Actinomycosis / by Frederic Eve.

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ACTINOMYCOSIS.[1]

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THE love of novelty is perhaps as strong in the present day as it was among the Athenians, and this applies to science as well as to fashion. The life of the pathologist and surgeon would be comparatively dull were it not that new diseases were constantly coming to light for him to study; or, what is perhaps more frequent, if old diseases did not assume fresh aspects from recent investigations. Generalisations in an imperfect knowledge of a subject are often too sweeping, and synthesis groups together diseases which analysis discovers subsequently to be absolutely dissimilar.

This was the case with actinomycosis, which appears to have been jostled about from pillar to post, having no definite resting-place in the classification of diseases. It has long been known to veterinary surgeons as a disease of cattle, which they called the "worm," probably on account of the circumstance that on squeezing a section of the morbid growth, worm-like masses could be expressed, such as are observed in epithelioma. In later days examples of it were described as lympho-sarcoma;

[1] Given in part before the Odontological Society of London.

and when occurring in the form of nodules in the internal organs, as scrofula or tubercle. I could point out at least three specimens in our museums, so described.

The true nature of the malady was discovered in cattle, in 1877, by Bollinger; and two years later, Ponfick of Breslau established the fact of its occurrence in man. I may briefly state that it belongs to the large group known to pathologists as the infective granulomata,[1] the infective element being a peculiar vegetable fungus, the growth and distribution of which are associated with tumours formed of granulation-tissue. The fungus gains access to the body by means of a lesion of some mucous membrane or of the skin. A primary tumour is thus established from which general dissemination may take place by means of the blood and lymphatic vessels, just as in cancer or tubercle.

I am able, in some measure, to illustrate the morbid anatomy of actinomycosis by means of a series[2] of preparations from the Museum of the Royal College of Surgeons (Nos. 2254 B, C, D, and 2274 B, C). This lower jaw of a heifer shows well the external form of the disease. It may be seen that there is a general expansion of the horizontal ramus such as might be due to the growth of a central tumour. In the next specimen of a lower jaw, a vertical section has been made to show its interior. The bone is expanded and infiltrated by a pale medulla-like substance which is punctated or dotted with numerous minute cavities. The growth infiltrates widely, and in some places has completely penetrated the jaw. The gum on the outer side of the teeth is thickened; and passing down through it into the substance of the bone are two sinuses marked by pieces of glass rod. These lead to the uppermost extension of the morbid growth, and it may have been through one of them that the fungus gained access to the interior of the bone. On pressing a section of the growth, worm-like masses of pultaceous material could be expressed from the small cavities above mentioned. This material, on examination under the microscope, was found to contain large numbers of actinomycetes,

[1] See *Ziegler's Pathological Anatomy*, by Dr. MacAlister, vol. i. art. 134.

[2] The specimens from cattle were presented by Mr. A. Lingard, and I described and showed them at the Pathological Society for him in 1886.

as the characteristic nodules of the fungus are called. In this case an enlargement of the lower jaw had been noticed for nine months before the animal was killed. No disease in any other part was found. Another specimen illustrates the disease in the upper jaw. The growth has filled the antrum, and forms a prominent projection on the face. In none of these specimens was there suppuration or ulceration.

Here are also two specimens of actinomycosis in the tongue of oxen. This organ becomes greatly enlarged and elongated, so that it may protrude several inches from the mouth. It is extremely hard and dense in texture, hence the affection is known as "wooden tongue." The changes in its substance are well shown in this tongue, which has been divided longitudinally. The section is studded with firm circumscribed nodules, varying in size from minute points to that of a pea; and often forming lines between the bundles of vertical muscular fibres. Each of these is composed of granulation-tissue surrounding a small mass of the fungus. The connective tissue of the tongue is much increased, especially along the upper border.

The characteristic appearances of the disease in internal organs are exceedingly well exhibited by this section of a human liver from the same museum. The cut surface shows several rounded deposits, the largest being two inches in diameter. They are yellowish-white in colour, and, owing to the presence of numerous apertures, have a honeycombed appearance. The liver and other viscera had undergone extensive lardaceous degeneration.

The patient, a lad, had previously suffered with symptoms referred to tuberculosis of the genito-urinary organs. There were scars as of tubercle in the ureters, and grey granulations (believed to be miliary tubercles) on the mucous membrane of the bladder. I made the post-mortem on this case in 1881, and supposed the disease to be tuberculosis. The microscopic appearances of the nodules in the liver and bladder confirmed me in this opinion, as in the sections of the former the actinomycetes fell out. On becoming acquainted with the naked-eye appearances of actinomycosis, I at once recognised the true nature of this case; and on cutting sections of the liver in celloidin demonstrated the actinomycetes, which had the same structure as in examples from cattle.

The actinomycetes themselves may be picked out or expressed from the growth. They appear also as golden yellow spheres, from the size of a grain of sand to that of a millet seed, floating in pus from abscesses.

A section of an actinomycotic tumour, examined with a low power, shows a number of rounded districts or areas. In the centre of each of these is an actinomyces surrounded by a zone of granulation-tissue, or in other words of leucocytes. If the section happens to pass transversely through the fungus, it is seen to consist of a central spherical homogeneous or finely granulated material, surrounded by a zone of delicate club-shaped

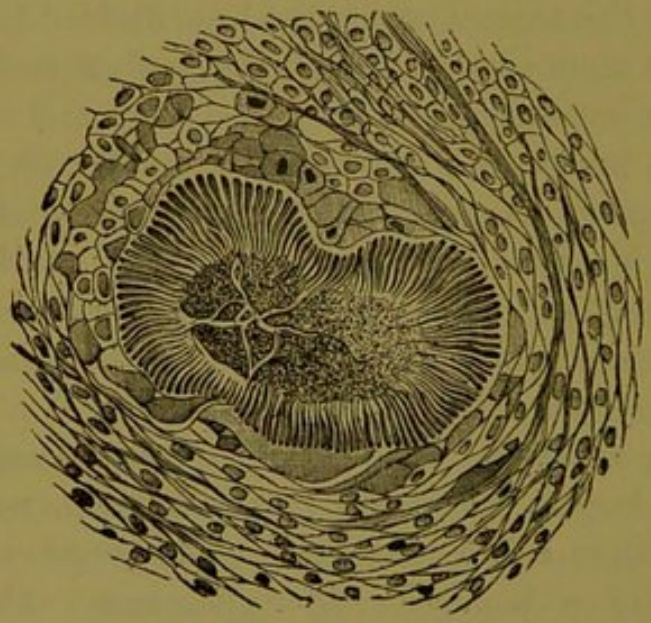

FIG. 1. (× 400.)

bodies which radiate from it. The appearance may be compared to a composite flower, such as the aster, the closely-applied club-shaped bodies representing the circumferential row of flowerets. The club-shaped bodies are enlarged and rounded at their outer ends, while their central ends become narrow and filamentous; and, in the accompanying drawing (Fig. 1), this may in some instances be traced into the central, apparently homogeneous, portion as a fine thread. The fungus appears to increase by the formation of nodular outgrowths from the central mass, leading to the production of a group with a mulberry-like outline, or even a radiated mass. A group may also be made up of a number of separate actinomycetes pressed together. Some

observers[1] have detected, by means of special staining agents, a network or tangle of fine filaments in the central, apparently homogeneous, part of the fungus, and extending outwards from this between the rays or club-shaped bodies in some instances into the surrounding tissues beyond the limit of the rays. The above are the usual appearances in oxen, and in many cases in man.

Dr. Theodore Acland has examined three specimens in man, which to the naked eye resemble actinomycosis, but in which the fungus was extremely different. In the early stage it took the form of rosettes composed of a number of radiating threads. The larger growths formed a ring of threads, with a hollow centre filled with degenerated cells and threads. These circles expanded like fairy rings, fused together, and formed larger areas. Whether this is one of the metamorphoses of the ray-fungus, an entirely different disease, or a contamination, cannot at present be determined in regard to these observations. The fact that Boström and Moosbrugger found filaments in the ordinary form of ray-fungus would lend some support to the first-mentioned conjecture. Moreover, the co-existence of the ordinary form of actinomycosis with spheres composed of leptothrix-like filaments, either in the affected organ or in some distant part, has been noted by some observers. Baumgarten, in a case of actinomycosis of the lung, found balls of filaments in the tonsils from which he thought the lung-disease was obtained. Roser observed spheres made up of a tangle of fine fibres, without any appearance of rays, in abscesses connected with actinomycosis of the neck. On the other hand, as opposed to this view, it is necessary to draw attention to the fact that the smallest actinomycetes are rayed, and have the same structure as the larger ones. This is well illustrated by the drawing, Fig. 2, showing two minute actinomycetes, each of them rayed on one side; they occupy opposite poles of a giant cell. It also suggests the possibility of the infective elements being carried to distant parts in leucocytes.

Clinically this disease in man presents itself under somewhat varying aspects. When attacking the maxillary region the first symptom is often severe pain localised in one or more teeth,

[1] An examination of Moosbrugger's figures suggests that the supposed filaments may be merely a differential staining of the ground substance between the rays.

which are frequently carious. A swelling soon appears about the lower, less commonly the upper, jaw, or near the angle of the jaw. After the lapse of weeks or months, the disease extends thence along the anterior border of the sterno-mastoid muscle to the clavicle, and ultimately culminates in a diffuse general enlargement of one side of the neck. It may also involve the face, and pass upwards over the temporal region. The swelling, at first circumscribed, becomes diffuse, soft, and fluctuating; but on opening the softened areas only a few drops of pus escape; and the tissues are found infiltrated by a soft spongy granulation-tissue. Crateriform openings appear on the skin leading into a system of intercommunicating fistulæ, which discharge a watery fluid. Nodules, not unlike softened lymph-glands, are sometimes observed in the integuments.[1] The discharges, as well as the granulation-tissue, contain the

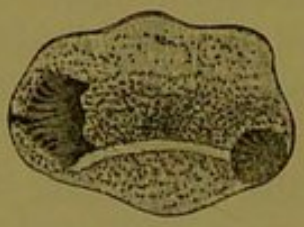

FIG. 2. (× 600.)

characteristic yellow grains. The progress of the malady is also marked by extreme chronicity, which, with the absence of acute local and general symptoms, distinguish it from ordinary inflammations. Rarely actinomycosis of the maxillary region takes the form of acute abscess.

In advanced cases of actinomycosis deep and devious abscesses are often formed, especially along the front of the spine. The abscess may be situated in the cervical region in disease of the neck and pharynx, or in the dorsal and lumbar region when the thoracic or abdominal viscera are affected. From these prævertebral abscesses sinuses track among the muscles of the back and open on the skin at various parts. The pus may find its way into the sheaths of the psoas muscles, giving rise to the usual appearances of psoas abscess, or an iliac abscess may develop

[1] A case of supposed actinomycosis was described in 1884 by Mr. Treves of Margate (see *Practitioner* xxxii. 287); but on investigation after the death of the patient (*Trans. Path. Soc.* vol. xxxv., 1884) the disease was determined to be alveolar sarcoma of the skin.

in connexion with disease of the vermiform appendix or pelvic organs. The vertebræ are usually superficially eroded and "worm-eaten," not extensively destroyed, and are roughened by osteophytes. One case is recorded in which the base of the skull was perforated. In actinomycosis of the lung and thorax pain in the side with pleurisy or pleuro-pneumonia are commonly the first symptoms. These soon disappear, and dulness over some part of a lung with evidences of general bronchial catarrh remain; a swelling may appear on the thoracic walls and discharge pus containing actinomycetes, or sinuses, connected with præ-vertebral abscess, form in the back. Disease of the liver is ushered in by pain in the epigastrium or merely a sense of fulness in the part. On examination the organ is found to be enlarged, and a distinct swelling may, in some instances, be observed on its surface. This becomes adherent to the integuments, which soften, and on opening the swelling a small quantity of pus and broken-down granulation-tissue are evacuated. Precisely these symptoms were present in a man aged about 55, whom I have had under observation for nearly two years. The man has several sinuses over the epigastrium which discharge watery fluid. Recently ascites and dropsy of the legs have appeared. The diagnosis remains uncertain, as I have been unable to find actinomycetes in the discharge. In other cases of actinomycosis of the liver pus makes its way through the diaphragm and points through the thoracic wall. Or again, beyond some enlargement of the organ with pain or discomfort, local symptoms may be absent.

The course of visceral actinomycosis is characterised by the same torpidity, being usually unattended with fever or severe functional disturbance of the affected organ. Temporary rises of temperature mark the presence of intercurrent attacks of inflammation of serous membranes and sometimes abscess-formation, but soon subside. There is gradually progressive emaciation and exhaustion, and death is often brought about by inflammation extending to the pleura, pericardium, or peritoneum, or by hydræmia and serous effusions, the sequences of lardaceous degeneration.

The duration of the disease in fatal cases, counting from the beginning of symptoms, varies from ten weeks to a year and a half or more, the average being about twelve months.

Secondary formations have been found in the liver, lung, kidney, spleen, intestines, brain, ovary, heart-muscle, and in the muscles and skin. In one of Ponfick's cases a growth had penetrated the internal jugular vein, and there was a large actinomycotic tumour projecting into the right auricle and ventricle.

The distribution of the disease in man may be gathered by the analysis of seventy-five cases (all those recorded up to 1886), by Moosbrugger. In twenty-nine the disease was in the neighbourhood of the lower jaw, in the mouth and neck ; in nine in the upper jaw and cheek ; in one case in the tongue, and in two involving the pharynx and œsophagus ; eleven in the intestines and abdominal viscera ; fourteen in the bronchial tubes or lung. In seven cases the seat of the disease could not be ascertained. The frequency of primary disease in or near the mouth and jaws may be gathered from the fact that in forty out of seventy-five cases it affected those parts. Up to the present time only four cases have been observed in the tongue in man, whereas lingual actinomycosis is not uncommon in cattle.

Experiments on animals, and other circumstances, such as the constant presence of actinomycetes and the nature of the new formation, place it beyond question that the ray-fungus is the *materies morbi*. The disease may be transmitted by inoculation from cattle to cattle. The experiments of Johne and Ponfick on cattle prove that the insertion of portions of the morbid growth in the subcutaneous and muscular tissues, and in the peritoneal cavity, are certainly followed by positive results. Small nodules show themselves in a month, and the disease assumes unmistakable dimensions in three or four months.

Typical growths appear in the lungs a few months after injection of the diseased tissue in a finely divided state into the circulation.

A rabbit was successfully inoculated by Israel in the peritoneal cavity with portions of an actinomycotic tumour from *man ;* but no marked development of the disease took place. Ponfick failed to inoculate either rabbits or dogs. In swine the same form of actinomycosis occurs as in man, and has a like distribution. Rounded nodules similar to actinomycosis were found by

Johne in the tonsils of twenty out of twenty-one healthy pigs examined.

Another disease closely resembling that under consideration was described by Virchow, and subsequently more fully by Hertwig and Dunker, in swine. It consists in the formation of minute nodules in the muscles. These lie between the muscle bundles. They are composed of a central portion made up of fine fibres and granules, and surrounded by club-shaped or elongated pyriform rays very like the ordinary variety of actinomycosis. Calcification, extending from the centre to the circumference, rapidly takes place. No zone of granulation-tissue is formed.

Israel and Boström claim to have cultivated actinomycetes in blood-serum. The cultivation, according to Israel, resembled the fungus as found in man and animals. Boström failed to reproduce the disease on inoculating animals with his cultivations.

The botanical position of the ray-fungus has not been, I believe, determined; it has been provisionally classed with the *Cladothrix* group of the *Bacteria*.[1]

Our information regarding the manner in which the fungus gains access to the bodies of men and animals is very limited. Man probably derives it from the same source as animals, and only rarely directly from them. It enters by an abrasion, wound, or other solution of continuity. Thus it has originated in the scar after removal of a cancer of the breast. The probability of carious teeth being the point of entrance is very strong. In a case of actinomycosis of the submaxillary region, Kappener detected ray-fungus clubs and leptothrix filaments in two carious teeth. Israel also found, after extraction, actinomycetes in the alveolus of a carious tooth from which the disease appeared very distinctly to have originated. Further, in a very large proportion of cases in which the mouth and adjoining parts were involved, caries of teeth or erosions of the gum and cheek co-existed. These parts may also be inoculated through slight wounds from articles of food; and grains, seeds, and pieces of straw (often chewed by rustics) have been suspected as the carriers. Particles of the fungus may be swallowed, and enter by some lesion of the intestine; or be introduced into the air passage by

[1] Crookshank, *Manual of Bacteriology*, p. 336 (1887).

inhalation of particles from the air or from a primary growth in the mouth.

It is worthy of remark that while over seventy cases have been recorded on the Continent, only seven had been published up to 1887 in England and America. This may be explained either by supposing that this disease often passes unrecognised in England and America; or that it is more common on the Continent. Should the latter surmise prove correct, the Teutonic fondness for sausages and uncooked ham may explain the diversity, especially from the fact that pork is affected as well as beef. When flesh is prepared in the usual way the morbid change is so evident that its transmission to man by diseased meat is improbable.

The direct inoculation of man from animals, as already mentioned, occurs rarely; for in the collection of seventy-five cases already mentioned, in only ten were the individuals engaged in occupations which brought them into contact with cattle—as farmers, peasants, and farm labourers; whilst in only two cases did the sufferers have directly to do with diseased cattle. In one of these, a case of actinomycosis of the tongue, the patient had opened and subsequently looked after a tumour of the jaw in a cow.

Prognosis.—In this respect almost the same rules may be applied to actinomycosis in man as in tumour-formations. When affecting cattle this disease may undergo spontaneous cure; but in man there is little probability of this result. Perhaps in some instances in which suppuration is unusually acute and abundant the fungus may be destroyed. Thus a case is recorded by Stelzner in which a cure took place after a simple incision into the tumour. And in two cases of Roser's the disease simulated acute abscess, and healing took place after incision, scraping of the walls of the abscess, and drainage. Further in more than one case of actinomycosis of the liver pigmented cicatrices have been found on the mucous membrane of the intestines; and scars were noticed in the ureters in the case observed by myself. But these lesions, although associated with it, are not necessarily attributable to actinomycosis.

It is evident that the chief indications in forming a prognosis

must be the seat of the disease, its duration, and the probability of metastasis having occurred. That operative measures are successful when undertaken for disease in a part admitting of complete removal, and of tolerably recent standing, is clearly shown by the result in nine cases treated in the Klinik at Kiel. In six of these cases the neighbourhood of the lower jaw, and in the remaining three the upper jaw and cheek, were affected. In seven healing occurred and the patients remained free from return for periods varying from four months to three years; one patient remained under treatment, and another, with extensive disease of the cheek and neck, died. Two other cases of primary actinomycosis of the lung, also terminated fatally. This, speaking from our present information, must be the necessary result of visceral actinomycosis.

Treatment.—It follows that operative treatment is confined to those cases in which, from its locality and extent, the swelling allows of complete extirpation. Recent and limited disease may, as already mentioned, be successfully dealt with by simple incision and scraping with the sharp spoon. When more extensive, the same indications hold good as in the case of tumours. The disease should be removed in its entirety, the incisions being preferably made through healthy tissues. But if too widespread for this, the morbid growth should be followed up and eradicated with the knife and sharp spoon until healthy structures are reached. This proceeding is liable to failure from the devious course taken by extensions of the disease. Local recurrences, indicated by increase of swelling and renewed formation of the peculiar granulation-tissue, may be dealt with in like manner; and cases have been brought to a successful issue after two or even three operations.

In cases beyond the reach of operative measures the injection of solution of perchloride of mercury has been recommended. It has further been proposed, when the liver is the seat of the disease, to lay it bare and scrape out the actinomycotic nodules. Apart from other objections the usually wide distribution of the nodules in this organ render such a proceeding as little likely to be successful as if undertaken for cancer.