ACTINOMYCOSIS IN CHILDHOOD:

A CLINICAL STUDY AND REVIEW

BY

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Actinomycosis or infection with the 'ray fungus' is a relatively rare condition in childhood but is nevertheless of importance in the differential diagnosis of chronic suppuration following appendicitis and of the chronic inflammatory conditions of the jaws, face, and neck. The pulmonary forms of the disease may simulate lung abscess, empyema necessitatis, or tuberculosis, and owing to the difficulty of making the diagnosis from examination of the sputum, the condition is possibly less rare than is generally supposed. In a collected series of six hundred and seventy cases of actinomycosis of all types occurring in the United States, Sanford and Voelker¹ include thirty-nine patients under the age of fifteen years. The following study is based on five cases of actinomycosis in children, three personally observed and two (cases 1 and 2) added from the records of the Hospital for Sick Children. In three of these the infection was primarily abdominal, and in two pulmonary. (Another case, that of a submaxillary abscess, occurring recently in the practice of the Hospital for Sick Children, is not included here but is being reported elsewhere by Mr. Charles Keogh). The autopsy on case 5 was the first to be performed on a patient with actinomycosis in a series of 11,500 autopsies carried out at this hospital.

Aetiology.

Although the term actinomycosis has been applied to infection with any member of the genus *Actinomyces*, it has been strongly recommended by Colebrook² and other workers that this description should be reserved for diseases caused by the *Actinomyces bovis*, and that infection with other strains should be distinguished by a different nomenclature. The *A. bovis* is actually the commonest member of the group to cause lesions in man, and is almost certainly identical with that described in cattle as the cause of 'lumpy jaw' and 'woody tongue.' Without entering into the vexed question of the classification of the actinomyces (which is made doubly difficult by the variety of names applied to the same groups by different

authors and by a considerable tendency of the organisms to vary in their morphological characters), it may be said that the great majority of the actinomyces are non-pathogenic inhabitants of the soil, whilst a small minority are responsible for specific infections of plants (potato and beet scab) and of animals. The *A. bovis* is, typically, an organism consisting of non-septate branching filaments, Gram-positive (but often retaining this stain somewhat irregularly), and is not acid-fast. It grows anaerobically at an optimum temperature of 37° C., but primary culture is often difficult and in many of the cases of human infection was unsuccessful. Actinomycotic pus is characterized by the presence of white or sulphur granules, best seen after shaking the pus with saline. These show a central mass of mycelium surrounded by the radial arrangement of filaments which has caused the name 'ray fungus' to be given to the organism. The terminal portions of the filaments may be clubbed, giving a characteristic picture on which much emphasis has been laid, but in lesions in man especially, the clubs are not always seen.

For practical purposes, the clinical diagnosis is justified by the finding of an organism having the above morphological characters, and producing pus containing the typical white or yellow granules. Colebrook² considers a diagnosis based on these criteria as comparable to that of pulmonary tuberculosis based on the finding of acid-fast bacilli in the sputum. The cases here reported are therefore described as examples of actinomycosis, without further qualification, although primary culture of the organism was unsuccessful.

Source of infection.—Although the organisms causing human and bovine infections are generally regarded as being identical, direct infection of man from cattle is exceptional. Colonel Hamerton³, pathologist to the Zoological Society of London, states that whilst actinomycosis of bovine type and the closely similar 'kangaroo disease' are of common occurrence amongst the bovines and marsupials in the Zoological Gardens, no case of human infection amongst the attendants has ever been recorded there. Many of the patients are town-dwellers, and a history of contact with infected cattle is exceptional. Transmission of the disease from man to man must also be rare, although the occurrence of the condition in three members of one family (Knox⁴) and in several inmates of an institution⁵ suggests its possibility. Two different theories of aetiology have been suggested, and have been discussed by Wright⁶, Mattson⁷, Colebrook², Lord⁸, and others.

Brostroem⁹ in 1890 drew attention to the frequent presence of fragments of vegetable matter in actinomycotic lesions in and around the mouth, and he isolated an aerobic branching filamentous organism from actinomycosis of the jaw in cattle, which he regarded as the cause of the disease. Subsequent investigations by other workers make it appear doubtful whether this organism was actually the one responsible. Since the widespread occurrence of such aerobic actinomyces in the soil and grass is well known, it was urged, and widely held, that infection of the mouth or tonsils took place by chewing

or inhaling fragments of infected straw or other vegetable matter. Wolff and Israel¹⁰, however, isolated from two cases of human infection an anaerobic organism which grew best at body-temperature and not at all in the cold. Their findings were subsequently confirmed by Wright⁶ and others, and this organism has now been generally accepted as the one responsible for true actinomycosis. Owing to its cultural characters, it appeared improbable that this infecting agent could, except in rare instances, be introduced on vegetable matter, and it was suggested by Wright⁶ that it might actually exist as a harmless inhabitant of the mouth or gastrointestinal tract, becoming pathogenic only when it gained entrance through some local lesion. Strong support has been given to this theory by Lord⁸ who has isolated typical *A. bovis* from the mouths of normal, human subjects, and by Naeslund¹¹ who has produced actinomycotic lesions in animals inoculated with the content of carious human teeth.

Although the theory of infection being conveyed on grass and grain still finds place in many text-books, the view is now generally held that fragments of vegetable matter impacted in the gums or tonsils serve only to cause lesions of the mucosa through which the organism, already present in the mouth, can gain entrance. Similarly, inhalation of a foreign body or inflammation of the appendix may cause local damage allowing pulmonary or abdominal infection to occur. A history of local trauma is not uncommon, and this appears particularly liable to influence the site of superficial lesions after the abdomen or lungs have been invaded.

Age and sex incidence.—Actinomycosis occurs at all ages, the youngest case quoted in most series being that described by Stokes¹² who isolated *A. asteroides* (not *A. bovis*) from a lung abscess in an infant dying at the age of twenty-eight days. It is principally a disease of early adult life and is rarer in early childhood than in adolescence. Brofeldt¹³, in a study of the disease in Finland, found in a series of 313 cases of which the ages were known, only eight examples in the first ten years of life as compared with fifty three and eighty nine in the second and third decennia respectively. It appears to affect boys more commonly than girls, though the difference in sex incidence is not as great in childhood as in adult life. Thus, the series reported by Sandford and Voelker¹ contained twenty seven boys and eleven girls under the age of fifteen (the sex of one child being unspecified), whereas eighty per cent. of the total series were males. This is probably due to the greater liability of males to trauma of all kinds, a factor which is less operative in childhood than in adult life.

Clinical features.

The disease is characterized by its chronicity, the profuse production of granulation and connective tissue, and the almost invariable tendency of the lesions to break down and suppurate. It advances with little regard to anatomical barriers and is liable to attack every tissue. The lymphatic system, however, usually enjoys a peculiar immunity (a point which is often helpful in differential diagnosis), and though ribs or vertebrae may be eroded,

or show periostitis (as in case 2), it is rare to find the bones extensively involved. Occasionally ulceration of a blood vessel occurs, and the disease becomes disseminated by the blood stream^{14, 15}. In one instance, Freed and Light¹⁶ claim to have obtained positive blood cultures.

The prognosis in the abdominal and pulmonary forms of actinomycosis is bad at all ages, but particularly so in childhood. Superficial lesions offer a reasonably good prospect of complete recovery if diagnosed early and adequately treated.

Oral and cervico-facial types.—Owing partly to the frequency of dental caries and to the liability of the gums to trauma, the mouth, and hence the cheek and neck, form the commonest sites of actinomycotic lesions. Thus of Sanford's and Voelker's¹ thirty-nine cases, thirteen had the jaw affected and eight the neck, cheek or scalp, and Figi and Cutts¹⁷ who reported fourteen cases from the Mayo Clinic of actinomycosis in children between the ages of two and fifteen years, found the lesion in ten instances in the cervicofacial area. This site of election is the more understandable when it is remembered that the organism has been demonstrated in the mouths and tonsils of normal individuals. A common sequence of events is that a hard swelling forms around the root of a carious tooth, or on the alveolar margin following dental extraction. This becomes a more or less chronic lesion, and either finally softens and discharges serous fluid or pus by several sinuses, or a reddish-purple indurated swelling appears on the neck or face externally. In some instances there is no demonstrable actinomycotic lesion at what is presumably the site of infection within the mouth and the external swelling is the first indication of the disease. The swelling may be extremely hard and comparable to the 'woody tongue' of cattle. It is firmly adherent to the deeper tissues, and may resemble an osteosarcoma. Though pain is usually complained of, it is seldom very severe, and the lesion may be hardly tender. The general health at this stage is little affected. After a variable time, often many weeks, softening of the facial lesion occurs, and pus containing the characteristic granules is discharged. If vigorous treatment is instituted whilst the lesion is still localized, the prospect of cure is good, though healing is often slow and there is a tendency for the local lesion to recur. When, however, the disease has spread within the skull or thoracic region, the prognosis is practically hopeless. Of the ten cases of Figi and Cutts, eight were alive and well after periods of from one to seven and a half years, one had died from infantile paralysis, and in one instance death had followed secondary pulmonary involvement.

Abdominal type.—Primary infection within the abdomen occurs in the majority of instances in the region of the caecum and accounts for twenty to thirty per cent. of all cases. In four out of the fourteen cases of Figi and Cutts the infection was of this type, and Edwards¹⁸, in a review of actinomycosis in childhood, records two out of six original cases with involvement of the caecum or appendix. This site appears to be liable to attack when

it becomes a *locus minoris resistentiae*. Occasionally the appendix is found heavily infected with *A. bovis*, but more frequently the disease follows an attack of appendicitis, when the appendix has undergone inflammatory changes from the action of other organisms. This is well illustrated by case 1 of the present series. The appendix was examined histologically after it had been removed, and again after the diagnosis of actinomycosis had been made, but showed chronic inflammatory changes only and no evidence of actinomycotic infection. In other cases it is probable that stasis and abrasion of the caecal mucosa have aided the entrance of the organism.

The symptoms of actinomycotic infection may appear almost at once after the original attack of appendicitis or may be long delayed and insidious in onset. In one instance (case 3), after two days' history of abdominal pain, a gangrenous and perforated appendix was removed and turbid fluid found in the peritoneal cavity. The temperature remained raised and pus continued to discharge from the abdominal wound and subsequently from the rectum and vagina. Extension to the thorax took place, probably within eight days of operation, and death occurred six weeks after the first symptoms. The history in cases 1 and 2 was longer. The patients came under observation nine and six months respectively after the original attack of appendicitis. In the first instance, in which the appendix had not been removed at the time of the original attack, the organ showed chronic inflammatory changes only. After appendicectomy had been performed, the temperature continued to swing and laparotomy two weeks later showed a glistening appearance of the abdominal tissues 'as if a snail had crawled over them' (Waugh¹⁹). This was followed during the subsequent five weeks by the appearance of a subphrenic abscess and extension to the thoracic wall. Death occurred about four months after the appendicectomy. Case 2 came under observation on account of a superficial swelling over the lower ribs which proved to connect with a large chronic abscess tracking extensively into the thoracic and abdominal walls, and probably connected also with the abdominal cavity. The patient died ten weeks after the appearance of the superficial swelling, and nearly nine months after the removal of a gangrenous appendix.

Cope²⁰ also described a more chronic type of peri-caecal actinomycosis, in which pain is practically absent in the earlier stages; the patient first came under observation on account of loss of weight or the presence of a hard indurated mass in the right iliac fossa. (This clinical picture appears to be rare in childhood.) Once softening of the mass and suppuration have occurred the later course and prognosis is essentially the same as in the more acute cases—swinging temperature, rapid emaciation, drenching sweats, and sooner or later extension throughout the abdomen or thorax, and death.

Whilst the primary site of invasion within the abdomen is almost always the caecum or appendix, the disease occasionally appears to arise elsewhere (see below); secondary involvement of other organs is common. The

organism may reach the liver by the portal route and give rise to multiple abscesses throughout the hepatic tissue; the appearance of the liver in these circumstances has been compared to that of sponges soaked in pus. Large collections of actinomycotic pus are frequently found in the pelvis, right iliac fossa, or below the diaphragm, and superficial abscesses may form over the lower ribs or abdominal walls. The tendency of the disease to spread to the thoracic wall and pleura is seen in cases 2 and 3 respectively. Once the condition has become established, it almost invariably progresses to a fatal termination in spite of treatment.

Thoracic type.—Whilst pleuro-pulmonary infection frequently occurs by extension of the disease from below the diaphragm, or from the pharynx or oesophagus, infection of the lung is the primary condition in from ten to twenty per cent. of all cases. Here again the disease seems particularly liable to invade the thorax when the latter has been damaged by some other agent. A preceding history of direct trauma to the chest (Huber and Berkowitz²¹) or inhalation of a foreign body has been several times recorded. Case 5 illustrates the latter factor particularly well. The patient inhaled a piece of cocoanut which he was chewing, and had a violent fit of coughing, which was followed by an attack of wheezing simulating asthma. Seven days later the temperature rose to 104° F., and remained raised almost continuously until death occurred. In some cases, pneumonia is possibly a predisposing cause, though it is often difficult to distinguish the 'pneumonia' from the onset of the disease. Landis and Norris²² quote a case of a boy of ten who had had pneumonia and empyema at the age of three, and had been in ill health since that time; at autopsy both lungs showed extensive actinomycosis. Although full clinical details are not given, it appears highly probable from the length of history that the disease had recently affected a previously damaged lung.

The condition may occur at any age. Apart from Stokes' patient, an infant of twenty eight days referred to above, pulmonary actinomycosis has been described in infants of twelve weeks (Husick²³), two years (Does, Gorter and Korthof²⁴), twenty six months (Skwortzoff²⁵), and two and a half years (Halpern and Levinson²⁶). After the age of five years, the condition becomes less rare, and the German and American literature contain a number of cases of pulmonary actinomycosis in children. In France, Nobécourt and Kaplan²⁷ have reviewed the literature and described one personal observation, whilst recently cases have been reported from Italy by Bollettino²⁸, from Holland by Does and others²⁴, and from Poland by Piankowna²⁹. In this country, the first case of pulmonary actinomycosis appearing in the literature was that of a boy of nine, reported by Powell, Godlee and Taylor³⁰ in 1889. Since that time a few isolated cases have been recorded.

Two types of the disease have been recognized, a bronchopulmonary and a pleuropulmonary, but the distinction does not appear to be one of much

practical importance. In either case the onset may be insidious, with loss of weight over a period of months before definite pulmonary symptoms become established, or, as is more usually the case, the onset is more abrupt and the course more rapid. A 'pneumonia' (case 4) is followed by delayed resolution and persistent cough. The child appears disproportionately ill, and the dulness in the chest so marked that an empyema is suspected. There is, however, relatively little displacement of the heart or trachea, and no pus, or a very small quantity only, is obtained on needling the pleural cavity. After a variable time, a superficial swelling containing thick pus is likely to appear

FIG. 1. Case 4.—Lipiodol injection, showing considerable deformity and obstruction of bronchi in right middle and lower lobes.

over the lower ribs on the affected side. Actinomyces should be suspected if this occurs in the absence of tuberculosis or of dulness to percussion to the level of the clavicle, since an empyema is unlikely to present on the chest wall until the whole of the pleural cavity on that side is filled. In case 4, the right upper lobe remained resonant, and the heart was only slightly displaced to the left, after the abscess had pointed on the chest wall. Rib resection showed that there was no collection of pus in the pleural cavity, and the pleura appeared healthy. This tendency of the organism to spread through tissues showing little naked-eye change, and to form an abscess at some little distance from the original site of infection is not infrequently seen.

The right or left lower lobe is usually first involved and though the destruction of lung tissue may be very great, it is striking that the disease (as in case 5) may remain limited to one lung. From dense consolidation, giving almost stony dullness on percussion, and greatly diminished or absent breath sounds over the affected area, the condition progresses to softening, suppuration and the formation of multiple abscesses. Clubbing of the fingers occurs early, but is not necessarily of extreme degree. Secondary infection of the affected lung tissue usually takes place as soon as the lesion begins to break down and gives the breath and sputum the peculiarly foul odour that is so often noted.

FIG. 2. Case 4.—28.12.32. Heart slightly displaced to left; dense opacity at right base, with marked thickening of pleura over whole of right lung.

The radiological appearances are similar in most of the published cases, a dense homogeneous opacity of the affected lower lobe, with little displacement of the heart. The process may extend to the mediastinum and cause an enlarged mediastinal shadow, but glandular enlargement is seldom demonstrable until secondary infection has occurred. The picture obtained with lipiodol injection is of interest. Fig. 1 shows the appearance seen in the earlier stages of the disease; there is blocking and deformity of the descending bronchi, and the oil fails to enter the area of the left lower lobe principally involved. Corresponding pictures were obtained on several

occasions in case 5, though here the left lower bronchus was blocked half an inch from the bifurcation. After extensive abscess formation had occurred and the boy had been coughing up large amounts of foetid sputum for some weeks, the oil entered the abscess cavities and spread throughout the greater part of the affected lung (fig. 5).

In the relatively few cases in which the diagnosis of pulmonary actinomycosis has been made in children during life, it has usually rested on the examination of pus obtained from the chest wall. It generally appears difficult to isolate the organism from the sputum, since little or no sputum is raised in the early stages before suppuration has occurred, and subsequently

FIG. 3. Case 4.—16.10.34. Right lung field considerably clear, with some residual opacity at right base.

the abundance of secondary infection obscures its presence. It is usually suspected by a process of exclusion. Tuberculosis is excluded in younger children by a negative Mantoux test and examination of the stomach washings, and in older children by direct examination of the sputum. As mentioned above, superficial abscess formation in the absence of other evidence of empyema necessitatis provides the best clue to the disease.

As in the case of abdominal infection, pulmonary actinomycosis in childhood has an extremely high mortality. Although occasional instances of recovery have been reported in adults (Preston³¹), I have not found any

record of one in a child. Cope²⁰ and Nobécourt and Kaplan²⁷ described patients who were still alive at the time their papers were published. By courtesy of these authors I learn that in both instances the children died shortly afterwards. Case 4 of the present series is therefore of particular interest, since the boy is not only still alive two and a half years after the onset of the disease (two years after the diagnosis was made from pus obtained from the chest wall), but his general health has steadily improved. Although he cannot yet be described as having completely recovered, the improvement in the physical signs and radiological picture is very marked. The lesion in the right lower lobe appears to have resolved slowly without having undergone extensive abscess formation, and the present state suggests a relatively small amount of pulmonary fibrosis and pleural thickening only (fig. 3).

Cutaneous type.—Cutaneous infection occurring as a primary condition is of extreme rarity, its incidence being estimated by Brofeldt¹³ as 1.6 per cent. of all cases. In many of the recorded instances there has been a history of local injury, such different agents as the horn of an ox, the claw of a cat (Vignolo-Lutati³²), the hoof of a horse, and the tooth of a man (Cope²⁰) having been at times incriminated. In other cases, the occurrence of lesions on the hands of those packing or handling straw, or on the feet of those walking barefoot on stubble, has suggested a primary infection from those sources. Carr, Johnson, and Power³³ recorded the cases of two children in which extensive cutaneous lesions were present over the sternum and abdominal wall respectively, and which the authors regarded as primary cutaneous infections. In the former case, however, the history strongly suggests that the skin lesion was actually secondary to infection within the thorax.

Secondary infection of the skin from a more deeply seated lesion is much more frequent, and probably accounts for about ninety five per cent. (Fraser³⁴) of the cutaneous cases. As mentioned above, the disease tends to extend to the surface from an abdominal or thoracic site, and involvement of the face frequently follows infection within the mouth.

The cutaneous lesion is first noticed as a firm swelling or nodule in the deeper layers of the skin, attached to the underlying tissues. If there has been an abrasion of the skin, it will fail to heal completely and the edges of the wound will become indurated. The skin at the site of the lesion is often reddish-purple or even blue in colour, and may be surrounded by a number of purple blotches or small flecks (Fischer³⁵). The swelling increases in size, and may remain hard as wood until it involves a considerable area, or multiple nodules appear surrounding it. It finally softens, and either discharges the characteristic pus by a number of small sinuses or causes extensive ulceration. The process is essentially a chronic one, and it may happen that a second or a third lesion will arise at the margin or in the scar tissue of a primary lesion that has healed.

An important point in diagnosis is the absence of involvement of the lymphatic glands, which are seldom affected unless infection with other organisms has taken place. The purplish-red colour of the skin, and the chronicity of the condition are also suggestive, but the diagnosis can seldom be made before the organism has been found in the pus.

Other types.—Occasional examples of primary actinomycotic infection of almost every organ have been described but most of these are so rare as to be little more than medical curiosities. Infection of the stomach, which is not very uncommon in animals, does not appear to be of the same importance in man. Stravinsky³⁶, who has recently reviewed the literature, found only eight examples of primary gastric infection, the youngest case being a male of nineteen. It appears that the presence of a chronic gastric ulcer may predispose to the condition. Secondary infection of the stomach from swallowed sputum might be expected to occur in children with pulmonary actinomycosis, and case 5 at post mortem showed two lesions in the fundus of the stomach which were at first taken to be of this type. Microscopical examination showed only the presence of secondary organisms in the sections. The female genital organs may also be the site of actinomycosis, though generally by the time the diagnosis has been made the disease has spread to such an extent that the primary infection is in doubt. Amongst sixty-six examples collected from the literature, Daniel and Mavrodin³⁷ include only one child. The patient, a girl of fifteen who had never menstruated, had been ill for a year with pain in the left loin. At post mortem the uterus was found to be of infantile type, and both ovaries almost entirely destroyed by actinomycosis. The renal tract is occasionally affected (Cecil and Hill³⁸), and examples of cerebral (D'Ewart and Dawson³⁹), aural, lachrymal, and pericardial actinomycosis are also recorded. The pyaemic form of the disease, in which any organ may be secondarily involved, has already been referred to.

Treatment.

Whilst treatment is unsuccessful in the great majority of abdominal and pulmonary cases in childhood, the relatively good prognosis in patients presenting superficial lesions only and the occasional recoveries reported in adults suffering from more extensive disease, encourage energetic treatment from the time the diagnosis is first made. The use of iodides has for long been regarded as specific therapy both for the bovine and human type of infection and, though its value has recently been called in question, the balance of opinion is still in its favour. A small initial dose of potassium iodide should be given in case of intolerance, and the amount rapidly increased. It will be found that most children suffering from actinomycosis will tolerate massive doses over long periods. As an alternative, tincture of iodine, starting with two minims and cautiously increasing, may be given in milk. When the patient is intolerant of oral administration, Lugol's iodine can be used intravenously.

Iodine is also used for local application, the tincture being applied to superficial lesions, and iodoform gauze being employed for packing abscess cavities. Johnson and Kernan⁴⁰ have recommended bronchoscopy and the injection of iodised oil (lipiodol) in the treatment of pulmonary actinomycosis, and Raimondi, Pardal, and Mazzei⁴¹ have also practised lipiodol injections. This was done by the cricothyroid route in cases 4 and 5, though it was found in both instances that there was blocking of the bronchi of the affected lobe in the early stages of the disease, and it was not until extensive cavitation (fig. 5) had occurred that the oil spread throughout the lung in case 5.

Copper salts have been extensively used recently in the treatment of the disease, and some good results have been claimed for them. Colebrook⁴² and Cope²⁰ have also recommended the use of vaccines consisting of fragments of the organism, and have obtained some promising results in conjunction with surgical drainage. X-ray therapy has been employed by a number of workers, but in children it does not appear to have given any very striking results. Surgical treatment has a limited application, and in visceral cases the aim should be to provide free drainage of abscesses rather than to attempt extensive removal of tissue. Local and superficial lesions can sometimes be successfully excised.

The use of insulin and glucose (one unit of insulin to three grammes of glucose, given intravenously) has been advocated by Jacobson⁴³ as an adjunct to other forms of general treatment, and in view of the chronicity of the disease this may prove of value in stimulating appetite and preventing wasting. The same author has employed non-specific protein shock, in the form of typhoid-paratyphoid vaccine with suggestive results.

Case records.

Case 1.—Abdominal type.

T. C., a boy aged eleven years, four months, was admitted to hospital on 20 November, 1923, under Mr. George Waugh with a history of having had an attack of appendicitis nine months previously, and intermittent pain in the right side of the abdomen since then. The child had not been operated on at the time of the original attack. Pain was unrelated to food, and there had been no vomiting but some nausea in the mornings. There had been no cough, and no sweating until three weeks before admission. The bowels were usually constipated, and there had been intermittent pyrexia. Family history and previous history were irrelevant. The child lived in London.

ON EXAMINATION. A pale child, temperature 99° F., pulse 133, respiration 24. The tonsils were enlarged, the tongue clean, the heart and lungs normal. Small discrete glands were present in neck; the abdomen moved well on respiration; there was no palpable tumour but some tenderness and rigidity of right flank. The lower border of liver extended one inch below costal margin. Urine was normal.

BLOOD COUNT. White blood corpuscles, 23,750 per c.mm.

X-RAY. A bismuth meal showed ileo-caecal stasis.

OPERATION BY MR. WAUGH (23.11.23). The abdomen was opened by a right paramedian incision, a small amount of free fluid being found present. Portions of the omentum were adherent to the lower abdominal wall, but not in connection with any evident pathological focus. The appendix was situated retro-caecally and was embedded in peri-appendicular adhesions. The caecum was unusually mobile. The appendix, which showed a marked degree of inflammatory change, was removed after extricating it from its bed of adhesions and the base invaginated. The peritoneum was closed.

Section of the appendix showed signs of chronic inflammation with great thickening of the walls. No streptothrix was seen in sections stained by Gram's method.

COURSE. The patient's condition was good following the operation, but the temperature rose irregularly to 103°, and on 30.11.23 (a week after operation) it was noted that there was dulness at base of the right lung and tenderness on pressure high up in the right flank. The urine contained a few hyaline casts and was sterile.

BLOOD COUNT (4.12.23). White blood corpuscles 22,000 per c.mm. Polymorphs., 70 per cent.; small lymphocytes, 20.5 per cent.; large lymphocytes 9 per cent.; eosinophils, 0.5 per cent.

8.12.23. An area of localized tenderness was found above the right iliac crest, just lateral to the erector spinae muscle. An incision was made over this point under general anaesthesia, and the underlying parts explored. The peritoneum was opened behind the ascending colon but only a slight amount of dry plastic peritonitis was found.

21.12.23. Thirty c.c. of one per cent. chloramine injected intravenously. Blood culture was sterile.

3.1.24. X-ray (screen) showed complete immobility of right diaphragm, which was not raised, but consistent with a subphrenic abscess. The temperature remained raised.

11.1.24. An exploratory laparotomy was performed by Mr. Waugh. The liver was found adherent to the peritoneum in the floor of the incision. There was much perihepatitis, and a large quantity of thick lymph was removed from between the liver and diaphragm. No pus was obtained. The cavity between liver and diaphragm was packed with iodoform gauze, and a tube was placed in the region of the hepatic flexure. Oxygen and camphor were administered during the operation and 20 oz. of five per cent. glucose in saline given intravenously.

Report on material from subphrenic region: 'No organism seen. Cultures sterile.'

14.1.24. The iodoform plug was removed followed by considerable discharge of foul-smelling pus. A drainage tube was inserted. The temperature continued to swing and the general condition deteriorated. On January 20, an icteric tint of conjunctivae was noted and a week later a swelling appeared over the right lower ribs in the posterior axillary line.

30.1.24. The swelling over ribs was incised, and thick white pus obtained. Forceps inserted into lumbar region and below right anterior costal margin and tube inserted.

EXAMINATION OF PUS. The films showed Gram-negative and positive cocci. The cultures were sterile.

The wound continued to discharge thick pus, and in the region of the original incision, the tissues became reddened and oedematous, with secondary abscesses pointing in several places.

Actinomycosis was suspected, and examination of the pus on 21.2.24 showed the presence of granules. In the fresh film, clubs were seen, irregular in shape and size, and in the stained film, filaments of Gram-positive branching streptothrix.

The patient was treated with pot. iod. gr. xx, and copper sulphate gr. $\frac{1}{2}$ t.d.s. for the following month, but as the general condition was steadily getting worse, he was removed from hospital by the parents on March 26, 1924, in a dying condition.

Case 2.—Abdominal type.

J. M., a girl aged eleven years was admitted to hospital under Mr. Higgins on 13.7.31, with three days' history of a swelling over the right lower ribs posteriorly. She had been hit by a cricket ball at this point several days before the swelling was noticed.

In January, 1931, a gangrenous appendix had been removed, and in April, 1931, she had suffered from an attack of influenza.

ON EXAMINATION. The patient was an ill-looking child; temperature 102° F., pulse 128, respiration 28. A large fluctuant abscess was situated over the right lower ribs posteriorly. The chest was dull to percussion at the right base. The abdomen showed nothing abnormal except an appendicectomy scar and slight rigidity on right side.

15.7.31. The abscess was incised and left open without drainage.

BACTERIOLOGICAL EXAMINATION. The pus evacuated was greenish yellow in colour, slightly blood stained, and contained sulphur yellow granules. A stained film showed pus cells and a fair number of Gram-positive branching filamentous organisms, having the appearance of *A. bovis*. On staining with Ziehl-Nielsen, no tubercle bacilli were seen. Cultures were sterile in seven days. A second examination of the pus made on the following day again showed the same organisms present. Subsequent examinations of pus on 29.7.31, 7.8.31, and 17.8.31, showed a few colonies of staphylococcus aureus only, but on August 21, 26, 27, and 31, and September 3, 7, 15, and 19, the typical mycelium was again seen. Cultures in each case grew staphylococcus aureus (and in one instance, coliform bacilli) only.

Examination of the faeces was repeatedly negative for actinomycosis; cultures made from the urine were sterile.

BLOOD EXAMINATION. 11.8.31. White blood corpuscles, 23,900 per c.mm.; polymorphs, 70 per cent.; lymphocytes, 24 per cent.; large monocytes, 6 per cent. 12.9.31. Red blood corpuscles, 2,300,000 per c.mm.; white blood corpuscles, 14,400; Hb., 35 per cent.; polymorphs, 88 per cent.; lymphocytes, 12 per cent.

COURSE. Although the abscess drained freely, the patient continued to have a swinging temperature (104°) and the general condition rapidly deteriorated. She was treated with increasing doses of potassium iodide without improvement.

X-RAY. 12.8.31. Showed periostitis of tenth and eleventh ribs.

OPERATION BY MR. HIGGINS. 13.8.31. An incision was made over the abscess and was extended in several directions; portions of the tenth and eleventh ribs were resected, and a large chronic abscess was discovered. It extended upwards deep to the lower ribs and superficial to the parietal pleura, and below extended medially to the region of the posterior abdominal wall. Much purulent debris was evacuated, and the abscess wall curetted. It was thought that the cavity was connected with the abdominal cavity, and related to the appendix removed in January, 1931, with a possibility of extension to the right lung and liver. The cavity was syringed with Dakin's solution and Carrel-Dakin tubes inserted. The abscess cavity remained open and drained thick offensive pus.

15.9.31. The chest showed fine crepitations at both bases, and the abdomen slight general distension; the liver and spleen were not enlarged. The abscess had extended towards the midline posteriorly.

18.9.31. Blood transfusion given (20 oz. of father's blood).

OPERATION BY MR. HIGGINS. 25.9.31. Extension of abscess incised, and the skin and subcutaneous tissues were found riddled with sinuses. The communication with the right posterior abdominal wall was still present.

The patient died on September 28, 1931, ten weeks after admission to hospital.

Post-mortem examination was not allowed.

Case 3.—Abdominal type.

I. N., a girl aged nine years, was admitted to hospital on October 17, 1933, under Mr. Eric Lloyd, with two days' history of abdominal pain, vomiting, and constipation. The pain was referred to the suprapubic region. She had previously been in hospital (6.6.32 to 16.8.32) with chorea and rheumatic carditis.

ON EXAMINATION. She was a pale ill-looking child, temperature 100° F., pulse 160, respiration 40. The tongue was furred and the heart enlarged to the left, with a soft systolic murmur at the apex. The lungs were clear. The abdomen showed no definite rigidity at the time of admission, but slight tenderness in the midline below the umbilicus; the abdominal reflexes were absent in the right and left lower quadrants. Generalized rigidity of abdomen developed a few hours after admission, Rectal examination was negative.

OPERATION BY MR. HINDENACH. A large quantity of free fluid (turbid but not offensive) was found in the peritoneal cavity, particularly in the pelvis and right iliac fossa. The appendix was greatly swollen, the distal end being perforated and gangrenous. The appendix was separated with difficulty from its mesentery, its base clamped, and the organ removed. The base could not be turned in, but the caecum was sewn over it. Drainage tubes were inserted into the pelvis and right iliac fossa. The pus obtained and cultured at the time of operation grew coliform bacilli only.

BLOOD COUNT (after operation). White blood corpuscles, 22,500 per c.mm. Polymorphs, 74 per cent.; lymphocytes, 20 per cent.; monocytes, 6 per cent.

COURSE. A profuse discharge continued to drain from both tubes, and the temperature remained raised, swinging to 102°. On the third day, there was distension of the abdomen and all feeds were vomited, and three days later the child began to cough and become increasingly restless. She was given continuous intravenous glucose for three days.

25.10.33. The chest showed dullness at the left base, and râles at both bases. Secondary haemorrhage occurred from the abdominal wound and the following day the discharge became faecal. Subsequently a large swelling was felt per rectum, filling up the pelvis, and pus began to discharge from the rectum and vagina. The signs at the left base persisted, with diminution in vocal fremitus and resonance in this area. On November 15 aegophony was noted at the upper level of dullness, and moist crepitations in the lung above. The left chest was aspirated posteriorly on October 18, but only a small quantity of blood stained fluid was withdrawn. The stained film showed this to be mainly blood; no organisms were seen, and cultures were sterile.

23.11.33. Eight c.c. of foul 'anchovy paste' pus were aspirated from the left pleural cavity posteriorly, medial to the angle of the scapula.

EXAMINATION OF PUS. No granules were seen. The stained film showed very degenerate material. A few Gram-negative bacilli and a fair number of branching streptothrix 'almost certainly actinomycosis' were noted.

Intense iodine therapy was commenced, but the child died suddenly on November 26, six weeks after the onset of symptoms.

Post-mortem examination was not allowed.

Case 4.—Pulmonary type.

N. P., a male, aged six years nine months, lived in London and had never been out of town except twice for the day (to Clacton), had had no known contact with cattle, or any farm or dairy worker. His father, a painter, was well; his mother and one older brother were well. His infancy was normal. He had pneumonia at two, pertussis at three years of age, and measles in May, 1932 (at the age of five years and three months) with uneventful recovery.

In August, 1932 (aged five-and-a-half years) he had pain of sudden onset in the right side of the chest, and was in bed for two to three weeks. He did not make a satisfactory recovery, and continued to have a slight cough. He was admitted to Victoria Park Chest Hospital in November, 1932, where he was x-rayed and the chest needled; no fluid was obtained. He was taken out of hospital against advice, and subsequently admitted to the London Hospital under Dr. A. G. Maitland-Jones on December 27, 1932.

ON EXAMINATION (28.12.32). A moderately well-developed, ill-looking boy, with marked pallor and definite clubbing of the fingers. There was a tendency to cyanosis of the lips and some slight cough and dyspnoea on exertion. No sputum was raised. The temperature was 104.5° F., respiration 40, pulse 130. A fluctuant swelling measuring three quarters of an inch by one and a half inches was situated on the right chest wall, at the level of the sixth and seventh ribs, just outside the mid-clavicular line. The skin covering it was dark red, and moderately tender. There were dilated veins over the right chest anteriorly. The chest showed diminished movement on the right side, with slight flattening of the lower ribs. The percussion note was normally resonant over the left chest, slightly impaired over the right apex, and stony dull over the right side of the chest to the level of the third rib above. Air entry was greatly diminished over the right lower lobe, with an area of bronchial breathing at the angle of the right scapula. Very occasional crepitations were heard at the right base. The apex beat was immediately external to the mid-clavicular line in the fourth interspace. The heart sounds were normal. No other signs of disease were found. The Mantoux test was weakly positive (1 in 1,000 dilution).

COURSE (4.1.33). The right chest was needled in four places, but no pus was obtained from the pleural cavity. The swelling was incised and drained, several cubic centimetres of thick yellowish blood-stained pus being evacuated.

Examination of the pus by Dr. P. N. Panton showed the presence of many pin-head yellow granules, with numerous filaments of Gram-positive streptothrix in the film, which appeared typical of actinomycosis. The organism at first grew anaerobically, but cultures subsequently died out.

Radiological examination (28.12.32) showed the heart slightly displaced to the left and a homogeneous opacity at the right base resembling consolidation, with marked thickening of the pleura over the whole of the right lung (fig. 2). Lipiodol was injected by the cricothyroid route on 11.1.33, and showed considerable deformity and obstruction in the bronchi in the right middle and lower lobes (fig. 1).

Intensive iodide therapy was started as soon as the diagnosis was made, the dosage being increased up to 120 grains a day for several weeks. The boy has had from 40 to 60 grains a day almost continuously during the past two years, except for one three-month period during which it was remitted.

The temperature and respiration rate fell to normal on the third day in hospital, and except for one or two slight rises (to 101°), the boy has been afebrile since this time. The chest wound continued to drain small quantities of sero-sanguinous discharge and thin pus for six to eight weeks, and then healed. A second small fluctuant swelling appeared on the chest wall, posterior to the old wound, five months later, but settled without incision.

The general health has improved slowly during the past two years, and the boy has gained eight pounds in weight. Apart from slight dyspnoea on exertion he is free from symptoms. The physical signs in the chest remained practically unchanged for nearly

FIG. 4. Case 5.—Left lung almost completely opaque, and heart drawn to left.

twelve months, although the x-ray showed some degree of clearing. Since this time there has been considerable improvement in both x-ray and physical signs. He now (January, 1935, aged seven years and ten months) has impaired percussion note over the right lower lobe only, and moderately good air entry in this area. The movement of the right chest is only slightly diminished, and the clubbing of the fingers is less marked.

Radiological examination (16.10.34) shows very marked clearing of the right lower lobe, with some residual shadowing at the base. (This case was shown at a meeting of the Children's Section of the Royal Society of Medicine⁴⁴ in January, 1933.)

Case 5.—Pulmonary type (autopsy).

K. S., a male, aged four and a half years, was an only child of healthy parents, living in an agricultural district in Kent. There was no known contact with actinomycosis, but frequent association with horses and cattle. He was well until July 7, 1934, when he inhaled a small piece of cocoanut pulp whilst running. This was followed by an attack of dyspnoea closely resembling asthma. Seven days later he had a sudden rise of temperature to 104° F., and respiration rate to 58, and he was diagnosed as having lobar pneumonia. The temperature remained raised until the eleventh day when there was a pseudocrisis. Subsequently the temperature continued to swing between 99° and 102° . There was grunting respiration and some asthmatic wheezing in the evenings.

FIG. 5. Case 5.—Lipiodol injection, showing multiple abscess cavities at left base.

Skiagrams taken on July 16 showed relatively little infiltration of left base; there was no sign of fluid. He was referred to hospital August 16, 1934, by Dr. A. F. Cole, of West Malling, to whom I am indebted for the previous history, and admitted under Dr. Cockayne.

ON EXAMINATION. He was a pale, wasted boy with considerable respiratory distress and frequent cough. His temperature was 101° F., respiration 40, and pulse 128. There was early clubbing

of fingers. No displacement of trachea was noted. The apex beat was not palpable. There was dullness half an inch to the right of the sternum. No cardiac murmurs were heard. There was diminished movement of the left side chest and stony dullness at the left base with diminished resonance over the whole of the left lung except at the apex. The breath sounds were diminished over the left lung except at the apex, and they were tubular over the lower part of the left upper lobe. The right lung was normal. The tongue was furred, the tonsils red. There were two carious right upper molars. The ears and abdomen were normal. A skiagram showed almost complete opacity of left chest with very little displacement of heart. An exploratory puncture was made on the night of admission in the eighth left intercostal space in the posterior axillary line, and a few drops of thick pus obtained with the needle one inch from the surface. White blood count: 32,450 per c.mm.

17.9.34. Operation under local anaesthetic. Openings made in eighth and ninth left intercostal spaces. No pus was obtained. The lung felt hard, but the pleura appeared normal. Two catheters were inserted.

18.9.34. Catheters removed. Mantoux tuberculin test was negative in 1 in 1,000 dilution.

The following day the wound began to discharge thick yellowish pus with extremely offensive odour.

PATHOLOGICAL REPORT on the yellow pus. On emulsion with saline, typical sulphur yellow granules were present. A wet film showed granules with rosette arrangements and radiating clubs. Stained by Gram and carbolfuchsin: Gram-positive cocci were seen in clusters and Gram-positive streptothrix of all sizes, occasionally in clusters. Stained with Ziehl-Nielsen, no tubercle bacilli were seen; the streptothrix was not acid fast. The streptothrix failed to grow aerobically or anaerobically.

COURSE. The patient was treated with increasing doses of potassium iodide (up to 60 grains four hourly), and with repeated lipiodol injections intra-tracheally. The general condition rapidly deteriorated, with extreme wasting. Clubbing of fingers became more marked, but not extreme. Temperature rose to 104° F. a week before death, which occurred one month after admission.

POST-MORTEM EXAMINATION. (Examination of brain not permitted.) The body was greatly emaciated: weight 25 lb., length 45 in., an open wound with a necrotic margin was present in left side of chest (eighth and ninth interspaces in posterior axillary line). The mouth was foul and contaminated with sputum, with two carious right upper molars but no induration of alveolar margin. The tonsils were small and sections showed some chronic inflammatory changes. The salivary glands and cervical glands presented no changes.

The whole of the surface of the left lung was purplish-red in colour, the visceral pleura being rough and indurated and its vessels

engorged. The parietal pleura had lost its glistening appearance and from the mid-axillary line backward the parietal and visceral pleurae were firmly adherent. There was no free fluid in the left pleural cavity, but a sinus surrounded by dense adhesions connected a large abscess in the left lower lobe with the external opening in the sixth interspace, and a small amount of thick green pus was adherent to the apex of the left upper lobe posteriorly. Medially, the parietal pleura was adherent to the pericardium.

FIG. 6. Case 5.—Left lung showing thickened pleura, fibrosis, and multiple abscess cavities; right lung unchanged.

The left pleura was found greatly thickened and indurated and the surfaces of the interlobar pleura adherent. The normal lung structure was completely destroyed, the greater part of both lobes presenting a honeycombed appearance due to multiple abscess cavities filled with foetid greenish-grey pus, which showed the presence of yellow granules after shaking with saline. The abscess cavities varied in size from two or three millimetres in diameter to one in the left lower lobe the size of a walnut; the lining of

the cavities was ragged and necrotic. Surrounding the cavities and underlying the pleura were areas of consolidation and dense fibrosis; the vascularity of the whole lung was increased. The main bronchi contained thick pus.

Histological examination of the left lung showed irregular areas of young fibrous and granulation tissue, and necrosis in the vicinity of the abscess cavities. Very many Gram-positive cocci and leashes of Gram-positive streptothrix were present throughout the sections; the latter showed a tendency to rosette formation in several areas, but no clubs were seen.

The right lung and pleural cavity appeared normal naked-eye and microscopically except for some terminal oedema and congestion at the base of the right lower lobe. The bifurcation gland was considerably enlarged and beginning to break down; one tracheo-bronchial gland on the left side was fibrosed, and the remainder slightly enlarged, but sections of these showed no evidence of streptothrix within them.

The heart showed no changes. The pericardium, though adherent to the left lung, was not indurated. The liver was in a condition of early fatty degeneration. The kidneys showed pallor of the cortices and microscopically some hyaline degeneration of the tubules. The pelvis of the right kidney contained a small calculus (the size of a split pea), and both ureters were distended with urine. Two calcified mesenteric glands were present in the right iliac fossa.

The stomach contained a small quantity of swallowed sputum, and there were two small areas of ulceration of the mucosa of the fundus. These had indurated margins, and were surrounded by areas of haemorrhagic staining. Histologically, many Gram-positive cocci but no streptothrix were seen in sections of the ulcers. The caecum and appendix showed post-mortem staining, but no evidence naked eye or histologically of actinomycotic infection. The peritoneum and other organs showed no abnormality.

Summary.

1. Actinomycosis, though rare throughout childhood, occurs even in early infancy. The disease is less uncommon in boys than girls. In most instances, the *Actinomyces bovis* is thought probably to exist within the mouth or gastro-intestinal tract, and to become pathogenic when it gains entrance to the deeper tissues through an abrasion or area of lowered resistance of the mucosa.

2. The clinical features of the commoner types of actinomycotic infection are described. The mouth provides the most frequent site of invasion, and next to this the caecum and appendix.

3. Five illustrative cases of actinomycosis occurring in children are reported. Three of these were of abdominal type, with extension to the thorax, and two were pulmonary. Of the latter, one is alive and shows improvement clinically and radiologically two-and-a-half years after the onset of the disease. The post-mortem findings in the other case are reported.

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