T H E S I S

For the Degree of M.D.,

o n

The Nature, and some of the more immediate after-effects of the Pus in

CEREBRO-SPINAL FEVER,

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These notes indicate the nature and more immediate effects of the pus found on the brain and spinal cord in cerebro-spinal fever. They are taken from patients admitted to Ruchill Fever Hospital during the epidemic of 1906-1908, and are mainly the results of post-mortem examinations, particularly of the brain and cord. But, to associate the results with the disease it has been deemed advisable to indicate

1. A brief outline of the history of illness,
2. Some notes of work done at the bed-side, such as blood counts, and cultures.

In the first case described no post-mortem examination was allowed.. In the other cases there are only given in detail those results relative to the subject.

George Stirling, aet. 20 years, was admitted to Hospital on 8th March, 1907. He was perfectly well on the previous day, and slept as usual at night. On the morning of the 8th at 11 a.m. he was suddenly seized with headache, occipital at the commencement, latterly general. Vomiting came on within an hour after. He had no nasal catarrh, no discharge from the nose or throat, no sore throat, and no tonsillitis. He became unconscious at 1 p.m. Examined at 3 p.m., he lay unconscious, with head retracted, arms and legs rigid, Kernig's sign well marked, breathing stertorous, face flushed, temp. 104°F. He remained thus till next morning, when cyanosis of the face became marked, and the pulse feeble and fluttering. He died at 9 a.m. on the 9th, having been ill for 22 hours.

The blood count was as follows;-

Date.	White cells p.c.m.	Red cells p.c.m.
8-3-07 at 3 p.m.	5,886	4,252,000
do at 12 midn.	6,432	4,876,000
9-3-07 at 8 a.m.	6,550	4,320,000

A culture was made from the blood, on the admission of the patient by the following method. The skin at the bend of the elbow was carefully cleansed with turpentine, followed by methylated spirit. A hypodermic needle and an all-glass syringe were sterilized by heating in water. The needle was plunged into one of the veins at the elbow and a little blood withdrawn in a syringe. Three drops were then allowed to fall on to a sloped agar tube and to spread over the surface. The tube was incubated at 37° C. for 48 hours, by which time small colonies had grown. They occurred as small round, translucent, whitish, wet-looking colonies, varying in size from a pin-point to a medium sized pin-head, and shelving off at the margin. Under the microscope they appeared yellowish and slightly granular. Films showed the presence of the Diplococcus intracellularis meningitidis of Weichselbaum. It was variable in size and staining power, and was Gram-negative.

About 1½ ounces of the cerebro-spinal fluid were removed by lumbar puncture, shortly after the admission of the patient. It was under considerable pressure and spurted from the puncture-needle as an opalescent, slightly milky fluid, with no masses of yellow pus, and no shreds of fibrin. On standing, a thin funnel-shaped web of fibrin, with the mouth of the funnel at the surface of the fluid, formed in the test tube. Examination of the uncentrifugalised fluid showed diplococci in enormous numbers lying free in the fluid, and aggregated round pus cells. They occured also in groups of four, and in short chains of three or four. The cells were mostly polymorphonuclear, and were undergoing degeneration, many having a fragmented nucleus; some being swollen up, shewing/

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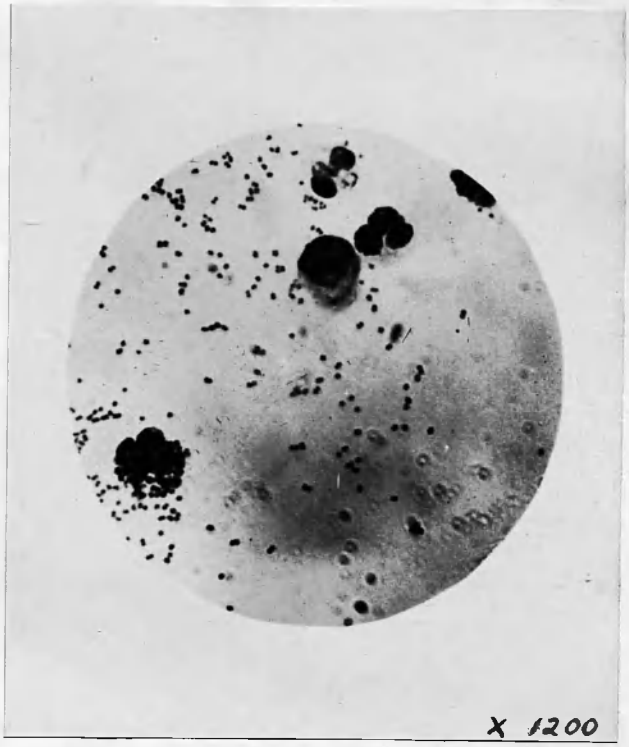

(1) Stirling. Spinal fluid uncentrifugalised, from a severe case, ill only 22 hours.

Shows (a) a great number of diplococci; (b) degenerated polymorphonuclear cells (the lowest one with diplococci); (c) one large mononuclear cell.

showing vacuolation, and staining badly; and others being quite disintegrated. Here and there were small mono-nuclear cells, with little protoplasm, like lymphocytes. Large mono-nuclear cells were also present, but were not such an outstanding feature as in some cases. They had a rounded or oval nucleus, filling a large part of the cell. They were variable in size, all intermediate stages between the small forms and the large forms being found. Diplococci appeared to be inside both the poly-morphonuclear, and the large mononuclear cells, but it is probable this appearance was due to their being on the surface of the cells, as elsewhere they were distinctly seen to be aggregated round them.

No phagocytosis of polymorphonuclear cells was seen.

Cultures grew readily at 37° C. on agar, on blood-smeared agar, and on blood serum. They did not grow at room temperature. They presented the same characters as those grown from the blood. Films showed a Gram-negative diplococcus. This organism in a 24 hours culture did not vary in size and staining, and was always Gram-negative. It was rather smaller than the staphylococcus, and was kidney-shaped, but more globular than the gonococcus, some being quite round. A film from an older culture had a faintly stained background of dead cocci, while the living deeply stained forms could be picked out here and there. These varied greatly in size, some being three or four times as large as the staphylococcus. Large round involution forms occurred, and sometimes one coccus of a pair was small and the other very large. In the older cultures, too, there were many which did not altogether lose gram's stain.

William Cummings, aet. 28 years, was admitted to Hospital on 3rd December, 1906. He felt quite well on 2nd December, taking his food well, and being in good spirits. On the evening of 2nd December he complained of headache, but he had no sore throat, no nasal discharge, no pain in ears, or ear discharge, and no conjunctivitis. At 2 a.m. he was sick and vomiting; headache was severe, and his neck was painful when moved. Next morning there was stiffness of arms and legs, and retraction of neck, and the patient was stuporose though often putting his hand to his head and crying out. Temperature 103° F.

By 7th December patient had improved a little, being able to hear and understand, to some extent, what was said to him. There was now for the first time muco-purulent discharge from nose and throat. Temperature varied between 101° and 103° F.

On 12th December he became worse. He was quite unconscious, breathing was stertorous, vomiting frequent, and loss of control of sphincters complete. He died in this condition on 15th December, 1906.

Blood-count.	Lcts. p.c.m.
4th Dec., 1906,	23,400
5th Dec.,	27,300
7th Dec.,	20,400
10th Dec.,	18,400
12th Dec.,	25,500
14th Dec.,	24,480

The Spinal Fluid, ran in a full stream from the puncture needle, as a very turbid fluid, with fibrinous shreds here and there. About 2 ounces were drawn off, which, on standing, left a copious yellow flocculent deposit, without formation of a funnel of fibrin. Diplococci were present in large numbers, a few being intracellular. A culture on agar grew colonies similar to those already described, and films showed Gram-negative diplococci. Polymorphonuclear cells were numerous, and in stages of degeneration. Mononuclear cells occurred in considerable numbers; some were small, with round deeply staining nucleus, many were a little larger than the polymorphonuclear cells, with rounded or oval nucleus, while a few had an indented or kidney shaped nucleus.

Post Mortem.

The scalp was reflected by the usual coronal incision. In order to ascertain the condition of the Foramen of Majendie without disturbing the relations of the parts a disc of bone was trephined ¼ of an inch below the/

the occipital protruberance, the dura and occipital sinus cut through by a crucial incision and the cerebellum exposed. The lateral lobes were gently separated by the handle of a scalpel. Pus was found between them extending right up to the foramen, and covering it over, but fluid could escape when pressure was applied at the sides.

The skull cap was removed; it was not adherent to the dura mater. The latter was congested, the veins coursing over it being large and full; it was not tough.

The brain was coated with thick yellow gelatinous pus, most abundant in the sulci, and following the vessels. In places it covered and obscured the vessels, but elsewhere it showed as two yellowish lines on each side of them. At the base it had collected in the space between the optic commissures and the crura cerebri. It did not extend forward under the frontal lobes, nor did it follow the olfactory lobes. There was none in the region of the cribriform plate. It was collected under the cerebellum, but limited by a well defined border so as to leave a free margin an inch broad under the lateral lobes. It extended between the lateral lobes of the cerebellum and also over the medulla, involving the region of the foramen of Majendie.

The pus was not free on the surface, but lay in the arachnoid membrane, so that none could be wiped off. A smear was made by incising this somewhat tough membrane, and withdrawing the pus on a platinum loop.

The brain matter was soft, pinkish, and easily torn; there was no localised area of softening.

The lateral ventricles were not dilated, but contained milky fluid with a considerable deposit of yellow pus in the descending portions of the posterior horns. The glistening surface of the ventricles was not destroyed. There were no dilated vessels. The choroid plexuses were bathed in thick pus.

The cord was exposed by cutting through the vertebral laminae. The dura was much congested and its veins full along its whole length, but it was not adherent to the bony canal. About 3 drachms of milky fluid excaped on opening the dural sheath. The cord was congested on its surface. Pus was not present all along the cord; it occurred at the cervical and lumbar swellings where the membranes are normally loose. Nor did it surround the cord, but was found as a band posteriorly. The cord was soft, and had to be hardened before it would cut.

A possible source of infection was now searched for. The floor of the cranial cavity showed no area of softening, a localised redness, or roughness, suggesting extension through/

through the bone from other parts. The surface of the cribriform plate was healthy and no pus was present on its surface. Forcible perforation of the petrous bones over the middle ears revealed the presence of pus in both. The tympanic membranes were healthy and unperforated.

In order to expose the relationship of the cavities of the nose and throat to the base of the brain the following procedure was adopted. The original transverse incision through the scalp was extended on each side to the mastoid process. The scalp and skin could now be reflected back down to the verebral column, and forward to the root of the nose; and thus on completion of the examination they could be replaced in position to preserve the natural appearance. A longitudinal saw-cut was made behind into the foramen magnum and in front through the cribriform plate and the sphenoid and occipital bones, also into the foramen magnum. The halves of the skull were now prized apart, exposing the nasal and pharyngeal cavities, the cribriform plate, and the sphenoidal and eth moidal sinuses. There was no tract found. A large quantity of purulent material was present in the nasal fossae, abutting on the cribriform plate, but there was no visible evidence of extension through the plate. The sphenoidal sinus, the body of the sphenoid, and the basilar process of the occipital bone were all exposed, and were seen to be healthy. The articulations of the Atlas and Axis with the skull were free from disease, and there was no trace of extension from the pharynx to the spinal canal.

Respiratory Tract. The soft tissues of the mouth and neck were removed as follows. The knife was driven up from the original ventral incision under the skin of the neck to the lower jaw, and carried round still under the skin to the mastoid region on each side separating the trachea and oesophagus and surrounding structures of the neck from the skin. The point of the knife was then pushed through the floor of the mouth close to the symphysis, and carried back on each side close to the jaw as far as the vertebral column. The tongue was now pulled through the wound below, and the attachments to the hard palate cut through. The tongue, tonsils, pharynx , larynx and oesophagus could now be separated en masse from the vertebral column. The lungs and heart were removed in the usual manner.

The pharynx contained purulent slimy material; it was congested, but there was no erosion of the mucous membrane. The congestion was marked on the epiglottis, but stopped abruptly at the rima, the larynx being free. The tonsils were about ½ an inch in the longest diameter, and were not ulcerated./

ulcerated. They cut easily and showed on section pockets filled with white cheesy material. There was no evidence of acute inflammation, and no peritonsillar areas of softening or abscess formation. Under the microscope they showed an increase of lymphatic tissue and enlargement of the follicles. Diplococci were found in the debris. Recent pleuritic adhesions were present at the base of the right lung attaching it to the diaphragm; they were soft and easily broken down.

The lungs were much congested and firm to the feel, but crepitant. On section they were intensely red, and a quantity of blood escaped on the knife. A little frothy material could be expressed. Large areas of firm dark irregular patches of broncho-pneumonia were present at both bases, especially on the diaphragmatic surface, and most marked behind. Pus could be pressed from the small bronchi. The larger bronchi were red and congested and contained slimy pus. The trachea was also congested, the redness diminishing in its upper portion.

Under the microscope the broncho-pneumonic patches had greatly dilated alveolar capillaries filled with blood. Some alveoli were collapsed; others contained polymorphonuclear cells in large numbers, epithelial cells having oval faintly staining nucleus, and large phagocytic "catarrhal" cells. The bronchi were filled with pus, and the epithelium was shed and lay in the pus.

The bronchial glands were large and red, their veins being greatly dilated and filled with blood. There was no cellular increase and no excess of polymorphonuclear cells. Cultures were made by searing the surface with a hot iron and cutting into the gland with a sterile knife, but no organisms grew.

The Heart was full of blood; the walls were not thickened, nor fatty.

The oesophagus and stomach were healthy; the lower portion of bowel was coated with greenish slimy material, the vessels were enlarged but indistinct, the mucous membrane having the hazy appearance of catarrh. Peyer's patches were congested and raised above the surface but there was no ulceration. The mesenteric glands were enlarged and red. No cocci grew in cultures, but there were bacilli.

The liver was normal. The gall bladder was full of thick greenish tarry bile.

The spleen was large and soft; the capsule was wrinkled. No organisms grew from a culture.

The kidneys were red and the capsule stripped easily. The cortex and medulla were normal. The pancreas was healthy.

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(2) Cumming. Section of Brain and Pus; shows (a) the thick layer of pus in the pia-arachnoid membrane, the portion near the brain being denser than that towards the dura. (b) the dilated blood-vessels in the brain.

The bone marrow appeared normal. The joints (hip, knee, shoulder, elbow and wrist) were not diseased.

In sections of the brain the pus is in a thick layer on the surface enclosed in the meshes of the arachnoid membrane and shut off from the subdural space by a dense fibrous layer. The dural aspect of this layer is covered with epithelium whose cells are not swollen. Towards the brain surface the meshes are looser, and the cells are loosely packed, but again near the pia where the vessels are more numerous, the meshes are finer and the cells closely packed. In parts the pus is separated from the brain surface by the epitheluim of the pia, but, here and there, there is no epithelium and the pus seems to invade the surface. In sections stained with weak carbol-fuchsin, diplococci are seen. The majority lie in spaces in the outer layers of the arachnoid membrane; some, however, are seen in the polymorphonuclear cells, these latter being degenerated. Near the brain the cocci are few, and nearly all are intracellular. None are found in the brain matter itself, or around the vessels dipping into the brain.

The pus consists chiefly of polymorphonuclear leucocytes, in all stages of degeneration, many of them having fragmented nuclei, and others showing loss of staining power and even complete disintegration. A striking feature is the number included in other cells.

Mononuclear cells occur in various forms;

1 Small cells with round dark nucleus and scanty protoplasm, indistinguishable from lymphocytes.

2 Cells of varying size, with small round or oval eccentric nucleus, and more or less protoplasm, staining well. Some of these attain a large size, and include other cells, chiefly the polymorphonuclear, the nucleus being pressed aside. Vacuolation is frequent in these. (macrophages)
Phagocytosis is a marked feature, many of the cells being three or four times as large as a polymorph, and containing one or two cells, with nucleus broken up. Sometimes the included cell is surrounded by a clear ring. Degeneration forms of this type are frequent; it is evident they do not all migrate back into the blood, but rather disintegrate and disappear.

3 Other cells with round or oval nucleus, and with well marked protoplasm, which is in some cases pointed, or even spindle shaped (embryonal cells).

4 Cells of the matrix of the arachnoid, with pale oval or pointed nucleus.

Fibrin is deposited as a meshwork, and as small amorphous masses. It is not as abundant under the pia mater as in some cases.

Blood vessels are large, numerous, and well filled with corpuscles. Some have altered endothelium as if it had been overstretched. Thrombosis is not apparent.

Young new-formed blood-vessels are not seen.

The brain substance does not appear to be much altered. The blood vessels are dilated; there is some oedema at the surface; and there is a perivascular increase of small cells. There are no cocci, and few polymorphonuclear cells.

Sections of the cord show changes similar to those in the brain. Pus is collected posteriorly in the arachnoid membrane. There is no appreciable alteration in the structure of the cord, and no tract of degeneration.

Sections of the nerve-roots show them to be surrounded by pus which finds its way also between the bundles, following the fibrous partitions. The blood vessels are not dilated to the extent sometimes found in chronic cases. The medullary sheaths are intact, and there is no degeneration or necrosis. The pus is present within and without the fibrous covering of the nerve-root, and it breaks up the root itself into bundles.

William Quinn, aet. 27 years, admitted 1st March, 1907.

He was quite well on 26th February, 1907, till 10 p.m., when he felt cold and shivery and out of sorts. During the night his relatives were wakened by him vomiting. When spoken to, he did not appear to hear. In the morning he seemed a little better; he was not sick; he could recognise people, and he could speak, though with difficulty. There was no nasal discharge; no sore throat; and no tonsillitis. Towards night, 27th Feb., 1907, he became worse, and could be roused only with difficulty. He continued thus till admission on 1st March. He was now unconscious, but every now and then was crying out and putting his hand to the back of the head. The head was retracted; limbs rigid; feet extended. Temperature, 105°F. He continued thus for 5 days and then began to improve. By 23rd March he was able to recognise people and to swallow his food, though the head was still retracted and he lay without moving. Emaciation was extreme. On 2nd April he had a relapse, temperature again reaching 105° F. and unconsciousness supervening. He began to improve again and by 4th May was conscious. Headaches were not severe, and the temperature was more settled. On 10th May, however, he again became unconscious, though occasionally crying out with pain. Ultimately he became comatose. Râles developed at the bases of both lungs, and he died on 3rd June, 1907.

Blood count.	Leucocytes p.c.m.	Red cells p.c.m.
1-3-07,	26,800,	3,884,800
2-3-07,	19,900,	4,352,000
3-3-07,	12,320,	3,688,000
7-3-07,	19,240,	3,452,000
10-3-07,	15,800,	4,888,000
11-3-07,	20,173,	4,388,000
14-3-07,	11,500,	4,648,000
24-3-07,	15,160,	4,616,000
1-4-07,	7,550,	4,312,000
2-4-07,	24,450,	4,288,000
3-4-07,	25,128,	4,350,000
4-4-07,	19,560,	
29-4-07,	16,480,	
11-5-07,	9,560,	
12-5-07,	9,480,	
18-5-07,	10,350,	
25-5-07,	9,350,	

The cerebro-spinal fluid (2nd March, 1907) flowed freely from the puncture needle, about 1 oz. being removed. It was yellow and purulent, and on standing deposited about 15 c.c.s of thick yellow pus, leaving the supernatant fluid slightly milky. A fine funnel of fibrin formed, with its mouth at the surface and lower end dipping into the deposit at the bottom.

Polymorpho-nuclear cells were many. They all had fragmented nucleus, but disintegration was rarely complete and there were few indistinct "fuzzy" forms. Mononuclear cells were numerous. They had large nuclei, which were kidney shaped as a rule, though some were rounded and filled a great part of the cell. Diplococci were sometimes seen inside them, but there were no included polymorphonuclear cells.

Diplococci occurred here and there but they were not numerous. They were found in both forms of cells. Some were free.

The cerebro-spinal fluid, on 14th March, flowed freely, and filled 2 test tubes (1½oz.). It was milky and not as yellow nor as thick as before. No fibrin formed on standing. The same elements were present as before, but in different proportions. All the cells were faintly staining, "fuzzy", irregular masses of protoplasm, with remains of nuclei here and there. They appeared as if in process of digestion rather than in simple disintegration. This would account also for the absence of the fibrin in the form of a funnel, since it also would be digested.

Diplococci were very numerous, and were extracellular.

After the relapse on 2nd April the cerebro-spinal fluid was under considerable pressure, and about 2½ ounces were removed. It was slightly turbid, and had very little deposit on standing. There was no formation of the fibrin funnel on standing.

A portion of the fluid was centrifugalised, films made and stained with dilute carbol-fuchsin. The greater part of the film was made up of cells in a more advanced state of digestion than in the previous film. Clear round remains of cells, containing faintly stained remnants of nuclei, were seen embedded in amorphous finely granular protoplasmic matter. Sometimes even the outline of the cell had disappeared and only a round amorphous mass remained, and there were others even further digested, where the faintly staining amorphous mass looked as if it were being dissolved away. But there had been a fresh shower of leucocytes, and these were scattered throughout the film. Some were well formed polymorphonuclear cells, With/

with definite trilobate nuclei; but others were degenerated, the nuclei showing fragmentation. Mononuclear cells occurred as small round deeply stained forms, though there were others larger and more faintly stained.

Diplococci were few and required careful search.

Post Mortem Examination.

The foramen of Majendie was examined by trephining a disc of bone as before shown. The lateral lobes of the cerebellum were exposed; they were non-adherent, so that they could easily be separated. There was no pus covering the foramen, which was quite patent, but it was limited by tough membrane (the thickened pia-arachnoid), whose sharp firm edges formed an aperture, through which the cerebro-spinal fluid welled out on pressure being applied to the brain at the side. There were no adhesions round about.

On removing the skull-cap the dura mater was found to be thick, but not congested. The brain bulged through on making an incision. The dura being removed the convolutions were seen to be much flattened. The arachnoid was tough and had to be incised before a culture could be taken, as a platinum loop could not be driven through. This thickening was specially marked in small areas, and along the blood vessels so that a patchy and streaked appearance was presented. The membranes, over the rhomboid space formed by the crura cerebri and the optic commissure, also were thickened. A very small amount of yellowish pus was present under the lateral lobes of the cerebellum, but none was present at the base of the brain. The cut surface of the brain was whiter than normal, and the venous radicles, being dilated, appeared prominent on the firm whitish background. The lateral ventricles were greatly dilated so that the outer wall was only ½ inch thick. There was much slightly turbid fluid in the cavities. A small amount of distinctly gelatinous yellowish pus was present in each descending cornu.

A smear from the pus on the under surface of the cerebellum obtained by making an incision in the tough arachnoid and withdrawing some pus on a platinum loop contained,

1 A great number of small mono-nuclear cells.
2 Many larger mononuclear cells, with kidney shaped nucleus at one side. (Many forms occur between 1 and 2.)
3 One or two cells about twice the size of a polymorph, and possessing several nuclei, like giant cells.
4 Very few degenerated polymorpho-nuclear cells.
5 Few diplococci.

The cord appeared normal. There was no pus anywhere along its length; the membranes were not thickened; and there was no granulation tissue.

The skull was sawn down the middle as before shown to obtain a view of the relationship of the nose and pharynx. There was no trace of bone disease, and no diseased tract between the nose or pharynx and the interior of the skull. The cribriform plate was unaltered. The roof of the sphenoidal sinus was thin but not diseased. The articulations of the skull and upper vertebrae were healthy.

Pus was present in the right middle ear. The tongue, pharynx, tonsils, trachea, and oesophagus were removed in mass as before shown. There was no ulceration of the pharynx, though the mucous membrane had a milky appearance and was congested. The tonsils were firm and were not ulcerated. Under the microscope they showed that the lymphatic tissue was predominant; the crypts extended deeply but were not dilated ~~and~~ nor filled with debris, and the solitary follicles were prominent. The trachea was unaltered in the upper part, but was red and congested below. The lungs were congested, and patched with areas of broncho-pneumonia at the bases; frothy fluid and blood could be pressed out.

Pus was seen in the bronchi and in some of the alveoli, and the epithelium of many bronchi was shed and disintegrated. Cultures from the bronchial glands showed no diplococci.

The oesophagus and stomach were healthy.

There was a small erosion at the lower end of the ileum, about half an inch above the ileo-caecal valve. It was $\frac{1}{4}$ inch in diameter with ragged edges and red base and looked like a small ulcer. Under the microscope, however, it simply showed loss of epithelium and congestion of the vessels below the surface. There was no cellular increase.

Peyer's patches were prominent, but were not ulcerated. Cultures from the mesentric glands grew no diplococci. The spleen was large, soft, and dark, and the capsule was wrinkled. The pulp was soft and could be scraped away with the edge of a knife.

The liver, pancreas, kidney and bladder, bones, bone-marrow, and joints were healthy.

Sections including the brain surface showed the pia-arachnoid membrane to be about $\frac{1}{8}$ inch thick in places. It was composed of fine strands of tissue, diffusely woven together and containing few cells, and bounded externally by a more compact thin membrane. The blood vessels were mostly near the brain surface and were dilated.

Polymorphonuclear cells were absent; the majority of the cells were round or oval, staining well, with small round or oval nucleus, excentrically placed. Smaller cells with little protoplasm and deeply stained nucleus were more numerous near the blood vessels, and were probably stages in the development of the larger cells. The pus had disappeared, and its place was not taken by granulation tissue. The polymorphs had either become disintegrated, or digested, or carried away by macrophages, leaving the arachnoid membrane distended.

There was still some unabsorbed fibrin lying in the meshes, massed here and there. The few cells lying free in the arachnoid membrane were mostly mononuclear macrophages. Fibroblasts were rarely seen. At some parts where the vessels were numerous the tissue was much more dense and fibrous, but it was not cicatricial. At the foramen of Majendie this dense layer was of some thickness, and might possibly interfere with the circulation, or with the perivascular lymph flow. (The foramen itself was quite patent.) The brain structure showed little change. There was no increased vascularity, no multiplication of cells, no cloudy swelling or other apparent degenerative change. Diplococcci and polymorphonuclear cells were absent. Where the thin outer fibrous rind of brain merged into the more cellular matter there were numerous spaces. These were increased in number and size. (This often occurs in chronic cases, but is infrequent in acute cases.)

John Watson, aet. 21 years was admitted on 6th March, 1907.

He felt quite well till the evening of 4th March, when he began to complain of pain in the back. He had previously had no nasal catarrh, was not feeling out of sorts, and was not "run down" in health. His back felt stiff, and stooping caused pain. He was quite clear mentally. Through the night he vomited several times. Next morning he looked dazed, but roused himself when spoken to; he did not feel sick and took some food. On the evening of the 6th he became unconscious and was admitted to hospital. He lay with his head retracted and his back arched, taking notice of no one, and crying out at intervals. He was well-nourished. Temperature, 105° F.

He remained in this condition for a week, then he rapidly lost flesh, and by the 20th he was extremely emaciated. He never fully regained consciousness, but gradually became weaker, and died on the 30th March, 1907, having been ill 26 days.

Blood count.	Leucocytes p.c.m.	Red cells. p.c.m.
6th March,	29,430	4,832,000
8th Do	25,380	
10th Do	14,150	4,536,000
15th Do	20,210	4,660,000
20th Do	14,790	
25th Do	13,560	4,415,000

A culture from the blood was made by the method adopted in the case of Stirling, and Gram-negative diplococci were found. The cultures were identical in appearance with those of the Diplococci of Weichselbaum grown from cerebro-spinal fluid, and acid was produced on certain sugar media.

The cerebro-spinal fluid, on 7th March, flowed freely, but did not spurt, from the puncture needle. It was yellowish, turbid, with shreds of fibrin; and on standing had little deposit, but formed a funnel of fibrin. A smear was made without centrifugalising the fluid. It showed a large number of polymorphonuclear cells with fragmentation of nucleus, many having undergone a certain amount of digestion; the protoplasm had flowed beyond the cell margin which had lost its round clear cut appearance. Mononuclear cells occurred here and there, some small, like lymphocytes, others large with oval nucleus. They were also degenerated and did not stain well, the nuclei being badly differentiated.

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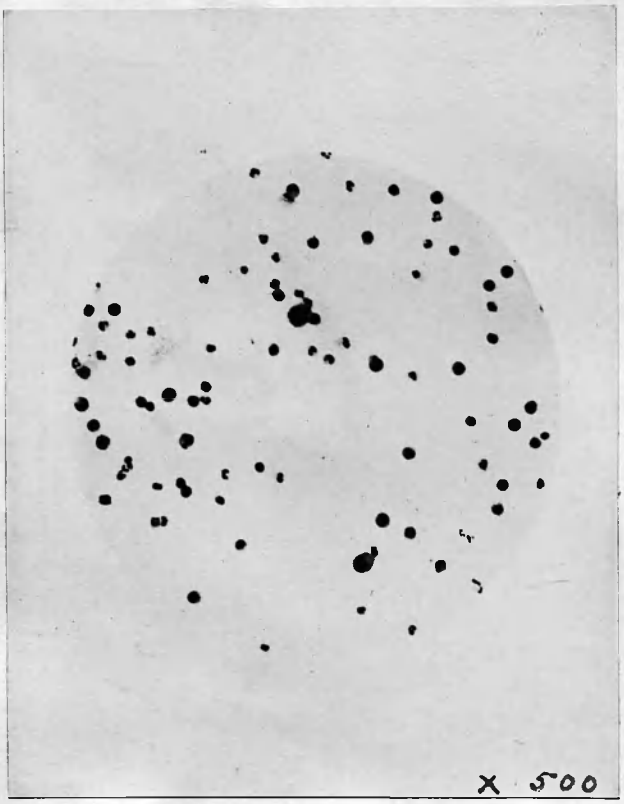

(3) Watson. Spinal fluid, after the acute stage. Sho
a great number of large mononuclear, and very few polymor
phonuclear cells.

Diplococci were few and were found in the cells.

Fluid removed on the 24th of March was turbid and whitish, with no shreds of fibrin. On standing there was little deposit, but a funnel of fibrin formed. A smear was made from the centrifugalised deposit, and stained with Carbol Fuchsin. The outstanding feature was the large number of mononuclear cells. They were of various sizes; a few were small, with deeply stained round nucleus, but the majority were much larger than polymorphonuclear leucocytes, and had large round or oval nuclei which were situated at one side. The largest of them sometimes contained remains of polymorphonuclear cells, and had the nucleus pressed to one side. Some were vacuolated. Polymorphonuclear cells were not numerous. Fragmentation of the nucleus occurred in almost every one. Digestion of the cells was not seen. Diplococci were few, and mostly intracellular. They were generally found inside the polymorphonuclear leucocytes, but occasionally they were seen in the mononuclear macrophages.

The foramen of Majendie was examined by trephining a disc of bone as before shown. There was pus between the lateral lobes of the cerebellum which extended right up to and occluded the foramen, so that no fluid could escape through it. The lobes were held together by the gelatinous pus.

The dura mater was congested, the veins coursing over it being large and full; it was not adherent to the skull cap.

The convolutions were flattened. Pus extended over both hemispheres, lying in the sulci and following the vessels. It was not free on the surface, but lay in the arachnoid membrane, which was tough. It was collected at the base of the brain, as a thick deposit, between the optic commissures and the crura cerebri; but it did not extend forward to the olfactory lobes. It was present on the under surface of the cerebellum, the margins of the lateral lobes being free. The upper surface of the medulla was coated right up to the foramen of Majendie.

There was no part where the inflammation seemed more severe or more advanced, such as is sometimes seen over the temporal lobe in extension of septic meningitis from middle ear disease. The pus was evenly distributed over both sides of the brain.

The brain matter was soft; almost diffluent. The lateral ventricles were dilated to a slight extent, and contained turbid fluid, with deposits of yellowish pus in the anterior and posterior cornua. The choroid plexus on each side floated in pus. There was no localised area of softening of brain substance.

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(4) Watson. Pus from knee-joint. Shows (a) a diplo coccus near the centre of the field; (b) pus cells.

The cord was surrounded by a red and congested dura which was not adherent to its bony canal. There was little pus on the cord, though a narrow band was present behind at the cervical and lumbar enlargements where the arachnoid membrane is looser in structure. There were no red areas of granulation.

The base of the skull was sawn through, by the method already shown. There was no evidence of extension from the nose or pharynx. There was no pus in the middle ears. The tongue, tonsils, and pharynx were removed together as shown for Cummings. The tonsils were large and measured almost half an inch in the long diameter. On section, the crypts were greatly dilated and filled with white cheesy material. A film of this material was made but no diplococci were found. There was no suppuration. The pharynx was congested and catarrhal, but there was no ulceration.

The lungs were red and firm, but spongy and crepitating between the fingers. There were no areas of collapse or consolidation; pleurisy was absent. On cutting with a knife they were seen to be red, and frothy blood escaped. Both bases were dark in colour and had a glassy appearance due to gastric juice digestion. There was pus in the bronchi. The trachea showed an ascending tracheitis. The bronchial glands were red and swollen; a culture was negative.

The stomach was healthy; there was some catarrh of the ileum. The mesentric glands were red and swollen; a culture was negative. The spleen was large and diffluent. A smear stained with carbol fuchsin showed diplococci, and these organisms also grew in culture.

The liver appeared healthy; the bile was dark and tarry.

The kidney showed some cloudy swelling. The capsule stripped readily.

Both knee joints contained about an ounce of oily-looking pus. The synovial membrane did not appear to be ulcerated; it was soft and pulpy and slightly thickened. There was no bone lesion. The pus consisted of polymorphonuclear leucocytes with a number of mononuclear cells having large round or oval nuclei. Diplococci were not infrequent; they were mostly extracellular. Cultures on agar smeared with blood grew colonies similar to those from the brain and spleen. There was no pus in the other large joints.

Sections of the brain show the pus in the pia-arachnoid membrane surrounding the vessels, and spreading out over the surface of the brain. It is not so dense as in Cummings's, and appears to be undergoing absorption.

Phagocytosis is active. Macrophages with single, oval or crescent-shaped, nuclei are numerous, and polymorphonuclear leucocytes may be seen included. Some are vacuolated, and others are pale-stained and degenerated. Polymorpho-nuclear leucocytes are numerous. There are also small momonuclear cells with deeply stained round nucleus. Here and there are round cells with deeply stained protoplasm and a round well marked nucleus; they have the characters of embryonal cells. Only occasionally is there one elongated and pointed like a fibro-blast. Fibrin does not occur in masses, but is seen in places as a network. There are no new formed blood vessels and no granulation tissue. There is no thrombosis.

The pia at some parts intervenes between the pus and the brain matter, but at other places it is absent and the pus merges into the brain substance.

The brain matter does not appear much altered in section. The larger vessels dipping into it are surrounded by cells in greater numbers than normal, some of them being polymorpho-nuclear. The epithelial lining of the ventricles is intact.

The pus on the cord presents the same characters as that on the brain.

Neuritis is not marked and there is no degeneration of tracts in the cord.

One vessel shows septic thrombosis; the endothelial lining is destroyed, and there is pus in its lumen.

The central canal is patent.

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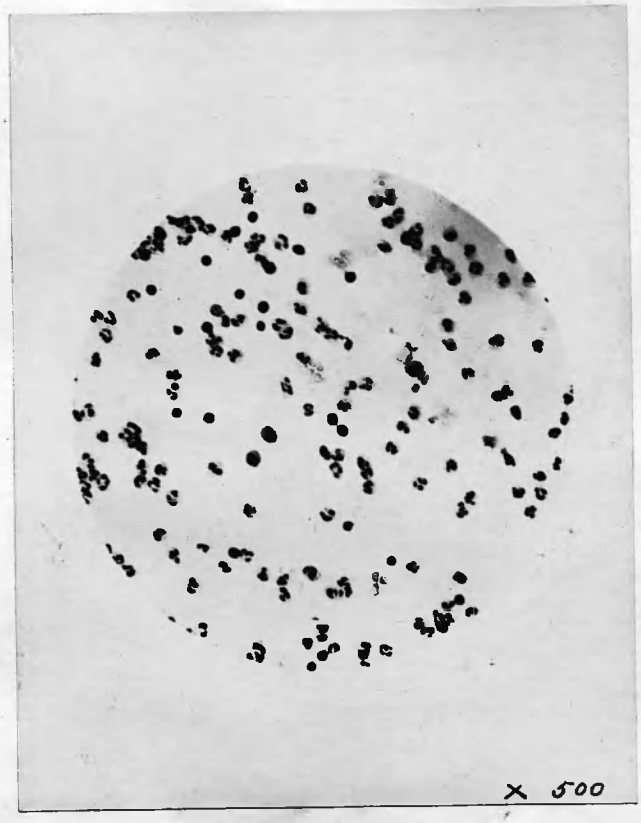

(5) Fitzpatrick. Spinal fluid 1. Shows (a) polymorphonuclear cells with fragmented nuclei; (b) small and large mononuclear cells.

Wm. Fitzpatrick, aet. 6 years. Admitted 20th January, 1907 to Ruchill Fever Hospital.

History.

Patient was quite well on Wednesday, 16th January. At night, on going to bed, he seemed dull. At 2 a.m. he wakened with vomiting. He did not seem to have headache. He had no convulsion. He went to sleep again and appeared to sleep all day, but when he was lifted up at 8 p.m. he could not speak, and was apparently blind. Next day he was rather better and asked for his "Dad", but he was still sick. There was no nasal discharge; no history of ear ~~disease~~ disease; no sore throat. On admission he was dull and apathetic; and lay with his head drawn back; the limbs were not rigid, but the fingers and hand were curled on the wrist; the feet were extended. Temperature, 104·2°F.

3rd Feb. The condition was not much changed. Opisthotonous was more marked. Emaciation was proceeding rapidly.

28th Feb. The patient developed râles at bases of both lungs and became cyanosed.

3rd March, 1907. Patient died.

Blood count. Date.	Leucocytes p.c.m.	Red cells. p.c.m.
21st Jan., 1907,	29,342	4,452,000
10th Feb., 1907,	18,112	4,500,000
24th Feb., 1907,	16,458	4,481,000

Cultures from the blood were negative.

The Cerebro-spinal fluid on 20th January flowed slowly from the puncture needle. It was clear, and measured about an ounce. There was no deposit, and no formation of fibrin on standing. In order to make a film for microscopic examination the fluid was centrifugalised for 5 minutes and the super-natant fluid drawn off. A drop of the residue was then placed on a slide and dried, then another drop added and dried, till sufficient for a film was obtained. Films were stained with carbol fuchsin and with Gram's stain. Polymorphonuclear leucocytes were numerous, but the mononuclear forms were more abundant than usual. They were of all sizes from small forms like lymphocytes to the larger and more typical macrophages. The latter had a large round or oval nucleus and sometimes were vacuolated. Diplococci were few. In addition there was a slender slightly curved bacillus about the length of the diameter of a red blood corpuscle. It often occurred in pairs end to end. (It has been described as a double infection in cerebro-spinal fever, but it is never found in freshly drawn fluid. It grows rapidly, and in two hours may be abundant in the fluid, even at room temperature. It liquefies gelatine, but produces no fluorescence. It is Gram-negative.).

The foramen of Majendie was examined as before. The lateral lobes of the cerebellum were adherent, but could easily be forced apart by the finger gently inserted between them. The foramen was covered by a film of clear gelatinous material. On pressing at the side of brain no fluid escaped, but on puncturing this membrane over the foramen, there was a free flow.

The brain was then exposed in the usual way. The dura was adherent to the bony vault. It was congested, the veins being large and full. The arachnoid membrane was tough and thickened in places giving a milky patched appearance to the surface. These thickened portions occurred along the vessels in streaks on each side; and at the branches, forming triangular areas between two vessels. The membranes were thickened also at the base of the brain, in the space between the optic commissures and the cura cerebri, stretching across like a sheet; between the medulla and cerebellum extending up to and including the foramen of Majendie; and below the lateral lobes of the cerebellum, but leaving a half inch margin all round. These are the most common situations of pus in acute cases. On the other hand there were one or two small areas of pus on the summits of the convolutions away from the blood vessels, these having so far escaped absorption.

The brain matter was not so soft as in acute cases, and did not tear readily. The ventricles were dilated and contained about 3 ounces of fluid. A small amount of yellowish gelatinous pus was present in the posterior cornu of each lateral ventricle.

The cord lay in its congested dura which was not thickened and not adherent to its bony surroundings. There was no pus present. The cord was soft and could scarcely be handled with safety.

The skull was sawn longitudinally as before. The cribriform plate was free from pus, the sinuses appeared healthy and there was no tract of disease leading to the brain surface. There was no pus in the middle ears. The Atlas and Axis articulations were healthy, and no trace of infection to the cord by this route was evident. The nose and pharynx contained a quantity of purulent slimy material, but there was no ulceration. The tonsils were small and did not protrude into the oral cavity.

Laryngitis was absent. Tracheitis was present to a slight degree, extending up the trachea for about 3 inches. Broncho-pneumonia involved half the diaphragmatic surface of the right lung, and pus could be pressed from the small bronchi. There was catarrh of the intestine but no ulceration. The mesenteric glands were enlarged and red. Cultures made after searing the surface showed bacilli but no diplococci.

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(6) Fitzpatrick. From Section of brain. Shows (a) fibroblasts in various stages of development, one of them lying in a mass of fibrin; (b) large mononuclear cells; (c) a degenerated and vacuolated mononuclear cell. in the pia-arachnoid membrane

The liver, kidney, pancreas, bones and large joints were healthy. Cultures from the spleen showed no diplococci.

Sections of brain under the microscope show the arachnoid membrane to be denser and more fibrous towards the dural surface, while the texture is looser and more cellular towards the brain. The outstanding feature is the great number of macrophages. Phagocytosis is evidently very active, and many cells are seen with others included. The macrophages are abundant. They are large cells, with single large round or oval nucleus. Sometimes where the cell is very large the nucleus is seen pressed to one side while the remainder of the cell is occupied by other cells, or by a vacuole. Polymorphonuclear cells are present but they are not numerous and are in stages of degeneration. There are small mononuclear cells with deeply stained nuclei. With the oil emersion lens a ring of protoplasm is seen to surround each. There are others with similar staining characters but with more protoplasm, and others again are larger and protoplasm is abundant. Thus there are intermediate stages between these small cells with dark nuclei, and the large macrophages. But on the other hand there are similar intermediate stages between the small mononuclear forms and connective-tissue cells. Some are seen with their small amount of protoplasm becoming elongated, then pointed at the ends; then the nucleus becomes oval and stains less deeply. These fibroblasts are often found lying in fibrin, sending their protoplasmic elongations into the amorphous mass, and appearing to feed on it.

There are no new-formed blood vessels, and granulation tissue is absent. Fibrin is present in small quantity, occurring under the pia in amorphous masses, and in the pia-arachnoid membrane as short rods and threads. In places it is surrounded by cells and is undergoing absorption. Young connective tissue cells in the outer layers of the arachnoid membrane indicate a tendency to fibrosis.

There is here evidence of (1) disintegration of polymorpho-nuclear leucocytes, and of (2) some of them being taken up by phagocytes, of (3) disintegration of fibrin, of (4) fibrin being eaten by fibroblasts, and of (5) a degree of fibrosis without formation of actual granulation tissue.

There is little change in the brain matter itself. The cells do not show any changes and there is no increased vascularity. A line of ~~vacuolation~~ clear spaces a short distance from the surface is here present as in other chronic cases and probably indicates a degree of oedema.

In the cord there was little change shown. There were no cells in the arachnoid membrane, and no fibrosis. Neuritis and degeneration were absent.

Hugh Harris, aet. 34 years. Admitted to Ruchill Hospital, 14th ~~July~~ Feb., 1907.

The patient was well on 8th January. He had no nasal discharge, or evidence of catarrh; no discharging ears, and no tonsillitis. On 9th January he felt out of sorts but was able to go to work. On 11th January he had pain in the back, headache and loss of appetite. He gradually grew worse, and was admitted on 14th January as ? Enteric Fever. After admission he was delirious, and frequently complained of pain in the head. Retraction of head was evident by 16th January, and lumbar puncture confirmed the diagnosis of cerebro-spinal fever. Emaciation became marked. The patient began to improve by the beginning of February, and was able to talk rationally. He was very weak, but there was no paralysis. In the beginning of March he began to complain of sharp burning pains at spots in both legs. He could put his finger on the spots; and in an hour or two after the onset of pain, a raised, red, oedematous papule, about ¼ inch in diameter would appear over each painful spot. These were very tender. Each spot remained about 5 days, then disappeared, leaving a brown stain. The attacks came on at intervals of about two a day, and two or three spots appeared with each attack. This occurred for about two months . Then in May pain of quite a different character came on. Sharp lightening pains would shoot down the right thigh, and were so severe that morphia had to be given. On pressure being applied along the course of the sciatic nerve the patient would start with pain. There were also tender points in the gluteal region, but they were variable in position, so that at one time patient would wince on pressure at a particular spot, but the next minute pain at that point would be gone, but would be transferred to another point. The knee-jerk was absent, but emaciation was so extreme that it would be impossible to place reliance on its absence. The senses of touch and pain on pricking patient with a needle were not altered. Patient gradually became weaker, and more stuporose, and died on 28th May, 1907.

Blood Count.	White corps. p.c.m.	Red Corps. p.c.m.
15-2-07	20,850	4,152,000
16-2-07,	16,050	3,141,000
17-2-07,	21,100	3,520,000
21-2-07,	28,266	3,708,000
29-2-07,	22,700	3,426,666
3-3-07,	24,800	3,596,000

6-3-07,	28,260	3,996,000
7-3-07,	23,732	
11-3-07,	12,800	
13-3-07,	12,700	3,736,000
24-3-07,	10,700	
16-4-07,	9,650	
30-4-07,	9,800	4,092,000
12-5-07,	9,770	
28-5-07,	10,150	

Cultures made from the blood on patient's admission were negative.

Cerebro-spinal fluid, drawn off on 16th January, 1907, flowed slowly from the puncture needle, about a half ounce being removed. It was turbid, and deposited fibrin on standing. Under the microscope it shows polymorpho-nuclear cells in stages of degeneration. There are a few large mono-nuclear forms, with large round nucleus filling the greater part of the cell. Diplococci are few but occur free in groups, and in the polymorpho-nuclear leucocytes. They are Gram-negative.

Cultures were made on agar and grown at 37o C. Colonies formed in 36 hours, and the diplococcus of Weichselbaum was recovered from them. No organisms grew at room temperature.

A further specimen of fluid was obtained on 3rd March, 1907. It was clear and flowed freely, 1½ ounces coming away. There was no deposit on standing, but the formation of a clear funnel of fibrin was distinct. A portion of the fluid was centrifugalised but little deposit was obtained, so a film had to be made by drying a drop on a slide, then placing on another drop and drying, till a suffieient amount was obtained. Such a film shows very few cells. They are mostly small mononuclear cells though a few polymorphonuclear and one or two large mo no-nuclear cells occur. They are partly disintegrated as if they had been in the fluid for some time. The type is thus different from the fluid first obtained and resembles that from a case of tubercular meningitis both in the number and in the form of the cells. There are no organ-isms.

The condition of the foramen of Majendie was examined by removing a disc of bone as before. The lobes of the cerebellum were adherent, but could be separated by gently inserting the finger. The foramen was distinctly patent, and was bounded by a sharp edge of thickened membrane. Fluid trickled through the opening, on pressure being applied at one side.

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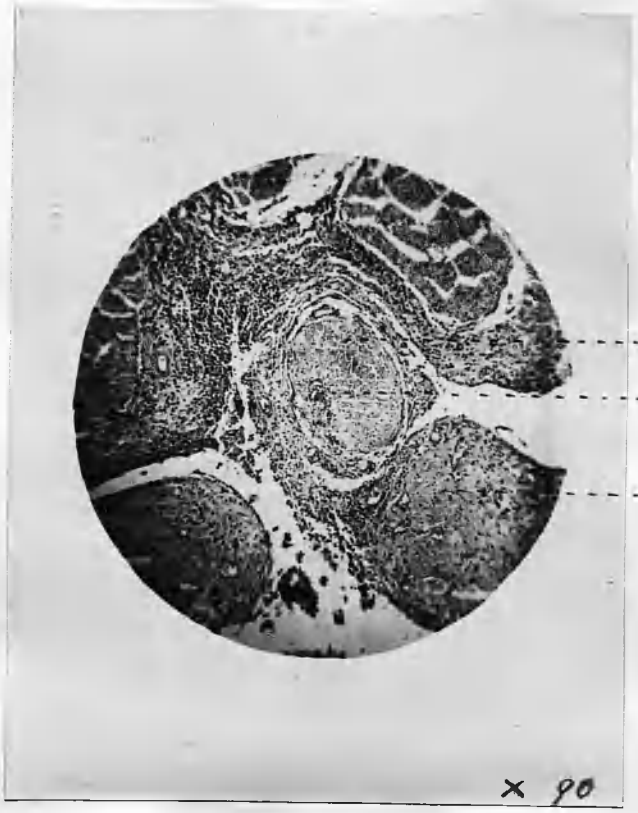

(7) Harris. From Section of spinal cord in lumbar region. Shows (a) in the middle of the field a completely necrosed nerve with two old vessels intact; it is being invaded with granulation tissue at its lower end; (b) granulation tissue surrounding the necrosed nerve; (c) a nerve broken up into islets; (d) degenerated nerves being invaded by granulation tissue.

The skull cap was then removed and the thickened dura exposed. It was adherent to the bone; it was not congested.

The convolutions were much flattened. The arachnoid membrane was thickened and pearly, especially alongside the vessels where it was distinctly opaque. There was no pus; no reddish area of granulation tissue, and no fibrin on the surface.

The brain matter was tough and white, the enlarged venous orifices being prominent on the white ground. The lateral and third ventricles were greatly dilated, so that the brain tissue at some parts was only ¼ inch thick. They contained turbid fluid, but no yellowish pus. The choroid plexus on each side was unaltered. There were no areas of softening.

Sections show the membranes to be thickened by an increase of fibrous tissue. Polymorphonuclear cells are absent. Large mononuclear macrophages are abundant. Fibroblasts occur in the outer layers. There is no granulation tissue, and no new formation of vessels.

The cord lay in a small quantity of turbid fluid enclosed in a thickened vascular dura which was adherent to the bony canal. Red patches of granulation tissue studded the cord along its length, and fixed it to the dura. The granulation tissue was abundant at the lumbar thickening, posteriorly; and also round the nerve roots which were involved. There was little granulation tissue in the dorsal region and here the membranes were pearly, and the vessels large and numerous. The cord like the brain matter was firm, and not diffluent as in some acute cases.

Sections in the lumbar region show many points of interest. Granulation tissue is taking the place of the pus; and the nerve roots are seen in all stages of neuritis and degeneration, some being completely necrosed.

The pus which has at one time surrounded the cord is becoming replaced in parts by granulation tissue, in other parts by simple fibroblasts, as in Fitspatrick's case. Polymorphonuclear cells are present, but they are scarce and are degenerating; fragmentation of nucleus occurs in them all. At some places, where the changes are less advanced, large macrophages occur with abundant protoplasm and round or oval nucleus; some have included polymorphonuclear cells, and others are vacuolated. In most parts the changes are further advanced. Young thin-walled blood vessels are abundant. The pus cells (microphages and macrophages) have given place to fibroblasts, and the fibrin has disappeared.

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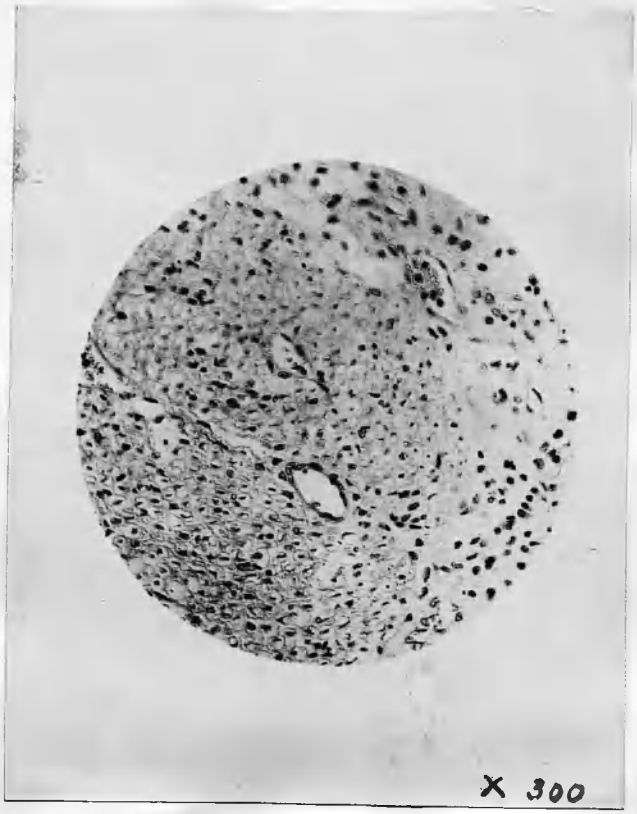

(8) Harris. From Section of spinal cord in lumbar region. Shows (a) a partially degenerated nerve (on the left) being invaded by granulation tissue (on the right).

The fibroblasts are seen in all stages of development. Some are small round cells, with round dark nucleus and just a ring of protoplasm; others have more protoplasm; others are beginning to elongate and have pointed ends; while still others have an oval nucleus. The more advanced forms have an oval pale nucleus, and a narrow protoplasmic fibre.

Fibrin occurs (1) as a network and as amorphous masses between the cells; (2) as a definite layer of pale-staining amorphous or faintly fibrillar material under the pia. The changes are somewhat different in the two situations. The fibrin among the cells is partly disintegrated, and partly absorbed by macrophages and fibroblasts; blood vessels have entered it, and granulation tissue is replacing it. Under the pia the changes are not as active. Some parts are undergoing no change; others contain a few young fibroblasts, and these latter are elongating and insinuating their processes in amongst the amorphous material, and living on it. In only a few places are blood vessels seen penetrating it. It would appear therefore that fibrin, where it is in masses, is acted on slowly and with difficulty and that it becomes replaced only after a long time by fibrous tissue, without, as a rule, the more active process of vascularisation and formation of granulation tissue.

No diplococci were found in sections stained with carbol-fuchsin, or Methylene blue.

Nerve changes are seen. The earliest commence as neuritis with increased vascularity of some roots, the dilated vessels running in the fibrous partitions separating the bundles; other roots show the bundles broken up into islets and containing nerve fibres which have lost their medullary sheaths; in others again the nerve fibres are represented by the merest outlines - small circular spaces with here and there an axis cylinder not quite gone, and represented in eosin-stained sections by a red point. Completely necrosed nerves are seen in sections as structureless masses, oval in outline, and enclosed in a sheath or surrounded by granulation tissue. The remains of nuclei are still apparent. In some cases the main artery and vein of the nerve lie intact, but dilated, and surrounded by the necrosed tissue. The so-called process of repair is seen in an invasion by granulation tissue. One nerve is seen without a definite sheath, its place being taken by young connective tissue cells, while thin-walled blood vessels penetrate from the periphery into the interior, and young fibroblasts with pale oval nuclei are scattered round them.

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(9) Harris. From Section of spinal cord in the thoracic region. Shows (a) degeneration in the column of Goll; (b) great dilatation of vessels in the posterior horn; (c) fibrin on the surface of the cord.

The blood vessels and cells are more numerous at the periphery, showing that the change takes place by invasion from without.

The sections thus indicate the history of nerve change, viz., increased vascularity and oedema; destruction of the medullary sheath; death of the axis cylinder; and necrosis of the nerve root en masse; ingrowth of new vessels. and proliferation of young cells.

The older vessels show in some cases a degenerative change in the outer and to a less extent in the middle coats, these being faintly stained and in parts hyaline. Sometimes the outer coat is invaded with fibroblasts. There is no destruction of the endothelium; and no thrombosis. In at least one vessel in the sections there is an atheromatous patch.

The most important change in the spinal cord in the lumbar region is the degeneration of many of the fibres, which occurs chiefly in the posterior portions to the mesial side of,and also including,the posterior horns. It is more marked and more localised on one side. (the severe neuralgic pain was on one side - the right). On the other side it is more diffuse. The medullary shea- sheath has disappeared from most of the fibres, leaving only the axis cylinders and even these are degenerated. There is no increase of cells in this area, and no fibrosis. In the anterior horn of one side there are patches of softening; some appear to be in relation to the blood vessels. There is one area of considerable size. The nerve tissue is destroyed and there is an extravasation of red blood cells. Small round cells with little protoplasm are scattered in it. Where a blood vessel is seen its walls are degenerated and hyaline.

The large nerve cells are little altered. The nuclei are well marked, and the granules large and distinct.

The central canal is large and contains cellular debris, but no pus.

Sections in the middle thoracic region show marked processes of repair. Polymorphonuclear leucocytes are absent, and the pia arachnoid interspaces, instead of being solid with cells, are left almost free again, except for unabsorbed fibrinous masses and rods here and there, and for occasional formative cells. But the fibrin under the pia mater is denser and shows distinctly the formation of fibrous tissue, without a typical stage of granulation. Young blood vessels though they occur here and there, are infrequently met with. Where they do occur fibroblasts are abundant. But apart from these, fibroblasts in all stages are seen. They are round cells, with nucleus large,round,deeply stained, centrally situated, and occupying the greater part of the cell; the protoplasm stains/

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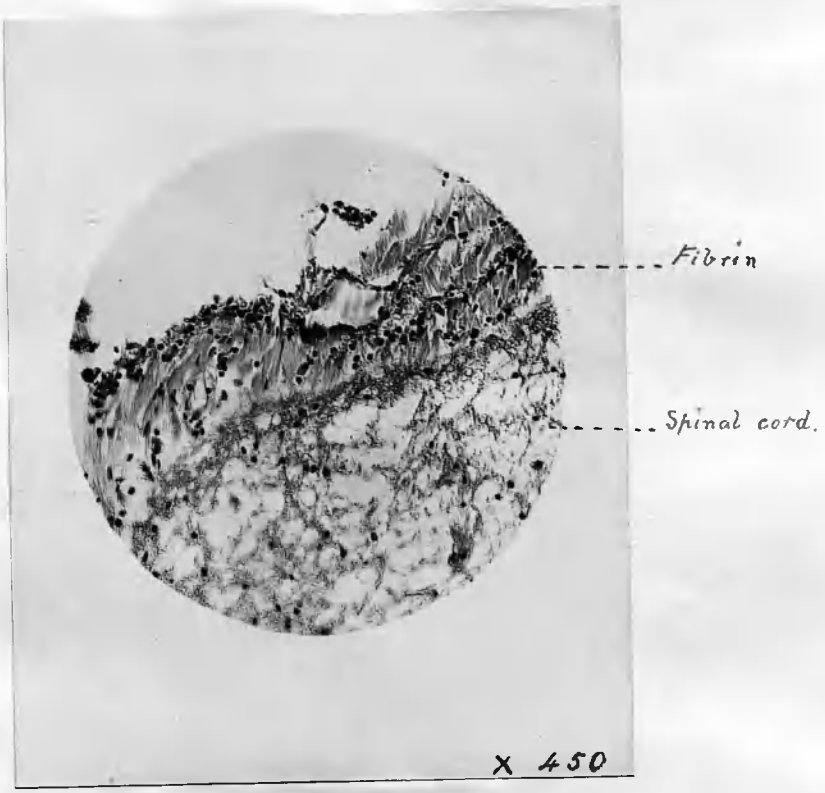

(10) Harris. Section of spinal cord in the thoracic region. Shows fibrin on the surface of the cord being replaced by fibrous tissue.

stains well with eosin. Older forms are seen as oval cells with protoplasm drawn out at each end. In some cases this protoplasm can be seen insinuating itself between the paler fibrin rods on which it appears to live. Adult cells are seen with long narrow pale nucleus and attenuated protoplasm. Thus without actual disintegration of the fibrin, and without much vascularisation, the change into fibrous tissue takes place, the fibroblasts acting like phagocytes.

The nerves are degenerated. Many of the fibres are without medullary sheaths, though actual necrosis has not occurred. The outstanding feature is the presence of numbers of large vessels. In some cases these occupy almost the whole nerve bundle; many are thin-walled and evidently newly formed, but others have more definite walls and appear to be vessels normally present, though enormously dilated. There is no replacement by granulation tissue. There is thrombosis of one or two vessels of the pia mater.

The cord in this region has two narrow bilateral tracts of degeneration just inside the posterior horns, and occupying the position of the Columns of Goll. Degeneration of fibres is not wholly confined to these columns, but occurs generally in the white matter. The medullary sheaths of many nerves have gone, and there is an increase in the connective tissue of the matrix.

The grey matter is broken up leaving spaces in its substance. The vessels are large and numerous, occupying a great part of the posterior horns. The multipolar nerve cells are indistinct, the nucleus is hazy, and the large granules are prominent. The central canal is obliterated, though it is represented by the irregularly placed cells of the epithelial lining.

The remainder of the post-mortem examination showed little relative to the subject.

The skull was sawn longitudinally as before and showed no lesion pointing to an invasion of the brain from the throat or nose. Otitis media was absent.

The pharynx was oedematous and congested, the cervical glands swollen; the tonsils were not enlarged and not ulcerated.

The lungs were red and oedematous, with large areas of broncho-pneumonia at the bases; there was no pleurisy. Cultures from the bronchial glands were negative.

The heart was pale and flabby. It was not fatty. There were patches of atheroma in the first part of the aorta.

The oesophagus and stomach were coated with slimy material. The bowel was congested, especially at its lower end; there was no ulceration. Peyer's patches were pink and swollen. The mesenteric glands were swollen and red. Cultures ~~showed~~ showed from the glands bacilli, but no diplococci. The mesentric veins were large and full. The kidneys, spleen, liver, pancreas, bones and bone-marrow showed unimportant changes. The large joints contained no pus.

Harriet Arthur, aet. 10 years was, admitted to Ruchill Fever Hospital on 18th January, 1907.

History.

The patient was quite well on 16th January. She had a good appetite and was not in the least out of sorts. She had no nasal catarrh, no sore throat, no tonsillitis, and no cough or pain in the chest. On going to school that morning (16th Jan.) she felt a slight pain in her back. The following day the pain was still there but it was not severe enough to prevent her going to school. She had a slight headache all day. During the night she "talked in her sleep." Next day (18th Jan.) she felt ill, and was very thirsty. She vomited anything she took to relieve the thirst. Headache became severe, and the pain in the back worse. She was admitted to Hospital the same day.

On admission (18th Jan.) she was drowsy. The headache was as severe as to make her scream out at intervals. The head was retracted and the muscles of the neck rigid. The arms were rigid and tremulous; the fingers were flexed and the thumbs turned in. The feet were extended; the knee-jerks absent; Kernig's sign well marked; Babinski's sign absent. There was hyperaesthesia of the legs, the slightest touch causing the patient to cry out. A few petechial spots were present in the skin in the left iliac region. The patient was well nourished.

After admission she began to improve, and by 23rd January she was able to answer questions readily, though she lay limp in bed with head still retracted. Emaciation, however, was just beginning to be noticeable. (The improvement is also seen in the blood count given below). At the beginning of February she had no headache, and no mental apathy; and the temperature had remained normal for a week. Retraction of the head was slight. Emaciation was considerable. She remained like this, till the beginning of March, when she had a relapse. The temperature showed great oscillations. Patient was stuporose, but at times screamed out as if with pain. Retraction of head was marked. Lumbar puncture was performed but no relief was obtained. Diplococci were found in the fluid. The patient gradually sank and died on March 16th, 1907.

On 19th January a small quantity of blood was taken from a vein in a sterilized syringe, and smears were made on agar and blood-serum and incubated at 37° C. No organisms grew.

Blood counts show a leucocytosis, this being mainly due to an increase in the polymorpho-nuclear cells.

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(11) Arthur. From Section of spinal cord. Shows proliferation of cells in the coats of vessels.

Date	White cells p.c.m.	Red cells p.c.m.
19th Jan.,	27,730	4,150,000
21st Jan.,	25,680	4,350,000
23rd Jan.,	20,350	3,880,000
25th Jan.,	12,200	
1st Feb.,	10,480	3,650,000
14th Feb.,	11,310	4,158,000
3rd Mar.,	28,150	4,335,000
4th Mar.,	27,230	
6th Mar.,	27,180	
10th Mar.,	29,360	4,546,000
14th Mar.,	17,280	

The Spinal fluid,(19th January,) flowed slowly from the puncture needle, and about half an ounce of yellow turbid liquid was removed. A copious deposit formed, and there was a well marked funnel of fibrin after a few hours. The funnel was opaque from the presence of entangled cells. Polymorphonuclear cells were abundant; mononuclear cells occurred but they were not numerous, nor large. Diplococci were found free and in the polymorphonuclear cells. Cultures were made on agar at 37° C. and grew the usual colonies; films from the colonies showed Gram-negative diplococci.

The brain was examined by first exposing the foramen of Majendie as shown for Cummings. The lateral lobes of the cerebellum were not adherent, and were easily separated by the handle of a knife. The foramen was patent and fluid was seen welling out. A small quantity of gelatinous pus was present between the lobes.

The vault of the skull was next removed and the congested dura exposed; it was not adherent to the bone. Large veins were seen coursing over it. The surface of the brain was congested, and the convolutions were slightly flattened. There were small areas of gelatinous pus here and there, more especially over the vessels, but also in places between them. The pia-arachnoid membrane was opaque and so tough that a "platinum loop" would not penetrate them to obtain a smear of the pus, - a small incision had first to be made with the point of a knife. Pus was also collected at the base of the brain, in the space between the optic commissure and the crura cerebri, and underneath the cerebellum, between it and the medulla.

The brain matter was soft and pink. The ventricles were dilated and contained about an ounce of turbid fluid, while a small quantity of gelatinous pus was collected in each descending cornu. The choroid plexus of each side was bathed in pus, and its vessels were engorged. The

fourth/

fourth ventricle was large enough to admit the tip of the little finger.

The spinal cord lay in its membranes, surrounded by a small quantity of fluid. The vessels were dilated. The arachnoid had lost its glistening character, and at places was thick and pearly. Small collections of pus were found along the posterior aspect, and here and there were little pink spots of commencing granulation.

Sections show a condition of affairs explained by the history; namely, changes due to a former attack (as seen in the increased number of small round cells, commencing granulation-tissue-formation and the changes in the blood-vessels) side by side with signs of a most recent attack (as seen in the collections of recently formed pus).

The pus is found posteriorly. lying in the meshes of the arachnoid. It consists mainly of polymorphonuclear leucocytes which show signs of degeneration, some having fragmented nucleus, and others staining badly. A few are seen inside the large macrophages. The latter are of variable sizes, have small oval nuclei, are sometimes vacuolated and show signs of degeneratio n. Some attain to a large size, and in these the nucleus may be pressed aside.

There are no newformed blood vessels in this pus, and no evidence of granulation tissue. At other parts of the section, the polymorphonuclear cells - and to a large extent the fibrin - have disappeared, and young embryonal cells are increased in number. These are in various stages of development. They are often scattered amongst the masses of broken down fibrin, and sometimes a cell may be seen insinuating its attenuated process into the debris. Fibrin occurs in masses, either amorphous or fibrillated. It is plentiful towards the surface of the cord, where it is collected both under and above the epithelium of the pia mater. Here it is dense, has a fine fibrillar structure, and stains faintly. Much of it is unchanged. In places, however, it has been invaded and replaced by small round cells. In the arachnoid meshwork it is broken down. In one part young thin-walled blood vessels have grown into it, and fibroblasts are collecting, thus showing commencing granulation-tissue formation. Well formed granulation tissue is not seen in the sections.

Many of the blood vessels are greatly altered. Some have their whole wall ~~invaded~~ transformed by embryonal cells, so that only a few of the original cells remain unaltered. Others have their endothelium destroyed. No thrombosis is seen.

The changes in the nerve-roots are not great. There are no dilated vessels, there is no necrosis and no invasion by granulation tissue, such as is seen in Harris' case. Some of the fibres have lost their medullary sheaths. The fibrous sheaths of some of the nerve roots are invaded by small cells.

The cord shows no tracts of degeneration and no fibrous change. There is an increased vascularity of the grey matter, which from the clear spaces in it, looks as if it had been oedematous. The central canal is patent.

The base of the skull was examined by the method before shown. There was no tract of infection found. Pus was found in both middle ears.

The stomach and intestine contained slimy mucus. There were several small red areas about ¼ inch in diameter under the mucous membrane of the ileum, but they were not ulcerated. Sections showed the submucous coat to be swollen and the vessels dilated, but there was no extravasation of blood. The bones were normal, and there was no pus in the joints. The spleen, liver, kidneys and pancreas showed nothing noteworthy.

Joe Docherty, aet. 24 years, admitted to Ruchill Fever Hospital, on 6th March, 1907.

He had been quite well till the evening of 1st March, 1907. He had had no nasal discharge, no sore throat, no tonsillitis, and no discharge from the ear. The illness began with a dull pain in the head, and loss of appetite. The headache became more severe during the two following days, and the patient was sick. He was admitted on 6th March, certified as "Enteric Fever?" After admission, retraction of the head was noticeable, delirium was marked and the patient screamed with pain. Gram-negative diplococci were present in the cerebro-spinal fluid, and there was a high degree of leucocytosis of the blood (27,100 p.c.m.). During the first few days after admission the head became more retracted, and vomiting more frequent. The patient continued thus till the beginning of April when he began to improve, and gradually became more rational. He still complained of slight headache; and he was very weak and emaciated. He could not move his legs in bed, and the knee-jerks were absent. On 17th April he complained of shooting pains down his legs so severe as to make him cry out. On 21st April large watery blisters appeared on the soles of both heels (not on the part resting on the bed). The blisters broke and left ulcers, which, becoming deeper and deeper, resembled perforated ulcers. There was still pain in the legs, but it was now gnawing, rather than shooting, in character. His legs gradually regained power, but the ulcers showed no signs of healing. They were about half an inch in diameter, extended down to the bone (oscalcis) and were steep-edged and lined with pale firm fibrous tissue. In June, i.e. after 3 months they began to slowly improve. In July, the patient had several attacks of neuralgic pains in the legs and in the left side of the chest, but these ceased after the lapse of a week. The patient was now able to be up. The ulcers on the heels were improving slowly.

On 30th October, 1907, he was dismissed, having been ill nearly 8 months. He was quite well mentally; he had regained his strength and weight; and the ulcers of the heels were almost healed.

	Blood - count.	
Date.	White corps. p.c.m.	Red corps. p.c.m.
14th Mar. 1907,	27,100	4,760,000
15th do	25,300	
26th do	29,080	5,056,000
27th do	43,600	
31st do	46,800	

1st April,	28,000	5,188,000
2nd do	29,431	
6th do	20,365	
6th May,	11,180	4,988,000
6th June,	10,430	
6th July,	11,150	
6th Oct,	10,280	5,150,000

Cultures made from the blood were negative.

A REVIEW OF 109 CASES.

The Mode of Infection.

The History.

Occasionally there are premonitary symptoms of malaise, weakness, loss of appetite, or general pain, (Enteric Fever may be simulated) but as a rule headache is sudden. There is no history of immediate otitis, of nasal discharge, of pharyngitis, or of tonsillitis. Usually the patient is perfectly well when headache suddenly supervenes. The position of the headache gives no clue as to the seat of origin. It may be temporal, or occipital, or frontal. Pain may first be felt in the back.

From Examination.

The results of examination, clinical or postmortem, are mainly of value from a negative point of view.

Ear inflammation is not an early symptom. The tympanic membranes examined early in 16 cases, were not even congested. Diplococci were found in the external ear in 8 of the 16 cases, but in one only did it answer all the tests for the diplococcus intracellularis meningitidis. The profuse muco-purulent nasal discharge met with in the disease is never an early symptom. In an examination of the base of the skull in 18 cases, by sections showing the relations of the nose and pharynx to the brain, there was no tract of communication to the brain. The cribriform plate was healthy; moreover, pus was often absent from the olfactory lobes, when it was thick elsewhere. The roof of the sphenoidal sinus was often thin, but never diseased. There was no tract through the bone (base of the sphenoid or the occipital). The articulations of the skull with the first two vertebrae were healthy. There never was any localised collection of pus on the brain (such as sometimes obtains in a spread from the ear) to indicate a source of origin. It was true, pus was usually found in one or other middle ear, but that was most probably an extension from the throat along the Eustachian tube.

Ulceration of the pharynx was not primary. The tonsils of 109 cases were carefully examined, and sections made in 9 cases. There was no indication that they were the source of infection. They were not acutely inflamed, nor ulcerated, and there never was a peritonsillar abscess or cellulitis or lymphangitis. The crypts were sometimes dilated and full of debris.

The specific diplococcus was usually found in them; but it was also found in the lungs and in the bowel. Cultures from the cervical and bronchial glands were negative. In one case only (Watson), out of 16 examined, was a culture of the diplococcus obtained from a mesenteric gland. This was a late septicaemia;and the organisms were also found in the blood and in the spleen. The lungs frequently showed patches of broncho-pneumonia, and sometimes pleurisy; but broncho-pneumonia is a late manifestation. The bowel appeared to be ulcerated in two cases (out of 109) but under the microscope the ulcers were found to be mere erosions and non-inflammatory; cultures from the mesentric glands in these cases did not grow the diplococcus.

It is noteworthy, too, that in the Glasgow epidemic of 1906-1908 where nurses, many of them run down in health, were working in close contact with 30 to 50 cases in an overcrowded ward, not one contracted the disease. This seems to go strong against an aerial infection, and to a slight extent against a food infection. In the patients' homes on the other hand contact cases would appear to occur occasionally. Four members from the same house were admitted to Ruchill Hospital within a week. A mother, and a baby at the breast,were admitted together, the baby having sickened 5 days before the mother.

From a review of all the facts it would not be surprising to find that infection occurs through the skin, by means of some outside agency, such as the flea. The manner in which the disease spreads, and its distribution in certain quarters of the city are quite in keeping with such a theory.

LEUCOCYTOSIS OF THE BLOOD.

There is always a marked leucocytosis in the early stages of the disease, the polymorphonuclear leucocytes being the chief cells affected. As the disease becomes less active the number falls, rising however with each true relapse. In 31 cases examined early the leucocytes commonly numbered from 20,000 to 30,000 p.c.m. In 4 they reached over 56,000, p.c.m. In one case (Stirling) the count was very low, (5,886, p.c.m.). This was a virulent septicaemia.

THE CEREBRO - SPINAL FLUID.

The character of the spinal fluid is very variable, just as the type of disease is very variable. In most cases diplococci are found, and there is no difficulty in the diagnosis. Ina few cases, such as that of Harris (see film from the second puncture) the cells are very few, small, and mononuclear, and organisms are rarely seen. Such a fluid resembles that from a case of tubercular - meningitis. The search for the organism here requires care. The best method of obtaining a film is to centrifugalise the fluid, and to place drops of the residue on a slide, drying the film after each drop. In this way there is an accumulation of films, and diplococci are more apt to be found. Diluted carbol-fuchsin is the best stain for picking them out, (in sections it is not so useful). Sometimes the diplococcus can be obtained in culture, when it is not seen in films.

The appearance of the fluid is useful as indicating the state of the pus on the brain , but it is not to be relied on for prognosis (though it is a guide) as complications are frequent and unforeseen.

In very acute cases (Stirling) the fluid swarms with diplococci, polymorphonuclear cells are not numerous, and ~~mononuclear~~ monuclear cells are few and far between; the diplococci appear to be collected round the cells, rather than inside them. In the ordinary severe case diplococci are plentiful and some are intracellular; and cells are numerous - at the commencement of the disease polymorphonuclear cells abound, but gradually mononuclear cells increase in number. Where the organisms are mainly intracellular, and the polymorphonuclear cells are disintegrating or are contained in phagocytes, and where an imperfect funnel of disintegrating fibrin forms in the fluid, the patient may recover rapidly (in a week) though on the other hand he may become a chronic case, and die of some complication. In cases that have become chronic the organisms are few, cells are scarce and are mainly mononuclear, and a thin clear funnel of fibrin forms in the fluid after some hours.

The quantity of fluid which drains off by lumbar puncture depends, as a rule, but not always, on the amount of hydrocephalus present. In chronic cases there is frequently a temporary improvement in the patient's condition after removal of the fluid; ill effects are rare.

The organism is a diplococcus, kidney-shaped, variable in size, usually smaller than the staphylococcus pyogenes aureus, and often rounder in form than the flat gonococcus.

It is always Gram-negative. (In cultures it may be less decisively so). It does not grow at room temperature but grows readily on agar (very slightly alkaline) or on agar smeared with blood, or on blood serum, the colonies appearing in from 24 to 36 hours, as small, round, whitish, translucent, wet-looking discs, varying in size from a pin point to a medium sized pin head, raised in the centre and shelving gradually to the edge. Under the microscope they appear yellowish and finely granular. In films from these cultures, the organisms are more variable in size, and occasionally occur in tetrads, and in short chains of 3 or 4. Older cultures are larger and vary in outline, and films show a faintly stained background of dead cocci, in which are scattered a few well-stained forms. The cocci die quickly. Involution forms occur. Some are round and may reach a very large size. Sometimes in a pair, one cocus may be normal in size, while its vis-a-vis may be four times as large. In these older cultures some organisms do not easily loose their stain by Gram's method.

A bacillus sometimes occurs in specimens of fluid and has led to a double infection being described. It is evidently a contamination, and is never found when aseptic precautions are taken. It growsreadily in cerebro-spinal fluid at room temperature and may be abundant in 2 or 3 hours. It occurs as a short slightly curved bacillus about 5 μ long. It is often in pairs, is slightly thicker at the middle than at the ends, and has rounded extremities. It grows readily in gelatine at room temperature and liquefies a small button at the surface.

The most frequently met with cells in Cerebro-spinal fluid are the polymorphonuclear leucocytes. They are most numerous in severe cases, though in the very severest they are fewer. Healthy cells, with well stained nucleus are seen where the disease is still active, but as it dies down, they disappear. They may include diplococci in their interior, and then often both they and the cocci die. Degeneration is very common. This may occur as a simple fragmentation of nucleus; but sometimes there seems to be a process of digestion, when the protoplasm of the cell becomes "fuzzy", badly stained, and spilled outside its normal limits. It gives a film a characteristic appearance, as if it were badly fixed. This digestive process aids the general disintegration, especially the disintegration of fibrin. Polymorphonuclear cells disappear in old standing cases, provided there are no relapses.

Mononuclear cells occur in two forms, with intermediate stages between the two. There are large cells, with round/

round, or oval, nucleus, and much protoplasm. These are the macrophages, and may be seen with other cells included, and sometimes with the nucleus pressed to one side. They may reach a great size, 4, 5, or 6 times as large as the polmorphonuclear cells (microphages). They are a characteristic feature of films of cerebro-spinal fluid. They become vacuolated, and degenerated; some may enter the blood stream.

Small mononuclear cells occur with round dark nucleus, and just a ring of protoplasm. These are found in chronic cases, and here the fluid comes to resemble that of tubercular meningitis.

Fibrin deposits, when the fluid is allowed to stand in a test tube, as a long funnel, with the mouth at the surface of the fluid. In acute cases it is dense and entangles many leucocytes. In chronic cases it is more transparent, and of finer texture. In some cases it is digested and does not form a funnel. Such indicates a similar process of digestion of the pus on the brain, with sometimes a rapid healing.

The appearnace of Cerebro-spinal fluid should therefore be studied as an aid in forming an idea of the nature of any particular attack of the disease.

THE P U S.

The pus is situated in the arachnoid spaces, or in what might be called the pia-arachnoid membrane. It is never free on the surface. It s distribution depends partly on gravity (it is more abundant on the posterior than on the anterior aspect of the cord) and partly on the looseness of the pia-arachnoid membrane in which it is situated, (it is abundant along the course of the cerebral vessels, and on the under surface of the cerebellum, where it is often limited by a definite margin.)

Diplococci are found in the pus in early cases. They are more numerous in the outer layers of the arachnoid than in the inner more vascular layers. The majority lie in spaces and are probably brought to this outer position by the exuding fluid. Those in the inner layers are more often intracellular. In <u>films</u> weak carbol-fuchsin is best for demonstrating the cocci. In <u>sections</u> thus stained the cocci may be hidden, so the methylene-blue method is better. By this, the sections are stained with methylene blue for an hour or more, and then partly de-stained with very dilute acetic acid.

The composition of the pus has been already described. It consists of polymorpho-nuclear leucocytes, large mononuclear cells, small mononuclear cells, sometimes fibroblasts, and fibrin. The small mononuclear cells are mostly stages in the formation of the large mononuclear cells and the fibroblasts; some of them are lymphocytes.

The fate of the pus is variable. It will be seen in the foregoing types that it is usually in process of absorption. Death is not always due to the immediate effects of the pus on the brain, but often to remote effects, such as toxaemia, hydrocephalus, exhaustion, or broncho-pneumonia.

(1) It (the pus) may be absorbed completely, as in the few cases, where after a severe attack of a few days, the leucocytosis of the blood rapidly falls, and the patient becomes absolutely well. (At the same time, pus may exist, say in the ventricles, without any apparent symptoms. Such is the case of a boy, aet. 10, who seemed to have recovered, and had been running about for 5 weeks, when he suddenly took a convulsion and died. At the post-mortem examination half a drachm of thick old-standing pus was found in the descending cornu of each lateral ventricle though the surface of the brain was free).

(2) It may be absorbed leaving a degree of fibrosis. Polymorphonuclear cells may disappear rapidly by lysis or by phagocytosis. Fibrin disappears more slowly. It occurs in two forms, (a) in a network enclosing cells, (b) in masses as for example between the pia and the brain. Where it is in a net work and is intimately associated with the disintegrating cells it may undergo fibrolysis. Where it is in masses the process is different. Fibroblasts, in different stages of development are seen scattered throughout the denser layers; some send their processes into its substance and live on it. Thus it disappears before the advancing processes.

The connective-tissue cells proper of the arachnoid membrane also show proliferation.

The result is that the pia-arachnoid membrane becomes tough, and in some parts thickened and fibrous. In the great majority of cases that die, there is left this fibrosis, though often it is very slight.

(3) It (the pus) may be replaced by granulation tissue. Young blood vessels grow into its substance; and fibroblasts increase in number, as the pus cells and fibrin disappear. The granulation tissue does not form a continuous sheet over the brain and cord, but is studded here and there, and may form adhesions with the dura mater. It does not invade the tissue of the brain or cord to any extent, but it may replace nerve roots necrosed en masse. There is thus produced a fibrosis of a coarser type than in 2.

SOME CHANGES PRODUCED by/at the seat of THE PUS.

(1) Changes in nerve structures.

Neuritis of varying degrees is common. In acute cases (Cumming's) the pus finds its way between the bundles of the nerve-roots, following the vascular fibrous partitions and dividing up the root. There may be simply congestion which may end in recovery, but in some cases the vessels become greatly dilated, and, occupying nearly the whole of a nerve press the fibres aside. In others the nerves become oedematous, and appear, in section, divided into islets; the medullary sheaths of the fibres break up and ultimately disappear; blood-vessels become numerous, and the cells in the adventitia proliferate. Where the inflammation has been severe, the whole root becomes necrosed. Sections show necrosis in all stages. The medullary sheaths of the fibres disappear, then the axis-cylinders break down and the whole root becomes structureless. In sections there might be some doubt as to the identity of the necrosed masses, but some show remains of axis cylinders, and others the remains of their main vessels in their interior. Moreover, all the stages of necrosis can be traced.

So-called repair commences with an invasion of the necrosed mass by new-formed thin-walled blood-vessels; fibroblasts surround the vessels; and so true granulation-tissue comes to occupy the place of the nerve.

That a mild neuritis may recover is seen in the case of Docherty, whose perforated ulcers were a result of the neuritis. The ulcers took five months to heal, but the patient was dismissed well.

Where the nerve roots are destroyed, degenerations may be traced into the cord. At the point of entry, individual fibres are seen degenerated; but at a higher level in the cord, as in Harris, whole tracts may be found degenerated. Vascular dilations in the grey matter may be extreme (Harris). Areas of softening may occur.

The central canal is sometimes obliterated, and sometimes dilated.

The brain in acute cases is soft, almost diffluent, and pink in colour; in chronic cases it becomes tough and cuts like soft cheese; it is greyish in colour, and the mouths of the veins are prominent. Under the microscope small cells may be seen, and there may be a degree of fibrosis. A line of separation in the brain substance, a short distance from the surface frequently occurs in sections of chronic cases.

Pus does not invade the brain to any extent. The vessels dipping into it are sometimes dilated, and there may be a perivascular increase of cells.

(2) Changes in the vessels.

In acute cases little change can be observed. In chronic cases the coats are frequently altered.

Hyaline degeneration is common (Harris). Sometimes there is a proliferation of the cells of the coats, and this may be extreme as in Arthur, where some vessel walls are completely changed into small round cells.

Thrombosis sometimes occurs in the smaller vessels, (Harris).

Septic thrombosis was met with only once.

(3) Hydrocephalus.

This is present to some extent in almost all cases of long duration. Sometimes it may be extreme, the walls of the lateral ventricles being reduced to $\frac{1}{4}$ inch in thickness. Several cases die from this alone; and it was with a view to the possibility of relieving the condition by operation, that the method of examination of the foramen of Majendie, by removal of a disc of bone from the skull behind, was adopted. In 21 cases of Hydrocephalus thus examined, the foramen of Majendie was definitely closed in 5; the lobes of the cerebellum were glued together in other 6; but in 10 cases there was no obstruction to the free passage of the fluid. (the layer of cells of the pia mater described as normally covering the foramen was not observed in these pathological cases).

On the other hand, the choroid plexus of each lateral ventricle was often bathed in pus; its vessels were often dilated and engorged; there were hyaline and other degenerations in vessels, in sections of the pus; and the perivascular lymphatics must be greatly altered. It is probable that these are potent causes of hydrocephalus; and thus, though operation might temporarily relieve the condition of pressure (as lumbar puncture sometimes does) it is questionable if it would ultimately allow of a cure.

(4) Septicaemia.

The blood was examined, by the method adopted for Stirling, in 31 cases. In two of these the diplococcus of Weichselbaum was found. One (Stirling) was a very virulent infection; the organisms swarmed in the cerebro-spinal fluid, and were seldom found in the cells; in blood-counts the leucocytes were under 6,000 per cub. m.; and the patient lived only 22 hours. The other case (Watson) was a late septicaemia. There was pus in both knee joints.

Cultures of the diplococcus were obtained from the blood, from the pus in the joints, from the spleen, and from a mesenteric gland; they answered the tests on sugars for the diplococcus of cerebro-spinal fever. The organism was found in smears of the pus in the joints, and of the spleen pulp.

(5) Emaciation.

There is always a degree of emaciation, and it may be extreme, some patients, in whom the disease has been long-standing being studies in the anatomy of the bones. It frequently comes on suddenly, and proceeds with such rapidity that one is forced to believe it is an active process, and not merely one of mal-~~administration~~ assimilation. The time of onset often agrees with that of the breaking down of the pus cells.

(6) Pus in the large joints.

This was found in two out of 109 cases. In one case (Watson) both knees were affected; in the other case (Finlayson), aet. 10 years, there was pus in the right knee-joint. There was no acute inflammation; the synovial membrane was oedematous, but was not eroded, and there was no bone lesion. Diplococci were found in the pus in both cases. In Watson, they were also found in the blood; in Finlayson, blood cultures were negative.

It will thus be seen that the immediate after-effects of the pus, especially as regards nerve and vessel changes, are often more to be dreaded than the ~~pus~~ primary attack itself.