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SCIENCE

Electric Enhancement of Bone Healing

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Abstract. *A human congenital pseudarthrosis of the tibia, unresponsive to conventional treatment, was stimulated to healing by direct electric current. The method was modeled after prior experimental work in vivo in rabbits. X-ray photographs, histological techniques, and electron microscopy confirmed the presence of newly formed bone in the defect region.*

Recent experiments (*1–7*) dealing with electrical stimulation of bone tissue may be divided into two types. *Electrode-sensitive* experiments (*3, 8–10*), which tend to be equivocal, relate to remodeling effects at the electrode sites with accretion occurring at the negative electrode and resorption at the positive. Other investigators have performed the *current-sensitive* experiments (*1, 4, 7*) which evaluate the effects of current in promoting healing of lesions placed *between* the electrodes. The latter method prevents misinterpretation of spurious results occurring at the electrode sites due to (i) the tissue–foreign body interactions, (ii) localized ionic imbalances, and (iii) possible heating effects. Our group (*5*) placed such experimental lesions between electrodes in rabbit femora and demonstrated that direct current in the range of 2 to 4 μa increases the normal healing process by a factor of 2 when compared to nonstimulated controls, in agreement with Yasuda *et al.* (*1*) and Iida (*2*).

We now describe the first case of human congenital pseudarthrosis of the tibia successfully treated with electric current; in this case we used the same experimental methods that produced bone consolidation in rabbits. Congenital pseudarthrosis is a rare, local dysplasia in which the possibility of effecting union by conventional methods is scant.

The pseudarthrosis in a 14-year-old male was followed since his birth. The child was braced until he was 4 years old, when he underwent a posterior bone graft which healed the defect. At the age of 11, the patient sustained trauma to the tibia, which fractured through the old pseudarthrosis site. He was treated with casting for 6 months. There was no evidence of healing. He then underwent an open reduction with the application of dual onlay bone grafts. The grafts resorbed and the nonunion persisted. One year later he was operated on again and underwent reversal of the diaphysis of the tibia which included the pseudarthrosis, with the concomitant insertion of an intramedullary rod. The defect did not heal despite rigid immobilization for 12 months.

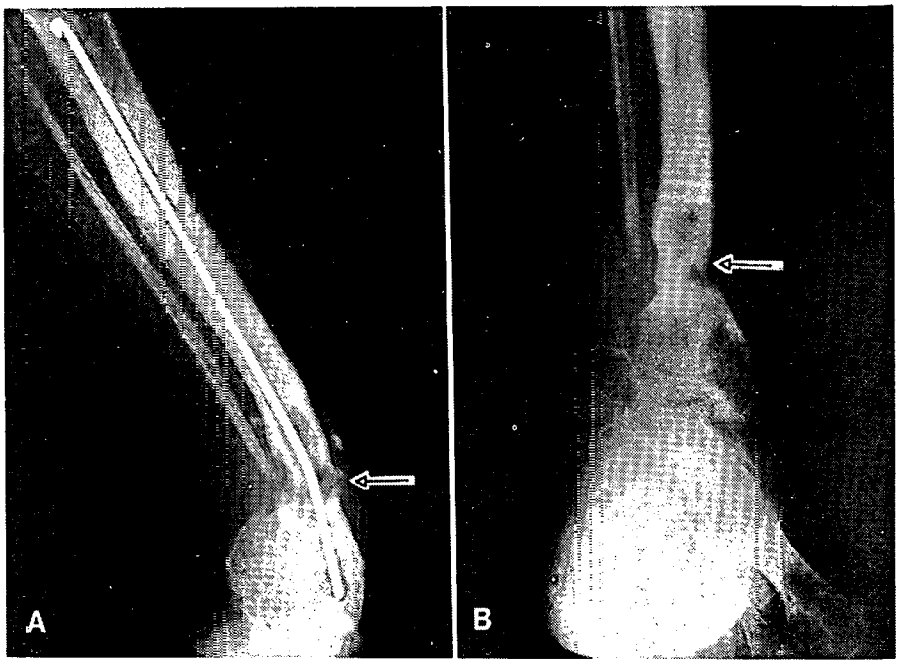

Fig. 1. (A) X-ray taken prior to the application of electric current. There is a rather prominent pseudarthrosis defect (arrow) with angulation. (B) X-ray taken 4 months after continuous application of 4 μa of current. The healing site (arrow) is being replaced by bone.

As an alternative to amputation of the limb, in October of 1970, direct electric current was passed across the pseudarthrosis defect and beginning bone union was obtained within 4 months.

Prior to electrical treatment, the previously inserted intramedullary rod (Fig. 1A) was removed; there was an obvious nonunion, with motion at the fracture site. A biopsy of the pseudarthrosis was performed. Two drill holes (0.25 cm) in diameter were made 1.9 cm proximal to and distal to the area of nonunion; platinum electrodes were inserted into the medullary cavity of the tibia through the drill holes. The platinum was insulated with shrinkable tubing up to the periosteum, such that the current path traversed bony tissue on both sides of the defect. A Steinman pin was placed in the calcaneus and proximal tibia to maintain alignment, the skin was sutured around the electric leads, and a long, leg plaster cast was applied.

The external circuit for the power supply (Fig. 2) consisted of two D cells (3 volts) in series with a 0- to 15-μa meter and a resistance of 0.63 megohm. The effective tissue resistance between the implanted electrodes was 0.14 megohm. The current, monitored continuously with a strip-chart recorder, did not vary from the 3.9 μa reached after completion of the surgical procedure. Thus, the potential difference across the platinum electrodes was 0.55 volt. During the entire treatment period (125 days) the current was applied at least 92 percent of the time. A total of 39 coulombs of charge was supplied to the patient during this treatment. Except for extremely brief checkout procedures, the polarity (distal lead positive) was kept the same during the treatment period.

Two months after electrical treatment was begun, the Steinman pins were removed, and 2 months later the cast and platinum electrodes were removed. The area was surgically inspected and a biopsy was taken. There was no evidence of motion at the pseudarthrosis site upon manipulation. X-ray photographs, histological studies, and electron microscopic investigations revealed beginning bony union (Fig. 1B).

Electron microscope studies of the pseudarthrosis before treatment (Fig.

3) reveal marked differences between bone and defect area. The bone at this transition area stains more densely (histologically and in electron microscope studies), suggesting the possibility of a barrier that prevents the bone from growing into the defect. The inset illustrates collagen coming from bone and forming a major component of the defect. However, bone and collagen appear normal. Some cells found in this defect area are typical fibrogenic-like cells with rough endoplasmic reticulum and normal mitochondria.

Electron microscope pictures taken after the electrical treatment revealed that collagen formation and osteogenesis was occurring in the former defect. Figure 4 shows a fibrogenic cell whose prominent features are a large nucleus, numerous cytoplasmic fibrils, mitochondria, rough endoplasmic reticulum, and Golgi complexes. The presence of rough endoplasmic reticulum indicates that these cells are actively synthesizing protein (*11*). Vesicles near the periphery have been observed by others (*12, 13*). It should be emphasized, in the present case, that scores of such small vesicles line the cell membranes. These vesicles are secretory, as is indicated by the dense band of material of uniform width surrounding the cells. This dense band of material is layered, two or three bands being sequentially secreted near one cell interspersed with collagen. One must consider the possibility that the vesicles may secrete mucopolysaccharides, precollagen materials, and apatite precursors (*13, 14*). The inset photograph is another view of these membrane-bound vesicles, secreting into the extracellular environment.

It is clear that electrical potentials play an important role in directing the architectural and structural development of bone. The success of applied electrical current in treating this difficult orthopedic condition warrants, in

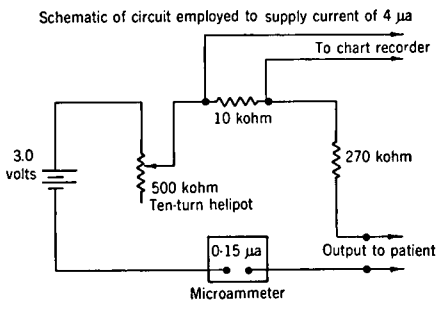

Fig. 2. Scheme of circuit for supplying current of 4 μa.

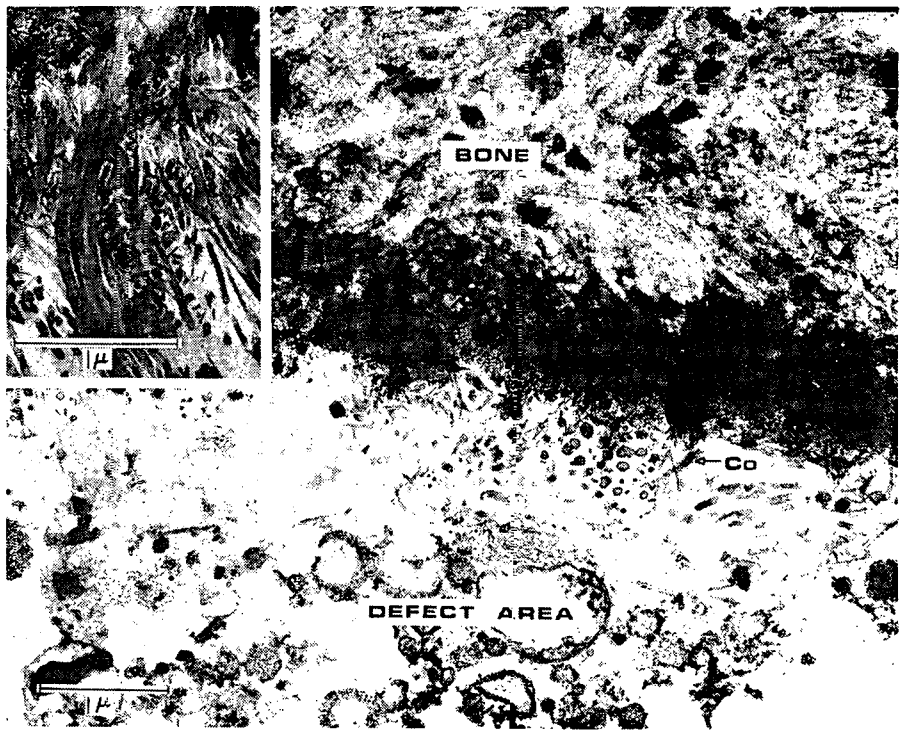

Fig. 3. Electron microscopy of a sample before electrical stimulation, showing the dark staining transition zone between bone and defect area. The inset of another section illustrates some of the prominent collagen fibers (*Co*) coming from the bone and entering the defect. This inset is a representative picture of the collagenous tissue lining the transition zone. The preparation was fixed with 10 percent formaldehyde buffered to *p*H 7.3 with phosphate. It was then postfixed with 1 percent osmium and stained with uranyl acetate and lead citrate.

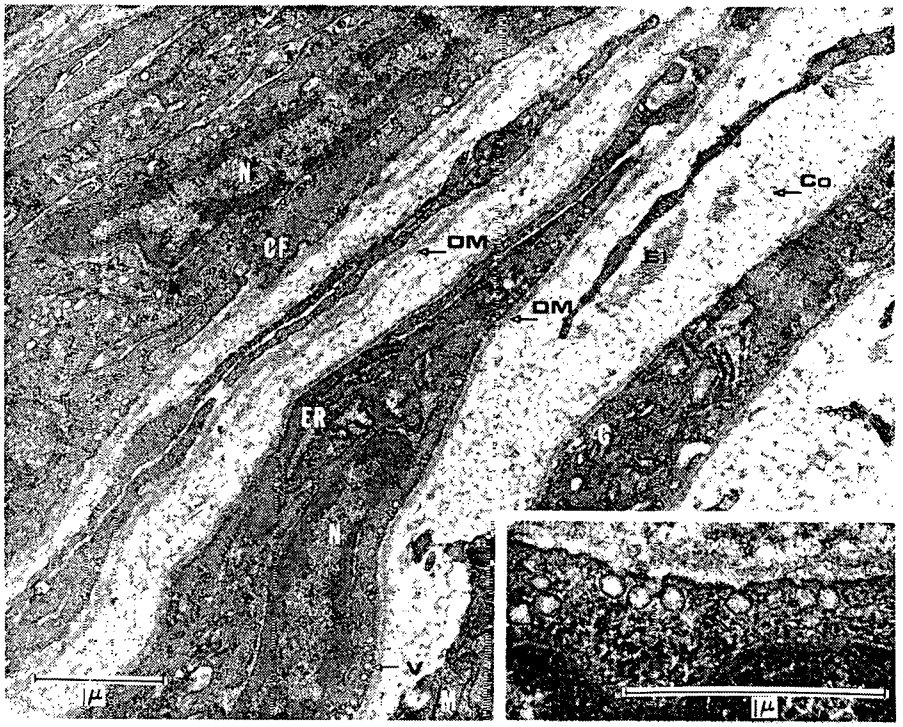

Fig. 4. Electron microscope sample after electrical stimulation. The vesicles (*V*) along the periphery of the cell are very prominent. The dense material (*DM*) is secreted by these cells. The inset is higher magnification of these vesicles. *N*, nucleus; *ER*, endoplasmic reticulum; *G*, golgi complex; *El*, elastin; *CF*, cellular fibrils; *Co*, collagen; *M*, mitochondria. The preparation was fixed with 3 percent glutaraldehyde and buffered at *p*H 7.4 with cacodylic acid. Postfixation and staining as in Fig. 3. The biopsy specimen was obtained 4 months after the one taken for Fig. 3. The area shown in this electron micrograph corresponds to the defect region shown in Fig. 3, and the magnification is exactly the same (except for the inset) as in Fig. 3.

our judgment, its application to other less rare problems, such as nonunion and delayed healing of fractures. Obviously, there are further ramifications. Understanding the coupling mechanisms linking electricity to basic cellular phenomena represents, in our opinion, a problem of primary biophysical importance.

We realize that this is only one case. However, the foundation for this report rests upon prior animal experimentation. In addition, the rarity of this disease precludes reporting more than one case at this time. The decision to experiment first with congenital pseudarthrosis in a human subject instead of delayed union was prompted by the treatment of choice, in this case amputation. In addition, the difficulties presented by this disease represent an extreme test of electrical stimulation. Fundamentally, we are motivated in presenting this report by its potential importance.

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