INFECTION OF WOUNDS WITH ACTINOMYCES

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Actinomycosis is now so widely known as a pathological entity that the presentation of another series of cases should be justified by at least some unusual feature of the syndrome or a contribution to the treatment of this difficult disease. The fact that over 80 per cent of cases in humans occur in the gastro-intestinal or respiratory system (Boyd 1943) is strong evidence in favour of infection through the mouth and digestive tract. The mode of entry is still obscure, but it seems probable that infection takes place through an abrasion in the mucosa.

The group of cases to be described presents an unusual feature, in that the streptothrix gained entrance through a known wound and in five patients there was evidence of involvement of bone (Table I). One other patient was infected at the site of a hypodermic injection. Bone involvement is common in the spine where the lesion is frequently a direct extension from a focus in the lung or paravertebral glands. These lesions have been well described by Cope (1938), Tubb and Tucker (1933), Holmes and Ruggles (1936) and Dixon (1939). Primary infection from a human bite has been described by Cope (1915), McWilliams (1917), Robinson (1944), and Burrows (1945).

CASE REPORTS

Case 1—W. D., male aged twenty-eight years. In 1944 he sustained a mortar bomb wound of the left buttock. There was considerable laceration of soft parts and a comminuted fracture of the subtrochanteric region of the femur. Treatment—Toilet of wound; packing with vaseline gauze; plaster spica. He was given two pints of plasma. Sulphathiazole (17½ grammes) and penicillin (700,000 units) were administered during the succeeding week. Progress—Two weeks later there was pyrexia to 101 degrees F. Inspection of the wound under anaesthesia revealed a sinus leading down to the fracture and much purulent discharge. There was no gross local oedema or redness. The sinus was opened up and repacked, and a new plaster spica was applied. A further course of penicillin was given (400,000 units). One month later there was recurrence of pyrexia. The sinus was still discharging. The wound was reopened, several sequestra were removed and the plaster was renewed. The pyrexia subsided after four days' treatment with suphanylamine (1 gramme every four hours). Four months after injury the fracture was united, but the sinus over the greater trochanter continued to discharge. Six months after injury the cavity was laid widely open under

<table>
<thead>
<tr>
<th>Case number</th>
<th>Age</th>
<th>Type of wound</th>
<th>Site of injury</th>
<th>Location at time of injury</th>
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<tbody>
<tr>
<td>1</td>
<td>28</td>
<td>Mortar bomb</td>
<td>Hip joint</td>
<td>N.W. Europe</td>
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<tr>
<td>2</td>
<td>27</td>
<td>Mortar bomb</td>
<td>Hip joint</td>
<td>North Africa</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>H.E. shell</td>
<td>Hip joint</td>
<td>N.W. Europe</td>
</tr>
<tr>
<td>4</td>
<td>19</td>
<td>Bullet</td>
<td>Upper chest</td>
<td>N.W. Europe</td>
</tr>
<tr>
<td>5</td>
<td>27</td>
<td>Mortar bomb</td>
<td>Lower chest</td>
<td>Italy</td>
</tr>
<tr>
<td>6</td>
<td>40</td>
<td>Hypodermic needle</td>
<td>Left arm</td>
<td>India</td>
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general anaesthetic through a transverse incision. Several sequestra were removed. Actinomycetes, demonstrated in the pus, sensitive to penicillin. In spite of surgical drainage, sulphonamide and penicillin, the sinus continued to discharge. 

**Bacteriological examination**—Direct examination of the pus, two months after injury, showed streptococci, staphylococci, a few diphtheroids and doubtful hyphae of actinomycetes. Aerobic cultures grew pyocaeus and spore-bearing bacilli. Anaerobic cultures grew diphtheroid bacilli. Four months later hyphae of actinomycetes were seen on direct examination and aerobic cultures produced a colony of actinomycetes after four days' growth. Six months later hyphae of actinomycetes were still present on direct examination, but culture grew bacillus coli only. 

**Case 2**—C. R., male aged twenty-seven years. In 1943 he sustained a mortar bomb wound of the right buttock with open fracture of the neck of the femur and complete sciatic palsy. Treatment—Primary excision of wound. Wound packed and hip spica applied. He developed an inguinal abscess which was drained by anterior incision. Progress—Three months after injury his general condition was fair. Pyrexia up to 101 degrees F. persisted. Examination showed a large abscess in front of the hip joint which was drained through an anterior incision. Several sequestra were removed and the limb was immobilised on a frame. A month later the pyrexia still persisted. 

A further large abscess under the gluteal muscles was drained through a posterior incision and several further sequestra were removed. Gradual improvement in general health continued. During the subsequent year the wounds healed slowly and the patient was allowed to get about with a cork raise on his sole (Fig. 1). The sinuses broke down after nine weeks and continue to discharge, in spite of several courses of sulphanilamide and penicillin (one million units). 

**Bacteriological examination**—Direct examination of the pus four months after the injury showed streptococci and a few diphtheroid bacilli. Aerobic culture was sterile; anaerobic culture showed streptococci and coliform bacilli. Six months later direct examination showed many acid-fast bacilli; coliforms, and staphylococci. Twelve months later (twenty-two months after injury) acid-fast actinomycetes were seen on direct examination, and were still present four months later.

**Case 3**—M. S., German prisoner-of-war aged fifty years. In 1944 he sustained a shell wound of right hip with compound fracture neck of femur and sciatic palsy. Treatment—Primary wound excision. Wound packed and limb immobilised in “Tobruk” plaster. He was given 180,000 units of penicillin in two days. Progress—During the succeeding three months several abscesses around the hip were incised and drained. Local penicillin instillations (5,000 units twice daily) were given. Six months later there was high swinging temperature to 102 degrees F. General condition was very poor; extensive pressure sores were present over sacrum and buttocks and he was incontinent of urine and faeces. There was profuse discharge from sinuses in front of and behind the right hip. Further courses of penicillin (100,000 units daily were given (total 1,200,000 units). Much general improvement followed. Two months later his general condition again became worse. Pyrexia persisted and there was much purulent discharge from the wound. The hip joint was laid open by reflecting the gluteal insertion. The posterior capsule was excised. The head of the femur was dead and was removed. Counter-drainage was effected in front of the joint. The wounds were packed open and plaster applied. A further course of penicillin (total 900,000 units) was given. Discharge around the pack continued. Two months later the wound was cleaner but purulent discharge continued.
Bacteriological examination—Direct examination of the pus eight months after injury showed large numbers of streptococci and hyphae of actinomyces. Anaerobic culture grew actinomyces. Four months later no actinomyces were seen on direct examination and culture grew only coliform bacilli, diphtheroids and streptococci.

Case 4—R. D., male aged nineteen years. In 1945 he sustained a through-and-through bullet wound involving the inferior angle of the left scapula, complicated by pneumohæmorrhax and paraplegia below the level of T.8. Treatment was by primary wound excision and closure. Penicillin (1,400,000 units) was given. Progress—Four weeks later both anterior and posterior wounds of chest were healed. There were high pyrexia, multiple bed sores, and urinary infection. He developed a large abscess over the right scapula, and another over the left elbow. Both were incised. Actinomyces were isolated from the pus from the elbow. A further course of penicillin (1,000,000 units) was given. The infection subsided in ten days. Wounds healed within three weeks and have remained healed since.

Bacteriological examination—Direct examination of the pus showed hyphae of actinomyces. Colonies of actinomyces were grown after five days' aerobic culture.

Case 5—G. G., male aged twenty-seven years. In 1942, while overseas, he sustained multiple shell wounds of head, with hemiplegia and a penetrating wound of the right lower chest. He came under the care of the writer when he returned to Britain ten months later. His general condition was poor. There was pyrexia up to 102 degrees F. There was a discharging sinus in the mid-axillary line on the right side. Radiographs of the chest showed pleural thickening and erosion of the twelfth rib (Fig. 2). Treatment—The sinus was explored. The twelfth rib was friable and there was a mass of soft granulations deep to it. Rib excised; no localised abscess found; wound packed open. Progress—Five months later the sinus was still discharging profusely. Examination of the pus showed a streptothrix, spores and hyphae. Repeated courses of potassium iodide (40 grammes three times daily), and of sulphonamide (1 gramme four hourly) were given, but there was no improvement. A course of deep X-ray therapy was given without effect. Six months later (twenty-three months after injury) there was persistent pyrexia and profuse purulent discharge.

Bacteriological culture grew actinomyces bovis (Hartz) anaerobically. Systemic penicillin (1,100,000 units) was administered by continuous drip. The sinus healed within two weeks and the pyrexia settled. A further course of penicillin was given and the sinus has remained healed.

Case 6—M. H., male aged forty years. This patient was seen with an indolent swelling over the outer aspect of the middle third of the arm. He stated that he had had an injection at this site six months previously in India. The swelling later became fluctuant and a pure growth of acid-fast actinomyces was cultured aerobically from aspirated pus in thirty-six hours. The organism was resistant to penicillin.

Comment—There is little in the clinical syndrome to distinguish this type of infection from the more general mixed infections complicating open fractures. The following points make one suspicious: 1) Profuse discharge without demonstrable sequestra or foreign bodies; 2) thin, non-clotting pus; 3) multiple frequent flares of cellulitis and abscess formation around the wound; 4) marked osteoporosis coincident with new bone formation; and 5) marked general toxaemia with anaemia, and failure to respond to routine therapy. Infection with actinomyces is seldom suspected till the organism is demonstrated in the pus. The pus is usually profuse, but "sulphur granules" were present in only one case.
Variability of actinomycetes—The actinomycetes show a great range of variability in their members, so much so that Lieske (1921) regarded the concept of species as untenable for this group. It has been agreed that this is an extreme view and that the identity of species is preserved (Table II). In the present series some traits appear to have a higher degree of constancy than others: 1) The general mode of growth; the firm woven consistency of the colony as opposed to a friable mass. 2) The mode of branching at the periphery where a circular fringe of hyphae growing just beneath the agar anchors the growth and determines the general character of the colony. 2) The capacity to bear aerial hyphae and the texture and colour of these is fairly constant. These features enabled any group of six to be distinguished from one another. The features embodied in Table II represent an average mean and are all liable to variation.

Haemolysis—On blood-agar each of the larger colonies is surrounded by a cloudy green ring about two millimetres wide. This merges into a wider ring of clear haemolysis which is, in turn, surrounded by a further ring of cloudy green. The change appears in two to four days. Contrary to expectation haemolysis was scarcely noticeable in the first subculture after isolation from pus, and increased only in the next one or two subcultures. It may have been merely fortuitous, but the two most haemolytic organisms occurred in the two most anaemic patients.

Spore-formation—The four non-acid-fast types (Cases 1, 3, 4 and 5) bear hyphae which break into short diphtheroid spores, and these were probably present in the pus where in quantity they would be difficult to distinguish from involution forms of diphtheroids. The diphtheroids

<table>
<thead>
<tr>
<th>Case</th>
<th>First culture</th>
<th>Type of growth</th>
<th>Early colony</th>
<th>Peripheral fringe</th>
<th>Aerial branching</th>
<th>Colour</th>
<th>Haemolysis</th>
<th>Acid fast</th>
<th>Penicillin sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Aerobic and micro-aerophilic</td>
<td>Adherent web</td>
<td>Matt, lens-shaped, yellow-grey, opaque</td>
<td>Comparatively wide. Stout hyphae, side branches at long intervals, angles acute</td>
<td>Early from two days</td>
<td>Dead white</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>Aerobic</td>
<td>Adherent web</td>
<td>Matt, highly domed, brown, opaque, cartilaginous</td>
<td>Narrow, delicate hyphae, side branches becoming parallel</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>Anaerobic</td>
<td>Adherent web</td>
<td>Matt, lens-shaped, yellow-grey, translucent</td>
<td>Narrow, delicate hyphae, side branches at large angles</td>
<td>1-4 weeks</td>
<td>Yellow-white</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>Anaerobic</td>
<td>Adherent web</td>
<td>Matt, smooth, almost flat, thin, translucent</td>
<td>Narrow, very fine hyphae, similar to Case 3 but not so wavy</td>
<td>1-several weeks</td>
<td>White or grey to olive-green</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>Anaerobic</td>
<td>A. bovis (Hartz)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Therapeutic response</td>
</tr>
<tr>
<td>6</td>
<td>Aerobic</td>
<td>Friable non-adherent</td>
<td>Dew drop, later matt, creamish, opaque</td>
<td>Narrow, stiff, sparse, disappearing with age</td>
<td>0</td>
<td></td>
<td>Slow, cloudy green orange</td>
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grown in culture were sometimes too few to account for the appearances of the fresh films. In the two acid-fast forms acid-fast rods were occasionally seen in large numbers in a pus cell, especially when filaments became scanty.

Isolation of actinomyces—It is difficult to grow the actinomyces from pus on artificial media. Successes recorded here followed several trials. Once started they are more easily propagated in subcultures.

Characteristics of the pus—The pus is thin, non-clotting and heavily loaded with polymorpho-nuclear leucocytes. Short branching hyphae may be obscured by other organisms or numerous specimens of pus may have to be searched before they are demonstrated. The filaments may break up into diphtheroid or coccoid bodies (spores) and one should regard pus containing such organisms with suspicion, especially when many are seen in pus cells. These diphtheroids and cocci are usually smaller than the natural organisms. For bacteriological examination swabs were taken from the depths of the wounds at operation or at routine changes of plaster. Direct films and blood-agar or glucose-broth cultures were made routinely (Fig. 3). In long-standing wounds the plates were dried in an oven for half an hour to inhibit B. proteus and B. pyocyaneus. Routine use clinically of penicillin and “phenoxtol” reduced the secondary infection and made the isolation of the actinomyces much easier. With experience it was found that certain modification of, or additions to, this technique were desirable:

1) A specimen of pus is preferable to swabs. “ Sulphur granules ” or tangled masses of hyphae may be visible to the naked eye.
2) Ziehl-Nielson staining short of full decolourisation was used to demonstrate the acid-fast actinomyces.
3) Phenoxtol-agar (2 per cent) proved useful in suppressing the growth of Gram-negative organisms.
4) The anaerobic and carbon dioxide jar was frequently used.
5) P. Amino broth, freshly boiled and cooled, was used for culturing micro-aerophilic organisms in the carbon dioxide jar.
6) Cultures were incubated for up to six days to allow for the slow growth of the actinomyces. The actinomyces was grown on at least one occasion in each of the six cases reported and in two it was isolated more than once. It seems reasonably certain that these organisms were not chance contaminants. Actinomyces were grown only from pus in which they had already been demonstrated and acid-fast forms retained their acid-fastness on culture. The only actinomycte contaminant found on old plates is a pink non-acid-fast variety.

Guinea pig inoculations—Four lots of three animals were inoculated intraperitoneally with agar cultures kept overnight in broth, from Cases 1, 2, 4 and 6. Owing to a technical fault the guinea pigs inoculated with cultures from Case 2 were not available for study.

Case 1—A guinea pig died on the thirteenth day and an autopsy showed a caseous mass in the abdominal wall and similar smaller nodules in the spleen. Histologically the lesions were typical of actinomycosis. Hyphae, coccoid and rod-like bodies were demonstrated. A second guinea pig died on the seventeenth day. Typical lesions and hyphae were found in the liver and spleen and a caseous mass occupied the space between the liver and duodenum.

Case 4—One guinea pig died on the fourteenth day. Lesions as already described were found in the spleen.

Case 6—One guinea pig died on the fourteenth day. At autopsy nothing definite could be found except one suspicious nodule in the liver.
DISCUSSION

The usual pathogen in man is the actinomyces bovis (Topley and Wilson 1946). Infection by aerobic, acid-fast and non-acid-fast actinomyces is rather infrequent. Mutation from anaerobic to aerobic types occurs in cultures but the opposite is very rare. Cope (1938) doubts whether the aerobic organisms can cause lesions in animals and man. In the present series there seems little doubt of their pathogenicity for the following reasons:

1) Of approximately fifty open fractures of the femur treated during the two years in question, only five failed to heal within a year. Three of these harbouring the actinomyces, one had a complicated sinus tract not amenable to radical surgery and one had sequestra on exploration. After sequestrectomy the wound showed signs of healing rapidly.

2) Metastatic spread was noted in one case (Case 4).

3) In another case (Case 6) a pure growth of aerobic actinomyces was obtained from a closed lesion.

4) Twelve guinea pigs were inoculated intraperitoneally with the organism. Four died. Nodules of granulation with loose strands of mycelia were detected in the spleen and mesenteric lymph glands at autopsy. One of these was an aerobic form.

![Graph showing penicillin sensitivity of actinomycetes in five patients.](image)

The mode of infection remains in doubt. Cope stated that the actinomyces is frequently found in the large gut and Boyd (1943) mentioned his experience of perianal lesions. Infection from the rectum is easy to understand in cases of wounds around the buttocks. In the two cases with chest injuries a fouled bed was common, as both patients were incontinent at some stage of their illness. On the other hand, infection may have been carried in by clothes or missiles at the time of injury. What factors determine the invasion of the tissues by the organisms remains doubtful.

**Treatment**—All patients had one or more operations. The site of infection was widely exposed and the wounds were treated by gauze packing. In the cases involving the femur, adequate splintage was provided. It may be suggested that the patients with involvement of the hip were not subjected to adequate drainage, or that they might have benefited from excision of the head and neck of the femur as advocated by the late G. R. Girdlestone. In reply, we would state that in two of the cases the sciatic nerve was already irreparably injured, so that posterior exposure of the affected joint was very extensive.

Three patients had prolonged treatment with potassium iodide, as advised by Cope, with little or no response. Chemotherapy by sulpha drugs in this group was disappointing,
in contra-distinction to the results obtained by Cope (1938), Ogilvie (1940), Lyons and Owen (1943), and Dorling and Eckhoff (1940). In spite of adequate dosage no permanent improvement was noted.

Three cases were treated by X-ray therapy. Two cases showed progressive improvement and one gave no response. In one patient (Case 6), infected with a penicillin-resistant strain of actinomyces, the lesion resolved after treatment by X-radiation.

Penicillin—The response to doses of the order one to one and a half million units was dramatic in the two patients with thoracic lesions. In both, the sinuses were healed and the patients afebrile within ten days of the beginning of treatment. Three patients with lesions involving the hip region did not heal on doses of this order; it remains to be seen whether they will do so on doses of penicillin up to eight or ten million units as recommended by Walker and Hamilton (1945), who claimed excellent results in a small group of cases treated over periods up to eighty days. The general condition of these patients has improved on prolonged treatment and the actinomyces is disappearing from the pus.

Ogilvie believes that the chemotherapeutic substance acts by damping down the secondary infection and the tissues then deal with the actinomyces. In the two cases here described which responded to penicillin, this explanation does not apply, for the concomitant organisms were insensitive to penicillin. It appears therefore that penicillin acts directly on the organism (Fig. 4). Results of local irrigation with zinc peroxide, penicillin and "phenoxetol" have been disappointing.

**SUMMARY**

1. Six cases of infection of wounds with actinomyces are described and the cultural characteristics of the organisms are discussed.
2. In three patients the infecting organism was an unusual aerobic form.
3. Possible sources of infection are considered.
4. The chronicity of the condition and the difficulty in treatment are stressed.
5. Penicillin and X-radiation hold out most hope of cure.

**REFERENCES**


