PULMONARY STREPTOTRICHOSIS

WITH

RECORD OF A CASE TREATED WITH VACCINE.

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W. S. Malcolm, M.B.,
5 Nelson Street,
Dundee.
In most old works on Veterinary Surgery are to be found descriptions of cases in which the jaws of cattle are affected with a great enlargement. Under various names this disease was known at a very early date and in 1826 a careful description was given by Leblanc of the affection as involving the jaws of cattle.

In 1845 Langenbeck noticed the yellow actinomycotic granules in the pus from a case of caries of the spine in a human being. This observation was published by Israel\(^1\) in 1878.

In 1857 Lebert\(^2\) published the first case of the disease in man and as the organism was not identified the colonies alone were figured. Libert's case was one of pulmonary disease supposed to be cancerous and terminating in abscess of chest wall.

In 1868 Rivolta\(^3\) noticed the granules in the contents of the swollen jaw of an ox.

In 1870 Hahn described the same appearance in wooden tongue.

In 1877 Bollinger\(^4\) made it clear that the disease was due to the presence of a fungus and Harz\(^5\) named it, because of its appearance, the ray fungus or Actinomyces.
In 1878 Israel recognized the ray fungus as the cause of disease in man and a year later Ponfick identified it as being the same as that found in the ox.

The first case suspected in this country was under the care of W. Knight Treves of Margate, and though the organism was not demonstrated Israel accepted it as genuine and included it in his book.

The first case confirmed microscopically was admitted to St. Thomas Hospital in October 1884. By employing Granif's method Acland was enabled to show the thread form of the organism.

In 1885 the first case recognised in America was discovered by Murphy and in France by Nocard and Lucet in 1888.

In 1890 Bostroem published an account of the characteristics of some ray fungi isolated from cases of human and bovine actinomycosis which he regarded as belonging to the same species.

In 1891 Wolff and Israel published an account of a ray fungus isolated from a case of human actinomycosis which differed in a number of characteristics from that of Bostroem and evidently belonged to a different species.

In 1893 Stewart and Muir recorded Scotland's first case - that of Leith being reported in the following
year - and in 1900 Bennett\textsuperscript{12} followed suit for Ireland. Since then other distinct species have been cultivated from isolated cases of disease in the human subject where the lesions resembled more or less closely those of Actinomycosis. The organisms from such sources differ according to their microscopic characters, conditions of growth, staining reactions and so on. The organism of Wulff & Israel is perhaps the typical one and it was from cultures of it derived from several cases of human actinomycosis that the vaccine used in this case was prepared.

The ray fungus develops from a small round spore into cylindrical threads which branch and form a network. Each single thread with its branches represents one whole single organism. It occurs in pus in these forms under the microscope and as granules or colonies of the size of a small pin's head visible to the naked eye. When crushed between cover glass and slide each of these is of tallowy consistence and under the microscope is seen to be composed of a central felted mass of threads with entangled spores with radiating clubs at the periphery. The colonies are opaque or translucent and their colour has been described as grey, white, yellow, greenish yellow, golden, sulphur, greenish.
most black and as being fish egg like or like jelly. The ray formation is not constant or necessary to form a diagnosis and the generic term streptothrix is perhaps preferable to the specific term ray fungus. In only a small percentage of cases has the organism been cultivated and a difficulty is thus created of determining particular species.

When not living as parasites on man and other animals the streptotrichetes are essentially either saprophytes living in the soil or parasites of higher forms of vegetable life. Acidfast species occur as natural parasites of grasses and other forms of vegetable life more particularly of the spikelets of certain grasses e.g. Phleum pratense L and Hordeum murinum L (Timothy grass and Wild Barley)

Harbitz and Grondahl obtained greatly varying results in an investigation to determine typical growth of the pathogenic fungus. Thus 27 strains were got from 20 cases by making cultures at different times from the same lesion and by inoculating media from pus, urine or sputum from the same patient. They conclude that the exciting cause of the disease in man in the large majority of cases is an anaerobic fungus showing no tendency to adopt an aerobic habitat.
(McDonald's\textsuperscript{15} streptothrix was aërobic; Wynn\textsuperscript{16} was both anaërobic and aërobic. So was Leith\textsuperscript{13}.)

Pure culture of 3 strains from air, of 2 from straw, of 3 from barley and oats and of 3 from manure were all aërobic and anegative result was got when injected subcutaneously, intrapleurally and intraperitoneally into rabbits and guinea pigs (Hagen\textsuperscript{14}).

It is possible that the fungus lives as a saprophyte on plants to enter man by chance and then to go on living a saprophytic existence until a focus of less resistance is offered when it at once becomes pathogenic.

Different species of organisms produce different results. The actino-bacillus of Lignières and Spitz, very common in South America, gives rise to a type of Actinomycosis of cattle affecting generally the tongue and neck in which no grains are found\textsuperscript{27} and it affects lymph glands more frequently than does ordinary Actinomycosis\textsuperscript{28}. The difference in species may account for the divergence of view noted in records of this disease as regards suppuration or nonsuppuration in affected glands e.g. Acland\textsuperscript{29} says the lymphatics shows no tendency to become affected and Lord\textsuperscript{30} that it penetrates the lymphatic system only in rare instances and extension from the tonsils by way of lymph channels is improbable.
Bevan on the other hand records a case giving evidence of lymphatic involvement where the fungus had been transmitted through the lymphatic chain from the diseased area and become arrested in a lymphatic gland. This was confirmed microscopically.

"A secondary abscess occurred in an auxiliary by direct extension through the lymphatics. This abscess was particularly rich in the characteristic granulose bodies."

From the habitat already mentioned one can readily assume a dispersion of fungus airwise to account for the incidence of the disease in those patients in whom one is unable to trace a more direct infection, and the high vitality of the fungus supports the view. Clivetien quotes an investigation where the organism resisted boiling water for 14 minutes and a dry heat of 140 - 1450 F. for 4 - 5 hours. One in twenty phenol had little effect; but 1. 1000 hydrarg perchlor killed it in 5 minutes.

"We cannot help inhaling the dust of a threshing machine and are exposed to the inroads of this organism in a thousand ways impossible to guard against. (Godlee)

Though there have been failures in the experimental inoculation of laboratory animals with the mycelium of nature accidental inoculation has been lamentably
successful.

Amongst cattle the tongue and **udder** are the parts most vulnerable and in a report[^31] on 85,445 ox tongues imported from the Argentine Republic into the City and Port of London we find 5.7% rejected on account of the presence of Actinomyosisis. Furthermore these were all tongues which had passed scrutiny before Export.

Cattle living on salt marshes, which are periodically covered by the sea, are more susceptible, the jaw being injured by sand shells.

In an investigation into the occurrence of Actinomyosisis in cows' udders Patterson[^32] found five affected out of 50 examined and in none of these was the lesion observed in any other part of the carcase. From this he judges the infection took place by the teat from bedding.

Leith was the first to describe this mode of infection.

In man the parts most accessible to external agencies are the integument and mucous linings with the ducts of glands leading thereon.

A pretty and convincing instance of skin inoculation is recorded by Schwartz[^21] whose patient was distinctly aware of a prick on his cheek while sleeping on grass
The number of such cases can be prolonged indefinitely. Lord\textsuperscript{35} found that organisms resembling actinomycetes in morphological and staining reactions can be demonstrated in the contents of carious teeth and in the tonsillar crypts of patients without actinomycosis. This prepares us for the inoculation of an abrasion of the cheek by a carious tooth\textsuperscript{36} by the clamp of an artificial denture\textsuperscript{37} by a dental instrument\textsuperscript{38}, by the incision of a gumboil, by the extraction of a tooth\textsuperscript{39} and subsequent inoculation from infected grain\textsuperscript{40}.

Further Lord found that the intraperitoneal inoculation of guinea pigs with the contents of carious teeth and the crypts of the tonsils gives rise to omental tumours histologically identical with actinomycotic tissue and containing typical club-bearing actinomyces granules. Similarly with scrapings from sound teeth.

Söderlund\textsuperscript{41} investigated 6 cases in which actinomycosis was limited to the salivary glands and in four of them particles of oats or barley were demonstrated in the centre of the tumour.

Again Cuff\textsuperscript{42} found the husk of an ear of wheat in the centre of an abdominal tumour which was actinomycotic. There was a connection with the ascending colon and the foreign body had been swallowed by the patient who picked
his teeth with straw.

Bertha records three indubitable cases of inoculation of the
1. hand - cutting oats with a sickle.
2. hand - threshing corn

Müller of the hand from a splinter of wood
Foulerton of the peritoneum at an operation for an annulet malignant stricture of the oesophagus.

The source of this type of case is inexhaustible. A few are given as instances of direct inoculation where the wound and introduction of fungus were simultaneous in all likelihood.

One realises the special risks of infection run by those whose employment brings them, or whose inclinations lead them to spend their lives in an environment of straws, grains or cattle. Cases 43 to 54 are additional examples. In 100 mixed cases Erving found that 36 had much to do with both live stock and grain.

The evident fact that a breach of the epithelial barrier facilitates the entrance of the organism into the tissues explains why the disease is more common in the appendix and rectum. According to statistics there are inflammatory changes and small ulcers, etc., in the
appendix in 75% of healthy adults. Again in this region the process of movement is retarded, faecal mass is becoming more solid and remains longer in the area. Solid particles themselves may cause abrasions. For the same reason the rectum is more likely to show superficial ulceration. The reason given for gastric ulcer not being oftener affected is that the acid of the stomach prevents the growth of the organism. Inoculation of the typhoid ulcer has been reported by Lange58 and by Maass59.

It is futile, however, to attempt to trace every case of actinomycosis to a grain, a straw or to an animal affected with lumpy jaw61. Foulerton60 has seen five cases caused by passing infected cotton through the mouth. There is a large class of cases where no history exists of a breach of skin or mucous membrane to facilitate an invasion by the fungus; but a catarrh already existing or induced by actinomyces themselves can lead to such a denudation of cells that an easy entrance to the body is obtained by fungus airborne or otherwise. Spread occurs by direct continuity or by bloodstream. Godlee's sixth case89 illustrates well the widespread diffusion of the disease by blood stream and further it is interesting to note that the lung was affected by
direct extension and had none of the characteristic embolic processes in it.

Fütterer's\textsuperscript{97} case furnishes a beautiful example, two actinomycotic nodules being found post mortem at the base of the tricuspid valve of the heart. Dean\textsuperscript{98} has recorded a case of pyaemio actinomycosis. McFadden, Delepine, Muir, Leith and others have seen cocci and bits of filaments within the protoplasm of leucocytes and Bridge\textsuperscript{55} has seen the same in the arterioles themselves.

Early in the history of the disease Israel\textsuperscript{57} pointed out that the point of maximum intensity of lesion might be quite remote from the point of entrance of the organism, and that from the point of entry one could only sometimes trace a thickened track leading to the diseased area. For example in the report\textsuperscript{31} already alluded to, actinomycosis was found involving the glands attached to the roots of ox tongues without trace of involvement of tongue itself and without the existence of disease in any other part.

Again in Godlee's 5th case\textsuperscript{89} the symptoms were those of an empyema in region of 8th R. rib mid-salvary. The autopsy revealed a large mass of typical actinomycosis 3 inches in diameter in the right lobe of
the liver, the oldest part of which was below and very closely adherent to hepatic flexure of colon, which however showed no sign of ulceration - another definite instance of closed door of entry.

The proof of direct contagion is not very convincing. McKinty says that at the Royal Victoria Hospital one of the earliest cases occurred in a nurse who had been attending a case of actinomycosis. Leith denies the possibility.

Von Baracz says a woman acquired actinomycosis of the face from a man similarly afflicted.

Ochsner records two cases bearing on this. A farmer developed alveolar actinomycosis and for six months previous to his illness he had driven a horse supposed to have lumpy jaw. The other patient was a cattle dealer who developed the disease in his upper jaw. He had been buying and selling cattle for 40 years. Many of these had lumpy jaw and he personally had treated them by incision and scraping.

It is not believed that the disease is communicated from one person to another or from animals to man as a rule, but in a discussion before the Chicago Surgical Society Dr. Carl Wagner related that one of the pupils of Prof. Sacchi, Surgeon Doges Hospital, Genoa
having opened an actinomycotic abscess touched his nose before he had disinfected his hands. His nose became infected and he succumbed in a short time to generalised actinomycosis.

Experimentally twenty-one healthy cattle were kept in close quarters with others suffering from Actinomycosis without in any case showing signs of infection. Therefore transmission direct from one individual to another is matter of considerable difficulty. Experimental transmission from one animal to another, and from man to animals, both directly and after artificial cultivation has been successfully accomplished.

There is no positive evidence of infection of human beings from eating the meat of infected cattle.

It has been proved by Johne and others that cattle fed on virulent cultures will not acquire the disease.

The appearance of an organ or tissue affected with actinomycosis varies according to the part diseased, according to its acuteness or chronicity and according to there being more or less mixed infection.

The presence of the fungus sets up irritation leading to proliferation of round cells about the focus and resulting in a nodule. The central cells nearest the infection degenerate, become fatty and greater or less
liquefaction results. The cells towards the periphery of the nodule become organised into new connective tissue. The ends of the streptothrix grow out in various directions and anliquefaction, and condensation become repeated. The result is a spongy tissue composed of little cavities communicating with one another and due to liquefaction of cells and bounded by fibrous tissue due to a less degree of virulence at a further distance from the organism. An uncomplicated infection with feeble virulence in tissues having a high degree of resistance will be followed by but little destruction.

With regard to the clinical course of the disease we do not always see the simple case of cause and effect which occurs in manifest accidental inoculation. Beginning usually insidiously, especially in its pulmonary and abdominal form, it progresses steadily, and to use Leith's words " May have produced very grave pathological lesions before it gives rise to any definite symptoms and may indeed run its entire course and cause death without affording the physician sufficient evidence of its existence to enable him to give more than a conjectural diagnosis.

Male aged 40 years, jute merchant complained of pain and swelling in precordial region.
Previous illnesses. 1 Mastoid disease 12 years ago.

2 Urinary calculi at intervals, have been passed. One required lithotritry.

Present illness. Roughly for 12 months patient's health had been under par. He felt languid, was disinclined for work or play. A cough started and was accompanied by pain about the left mammary region. The pain was so great that he supported the part when coughing. About 1st Feb. 1910 he observed a swelling where the pain was felt between the left nipple and the sternal margin. This increased in size and tenderness and compelled medical advice.

March 6/1910. Diffuse swelling between lower four inches of sternum and the anterior axillary line. Skin unchanged in colour. Percussion absolutely dull and the parts so excessively tender that examination was difficult. Neither cough nor spit were prominent. Temperature never exceeded 100°F. Pain very great. A consultant diagnosed a sarcoma of lung; but later, deep fluctuation was suspected. Under chloroform an incision liberated pus with sulphur yellow granules. Counterincised and drained Diagnosis of actinomycosis confirmed microscopically. Incisions joined and prolonged to length of 6 inches, a flap raised and soft
parts curetted and ribs laid bare. Bleeding excessive. Lotion of 2% Carbolic used and parts swabbed with a watery solution of iodine and iodide of potash gr 30 given daily. Many pockets of disease had from time to time to be cleared out. Notice was now taken of the cough and the sputum - always scanty - was found to contain the mycelium and was haemorrhagic on several occasions. Temperature for a time ranged between 100°F and 102°F, seldom reaching the latter figure. General health improved by a visit to the country; local condition unsatisfactory and towards the end of August 1910 under chloroform 3 or 4 inches of the internally eroded 3rd to 6th ribs were resected laying bare the pericardial sac, the interna surfaces of sternum, and adjacent ribs were curetted and mediastinal tissue removed. A good recovery was made and potassium iodide continued, the dose sometimes reaching gr180 daily. At the end of two years one found periodic pain, swelling and a scanty discharge of pus, which had gone on more or less since the operation. Patient's blood pressure was only 95, the iodide was omitted and through Sir Almroth Wright a vaccine was obtained.

This vaccine is a stock one prepared from pure
cultures of human actinomycosis. A culture is taken in glucose agar tubes by inoculating with granules crushed in normal saline, and grown anaerobically. The growth is removed from the agar and thoroughly shaken to break up the filaments into fragments, which then have somewhat the appearance and size of tubercle bacilli. It is heated for an hour at 60°C to sterilize and standardized by enumeration of its component units. This is the actino-fragment content of the vaccine.

Treatment was started in August, 1913 by weekly subcutaneous injections of 2½ million actino-fragments. The dose was gradually pushed up to 10 million with a like interval between the injections; but this dose proved much too large. The temperature was no index; but the patient's sensations and a local reaction were. The patient felt thoroughly out of sorts and depressed when overdosed, and if one neglected this indication for two weeks, there were two small conical tumours which rose out from the pericardium, and receded only when the dose was lessened sufficiently. This was noticed twice, and ultimately it was found that a dose of 4 million had no bad effects and under it discharge has now ceased for some time and the irregularities have
gradually disappeared from the pericardium. Between 60 and 70 injections have been given and the improvement was very pronounced from the start.

Fortunately one cannot confirm or refute one's conceptions of this case by post mortem findings; but a study of recorded infections of lung by streptothrices enables one to assume that the course of infection was by inhalation with uneventful passage through the bronchial mucosa into lung tissue, hence by continuity towards the periphery affecting the overlying pleura and reaching the mediastinal tissue and finally after passing the bones, becoming intercostal and subcutaneous.

This patient was a male. Season incidence occurs in proportion of 65 male to 35 female. Males are more liable to chew straw and be brought into contact with infection. His age 40 is rather over the period of greatest incidence as 60% occur between the ages of 15 and 35 years. His occupation didn't lend itself to infection especially, but his holidays were always spent in farm houses in the country.

Seasonal incidence of pulmonary actinomycosis is said by McKinty to occur late in Spring with symptoms dating from variable time anterior to that. Our patient's symptoms were at their maximum early in March.
The Incubation as in other pulmonary cases was longer than in jaw or superficial lesions and probably lasted for months.

The case cited is one type where the brunt of the attack has fallen on the chest wall. Other cases have run their course to recovery or death without involvement of the parietes.

In the bronchial form the germ becomes established on the surface of the bronchial mucous membrane resulting in a chronic catarrh of the bronchi with actinomyces in the sputum. This purulent bronchitis appears to be the earliest sign of actinomycosis in the lung and is rarely recognised in this stage during life. In Canali's case after some intercurrent feverishness cough and spit alone were present, the latter becoming foetid. No additional symptoms occurred for several years until she finally passed from observation with no damage to health. Henry recognised a case, and his patient, an old woman, died shortly afterwards of pneumonia followed by empyema. The filaments were confined to the bronchial secretion. Leith in his case of actinomycosis of the hepatic flexure of the colon found post mortem an independent infection of the bronchi by inhalation.
Extension to the adjacent alveoli leading to catarrhal exudation with desquamation of epithelium allows the entrance of the parasite to the connective tissue framework of the lung itself and constitutes the early stage of pulmonary involvement.

Wynn\(^\text{16}\) thought that in his case the spread into the alveoli was heralded by a rise of temperature. Failing that one would expect to diagnose the spread by a change of physical sign, and in the sputum by a change in the proportions of the respective epithelial linings of tubes and alveoli. The development in the lung is insidious. There is peribronchial infiltration of parenchyma which by softening and confluence produces abscess cavities. Parts around and between are in reactive connective tissue proliferation leading to a scarred thickening of lung parenchyma with shrinkage and recession of chest over part affected. The shrinkage of lung may produce bronchietatic cavities recognisable by their lining.

The signs in the lung vary according to the involvement. There may be very few\(^5\) (case 9) and according to Israel\(^\text{17}\) in lung actinomycosis limited in extent the whole process can take place without the patient feeling ill, without his capacity for work becoming markedly injured, without harming appetite, digestion or sleep. There
is always a bronchial catarrh which is usually overlooked, usually consolidation, sometimes cavitation or effusion into pleural cavity or empyema or fibrosis.

The case No. 90, claims to be the first example of Actinomycosis of lung in the human subject that has been recognised during life in this country.

During the initial stage there is a feeling of being poorly, of being unaccountably weak and breathless. There may be months of lethargy, not alleviated by tonics or change of air. Cough is usually the first symptom of complaint and lasts throughout the illness, becoming more and more severe. There may be no spit at all or it may be scanty. There may be "a little daily" or it may be profuse e.g. coughed up 2 pints of offensive matter. Two types are described.

1. Clairy, mucilaginous, often quite watery.
2. Purulent, more or less bloody, more or less foetid.

The second type may have a characteristic homogeneous pinkish colour or be deeply blood-stained. It generally has a distinctly bad odour.

Fever is present in nearly all cases. Usually it is a first symptom, but sometimes starts later with
extension of the disease. There may be "no temperature", "Up 3/4°", "little or no fever". An evening rise is not common unless the disease is accompanied by suppurative changes, which are later. The disease may go on for a long time without a rise. Later there is an evening rise with a fall next morning not going down to normal. "Fever subsided with the discharge of masses of bloody pus with a terrible odour". The temperature is dependent on the extent and nature of the lesion, and later by the development of the pus forming centres.

Pain occurs in most cases in the side affected and may be constant and severe.

Emaciation is gradual and often extreme. With an early diagnosis there may be only a few lbs. lost or no diminution in weight.

Invasion may be succeeded by a markedly slow chronic and insidious process to which no attention may be drawn until in a metastatic area has been discovered in a distant part, the causal organism found and the oldest pathological lesion discovered and proved by its extensive growth of interstitial tissue.

Israel has stated that in lung actinomycosis haemoptysis of severe amount is not on record. Bridge's fifteenth case died of haemoptysis and on repeated examination
no T. B. were found, only actinomyces. Further, the onset may be an attack of haemoptysis from an area of deep-seated dulness in an upper lobe. All degrees of haemorrhage have been described. The sputum has been "tinged", "at first bloody", pinkish mucopus", "later slightly pulmonary haemorrhage occurred" and "Blood flecked for weeks".

In his remarks on differential diagnosis Israel regarded the basal seat of actinomycosis one of the main criteria in distinguishing that disease from tuberculosis.

Several of Bridge's cases were apical, namely 9, 14 & 16. Knox's first case had a sinus in the back leading to the apex. Martin's first case was apical in origin and so on.

Godlee's fourth case combines these two features in having slight haemoptysis and apical signs.

The course taken by the disease is towards more and more consolidation, dulness, reduced motion, bronchial breathing, rales and finally cavitation. Case nine with a cough for several months had "barely slight bronchial breathing at the right apex".

One case had all the signs of apical phthisis, but T. B. were absent and actinomyces were not found till
4 months later. Again there was cough, spit, T.B. present and 1° of fever. After several years fever reached 102°, marked consolidation, actinomyces present. No T.B.

Thus the physical signs are similar and in both actinomycosis and tuberculosis of lung there may be cough, scanty spit, sometimes night sweats, pallor, sometimes shortness of breath, sometimes bloody spit, as well as loss of weight. Further T.B. and actinomyces may be present simultaneously in the spit (Case 17). In this case the T. B. disappeared under administration of tuberculin but the streptothrix persisted.

The disease has a tendency to involve adjacent parts but it may be limited throughout to pulmonary tissue and end there in death or recovery. Thus Bridge's eighth case which ended in death lasted for 3 years without involving chest wall.

Post mortem the bronchi may shew little evidence of epithelial lining, and may have their lumina filled with small round cells in various stages of degeneration. The walls may be infiltrated by pus which may be traced to various distances into the surrounding tissue, and be found filling the alveoli themselves. Conditions may be manifested in the lung...
of both acute and advanced chronic inflammation. The former is illustrated by numerous abscesses and tracts of suppuration in various portions of lung tissue, the latter by advanced interstitial pneumonia, the alveolar arrangement of lung tissue being scarcely discernible. In those areas where the alveoli have retained their outline, lumma may be filled with small round cells and their walls be greatly thickened. Thickened arteries may also be seen.

Unless the grains or threads of actinomycosis be found in the expectoration or until the growth invades the chest wall the diagnosis is difficult. When the foci are small and the lesion centrally placed no physical signs may be available and diagnosis is only possible in presence of a specific spit.

It is rare for a case to show spontaneous arrest and apparent cure without active treatment. Grant records such an one.

Another most interesting case is given in Entenso as it illustrates symptoms met with repeatedly in recorded cases. Boy, 16 years, wasted, dry cough, diarrhoea, no spit, peculiar odour breath, signs consolidation left lower lobe, coughed up large quantities offensive pus, odour as breath. Signs of dry cavity later. Put on
weight, cured spontaneously. Twelve months later, hard lump, attached to rim pelvis. Rapid loss of weight, intra-peritoneal abscesses, faecal fistula, bed sores, ultimately tissues again victorious and spontaneous cure.

Hichens's case coughed up 4 lung stones - recovered. Knox one case cured under iodide.

Hudson & Flexner's case of skin actinomycosis is of interest from the evidence given of infection of lung by airborne fungus.

In lung infection the parasite progresses by continuity of tissue until it has reached the pleural surface of lung. The two surfaces usually adhere, at least in part. The parasite grows across the adhesion to the chest wall, becoming intercostal and later subcutaneous.

One of Bridge's cases had cough and pain for months, and though there was no rise of temperature and only a trifling spit with specific content three or four quarts of bloody fluid were aspirated at one operation, and post mortem there were no adhesions and the lung was compressed into the size of a large human fist. Another post mortem showed a large mass of soft material occupying the pleural cavity. It was pulvaceous and canary coloured, much resembling coarse, badly made mortar. In this case the fungus flourished between the layers of
the pleura.

In cases where there is obliteration of the pleural cavity, as in Israel's⁶, there is an insidious onset in the lung, and a spread to the chest wall without pleuritic symptoms; but usually the disease manifests itself with the onset of acute feverish chest disease usually resembling pleurisy and exhibiting frequently a combination of adhesive and exudative pleurisy where the non-obliterated part of the pleural cavity becomes filled with effusion. Many a patient mistakenly dates the start of his illness from this acute pleurisy occurring in the course of a chronic process in the lung, which had escaped recognition. At this stage, therefore, Israel exhorts us to recognise whether the pleurisy is a primary one or a secondary, as shown by signs of recession, and he himself⁵⁷ was lead to a diagnosis of his 19th case by careful comparison of the volume of the sides of the chest and by a differential diagnosis between actinomycosis and tuberculosis. After his illness had gone on five months one patient had painful and difficult breathing, dyspnoea on exertion, foetid breath, no cough, no expectoration, but signs of slight effusion left base. The first aspiration obtained 27 ounces of turbid, straw coloured fluid. Two weeks later
13\frac{1}{2} ounces of thick, stringy, turbid reddish fluid were got; No T.B. Three months later a third aspiration was unsuccessful. Two weeks later 1\frac{1}{2} inches of 7th rib resected and pleura incised, releasing 3 ounces of offensive pus. Exploration with finger shewed adhesions. Six weeks later 7th rib removed, no cavity found but finger passed into a soft pliable tissue that bleed freely. The diagnosis was only made six weeks later still, from granules in the pus. Godlee says that if "the amount of pus is less than was expected and the finger passes into an indefinite soft mass, which bleeds with great freedom and breaks down easily before the finger in all directions - these are almost unmistakeable when they have been felt two or three times".

On evacuating what is assumed to be an empyema one may enter where the pleural layers are adherent and go into a cavity of lung which may communicate directly with a bronchus.

Extension to the chest wall may occur after one year of lung disease and during an eight-day fever without an exudative pleurisy - Israel's twentieth case - or again the illness may start with general pains, and in two months there may be a rise in
temperature with heats and sweats and intermittent cough and in 4 months the swelling may appear with other metastatic abscesses. - Israel's case 22.

Instead of extension to chest wall metastases may occur. A lesion in the R. lung was proved definitely post mortem to be the oldest with subsequent general infection of the rest of lungs and lesions in brain, kidney, heart and muscle.

As a result of the specific infection of neighbouring parts from direct continuity the diseased part of the lung becomes blended with its surroundings, and actinomycotic swelling may appear anywhere on the thoracic wall, more usually laterally and behind than in front. Not rarely it spreads to the precordia (our case) through the anterior mediastinum or into the abdominal cavity, behind, through or in front of the diaphragm.

Israel said long ago that the first consultation with a doctor may take place only when the tumour has appeared in the chest wall. This is what happened in our case, and what has happened in others. In fact, sometimes advice has not been sought until after rupture has occurred and a chronic sinus or sinuses remain defying ordinary antiseptic treatment. This all emphasizes what has already been said about the treacherous
unnounced start and advance of the primary visceral disease, which has in cases reached this stage with symptoms only of languor and of pain in addition when the pleura has been affected. The point of this is that a class of case has been mistakenly described as of primary skin affection with secondary involvement of internal organs. Such, of course, is possible; but in undoubted cases of skin inoculation a history of such is not difficult to find, and when a post mortem examination has been made the source of the infection is traced to old foci in the being, which prove their seniority in the amount and density of their fibrous tissue and in other signs of chronic change.

Besides, a tumour starting from it cutaneously and subcutaneously is likely to arrest early attention to its presence before it has started to grow inwards - a course which it doesn't usually follow. Cases 87 & 88 are instances.

On the other hand there may be a history of an illness extending backwards for 6 months, including a pneumonia or a pleurisy with apparent recovery. Then there is a settled pain with perhaps effusion, when over pleura, which may become absorbed while the actinomycotic swelling is increasing. (Israel's 19th case) or signs of pericarditis may occur as friction or effusion.
Sometimes there are practically no other symptoms; at other times dyspnoea may be present with severe cough, profuse foetid expectoration, with fever and night sweats, pallor and emaciation. As the involvement becomes intercostal physical heart and lung sounds are obscured and physical signs may be uncertain on account of state of skin. While in the lung, the reactive connective tissue, proliferation limits rapid spread. Once outside the lung the spread is much faster and the affected part bulges. Patient stoops to that side, the spine being curved with concavity to that side. An instance of extensive invasion of subcutaneous tissue is given by Foulerton where from an intercostal space in front the lesion spread to the umbilicus and upwards and backwards over the shoulders and then down to the level of the lower angle of the left scapula. "The skin itself is infected only in slight degree except that it is punctuated here and there by small ulcers, which mark the sites of discharge of small abscesses which form in the subcutaneous tissue. The dusky appearance is due to subcutaneous changes."

The swelling becomes prominent. Knox reports one as being soft, nonfluctuating, varying in size from time to time. It didn't break down and ultimately
disappeared. Other cases are recorded than our own where at this stage though cough is present there is no spit. Temperature may become more hectic, flesh lost more quickly, swelling more prominent, and the tumour more resistant in certain parts, softer in others due to abscesses formed within the infiltrated zone which communicate with each other through subcutaneous pus-filled openings. Its limits become less well defined, and it is finally transformed into a painful growth. After rupture or incision and emptying of purulent contents one finds a highly perforated tissue, which breaks down on light pressure with copious bleeding. In the bottom of the ruptured or opened abscess may be discovered one or more fine openings through which the sound penetrates to such an extent as to raise suspicion of intrathoracic origin for the suppuration. The pus itself may be thick and tenacious and appear like pale anchovy sauce or may be yellowish green or a thin clear syrupy fluid containing occasional or innumerable bodies varying in size from a pin point to large pin head, of a pearly grey to yellowish white colour. These characteristic bodies if present settle the diagnosis. Apart from them astreptothrix may be obtained in pure culture and without physical signs of disease of lung further exploration showed
asinus leading into a small cavity in the underlying lung. Occasionally haemoptysis occurs after these explorations and very free local haemorrhage, and though cough may be present spit may not yet be. Too often has the investigation of the sputum, when scanty in amount, been overlooked, and only examined after the presence of the fungus has been demonstrated in pus obtained through the thoracic wall. Often the cough seems to develop only after a condition of abscesses on chest wall exists, but with chest retraction showing a previous insidious course. On incising an abscess the cavity opened may communicate freely with a bronchus (case three) and medicaments applied externally may manifest themselves in the spit. The wounds may be all languid with purplish edges, pale and large granulations and have dirty yellow granules among the thickest pus which may adhere. The swelling may rupture 10 weeks after being first noticed, and may be noticed 49 days after a pleuro-pneumonic onset (Israel) or 42 days after a broncho-pneumonia (Hodenpyc).

The post mortem report that follows is interesting taken along with our own case. "Besides extensive changes in lungs, the mediastinal tissue as dense and purulent and penetrated by numerous sinuses running in all directions and traced to the lung apices. The whole of the
posterior surface of the manubrium and corpus sterni as well as the sternal ends of the first 3 pairs of ribs was markedly eroded and had osteophytic deposits with thickened and purulently infiltrated periosteum" &c.

Also these instances of pericardial affection.

Pericarditis - sero fibrinous Weigert\textsuperscript{99}.

Fistula leafing through the obliterated pericardical sac to the heart &c. Konig and Israel\textsuperscript{100}.

Right and left lung adherent to the pericardium, which shows fresh pericarditis and a focus on the left ventricle - Ponfick\textsuperscript{7} S31, and finally in Israel's case\textsuperscript{25} under where the lobe of the R lung was adherent to the pericardium and permeated by abscesses.

Diagnosis. The discovery of the fungus in one of its many forms or the evidence of a serum reacting are the only positive evidences of the disease.

The serum can only be used in differentiating mycotic diseases from those of bacterial origin or in diagnosing a mycosis belonging to a group which includes actinomycosis. The group is a small one and the members of it can be excluded otherwise\textsuperscript{101}.

The fungus is pleomorphic and variable in size according to Foulerton\textsuperscript{77}; it occurs in three forms, the first two being recognisable positively
1. the classic grain or tuft.
2. mycelium in earlier stages of fragmentation when it is breaking up into rod forms.
3. When fragmentation is complete and when sporulation has occurred the stained film shows then only irregular bacillary forms and spherical spores, both staining deeply with Gram's method, the spores resembling pus cocci. Failure to obtain growth from these spores raises suspicion that the spherical forms do not represent cocci since none of the known gram-staining pathogenic cocci are difficult of growth on artificial media.

An early and reliable diagnosis is possible by the two methods of gram stain and bouillon culture, but we are not in a position to determine the earliest time during the course of the disease when we may reasonably expect to find the germ in the sputum of pulmonary streptothricosis.

In the case of the abscesses making their way to the chest surface, aspiration may withdraw specific material especially if tried at different depths. Exploration with the finger after incision may discover "the indefinite spongy walls easily breaking down before the finger in all directions and bleeding very freely."
The Pulmonary form of streptothricosis has the clinical symptoms and signs of chronic phthisis. In many cases an exact diagnosis on clinical grounds is impossible but with
a. Pleural effusion with retraction of some parts of the thorax due to fibrous changes in the lungs.
b. Swelling of the wall of the thorax from perforation of an intercostal space, with shrinking of lung causing retraction of chest walls.
c. Failure to find typical T.B.

One ought to look for positive signs of streptothricosis.

Prognosis. Hodenpyl's collected pulmonary cases all died 70.

Foulerton's case mortality was 85. 90%.

Erving 76 in 20 cases had, recovered 10%, improved 10%, not improved 5%, died 75%.

Where the entire focus cannot be safely subjected to surgical treatment the prognosis is grave, but not hopeless, e.g. of 14 cases subjected to surgical treatment 79 the only 2 recoveries had radical operations with resection of 4 or 5 ribs and cauterisation of the disease cavity of the lung. All those died who were simply incised and drained. Prognosis is influenced by the
greater resisting powers of some individuals. There are many spontaneous recoveries, as well as recoveries under treatment. Early diagnosis and thorough medication are important along with surgical measures when applicable.

Treatment. The keen struggle between the organism and the cell life it provokes, to which the morbid appearances bear witness, points to the wisdom of trusting in treatment largely to the maintenance of the vital powers of the unfortunate host whilst endeavouring to impair that of the parasite.

The remedial measures which were employed in this case are alone considered and they are named in the order of their use.

1. Surgical measures and iodine locally.
3. A stock vaccine.

1. In our case, as in a large proportion of cases treated only surgically, repeated operations were necessary. The disease exhibited great stubbornness and recurred invariably after incision and drainage, after incision and scraping and after a very radical operation which was believed to be a complete excision of all affected tissues. Guided when necessary by X rays
surgery is indispensable. The employment of surgical measures enabled the use of a solution of iodine to the exposed, affected tissues; but in advanced cases where the disease has come to the surface—after long wandering, it is a matter of the utmost difficulty to make the application to deep-lying pockets and sinuous channels. Cataphorësis was not employed, but doubtless it has its uses in such circumstances as well as injections into the tissues surrounding the focus.

2. The exhibition of potassium iodide is now of long standing. It seems to have no specific action on the ray fungus as 1% doesn't kill in culture (Nocard). It must be given for months and in large doses. Coterill¹⁰² found recurrence from incomplete dosage. Others have found the disease extend under ordinary doses but become checked by larger doses 25 and 81. Vascularity is an important factor in bringing the iodide into contact with the diseased tissues and the results when less highly vascular tissues are attacked may be less satisfactory. With an abscess existing the actinomyces remain away free from the circulation in which the iodide is carried. So long as no abscess had formed Ochsner's patients invariably recovered under iodide of potash⁵⁴.
The method of dosage adopted latterly was that advocated by Wild\textsuperscript{25}. A solution of one ounce of iodide of potash was made in eight ounces of water and half an ounce to an ounce of this was given in a cup of milk at short intervals. On account of the rapid elimination of the iodide a more marked effect is given in this way. Enormous quantities of the iodide were taken by our patient, and even Wild’s records for quantity were exceeded.

Potassium iodide in the majority of cases has been used with great success. Our case must be included in the refractory ones.

3. The vaccine treatment of this disease was initiated, in this country at least, by Wynn\textsuperscript{16} and that successfully. Monsarrat\textsuperscript{103}, Whittier\textsuperscript{104}, Harbitz and Grondahl\textsuperscript{14}, Kinnicutt and Mixter\textsuperscript{82}, Haynes Lovell\textsuperscript{105}, Collie\textsuperscript{106} and Foulerton\textsuperscript{77} are the only published references to vaccine treatment the writer has discovered. The method of preparing and employing the vaccine/have already been noted. Its prompt remedial effect was most encouraging and as this occurred at the critical time when further surgery was impossible and iodide had been given up in despair one feels impelled to hope that in this as in other infections the appropriate vaccine has a place in treatment.
As one becomes familiar with this class of diseases and when their early diagnosis becomes the rule one is justified in looking forward to the time when this vaccine will be the earliest and deadliest weapon of attack employed on the invader.
Summary of Conclusions.

1. Streptothricosis is not so rare as formerly thought, and is recognised oftener and earlier, where bacteriology is most studied.

2. The onset of pleurisy apparently primary may be secondary to the chronic process of pulmonary streptothricosis.

3. The disease may be present as a swelling on the chest wall from bronchial-pulmonary-pleural infection before the victim consults his doctor.

4. Diagnosis is often obscure but delay in the use of aspiration and incision is blameworthy.

5. In every case suggestive of tuberculosis of lung the sputum should be examined for streptothrix as well.

6. In all cases of sinuses of obscure origin in chest or back which are not tubercular, suspect streptothricosis and examine the sputum.

7. Some of the cases recorded as primary cutaneous with secondary spread to the lung have lung as the starting point, with secondary involvement of integument.

8. It is possible to have mixed infection of T.B. and streptothrix and of the latter with cocci and bacilli.

9. It is not unusual to have haemoptysis.

10. In treatment give the appropriate vaccine early.

11. In mixed infections treat each infection with its
corresponding vaccine.

12. When surgical measures are used give potassium iodide.

13. Very young mycelium is resistant to all stains; old threads also fail to stain.

14. The active infectious agent in the tissues is apparently the rod segment.

15. The fungus of nature is the cause of the disease in man and animals.

16. It can remain in the host for very long periods without manifesting its presence.

17. Occasionally it spreads by lymph channels.

18. The lung apex is quite commonly affected and the supposed selection by the fungus of a basal site in the lung is a misleading point in differential diagnosis from tubercle.

19. Cases elude diagnosis from ignorance of observer of the various forms of the fungus.

20. Prognosis is improved from the availability of a stock vaccine for treatment.
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