FURTHER EXPERIENCE IN THE MANAGEMENT
OF CHRONIC OSTEOMYELITIS

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Since the author's previous communication (Rowling 1959), in which fifty-eight cases were reported, further experience has confirmed the view expressed in that paper that chronic osteomyelitis is now a curable disease. Cure depended upon three main factors: adequate excision of diseased tissue; plastic reconstruction; and effective antibiotic treatment.

Of the three factors, wide excision of all sclerosed bone and fibrosed soft tissue as well as sequestrectomy, as was considered previously, is essential. The need for thorough surgery often resulted in operations of considerable magnitude, leaving a dead space to be filled by variable tissue, but this gave apparent cure in sixty-nine out of a total of seventy-seven consecutive cases (89.5 per cent).

Antibiotics alone cannot cure chronic osteomyelitis. They have therefore been used to control the spread of bacterial growth during operation and to prevent persistent infection. An antibiotic is now available which has been shown to penetrate even into avascular bone, but the basic principles of cure remain unchanged: without operation there can be no certainty that bactericidal levels are reached throughout the lesion or that the concentration can be maintained. Antibiotic drugs are used, as before, only in conjunction with surgery, and it cannot be emphasised too strongly that the first meeting of the antibiotic and the organism must be at operation in order to prevent resistance to the antibiotic.

CHOICE OF ANTIBIOTIC

In the past penicillin was the antibiotic of choice in treating staphylococcal bone infections. Penicillin-resistant bone infections are now so common (Harris 1960, Gilmour 1962, Sandeman 1965) that this drug is no longer considered best. There is also no evidence to suggest that penicillin itself, or its newer semi-synthetic derivatives, can penetrate avascular tissues. Many other anti-staphylococcal agents are of course available, of which some are bacteriostatic, but in osteomyelitis a bactericidal agent is essential; others, while effective, often produce toxic reactions especially when given in high dosage for prolonged periods.

Fucidin (sodium fusidate B.P.) was introduced into clinical medicine in 1962 and has been the subject of a considerable number of laboratory and clinical papers. A degree of synergism has been shown in vitro (Barber and Waterworth 1962, Waterworth 1963) between Fucidin and penicillin. The combination has also been shown to lessen the risk of resistance (Jensen and Kiae 1963). In the management of subacute or chronic osteomyelitis, Chater (1963) reported six patients whose infection healed after operation and concurrent administration of Fucidin and penicillin. Sinuses had been present for periods varying from three months to four years. Crosbie (1963), on the other hand, reported two long-standing cases of osteomyelitis which responded to Fucidin alone.

More recently, Hierholzer, Knothe, Rehn and Koch (1966) undertook a systematic investigation of Fucidin in the treatment of forty patients with chronic bone infection. Concentrations of the antibiotic were determined in serum, in bone and in sequestra. After several days' treatment at a dosage of 1.5 grammes per day they were able to show a mean concentration of Fucidin in infected bone of 7.3 micrograms per gramme. Not only did the authors conclude that Fucidin concentrations in chronically infected bone were adequate to inhibit the growth of staphylococci, but they also suggested that their findings justified a change
in the prevailing view that antibiotics could not penetrate into infected bone in adequate concentration.

Because of the in vitro evidence of a degree of synergy and the vital importance of preventing the development of antibiotic resistance, patients in the present series of cases were treated with a combination of Fucidin and penicillin. The antibiotics were given in a combined preparation containing 167 milligrams of Fucidin and 100 milligrams of calcium phenoxymethyl penicillin per capsule. The dosage varied, but an average of four capsules was given four times daily for two weeks, three capsules were given four times daily during the third week, and thereafter the dose was gradually reduced to two capsules three times a day for six to eight weeks. Sometimes treatment was continued longer. In some patients a 2 per cent solution of sterile Fucidin powder was introduced twice daily into the operation site to supplement the oral antibiotic.

**PATHOLOGY**

Details of the twenty-nine patients treated in this series are given in Table 1; the youngest patient was nine years old and the oldest seventy-six. The duration of the infection varied from a few months to fifty years; fourteen of the twenty-nine patients had suffered from the disease for four years or more. Acute or subacute osteomyelitis was the primary cause in ten patients and injury in another eleven. Miscellaneous causes, including infected haematoma, secondary infection in a tuberculous joint and cellulitis accounted for the remaining eight.

The sites involved were: tibia (eighteen patients); femur (eight patients); humerus (three patients); ulna (two patients); fibula (one patient). In three patients two bones were involved.

Before operation coagulase-positive staphylococcus aureus was cultured from the discharge in most patients. Sometimes there was a mixed bacterial colony including pyocyanus, escherichia coli and proteus. All the staphylococci were sensitive to Fucidin. In one patient a Fucidin-resistant strain was subsequently cultured, but primary healing occurred.

**PROCEDURE**

The patients were prepared for operation in the usual way; anaemia was corrected and other septic foci were eradicated. Diabetes and amyloid disease were excluded by testing three specimens of urine before operation, and no patient was found to have these diseases (neither of them is a bar to operation, but each is an imperative indication for cure).

Before operation three swabs of the lesion were tested for antibiotic sensitivity. Antibiotics were not used until the day before operation, when Fucidin and penicillin were given for twenty-four hours in full dosage. Intramuscular cloxacillin, 500 milligrams, replaced the dose of Fucidin immediately before operation, which at that time could be given only orally. Since then, O’Garra (1968) has reported on the use of intravenous Fucidin in two cases.

At operation the sinus was probed and followed to its extremity. Most of the mature fibrous tissue was excised. Meticulous clearing of all scar tissue was not done, but it was nevertheless considered unwise to leave too large a reservoir of avascular tissue where even Fucidin might not penetrate easily. All sequestra were removed and the cavity was fully explored; only the most avascular sclerosed bone was removed.

Relatively little surgical judgement was required previously when cure demanded total excision of the lesion; anything less might be followed by recurrence and extension of the disease. While the more limited operation carried out in this series is less demanding of technique it is more demanding of good judgement; thorough exploration is still imperative and cowardly or careless surgery still can lead to failure.

The cavity left after excision was treated by reconstructive surgery if the normal tissues lent themselves readily to it. In the outer thigh a little further excision of the fibrous tissue usually allowed the use of muscle graft from the vastus lateralis. Elsewhere, notably when the whole tibial shaft was involved, reconstruction was difficult and is now no longer considered
TABLE I
CLINICAL DETAILS OF TWENTY-NINE PATIENTS WITH CHRONIC OSTEOMYELITIS

<table>
<thead>
<tr>
<th>Case number</th>
<th>Age (years)</th>
<th>Site of lesion</th>
<th>Origin</th>
<th>Duration of infection (years months)</th>
<th>Result</th>
<th>Duration of follow-up (years months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38</td>
<td>Lower tibia</td>
<td>Infected compound fracture</td>
<td>13 0</td>
<td>Primary healing. Has remained healed</td>
<td>4 9</td>
</tr>
<tr>
<td>2</td>
<td>17</td>
<td>Lower tibia</td>
<td>Acute osteomyelitis</td>
<td>1 2</td>
<td>Primary healing. Has remained healed</td>
<td>4 8</td>
</tr>
<tr>
<td>3</td>
<td>37</td>
<td>Whole fibula</td>
<td>Acute osteomyelitis</td>
<td>24 0</td>
<td>Primary healing. Has remained healed</td>
<td>4 3</td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>Lower ulna</td>
<td>Acute osteomyelitis</td>
<td>0 11</td>
<td>Primary healing. Has remained healed</td>
<td>3 11</td>
</tr>
<tr>
<td>5</td>
<td>19</td>
<td>Femoral shaft</td>
<td>Acute osteomyelitis</td>
<td>10 0</td>
<td>Primary healing. Has remained healed</td>
<td>3 9</td>
</tr>
<tr>
<td>6</td>
<td>53</td>
<td>Lower femur</td>
<td>Probably infected haematoma</td>
<td>0 4</td>
<td>Primary healing. Has remained healed</td>
<td>3 9</td>
</tr>
<tr>
<td>7</td>
<td>32</td>
<td>Upper ulna, Lower humerus</td>
<td>Secondary infection in tuberculous joint</td>
<td>6 0</td>
<td>Occasional slight discharge. Invariably no pathogens cultured</td>
<td>3 6</td>
</tr>
<tr>
<td>8</td>
<td>76</td>
<td>Head and neck of femur</td>
<td>Infected nail-plate</td>
<td>0 8</td>
<td>Primary healing. Has remained healed</td>
<td>3 5</td>
</tr>
<tr>
<td>9</td>
<td>68</td>
<td>Upper tibia, Lower femur</td>
<td>Infected operation wound (arthrodesis)</td>
<td>25 0</td>
<td>Primary healing. Has remained healed</td>
<td>3 3</td>
</tr>
<tr>
<td>10</td>
<td>24</td>
<td>Lower tibia</td>
<td>Infected compound fracture</td>
<td>0 8</td>
<td>Primary healing. Has remained healed</td>
<td>3 3</td>
</tr>
<tr>
<td>11</td>
<td>35</td>
<td>Femoral shaft</td>
<td>Infected Kuntscher nail</td>
<td>0 11</td>
<td>Primary healing. Has remained healed</td>
<td>3 2</td>
</tr>
<tr>
<td>12</td>
<td>17</td>
<td>Upper femur</td>
<td>Infected fracture-haematoma</td>
<td>3 8</td>
<td>Primary healing. Has remained healed</td>
<td>3 2</td>
</tr>
<tr>
<td>13</td>
<td>41</td>
<td>Lower tibia</td>
<td>Infected compound fracture</td>
<td>5 3</td>
<td>Intermittent clear discharge for 3 months; healed after removal of foreign body. Thereafter remained healed</td>
<td>3 2</td>
</tr>
<tr>
<td>14</td>
<td>19</td>
<td>Upper tibia</td>
<td>Acute osteomyelitis</td>
<td>5 0</td>
<td>Primary healing. Has remained healed</td>
<td>3 1</td>
</tr>
<tr>
<td>15</td>
<td>73</td>
<td>Lower femur, Upper tibia</td>
<td>Acute osteomyelitis</td>
<td>4 1</td>
<td>Slow primary healing. Has remained healed</td>
<td>2 9</td>
</tr>
<tr>
<td>16</td>
<td>21</td>
<td>Middle tibia</td>
<td>Infected compound fracture, Non-union</td>
<td>0 5</td>
<td>Slow primary healing. Fracture united. Has remained healed</td>
<td>2 8</td>
</tr>
<tr>
<td>17</td>
<td>42</td>
<td>Upper tibia</td>
<td>Brodie's abscess</td>
<td>0 2</td>
<td>Primary healing. Has remained healed</td>
<td>2 6</td>
</tr>
<tr>
<td>18</td>
<td>17</td>
<td>Humeral shaft</td>
<td>Acute osteomyelitis</td>
<td>6 0</td>
<td>Primary healing. Has remained healed</td>
<td>2 4</td>
</tr>
<tr>
<td>19</td>
<td>53</td>
<td>Mid-shaft tibia</td>
<td>Primary subacute osteomyelitis</td>
<td>1 7</td>
<td>Primary healing. Has remained healed</td>
<td>2 1</td>
</tr>
<tr>
<td>20</td>
<td>35</td>
<td>Middle and upper tibia</td>
<td>Acute osteomyelitis</td>
<td>21 0</td>
<td>Primary healing. Has remained healed</td>
<td>2 0</td>
</tr>
<tr>
<td>21</td>
<td>26</td>
<td>Upper tibia</td>
<td>Infected subperiosteal haematoma</td>
<td>0 6</td>
<td>Primary healing. Has remained healed</td>
<td>1 10</td>
</tr>
</tbody>
</table>
essential: in such patients the skin was closed over a potential haematoma, usually after the wound had been flooded with 2 per cent Fucidin solution. In this series full thickness skin grafts were not needed, though there should be no hesitation in using this method if it is indicated. One or two drains were inserted through normal skin and totally occlusive dressings applied; the limb was enclosed in a well padded plaster or splint and elevated.

Suction drainage was continued for forty-eight hours, the first bottle being changed after twenty-four hours. Cultures from these bottles were nearly always sterile. Latterly, a solution of 2 per cent Fucidin was usually introduced into the wound through the drain twice a day: aseptic precautions were meticulous. Suction was applied for half an hour before the next local introduction. The volume of fluid introduced varied with the size of the cavity; it was given very slowly and was stopped if the patient complained of pain. The duration of local treatment, which varied between one and six weeks, depended on the rate of healing, which naturally varied with the site of the lesion, the age of patient, the density of fibrosis and the duration of infection. Absolute criteria for the duration of local therapy are not yet fully understood, but should become apparent as further experience is gained.

The wounds were dressed in the operation theatre on the fourteenth day after operation; immobilisation and elevation were usually continued for a further two weeks. A prolonged and careful watch was kept for any evidence of pyrexia or inflammation in the wound. The patient himself is often the best judge of a reactivation of infection and may volunteer information before signs become apparent.

**RESULTS**

Cure of chronic osteomyelitis can be only certain when the follow-up has extended over many years. However, in this series of twenty-nine patients, fourteen have been followed up.
for three years and over and a further thirteen for at least one year. On this basis, the results may be regarded as encouraging. Alternatively, it seems reasonable to use the incidence of primary healing as a measure of the effectiveness of treatment. Primary healing took place in twenty-five out of the twenty-nine patients. Their wounds have remained healed. (Two of these patients died from other causes seven and twenty-two months after operation.)

In three of the other four patients there was either a recurrent discharge or transitory breakdown in the immediate period after operation, but thereafter the wounds healed and have remained healed for not less than a year. In one of these three patients (Case 13) the cause of breakdown was a foreign body.

The affected leg of the remaining patient (Case 23) was severely oedematous and raw with eczema; the whole foot was rigid and painful. Culture revealed a copious growth of haemolytic streptococci, coliforms and proteus. He refused amputation until surgical exploration under Fucidin had failed. A below-knee amputation then healed by first intention. The case is included in the series only because it is rigidly consecutive.

In the series as a whole there have been no local complications such as pathological fracture or persistent pain. Pain before operation and stiffness in adjacent joints were not aggravated, and in most patients were improved; bone regeneration was satisfactory in all.

It is particularly encouraging that no toxic reactions to the drugs were noted, even though the Fucidin and penicillin combination was given for up to twelve weeks with an average total dose of seventy to eighty grammes of Fucidin. One patient complained of gastro-intestinal disturbance; this was never severe enough to warrant stopping the drug and was eased by giving the drug after meals or with an antacid. Another patient developed melaena but, because this has never been reported with either Fucidin or penicillin, it was possibly not related to the antibiotic therapy.

DISCUSSION

In the author's experience over the past sixteen years chronic osteomyelitis has been curable—at a price. The price paid for a 90 per cent chance of cure was twofold: antibiotics of varying toxicity had to be given for six to eight weeks or longer, and radical surgery was often needed. This approach was based on the belief that unless all tissue bearing a poor blood supply was excised the antibiotic could not be expected to reach the organisms in bactericidal concentration. Meticulous and often hazardous excision of all fibrosed soft tissue and sclerosed bone was vital: this had to be followed by the complete closure of the cavity with a muscle graft or a full thickness skin flap to ensure that a free blood supply containing the antibiotic reached the whole of the operation site. An operation of this magnitude often took three or four hours. Apart from the immediate and delayed hazards of the operation itself, such radical bone excision involved the risk of fracture until regeneration had occurred.

The price of cure appears to have been considerably reduced by the advent of an antibiotic with penetrating qualities. Equal care and greater judgement are required in treatment but, given Fucidin cover, the results appear so far to be equally good with a much less radical operation. It now seems unnecessary to excise more than the sequestra and most of the fibrous tissue. Reconstructive surgery to fill in the resulting cavity is seldom required, partly because the cavities are small and partly because suction drainage alternating with the introduction of Fucidin solution locally allows the cavity to close naturally without risk of an infected haematoma. With increasing experience, the extent of surgery has become even more limited. Early in the series patients were probably overtreated as regards the amount of tissue excised.

Despite the major change which has been brought about by the use of an antibiotic which can penetrate into avascular tissues, it must be stressed that the fundamental approach to the management of chronic osteomyelitis remains unchanged. The exhibition of antibiotics for days or weeks pre-operatively cannot be too strongly condemned. This cannot cure the
infection; it can only encourage resistant strains of staphylococci to develop. A high concentration of antibiotic must be delivered for the first time into the infected area as near to the moment of tourniquet release as possible.

Local Fucidin has been used more often in the more recent cases because of the impression that it contributes to a better result. Any haematoma which forms after operation carries an adequate antibiotic concentration for perhaps forty-eight hours, but the levels probably fall off after this period, thus increasing the risk of the development of resistant organisms. It seems logical to instil Fucidin solution into the wound through the drain in an effort to ensure that the cavity remains free from infection. Occasionally, the patient has found the pain of this intolerable, when it was either discontinued or the volume of the instillation decreased. It has not been used near a growing metaphysis. Further experience will be necessary before a final comment can be made on the local use of Fucidin as a supplement to systemic administration.

We cannot yet speak of cure. It can only be said that the wounds have remained healed up to the time of writing in all the surviving twenty-seven patients, though healing was slow in three and recurrences may yet occur in two. Thus a good prognosis can be given in 86 per cent of patients.

SUMMARY

1. The treatment of twenty-nine consecutive patients suffering from chronic osteomyelitis is reviewed. With the advent of an antibiotic, Fucidin, which has the ability to penetrate in significant amounts into tissues carrying a poor blood supply, a more limited surgical procedure has become possible.

2. A successful outcome, as judged by primary healing, was achieved in 86 per cent of patients treated with a combination of surgery and Fucidin with penicillin. This compares favourably with the results achieved in a previous series in which more radical surgery was undertaken.

3. Although Fucidin has advanced the treatment of chronic osteomyelitis, it is still essential to use surgery as well.

4. Fucidin caused no toxic effects despite an average total dose of seventy to eighty grammes. Resistance of the staphylococcus developed in vitro in one patient, without affecting a satisfactory clinical outcome.

REFERENCES


WATERWORTH, P. M. (1963): Apparent Synergy between Penicillin and Erythromycin or Fusidic Acid. Clinical Medicine, 70, 941.