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ANTIBIOTIC PROPHYLAXIS IN OPEN AND CLOSED FRACTURES

A Controlled Clinical Trial

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The value of prophylactic antibiotics in fracture surgery was studied in a series of 90 patients with open fractures of various bones and 180 patients with closed malleolar fractures treated by open surgery. Dicloxacillin and benzyl penicillin were compared to saline (placebo).

The soft tissue lesions of the open fractures were divided into Grade I wounds and Grade II & III wounds. Of the patients with Grade I wounds, 17 received dicloxacillin, 21 benzyl penicillin and 17 saline. No major infections occurred. Twelve patients with Grade II & III wounds were treated with dicloxacillin, 10 with benzyl penicillin and 13 with saline. In the saline group, 2 patients developed a deep infection.

Fifty-eight patients with closed malleolar fractures received dicloxacillin, 59 benzyl penicillin and 63 saline. Two infections developed in the placebo group. A statistically significant difference was found between the number of infections in the antibiotic groups and the number in the placebo group.

Superficial thromboplebitis following the antibiotic infusion occurred in 16 per cent of the dicloxacillin treated patients and in 1 per cent of those treated with benzyl penicillin or placebo.

Key words: antibiotics; fractures; wound infection

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Antibiotic prophylaxis is routinely used in many departments of orthopaedic surgery in connection with skeletal surgery. Its efficiency has been confirmed in clinical practice (Amstutz 1970, Aglietti et al. 1973, Ericson et al. 1973, Lidgren & Sandegård 1977, Wilson et al. 1975).

The present report considers the clinical efficiency of antibiotics in preventing postoperative wound infections in open and closed fractures.

PATIENTS AND METHODS

This study was performed over 30 months, from August 1974 to January 1977.

Two groups of patients were studied: 90 patients with fractures and concomitant skin and soft tissue injuries, and 180 patients with closed malleolar fractures treated by open surgery. The skin and soft tissue injuries were classified as stab wounds and lacerations. Stab wounds (Grade I) were defined as skin injuries of less than 2 cm, without loss or contusion of soft tissue, caused by external or internal perforation. Lacerations (Grade II & III) were defined as wounds exceeding 2 cm with a varying degree of soft tissue damage. The grading refers to that of Gustilo & Anderson (1976). Fifty-five of the patients had stab wounds (Grade I) and 35 had laceration (Grade II & III) injuries. Of the patients with stab wounds, 30 were men with a mean age of 44 years (range 17 to 85 years), and 25 women with a mean age of 69 years (range 16 to 85 years). The corresponding distribution among the laceration injuries was 29 men with a mean age of 42 years (range 16 to 74 years), and 6 women with a mean age of 57 years (range 49 to 66 years). These patients constituted all patients treated for shaft fractures of the limbs during the investigation

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Table 1. Number of stab wounds and lacerations in the different locations of the extremities

Fracture location	Stab wound	Laceration	Total
Upper arm	6	4	10
Fore arm	18	1	19
Thigh	2	1	3
Lower leg	23	14	37
Ankle	4	13	17
Midfoot	2	2	4
Total	55	35	90

period who had skin and soft tissue injuries. The laceration injuries were often caused by traffic accidents while penetrating wounds were caused primarily by low energy trauma.

Table 1 shows the fracture location in the open fractures. Shaft fractures of the lower leg were the most frequent and also caused the greatest therapeutic problems; the skin injury was often considerable, particularly when high energy trauma prevailed.

The closed malleolar fractures included all those treated surgically during the period of the study. Of the 180 patients, 88 were men with a mean age of 43 years (range 17 to 80 years) and 92 women with a mean age of 51 (range 19 to 78 years).

The treatment of the skin and soft tissue injuries was surgical excision of necrotic and contaminated tissue and primary suture. The fractures were predominantly treated by external fixation with a plaster cast or percutaneous pin fixation as recommended by Hoffman and Vidal-Adrey. The only internal fixation used was cerclage wires or lag screws. The closed fractures were all treated within 12 hours with open reduction and internal fixation using wire-loops, small nails and clamps. Postoperatively a below-knee plaster cast was applied. This was changed after 2 weeks when the sutures were removed. The total plaster immobilization period was 6 to 8 weeks.

The patients were treated with either dicloxacillin, benzyl penicillin or saline (placebo). The drugs were packed in coded boxes according to random number, each box containing divided doses for a treatment period for one patient. The patients were randomly allocated to treatment and the drugs were given by intravenous infusion during 30–60 minutes. The first dose was given preoperatively and the infusions were repeated every 6 hours for 2 days, i.e., 8 doses were given altogether. Each dose contained either 2 g dicloxacillin, 3 million IU benzyl penicillin or 100 ml of saline.

The patients were given no other antibiotic therapy. All patients were followed until the wounds had healed. All complications were recorded. Aerobic and anaerobic bacterial cultures were taken in cases of prolonged wound healing or wound drainage. Late infections and fracture healing were not evaluated in this study. The code was broken when all patients had been followed up.

Complications of healing were defined as follows: A wound was considered superficially infected when signs of inflammation were present, i.e., suprafascial drainage and a positive bacterial culture. Deep infection was defined as a subfascial process going down to the bone or osteosynthesis material. Superficial thromboplebitis was defined as a palpable fibrotic vessel or visible inflammation along the course of the infused vessel.

Statistical analysis was performed using the chi-square-test.

Difficulties in dissolving the dicloxacillin powder creating floculation were often encountered, leading to discontinuation of the prophylaxis in 5 patients. These patients are not included in the study.

RESULTS

In the 55 patients with stab wounds, superficial infections occurred in 2 patients in the placebo group and in one following dicloxacillin treatment (Table 2). All these patients had sustained tibial shaft fractures and the wounds had necrotic skin areas. No deep infections occurred in this group.

Five superficial infections occurred in the 35 fractures with laceration injuries. Two of these were in the group treated with dicloxacillin, one in the group treated with benzyl penicillin and 2 in the group receiving placebo (Table 2). Two deep infections occurred in patients with lacerations, both in the placebo group. In one of the infections hemolytic streptococci were cultured (Table 3). Since that patient had a throat infection it is possible that this was a secondary infection. The other infection developed in an anterior skin flap following a Symés amputation. Cultures from the wound and the blood in that patient revealed penicillin-sensitive Staphylococcus aureus and Enterococci. Treatment with penicillin and with secondary revision was unsuccessful and a below-knee amputation was finally performed.

The closed ankle fractures were complicated by superficial infections in 18 cases. Two patients in the placebo group developed deep infections (Table 2). Staphylococcus aureus resistant to penicillin was cultured in both cases. Both healed eventually without osteitis.

Table 2. Frequency of superficial and deep infections according to treatment in open and closed fractures

	Open Fractures				Closed Fractures	
	Grade I $n=55$		Grade II–III $n=35$		$n=180$	
	Superf inf	Deep inf	Superf inf	Deep inf	Superf inf	Deep inf
Dicloxacillin $n=87$	1	0	2	0	4	0
Benzyl penicillin $n=90$	0	0	1	0	8	0
Saline $n=93$	2	0	2	2	6	2
Total	3	0	5	2	18	2

Regarding the superficial infections, there are no statistically significant differences within the sub-groups or in the total material. The bacteriological patterns (Table 3) reveal some traits, however. The most frequently cultured organism was Staphylococcus epidermidis. It was found mainly in the placebo group. Staphylococcus aureus resistant to penicillin was predominantly cultured from patients receiving penicillin and dicloxacillin. Gram negative bacteria were infrequent. All these infections healed eventually with local treatment. Whether or not supplementary treatment with systemic antibiotics was instituted seemed to make no difference.

All the deep infections occurred in the placebo group. There is no statistically significant difference between the results of treatment in the fracture sub-groups. When the two groups treated with antibiotics are compared with the placebo group there is such a difference ($P < 0.01$). However, it must be emphasized that the patients with open fractures were subjected to early treatment rather than true prophylaxis as opposed to the patients with closed fractures. The main cause of deep infection was Staphylococcus aureus.

Complications of treatment

In the dicloxacillin group a rash was found in one patient, while 2 patients complained of itching and of nausea, respectively. Superficial thromboplebitis was found in 16 per cent in this group. In the other two treatment groups the only complication recorded was superficial thromboplebitis in one patient in each of the groups.

Table 3. Bacteria found in the superficial and deep wound infections in the various treatment groups in the total material

	Dicloxacillin		Penicillin		Placebo		
	Superficial	Deep	Superficial	Deep	Superficial	Deep	Total
Staph aureus resistant type	3	–	4	–	1	2	10
Staph aureus nonresistant	1	–	–	–	2	1	4
Staph epidermidis	–	–	3	–	6	–	9
Pseudomonas	1	–	1	–	1	–	3
Streptococcus	–	–	–	–	–	1	1
Entrococcus	–	–	–	–	–	1*	1
Other	2	–	1	–	–	–	3
Total	7	–	9	–	10	5	31

* Mixed with Staphyloccus aureus in one wound.

DISCUSSION

Open fractures represent a major therapeutic problem because the results of treatment are often jeopardized by infection. Lidgren & Lindberg (1972) found a total infection rate of 15 per cent after open fractures. In patients with large soft tissue lacerations the infection rate increased to 50 per cent. The importance of adequate debridement has been emphasized in large series (Brown 1973a, b, Copeland & Enneking 1965, Daland 1934, Davis 1948, Edwards 1965 and 1970, Epps & Adams 1961, Gustilo 1971, Gustilo & Anderson 1976, Gustilo et al. 1969). In these reports it is stated that the most important factor determining the outcome of healing is the soft tissue damage, the extent of which is directly related to the energy of the trauma.

No antibiotic can replace proper surgical management. The wound should be thoroughly cleaned and all damaged tissue removed, so that clean, viable tissue surfaces are obtained in all parts of the wound. Special care should be taken to remove all damaged muscle tissue. In doubtful cases secondary closure is recommended (Epps & Adams 1961).

In the present study primary skin cover was always attempted. In only a few patients was delayed primary suture applied. These wounds all healed without complications.

The fractures which caused the greatest problems were the tibial shaft fractures. This is in agreement with previous publications (Cox et al. 1970, Edwards 1965, Mattsson 1975, Norberg 1976, Rosenthal et al. 1977, Veliskakis 1959). Stable fixation is recommended for good healing of the wound as well as the fracture (Müller et al. 1979). However, the majority of our fractures may not have met the criterion of stable fixation according to the AO school (i.e., those treated by pins incorporated in plaster or in internal fixation consisting of a cerclage wire). Rittman et al. (1979) have shown that internal fixation with plates or intramedullary nails does not increase the risk of infection.

The present material is too small for extensive conclusions. However, the low frequency of infections among the patients with open fractures is striking. There might be several reasons for this, such as the short interval between the accident and admission as is the case in an urban area, and the meticulous revision done by surgeons not knowing what treatment, if any, the patients were being given. The same number of infections was found among the patients with Grade II & III open fractures and closed ankle fractures. The patients with the latter ailment might have been suffering from other conditions lowering their resistance to infection.

The present study may indicate that prophylaxis has a place in the routine treatment of open fractures with severe soft tissue damage (although this is by no means proved). This is in agreement with previous studies by Patzakis (Patzakis et al. 1974, Patzakis 1975), who compared equivalent groups without antibiotic treatment and those treated with a combination of penicillin and streptomycin, and cephalosporin. The infection rates of these groups were 14, 10 and 2 per cent, respectively. Rittman et al. (1979) found antibiotics beneficial in laceration injuries.

It has been shown in animal experiments as well as in clinical series that prophylaxis should start within 3 hours after the injury or operation to be maximally efficient (Alexander et al. 1960, Burke 1961, 1975, 1976). Circulatory disturbances arise after this period and the bacteria begin to multiply (Bowers et al. 1973). In accordance with this it is recommended that antibiotic administration be started as soon as possible after the patient is admitted to the hospital. Concerning open fractures, it is a matter of dispute whether the preoperative administration of antibiotics is prophylaxis in its true sense or an early treatment. It should be emphasized that surgery represents a new trauma, leading to hyperemia of the fracture region with local concentration of antibiotics (Bergman 1979, Kondo 1972). Burke (1976) stated that the prophylaxis need not be continued for more than 3 hours although Patzakis (1975) recommended 3 days. For the present study 2 days were chosen.

The choice of antibiotics for prophylaxis is a rather difficult question. Lidgren & Lindberg (1972) stated that a change in the bacterial flora in orthopaedic infections has occurred during a 10-year period from Gram-positive (78.8 to 57.0 per cent) to Gram-negative (23.6 to 40.5 per

cent). In a series of infections following general surgery, Bröte & Niléhn (1976) reported that 45.3 per cent of the strains were sensitive to penicillin G. In our experience, Staphylococcus aureus is the predominate cause of infection (Backelin et al. unpublished data).

Lindgren & Sandegård (1977) recommended benzyl penicillin or, under special circumstances, isoxazolyl penicillin combined with ampicillin. Gustilo (1971, 1976) tried penicillin in combination with various broad spectrum antibiotics and finally recommended cephalosporin derivatives. The present study does not indicate a clear-cut superiority for either of the two antibiotics used. It might be stated that penicillin seems to be better than no antibiotic at all and that the use of dicloxacillin is a further improvement. In the bacteriological situation described (Table 3) there seems to be no need for broad spectrum antibiotics, which might cause an ecological disturbance. These hypotheses are all in accordance with other results of ours (Backelin et al. unpublished data).

The most common complication of prophylaxis encountered in this trial was superficial thromboplebitis following intravenous administration. This was particularly common in the dicloxacillin group. This has been shown in animal studies. Gottlob (1972) studied different isoxazolyl penicillins, benzyl penicillin and ampicillin and found that dicloxacillin gave the highest incidence of endothelial damage. This was verified also by Sinapius & Brundel (1975), who showed that a 5 per cent solution of dicloxacillin caused maceration of the vascular endothelium. Because of these experiences we prefer cloxacillin and benzyl penicillin for intravenous administration.

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REFERENCES

Aglietti, P., Salvati, E. A. & Wilson Jr., P. D. (1973) A study of the effectiveness of a surgical unidirectional filtered air flow unit during total prosthetic replacements of the hip. *Arch. Orthop. Unfallchir* **77**, 257–268.

Alexander, J. W., McGloin, J. J. & Altmeier, W. A. (1960) Penicillin prophylaxis in experimental wound infections. *Surg. Forum* **11**, 299–300.

Amstutz, H. C. (1970) Complications of total hip replacement. *Clin. Orthop.* **72**, 123–137.

Backelin, B., Bergman, B. & Brandberg, Å. Unpublished data.

Bergman, B. R. (1979) Study of the concentration of dicloxacillin and benzyl penicillin in fracture surgery. *Scand. J. Infect. Dis.* **11** (3), 225–228.

Bowers, W. H., Wilson, F. C. & Greene, W. B. (1973) Antibiotic prophylaxis in experimental bone infections. *J. Bone Joint Surg.* **55**-A, 795–807.

Brown, P. W. (1973a) The prevention of infection in open wounds. *Clin. Orthop.* **96**, 42–50.

Brown, P. W. (1973b) The open fracture. Cause, effect and management. *Clin. Orthop.* **96**, 254–265.

Bröte, L. & Niléhn, B. (1976) Wound infections in general surgery with special reference to the occurrence of Staphylococcus aureus. *Scand. J. Infect. Dis.* **8**, 89–97.

Burke, J. F. (1961) The effective period of preventive antibiotic action in experiment incisions and dermal lesions. *Surgery* **50**, 161–168, 184–185.

Burke, J. F. (1975) Preventive antibiotics in surgery. *Postgrad. Med.* **58**, 65–68.

Burke, J. F. (1976) Pin pointing the critical hours in wound sepsis: Timing is the key in preoperative antibiotics use. The Surgical Team. Jan–Feb, 30–32.

Copeland, C. X. & Enneking, W. F. (1965) Incidence of osteomyelitis in compound fractures. *Am. Surg.* **31**, 156–158.

Cox, G. W., Burke, J. F. & Evans, E. (1970) Compound fractures of the tibia. *South. Med. J.* **63**, 1409–1414.

Daland, E. M. (1934) A study of two hundred and thirty-six compound fractures treated at the Massachusetts general hospital. *New Engl. J. Med.* **210**, 983–995.

Davis, A. G. (1948) Primary closure of compound-fracture wounds. *J. Bone Joint Surg.* **30**-A, 405–415.

Edwards, P. (1965) Fractures of the shaft of the tibia: 492 consecutive cases in adults. Importance of soft tissue injury. *Acta. Orthop. Scand.*, Suppl. 76.

Edwards, P. (1970) Frakturer på underbenet – den akuta hudskadan. Read at the XXVIIth meeting of the Swedish Medical Association, November 26, 1970.

Epps, C. H. & Adams, J. P. (1961) Wound management in open fractures. *Am. Surg.* **27**, 766–769.

Ericson, C., Lidgren, L. & Lindberg, L. (1973) Cloxacillin in the prophylaxis of postoperative infections of the hip. *J. Bone Joint Surg.* **55**-A, 808–813.

Gottlob, R. (1972) Endothelschädigungen durch introvasale Injektion von Arzneimitteln. *Arzneim. Forsch.* **22**, 1970–1975.

Gustilo, R. B. (1971) Management of open fractures. *Minn. Med.* **54**, 185–189.

Gustilo, R. B. & Andersson, J. T. (1976) Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones. *J. Bone Joint Surg.* **58**-A, 453–458.

Gustilo, R. B., Simpson, L., Nixon, R., Ruiz, H. & Indeck, W. (1969) Analysis of 511 open fractures. *Clin. Orthop.* **66**, 148–154.

Kondo, S. (1972) Experimental studies on the chemotherapy of open fractures (Part 5): Clinical studies on the distribution of glycosidic antibiotic concentrations in bone marrow and in fracture hematomas. *Bull. Osaka Med. Sch.* **18**, 98–114.

Lidgren, L. & Lindberg, L. (1972) Orthopaedic infections during a 5-year period. *Acta Orthop. Scand.* **43**, 325–334.

Lidgren, L. & Sandegård, J. (1977) Infektionsförebyggande rutiner vid frakturkirurgi på svenska sjukhus 1975. *Läkartidningen* **74**, 640–642.

Mattsson, S. (1975) Behandling av diafysärt underbensbrott. *Läkartidningen* **72**, 2039–2041.

Müller, M. E., Allgöwer, M., Schneider, R. & Willenegger, H. (1979) *Manual of internal fixation.* 2nd Edition. Springer Verlag, Berlin, Heidelberg, New York.

Norberg, L. (1976) Öppen cerclage behandling af tibia diafysfrakturer. Dissertation Göteborg.

Patzakis, M. J. (1975) The use of antibiotics in open fractures. *Surg. Clin. North Am.* **55**, 1439–1444.

Patzakis, M. J., Harvey, J. P. & Ivler, P. (1974) The role of antibiotics in the management of open fractures. *J. Bone Joint Surg.* **56**-A, 532–541.

Rittmann, W. W., Schibli, M., Matter, P. & Allgöwer, M. (1979) Open fractures. Long term results in 200 consecutive cases. *Clin. Orthop.* **138**, 132–140.

Rosenthal, R. E., MacPhail, J. A. & Ortiz, J. E. (1977) Non union in open tibial fractures. *J. Bone Joint Surg.* **59**-A, 244–248.

Sinapius, P. & Bründel, K. H. (1975) Endothelschädigung durch die halbsynthetischen penicilline Cloxacillin, Dicloxacillin und Flucloxacillin. *Vasa* **4**, 54–58.

Veliskakis, K. P. (1959) Primary internal fixation in open fractures of the tibial shaft. *J. Bone Joint Surg.* **41**-B, 342–354.

Wilson, P. D., Salvati, E. A. & Blumenfeld, E. L. (1975) The problem of infection in total prosthetic arthroplasty of the hip. *Surg. Clin. North Am.* **55**, 1431–1437.

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