.

Therapeutically, I have not seen any sign of its

* See Fig.7.

doing any good beyond relieving, temporarily, urgent symptoms.

Many cases of recovery after lumbar puncture in these forms of meningitis have been recorded, with and without injection of antiseptics.

It would appear as if the source of the infection and type and virulence of the organism have an important bearing on prognosis.

Where there is an acute bacteriaemia, as shown by the organism being found in the spleen and heart, the effect of locally draining the meninges would seem to offer slight hope. I have isolated the infective organism from the spleen, in culture or smear, or both, in three cases in which it was examined bacteriologically.

There remain seven cases not definitely diagnosed. Lumbar puncture was performed in five of these and failed to decide the diagnosis, partly because no cultures were taken.

One of these cases was a boy, aet 6 years, admitted to a surgical ward for fits. He was knocked down by a bicycle, developing fits five days later. He had previously been in good health, but had had multiple abscesses of scalp. He was supposed to have a fractured skull. On admission to a surgical ward there were active meningitic symptoms, and the

notes say early optic neuritis. The temperature was up to 105° twice. Lumbar puncture was done with difficulty giving a blood-stained fluid, which rendered its microscopical examination difficult. There was some polymorph leucocytosis; if all due to the blood contamination, there must have been a large leucocytosis of the blood.

A second lumbar puncture under an anaesthetic next day gave same blood-stained fluid, increased in amount. I could find no organism. A culture was not taken. The boy died on the third day of the attack.

Post-mortem there was definite congestion and a turbid effusion under the membranes; no tubercles; no pus; no large collection of fluid.

The liver showed fatty changes, the spleen some congestion. The pericardium contained an excess of straw-coloured serous fluid. Under the epicardium I found two small pustules, like tubercles, only more opaque and yellowish. These in smears and culture gave typical staphylococcus pyogenes aureus. There were no vegetations on the valves. Was this a case of fulminant meningitis, connected with the septic scalp and injury?

Unfortunately the spinal fluid was not cultivated nor the meningeal effusion post-mortem.

Maiella found that in septic (staphylococcal) meningitis artificially produced in dogs, that a leucocytosis of the fluid did not occur, nor did pus form; unless the animal lived about a week.

When I saw this case his head had been completely shaved with a view to operative treatment; the supposed depressed fracture was obviously a "hot-cross bun" shaped cranium, the result of previous rickets.

I remember the case of a Swedish sailor admitted to the Edinburgh Royal Infirmary, as a possible pneumonia. There were no physical signs and he died the same night, having been exceedingly drowsy and irritable. He had only been ill three days. At post-mortem, there was congestion and cloudy swelling of several of the organs; a pure culture of staphylococcus being obtained from the heart and spleen; no other cause of death being discovered.

Among my cases have been five whose deaths have been attributed to cerebral injury, in whom definite cerebral injury has been followed by meningitic symptoms, and death.

Two of these developed tubercular meningitis with death in 13 and 14 days, and definite advanced tubercular meningitis; the cerebral changes being much in advance of the changes elsewhere, at post-mortem.

The other three consisted of two cases of primary pneumococcal meningitis already described, in which death occurred on the third and fourth day respectively; the fifth case being the case described above where staphylococci were obtained from the heart.

I have recently heard of another case where a child, aged 5 years, was knocked down by a bicycle, became drowsy about 36 hours later, was admitted to a Cottage Hospital, for concussion; and died with meningitic symptoms, on the fifth day after the injury was received. Post-mortem there was a dense collection of pus over the surface of the brain. The child was quite well before the accident.

I have twice been asked at inquests whether a meningitis can be definitely attributed to a cerebral injury. It is at least strange that I should meet with six cases in about eight months, all developing meningitis apparently in perfect health, directly after a cerebral injury.

Another case, a boy of five, after being less well than usual for two days, suddenly developed fits at night, about two hours before admission, and died about 12 hours after admission. The fits suggested epilepsy. They persisted in spite of treatment,

chloroform only having a very temporary effect.

Lumbar puncture gave an excess of fluid showing a fairly large lymphocytosis; no coagulum formed in it. A culture was not taken. Fits persisted till death, which occurred suddenly. At autopsy there was no evidence of meningitis, not even as much congestion as I had expected after the continuous fitting. The liver was large, pale, and showed fatty changes. The other organs were apparently healthy. This may have been a case of status epilepticus.

The ears were examined with a negative result; the tympani were punctured, with no effect.

Another undiagnosed case was that of a girl, aet 5 years. Taken ill with headache on Saturday, she became unconscious on Sunday afternoon, was admitted that evening, and died that night. She had been well before.

There was general twitching; face drawn to one side; no physical signs present. Ophthalmoscopic examination gave some redness of disc, distension of veins and blurring of edges of one disc; head slightly retracted.

There was nothing in the history to help; lumbar puncture was not performed.

At autopsy, brain showed marked congestion: some effusion under membranes; no tubercles seen; liver pale and showing fatty changes; kidneys pale; lungs showed slight congestion at bases; other organs showed nothing abnormal.

Here again no culture was taken from the meningeal effusion. It seems to me to have been most likely an acute fulminant meningitis.

There was nothing in the ears.

With reference to these cases dying with convulsions and possibly from fulminant meningitis, I have found on looking through some St. Thomas' Hospital reports, several cases where the actual cause was not diagnosed post-mortem.

In 1905, two such cases were reported, admitted for "convulsions and fits of doubtful causation"; an infant of 12 months and a man of 38. Nothing was found post-mortem, the man being "possibly status epilepticus".

In Vols. XXXIII. and XXXIV. there are cases quoted of meningitis with optic neuritis clearing up with complete recovery. These would appear to be cases of serous meningitis.

In 1903 an interesting case is reported as being admitted for fits, discharged and readmitted later on,

dying ten weeks after with tubercular meningitis. Had this child died during the fits when first admitted, would there have been naked eye evidence of tubercular meningitis?

Several of my cases, tubercular, pneumococcal and one or two of these undiagnosed cases have been sent away from the casual department, the fits being supposed to be epileptic, or teething. In 1903 another case died "possibly status epilepticus". In 1899 a case is mentioned which was admitted as one of infantile convulsions, discharged as cured four days later, and admitted later to a fever hospital, dying in four days "with phthisis and tubercular meningitis".

Two cases of fulminating cerebro-spinal fever are reported from Belfast,⁽¹⁾ dying in a few hours with very little meningeal evidence: also a case of fulminant meningitis from the London Hospital⁽²⁾: lumbar puncture gave a clear sterile fluid in excess. Early optic neuritis was present. Post-mortem only congestion of the meninges was to be seen.

I have also quoted elsewhere cases showing no naked eye evidence of meningitis post-mortem - tuberculous meningitis, without tubercles; streptococcal meningitis without pus (Wilson); pneumococcal meningitis with no macroscopic evidence of it.

(1) Brit. Med. Journ. Vol. I. 1907, p.1537.

(2) Brot. Med. Journ. Vol. I. 1907, p.992.

Another case was that of a boy, aet 1 year, who died after a long illness of five weeks with symptoms of meningitis. Lumbar puncture gave slight excess and a turbid fluid, which was not examined.

At autopsy the brain was very soft and the right temporo-sphenoidal lobe breaking down. There was no definite pus; some purulent matter at base. No culture was taken. The pathologist diagnosed septic meningitis with abscess, on the strength of a very minute amount of muco-pus in both middle ears. I have seen exactly the same condition at autopsy in a case of tubercular meningitis. This is a case where adequate examination of the spinal fluid might have been of great diagnostic value. The other organs of the body were reported healthy. I am inclined to diagnose posterior-basic meningitis owing to the history, the persistent vomiting, and the persistently low temperature; there is also a clinical note "apparently blind" which supports this diagnosis.

Another case was a child of seven months, under treatment for wide-spread eczema. I did not have charge of this patient, but was sent for, as it was in convulsions. Up to that it had been doing very well under lotio calamine.

When I saw it, it was in a marked convulsive fit which quieted under chloroform; only to return an hour later, being this time rather hemiplegic, involving left side of face and right arm and leg.

I performed lumbar puncture which was followed by a decided improvement; the fits recurring a few hours after, with sudden death before I could reach it. Lumbar puncture gave a large excess of fluid containing a large number of blood corpuscles and a slight excess of lymphocytes.

At the post-mortem next day, the pathologist reports: "brain very soft and pulpy; blood clot on either side of longitudinal sinus between dura and brain; blood extravasation under membranes; no sign of tubercles; some milky exudate under membranes; thymus much enlarged." The temperature rose from 99° the previous morning to 99° that night; and 101° the morning of the attack to 106° before death; so the temperature was apparently rising before the fits began.

This is a case where blood in the spinal fluid was probably of diagnostic importance, though at the time I thought it was due to the operation; as it apparently agreed with the appearance of blood contamination in other cases, where no cause for it was vouchsafed post-mortem.

Another case similar in this respect was that of the meningitis due to the pneumo-bacillus where there was haemorrhage into the ventricles, and a blood-stained fluid obtained by lumbar puncture. There is another interesting point in this case. Why should it have developed fits; were these productive of the haemorrhages or vice versa, as the rising temperature might suggest? and what relation did these phenomena bear to the enlarged thymus? Another case of infantile eczema had suddenly died not long before, in which a post-mortem was not performed. It was suggested the calamine lotion was to blame, as it was used in both. There is, however, an article by E. Feer in which he attributes "eczema deaths" to a condition of status lymphaticus. He mentions the popular dread of external treatment for fear of "driving it in"; and occurrence of fever and convulsions; and death, with symptoms of cardiac failure and dyspnoea, which follows even careful treatment. From a number of fatal cases in his own experience and a study of 30 other cases, he believes death to be due in most instances to "status lymphaticus".

The two remaining cases have been already described. "M.M." has been referred to as showing

decided symptoms of intracranial pressure, papillitis and flame haemorrhages, as well as very marked constitutional symptoms and a large persistent lymphocytosis. It was thought at one time tubercle bacilli were present.

The symptoms cleared up after mastoid operation with exploration of dura and brain for abscess.

The papillitis continued intense for a considerable time afterward.

I also referred to the appearance of diplococci which bore some resemblance to pneumococci, and which were found when the child was apparently well and on the point of being discharged. They were accompanied by a very few polymorph cells.* No cocci or polymorphs had been seen in earlier tappings; but the pus from the ear apparently contained pneumococci. The lymphocytosis of the fluid was still very marked.

Was this case one of double otitis media with a cerebral complication - meningitis serosa benigna - cured by the removal of septic focus and relief of the congestion by trephining and lumbar puncture? (Only one ear was operated upon; the other otorrhoea was free) or was it a case of tubercular cerebral disease accompanied by double otorrhoea and cured by treatment?

* See Fig.13.

I do not understand the persistent lymphocytosis, but can hardly believe it was due to tubercle.

The last case, C.J., a boy of 3 years, was admitted for meningitis and found to have pneumococcal empyema. He nearly died after the operation from sudden collapse; then improved, the temperature falling to normal. The meningitic symptoms then became worse, with much irritability, restlessness and intense head retraction. Lumbar puncture, repeatedly done, gave marked temporary relief, a large excess of normal fluid being removed under high pressure; albumen not increased, and no leucocytosis; a few lymphocytes only being found with difficulty. The later tappings gave less relief, were much less in amount, while the symptoms were more marked. Quincke regards this combination as pointing to automatic closure of the foramen magnum by the brain itself. A culture was not taken. An autopsy was refused. There was a marked terminal rise in temperature. The ophthalmoscope revealed no definite optic neuritis, but some early changes. The repeated lumbar puncture may have prevented the development of a decided optic neuritis.

Was this serous meningitis? or septic meningitis complicating empyema with closure of the communication at base of the brain?

I am in favour of the latter explanation, as I have had another case with negative evidence obtained by lumbar puncture in this condition.

Appended is an analysis of the chief data, which I have compiled from my notes of those cases of tubercular, septic and post-basilar meningitis, which form the bulk of the material referred to in this thesis. I have only included those cases in which the diagnosis was beyond a doubt.

The other cases of acute poliomyelitis, meningism and hydrocephalus have all been described elsewhere.

I might refer again to two cases of acute poliomyelitis, which at first closely simulated meningitis. "J.A." when in the out-patient room lay rigid with head retracted exactly like a meningitis; when seen later in the ward, he was quite different. "L.W." for some time suggested meningitis there being cervical rigidity not definite retraction. There was paralysis of left arm and leg with early improvement, as seen in a case of tubercular meningitis; and as recorded by Canby Robinson (5 cases). The typical electrical alterations were found later. There was also a small but definite spinal lymphocytosis; but not the typical coagulum; nor were tubercle bacilli

found. This child went out almost a complete recovery.

I have, however, discovered a note, which was mislaid, referring to a case apparently of "meningism".

It was an infant of seven months, admitted with symptoms of meningitis and broncho-pneumonia. It died after a fit, and post-mortem there was no sign of tuberculosis. The lungs showed broncho-pneumonia and the brain congestion with some excess of fluid under the membranes. This would seem to corroborate the views of Nobecourt & Voisin referred to under "meningism", that there is hyperemia and increased fluid in the meninges in pulmonary disease in children, which may account for some of the cerebral symptoms seen in those diseases.

Lumbar puncture was not performed in this case.

It only remains for me to acknowledge the kindness of the Staff of the Queen's Hospital for Children, in allowing me to refer to these cases, which were in their wards: also to express my regret at having failed to make better use of that material.

ANALYSIS OF 32 CASES OF MENINGITIS.

Comparing various conditions as to cerebro-spinal fluid
and clinical symptoms.

	Tubercular	Septic	Posterior-basic	Totals
Number of cases	16	8	8	32
Age (i) Under 1 year	5	5	7	17
(ii) Under 2 years	12	7	2	21
(iii) Average age	2 yrs. 1 mo.	3 yrs. 4 mo.	9 $\frac{1}{4}$ months	-
Average duration of disease	3 wks (= for 13 cases)	6 days (for 8 cases)	6 wks (for 8 cases)	-
Absence of marked symptoms	None	None	None	-
Eye (i) Squint	13	4	3 (slight)	20
(ii) Changes in fundus	Choroidal tubercle - 2 optic neuritis - 5	Optic neuritis - none	Pallor (? atrophy) of of disc - 3. Optic neuritis - none.	-
Fits	10	5	None	15
Marked vomiting	4	3	8	15
Temperature (i) Terminal rise	11	All of 10 cases	1	
(ii) High or fairly high range.	8	All of 10 cases	3	
(iii) Low range	5	None	6	
Retraction marked	4	4	7	15
Opisthotonus	2 (simulated post-basic)	None	4	6
Kernig's Sign	Noted, present in one and absent in three.	Noted present in 1	Noted present in 3	
Herpes labialis	1	2	1, also purpuric rash	
History of Accident	2	2	None	
<u>Spinal Fluid:-</u>				
1. Increased amount	5	7	6	18
2. Increased pressure	7	5	5	17
3. Albumen increased	7	3	5	15

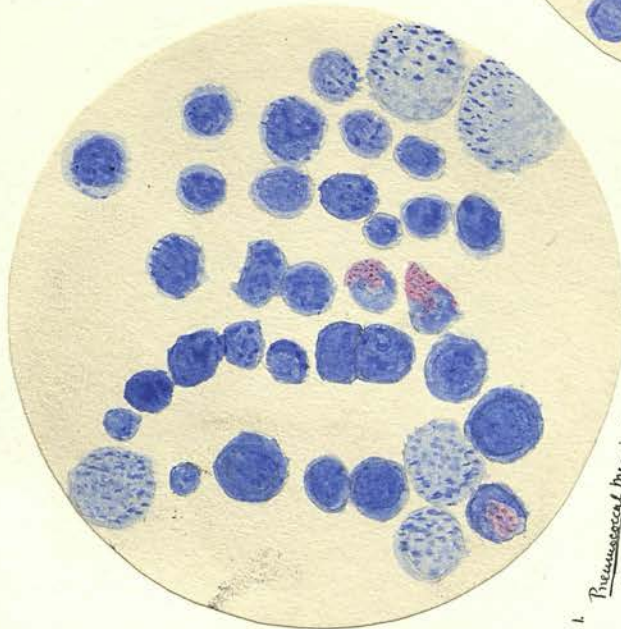
	Tubercular	Septic	Posterior-basic	Totals
Albumen not appreciably increased.	6	5	3	14
4. Naked eye (i) Clear fluid.	2	3 (2 became turbid at end)	2	5
(ii) Opalescent or turbid fluid.	14	7 (2 only turbid in final tapping)	7	28
5. (i) No leucocytosis	1	1	1	3
(ii) Lymphocytosis (pure)	7	2	None	9
(iii) Polymorph leucocytosis (pure)*	None	None	4	4
(iv) Mixed leucocytosis	8	5	4	17
(v) Mixed with polym. predominating	2	4	4	
(vi) Mixed with lymph. predominating	4	1	None	
	In addition 2 more cases in which polym. predominated at the beginning in one, and at the end in the other.			
(vii) Organism found in film	{ Tubercle Bac. in film or in coagulum in 13 (not looked for in 3) Intracellular coccus in 1.	{ Pneumococcus - 6 Pneumobacillus - 1 Streptococcus - 1	{ No cocci found in 3 Intra-cellular diplococci in 6.	29
(viii) Organism found in culture	Diplococcus (gr.-neg.) in 3.	As in films	{ Gr.-neg. diplococcus in 3. Gr.-positive diplococcus in 1.	

* i.e. lymphocytes being present only in negligible quantity,

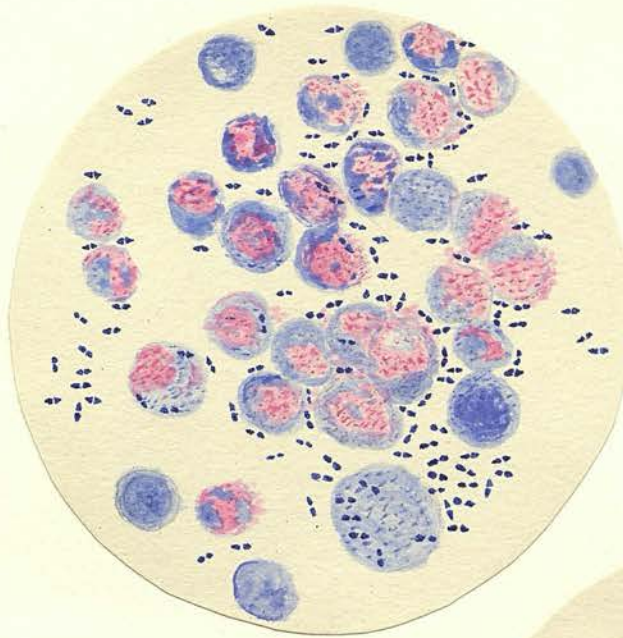
N.B. Only cases have been included in which the diagnosis has been beyond doubt, and in which lumbar puncture has been performed.

These illustrations are copies of actual fields as seen under the 1/12 oil immersion lens. They are an attempt to reproduce what is present: not an effort to show typical pictures. They are not composite except in the case of Figs. 22 and 23 where cells containing cocci have been sought out.

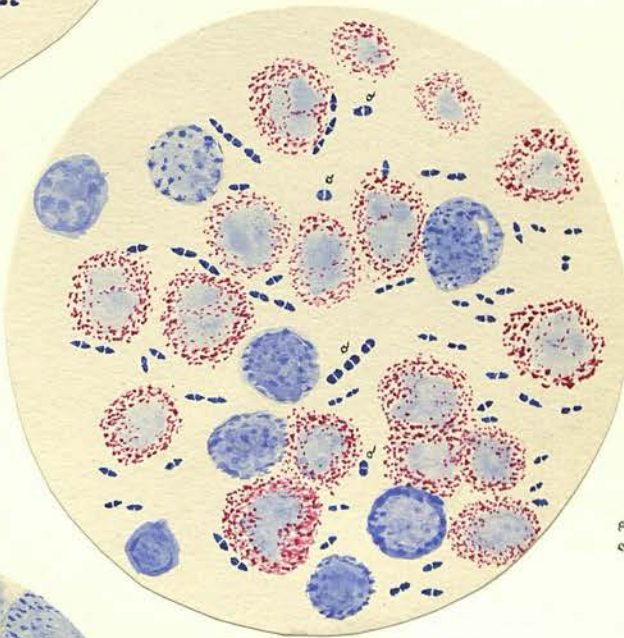
I have been unable to accurately depict the changes seen in the polymorphs in various conditions: though I have done so as far as possible.



1. Pneumococcal Meningitis. Case Hg.
 Film Spinal fluid: 7th day of illness: 3 days before death. 2nd tapping.
 Almost pure lymphocytic fluid. No organisms seen.
 [Giemsa stain.]



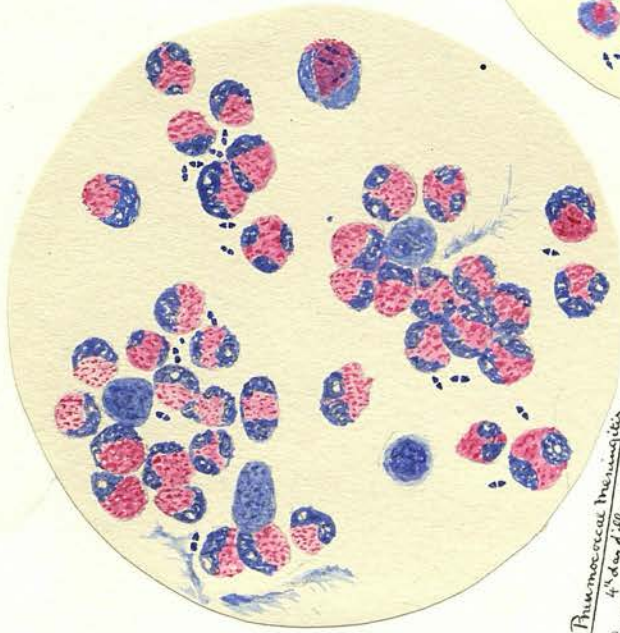
2. Pneumococcal Meningitis (Same as No. 1) Case Hg.
 Film Spinal fluid 24 hours before death.
 Large polymorph leucocytes, also a few mononuclear
 forming with pneumococci.
 Polymorph cells very altered. [Giemsa stain.]



3. Pneumococcal Meningitis
 Film Spinal fluid. Few hours before death: 3rd day of illness
 (Primary: following fall on head Feb. 8/10).
 Cells very altered. Epine pneumococci, also some
 coarse bean-shaped structures (c), also appearing in cells being gran. positive

(All drawn with Oil Immersion lens 1/14)

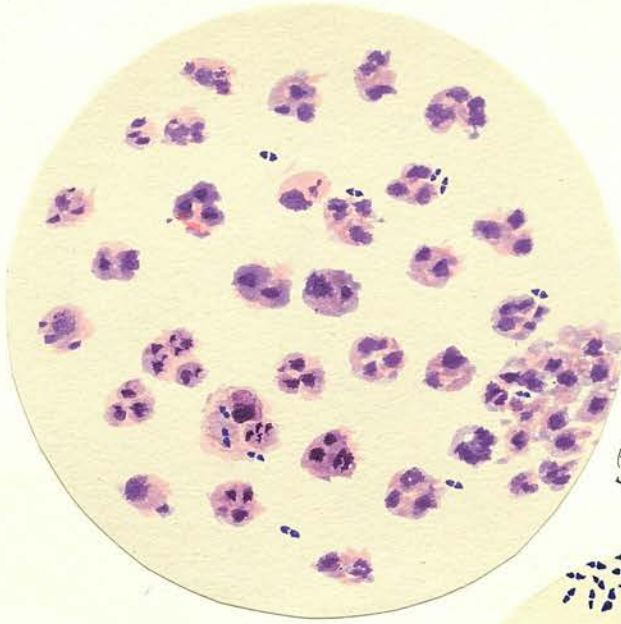
N.B. These are all as actually seen under the oil immersion lens field.
 They are not composite pictures.



4. Pneumococcal meningitis

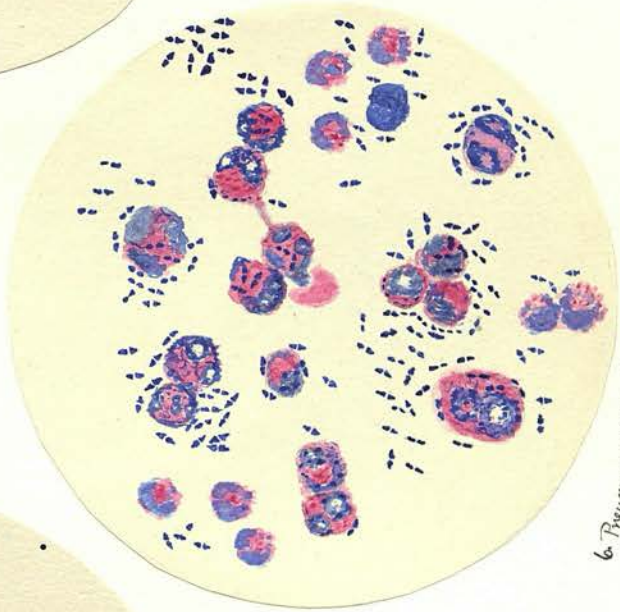
4 days of illness: few horns before death
 Many pneumococci: few mononuclear
 many cells well preserved
 (Pneumococci often injure & head, but not mid)

[Gruner stain]



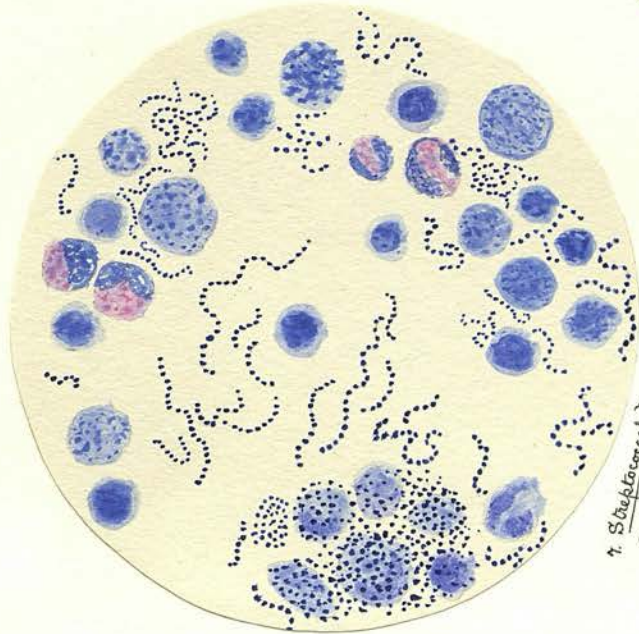
5. Pneumococcal meningitis (Same as No. 4)

Same fluid stained Gruner method; showing
 few foamy organisms.

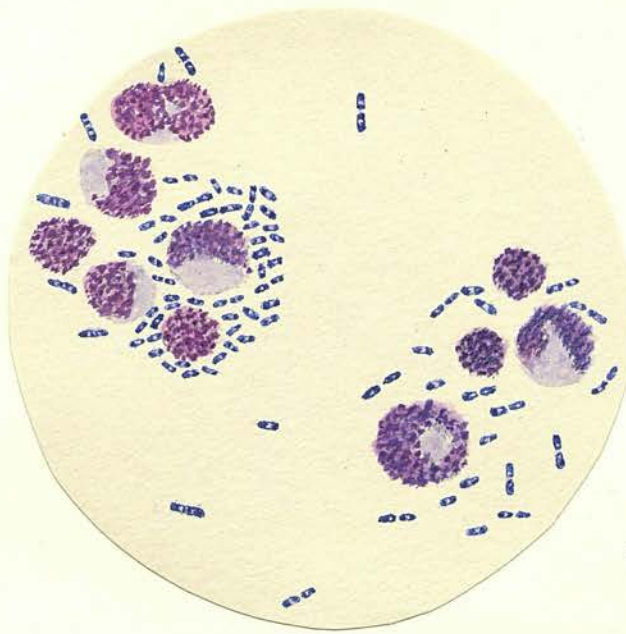


6. Pneumococcal meningitis

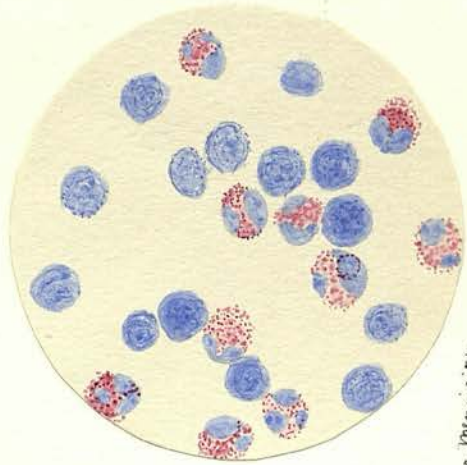
Film spinal fluid about 36 hrs before death: about 6/6 8 days of illness.
 Very few mononuclear. Swimming with pneumococci. Some intracellular
 showing 8 other heads - especially 12 with swimming. [Gruner stain]



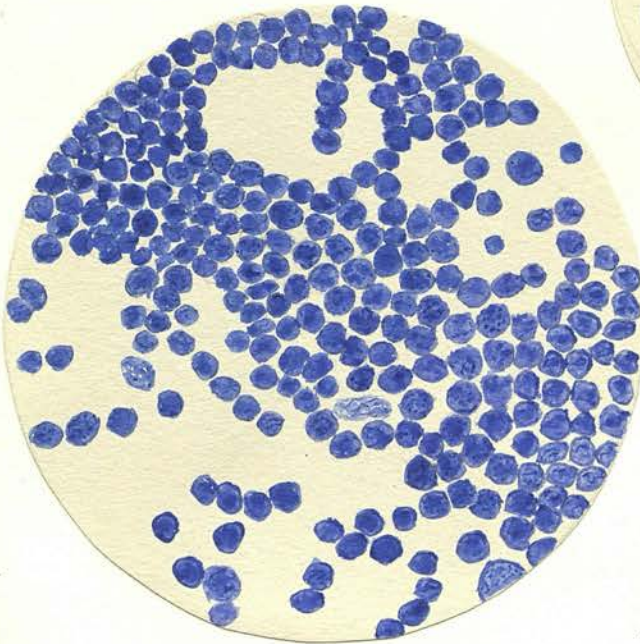
7. Streptococcal Meningitis
 Spinal fluid: Few WBCs
 Very few polymorphs: Very large lymphocytes.
 (Meningitis 3 hrs. containing streptococci in fluid)
 [Fleming's strain]



8. Meningitis and Ventricular haemorrhage
Pneumobacillus in Spinal fluid: and in meninges, pneumonia
 Very few leucocytes in spinal fluid; those included in smears.
 C&G H.P. Abscess in test. [Leishman's stain]
 Film from spinal fluid: obtained immediately after death.



9. Tubercular meningitis
 Film spinal fluid 2nd day of illness: Death on 5th day.
 One tubercle bac. found in corresponding film.
 mixed leucocytes. No cocci seen. [Giemsa stain]

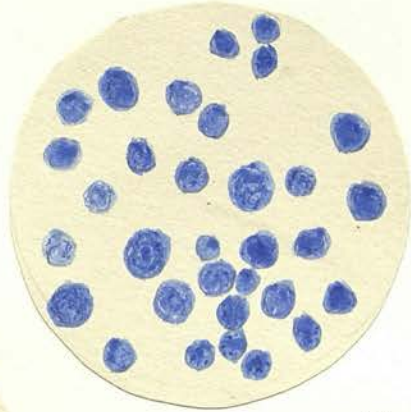


10 Tubercular meningitis

Film spinal fluid, showing large pure lymphocytes. [Giemsa's stain]

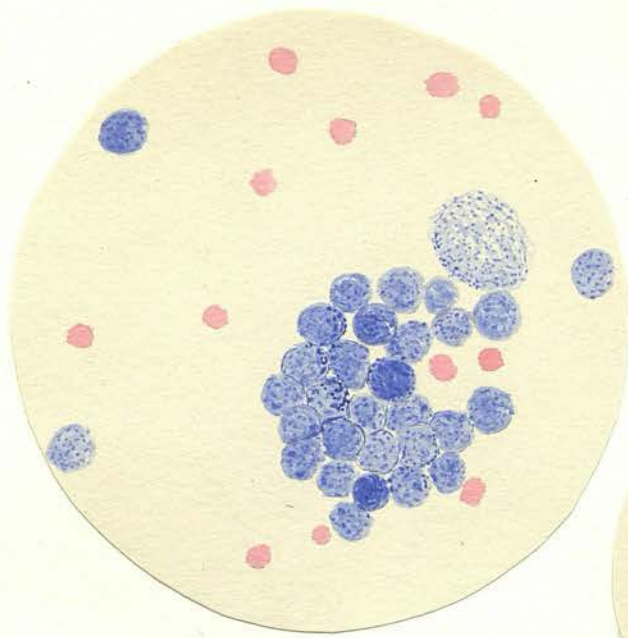
N.B. Small mononuclear predominates in tubercular infection; when even when the polymorph is in excess, the type of mononuclear is the small cell

When in septic and post-brain meningitis the type of mononuclear cell is larger and there are more faint-staining large, foamy granular cells of the mononuclear type.



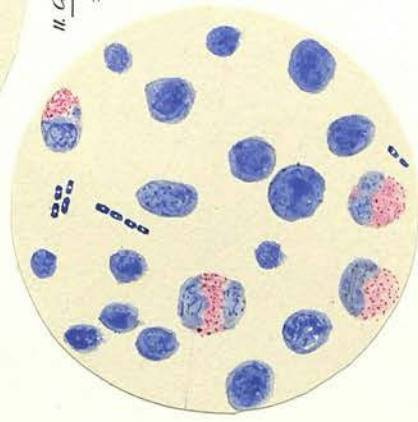
12. Case M.M. decembris in text

Film spinal fluid, 2nd lumbar puncture - about 3 or 4 weeks of illness day before operation. Pure, large, lymphocytes.



11. Acute tubercular Polymenicitis

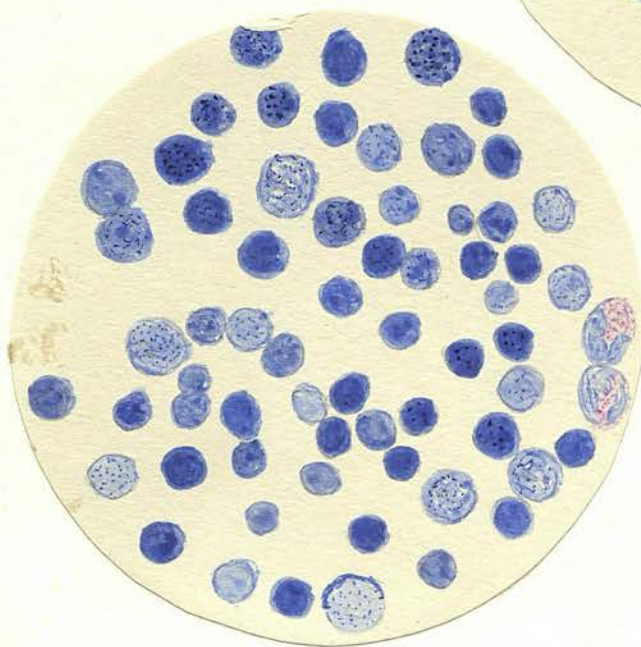
Film spinal fluid, showing large lymphocytes and some red blood cells. Taken 5th day of illness: No tubercle bacilli. No eosin. No polymorphs seen. Lymphocytes seen in the largest smear - but in text: There are many 'clumps' like this. [Giemsa's stain]



13. Case M.M.

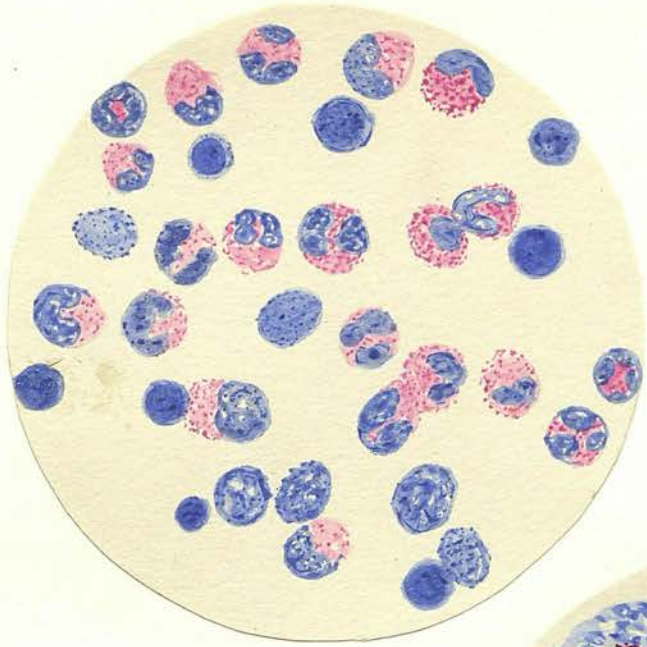
Film spinal fluid, last lumbar puncture: 3 weeks after last exam in 1912. Shows large lymphocytes and presence of a few polymorphs and eosinophilic granular cells. About: left hospital a few days later: it has been well since.

(all drawn with oil immersion 1/2)

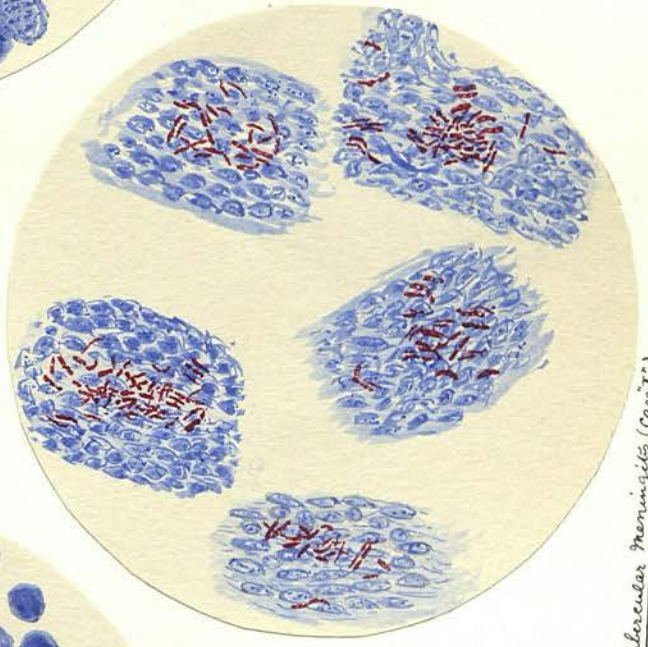


14. Tubercular meningitis (Case I.)
 Film spinal fluid first tapping.
 Pure lymphocytosis.

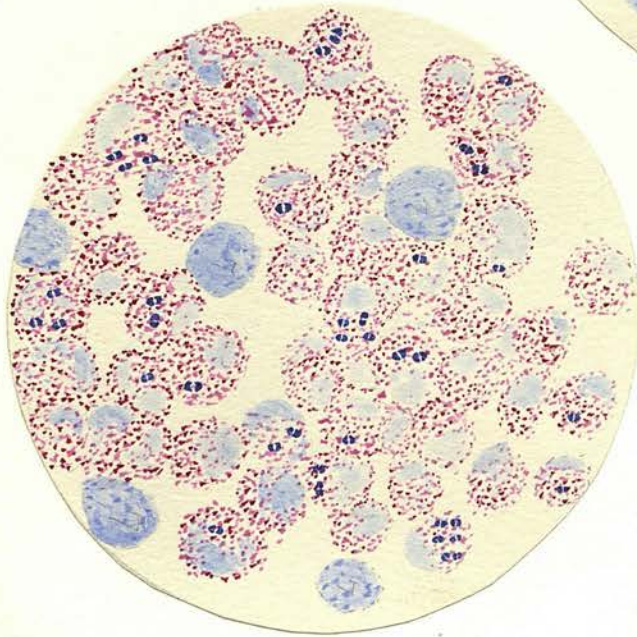
These are all from the same
 case of
 Tubercular Meningitis



15 Tubercular Meningitis (Case I.)
 Film spinal fluid: 10 days later than that
 shown in fig. 14. 1 week before death.
 No organisms seen Culture Sterile.
 Polymorphs, now predominant. May show various
 degenerative changes - vacuolation, etc.
 This case clinically simulated post-tuberc
 meningitis (see photographs)



16. Tubercular meningitis (Case I.)
 Conspicuous from spinal fluid, stained for tubercle bacilli.
 In each of these 5 places seen on the same slide, are large
 clumps of bacilli, readily seen. This is an unusual
 abundance of bacilli, to find in one slide.



20. Posterior Basic Meningitis

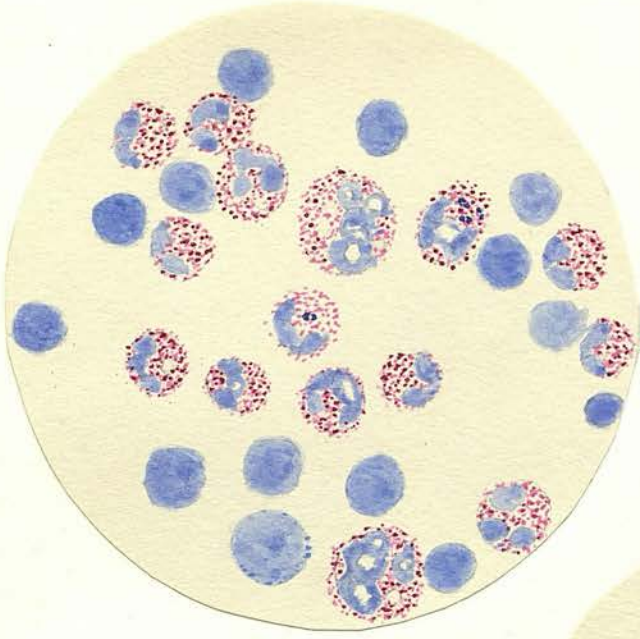
Film Spinal fluid 2nd week of illness.

Very large leucocytes, mostly poly morph

Many intra cellular bean-shaped diplococci.

Cells very much degenerated.

[Jenner's stain]



21. Posterior Basic Meningitis (same case as fig 20)

Film Spinal fluid same case as fig 20. but 10 days

later: about 2 weeks before death. Fluid became

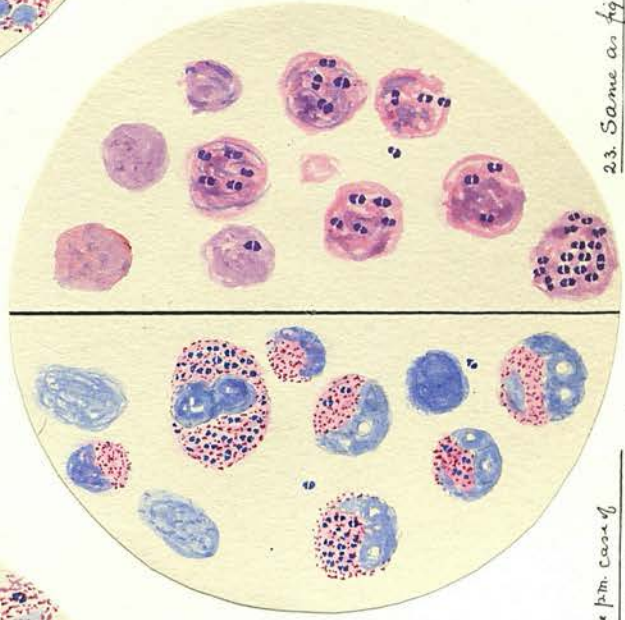
difficult to get on account of clotting, at the

foramen magnum.

Much fewer cocci; more mononucleoh

Cells show marked vacuolation

[Jenner's stain]



22. Same case from Venetia 1st m. case of

Posterior Basic Meningitis: no cocci found

in spinal fluid, which was very scanty.

Note diplococci in cells.

[Jenner's stain]

23. Same as fig 22 but stained by Gram's method (Wigzell's modification)

Shows gram-positive diplococci; mostly intracellular.

(All drawn with Oil Immersion lens 1/10)



Case I: Tubercular meningitis

This photograph does not fully do justice to the very marked retraction of opisthotonus: This developing early in the case produced a strong resemblance to post-tubercular meningitis: Examination of the Spinal fluid gave copious tubercle bacilli on several occasions (see figs 14, 15, 16) and lymphocytes as well; becoming a mixed leucocytosis.

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