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By Sheridan Delépine, M.B.

[With Plates XXVII, XXVIII, and XXIX.]

Preliminary remarks.—Dr. Gamgee had promised to give a complete account of the nervous phenomena observed by him during the time the case was under his care. Owing, however, to a sudden illness he has been unable to carry this intention out, and after waiting several months I find myself obliged to take the entire responsibility of a communication which I had hoped might have been a joint one. In order to compensate in some measure for the absence of Dr. Gamgee's observations, I have asked the Registrar (Dr. Sisley) to give me a short abstract of his report on the case. This he has kindly done. By putting together the data which I had obtained from Dr. Gamgee's original communication and those provided by Dr. Sisley, I am able to give the following short clinical sketch. I must, however, repeat that Dr. Gamgee intended to give a much fuller account of the nervous symptoms than I am able here to do.

History.—The patient, a decorator, sixty-five years of age, was admitted to St. George's Hospital, under Dr. Gamgee's care, on the 15th of August, 1888.

In 1887 he suffered from a series of abscesses of the abdominal wall, and was treated during about four months by Dr. Roberts and Mr. Beck at the University College Hospital. After leaving the hospital, and being readmitted once more on account of the formation of a new abscess, he was sent convalescent to Eastbourne. On coming back to London (five or six weeks before his death) the patient had cough, dyspnœa, and pain in the left side of the chest.

Four weeks before his death he noticed for the first time loss of power in the right leg and arm.

On admission (seven days before his death), the man was spare, pale, and looked very ill. He had cough and dyspnœa. The physical signs of effusion into the left side of the chest were present. Several scars were observed on the chest and abdomen. There was loss of power in the right arm and leg. There was no ankle-clonus, no knee-jerk, no loss of sensation, no hyperæsthesia, no reaction of degeneration, no headache. Soon after admission

Dr. Gamgee observed an attack of Jacksonian epilepsy affecting the right side of the patient, and lasting five minutes. The clonic convulsions began in the deltoideus and extended down the arm, there being ultimately flexions of the wrist. The leg was less affected than the arm.

Six days before death he had a similar attack lasting three minutes.

Five days before death he was seen by Dr. Ferrier, who confirmed entirely the previous observations, with the exception of those relating to the convulsions (the patient having had no attack in his presence).

Four days before death his chest was tapped, and 8½ oz. of thin, purulent, bloody fluid was drawn off.

Three days before death there was an unobserved attack of convulsions.

The day before death the lines under the right eye were more distinct than those under the left, and the right pupil was dilated.

On the 22nd of August the patient became delirious and died.

Post-mortem examination.—The autopsy was made on the 22nd of August, 1888, twenty-nine hours after death, by Mr. W. L. Dickinson. I was also present and am responsible for the following statements.

Note.—Permission had been obtained with some difficulty for the examination of the head and thorax. I was not allowed to remove any part of the skin.

General appearances.—Height of body five feet three inches. Body spare.

I. *External parts.*

1. *Skin.* Numerous scars were found in the skin covering the outer aspect of the right arm, the anterior aspect of the chest and belly, and the left forearm. These cicatrices were most abundant on the right side of the body, and more especially on the outer aspect of the upper part of the right forearm.

Of the several groups of scars found on the thorax and abdomen one deserves special mention. It was situated quite near to and on the right side of the umbilicus. The cicatrices were large, some measuring an inch and a half in diameter, and even more; they were generally rounded, but owing to their close proximity they had in many places coalesced. They were not unlike syphilitic scars; but no deformity of bone nor any genital syphilitic sore could be discovered, even after very careful search.

2. *Hands and feet.*—The hands and feet were distinctly swollen,

and this swelling was much more marked on the right than on the left side. On the right side the thumb and big toe were more swollen than the rest of the hand and foot, the swelling being most marked about the small joints.

The right forearm was distinctly swollen. All the parts thus altered were very much smoother than the corresponding parts of the other side.

The *post-mortem* lividity was more marked on the right side than on the left. (Before taking note of these points I carefully ascertained, by examination of the body and by questioning the attendants, whether the body had been lying on the right side, and I found it had not.)

II. *Thorax.*

1. The *left pleura* measured an eighth of an inch in thickness in several places. In the upper third of the chest its two layers were adherent; in the lower two thirds they were separated by sero-purulent fluid mixed with blood, of which about three pints were removed. This fluid on microscopical examination was found to contain a moderate amount of swollen and degenerated pus-corpuscles, a few red blood-corpuscles, and a large quantity of granular débris, chiefly fatty. The surface of the pleura was scraped and the scrapings examined, and were found to be composed of the same elements, *plus* fibrinous shreds. No micro-organism was discovered, with the exception of some which could not be distinguished from ordinary putrefactive organisms (*chiefly micrococci*). The right pleura was also thickened; its layers were united by dense adhesions all over the upper lobe of the lung.

2. The *lungs* weighed, together, 4 lbs. In the left lung the lower lobe was collapsed, the upper lobe congested, œdematous, and indurated. Sections made perpendicularly to its surface, and including the whole of the thickened pleura, showed microscopically the following things :—Serous layer very much thickened, composed of fibrous tissue, becoming very loose towards the surface; this layer contained a number of vessels of old formation. These vessels were distended with blood. The subserous or perilobular tissue was slightly increased in amount. The carbon pigmentation was not unusually great for a man of sixty-five. The interlobular septa were not generally thickened, but there was a small amount of small cell infiltration around a few small vessels. Several of the medium-sized vessels had their intima thickened.

Most of the vessels were distended with blood, and the vasa vasorum formed a very conspicuous network in the adventitia of some of the larger ones.

The alveolar walls were not distinctly thickened. The elastic fibres were very distinct (as they are usually in old age). The capillaries were intensely congested.

The lining epithelium was swollen. Here and there the cells had begun to desquamate and to accumulate within a few alveoli.

Sections through the root of the lung, examined macroscopically and microscopically, did not reveal any trace of granulomatous growths or of abscesses. The lymphatic ganglia were indurated and intensely pigmented (carbon infiltration).

The bronchi were in a state of chronic congestion and bronchitis; their fibrous tissue was increased in amount, and the cartilages were eroded.

3. The *pericardium* was apparently healthy.

4. The *heart* weighed 12 oz. Its muscle was flabby. The mitral valve was slightly roughened and dilated.

III. *Abdomen.*

1. *Peritoneal cavity.*—The peritoneal cavity was apparently healthy. The ligamentum teres was thickened and much congested.

A section made transversely through it, near the anterior border of the liver, showed, under the microscope, intense congestion of the vessels, and great thickening of the serous layer covering it. No special parasite could be found in the folds of the suspensory ligament, except at the junction of its layers with the serous capsule of the liver, in the region which will be more specially described further on.

2. The *intestine* and the *stomach* were apparently healthy; at any rate they did not show any sign of any important lesion. They were entirely free from adhesions, and were only very moderately and uniformly congested.

3. The *spleen* weighed 4 oz., and looked healthy.

4. The *kidneys* weighed 10 oz. together. They were similar in size and general appearance; their surface was slightly granular, and both were congested.

The right kidney, on section, presented in the cortex two small yellow patches; one was situated immediately under the capsule, and projected slightly beyond the surface of the organ. The other

was situated more deeply, *i. e.* about 3 mm. below the surface; it was not more than 18 mm. distant from the former. Both these patches measured about 5 mm. in their greatest diameter. The more superficial one was distinctly conical in shape, with its apex turned towards the medulla. The deeper one was irregularly oval.

They were both pale ochre yellow in colour, and looked somewhat granular; they were very sharply defined and firm, but were not surrounded by any distinct capsule. There was no softening of their central parts.

Scrapings examined microscopically showed nothing special; granular débris abundant; epithelial cells and spindle-shaped cells. No organisms comparable with those found in the liver or brain could be discovered.

Sections made perpendicularly to the surface of the organ in the region of these nodules were examined with the following results: —The capsule was thickened. Gradually expanding into the superficial nodule referred to above, in the neighbourhood of that swelling the capsule was more cellular than usual, the cells being mostly long and spindle shaped. The superficial nodule projecting over the surface was almost entirely composed of spindle-shaped cells arranged in bundles, crossing each other in various directions, presenting an appearance hardly distinguishable from that of a spindle-celled sarcoma.

The subcapsular layer of the cortex was infiltrated with small cells; this was chiefly noticeable in the regions corresponding to the apices of the medullary rays and, to a lesser extent, to the regions corresponding to the interlobular vessels.

The same small-celled infiltration and a certain amount of interstitial fibrosis were found disseminated through the cortex around some of the vessels and of the Malpighian bodies.

All the vessels, large and small, were intensely congested, and in a number of them leucocytes were more abundant than usual. These leucocytes were very unequal in size and stained more or less deeply. The small ones were more regularly round and stained deeper than the large ones.

In addition some of the vessels contained an unusually large amount of granular matter (some staining deeply with hæmatoxylin). The vessels which contained the greatest amount of that granular matter had generally their coats thickened (chiefly their intima).

A large number of endothelial cells had been shed in many of

the arteries, some of which were almost or entirely obliterated by these cells.

The convoluted tubules just under the capsule and in the neighbourhood of the small tumour described above were dilated, a few of them formed cysts barely visible to the naked eye. The largest of these cysts were lined with flattened epithelium ; in the smaller ones the epithelium was more transparent than usual, and the nuclei more distinct, but the cells were not much atrophied. Some of the collecting tubules were distended with small proliferating cells.

In the Malpighian bodies the epithelium lining the capsule of Bowman was generally in a state of proliferation. A few Malpighian bodies were found in various degress of atrophy ; some had undergone a kind of fibro-hyaline degeneration ; these were found in the midst of those patches where interstitial changes could also be noticed. The deeper small yellow patch had a structure very different from that of the superficial one. The arrangement was mainly that of an adenoma. The tubules were much enlarged and irregularly convoluted, lined with very large cells having almost entirely lost the character of renal epithelium, some being like large liver-cells, distended with a large globule of fat, others being columnar. The walls of some of the enlarged tubules were folded so as to form projections into the enlarged lumen of the tube, and being lined with epithelium these convolutions gave to some parts of the nodule somewhat the appearance of a papilliferous cyst-adenoma in way of formation.

5. *The liver* weighed 2lbs. 14oz. On the upper surface, near the anterior margin and to the left of, but quite close to, the attachment of the suspensory ligament of the liver there was a slight antero-posterior furrow, extending as far as the anterior margin of the organ so as to produce a notch in it. The anterior border of the organ was thicker and more rounded than usual. Another shallow depression or groove of the same nature was also found in the middle of the upper surface of the right lobe. Little more than this could be seen before opening the organ ; the capsule, however, was very thick and opaque in the region of the groove found on the left of the suspensory ligament, this thickened capsule being continuous with the thickened suspensory ligament already described. An antero-posterior section made just on the left of the falciform ligament, so as to divide the liver in the region of the groove, revealed a large yellow, semi-cheesy and semi-purulent

looking lobulated mass. Its buff yellow colour contrasted strongly with the dark purplish, red, congested liver substance surrounding it. It was irregularly oval in shape; its antero-posterior diameter being the longest, and measuring 32 mm., the shorter axis measuring nearly 25 mm. The description of this abscess will be completed further on. A section made in the region of the depression found in the right lobe exposed a number of small, yellow, cheesy-looking, rounded patches, separated by narrow zones of intensely congested liver tissue. The largest of these patches measured about 3 mm., the smallest were not so sharply defined and were hardly visible. On making more sections through the organ, it was found that near the right border there were some very deeply congested areas, presenting the appearance of advanced passive congestion, some looking almost cavernous. These areas were separated by paler strands, looking almost anæmic and feeling somewhat softer than the other parts. The liver generally presented an unequally congested appearance.

The large nodule, situated near the insertion of the falciform ligament, was composed of an anterior portion which was softer and from which pus escaped pretty freely, and a posterior part firmer, and looking more like a mass of large granulomata than like an abscess. After scraping the surface of the anterior portion of the abscess, a small amount of pus was removed and a honeycombed stroma of fibrous tissue was brought out very clearly. The abscess was thus shown to be alveolated, each of the small compartments measuring on an average about 3 mm. in diameter; there were, however, many smaller alveoli. Others were on the contrary larger and evidently produced by the coalescence of several small abscesses. In the posterior portion of the tumour the small cheesy-looking nodules were separated by a larger amount of fibrous tissue or of indurated liver substance, in favorable sections they could be seen to be continuous one with the other, the isolated abscesses being simply the extremities or sections of ramifying tracts, originating at the periphery of the older multilocular abscess described above. These tracts measured from 2 mm. to 3 mm. in diameter, and were therefore quite visible to the naked eye. The liver tissue, through which they advanced, was distinctly indurated and more or less replaced by translucent and congested fibrous tissue. Several nodules of the same kind could easily be recognised in the thickened serous coat of the organ, over the older parts of the abscess. The pus which escaped from the surface of the section, or which could

be scraped off from the abscess, contained a number of yellowish white, nearly opaque bodies, very small and just visible to the naked eye; these were generally surrounded by a layer of pus-corpuscles.

Examined microscopically these small bodies were found, as expected, to be typical actinomycetes. The rest of the material was composed of well-formed, rather large pus-corpuscles, many of them arranged in small clumps, in the midst of which fine radiating filaments could be made out even with a power magnifying only 300 times. Under a higher power these masses presented the appearance represented in fig. 1, Plate XXIX. Besides these two forms of actinomyces, and the pus-corpuscles, débris of spindle-shaped cells, of epithelial looking cells, as well as granule-cells, oil-globules, and granular débris were found abundantly. More details regarding the morphology of the fungus will be found further on. Sections of the liver, examined microscopically, yielded the following data:

Falciform ligament: At the place where this ligament joins the liver, and all along its length, this ligament was, as already said, thickened and congested.

The subserous layer was thickened and much congested. It contained a great number of small round-cells escaped from the vessels, and of spindle-cells resulting from the proliferation of connective-tissue corpuscles. The fat enclosed between the two layers was in the same state of congestion and infiltration. No abscess was found in the ligament itself, but at the place where it merged into the capsule of the organ, near the anterior border of the liver, the large abscess already described was found, and the oldest part of that abscess was found near the place where the layers of the ligament separated and became continuous with the capsule. In that region the serous coat was replaced by embryonic myxomatous-looking tissue, very vascular and very soft. In the same region the capsule of Glisson was very unequally thickened; some parts of it being replaced by connective tissue, almost entirely composed of spindle-cells, and not unlike sarcomatous tissue. At the place of insertion of the suspensory ligament this layer was twenty or thirty times its normal thickness, and had evidently invaded the subjacent hepatic tissue. This thickening of the capsule diminished gradually and rapidly, so that at a distance of about two centimetres from the suspensory ligament the capsule of Glisson, notwithstanding its being congested and infiltrated with small cells, was not very much thicker than

normal. It was in the midst of that newly-formed connective tissue, continuous with that of the capsule, that the large mass of abscesses was found. A noticeable feature of this tissue was that at the upper and anterior part of the patch, viz. where the lesion was evidently oldest, the partitions which it formed between the various extensions of the abscess were very much narrower than the diameter of the alveoli. These partitions were evidently in a state of infiltration and degeneration, being composed of small cells staining badly, and separated by very little intercellular substance. In the midst of that degenerated tissue a number of leucocyte-looking cells, staining very deeply, and very granular, were found in some places very abundantly. These cells were very much like those filling up the small central cavity of each subdivision of the abscess. Only a few distinct vessels or even bundles of fibrous tissue could be found in those trabeculæ, and the liver-cells seemed to have entirely disappeared. Small hæmorrhages were not uncommon in those regions.

In the younger parts of the tumour, *i. e.* at the advancing posterior margin, the partitions between the alveoli of the abscess were very much thicker than the alveoli themselves. The connective tissue of these trabeculæ was chiefly composed of a large number of large, embryonic-looking spindle-cells. In the midst of that young connective tissue a number of large vessels, many with more or less thickened intima (arteritis obliterans), were found, as well as numerous large and tortuous bile-ducts. These bile-ducts were lined with an unusually luxuriant columnar epithelium ; and where these ducts were numerous the appearance recalled to mind the early stages of a columnar adenoma.

The lumen of many of the vessels was occluded by a thrombus or by accumulation of leucocytes or of large oval cells, staining less deeply than leucocytes, about one third larger than them, and evidently the result of proliferation and desquamation of the endothelium of vessels. (This desquamation of endothelium is a process common to a great many states, and I have had more than once occasion to allude to it. The subject has been much studied by Dr. Handfield Jones. I have reason to believe that it also goes on constantly in health, and that it is an important mode of origin for some of the cellular elements of the blood.)

The vessels which were not occluded by endarteritis or thrombosis were distended with blood, causing congestion of the parts.

One of the obstructed veins contained a calcareous mass (phlebolith) just visible to the naked eye. No parasite could be found in the concretion. In the midst of this recent tissue the liver elements were not entirely destroyed, but remained between adjacent abscesses in the shape of rows of flattened cells. These cells were, however, in an advanced state of atrophy, produced partly by the collateral pressure due to the growths of the abscesses, and partly to the gradual advance of the connective tissue along the capillary vessels, this part of the process resembling much what is observed in certain varieties of the so-called hypertrophic cirrhosis. (It is to be noted, however, that in this case, as in many of the cases which by their structure are allied to hypertrophic cirrhosis, there is neither apparent nor real hypertrophy of the organ, even in the parts which are most affected.)

The study of the abscess itself was not of less interest than that of the surrounding tissue; its most remarkable feature was its lobulated arrangement due to its being composed of a number of branches or purulent tracts ramifying in various directions from the point where the tumour originally started. It was impossible to discover any relation between that branching and the arrangement of the lobules or the distribution of the vessels or ducts of the organ.

(In the absence of the proofs which I have already recorded, this would almost be enough to support the theory that the abscess was formed in the midst of previously modified tissues.) In each sufficiently large alveolus of the abscess (some of the largest cavities are evidently produced by the disappearance of the septa between adjacent alveoli) one or several typical actinomycetes were found.

It is interesting to note that a large and probably mature actinomyces is multilobulated, and that its shape corresponds very much to that of the multiloculated abscess. One is often misled regarding the size of these actinomycetes by the fact that, owing to their large dimensions, the tips only of the diverging branches are found in certain sections, so that several small organisms may seem to be present in the same large cavity, or even in cavities which are apparently separated one from the other by partitions, and yet both the small abscesses and the typical organisms which they contain may be nothing more than the advancing branches of a large abscess and of the large actinomyces which it contains. It is an unfortunate feature of this parasite that when it has reached a large size the pus immediately round it is generally very soft or

non-coherent, so that it is impossible to retain the parasite in microscopical sections without resorting to special technical means (embedding in celloidin).

The form of the organism, which is generally known, was found only in the centre of abscesses of comparatively large size; at the margin of these abscesses and in the small patches of small round-cells preceding the well-defined abscess, no corresponding organism could be discovered.

There were in some of the abscesses small masses of radiating filaments, with few or no clubs connected with them. These were better seen in fresh specimens than in those kept for some time.

These tufts of branched filaments were, however, never found quite at the margin of the abscesses, but, on the contrary, were in the midst of the soft pus filling up some of the older abscess cavities.

In the neighbourhood of the large abscess just described the following changes could be observed:

Nodular patches of small-celled infiltrations of the capsule of Glisson; the adventitia of the bile-ducts was generally the part most affected. The bile-ducts, although never obliterated, showed some signs of dilatation from retention. Their columnar epithelium, as already remarked, was large and unusually distinct. The accumulation of small cells in the coats of the vessels seemed to have caused obliteration of some of them, this process being, of course, helped by thickening of the intima; others were, as already described, in connection with the walls of the abscess, partly or completely obliterated by arteritis obliterans, or endophlebitis (the endophlebitis was not general), by thrombosis, or by desquamation of the endothelium; in some vessels the serous layer of the intima had separated *en masse*, and the blood had passed between it and the elastic lamina, giving thus rise to a kind of laceration, which to my knowedge has not been described, but is apparently of little importance in this case.

The intralobular capillaries and vessels were in many places in a state of intense congestion, quite similar to what is observed in cases of pylephebitis obliterans around the obstructed area.

The liver-cells between the distended capillaries were in various degrees of atrophy and pigmentation. In some regions the capillaries, instead of being distended with ordinary blood-corpuscles, were filled up with degenerated, granular, small round-cells. Young connective tissue formed a sheath round some of these capillaries, and

in some places each liver-cell had an investment of connective tissue, so that a distinct intralobular cirrhosis existed in such regions.

Besides the atrophy of a number of cells, inflammatory changes, such as swelling, vacuolation, multiplication of nuclei, fatty degeneration were observed in large tracts of hepatic tissue.

These changes, which have been described in connection with the area surrounding the large abscess, were found also in the two other parts of the organ which have been described as showing distinct lesions. In the upper part of the right lobe the changes were chiefly due to congestion, infiltration, inflammation, and degeneration, and seemed to correspond to the stage immediately preceding the appearance of abscesses.

At the extreme right margin of the organ the changes were chiefly those of collateral passive congestion, such as is observed in the neighbourhood of obliterated vessels. This form of congestion is observed in the liver only when the obliteration of vessels is very extensive, or affects the terminal branches of the portal vein and hepatic artery.

IV. *The cranial cavity and spinal canal.*

1. The skull-cap having been removed the membranes covering it appeared at first sight to be normal. A more careful examination, however, revealed a slight adhesion and thickening of the pia mater in the region of the posterior end of the left upper frontal and adjacent part of the ascending frontal convolutions. There was little superficial congestion visible.

The upper parts of the left ascending frontal and parietal convolutions, as well as the posterior parts of the upper and middle frontal convolutions, were flattened and broader than usual, whilst, naturally, the intervening sulci were partly obliterated. The brain was also much softened in the same region, the softness amounting to fluctuation in the upper parts of the ascending frontal convolution. There the cortex felt as if it were merely a thin membrane covering a large cavity full of fluid,

All this was very much more distinct after the brain had been removed from the cranium than before, and then the flattening of the central parts of the left hemisphere, the softening, and the fluctuation became extremely evident, as well as a distinct enlargement of the same part of the organ.

On passing gently one finger along the inner surface of the left hemisphere one could feel distinctly that the inner aspect of the

upper ends of the ascending frontal and parietal convolutions was softened. The marginal convolution was also slightly softened in front of and behind that region, but the gyrus fornicatus felt quite firm.

The vessels examined, as far as it could be done without injuring the organ, did not show any trace of disease or excessive congestion.

2. *Vertical frontal sections* having been made after preparation of the organ a number of large and small abscesses, in various stages of development, were found in various parts of the brain. The most important of these abscesses was found, as was expected, in the white and grey matter of the upper part of the ascending frontal convolution and adjacent regions. In order to avoid a very lengthy description of these lesions they will first be enumerated, and their most salient features will afterwards be described.

A. *In the right frontal lobe* the following abscesses were found:

(1) At a distance of about 25 mm. from the anterior extremity of the brain, in the white matter underlying the anterior portion of the gyrus fornicatus, a group of small abscesses not softened yet, and measuring about 15 mm. × 18 mm. These abscesses were situated just in front of the genu corporis callosi, their border nearest to the surface being at a distance of 5 mm. from the bottom of the calloso-marginal sulcus.

2, 3, 4. At a distance of about 40 mm. from the anterior extremity of the hemisphere and at the level of the genu, several abscesses were found in different regions of the white matter. They all measured about 5 mm. in diameter. (Plate XXVII, fig. 1.)

(2) One of them was situated at the basis of the middle frontal convolution, its border nearest to the surface was at a distance of 10 mm. from the bottom of a secondary sulcus.

(3) Two small abscesses were found among the fibres of the corpus callosum at some distance from the middle line, their innermost border at about 10 mm. from the median surface of the hemisphere.

(4) Another one was found just under the grey matter of the orbital convolution formed by the reflected second frontal. The border of that abscess was at 4 mm. from the surface of the convolution.

B. *In the left frontal lobe* were found:

(5) One small abscess, 25 mm. from the anterior end of the lobe on the white matter of the upper frontal convolution. Its border nearest to the surface was 5 mm. from the side of the upper frontal sulcus.

(6) Another small abscess, 45 mm. from the anterior end of the lobe, situated near the posterior end of the inferior frontal sulcus, and just in front of Broca's convolution. Its border nearest to the surface was 6 mm. from the bottom of the inferior frontal sulcus. (Plate XXVII, fig. 1.)

c. *In the region of the motor areas*, i. e. *the frontal and parietal lobes about the fissure of Rolando*, were found:

(7) A large abscess implicating the upper part of the ascending frontal and ascending parietal convolutions, as well as the posterior part of the superior frontal convolution. Its anterior margin was 80 mm. from the anterior extremity of the brain; its posterior margin 60 mm. from the posterior end of the hemisphere. These measurements were taken after hardening of the brain in Müller's fluid, and in a projection of the lesions on an imaginary horizontal plane. The internal margin of the abscess was not more than 2 or 3 mm. from the surface of the paracentral lobule, its outer border about 35 mm. from the same surface. The abscess measured about 32 mm. from side to side, and 25 mm. from before backward.

Its antero-internal part was much nearer the surface than the postero-external part. In fact, near the anterior border of the upper part of the ascending frontal convolution, the lesion was so superficial that it was almost impossible to discover any trace of unaltered grey matter over an area measuring about one square centimetre. This was the region where the membranes were thickened and adherent. The grey matter of the ascending frontal convolution was either very nearly or entirely destroyed over an area bounded in front by the precentral sulcus, and behind by a line parallel to that suleus, and 4 mm. further back; above by a line parallel to the median fissure, and distant about 3 mm. from it, and below by another line parallel to the first and about 25 mm. from the median fissure. The grey matter of the immediately adjoining portion of the superior frontal convolution was also destroyed or very nearly so.

This abscess was imperfectly subdivided by partitions of congested and half disintegrated brain tissue into a number of compartments, the largest of which measured about 15 mm. in diameter. This large mass was forming the most internal and anterior portion of the group. Smaller divisions extended backwards and downwards into the white substance underlying the

parietal convolutions. These smaller alveoli measured on an average 5 or 6 mm. in diameter. (Plate XXVII, fig. 2.)

D. *Temporo-sphenoidal lobe.*

(8). Another abscess was found at the junction of the temporo-sphenoidal lobe with the basal portions of the brain just behind the insula. (Plate XXVII, fig. 3.)

This abscess was in contact with the grey matter covering the inferior wall of the fissure of Sylvius, quite at the bottom of the fissure. It measured 10 mm. by 5 mm.

This abscess had apparently destroyed some of the fibres passing from the temporo-sphenoidal lobe into the adjacent basal white matter.

3. *Structure of the cerebral abscesses.*—These abscesses differed in many respects from those found in the liver; their walls were thinner and the quantity of pus which they contained was larger. In none was there any typical actinomyces found. All through the pus, however, except quite near the margin of the abscesses, a number of small clumps of pus-corpuscles, with branching filaments radiating from their centre, were found. On searching carefully for a long time a few small clubs were found connected with several of these filaments. These clubs were the result of an expansion of their sheath, just as the more advanced clubs found in the liver. These young clubs, and the complete resemblance between the mycelium forming the central portions an ordinary actinomyces and the mycelium found in the small clumps above described, as well as in similar clumps found in the liver by the side of the more typical organism, made it quite evident that the parasite present in the brain was an early form of the very same organism as that found in the liver. The fresh pus on being removed from the abscess presented the general appearance of moderately thick, creamy, laudable pus.

On spreading it on a glass plate minute clumps could be seen all through it, but they were barely visible to the naked eye, and certainly very much smaller than the ordinary grains found in the pus of actinomycotic abscesses. These clumps when examined with a high power, showed the appearance described above. When compressed carefully, a number of rather coarse branching filaments with a well-marked wavy appearance could be distinctly seen without any other preparation.

The appearance of these filaments was so remarkable that even

before the liver had been examined I felt nearly certain that the case was one of actinomycosis. This was confirmed by the examination of the other organs. Near the margin of the abscesses the pus was lumpy, owing to the presence in it of débris of nerve tissue; there were also many small hæmorrhagic foci in this marginal zone.

4. *The brain substance surrounding the abscesses* was much altered; generally speaking the lesions were those of encephalitis, followed at the margin of the abscesses by the production of connective tissue which gradually replaced the degenerated nervous elements. The changes seemed to have occurred in the following order: Intense congestion of the vessels and endarteritis in many of them; mall cell infiltration of the coats, chiefly the adventitia; thrombosis of some of the vessels.

The red blood-corpuscles found in many of the vessels, also those found in the hæmorrhagic patches so common at the periphery of the abscesses, retained the dyes used for staining bacteria very strongly, and often more so than the bacteria themselves.

Some of the small arteries contained also leucocytes full of small granules staining very deeply; some of these granules were elongated and projected beyond the surface of the corpuscle.

In a few vessels bacilli were also found, but it was not possible to ascertain whether they were adventitious products or not. They looked, however, not unlike segments of the more typical filaments found in the abscesses, and were probably early forms of the organism, and it is quite probable that the granules found in the leucocytes represent still earlier stages in the growth. Such observations can, however, hardly be taken as equivalent to satisfactory proofs, and must be received simply as indications of the probable course of things.

The nerve-cells were swollen, their nucleus enlarged, and in some of them had divided.

The grey and white matter were infiltrated with leucocytes, and patches of the nervous tissue had undergone necrosis. It is in the midst of that necrosed tissue that the abscesses seemed to have formed; the walls of many of the smaller vessels had given way, and hæmorrhages had taken place, so that the pus was mixed with blood at places. The connective tissue was increased at the margin of the abscesses.

The growth of the abscesses does not seem to go much faster than the infiltrations and necrosis of the surrounding tissues, so that

the abscesses must take gradually the place of equivalent portions of brain tissue. There were, however, indications in a few places of compression of the tissues surrounding the abscesses. This was specially well seen in the scanty remnants of cortex covering some of the parts of the largest abscess. There was also distinct swelling of the affected parts of the organ. As the pus continues to accumulate, distinct mycelial masses begin to be visible and soon acquire the appearance already described.

Thus it is evident that marked inflammatory and degenerative changes occur in the brain before the abscesses appear, and that the abscesses have to reach a certain size before a distinct mycelium of actinomyces can be found in them.

5. *No trace of secondary degeneration could be discovered* in the crura cerebri, medulla oblongata, or spinal cord, although a large number of sections of these various parts had been examined after appropriate staining. There seemed, however, to be some swelling of the axis-cylinders in the crossed pyramidal tract; but at the most this change was very slight and very difficult to prove.

Discussion of the case.

This case presents so many points of interest, even from a purely pathological point of view, that it will be necessary to consider it under various aspects, for

(1) It gives an opportunity to follow the life-history of the fungus known under the name of *Actinomyces hominis*, and to study some of the forms under which it may present itself.

(2) It shows how the various parts of the body may become infected, and what are the various lesions which can be produced by that infection.

(3) The brain lesions are so definite, and have affected such important regions, that the case may be considered as if it were a physiological experiment by which the functions of certain parts of the brain can be determined.

(4) In the study of the case certain technical points have been made out which it may prove useful to discuss.

This multiplicity of aspects is, of course, not special to this case, and it would be easy to find a great many more points of interest in it as well as in other cases, but there are limits within which it is wise to remain, and I must be satisfied with exposing those points which have more specially attracted my attention.

A. *Etiological and morphological remarks.*

1. It seems evident that the organism which we know under the name of actinomyces does not penetrate into the body under the form with which we are acquainted. This is not only due to difference of size, but evidently to morphological changes. This is proved by the fact that no actinomyces (I of course use the word actinomyces with reference to the known form only), even of the smallest size, could be discovered at the advancing margin of large abscesses, in the midst of smallest abscesses or patches of infiltration, or in those blood-vessels which showed evident signs of the presence of some irritating material in the blood. A careful study of the pus contained in the large abscesses, and of the contents of the vessels in the parts where lesions are evidently of recent origin, leads me to the conclusion that—

2. Small micrococcus-like spores are produced by the filaments composing the mycelium and the core of young clubs. These spores can easily be seen within and between the filaments, and similar bodies can occasionally be found within the clubs after proper treatment (see technical remarks), and small granules of the same size may also be seen among the cells surrounding the parasite.

3. These spores do not seem to be able to pass easily through the layer of leucocytes which accumulate round the mother organism, and they are apparently nearly all absorbed by leucocytes and the greater number of them destroyed. This statement is not based on any perfectly conclusive direct observation of the facts implied by it, for owing to the constant process of degeneration taking place in the cells and of the walls of the abscesses, the boundary layers of these lesions are full of granules of different kinds, some fatty, some albuminous, and I have been unable to come to any positive conclusion regarding the presence or absence of the spores in these regions. But I have noticed that among the leucocytes surrounding the parasite many were very granular, and stained much deeper than the others. Then I have found a few leucocytes presenting the same appearances in the degenerated walls or partitions of the abscesses, and also in some of the vessels of regions in which changes were beginning to appear. Finally, in young abscesses I have found occasionally a leucocyte in the centre of a young colony, with filaments apparently radiating from it. The difficulty there is in staining these spores differentially has, however, not allowed me to trace them so satisfactorily as I

would have wished. There are, however, two forms of collateral evidence in favour of the view which I support here.

(A) It has been extremely difficult to discover any free organisms in more than a few of the vessels, even in those parts where changes were quite manifest (and even when found these organisms were of doubtful import). From this it would appear that the parasite must be carried from place to place by something else than the plasma, and must pass from the vessels into the tissues without having necessarily escaped into the plasma; hence it seems almost necessary to admit that the spores are carried by the leucocytes. (I put aside for the present transmission of the parasite by the lymphatics, because the lesions in the brain clearly indicate that the blood-vessels may ultimately become the channels of invasion, and it is on the brain lesions that much of what I advance is based.)

(B) The evident passage of the virus through several organs without the formation of colonies seems to indicate that the organism is not freely disseminated through the blood, and yet that it is under a form which can be easily circulated.

4. Besides spores, some potent poisonous material must be produced by the ray fungus, otherwise it would be difficult to account for the extensive changes which may be observed in several organs where no colony can be discovered, and also for the very marked irritative and necrotic changes which precede the appearance of the fully formed actinomyces, or are observed at the margin of the abscesses.

5. The spores having overcome the leucocyte containing them, and finding tissues of vitality lowered by the poison referred to above, begin to elongate and protrude beyond the dead body of their host. These filaments, all growing from a centre, are necessarily bound to radiate from that centre owing to collateral resistance. They soon branch, and in some cases begin to branch dichotomously. The ramifications of Cladothrix filaments are said to be false ramifications, but in actinomyces the branching is most clear and like that which is observed in moulds. At this stage the protoplasmic contents of the filaments can be distinguished from a thin sheath, and it is often possible to see that the protoplasma has subdivided into a number of small spheroidal segments.

6. During the development of these filaments an active fight seems to take place with the surrounding leucocytes. The pus of young abscesses is full of small clumps, composed of a central

small radiating mycelium, with, sometimes, a degenerated leucocyte quite in the centre, and a peripheral zone of leucocytes, rendered more or less pyriform by mutual pressure, and staining much more deeply than the surrounding ones. It is perhaps at that stage that the greatest number of spores becomes absorbed by the leucocytes. Some of the leucocytes surround entirely the filaments which they have attacked. The filament seems in some cases to have perforated them.

7. Soon the growth of the organisms becomes more marked in some directions than in others, so that from spherical it becomes more or less elongated, lobulated or stellate. This is probably owing to the unequal resistance offered by the various leucocytes and the débris of degenerated tissues.

8. Meanwhile, the sheath of the filaments becomes more distinct, and around the swollen extremity of some of the filaments it becomes very much thicker indeed, so that a certain number of lateral and terminal filaments assume the well-known club-shape. It must be remembered, however, that this change does not take place in all filaments, and that many of them retain their original form, extending beyond the filaments which have become claviform. The filaments which do not become claviform are evidently the growing ones.

9. The thickened sheath of the clubs soon becomes separated from the central filament through the accumulation of some material apparently fluid or semi-fluid. Owing to this the size of the clubs may become considerable.

10. Ultimately the central filament breaks up into segments and disappears, and the empty sheath remains.

11. Before this stage has been reached it often happens that, in the central portions of a large actinomyces, some calcareous salt becomes deposited. This material is soluble without effervescence in various acids, and is probably of phosphatic nature. As it disappears under the action of the acid the greenish yellow colouration, which the large masses of actinomyces have acquired, disappears, so that the pigment seems to be chiefly connected with the infiltrating salt. The calcareous deposit seems to take place indistinctly within and between the filaments, and is evidently not a structural element, but the result of a precipitation of salts contained in the fluids of the invaded organism.

12. This may account for the differences there are between the

bovine and the human actinomycosis. Owing, probably, to the nature of their food the fluids of the body of herbivorous animals contains more calcareous salts than those of the tissues of carnivorous or omnivorous animals, or else their salts are more readily deposited owing to the reactions of the fluids. This is shown by the composition of their urine. Calcareous deposits would consequently take place more readily in the tissues of herbivorous than in those of other animals, and this would account for the greater tendency which the organism has to assume in them the claviform appearance which seems, from what precedes, to be the result of an arrest of growth. This would certainly not account for all the differences, for thick claviform filaments, staining readily by Gram's method, have been found in the midst of giant-cells in the bovine disease, whilst such an appearance is not common in man This, however, might be explained by a difference in the vital activity of the cells. This difference certainly exists, and is well shown by the feeble resistance which some species of animals (chiefly herbivorous) offer to the growth of micro-organisms.

13. It is certainly diffcult to demonstrate the existence of a mycelium in the midst of the calcareous material infiltrating the central portions of the fungus, as found in cattle, but it is often easy to recognise, chiefly in specimens mounted in glycerine, a large number of small spherical granules of about the same size as that of the tapering ends of the clubs.

14. I must allude here to the connection between the *filiform* and the *claviform* varieties of the organism. It has long been known to German observers that both forms may occur in the same case. They have also very early described the way in which the filaments expand to form the clubs. (All these facts had been established more than six years ago.) It was rather unfortunate for English observers that in the first case observed the demonstration of the clubs was a matter of difficulty. Dr. Acland, however, notwithstanding this difficulty, did not hesitate in describing his first case as one of actinomycosis. Dr. Crookshank, in his communication to the Royal Medical and Chirurgical Society, impressed by the discussions which had arisen in connection with this absence of clubs in the cases of actinonomycosis described in England, devoted much time to the demonstration of the existence of clubs in human cases, and was led to affirm that they were present in all cases, thinking probably that in this way

the similarity between the human and the bovine actinonomycosis was best established. He confirmed the observations made several years before by Israel, Böllinger, Ponfick, Johne, and otl ers, touching the relation of the filaments and of the clubs. He suggested also that the clubs might be Basidia, from which it might be inferred that the actinomyces belonged to the higher fungi (Basidiomycetes). Now, the importance attached to the clubs on this occasion by Dr. Crookshank is, I believe, not quite justified, and the present case shows well how possible it may be for the filamentous (or mycelial) form to be the only one present in some abscesses.

15. The case also goes very far in proving that in lesions which have not existed for more than five or six weeks clubs are not likely to be found, but that at the end of that time the ends of the filaments are certainly getting club-shaped. (The patient did not show any sign of paralytic trouble till four weeks before his death, and as he was suddenly taken with chest troubles five or six weeks before his death it is reasonable to date from that period the penetration of the parasites into the vessels and its dissemination through the system.) Judging by the size of the large actinomycetes, they would at that rate take several months to reach the size which they had attained in the liver, a supposition supported by the history of the case.

16. As I have alluded to the opinion of Dr. Crookshank regarding the place which the actinomyces should occupy among the fungi, I may as well mention that, although I do not feel competent to discuss a botanical question of such difficulty, I have been struck with the strong resemblance which the organism has to some of the mould fungi generally classified among the *Ascomycetes*. Although from the description I have just given it is evident that I do not believe that the clubs are homologous with gonidiophores, I cannot help referring to the remarkable analogy of arrangement there is between the parts of an actinomyces and those of the sphacelium of a Claviceps (one of the *Pyrenomycetes*). This analogy is better marked when the specimens are examined *au naturel* than after they have been altered and disfigured by the use of numerous reagents. It is difficult to say for certain that the clubs are Asci ; some of them contain small bodies which might be spores, and these bodies disappear after a time. Before the mycelial filaments have been stained they look much larger, and their

branching is much more easily observed than after. After staining, their sheath generally becomes invisible, so that the slender protoplasmic core only remains visible. For this reason it is difficult to get an accurate idea of the real appearance of the organism unless it is examined unstained and fresh. Notwithstanding the analogies just mentioned it must be owned that if the actinomyces be a mould, as I believe it to be, it is one the hyphæ of which are of very small diameter. It must be kept in mind, however, that the question of size is of little importance in this case, for it would be difficult to find an organism more polymorphous than the actinomyces. Cocci, filaments (Streptothrix or Cladothrix filaments or hyphæ), and clubs are all exceedingly variable in size and shape. My conclusions on this point are therefore analogous to those of the earliest observers and discoverers of the disease, with that exception, that I believe with Boström and Paltauf that the clubs are the result of an arrest of growth. However it is not certain that they are the result of a degeneration process, and might be considered simply as more differentiated parts, and possibly as equivalent to Asci.

17. I have several times found an organism in the tartar encrusting the teeth and in the crypts of the tonsils, which closely simulates the actinomyces. Lately one of my friends brought me a specimen of that organism removed from his own mouth, a thing which naturally filled him with anything but pleasant feelings, for he knew all about the parasite and the way in which it is supposed to invade the organism. I was, however, able to comfort him very rapidly. The pseudo-actinomyces is composed of filaments radiating from a centre, and a number of club-like bodies are found at the periphery of the mass. When these are treated by hydrochloric acid they are seen to be composed of filaments held together by calcareous salts, and on further addition of iodine they can be proved to belong to nothing else than the simple *Leptothrix buccalis*.

B. *Technical remarks.*

It may be well to follow the description of the parasite by some remarks on the best ways to display its structure:

1. As already remarked by most observers, the clubs show much better in fresh specimens than in stained ones; but it is generally admitted that this is not true of the mycelium.

I found during my investigations that:

(*a*) Specimens preserved in *Müller's fluid* showed the filaments and clubs extremely well without further preparations; they lost, however, their sharpness of outline after they had been mounted in glycerine or Farrant's solution. (Plate XXIX, fig. 1.)

(*b*) *Strong acids* are very useful for the demonstration of the structure; fuming hydrochloric acid is by far the best reagent for the study of the morphology of actinomycetes when one wants to demonstrate rapidly the arrangement of the filaments and of the clubs and their connection. One has only to pick out a small clump of pus containing either the young or the fully formed parasite, to add a drop of strong hydrochloric acid to it, and press gently the cover until the specimen becomes sufficiently thin to be examined with the highest powers. The preparation is then sealed to prevent the fumes of hydrochloric acid corroding the brass-work of the microscope. A preparation can thus be obtained very rapidly, and in which more can be seen than when much more elaborate methods are used. (Plate XXIX, figs. 2, 3, 4, 5.)

In preparations of this kind it is not uncommon to find the clubs segmented, or even moniliform. This is the result of pressure, and can be produced at will. Glacial acetic acid renders the clubs very transparent and soft, and they seem at times to be dissolved, but this is generally due to excessive pressure being used.

(*c*) *A 10 per cent. solution of caustic potash* is very good also for the demonstration of the mycelium. The clubs at first become so transparent that they are difficult to see, but after a time they become visible again. By using boiling potash the mode of branching of the filaments can be demonstrated with great ease. By all these methods the spores can be brought out, but more specially by the last.

All these rapidly prepared specimens are most useful for the study of the morphology of the actinomyces, and by comparing specimens quite fresh with some acted upon by the powerful reagents just mentioned one is struck by the little alteration which is produced in those parts which can be well seen without preparation. (Plate XXIX, figs. 6, 7, 8, 9, 10, 11, 12, 13.)

2. When permanent specimens are wanted, and one wants only to demonstrate the presence of the organism, nothing can be better than the ordinary histological methods, thus:

(*a*) *Picrocarmine* stains the clubs very well, and filaments may even be seen, though not clearly, after mounting either in glycerine, Farrant's solution, or Canada balsam. Specimens can be

obtained thus which are quite as clear and demonstrative as those prepared according to the various complicated methods which have been recommended at various times.

(*b*) *Hæmatoxylin* is also very good, and according to the variety of stain used, or the time taken in staining the specimen, it is possible to leave the clubs unstained or to stain them slightly. Hæmatoxylin sometimes stains the spores; sometimes it stains the mycelium diffusely; sometimes it does not stain it at all.

When the specimens are double stained with eosin, acid magenta, or rubin S., or picric acid, the clubs are almost instantaneously stained red, pink, or yellow, and the contrast thus obtained is very good.

Young filamentous colonies have some affinity for eosin, so that if after a specimen has been stained with logwood it is stained with eosin, all the small colonies will appear in the midst of the blue pus like so many pale yellowish-pink spots, and as the leucocytes surrounding them immediately stain deeper than the rest of the pus, the young organisms are easily discovered, even in a specimen which has been prepared simply for the purpose of displaying ordinary structures.

I insist upon the fact that by ordinary histological methods it is very easy to recognise actinomycetes when they are present in an organ, because it has been said that the parasite had escaped the notice of observers simply because proper methods had not been used to demonstrate its existence. It has even been said on that basis that the disease would probably prove to be pretty common. That it is not quite so rare as was supposed at first is perfectly evident, but it does not seem to me possible that a parasite which is so easy to demonstrate should have escaped the notice of the large number of competent observers constantly at work if it were as common as some would believe. It might be said that the case on which I base this statement was an unusually clear one, but I may say in answer, that in order not to be deceived by such an accident, I have applied to other specimens the various tests which I have referred to with exactly the same result as in the present case. I have even been fortunate enough to obtain through the kindness of Dr. Taylor some of the pus got from the Brompton case, on which he and Dr. Crookshank gave such an interesting demonstration, and I have found that in that case the actinomyces and the details of structure I have referred to

could be demonstrated by simple methods with greater ease still than in my own specimens.

3. When brilliantly and deeply stained specimens are required for the purpose of demonstration, almost any of the bacteriological methods known can be used, but Gram's method is undoubtedly the best for bringing out the mycelium, if nothing more than the demonstration of its existence be required. Simple watery solutions of the usual anilin dyes answer quite well, the addition of anilin or carbolic acid being unnecessary. The chief cause of the difficulty one experiences in staining the ray fungus in sections so as to exhibit fully its structure, comes from the fact that it stains very much like surrounding tissues, so that when these are decolourised by the usual methods the fungus is decolourised at the same time; however, by taking care of not pushing the decolourisation too far, it is easy to keep the filaments stained with fuchsin, gentian violet, methyl-violet, methylene blue, &c. (Plate XXVIII, fig. 2.)

The filaments can be stained with methylene blue after the preparation has been stained with fuchsin and decolourised by sulphuric acid, as in staining for *Bacillus tuberculosis*; in such a case, if clubs happen to be present, they may retain a dark red colour; if instead of sulphuric acid acetic acid be used the clubs are more easily demonstrated. Clubs stain well with eosin, aurantia, acid magenta, rubin S., picric acid, &c. They can also be stained very rapidly with sloelin. All this indicates that their sheath is composed of differentiated matter (when the central filaments is present it stains, like the rest of the mycelium, with ordinary basic anilin dyes). The sheath of the filaments also takes these stains, but owing to its thinness this reaction is generally difficult to see. (This contrast between the affinities of the sheath and of the protoplasmic contents is well seen in some bacteria. In 1883 I had already attracted attention to the fact that the differential staining properties of the *Bacillus tuberculosis* were due to the presence of a sheath, and that within that sheath it was often possible to stain the active protoplasma or spores with methylene blue. In 1881, in an unpublished investigation on lochial discharges, which I was carrying out jointly with the late Dr. Angus Macdonald and Dr. P. Wells in the Edinburgh Maternity, I had also noticed that around streptococci filaments there was commonly a thin sheath which stained quite differently from the cocci.)

I have lately studied the reaction of the various parts of the hyphæ of moulds with analogous results, and in some moulds th hyphæ terminate in club-shaped extremities with a central core of protoplasma, and present very much the same appearances as the clubs of actinomyces, either before or after staining. My friend Dr. Slater has made numerous observations confirming entirely this statement.

4. The method which I feel inclined to recommend for the purpose of preparing permanent specimens showing the relations of filaments and clubs is the following one, which is a modification of Gram's method. (The ordinary Gram's method did not yield in my hands very satisfactory results when large sections of brain and also of liver had to be stained; that is the only reason why I felt obliged to alter it.)

(1) Specimens are either hardened in spirit or in Müller's fluid; they stain equally well whether the one or the other method is used.

(2) Sections of almost any size can be left in a weak, watery solution (without anilin) of gentian violet or methyl-violet (preferably the extra-dahlia variety) for from one to forty-eight hours or even longer; or else they may be spread on a slide and saturated alcoholic solution of methyl-violet poured on them. (This answers best for the brain.)

(3) After staying a few minutes in the alcoholic solution, or several hours in the watery, the preparations are rapidly passed through distilled water.

(4) They are then left for half a minute or a minute in Gram's iodine solution. (This step is not absolutely necessary if the following ones are carried out sufficiently rapidly, but the mycelium comes generally out very much better when iodine has been used than when it has not.)

(5) The preparations are then partly decolourised on the slide in a semi-saturated solution of eosin, fuchsin S., rubin S. or aurantia (eosin is the best) in absolute alcohol. This should be done rapidly; half a minute is enough generally, and the dehydration is rapidly completed by adding absolute alcohol.

(6) The decolourisation of the specimen is completed on the slide by means of oil of cloves, a thing which takes a very short time when the specimens have been rapidly stained with methyl-violet.

(7) Immediately the specimen has acquired the proper colour

the action of oil of cloves is stopped by removing it as far as possible by means of filter paper, and by flooding the preparation with xylol. (This method gives the best results when properly carried out, but when the oil of cloves is deeply coloured by the violet, the xylol is liable to cause a precipitation of the pigment in the specimen, so that it is well to use oil of cloves pretty freely.)[1]

(8) The specimen is then mounted in xylol Canada balsam. Very good results can be obtained by this method in an exceedingly short time. Some section of brain stained thus in five minutes showed the mycelium much better than preparations over which a great amount of time had been wasted. (I think one is often misled by the idea that slow staining gives generally better results than quick staining, but, when owing to slow staining the tissues surrounding bacteria become very deeply stained, it is often impossible to decolourise them without decolourising the bacteria at the same time. Slow staining, however, gives generally more permanent results.) (Plate XXVIII, figs. 1 and 3.)

5. One can obtain good preparations of the clubs by staining the specimens with eosin, fuchsin S. or sloelin, and decolourising them afterwards with a weak alcoholic solution of potash. In this way elegant preparations can be obtained in a few minutes, and although perhaps not quite so gorgeous in appearance as those prepared by Plaut's method they show very often a great deal more.

6. To demonstrate the meaning of the constrictions often observed in the clubs, and to which the idea that they might be gonidiophores was in part due, two methods can be used:

(1) The specimens can be macerated in potash or hydrochloric acid and a cover glass pressed upon them gradually, when, by watching a few clubs, it will be possible to see them becoming irregularly constricted or even taking a regular moniliform appearance; the same effect can be obtained by simple teasing.

(2) A thin section of an actinomyces is placed on a slide, and after staining or not it is allowed to dry; if then it is mounted most of the clubs will be found to be subdivided into small segments, and in the young clubs a central filament can be seen to unite these various transverse segments. (Plate XXVIII, fig. 2.)

[1] I have used this method of washing the oil of cloves out of clarified specimens, by means of benzol, chloroform, turpentine and xylol, for several years now, and have generally found it useful when properly carried out. For bacterial preparations I, of course, use only turpentine or xylol

c. *Pathogenetic remarks.*

The general description of the case having been given chiefly with the view of demonstrating the changes observed in various organs, there remains only to connect the facts recorded by a few remarks.

1. It seems evident that in this case the point of entrance of the parasite was the skin, and not any part of the alimentary mucous membrane, as is generally found in similar cases.

2. The skin of the arms and then of the abdomen was first affected, and, from the chronic nature of the abscesses there formed, and their mode of extension, it seems evident that these abscesses were the result of an inoculation, and not simply [illegible] lesions through which parasites accidentally entered into the system.

3. For several months it is evident that the germs must have been carried from one place to another by means of the cutaneous lymphatics. There is, however, a strange feature of the case which is difficult to explain on that hypothesis, namely, the diffusion of the organism over a large area, and the existence of large tracts of skin entirely unaffected between regions where abscesses were numerous.

4. One of the last of these groups of abscesses occurred in the region of the umbilicus, and had apparently cicatrized two or three months before the death of the patient. There the superficial spread of the disease seemed to have ended, and internal troubles must have begun soon after.

5. Judging by the history, the appearance, and the size of the abscess of the liver, it must have been at least two months old when the patient died. Its situation at the point of attachment of the falciform ligament and in the neighbourhood of the ligamentum teres, as well as its independence from the distributions of ordinary vessels, may be taken as almost indisputable proofs of the transmission of the germs through the small veins or lymphatics which accompany the ligamentum teres, as it passes from the umbilicus to the liver.

6. At this stage the mode of invasion must have altered. Five or six weeks before death some of the germs must have passed into the blood and been distributed all through the body.

7. Their passage through the lungs seems to have started inflammatory processes of an ill-defined nature.

8. A few of the germs arrested in the kidney and causing obstruction of very small vessels may have given rise to the peculiar growths described in that organ, and resembling so much in their structure the tissues found about the abscess in the liver.

9. But, through some reason or other, a larger number of these particles must have reached the brain and rapidly started mischief in that organ. Allowing a few days for the congestive, necrotic, and inflammatory lesions to take place and to give rise to nervous symptoms, it is evident that the infection of the brain must have taken place very nearly at the same time as that of the lungs. We can therefore consider the large abscesses found in the brain as having grown in the space of about six weeks at most. It was only four weeks before death that the paralytic symptoms were noticed, and these were slight at first, so that the abscess causing them must have been very small at first. Six days before the death of the patient there was no complete paralysis and no indication of degenerative changes in the cord. An absence of degeneration which was confirmed *post mortem*, and proves that the lesions of the motor areas could not have existed long. The main abscess must have therefore grown very rapidly to reach the large size which it had acquired at the time of death.

10. A short time before death another shower of spores must have been disseminated all through the frontal lobes by the anterior cerebral artery.

11. The situation of all these abscesses at some distance under the cortex indicates that the parasite must have been able to pass readily through small vessels, and became really arrested in the smallest arterioles or even in the capillaries supplying the grey matter and the subjacent white matter.

D. *Physiological remarks (neurological).*

1. In order to understand fully the relations of the lesions found after death with the symptoms observed during life it is important to keep in mind—

(1) That out of all the abscesses described above only one group was situated in the motor areas, and that therefore all the others, although probably causing certain disturbances of function, probably did not give rise to any of the phenomena recorded in this case, with the exception perhaps of the final delirium.

(2) That a small portion only of the cortex was entirely destroyed,

in a region corresponding to the boundary layers between several motor centres (forearm, wrist, and hip).

(3) That a greater portion of the cortex was undermined by the abscess, and that probably its direct connections with the motor tracts were severed. The portions thus partly isolated corresponded to parts of the centres for various movements of shoulder, arm, wrist, fingers, and legs.

(4) That around the region thus undermined there was a peripheral zone where the cortical layers and subjacent white matter were congested and irritated, and this zone implicated chiefly the centres for muscles of the head and face, shoulder, arm, wrist and fingers; hip, leg and foot; and trunk.

The centres above referred to are, of course, Ferrier's centres or areas, advantage being also taken of the confirmatory and additional experiments and observations of Horsley, Schäfer, Beevor, and others.

2. From what has just been said we should therefore surmise that during life there had been—

(1) Paralysis or paresis of the leg and arm.

(2) Convulsions (Jacksonian epilepsy) of the shoulder, arm, wrist, and fingers, of the leg, and perhaps also of some of the head-muscles and trunk-muscles.

3. Moreover, from the situation of the most superficial and older parts of the lesion, we should expect that the muscles most affected by convulsions would be the shoulder-muscles (deltoideus among others), the elbow- and wrist-muscles (biceps, supinator longus, and flexors of fingers, and also, and perhaps to a greater extent, the pronator and extensor muscles), the hip- and knee-muscles (chiefly the flexors), and the trunk-muscles. Other muscles might also have been affected to a lesser degree, viz. muscles of the neck, of the eyes, and the muscles of the foot.

4. As the gyrus fornicatus seems to have entirely escaped there should have been, if Ferrier, Horsley, and Schäfer be right, no loss of tactile sensibility. If, on the contrary, Schiff and Munk be right, there should have been distinct loss of sensibility.

By looking more minutely into the lesions, further points might be made out, but the difficulty of finding the areas which in the human brain correspond perfectly to those discovered in the monkey would render a more minute study probably fruitless, for the present at least.

5. If we now pass to the phenomena observed by Dr. Gamgee during life, and confirmed by Dr. Ferrier, who, at the invitation of Dr. Gamgee examined also the case a few days before death, we will find the following among the most prominent:

Four weeks before death patient noticed loss of power in right leg and arm.

Seven days before death (1) paralysis (or paresis) of right arm and leg. (2) No anæsthesia or hyperæsthesia of parts affected. (3) No reaction of degeneration. (4) Attack of Jacksonian epilepsy lasting five minutes; right side affected; right leg less affected than right arm, convulsions beginning in deltoideus and extending downwards; wrist bent up. (5) No knee-jerk; no ankle-clonus.

Six days before death another attack of convulsions, lasting three minutes.

Five days before death was the day on which Dr. Ferrier saw the patient. Copy of Dr. Ferrier's notes: (1) "Jacksonian epilepsy. (2) Arm and leg absolutely paralysed. (3) No affection of face. (4) Perfect retention of sensibility, tactile and muscular, feels and localises the slightest touch, and indicates with perfect precision the movements of any joint = cortical paralysis without loss of sensibility."

Three days before death an attack of convulsions.

The day before death right pupil dilated.

Last day delirium.

Thus Dr. Gamgee's case affords a complete confirmation of Dr. Ferrier's statements regarding the function of the portions of the cortex affected in this case.

This case also confirms entirely the later observations of Professors Schäfer and Horsley on the trunk-centres, and gives a full confirmation of the views advanced by Ferrier and supported by Horsley and Schäfer regarding the localisation of tactile sensibility, whilst, of course, it infirms to the same extent Schiff and Munk's views.

6. There are some points of great interest in the phenomena recorded, when they are considered in the light of the lesions observed after death.

(1) A very small part of the arm and of the leg areas was entirely destroyed, and even if the whole of the parts undermined by the abscesses be taken into account, not more than one half of

the arm area and one sixth of the leg area were destroyed or disconnected, and yet the paralysis of arm and leg was nearly complete. It is interesting, however, to note that the paralysis of the arm was more complete than that of the leg, although, for obvious reasons, the patient noticed loss of power in the leg before he was aware of loss of power in the arm.

(2) The most superficial cortical lesion was near the shoulder centre; in that region the membranes were slightly thickened and adherent. The other portions of the brain, which surrounded the superficial portion of the abscess, were undermined by the deeper parts of the same abscess, so that any irritation starting from the points of adhesion could have produced motion only by extension to parts of the cortex, situated near the margin of the deeper lesion. It is perhaps one of the most interesting features of this case that Dr. Gamgee was able to witness one of the attacks of convulsions, during which he noticed that the shoulder-muscles were first affected, then those of the arm and forearm, finally the wrist was flexed. The leg was convulsed less than the arm. The trunk was also affected, but to what an extent is not recorded. If we suppose a wave of irritation starting from the place where the membranes were adherent, that wave would have affected (1) the shoulder and arm areas. (2) The elbow and forearm areas. (3) The wrist and fingers areas. (4) The trunk and leg would also have been affected early, but to a much lesser extent than the arm. (5) Some of the head-muscles should also have contracted; according to Horsley and Schäfer's experiments the ears should have been strongly retracted; this was not observed, but retraction of the ear is a movement seldom observed in man, chiefly owing to the small size of the ear-muscles. The absence of rotation of the head and of deviation of the eyes is of great interest in showing that these areas do not correspond to the posterior part of the middle frontal convolution, which was the portion of the head area nearest to the abscess.

(3) The dilatation of the right pupil is of interest in showing a unilateral dilatation of the pupil when, probably, only the posterior portion of the head area was stimulated. This would, of course, complete the remark which we have already made regarding the probable absence of any area corresponding to the muscles of the head and neck in the same posterior part of the head area.

7. The marked œdema which I noticed *post mortem* (I was careful to eliminate the possibility of *post-mortem* gravitation of fluids) in

the right arm and leg, and more especially in the foot and hand, suggest the existence of vaso-motor disturbances previous to death, due to the irritation of the hand and foot cortical areas. Whatever be the cause, this is certainly an interesting instance of well-localised nervous œdema (Laycock).

General conclusions.

The following points seem to have been gained by the study of this case:

(1) Actinomycosis may begin in the skin, extend through the lymphatics, and penetrate into some internal organ.

(2) The parasite may after a time be disseminated through the system by means of the blood-vessels.

(3) It may pass through organs without apparently producing typical lesions, but nevertheless it may cause serious inflammation, which has apparently nothing specific.

(4) It is disseminated under the shape of small spores, and afterwards grows into branched filaments which, when unstained, have the appearance of a mould mycelium (when stained by Gram's method they look like Steptothrix or Cladothrix filaments).

(5) After five or six weeks, clubs begin to appear, and are the result of the thickening of the sheath of some of the filaments; after a time the protoplasmic core breaks up into small rounded masses which may be spores, and finally the sheath of the clubs remains empty.

(6) The fungus has all the characters of a mould fungus (although septa have not been seen in the filaments). The clubs have strong analogies with *Asci*, and the fungus belongs probably to the *Ascomycetes* and possibly to the family of the *Pyrenomycetes*.

(7) Considerable irritation of the tissues, and vascular disturbances, often rapidly followed by necrosis, result from the infection of a part, and this is manifest several days before the organism can be demonstrated. This seems to indicate the elaboration of some virulent poison in the early stages of growth.

(8) In the brain a large abscess can be formed in a few weeks under the influence of this parasite. Owing to the small size of the spores, or the way in which they are carried by leucocytes, areas supplied by several small vessels may be affected at the same time, so that the lesions must generally be multiple.

(9) In this case the symptoms observed during life corresponded to those which Ferrier has described as resulting from affections of the parts of the brain implicated in this case. The absence of tactile anæsthesia supports also the views of this observer on the localisation of tactile sensibility, and disproves the views that the motor areas are also tactile areas as supported by Schiff and Munk.

Note.—I have not attempted to give the literature of the subject because I am aware that several papers of great importance have been written in London, or are being written on the subject of actinomycosis. I present the case as one of great interest *per se*, and one which has been studied independently of any preconceived idea.

The chief facts of the case were communicated to Dr. Acland and several friends during the months of February and March, but many facts concerning the morphology of the actinomyces I had ascertained previously. From what I heard at the Royal Medical and Chirurgical Society I feel inclined to differ from Dr. Crookshank regarding the morphology of the actinomyces; however, as I have not yet seen his full report, I simply give my facts and they will speak for themselves.

On the day on which this paper was communicated Mr. Eve showed a specimen of *Actinomyces hominis* in which clubs were easily demonstrated, as well as the mycelium, supporting thus one of my contentions regarding the ease with which clubs can be demonstrated. About three weeks later Dr. McFadyean communicated observations on a case of *Actinomycosis bovis*, in which nearly all the points which I had advanced concerning the human parasite are recorded as being present in the bovine disease. It must be said that most of these points have been familiar to German observers for more than six or seven years. I need only refer here by name to the work of Israel, Bollinger, Johne, Ponfick, Pflug, Hink, Harz, De Bary, Acland, Eve, Shattock, Taylor, and Crookshank. The most complete history of the subject will, I am informed, be found in Crookshank's reports in the 'Annual Report of the Agricultural Department of the Privy Council Office on the Contagious Diseases, &c., for the year 1888,' which will soon appear, and a most condensed and lucid account of the subject by Dr. Acland will be found in the new edition of 'Quain's Dictionary.' I need only add that Bollinger has recorded lately a case of primary actinomycosis of the brain which differs considerably from the present one.

May 21*st*, 1889.

EXPLANATION OF PLATE XXVII.

To illustrate the report of a case of Actinomycosis Hominis by Dr. Delépine.

This Plate shows the appearance of three frontal sections of the brain (anterior aspect), about two thirds natural size.

(*Note.*—Owing to some accident in the printing, the sulci and internal cavities of the brain are represented as being much larger than in the originals, with this exception, the drawings represent *accurately* what could be seen in the actual sections.)

FIG. 1.—Section through the middle of the frontal lobe. 1. Left anterior cornu of the left lateral ventricle. 2. Genu of corpus callosum.

a, b, c, d, e. Small abscesses (described in the text as Nos. 1, 2, 3, 4, 6).

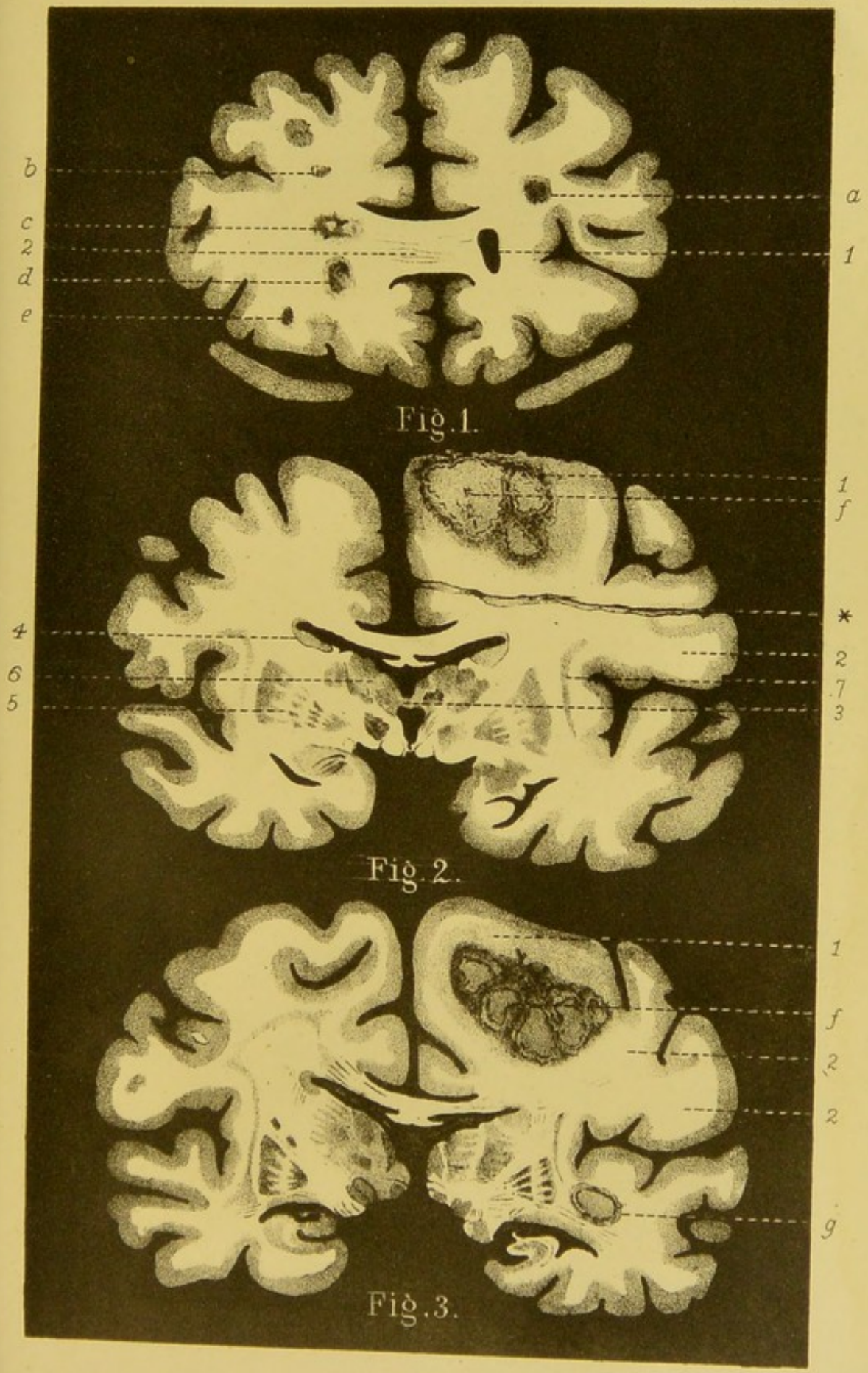
FIG. 2.—Section through the ascending frontal and the ascending parietal convolutions. 1. Ascending frontal convolution. 2. Ascending parietal convolution. 3. Middle commissure. 4. Nucleus caudatus. 5. Nucleus lenticularis. 6. Thalamus opticus. 7. Claustrum.

f. Large abscess (No. 7 in the text). This abscess was exposed by removing a thin slice from the upper part of the left hemisphere. The portion represented above the line * is therefore on a plane posterior to that of the rest of the section.

FIG. 3.—Section through the same convolution as those represented in Fig. 2, but a little further back. 1. Ascending frontal convolution. 2. Ascending parietal convolution.

f. Large abscess (No. 7, text).

g. Abscess (No. 8, text).



Sheridan Delépine del. (Aug 1888 - Apr 89).

Danielsson & Co lith.

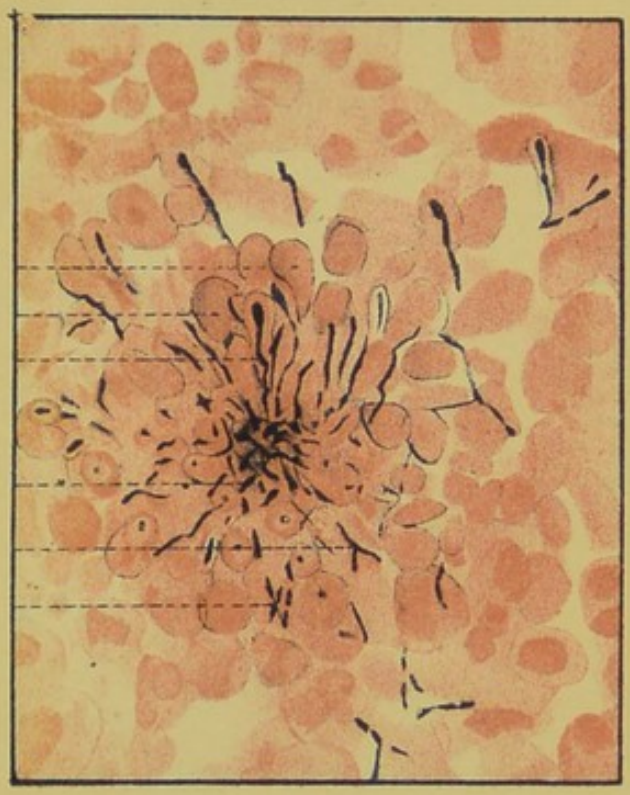


Fig 1

Fig 2

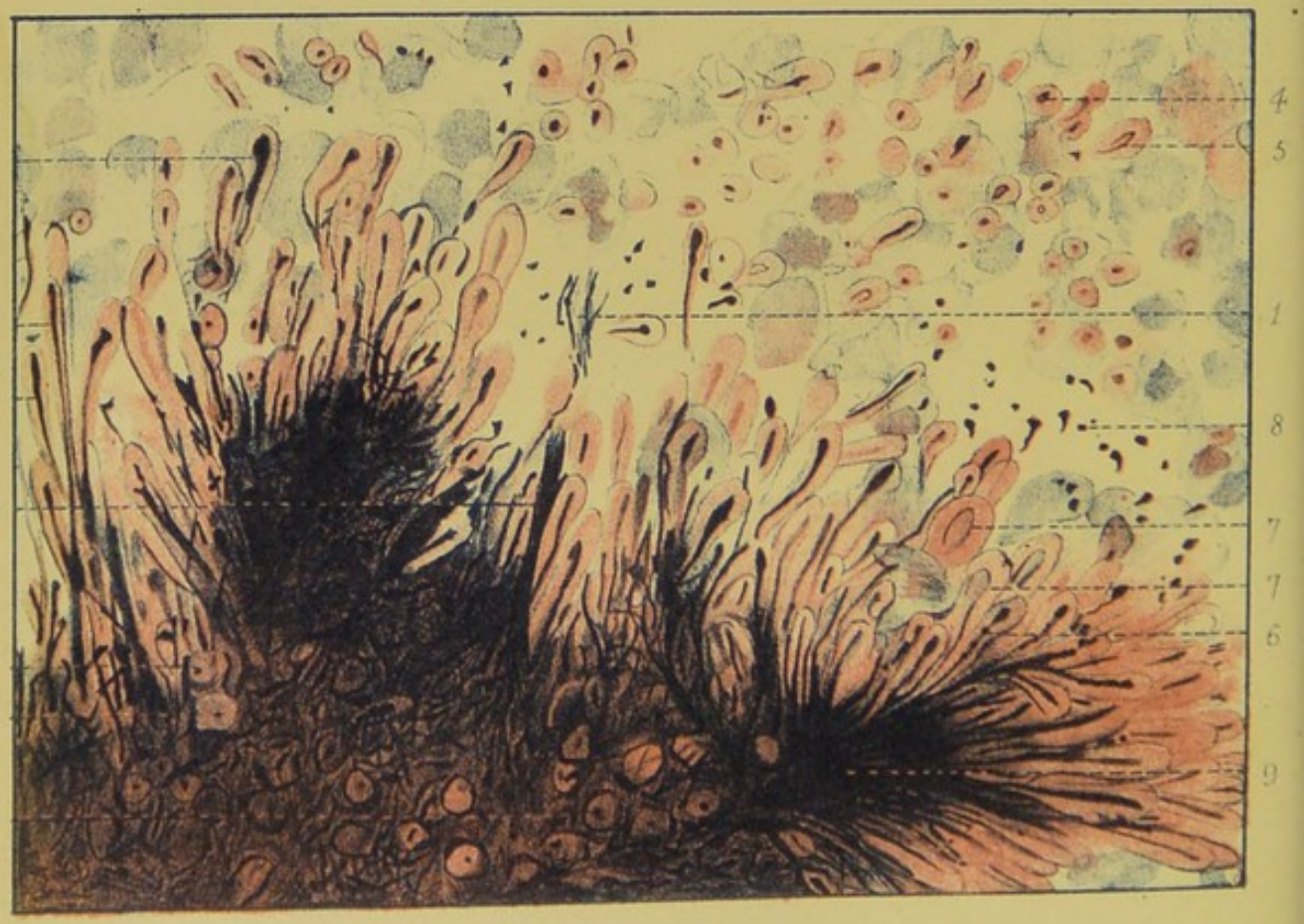


Fig 3

Sheridan Delépine del (March April 1889). Danielsson & Co chromo-lith.

EXPLANATION OF PLATE XXVIII.

To illustrate the report of a case of Actinomycosis Hominis by Dr. Delépine.

FIG. 1.—A young actinomyces found in the pus from one of the large cerebral abscesses (No. 7). (Stained by the rapid Gram's method described in the text.) × 1100. 1. Pus-corpuscles deformed by pressure, and staining deeper than the others. 2. Filament distinctly clubbed, and covered with a thick sheath (young club). 3. Bacillary form of the organism. 4. Branched filament. (Cladothrix form in its early stages.)

FIG. 2.—Portion of the margin of a medium-sized actinomyces from one of the large hepatic abscesses. (Stained with carbolised fuchsin, and double stained with methylene blue after decolouration by acetic acid.) × 1100. 1. Large clubs, forming the apparent border of the organism. 2. Mycelial filaments, extending beyond the clubs. 3. Mycelial filament slightly thickened at its peripheral end (young club). 4. Mycelial filament, with a thickened differentiated sheath (young club). 5. Large empty club (old club). 6. Clubs broken up into segments, owing to accidental stretching (this appearance has misled several observers).

FIG. 3.—Portion of the periphery of a pretty large actinomyces from one of the large hepatic abscesses. This shows two lobate projections, in one of which (9) the radiating arrangement of the mycelium is well shown. (Stained in weak watery solution of dahlia violet for three days, then treated with Gram's iodine solution and double-stained with eosin.) × 1100. 1. A fasciculus of simple filaments staining badly. 2. A young club with thick protoplasmic core and thin sheath. 3. A young club with thicker protoplasmic core. 4. Older clubs seen from above. 5. Older clubs seen obliquely. 6. Clubs with protoplasmic core segmented and assuming a streptococcus form (note the sheath is neither torn nor deformed). 7. Old clubs with thick sheath and no protoplasmic contents. 8. Free micrococcus-like bodies, varying in size, possibly spores. 9. Portion of the organism where the plan of section passes through the axis of one of the lobate projections, so that the radiating arrangement of the mycelial filaments is better shown than elsewhere.

EXPLANATION OF PLATE XXIX.

To illustrate the report of a case of Actinomycosis Hominis by Dr. Delépine.

(*Note.* — All the specimens represented in this plate are magnified 1100 times in diameter.)

FIG. 1.—A *small actinomyces* from one of the liver abscesses (× 1100). (Examined in *Müller's fluid*, unstained.) *a. Young filaments* growing rapidly, after passing through a barrier of cells. *b.* Filaments becoming club-shaped. *b'.* Clubbing of one of the filaments evidently due to arrest of growth in one direction, produced by *mechanical obstacle.* *c.* Large cells probably resulting from the proliferation of *fixed connective-tissue corpuscles.*

d. Pus-corpuscles.

(Note the strong analogy of structure with a mould.)

FIGS. 2, 3, 4, 5.—Portions of a *medium-sized actinomyces* from one of the hepatic abscesses (× 1100). (The specimen had been treated with *fuming hydrochloric acid*, and slightly compressed.)

Fig. 2. Portion of the margin where the clubs are small and distinctly branching. *a. Young clubs, moniliform* in shape owing to teasing. *b.* Much thickened filament forming the base of a number of clubs.

Fig. 3. *Older clubs*, all *distinctly branching* from one filament. *a.* Transverse *segmentation* produced by pressure.

Fig. 4. Part of the *mycelium* composed of branching filaments. *a.* Thickening corresponding to the base of one or several clubs.

Fig. 5. Small clubs, apparently containing small *spores.*

FIGS. 6, 7, 8, 9, 10.—Portions of a *large actinomyces* from one of the abscesses of the liver. (Treated with *liquor potassæ*, and examined in *saline solution.*)

Fig. 6. *Very young club*, formed by thickening of the end of a mycelial filament.

Fig. 7. *Young club*, showing a *sheath* and a *protoplasmic core.*

Fig. 8. *Older club*, with a distinct *space* between the sheath and the central filament.

Fig. 8'. Clubs in the same stage seen obliquely.

Fig. 8''. Branching clubs altered by pressure.

Fig. 9. *Large club* flattened by pressure. *a.* Protoplasmic core, soft and flattened. *b.* Harder sheath, split at several places. *d.* One of these slits. *c.* Space between the core and the sheath.

Fig. 10. *Empty old club*, rendered moniliform by pressure (appearance often mistaken for segmentation and production of conidia).

FIGS. 11, 12, 13.—Actinomyces obtained from pus removed from the *pleural cavity.* (The preparation from which this drawing has been made had been prepared from pus, which Dr. Taylor of the Brompton Hospital had kindly given me; as there was no difference between these specimens and those obtained from the hepatic abscesses, I have not thought it necessary to make two drawings.) Specimen treated by *boiling liquor potassæ.*

Fig. 11. A flattened clump of branched filaments (*mycelium*), with *spore-like bodies between them.*

Fig. 12. Some of the filaments with *spore-like granules* in them.

Fig. 13. *Branching wavy filaments* (Cladothrix), isolated by teasing.

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Fig. 1.

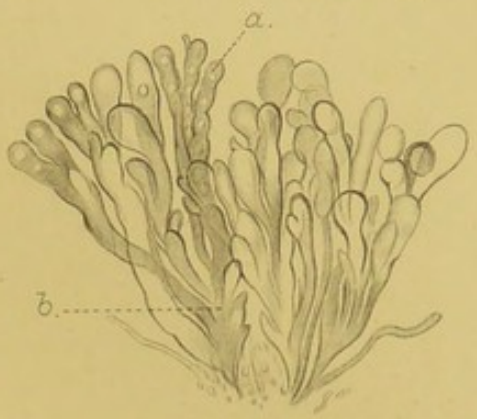

Fig. 2.

Fig. 3.

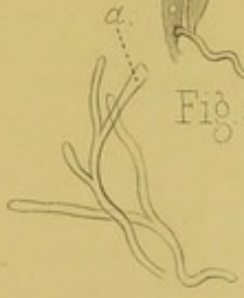

Fig. 4.

Fig. 5.

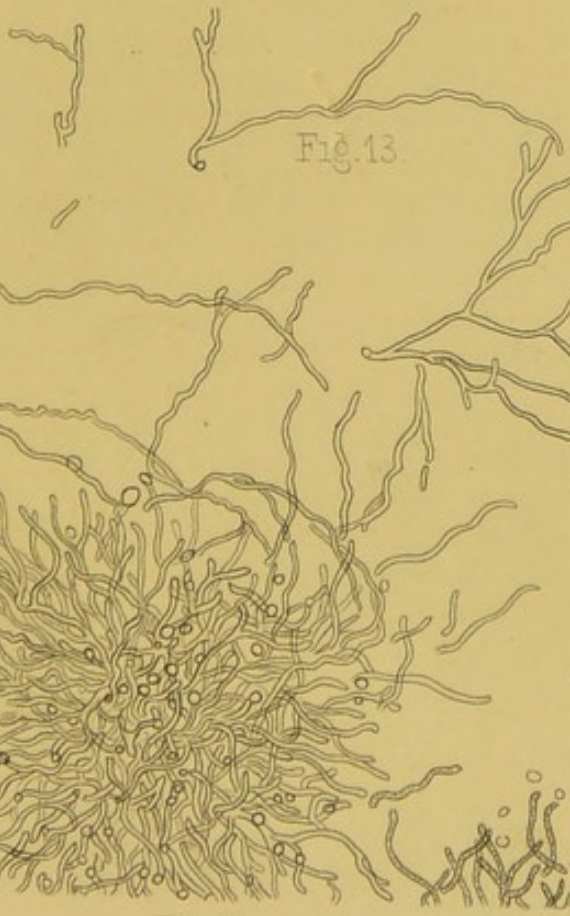

Fig. 11.

Fig. 12.

Fig. 8'.

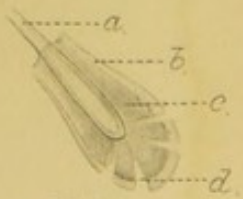

Fig. 9.

Fig. 13.

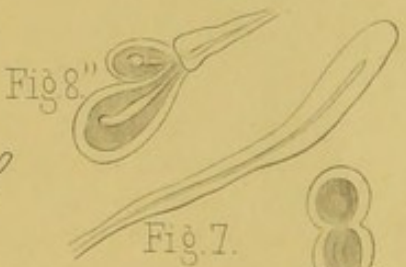

Fig. 8".

Fig. 7.

Fig. 10.

Fig. 8.

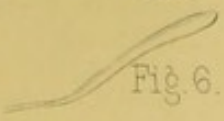

Fig. 6.

Sheridan Delépine del. (Feb. 1889).

Danielsson & Co. sculp.