rarely spreading on to the dorsum of the foot and associated with pain, but the swelling which, when associated with pain and redness, is described as typical of the condition has only been seen in 1 case.

4. *Sensation*.—In no cases could distinct objective impairment of sensation be found.

5. *Knee-jerks*.—In these early cases the knee-jerk was often present and perhaps unusually brisk.

6. *Ataxia*.—This has not been noted in our cases, in the absence of palsies the difficulty in maintaining the equilibrium has usually been attributed by us to the painful condition of the feet. There has always been the ability to describe passive movements of joints.

In the more advanced cases these types of sensory symptoms predominate, hyperæsthesiæ being most pronounced. The motor symptoms did not present any appearances that we are not accustomed to see in the neuritis of alcohol, and in none of the cases in which mental alteration was present could this latter poison be excluded. In no cases were the cranial nerves, the intercostals, or phrenics affected.

CLINICAL AND PATHOLOGICAL NOTES ON A CASE OF HUMAN ACTINOMYCOSIS.*

WITH CONCLUSIONS DRAWN FROM IT AS TO THE NATURE OF THE DISEASE.

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ON March 8th, 1898, a big, well-built man, aged 23, was admitted to Sir Patrick Dun's Hospital, Dublin, under the care of Dr. Bennett, Professor of Surgery at Dublin University. He complained of a large inflammatory swelling round his neck, which made him carry his head bent on his chest. The patient could in no way account for his illness, as though attending cattle there had not been a sick beast amongst them.

History.—This swelling had started four months previously as a small hard lump below the lobule of the left ear between the angle of the jaw and the mastoid process. It grew to the size of an orange in three weeks, caused him great pain, and prevented him opening his mouth, so that he got a doctor to incise it. This gave slight relief, but only blood escaped from the incision.

Condition on Admission.—The swelling went on increasing and extending, so that on admission to hospital he had a large, brownish-red, brawny swelling, extending from the lobule of the left ear round the back of the neck to the right ear, passing round the right side and front of the neck and down on the sternum. Fluctuation could be detected over a large part of the back of the neck, and at several places there were deep sinuses discharging fetid brownish pus, while at other parts there were small fungoid masses projecting from the surface. The only parts tender to the touch were those which the swelling had most recently extended to.

Diagnosis.—From the history and appearance of the case, Dr. Bennett made the diagnosis of actinomycosis, and being house-surgeon in the hospital at that time I was able to collect all the pus from the large abscess at the back of the neck, which was opened shortly after his admission.

Examination of Pus.—The pus, which was very fetid and blood-stained, was spread out in a thin layer on a large piece of plate glass laid on a black surface, and everything at all resembling actinomycetes granules was picked out and examined fresh and stained. No typical granules were found, but only a few small masses like inspissated pus about the size of a pin's head. Examining these fresh, they were seen to consist of small fat globules and pus cells, and in only one of them could I find what resembled a single club. Preparations stained by Gram's method showed long convoluted chains of what looked like streptococci, and very like what is depicted in von Jaksch's *Clinical Diagnosis* (English Edition, 1839, p. 353). The pus and scrapings from the walls of the abscesses were frequently examined later on, but nothing further was ever found during life.

Cultivation Experiments.—Aërobic cultures were made several times, but nothing resembling actinomycetes or any streptothrix form was found. Anaërobic cultures were not made.

Later History.—Some weeks after the opening of this abscess another formed over the sternum and opened of itself, and a little later another was opened at the vertebral border of the scapula, scraped out and plugged with beta-naphthol. At about this period the patient developed signs of tuberculosis of the lungs, especially the right, but no tubercle bacilli could be found in the sputum, and it was considered that the lung affection was due to extension of the abscess at the right scapula into the lung. This was proved later on by the patient expectorating the tincture of benzoïn emulsion, which was being used at the time for wash-out out the abscess cavities owing to their number and the risk of constantly applying strong antiseptics to so large an absorbing surface. During the next three or four months abscesses kept on forming about the back and neck, which were opened and scraped out, and then either plugged or swabbed out with almost every conceivable antiseptic; but most of them proved quite intractable and kept on discharging, while a

few healed up. A notable feature about all these abscesses was that they never communicated in any way with each other, arising, as it were, spontaneously at comparatively distant parts.

Death.—During the last three months of his illness the patient emaciated to an extreme degree from the profuse suppuration, and died on November 24th, 1898, with advanced amyloid disease and all its usual symptoms after an illness of almost a year's duration. Throughout the illness the temperature kept more or less above normal, usually dropping when an abscess was opened but finally becoming hectic.

POST-MORTEM EXAMINATION.

External Appearances.—The body, which was examined forty-eight hours after death, was greatly emaciated, all the bones visible, no subcutaneous fat, skin straw coloured. On the back of the neck the skin was hard and thickened, dark brown coloured, and covered all over with sinuses, some of which were discharging a thick brown-coloured pus. This condition extended over the entire back of the neck from the occiput to the first dorsal vertebra. There was an old sinus 1 inch above and internal to the lower angle of the right scapula, which was closed. (This had internal relations described below.) Several old healed sinuses were also present over the dorsal vertebrae and right scapula, and one behind the angle of the lower jaw on the right side.

Abdomen.—The abdomen was full of clean straw-coloured fluid, all the viscera pale, liver and spleen much enlarged.

Lungs.—Both thoracic cavities were full of straw-coloured fluid. The apex of the right lung was adherent, especially posteriorly, but the adhesions were easily broken down except at the angle of the third rib, where the lung tissues had been torn in trying to separate it from the rib. On doing this a distinct roughness was felt in the lung, due to a piece of necrosed rib superficially buried in the lung tissue. There was a ragged hole at the angle of the third rib about the size of a pea, from which brownish pus exuded on squeezing the intercostal spaces above and below it. On enlarging this hole the rib could be felt necrosed and the finger poked down beneath the skin of the back in the direction of the closed sinus at the angle of the right scapula, but even with a probe this scar could not be completely reached. No communication in any other direction could be established. This was the sinus where fluid was syringed into the lung from the skin during life. The apex of the left lung was much more adherent than the right, and parietal and visceral pleurae had to be stripped together. No ulceration into the lung was visible, but on looking at the chest wall the lateral surface of the second dorsal vertebra and adjacent head of the second left rib were seen to be quite rough and necrosed, but no communication any deeper into the vertebrae or soft parts could be made out, nor was there any pus here. The right lung was firm and hard at the apex; the base purple and cedematous, anterior margin pale and emphysematous. On section the apex was solidified and red coloured, studded over, especially under the pleura, with small white spots, not raised or hard, and not very like tubercles. There was also one other patch that exactly resembled a true corpus luteum, with a reddish jelly-like central mass, surrounded by a tortuous whitish margin. The left lung presented somewhat similar appearances. The rest of the lung tissue in both lungs was merely congested and cedematous.

The other viscera presented nothing of special interest. All the abdominal organs were amyloid, and the heart looked exactly like brown atrophy, but showed no change microscopically to confirm this view.

On examining a section of the skin stained with logwood and counterstained with acid fuchsin and picric acid (van Gieson), the epidermis and dermis are seen to be unaffected, except where the abscesses broke through the skin. There is, however, great congestion of the vessels of the true skin.

The lesions are mainly situated in the subcutaneous tissue, which is greatly thickened and very dense, and consists largely of granulation tissue in various stages of development. In the least affected parts there are masses of dense connective tissue, with patches of round-cell infiltration, and more recent tissue composed of young connective tissue cells, small round cells, and polymorpho-nuclear leucocytes. There are some places where the tissue is composed of large round cells, with almost clear protoplasm and a large nucleus not very rich in chromatin, usually with a nucleolus; some of them are vacuolated, and appear to include red corpuscles, which are freely present between them; they give no special reaction to polychromatic methylene blue, and are most likely the hyaline connective tissue cells described by Unna in Orth's *Pathology*.

Passing on to the more affected parts, the tissue consists of very vascular granulation tissue which in places, in the neighbourhood of the actinomycetes, has been extensively infiltrated with polymorpho-nuclear leucocytes, and in some parts broken down into actual pus. In these latter places the actinomycetes has usually fallen out of the section, but it can be frequently seen surrounded by a wide zone of polymorpho-nuclear leucocytes and remains of granulation tissue.

The actinomycetes, with van Gieson's stain, examined with a low power, usually appears as an irregularly round or oval maroon-coloured dense mass, about 0.15 mm. in diameter on

*Read before the Pathological Section of the Royal Academy of Medicine in Ireland.

an average, with a thin clear pale-pink coloured outer zone, and a central area of the same maroon colour which is much less dense, and sometimes contains a few polymorpho-nuclear leucocytes as well (Fig. 1).

Fig. 1.—Streptothrix mass in subcutaneous tissue showing an arrangement of threads and surrounding leucocytes. Leitz, Obj. 7, Oc. 1.

This whole appearance is due to the presence of a dense ring of streptothrix threads, which are composed of a delicate membrane enclosing the protoplasm of the thread (Fig. 2).

Fig. 2.—Part of Fig. 1 highly magnified, showing uneven staining, swelling, and true branching of the threads. Zeiss oil immersion, comp. Oc. 4.

This protoplasm, which is not evenly distributed throughout the thread, stains feebly with logwood, while the membrane stains pink, the result being a sort of maroon colour.

The outermost pink zone consists of the ends of the threads, which are for the most part void of protoplasm, while the central zone is made up of threads in much smaller quantity

than the middle zone. Immediately outside the thin pink zone there is usually a zone of leucocytes which are very few in number, causing a semitransparent appearance, and outside this again there is frequently an actual break in the tissue, probably due to shrinkage in preparation. The more advanced the process of breaking down in the tissues is, the better is this appearance seen.

When sections are stained with carmalum and Wiegert's fibrin stain the low power appearances of the actinomyces are just the same as with van Gieson if one substitutes shades of violet for the maroon colour seen with the latter stain.

Examining sections of the skin, stained by carmalum and Weigert with a 1 in 12 Leitz oil immersion, one sees masses of threads about the thickness of diphtheria bacilli, sometimes exactly like them, with their polar granules stained, but usually five or six times as long. The membrane is stained pink, while the protoplasm is unevenly stained violet, sometimes like long chains of cocci exactly resembling what I found in the pus during life, at other times much longer masses of protoplasm are stained, and thus there is a gap where the membrane only can be seen, and again these bacillus-like forms with a little violet granule at either end.

These threads undoubtedly form true branches which go off at a right or acute angle (Fig. 2). The stained protoplasm does not usually run direct from the stem into the branch, but there seems to be a direct continuity of the membrane.

The outside pink zone which I have described above is the representative of the clubs described in actinomycosis, and consists, as I have said, of the membranes of the threads. These free ends of the threads may or may not contain stained protoplasm, most frequently not, and in either case they may be swollen up into club-like masses just like the involution forms of diphtheria bacilli, but are just as often of even calibre all along, and moreover they are not confined to the outer zone, but are just as frequently seen in the middle or central zone.

The microscopic appearances of the affected parts of the lung show a double infection, namely tuberculosis and actinomycosis.

The consolidated apices are affected with broncho-pneumonia of a diffuse character. The alveoli are full of alveolar cells and leucocytes; the bronchi have greatly thickened fibrous coats, while all their coats are extremely congested and infiltrated with round cells and the epithelium almost completely desquamated.

In the more affected parts where the specific changes are to be found, the lung tissue is quite unrecognisable and replaced by a very vascular granulation tissue, which in places, especially round caseous patches, has become firm fibrous tissue. Throughout this tissue there are numerous caseous nodules full of giant cells and which contain tubercle bacilli.

So far the changes described do not differ from those in any tuberculous lung, but lying in this same tissue with the caseous nodules one can see the actinomyces, the tissue around being usually infiltrated with leucocytes just as in the skin. The process in the lung, however, seems to be much less advanced than in the skin, as there are several actinomyces groups simply lying in the granulation tissue with no surrounding zone of leucocytes.

From the descriptions of the micro-organisms found in the tissues in this case I think it is evident that we have one of the species of streptothrix to deal with.

There are now numerous cases of what may be collectively termed actinomycosis, both in man and animals, which have been described in this country and abroad. From these writings there can be little doubt, as Dr. Dean points out, that actinomycosis is due to different species of a common streptothrix genus. I may say here that I think it best to place the streptothricæ by themselves till something definite is made out as to their position among microbes. The existence of different species of streptothrix causing actinomycosis seems to be the only way of explaining the anaerobic or aerobic conditions necessary for the growth of the micro-organisms in different cases, besides a number of other variations in culture media.

The present case was undoubtedly not due to an aerobic organism, and unfortunately anaerobic cultures were not made. It was, however, a case of what is generally called

actinomycosis, and was clinically diagnosed as such before any micro-organism was even looked for.

Moreover, the arrangement of the micro-organisms in the tissues, the true branching, the uneven staining of the protoplasm, and the tendency to form swellings at the ends of the threads; all these points leave no doubt that it was a streptothrix infection (See Fig. 2).

As already said, I only found a single object resembling a club in the pus from one of the abscesses, but absolutely nothing else during life or *post mortem*. What the clubs are I do not venture to say, but I do not believe they are degeneration forms; for if tissues from actinomycotic cattle are stained by Gram's method a beautiful radial arrangement of clubs stained deep violet is shown, but I have never seen any mycelial thread stained.

I have seen two cases of human actinomycosis, and examined tissues from three others, and in only one case in which quantities of pus were coughed up were the clubs visible, and easily seen by squeezing out one of the "granules" found in the pus, and examining with a low power. In the other three cases the appearances were precisely similar to those in the present case.

The extracorporeal relations of these streptothricæ and their mode of infecting the animal are still unexplained, but there have been a number of researches, especially those of Jensen and Johne, cited by Crookshank, which point to their having origin amongst the cereals. Several experiments by different investigators tend to show a possible connection between the tubercle and Timothy grass bacilli and actinomycetes. For instance, Lubarsch and Schulze produced actinomycotic-like growths in animals from the Timothy grass bacillus and Eppinger's streptothrix. Bates produced mycelial growths with clubs in animals by injecting tubercle bacilli into the brain. The most extraordinary results were those of Friedrich and Nösske, who by injecting definite quantities of tubercle bacilli into the left ventricle of rabbits, produced a growth of tubercle bacilli, especially in the kidneys, composed of a dense mass of bacilli surrounded by a ring of clubs.

These experiments taken together seem to me to suggest a possibility of our finding the primary source of tubercle bacilli amongst the cereals or some other members of the vegetable kingdom.

In conclusion I wish to thank Dr. Wigham for the time and trouble he has spent in the photo-micrograph department on the photographs.

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NOTE ON THE DIALYSIS OF THE TOXINS THROUGH COLLODION WALLS.

BY

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M.D. M.D.

THE details of our technique for the dialysis of living cultures have been previously described in this JOURNAL.¹ It is sufficient to remind the reader that it consists in cultivating a given microbe in a collodion sac suspended in some cultivating medium. The object of our present investigations was to see whether mild toxins dialyse, partially or wholly, through the walls of a collodion sac, and whether they then retain their pathogenic properties. The microbe chosen was the bacillus pyocyaneus, because its pathogenic properties had been already studied by several observers and one of us (R.), and because it secretes a colouring matter rendering its recognition easy.

We have observed that toxins pass through the collodion walls in small quantities, but that the time they take in doing

so is comparatively long, depending on the thickness of the tube and on the nature of the liquid in which the sac is suspended.

A comparison of toxin filtered through a Chamberland candle with toxin obtained by dialysis, showed that the first had greater pathogenic properties than the second. Nevertheless, we succeeded in reproducing with the latter all the symptoms without exception, typical arthritis even, provided the quantity injected was sufficiently large. A guinea-pig, for instance, injected with 20 c.cm. (per kilog. weight) of filtered toxin died in three hours, but more than double the quantity of the toxin obtained through dialysis of a culture of the same age and the same breed was necessary in order to kill an animal of the same weight in forty-eight hours or thereabouts. Even under such conditions death was not constant.

Nevertheless, whenever the dose of toxin obtained by dialysis exceeded 20 c.cm. (per kilog. weight) the animals died from cachexia after a shorter or longer period.

The pathogenic properties of the dialysed substances varied according to the length of the dialysis. The toxins dialysed from living cultures during ten to thirteen days, a short period of fever, diarrhoea, and sleepiness predominated, though diarrhoea was less frequently present than the other symptoms. Convulsions occurred but rarely, and were produced only by toxins which had dialysed during a period of thirty to forty days.

The dialysed toxin injected in the dose of 5 to 10 c.cm. (per kilog. weight) produced no or hardly any apparent symptoms, but conferred immunity. The colouring matter (pyocyanine) dialysed only when the sac was not too thick.

We have stated already that the nature of the liquid surrounding the sac of collodion had great influence on the amount of toxin which dialysed through. We noted that if a collodion sac filled with a bouillon culture was suspended in distilled water, the surrounding water became far more toxic than when the surrounding medium was bouillon or peptonised water. The naked-eye characters of the cultures also differed according to whether these were immersed in one or other of the liquids. The cultures made in sacs suspended in bouillon, for instance, lost the greater part of their water, became viscous, and resemble those made in collodion sacs introduced into an animal's peritoneum. The bacilli appeared deformed, many became granular, others assumed a coccil form, and those seemingly normal were less vigorously motile than usual.

We have studied only casually, so to speak, the virulence of bacilli in collodion sacs, and in the few experiments we have made this virulence appeared to follow no regular rules.

To resume, the various toxins of the bacillus pyocyaneus dialyse, but not in their entirety. The time they take in thus dialysing is comparative long, and their pathogenic properties vary according to the length of the dialysis.

It is extremely probable that the immunising substances are among the first to dialyse. Advantage might possibly be taken of this property in the manufacturing of vaccines.

REFERENCE.

¹ BRITISH MEDICAL JOURNAL, November 3rd, 1900, p. 1305.

A CASE OF RENAL COLIC ATTENDED BY THE PASSAGE OF CASTS OF THE URETER (URETERITIS MEMBRANACEA).

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IT is well known that renal colic may be caused by other conditions than the passage of a renal calculus, and such causes as the passage of uric acid or oxalate of lime crystals, tuberculous *débris*, or hydatids from the kidney have been recorded, and to these psorospermiosis has recently been added.

The passage of casts derived from the mucous lining of the ureter itself seems, if one may judge by the absence of literature on the subject, to be a rare occurrence, and the following case is therefore interesting.

History.—Mrs. P., a lady of just over 60, was first seen by me about fifteen months ago for repeated attacks of agonising pain in the left loin,