The Journal of
Bone and Joint Surgery

American Volume

VOLUME 60-A, No. 7 OCTOBER 1978

Treatment of Orthopaedic Infections with Electrically Generated Silver Ions

A Preliminary Report*

BY ROBERT O. BECKER, M.D.†, AND JOSEPH A. SPADARO, PH.D.†, SYRACUSE, NEW YORK

From the Veterans Administration Hospital and the Department of Orthopaedic Surgery, State University of New York, Upstate Medical Center, Syracuse

ABSTRACT: **Electrically generated silver ions have been shown previously to be a potent antibacterial agent with an exceptionally broad spectrum as indicated by *in vitro* testing. The present study reports on clinical experience using electrically generated silver ions as adjunctive treatment in the management of chronic osteomyelitis. Fourteen patients had fifteen treatment attempts: thirteen for chronic osteomyelitis of the tibia, one for acute and chronic pyarthrosis and osteomyelitis of the knee, and one for a chronically draining sinus after total hip replacement. Wound débridement, silver ion iontophoresis, and subsequent wound care (usually provided by the patient) resulted in control of the infection in twelve of the fifteen treatment attempts and in healing of the non-union after follow-up ranging from three to thirty-six months. The other three attempts led to two partial and one complete failure.**

In the treatment of chronic osteomyelitis, many antibiotics have been used locally and systemically to control the infecting organisms, but none of the agents used either singly or in combination has been consistently effective[4,5,7,10,13,14]. For the past three years we have been evaluating the possibility of using silver ion iontophoresis as a bactericide in infected tissue.

The bactericidal properties of silver have been known for a long time[6], but as currently applied its clinical utility is limited. The diffusion of silver ions from a metallic surface such as silver foil is negligible due to its low solubility in aqueous solutions. Silver compounds that dissociate easily, such as silver nitrate, are locally sclerosing, and if used in large amounts the absorbed nitrates or other cations may be toxic. Most silver compounds that are non-toxic, such as the silver proteinates or silver sulfadiazine, are only sparingly dissociable[6]. Recent studies indicated that the bactericidal properties of silver sulfadiazine are at least in part due to the attached silver[9], although the action of silver on bacteria is not known. There is some evidence that it interferes with cell-membrane function, cellular DNA, and the respiratory chain of enzymes[9,11,12].

Free silver ions coming from a silver anode, because of their small size, can penetrate to some extent any structure that has an aqueous component even when the structure is avascular. The penetration is the result of both diffusion and ionic migration along a voltage gradient. Since silver ions combine with many proteins to form relatively insoluble compounds, silver ions must be present in the tissues in some excess to exert their full bactericidal effect. With ions being released continuously from the anode, the necessary excess of ions in the tissues is assured. At the same time, silver is minimally toxic[6] and the amount administered by iontophoresis is far below the level necessary to produce a detectable body burden. In our previous study of electrical stimulation of bone growth, in which we used pure silver electrodes as cathodes implanted in bone to produce cellular stimulation, no localized necrosis was evident[1]. Based on this experience, it seemed possible that with the same silver electrode we could deliver silver ions for their bactericidal effect and electric current for fracture

* Supported by the Veterans Administration Research Service, Project No. 098-14-7718-01, and by the Ritter Company, Division of Sybron, Incorporated.

† Veterans Administration Hospital, Irving Avenue and University Place, Syracuse, New York 13210.

healing in the treatment of non-unions complicated by infection.

At the beginning of our study, we did not know what organisms would be susceptible, what the local cellular toxicity might be, and whether the ions would be efficient in a clinical situation. We attempted to study each of these problems. The effects of electrically generated silver ions on a fairly large number of microorganisms were evaluated. While some minor differences in susceptibility were noted, all of the organisms that we tested were sensitive to the electrically generated silver ion, including some that were resistant to all known antibiotics[2,12]. The minimum inhibitory concentrations for silver ions were determined for a variety of bacteria. These were compared with the minimum inhibitory concentrations of antibiotics and found to be at least an order of magnitude lower on either a weight or a molar basis[2]. We also obtained some evidence that electrically generated silver ions are fungicidal[3].

The depth of penetration into bone of silver ions electrically generated at the anode and moving along a voltage gradient is not known. In agar gels containing proteins, chlorides, and bacterial nutrients, we could not demonstrate penetration of more than one centimeter with any of the variations in electrical current or potential, shape of the electrode, or composition of the gel that we employed[3,12]. For the purposes of this study, we assumed that the penetration into bone was similar and at the most one centimeter.

The mechanism of the action of silver ions on bacteria has not been explored fully. In the case of gram-positive cocci, electron micrographs of bacteria treated *in vitro* with silver anodes showed that incomplete septa formed in the cells as well as dense, enlarged mesosomes. There was also some separation of the plasma membrane[11]. In *Escherichia coli*, the induction of β-galactosidase was almost completely inhibited by the silver anode[11]. It would therefore appear that the cell membrane is the primary site of growth-inhibiting action on *Escherichia coli*, *Staphylococcus aureus*, and similar organisms. There was no indication that the action was merely the result of gross protein precipitation, since this would affect all cells, not specifically bacteria.

Toxicity for mammalian cells was also evaluated in our laboratory (unpublished observations) using cultures of mouse fibroblasts grown in the presence of anodes of pure silver wire which were subsequently energized at the levels used clinically. After two hours the fibroblasts in the immediate vicinity of the energized wire became rounded, but they were not lysed and their cell membranes remained intact as shown by the trypan-blue exclusion test. On subculture, these fibroblasts reproduced and their progeny had normal morphology and showed normal replication.

The chronic nature and variable behavior of osseous infections and the difficulties in isolating the effects of the different parts of the treatment program, such as meticulous wound care and the like, are well known. Despite the fact that such factors were operative in the clinical study to be described, our preliminary results have been so gratifying that we believe that it is worth while to report on them at this time.

Methods

To use silver iontophoresis in the treatment of osteomyelitis, standard surgical treatment was required, including débridement with removal of all dead bone and the opening of all pockets of infection, before beginning the iontophoresis. During the course of treatment, the affected part must be immobilized adequately and free drainage of secretions must be maintained. Because the depth of penetration of the silver ions into the tissues (even the soft tissues) was assumed to be no greater than one centimeter using the method of iontophoresis employed, systemic antibiotics in standard doses were given as adjuvant therapy after débridement. In twelve of the cases, this treatment was continued for ten days or less (average, seven days) and then stopped with no ill effects that could be attributed to the early cessation of antibiotic treatment. In no cases were high doses employed as primary therapy. Obviously, an area of sclerotic bone too thick to be penetrated by the migratory silver ions will not be sterilized. Therefore, during the initial débridement a vigorous attempt must be made not to leave any area of sclerotic bone that is more than one centimeter thick.

With a few exceptions (Table I), two treatment programs, each with its own type of electrode, were used: one for cases of infected non-union in which the wound could be closed after débridement, and the other for cases of osteomyelitis in which the bone was saucerized and the wound was left open.

In infected non-unions in which the wound was to be surgically closed, a wire of 99.99 per cent pure silver, 0.625 millimeter in diameter, was inserted directly into the non-union at the conclusion of the débridement. The length of the electrode was determined by the extent of the non-union and by the position of the wire, which was placed either along the fracture line or across the fracture. The electrode was insulated with Teflon except for the terminal eight centimeters. This terminal portion was trimmed to the desired length at the time of surgery. To fix the wire in place, a 2.8-millimeter (7/64-inch) drill-hole was made through the cortex. The distal end of the Teflon-coated portion of the wire fitted tightly in this hole. Initially the electrode was made electrically positive with respect to a skin-surface electrode with a current of one microampere per centimeter of exposed wire produced by a constant current device. This current was usually maintained for the first twenty-four hours after surgery. At the end of this time the current was reduced to 100 nanoamperes per centimeter and the electrode was made negative to stimulate bone production. This treatment, with daily monitoring of the voltage and current, was continued without interruption until 1.5 to 2.5 joules of total energy had been delivered, during a period of about six weeks[1].

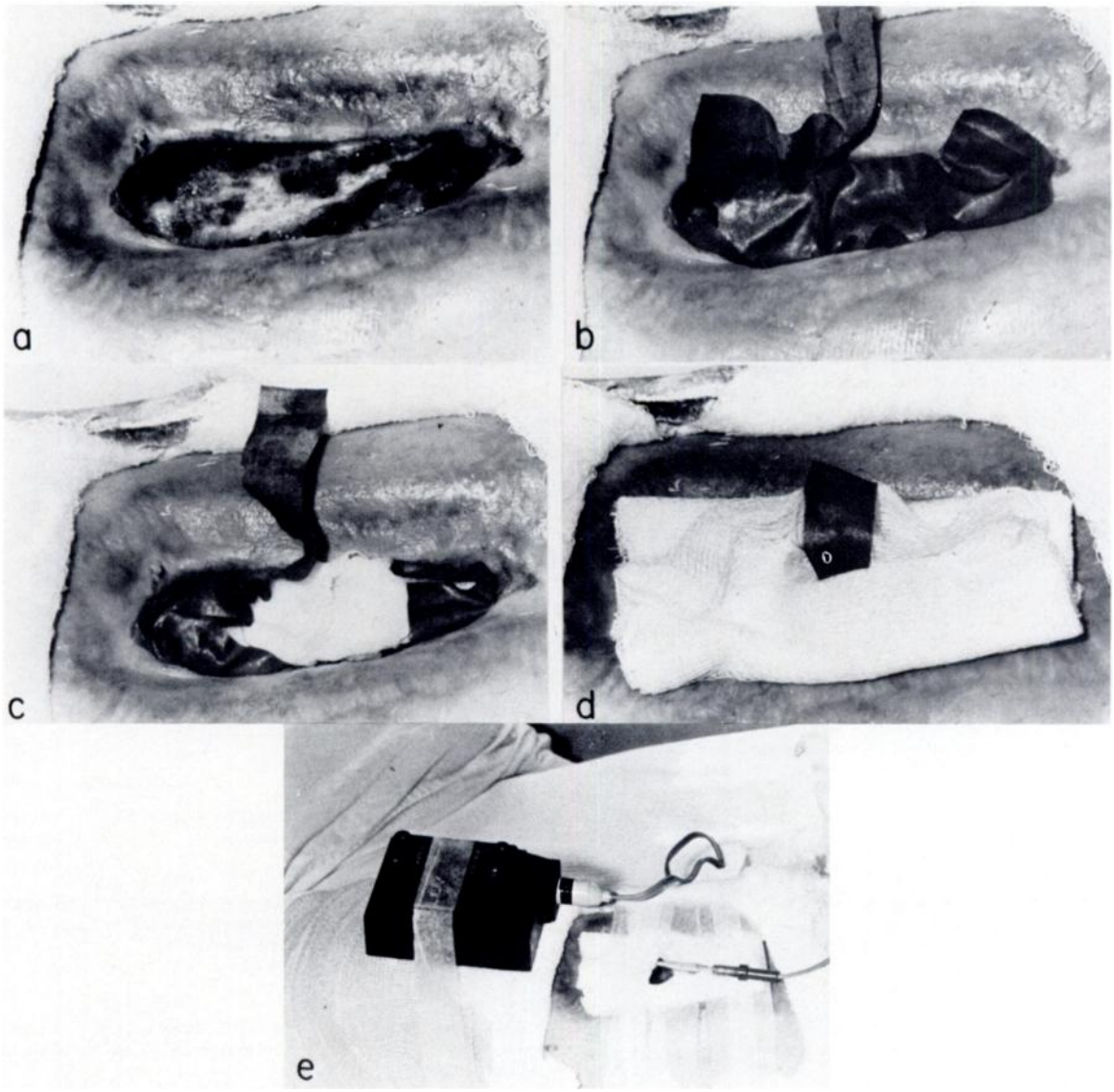

FIG. 1

Case 6. Application of silver-nylon sheet to saucerized, infected tibial non-union. *a*, The wound as seen through window in cast. *b*, Saline-wetted silver-nylon sheet placed in contact with all wound surfaces below skin level with a "tail" left out to establish electrical contact. *c*, A gauze stent moistened with normal saline packed over the silver nylon. *d*, Dry sterile gauze placed over entire wound, with tail protruding. *e*, Constant voltage source with positive lead connected to the silver nylon. The other electrode (not shown) is placed on the skin with electrode paste and its position is selected to enhance movement of silver ions into infected regions of the wound bed.

The current was then disconnected and the implanted silver wire was easily withdrawn from the wound manually without the need for surgery or anesthesia.

In the other type of case, in which there was established osteomyelitis and the wound was left open after débridement and saucerization of the bone, the active electrode (anode) was a sterile silver-impregnated conductive nylon fabric cut to the size necessary to cover the tissue in the depth of the wound, leaving a "tail" that extended out of the wound for electrical contact.

The silver nylon material was prepared daily for each patient. First it was cut to the appropriate size. Then, in a clean bench (Envirco, Model MB 24), it was sterilized by a thirty-minute soak in 70 per cent alcohol, washed in sterile water, air dried, and sealed in sterile plastic envelopes. At the time of application, the nylon was removed from the sterile envelope and cut to size using sterile instruments. It was then thoroughly moistened with sterile normal saline except for the "tail" which was kept dry. The moistened nylon was packed into the wound with sterile hemostats, so that it contacted all surfaces. Any excess at the skin margin was turned down into the wound. No nylon was allowed to remain in contact with the skin. A stent of gauze, cut to fit and saturated with sterile normal saline, was packed over the silver nylon. A dry sterile dressing was then taped over the wound in such a way that the tail came out through the dressing without touching the skin (Fig. 1). The silver nylon was connected to the positive lead of a voltage-controlled generator set to maintain 0.9 volt with respect to the skin-surface electrode. This limit was set to avoid hydrolysis and yet provide nominal current densities on the order of one microampere per

TABLE

Case	Sex	Age (Yrs.)	Diagnosis	Bacteria	Previous Antibiotic Treatment	Concomitant Antibiotic Treatment
				Osteomyelitis with Bone Discontinuity		
1	M	56	Fract. prox. ⅓ tibia; non-union, osteomyelitis, 5 yrs.	*S. aureus*	Lincomycin, 500 mg qid, continuously 1 yr. pre-admiss.	Clindamycin, 300 mg q 8 hrs. for 4 wks. postop.
2	M	25	Fract. tibia, mid-distal ⅓; osteomyelitis and non-union, 3 yrs.	*S. aureus*	Not known	Clindamycin, 300 mg IV q 6 hrs. for 3 days postop.
		27	Repeat treatment after 2 yrs.	*S. aureus, Enterobacter aerogenes*	Clindamycin after previous attempt	Cefazolin, 1 g q 6 hrs. IV for 7 days
3	M	26	Non-union tibia, mid-distal ⅓, 12 yrs.; multiple procedures; persistent drainage	*Pseudomonas aeruginosa*	None for year pre-admiss.	Oxacillin, 1 g q 6 hrs. for 6 days postop.
4†	F	54	Fract. tibia, mid-distal ⅓; non-union, 3 yrs.; infected screw track, 2 yrs.	*S. aureus*	Clindamycin, 10 wks.; oxacillin, 1 wk.; cephalothin, 1 wk.; erythromycin, 16 wks., during year pre-admiss.	Cefazolin, 1 g q 6 hrs. IV for 3 days; dicloxacillin, 250 mg q 6 hrs. for 7 days postop.
5†	M	33	Fract. tibia, mid-⅓; open red., soft-tissue slough; osteomyelitis, active drainage, 3 yrs.	*S. aureus, Enterobacter cloacae, Enterobacter aerogenes, Pseudomonas aeruginosa*	Gentamicin, penicillin G, penicillin UK for 7 mos. pre-admiss.	None
6	M	28	Fract. tibia, mid-⅓; osteomyelitis, drainage, 2 yrs.	*Pseudomonas aeruginosa, β-hemolytic Streptococcus*	Cephalosporin, débrid., Betadine	Carbenicillin, 80 mg q 8 hrs. IV for 7 days postop.
7†	M	53	Old fract., patella; pyarthrosis, knee; multiple surg. procedures; gross drainage	*S. aureus, β-hemolytic Streptococcus, Acinobacter calcoaceticus, Enterobacter cloacae*	Betadine packs, erythromycin for 5 mos. pre-admiss.	Cefazolin, 250 mg qid for 15 days, until 4 days pre-surg.; oxacillin, 1 g q 4 hrs. IV for 10 days postop.
8	M	55	Infected total hip replacement; prosthesis removed; draining sinus; pain	*Proteus mirabilis*	Gentamicin and clindamycin for 1 mo. before silver treatment	Carbenicillin, 80 mg q 8 hrs. for 3 days; clindamycin, 150 mg qid for 5 days after start of silver treatment
9	F	26	Open, comminuted fract. mid-tibia, loss of 10-cm segment; grossly infected, 1 mo.	*Klebsiella pneumoniae, Serratia liquifaciens, Streptococcus viridans, Enterococci, sp. undetermined*	Cephalothin IV or cephalexin continuously for 1 mo. pre-admiss., Betadine locally	Cefazolin, 1 g q 6 hrs. IV for 7 days pre-surg.; gentamicin, 80 mg q 8 hrs. for 7 days postop.
10	M	30	Fract. tibia, mid-⅓; non-union, 3 yrs.; 2 episodes of drainage	*S. aureus*	Cephalosporins for 3 days, 5 mos. pre-admiss.	Cefazolin, 1 g q 6 hrs. IV for 5 days
11	M	48	Fract. dist. ⅓ tibia; multiple surg. procedures; non-union, 2 yrs.; osteomyelitis, active drainage, 8 mos.	*Pseudomonas aeruginosa, S. aureus*	Cefazolin, gentamicin for 1 mo.	Cefazolin, 1 g q 6 hrs. IV for 10 days
				Osteomyelitis without Bone Discontinuity		
12	M	59	Tibial osteomyelitis secondary to direct trauma	*Enterobacter cloacae, S. aureus*	Oxacillin for 4 mos. pre-admiss., Betadine locally	Dicloxacillin, 500 mg q 8 hrs. for 14 days
13	M	49	Tibial osteomyelitis secondary to open fract., 30 yrs.	*E. coli, Streptococcus viridans*	Cephalexin, ampicillin 1 mo. until silver treatment	Ampicillin, 250 mg q 8 hrs. for 10 days
14	M	54	Tibial osteomyelitis secondary to open fract., 35 yrs.	*Pseudomonas aeruginosa*	Gentamicin 8 days, tetracycline 3 mos., ampicillin 1 yr., cephalexin 2 mos. during 18 mos. pre-admiss.	Cefazolin, 1 g IV q 6 hrs. for 2 days

* $+\mu a$ = anodic constant current for bacteriostasis; $-\mu a$ = cathodic constant current for osteogenesis; $+v$ = anodic constant voltage for bacteriostasis applied continuously at first and then intermittently.

† See Case Reports.

Electrical Treatments			Concomitant Surgical Treatment	Follow-up (Mos.)	Results	Remarks
Elec-trode Type	Current or Voltage*	Time (Days)				
Silver wire	+3 μa −0.3 μa	2 48	Tibiofib. synostosis near lesion; bone graft.	36	Partial failure; synostosis wound healed; occas. minor drainage from primary site, antibiot. required once	Silver treatment used as "cover" for synostosis in infected area near primary drainage site
Silver wire	+6.7 μa −0.62 μa	1 47	Min. dissection; bone graft	30	Total failure; non-union failed to heal, drainage absent during treatment but recurred 2 mos. postop.	Patient refused saucerization during this 1st attempt
Silver nylon	+0.9 v	26	Sequestrectomy, saucerization	5	Wound and bone healed, no drainage	Fully ambulatory in short cast after this 2nd attempt
Silver wire	+1 μa −1 μa	1 20	Slight curettage; bone graft	24	Bone healed, no drainage	Full weight-bearing
Silver wire	+3.5 μa −1.1 μa	0.5 42	Min. dissection; trough across fract. to contain wire	14	Bone healed, no drainage	Full weight-bearing
Silver nylon	+0.9 v	24	Débrid., sequestrectomy	12	Bone and wound healed, no drainage	Full weight-bearing
Silver nylon	+0.9 v	40	Débrid.	8	Bone and wound healed	Full weight-bearing; one brief episode of slight drainage after premature return to work against advice
Silver nylon Silver wire Silver wire	+0.9 v −200 na/cm −100 na/cm	7 21 21	Débrid., silver-nylon pack; Charnley fusion (see Case Reports)	16	Bone and wound healed, no drainage	Full weight-bearing
Silver wire	+0.9 v	13	None; silver wire inserted in sinus tract for 3 hrs. a day	12	Partial failure; clinically fused hip, drainage markedly less (one 10 × 10-cm gauze pad per day); no pain	Ambulatory with single crutch
Silver nylon	+0.9 v	8	Débrid., sequestrectomy	7	Wound completely closed, no drainage; bone grafts incorporated	5 wks. after silver treatment, split-thickness skin graft; 5 mos. later, 15-cm. fib. strut and iliac-bone graft; still not weight-bearing
Silver wire	+8.3 μa −0.92 μa	2 49	Débrid.	5	Wound and bone healed, no drainage	Fully ambulatory in short cast
Silver nylon	+0.9 v	29	Saucerization	6	Wound and bone healed, no drainage	Fully ambulatory in short cast
Silver nylon	+0.9 v	49	Débrid.	14	Healed, no drainage	
Silver nylon	+0.9 v	29	Débrid.	12	Healed, no drainage	
Silver nylon	+0.9 v	49	Débrid.	3	No drainage, wound 75% healed, cultures sterile	

square centimeter at the silver-nylon anode. (The delivered current varied with the size of the silver nylon and the total resistance in the wound cavity.) Initially the electrical treatment was continuous. (The longest period of continuous treatment so far has been four days.) Thereafter the electrical treatment was administered intermittently, still with the silver nylon as the anode, for three hours per day.

In this regimen of intermittent current, the silver-nylon packing was removed at the end of each three-hour treatment and the wound was irrigated with 50 per cent hydrogen peroxide in normal saline. These irrigations were done every four hours except at night, when a sterile saline pack was applied, which was permitted to dry until treatment was resumed the following day. We found that the patients could easily be taught this technique of wound care. In all cases in the present series, the wound irrigations and dressings were self-administered. Daily whirlpool treatment was found to be advantageous and was used when possible. Local bactericidal agents such as Betadine (povidone-iodine) and pHisoHex were found to interfere with the treatment since they seemed to retard the growth of granulation tissue. No such difficulties were noted with hydrogen peroxide. After all of the exposed bone was covered with granulation tissue, the silver-nylon treatment was discontinued, and thereafter the wound was irrigated daily with 25 per cent peroxide. In no patient in whom the nylon fabric was used was further silver ion treatment required. Spontaneous healing by epithelialization without skin-grafting or secondary closure occurred in all but one patient (Case 9), in whom there was an area of skin loss about 12.7 centimeters long which had developed before admission to this study (Table I).

The skin-surface counter-electrode used to complete the electrical circuit in both types of treatment was made of carbon-filled silicone rubber and was securely taped over conductive cream to ensure good contact. Because the current and silver ions follow a preferred pathway from the treatment electrode to the skin electrode, the position of the surface electrode was changed daily from a site proximal to the treatment electrode to one distal to it. In the patients in whom the wound was saucerized and the silver-nylon fabric was used, a site on the same limb directly opposite the saucerized area was used most often, since penetration of ions directly into the wound was desired.

Electrical Generators

Two types of electrical generators* were used, one voltage-controlled and the other current-controlled. The voltage-controlled unit, when set for the desired voltage range (0.9 volt or less), delivers the maximum current possible as established by the total circuit resistance. This type was used when the wound was left open or in the presence of pyarthrosis when the silver-nylon sheet was used as the anode. The current-controlled unit was used with the implanted silver-wire electrode and was set for the desired current of one microampere per centimeter of silver-wire electrode (positive) for bacteriostasis and 100 nanoamperes per centimeter (negative) for stimulation of bone formation. This type of unit automatically increases the voltage delivered as the circuit resistance increases. Therefore, the generator is equipped with an audible alarm which sounds when the voltage exceeds the maximum limit of 0.9 volt. Generally, large increases in resistance were caused by poor contact at the surface electrode and were easily correctable. Both types of unit were powered with rechargeable nickel-cadmium batteries and had external jacks to permit ready monitoring of current and voltage.

* Manufactured by the Ritter Company, a division of Sybron, Inc., Rochester, New York.

Clinical Results

To qualify for this study, patients had to have a long-standing infection involving bone and to have had standard treatment with antibiotics and wound care without success. Throughout the study period, all patients who fulfilled these criteria were placed on either the silver-wire or the silver-nylon mesh program, depending on the type of wound. No patient who fulfilled these criteria was treated by other methods during the study period. The series was therefore consecutive.

During the three years from October 1974 to December 1977, fourteen patients with chronic bone and joint infections resistant to other forms of treatment received fifteen courses of silver ion treatment (Table I). One patient who refused to have a saucerization and was treated unsuccessfully in 1974 (Case 2) was treated again with success in 1977, when complete débridement and saucerization was performed. To the extent that each patient had had previous extensive treatment for the osteomyelitis, it was assumed that in each there was an internal control. All patients were followed up by personal examination and repeated roentgenograms until the success or failure of the treatment could be established.

In twelve of the fourteen patients treatment was considered successful and in all fourteen patients (including the failure) treatment resulted in markedly reduced bacterial flora in the wound as shown by sequential colony counts. In no case were any undesirable side effects of the silver treatment apparent. Three case reports are presented in some detail to illustrate how the infections responded.

CASE 4. A white woman, fifty-four years old, was admitted on March 12, 1976, with a history of having sustained a closed fracture of the distal part of the right tibia in a skiing accident in 1974. The fracture had been reduced and immobilized in a cast initially, but six months later there was no evidence of healing and bone-grafting with compression-plate fixation was performed. Eight months after this procedure, there still was no evidence of healing. In addition, one of the fixation screws had backed out, penetrating the skin, and the wound had become infected. All internal fixation was removed and the patient was treated by a series of plaster walking casts.

On admission to our hospital, there was motion at the fracture site and the skin at the site of penetration by the screw was soft and discol-

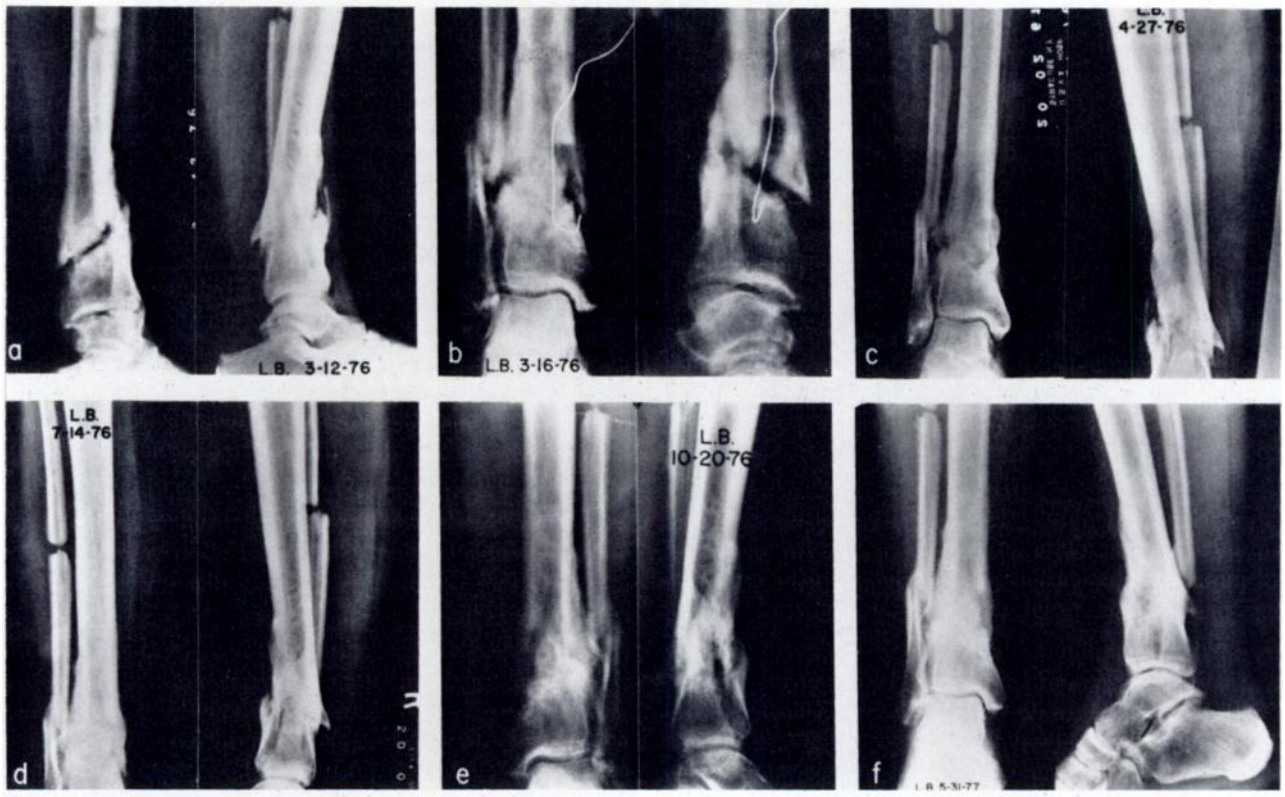

FIG. 2

Case 4. Serial roentgenograms of an infected three-year-old non-union (see Case Reports). *a*, On admission. *b*, Immediately after placing silver wire in trough across fracture. *c*, At time of removal of electrode. *d* through *f*, Sequential roentgenograms up to fourteen months after treatment was instituted.

ored, but there was no active drainage. Roentgenograms (Fig. 2, *a*) showed non-union. At operation on March 16, 1976, the fascia was found to be discolored and thickened throughout the entire area underlying the original incision, and the site of the screw track was filled with a soft, brownish material. Dissection of the bone was kept to a minimum and the non-union site was visualized by means of a short trough made in the medial aspect of the tibia which extended across the fracture site and ended distally at the infected screw hole. No attempt was made to curet the site of non-union, which was composed of sclerotic fibrous tissue.

A 2.8-millimeter (7/64-inch) drill-hole was made through the tibial cortex just proximal to the proximal end of the trough and a silver electrode six centimeters long was inserted through it along the trough and into the infected screw hole (Fig. 2, *b*). The wound was then closed and a long toe-to-thigh cast was applied. Postoperatively the patient received one gram of cefazolin intravenously every six hours for three days. Then the wound cultures grew coagulase-negative staphylococci, sensitive to dicloxacillin, and the patient was given dicloxacillin, 250 milligrams every six hours, for one week more, after which no antibiotic treatment was employed. Electrical treatment (silver wire as the anode) was begun immediately after operation using a current of 3.5 microamperes for twelve hours. The current was then stopped for twelve hours to permit the electrode surface to stabilize and a current of 650 nanoamperes in the opposite direction (implanted wire as the cathode) was applied and gradually raised over a period of four days to 1.1 microamperes. This current was administered continuously for six weeks until April 27, 1976, when the cast was taken off and the sutures and electrode were removed (Fig. 2, *c*). All wounds were well healed and there was no evidence of infection. At that time the patient had received 2.62 joules of cathodic electrical energy. A new long cast was applied and the patient was discharged walking with crutches and partial weight-bearing. On June 16, 1976, clinical union was evident and roentgenograms showed bone formation across the site of non-union. A below-the-knee walking cast was applied, and on July 14 healing was sufficient for full weight-bearing without support (Fig. 2, *d*). When the patient was last seen, on May 31, 1977, she was ambulatory bearing full weight, and showed no signs of infection (Fig. 2, *f*).

CASE 7. A fifty-three-year-old white man was admitted on August 27, 1976, with an exacerbation of a chronic infection in the left knee. He had had a transverse fracture of the patella on September 21, 1969, for which a partial patellectomy had been done. Postoperatively, because of continuing pain and limited motion, the knee was manipulated under anesthesia on December 9, 1969, but this caused a fracture of the retained patellar fragment and on December 18 the rest of the patella and scar tissue in the quadriceps mechanism were excised. After this procedure there was an extensive skin slough and skin-grafting was performed on January 26, 1970. Thereafter the patient regained only 10 degrees of active flexion of the knee. On May 7, 1974, he was readmitted ten days after a puncture wound of the knee with clinical evidence of infection involving the joint and suprapatellar bursa. After débridement and drainage, *Staphylococcus aureus* was cultured and the patient was treated with Lincocin (lincomycin), 500 milligrams every six hours for four months. A persistent draining sinus developed and the patient was readmitted on March 31, 1976. A sinogram showed a communication between the infected suprapatellar bursa and the knee joint. Surgical débridement was again performed and the patient was given erythromycin, 500 milligrams every six hours for two months, but the drainage persisted and when the knee was examined on August 27, 1976, it was swollen, hot, and tender with thick, yellow pus draining from the sinus tract.

Treatment with intravenous cefazolin sodium, one gram every six hours, was started. Cultures revealed a mixed flora composed of several species of gram-positive and gram-negative organisms. Because the patient had delirium tremens on the third hospital day, surgical drainage was not carried out and the profuse drainage did not cease despite continued antibiotic therapy. After successful treatment of the delirium tremens, a knee fusion was performed on September 28, 1976. The joint and the suprapatellar bursa were found to be filled with purulent exudate and were in direct communication (Fig. 3, *b*). The bone ends were

resected despite the presence of gross pus and a Charnley clamp was applied. However, the clamp was adjusted to *distract* the knee initially to provide a space for inserting the silver-nylon material and to prevent possible adherence of the fabric to the large cut surfaces of the femur and tibia (Fig. 3, *c*). A tail of the nylon fabric was left protruding through the loosely closed wound, and the limb was immobilized in a plaster splint. A current ranging from twenty-one to eighty-three microamperes with the voltage-control unit set at 0.9 volt was applied with the implanted silver nylon as the anode and the carbon-silicone surface electrode as the cathode. The intravenous cefazolin that had been started two weeks before the knee fusion was discontinued four days before the fusion and oxacillin, one gram intravenously every four hours, was started at the time of fusion and continued for ten days postoperatively. No antibiotic solution or other agent was used locally. Postoperatively, the patient's temperature rose to 38.3 degrees Celsius and then subsided within seventy-two hours. The drainage from the wound continued, but it became serosanguineous and ceased by the fifth postoperative day. The periarticular edema, redness, and pain resolved rapidly. One week after operation, on October 5, 1976, the silver-nylon packing was removed under anesthesia and the cut surfaces of the femur and tibia were inspected. These were clean and without evidence of infection. A silver-wire electrode five centimeters long was placed in the medial condylar area of the fusion site and the Charnley clamp was reapplied to produce compression of the cut surfaces and to fix the electrode securely in position. Postoperatively, an average current of twenty microamperes was applied with the wire as the anode. On the first day, after tightening the clamp the patient had a fever rising as high as 38.3 degrees Celsius but this resolved within forty-eight hours. The electrical current at that time was reversed to a cathodic current of 200 nanoamperes per centimeter, which was applied to stimulate bone formation. Thereafter the patient remained asymptomatic. The oxacillin was discontinued ten days after tightening the clamp while the current was continued for three weeks at 200 nanoamperes per centimeter and then was dropped to 100 nanoamperes per centimeter for an additional three weeks. Technetium polyphosphate bone scans (Fig. 3, *d*) showed growth in the lateral compartment (away from the electrode) after two weeks of current at 200 nanoamperes per centimeter and additional growth in the medial compartment (near the electrode) two weeks after the amount was reduced to 100 nanoamperes per centimeter.

On November 17, 1976, after six weeks of electrical stimulation with a total of 1.04 joules delivered, the electrode and Charnley clamp were removed. Clinically the fusion was solid and roentgenograms showed active bone formation (Fig. 3, *e* and *f*). The operative wound was completely healed, and there was no drainage. A walking cylinder cast was applied and worn until it was removed on December 4, 1976. The patient was last seen on March 2, 1978, at which time he was walking with full weight-bearing, no pain, and no evidence of infection, and the fusion remained clinically and roentgenographically solid.

CASE 5. A white man, thirty-three years old, was admitted on May 17, 1976, with an infected non-union three years after a fracture of the left tibia. His initial treatment had been internal fixation with a compression plate which was removed seven days later because of a severe infection and skin loss. A cross-leg pedicle flap was performed two years later, lessening the area of ulceration of the skin but not eliminating the drainage. He was transferred to our institution for amputation, where examination showed an ulcer measuring one by three centimeters over the middle third of the tibia, marked surrounding erythema and edema, and exposed, infected bone. Clinically there was gross instability of the fracture and roentgenograms showed non-union and osteomyelitis (Fig. 4, *a*). Cultures showed a heavy growth of *Staphylococcus aureus* and *Pseudomonas aeruginosa*. However, since there were no systemic signs of infection, the leg was treated with immobilization and dressings and no antibiotics were given. To secure stability of the fragments before attacking the infection, proximal and distal tibiofibular synostoses were performed on May 25, 1976. Following this procedure, some motion could still be demonstrated at the site of non-union, but it was much diminished. However, copious drainage persisted and the area of exposed bone did not decrease (Fig. 4, *b* and *c*). On January 6, 1977, the tibia was debrided and several sequestra were removed. Cultures now showed heavy growth of *Staphylococcus aureus, Enterobacter cloacae, Enterobacter aerogenes, Pseudomonas aeruginosa,* and several uniden-

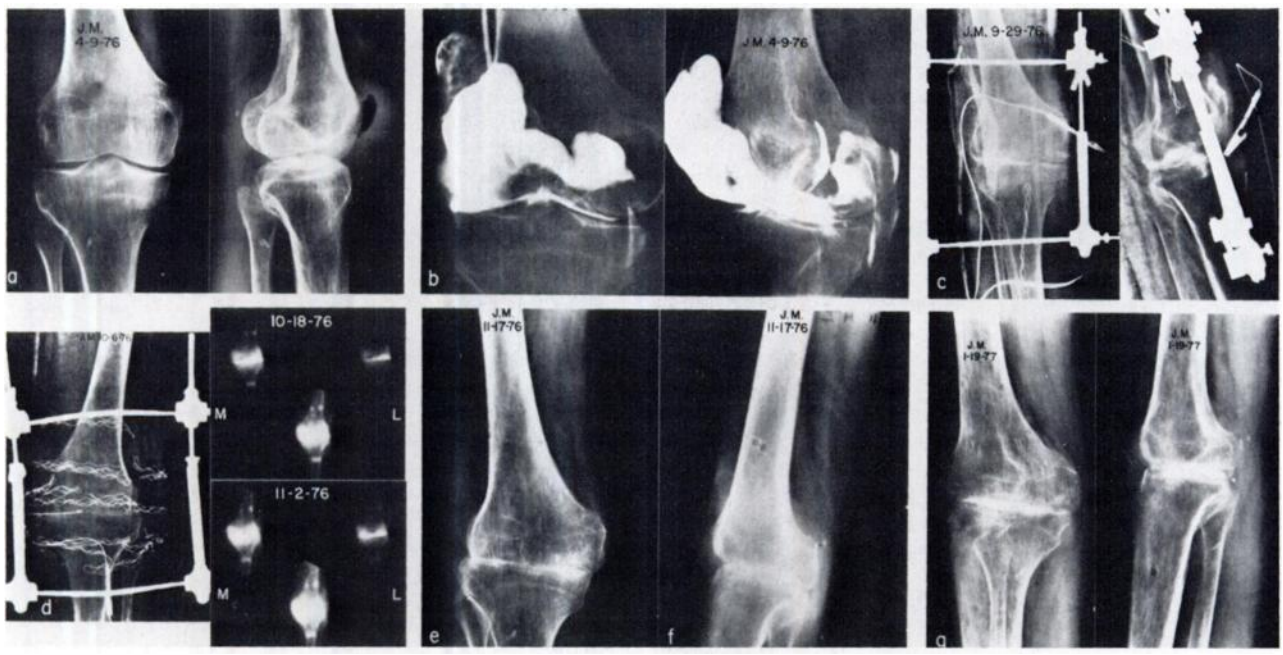

FIG. 3

Case 7. Serial roentgenograms of a chronic postoperative pyarthrosis of the knee treated by Charnley fusion and silver iontophoresis (see Case Reports). *a*, Prior to treatment. *b*, Sinogram prior to treatment, showing communication between draining suprapatellar bursa and knee joint. *c*, Immediately after debridement, resection of bone ends with Charnley clamp adjusted to distract the bone ends to make room for the silver-nylon fabric which was inserted between them and in the suprapatellar bursa. The fabric is visible in the lateral roentgenogram. *d*, After removal of fabric, insertion of a silver-wire electrode between medial femoral and tibial condyles, and application of compression by the Charnley clamp. The top bone scan, made after two weeks of treatment with 200 nanoamperes of current per centimeter, shows the isotope deposition at the electrode site to be less in the medial compartment, adjacent to the electrode, than in the lateral compartment. The bottom bone scan, after two weeks of current at 100 nanoamperes per centimeter, shows isotope deposition to be increased in both compartments compared with the previous scan. *e* and *f*, Anteroposterior and lateral roentgenograms at the time of removal of the Charnley clamp. *g*, Two months after removal of the Charnley clamp.

tified gram-negative organisms. No antibiotics were given at any time. After the débridement and sequestrectomy, the silver-nylon packing was applied using an 0.9-volt constant voltage source and an average current of 100 microamperes continuously for four days. The current was then changed to one three-hour electrical treatment with the silver-nylon electrode per day as previously described, providing an average current of eighty-five microamperes. Immediately before the intermittent treatment was started, a few colonies of Pseudomonas grew out in the culture from the drainage. By January 24, 1977, granulation tissue had covered the exposed bone. Active electrical treatment was reduced to one three-hour session every other day. Whirlpool therapy and dressing changes with peroxide every four hours were continued daily. The last electrical treatment was given on February 7, 1977, at which time the wound had closed to the extent that insertion of the silver-nylon pack was difficult. By that time, a total of forty-two joules (anodic) had been delivered to the wound. On February 17, 1977, the patient was discharged with the wound completely healed, and roentgenograms at that time revealed new-bone formation at the non-union site (Fig. 4, *d*). The patient was instructed to walk with crutches and partial weight-bearing. On April 6, the non-union was clinically solid and roentgenograms showed sufficient bone healing to permit full weight-bearing (Fig. 4, *e*). The patient was last seen on May 18, 1977, when he was bearing full weight and the wound was completely healed and dry. Roentgenograms at that time showed almost complete healing of the non-union (Fig. 4, *f*).

Of the fifteen treatments, one resulted in total and two in partial failure. A total failure was defined as failure to heal the pre-existing non-union and to control the infection. A partial failure meant healing of the previous non-union, if present, and marked reduction in drainage, but not eradication of the infection.

Case 2 was a total failure. This patient, with an infected non-union of the distal part of the tibia treated in 1974, refused complete saucerization. An attempt was made to achieve union and to control the infection using a silver-wire electrode inserted through a surgical approach located at a distance from the draining sinus. The dé-

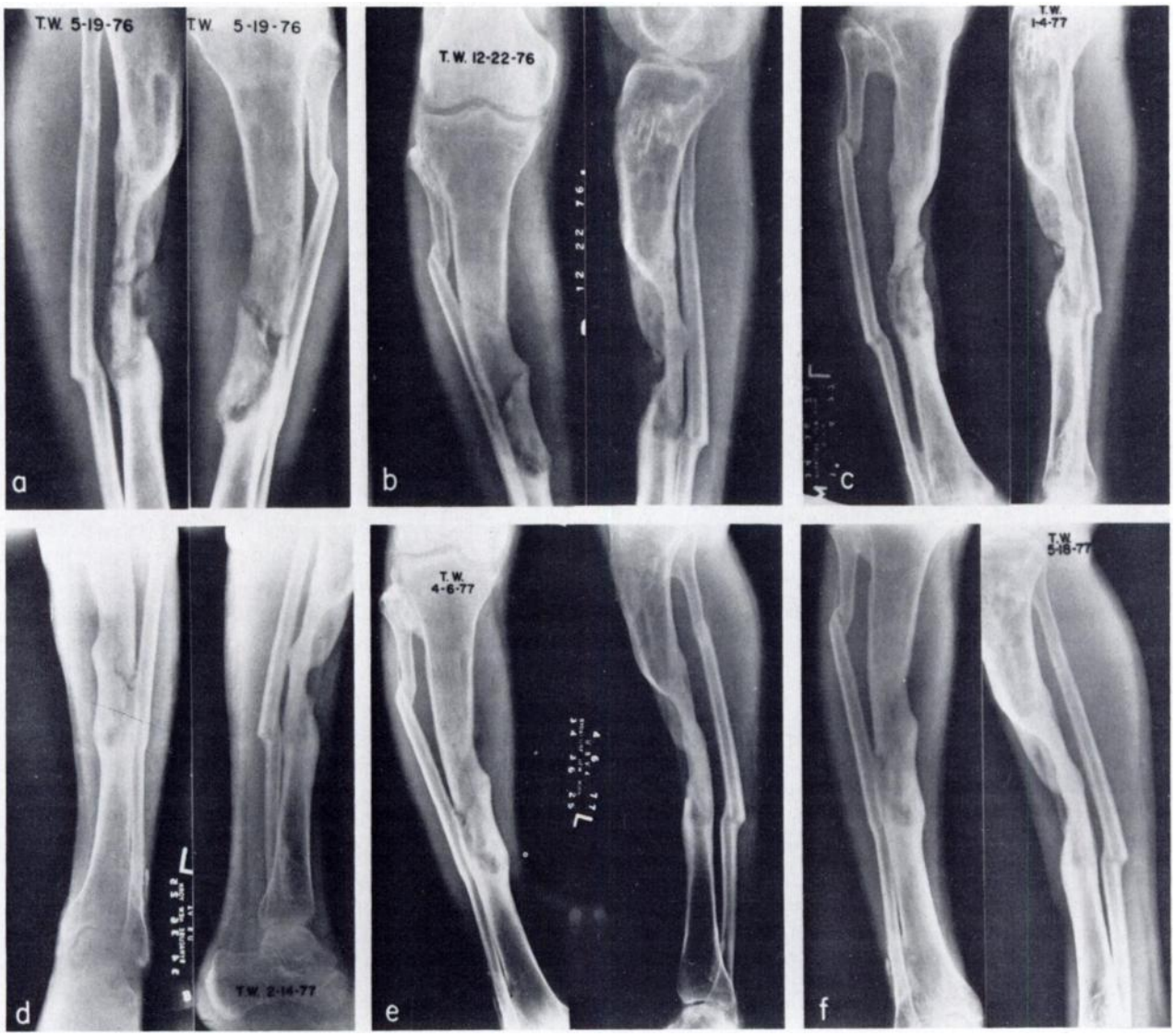

FIG. 4

Case 5. Serial roentgenograms of an infected non-union three years after a postoperative infection with skin slough (see Case Reports). *a*, On admission, showing non-union, sequestra, and tibial defect. *b*, Seven months after tibiofibular synostosis performed to increase stability. *c*, Before saucerization and silver-nylon treatment. *d*, After five weeks of silver-nylon treatment, when the wound was completely closed without drainage. *e*, Two months after all treatment was stopped. *f*, Five months after all treatment was stopped.

bridement was inadequate and while drainage from the sinus stopped during treatment, it recurred within a week after treatment was ended and the non-union persisted. This patient was treated again in 1977, at which time a complete saucerization and treatment with silver nylon was carried out, resulting in bone union and complete epithelialization with no drainage.

Case 1 was considered a partial failure, although the procedure performed in this instance was not the one described and was not designed to treat the infected non-union of the tibia directly by the silver ion treatment, but rather to prevent spread of the infection to an adjacent tibiofibular synostosis performed to stabilize the non-union. For five years this patient had had an infected non-union of the proximal third of the tibia, with a one by four-centimeter area of the anterior surface of the tibia exposed. At the time that this patient was seen, testing of the silver-nylon material had not been completed, and it was elected to do a tibiofibular synostosis in an attempt to secure stabilization without direct treatment of the osteomyelitis. The open draining area was close to the site of the synostosis performed at the level of the fibular neck. We therefore inserted a silver-wire electrode through the fibula into the tibia in the region of the synostosis to prevent infection. The surgical wound healed primarily with no drainage and union of the synostosis was established by eight weeks. Thereafter, drainage from around the exposed tibia ceased except for occasional minor episodes associated with excessive activity, and the wound gradually closed except for a few sinus tracts less than one millimeter in diameter. While the control of the active infection can be attributed to the stabilization of the non-union by the synostosis, we believe that the silver-wire electrode helped to prevent infection of the synostosis wound and helped to secure union under these unfavorable circumstances.

Case 8 also was considered to be a partial failure. This patient had had a deep infection after total hip replacement with subsequent removal of the implant. The wound was left open and treated by whirlpool baths and irrigations with hydrogen peroxide. It healed partially, leaving a residual sinus tract about one centimeter in diameter that extended to the acetabulum. However, the drainage from the sinus was profuse and any movement of the femur was extremely painful. The patient refused immobilization in a spica cast and as an alternative, silver wire treatment was instituted. The electrode was inserted twice weekly and electrical treatment was given for three hours. The only additional local treatment was daily peroxide irrigation and drainage by means of an in-and-out tube. The patient was also given carbenicillin for three days and clindamycin for five days after the beginning of the electrical treatment. During the six weeks of the silver treatment, the drainage diminished by approximately 75 per cent, the depth of the sinus was reduced by one-half, and range of motion at the hip was reduced markedly and became painless. The patient again refused immobilization in a spica cast and was discharged using a walker. Twelve months later he was ambulatory with one crutch and partial weight-bearing on the affected limb. Drainage persisted, but he changed the dressing only once a day and only one ten by ten-centimeter gauze pad was required daily.

Discussion

In this small series, the silver ions seemed to have been an effective local antibacterial agent with advantages over other antibiotics that included: activity against all of the bacterial types encountered in these patients, negligible toxic effect on local tissues, and penetration of poorly vascularized tissue to a distance that is believed to be about one centimeter. The main disadvantage appears to be the limited zone in which the ions are active. Excision of most of the infected tissue therefore is a prerequisite to successful use of silver iontophoresis. The antibiotic activity of silver ions at present is attributed to electrochemical action. If this is so, it may be possible to increase the volume of tissue in which the bactericidal effect is achieved by such techniques as short-duration high-current pulses (of more than one milliampere) applied to the electrodes. *In vitro* experimentation in this area is being pursued at present.

The treatment regimen used in this series (excluding Case 2) included careful initial surgical débridement, good daily wound care, and appropriate immobilization, all measures that contributed to the successful treatment of these patients. Although the relative importance of the contributions of these measures to the successful outcome in these patients could not be assessed, the previous failure of this type of treatment in these patients and the rapid subsidence of the infection once treatment with silver ions was initiated convinced us that the silver iontophoresis had had a beneficial antibacterial effect.

An added benefit, which was unexpected, was the deposition of substantial amounts of new bone produced during treatment with the silver-nylon anode seen in Cases 2, 5, 6, 7, and 11, all patients who had a pre-existing non-union in addition to osteomyelitis. Our previous experience with wire electrodes directly implanted in bone had indicated that osteogenic activity was confined to the region of the cathode. In these patients, the silver-nylon fabric was applied to the bone surface and not implanted within the bone, but the position of the surface electrode (cathode) was such that the maximum current flow would be through the bone including the non-union site. The present findings suggest that the osteogenic effect may be related to the passage of current and not to its polarity, as was previously thought. The lack of osteogenic response around an embedded anode found in prior studies may have been due to corrosive electrochemical effects. In general, our previous conclusions regarding the optimum current per centimeter of electrode and the optimum total energy for osteogenesis were substantiated in this study[1,8].

Silver would appear to be the metal of choice for im-

planted electrodes used for bone stimulation. Its antibacterial properties, when it is the anode, would assist in controlling a quiescent pre-existing or operatively acquired infection.

The results obtained with the silver-nylon electrode in open osteomyelitis would appear to warrant further investigation of its use as an antibacterial dressing after wound débridement.

NOTE: The authors would like to thank Ms. Sharon Chapin for technical assistance.

References

1. BECKER, R. O.; SPADARO, J. A.; and MARINO, A. A.: Clinical Experiences with Low Intensity Direct Current Stimulation of Bone Growth. Clin. Orthop., **124:** 75-83, 1977.
2. BERGER, T. J.; SPADARO, J. A.; CHAPIN, S. E.; and BECKER, R. O.: Electrically Generated Silver Ions: Quantitative Effects of Bacterial and Mammalian Cells. Antimicrob. Agents and Chemother., **9:** 357-358, 1976.
3. BERGER, T. J.; SPADARO, J. A.; BIERMAN, RICHARD; CHAPIN, S. E.; and BECKER, R. O.: Antifungal Properties of Electrically Generated Metallic Ions. Antimicrob. Agents and Chemother., **10:** 856-860, 1976.
4. CLAWSON, D. K., and DUNN, A. W.: Management of Common Bacterial Infections of Bones and Joints. J. Bone and Joint Surg., **49-A:** 164-182, Jan. 1967.
5. FROST, H. M.; VILLANEUVA, A. R.; and ROTH, H.: Pyogenic Osteomyelitis: Diffusion in Live and Dead Bone with Particular Reference to the Tetracycline Antibiotics. Henry Ford Hosp. Med. Bull., **8:** 255-262, 1960.
6. HILL, W. R., and PILLSBURY, D. M.: Argyria; The Pharmacology of Silver. Baltimore, Williams and Wilkins, 1939.
7. KELLY, P. J.; MARTIN, W. J.; and COVENTRY, M. B.: Chronic Osteomyelitis. II. Treatment with Closed Irrigation and Suction. J. Am. Med. Assn., **213:** 1843-1848, 1970.
8. MARINO, A. A., and BECKER, R. O.: Electrical Osteogenesis: An Analysis [letter]. Clin. Orthop., **123:** 280-282, 1977.
9. MODAK, S. M., and FOX, D. L., JR.: Binding of Silver Sulfadiazine to the Cellular Components of *Pseudomonas Aeruginosa*. Biochem. Pharmacol., **22:** 2391-2404, 1973.
10. ROWLING, D. E.: Further Experiences in the Management of Chronic Osteomyelitis. J. Bone and Joint Surg., **52-B:** 302-307, May 1970.
11. SPADARO, J. A., and BECKER, R. O.: Some Specific Cellular Effects of Electrically Injected Silver and Gold Ions. Bioelectrochem. and Bioenergetics, **3:** 49-57, 1976.
12. SPADARO, J. A.; BERGER, T. J.; BARRANCO, S. D.; CHAPIN, S. E.; and BECKER, R. O.: Antibacterial Effects of Silver Electrodes with Weak Direct Currents. Antimicrob. Agents and Chemother., **6:** 637-642, 1974.
13. SYMPOSIUM: The Management of Gram Negative Bacillary Infections in Orthopaedics. Moderator, E. O. Henderson. *In* Proceedings of The American Academy of Orthopaedic Surgeons. J. Bone and Joint Surg., **51-A:** 1022-1026, July 1969.
14. WALDVOGEL, F. A.; MEDOFF, GERALD; and SWARTZ, M. N.: Osteomyelitis: A Review of Clinical Features, Therapeutic Considerations and Unusual Aspects (Second of Three Parts). New England J. Med., **282:** 260-266, 1970.