TREATMENT OF ACUTE OSTEOMYELITIS IN CHILDHOOD

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A protocol of treatment for acute haematogenous osteomyelitis has been evaluated in 75 children. Intravenous cloxacillin and benzylpenicillin were given in hospital until the child had improved after which oral antibiotics and immobilisation were continued at home for a total of six weeks. Oral cloxacillin was used most frequently as *Staphylococcus aureus* was the major pathogen. Simple drainage of subperiosteal pus was carried out in the 17 children with clinical evidence of an abscess.

Ninety-two per cent of the 55 children with acute osteomyelitis diagnosed early were cured by a single course of antibiotics without an operation and with less than one week in hospital. Only 25 per cent of the 12 children with late-diagnosed acute osteomyelitis were cured with a single course of antibiotics and an operation. A longer period in hospital, a prolonged course of antibiotics, and secondary operations were required to cure the other children. Seven (88 per cent) of the eight neonates and infants with acute osteomyelitis were cured with a single course of antibiotics and an operation with only one to two weeks spent in hospital. The remaining infant was cured with a further course of antibiotics.

The overall cure rate with a single course of treatment was 83 per cent, and the remaining children were cured with further treatment. More children would be cured with a single course of antibiotics and immobilisation without the need for surgical intervention if treatment was started within one to two days of the onset of the illness rather than after four to five days when the disease is more advanced with the formation of an abscess.

Over the past decade many reports have shown that acute haematogenous osteomyelitis can be cured in childhood (Nade 1974). The methods of treatment include antibiotics, drainage of subperiosteal pus and immobilisation but there is considerable difference of opinion as to how these methods should be used. Our protocol of treatment was designed to achieve a rapid cure with the minimum amount of inconvenience for the child and for the family. The duration of intravenous antibiotic therapy as well as the length of hospital stay were kept to a minimum, operation being undertaken only when there were clinical signs of an abscess, and oral antibiotics and immobilisation of the limb were continued at home for six weeks in all. In this paper we report the details of this protocol, the early and late results achieved in 75 children, and a classification of acute haematogenous osteomyelitis which was found to be a useful guide to treatment and prognosis.

THE PROTOCOL

When the child is first seen, standard anteroposterior and lateral radiographs of the affected bone are taken and blood is collected for estimation of the haemoglobin, white cell count and erythrocyte sedimentation rate. The blood is also cultured and swabs are obtained from any infected lesions of the skin or upper respiratory tract.

Antibiotics. Cloxacillin in a dosage of 100 to 200 milligrams per kilogram body weight per day and benzylpenicillin in a dosage varying from 250 000 to 1 000 000 units are given intravenously every six hours. If the child is known to be allergic to penicillin, cephalothin is given instead of cloxacillin. The antibiotics are given via a paediatric burette incorporated into the intravenous line. Twenty to 30 millilitres of intravenous fluid are delivered into the burette to which the dissolved antibiotics are added and the concentrated solution is infused over a period of 5 to 10 minutes. As soon as the antibiotic sensitivities of the pathogen are available a single appropriate antibiotic is selected which is usually cloxacillin for *Staphylococcus aureus* and benzylpenicillin for Group A β-haemolytic streptococci. If bacteria are not isolated the antibiotics used initially are continued.

Intravenous antibiotics are continued until the child is seen to be clinically well, with less fever, and a decrease in the local signs. At this stage cloxacillin, phenoxymethylpenicillin (penicillin V) or cephalexin in a dosage of 100 milligrams per kilogram body weight per

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day are given by mouth in four doses. Food is not allowed for two hours before or for one hour after each dose. Antibiotic syrup is given to young children who are unable to take capsules or tablets. The children return home two days later, as long as they are well and tolerating the oral antibiotics. They are reviewed two weeks later and again after completing six weeks of treatment.

Surgical intervention. Incision and drainage of pus is carried out whenever there are clinical signs of an abscess. The soft tissue abscess is drained, the pus is cultured and soft tissue specimens are collected for histological examination, but the underlying bone is not drilled. In children with extensive bone destruction the biopsies are essential for the differential diagnosis from Ewing's sarcoma.

Immobilisation. With osteomyelitis of the shoulder girdle or humerus, the arm is supported in a sling. For osteomyelitis of the pelvis, bed rest is usually sufficient for inpatients but a hip spica is applied before the child returns home. Skin traction is applied to the leg whenever there is osteomyelitis of the proximal femur and a hip spica is also applied before the child returns home. Removable plaster splints are used for more distal parts of the skeleton and the plasters are completed before the children are discharged home.

Further treatment. At the end of six weeks a careful clinical examination is carried out and the initial haematological and radiological examinations are repeated. If the bone is still tender the oral antibiotics are continued for a further six weeks but in the absence of deep tenderness children with an elevated erythrocyte sedimentation rate, with or without lytic areas in the bone, are not given further antibiotics. All children are reviewed until radiological bone healing has occurred.

THE PATIENTS

Seventy-six children presented between January 1975 and December 1977 to The Royal Children's Hospital in Melbourne with their first attack of acute haematogenous osteomyelitis. Seventy-five of these children were included in this study but one child, who had an inherited severe immune deficiency, was excluded. The age distribution is shown in Figure 1. Forty-seven of the children were boys. The diagnosis of acute osteomyelitis was confirmed in all children by the radiological appearance of subperiosteal new bone or more extensive bone changes at some stage during the course of their illness. Osteomyelitis was observed in most bones but was more common in the bones of the leg (Table I). Patients with spinal osteomyelitis and discitis were not included in this study as the treatment used in this department has previously been reported by Menelaus (1964). The clinical stage of the disease and the age of the child were used to classify the children into three groups.

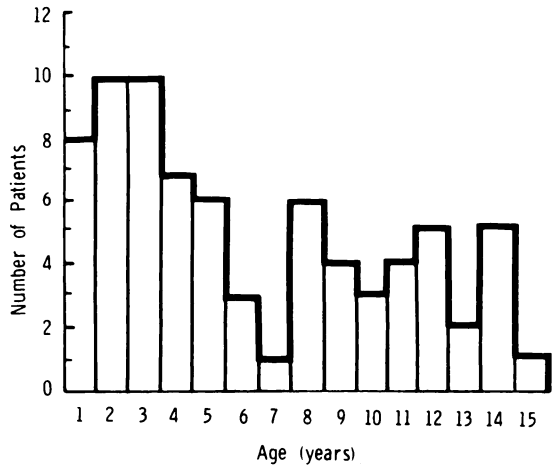

Fig. 1

Age distribution of patients with acute osteomyelitis.

Table I. Incidence of osteomyelitis at various sites

Site	Number of patients
Humerus	5
Radius	3
Ulna	1
Pelvis	8
Femur	22
Tibia	17
Fibula	9
Calcaneum	7
Talus	3

Group 1: early-acute osteomyelitis (55 patients). This was the major group and included children over the age of one year with an acute febrile illness of less than 48 hours' duration with localised pain, tenderness and swelling but without an abscess. The initial radiographs were normal except for swelling of the soft tissues. Half of the children had an erythrocyte sedimentation rate greater than 50 millimetres in the first hour and in three it exceeded 100 millimetres; 14 children had normal levels of less than 15 millimetres in the first hour.

Group 2: late-acute osteomyelitis (12 patients). This group included children over the age of one year who had severe osteomyelitis with an abscess. They presented five or more days after the onset of their illness and the radiographs usually showed bone destruction. The pelvis and the proximal humerus were particularly common sites in this group. The ages varied from 15 months to 13 years, but half of the children were over 10 years of age. The erythrocyte sedimentation rate was always elevated and 10 of the children had values greater than 50 millimetres in the first hour.

Group 3: neonatal and infantile acute osteomyelitis (eight patients). The diagnosis was often difficult in the five

neonates because of the variable clinical features. Two neonates were severely ill with septicaemia and pneumonia, and the lack of spontaneous movement of the limb was the first indication of osteomyelitis. The other babies were reasonably well and presented late with local tenderness and a large abscess and radiological evidence of subperiosteal new bone and areas of bone destruction. In all but one the erythrocyte sedimentation rate was raised but only two babies had levels exceeding 50 millimetres for the first hour.

BACTERIOLOGY

Blood was cultured from all patients and subperiosteal pus was cultured from 17 children. The types of bacteria isolated are shown in Table II. Thirty of the 55 children in Group 1 had positive blood cultures, while in Group 2 six children had positive pus cultures and five had positive blood and pus cultures. In Group 3, two children had positive blood cultures, one had a positive pus culture and two had a positive blood and pus culture.

Table II. Bacteria isolated from blood and pus

Bacteria	Number of patients			
	Group 1 *n=55*	Group 2 *n=12*	Group 3 *n=8*	Total *n=75*
Staphylococcus aureus	21	11	4	36
Group A β-haemolytic streptococcus	1		1	2
Haemophilus influenzae (Type b)	1			1
Staphylococcus albus	5			5
Achromobacterium	1			1
Diptheroides	1			1

Staphylococcus aureus was the commonest organism cultured in each group. The staphylococci were carefully monitored and, except for two isolates, all the cultures were resistant to benzylpenicillin but sensitive to cloxacillin and cephalothin. The Group A β-haemolytic streptococci were sensitive to benzylpenicillin. *Haemophilus influenzae* (Type b), sensitive to ampicillin, was isolated from the blood of a three-year-old child with osteomyelitis of the distal radius. *Staphylococcus albus, Achromobacterium* and diphtheroides were only isolated from blood cultures and may therefore represent skin contaminants.

METHODS OF ASSESSMENT

The initial response to treatment and the response after six weeks were assessed in every child. Sixty-four of the children were also reviewed two-and-a-half to four years later. This period of review was selected as it was well beyond the seven-month period during which most of the recurrences have been reported to occur (Blockey and Watson 1970). Forty-eight of the 55 children in Group 1, eight of the 12 in Group 2 and all of the neonates and infants in Group 3 were included in this review which included a careful history, physical examination and radiological examination of the affected bone. The 64 children reviewed represented all the children who were still living in the State of Victoria, the other 11 children had either moved to another state or had left Australia. Seven of the 11 children had been in Group 1 and had responded rapidly to antibiotic therapy and had shown complete bone healing within one year of the initial six-week course of treatment. The other four children had been in Group 2 and had had drainage of an abscess as well as antibiotic therapy and immobilisation. Three children responded rapidly to their treatment and follow-up radiographs showed that bone healing had been achieved with a single course of treatment. The fourth child had deep tenderness after the initial six-week course of treatment but was unavailable for follow-up. It was concluded that the 11 children were representative of the overall group and that their exclusion from the late review did not adversely affect the results.

RESULTS

Group 1: early-acute osteomyelitis. Fifty-one of the 55 children in this group had a rapid systemic and local clinical response in the first 24 to 48 hours of antibiotic treatment. Intravenous cloxacillin and benzylpenicillin were given during this period and were continued in the 25 children with negative blood cultures and in the seven children with positive blood cultures for *Staphylococcus albus, Achromobacterium* or diptheroides. Cloxacillin alone was used in the 21 children with positive *Staphylococcus aureus* blood cultures while benzylpenicillin alone was used in one child with a Group A β-haemolytic streptococcal infection; ampicillin was given to the only child in this series infected by *Haemophilus influenzae* (Type b). Intravenous antibiotics were given for an average of three days (range two to five days) before starting the oral equivalent. One to two days later the children returned home so that the average period in hospital was five days (range from four to seven days). When reviewed two weeks later the 51 children were well but four children had refused to take the cloxacillin syrup because of its unpleasant taste. Cephalexin syrup proved to be a satisfactory alternative.

When the 51 children were reviewed at the end of six weeks, 31 were found to be clinically normal with normal erythrocyte sedimentation rates and with radiographs which showed only a fine line of subperiosteal new bone and diffuse osteoporosis without any evidence of active infection (Table III). However, 20 patients had mildly elevated erythrocyte sedimentation rates with or without metaphysial lucencies. The elevated erythrocyte sedimentation rates were between 15 and 30 millimetres in the first hour and were seen in

Table III. Results after six weeks treatment

Result	Number of patients			
	Group 1 *n=55*	Group 2 *n=12*	Group 3 *n=8*	Total *n=75*
Normal	31	3	3	37
Metaphysial cavities	11		5	16
Elevated ESR*	6			6
Metaphysial cavities and elevated ESR	3	4		7
Tenderness and metaphysial cavities	3	1		4
Tenderness, metaphysial cavities and elevated ESR	1			1
Tenderness and sequestrum		4		4

*ESR Erythrocyte sedimentation rate

Table IV. Late results

Results	Number of patients			
	Group 1 *n=48*	Group 2 *n=8*	Group 3 *n=8*	Total *n=64*
Cure with initial six week course of treatment	44	2	7	53
Cure with initial 12 weeks of antibiotics	3	2	1	6
Cure with over 12 weeks of antibiotics		1		1
Cure with further antibiotics and surgery	1	3		4

children who initially had levels between 50 and 100 millimetres in the first hour. The metaphysial lucencies consisted of single or multiple cavities within the metaphysis. Forty-four of the 48 children available for review two-and-a-half to four years later (Table IV) were clinically and radiologically normal. They had been cured with the initial six-week course of antibiotic treatment, the metaphysial lucencies having healed spontaneously.

Four of the 55 children in Group 1 took five to six days to respond to the intravenous antibiotics. *Staphylococcus aureus*, sensitive to cloxacillin, was grown from the blood, and intravenous cloxacillin was continued for seven to nine days before starting the oral equivalent. The children returned home 9 to 11 days from the start of treatment. When reviewed two weeks later the four children were well, but at six weeks each child had deep tenderness and metaphysial lucencies, and one child also had an elevated erythrocyte sedimentation rate (Table III). A further six week course of oral cloxacillin was given to three children but the fourth child did not comply with the antibiotic treatment and 12 months later the osteomyelitis recurred. The cavity within the bone was opened and a further course of cloxacillin was given for six weeks. At the late review all four children were clinically and radiologically normal (Table IV).

Group 2: late-acute osteomyelitis. In addition to the antibiotics and immobilisation these 12 children were treated by incision and drainage of an abscess. Intravenous cloxacillin and benzylpenicillin were given for the first 24 to 48 hours followed by cloxacillin alone in the 11 children with positive cultures of *Staphylococcus aureus*, and cloxacillin and benzylpenicillin in the child with negative cultures. The severe pain experienced by these children was rapidly relieved by drainage of the subperiosteal pus, but the toxic features and fever lasted two to three days longer than was the case for the majority of patients in Group 1. As a consequence, the intravenous antibiotics were given for an extra two to three days and the period in hospital was extended to between 7 and 14 days.

After the six weeks course of treatment only three children were clinically normal with normal erythrocyte sedimentation rates and with radiological abnormalities confined to subperiosteal new bone and diffuse osteoporosis (Table III). These children had responded more rapidly to their initial treatment than the other children in this group. A further four children were clinically normal but their erythrocyte sedimentation rates were between 15 and 30 millimetres for the first hour and metaphysial cavities were noted on the radiographs. Oral cloxacillin was given for a further six weeks to three of the four children because of the extent of the bone destruction. The bone healed during the following two years.

At the six-week review one child had deep tenderness as well as metaphysial lucencies but bone healing occurred after a further six weeks course of oral cloxacillin. Four children were noted to have deep tenderness and a sequestrum. These children were over the age of 10 years, had severe osteomyelitis with large abscess cavities and had responded slowly to the intravenous antibiotics. In one child a small sequestrum resolved with further antibiotics while in three children the sequestra persisted despite antibiotics being given for several months. Acute flares occurred in these three children from 8 to 14 months from the onset of their disease and sequestrectomies were performed and further antibiotics given. Final review of eight patients, including four without a sequestrum and four with one, was made (Table IV). The four children without a sequestrum were normal. Complete healing after a further course of antibiotics had occurred in one child with a sequestrum and also in the other three children one-and-a-half, two and three years after sequestrectomy.

Group 3: neonatal and infantile acute osteomyelitis. Seven of the eight neonates and infants were initially given intravenous cloxacillin and benzylpenicillin while one infant, who was allergic to penicillin, was given

intravenous cephalothin. Intravenous cloxacillin and benzylpenicillin were continued in the three children with negative cultures, while cloxacillin alone was used in three of the children with positive *Staphylococcus aureus* cultures. Cephalothin was used in one child with a positive *Staphylococcus aureus* culture and benzylpenicillin alone was used in the child with a Group A β-haemolytic streptococcal infection. In five children an abscess was drained.

All the children responded rapidly to their treatment. Intravenous antibiotics were continued for five to nine days and all children were discharged home between the seventh and fourteenth day. At the end of six weeks all the neonates and infants were clinically normal but five children had metaphysial lucencies. A second six-week course of oral cloxacillin was given to one child with extensive bone destruction.

Final review of the eight neonates and infants showed that in each case the infection had been cured without further treatment and that remodelling of the bone had occurred over the first year (Table IV). One child, who had a Group A β-haemolytic streptococcal osteomyelitis of the distal radius with an abscess, had a partial arrest of the distal radial growth plate with radial deviation of the hand.

Combined results. Eighty-three per cent of the 64 children included in the late review were cured with their initial six-week course of treatment. However, when the results in each group were analysed separately it was observed that the initial treatment had been successful in 92 per cent of patients in Group 1, in 25 per cent of patients in Group 2, and in 88 per cent of patients in Group 3. The late review also showed that a cure had been achieved in seven children with further courses of antibiotics, and in four other children with further courses of antibiotics and operative drainage or sequestrectomy. At late review no child had residual infection but one infant had a permanent partial arrest of the growth plate of the distal radius.

DISCUSSION

The protocol of treatment used in this study has been shown to be simple and effective. The overall cure rate achieved with a single course of treatment was 83 per cent which is similar to the cure rates reported by Blockey and Watson (1970) and Blockey and McAllister (1972). Although many authors group the results of all their patients together, Green (1967) and Khazenifar, Weighill and Stanley (1978) have shown that the stage of the disease and the age of the child need to be taken into consideration. We agreed with this and classified our patients into early-acute osteomyelitis, late-acute osteomyelitis and neonatal and infantile acute osteomyelitis. We routinely use this classification as it enables us to give the parents realistic information about the expected period in hospital, the likelihood of further treatment being required and the ultimate prognosis.

Our results indicate the importance of early diagnosis within the first 24 to 48 hours and before a clinical abscess appears; a cure can then be achieved with a single course of antibiotics and immobilisation without the need for operation. In this series a delay in diagnosis of four to five days was the major factor responsible for children presenting with a clinical abscess. In the neonatal and infantile group the local symptoms and signs of osteomyelitis were frequently not detected until an abscess had formed. On the other hand most of the older children had sought medical care within one to two days of the onset of their illness, and although the site of the acute problem was noted the correct diagnosis was often not made until many days later. This was most commonly seen in children over the age of 10 years with osteomyelitis of the pelvis and proximal humerus. Delayed diagnosis of septic arthritis also occurs in these age groups for similar reasons (Cole, Elliott and Jensen 1975).

The choice of antibiotics used within the first 24 to 48 hours was based on our observations that during the previous five years *Staphylococcus aureus* had been the most commonly found organism and Group A β-haemolytic steptococcus the second most common. The pattern of the organisms we cultured was in keeping with this experience. The majority of children with an abscess had positive blood and pus cultures but pus cultures were often positive when blood cultures were negative although the patterns of organisms were the same. It was noted that half the children without an abscess had negative blood cultures but, as all these children responded rapidly to cloxacillin and benzylpenicillin, we did not feel that it was necessary to aspirate the site of the osteomyelitis to achieve a higher number of positive cultures.

Cloxacillin proved effective against *Staphylococcus aureus* and the cephalosporins were effective alternatives. Clindamycin, which has also been shown to be an effective agent, has been reported to produce pseudomembraneous colitis in adults (Tedesco, Barton and Alpers 1974) and although this serious and potentially fatal complication appears to be rare in children it is still a matter of concern (Wharton and Beddow 1975; Geddes *et al.* 1977). Fusidic acid has been shown by Blockey and McAllister (1972) to be effective, but in this hospital it is reserved for use against staphylococci which are resistant to cloxacillin. We will continue to use computer techniques to monitor the types of bacteria in the community and their antibiotic sensitivities. The antibiotic regime will be changed if sensitivities change.

We agree with Tetzlaff, McCracken and Nelson (1978) and with Kolyvas *et al.* (1980) that the results achieved with a short course of intravenous antibiotics followed by oral antibiotics for six weeks are as good as those achieved with prolonged intravenous therapy (Dich, Nelson and Haltalin 1975). In our study we have

also shown that oral antibiotics can be successfully continued at home and this programme significantly reduced the time in hospital, the inconvenience for the child and the parents and the overall cost of treatment. Tetzlaff *et al.* (1978) and Kolyvas *et al.* (1980) have recommended that oral antibiotics should only be given in hospital but, although it is more difficult to ensure compliance with home therapy, the parents in our study made a concerted effort to give their children the antibiotics in the prescribed manner; it is important to start the oral antibiotics in hospital to ensure that the child is able to tolerate them. Some difficulties were encountered with the cloxacillin syrup which had an unpleasant taste but the cephalexin or flucloxacillin syrups proved to be suitable alternatives.

The dose of antibiotics was regulated according to the clinical severity of the disease and the response to treatment. As the majority of the patients responded rapidly we did not consider that it was necessary to regulate the dose according to the blood levels of the antibiotics or to the *in vitro* serum bactericidal titres which have been recommended by others for routine use (Tetzlaff *et al.* 1978; Bryson *et al.* 1979; Kolyvas *et al.* 1980). However, these tests may be helpful in patients who are responding slowly to the antibiotic treatment.

In this study, a six-week course of antibiotics was always used. It is possible that the three-week course of treatment recommended by Blockey and Watson (1970) would have been sufficient for the children in Group 1 but a six-week course appears to be essential for children with more advanced disease. We are in agreement with Blockey and Watson (1970) that further treatment is not required for children with metaphysial lucencies and elevated erythrocyte sedimentation rates as long as deep tenderness is absent. We also observed that the metaphysial lucencies progressively healed over the following one to one-and-a-half years without further treatment.

We agree with Blockey and Watson (1970) that operation should only be done when there is clinical evidence of an abscess. Using this indication, only 22 per cent of the children in this series needed an operation as compared with 50 per cent (Blockey and Watson 1970), 75 per cent (Khazenifar *et al.* 1978) and 89 per cent (Wharton and Beddow 1975) of other series. These findings indicate that the number of children with clinical evidence of an abscess varies in different centres reflecting differences in the virulence of the organism, the resistance of the host or a delay in presentation to hospital.

Mollan and Piggot (1977) have a different approach and recommend that surgical exploration is mandatory in all cases, regardless of whether there are clinical signs of an abscess or not. However, if such a policy had been used in our study, 78 per cent of the children would have had an unnecessary operation and an unnecessary scar.

The operation was limited to incision and drainage of the abscess. We did not drill or unroof the bone because, when these procedures were previously used as a routine in this department, pus under pressure had rarely been found. This view is supported by Gilmour (1962) and by Blockey and Watson (1970). It is also unlikely that more extensive surgery would have prevented the formation of sequestra in our older children with large subperiosteal abscess cavities since interruption of the blood supply to the bone would have occurred before the children presented to this hospital.

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