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Control Mechanisms and the Action of Weak Electric Currents in the Acceleration of Wound Healing and Fracture Union

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Evidence is mounting on the action of weak electricity in accelerating wound healing, fracture union, in the improvement of certain other pathological conditions, and in other growth processes.[1] These weak electric currents are almost always of the direct type; the current can reach the site of action either from implanted encapsulated battery, resistor and electrodes,[2] or the battery with its limiting resistor may be on the outside, with electrodes piercing the skin; it can also be from the surface of the skin via flat electrodes fed from a source of the potential difference,[24] or again via electromagnetic waves from a pulsed high peak power high frequency powerful radio transmitter.[30]

This paper briefly describes the methods used, and then outlines possible mechanisms of action of such currents. Bioelectric and dc fields have been linked up with the following:

1. Cellular migration[8]
2. Tumor formation[21]
3. Morphogenesis[31 25]
4. Regeneration of amphibian limb[4 7]
5. Tissue repair[1]
6. Growth[9 23]
7. Behavior[29]
8. Sleep states[11]
9. Rapid multiplication of microorganisms[34]

Many years ago, Burr[10] showed that a decrease in electric positivity paralleled fibroblast proliferation. In the fifties, Japanese workers reported on certain effects of minute electric currents on bone in animals.[22]

Thereafter, Bassett and Becker[6] reported on a mechanical to electrical conversion effect, due to semiconductor characteristics in bone. In 1964 they demonstrated[2] the effects of certain types of electric currents of bone in vivo; they reported massive new bone formation at the cathode of encapsulated battery-resistor packs with electrode tips a few millimeters in the medullary cavity and currents of 10 and 100 microamperes for 2-3 weeks. Others have also reported on the treatment of bony defects and fractures in animals and humans by electricity.[13 14] In 1966 Wolf, Wheeler, and Walcott[36] showed that ordinary gold leaf applied directly to skin ulcers speeded tissue repair according to a postulated cathodal relativity concept. Wheeler and Walcott later published results of electrotherapy in many human cases of skin ulcers with weak direct currents via electrodes from an external source.[35]

Others[24] have shown in rats that electric fields (dc 100V, 3 c/s 200V and 30 c/s 200V) are capable of lessening the loss effects in bone by immobilization, and that similar strength but alternating current produced tumor-like growths.

Finally a number of workers have reported on the beneficial effects of athermal pulsed high peak power radio frequencies in the 27 Mc/s region. These range from rapid resolution of experimental hematomas in rabbits,[16] acceleration of wound healing,[12 37] speeding up of fracture union,[39] and other pathological conditions such as subacute sinusitis,[33] intermittent claudication,[20] bursitis with calcification,[18] experimentally induced formalin arthritis in rats,[26] and finally in stroke victims.[27]

The way these weak electric currents act in the body has been postulated to be by semiconduction and charge transfer in biological tissues by conduction bands; also by transduction and biological piezoelectricity.[32 37]

It has been shown that mechanical deformation of bone can produce measurable dc potentials. Also that bone behaves as a semiconductor with diode properties appearing at the junction between fibrous collagen (n-type) and crystalline apatite (p-type).[3 6] By using electron spin resonance, it was further shown that results obtained were consistent with the idea that charge carrier movement was present, of a nature required for the bone to act as a semiconductor. Dense compact bone[15] consists of minute crystals of hydroxyapatite, embedded in a mucopolysaccharide hyaluronic acid, and in fibres of the protein collagen, which is also in a semicrystalline state. Most of the apatite is arranged in a precise relationship to the structural pattern of spiral regular repeating collagen. This postulated diode junction responds to stresses on the bone by generating minute electric currents and this in turn stimulates bone cells to grow more new collagen fibres which orient themselves in certain positions and produce structural changes in bone to enable it to better resist the applied stress.

Calcium homeostasis is controlled through a negative feedback mechanism via the parathyroids.* Also a stress and deforming force results in a change in bony structure needed to resist the force. So therefore we can see here another negative feedback mechanism, namely an environmental signal, a transducer, and a response, which will tend to damp the effect of the excessive signal. We can now see how bending and stressing a bone could generate minute electric currents by:

1. Bending of collagen fibres,
2. Deforming mucopolysaccharide molecules,
3. Stressing of collagen-apatite (p-n) junctions.

The minute electric currents thus produced vary with the rate, duration, magnitude, and direction of the deforming force. Regions under compression which become concave are usually negatively charged and vice versa. Clinically a concave region of bone will tend to build up more bone, and a convex region of bone will tend to break down. Therefore it seems reasonable to assume that electrical negativity is associated with the building up of bone, and vice versa. This was well shown by Bassett and Becker. Bassett further speculates that bone being rigid and incompressible normally, tissue fluids cannot move freely to nourish various parts and components of bone, but now under a stimulus of minor skeletal deformations, a to and fro electrical signal could act as a pump to promote the ebb and flow of ions, etc. It would almost certainly depend on the innumerable diode properties of collagen-apatite units near osteocytes. Increase in electric generation would activate cells in the region to produce more bone and stabilize conditions, while diminished current would result in starvation

*Calcitonin mechanisms are not considered here.

and ultimate death of osteocytes. It has also been observed recently that parathormone influences the electrical conductivity in cellular membranes and therefore points to the fact that bone destruction (osteolysis) is electrically controlled. It should be remembered at this stage that Bassett's postulate only includes a direct current component of electricity. He has also shown that if minute dc is applied to drops of collagen in solution, a band of collagen started forming near the cathode and at right angles to the direction of the electric field. If on the other hand the electrical signal is alternating, the electrically charged molecules would tend to move to and fro, except perhaps if the number of cycles was very low (1-5 c/s) or if one of the two phases was dominant.

In wound healing, the role of exudate, granulation tissue, and enzymes is important. The enzyme collagen proline hydroxylase for example initiates the onset of collagen synthesis and deposition. The conversion of proline to hydroxyproline is an important step in the manufacture of collagen, since this collagen is the only animal protein containing hydroxyproline; the enzyme catalysis the hydroxylation of certain propyl residues in peptide linkages to form collagenous hydroxyproline. Ascorbic acid probably functions as a co-factor for the enzyme.

A cell should be visualized as a group of macromolecules bound together by a complex system of communications regulating both their synthesis and their activity; living things could not survive and multiply were it not for complex regulatory networks that interconnect different parts of their macromolecular structure, and which are based on negative feedback. Various cellular processes should be mentioned as possibilities for the site of action of weak dc currents, and consideration should therefore be given to nucleic acid regulation of protein synthesis, metabolic pathways, interaction of cell-to-cell connections, humoral and hormonal influences, free radicals, etc. Enzyme feedback mechanisms, and resonant phenomena should be especially mentioned. In biological amplification for example, a small input is converted into a large output by enzymes grouped in series, so that each catalysis the conversion of the next enzyme in the series.

Finally it should not be forgotten that [..." very weak dc is the stimulus. This is produced directly and primarily by electricity from a battery or by electrostatic fields, whereas in the case of athermal pulsed high peak power alternating electromagnetic energy, the to and fro very rapid oscillations generated in molecules and dipoles will lead to the secondary production of minute dc. The end result is approximately the same in both cases, namely the speeding up of wound healing and fracture union by a process of accelerated collagen deposition, and a faster calcification and ossification..."] as outlined above.

Add this statement

NOTE ADDED IN PROOF

Since going to press, further work in this domain has been brought to our notice.

Digby for example,[38] proposes that the small dc potentials developed across growing regions of mammalian bone are generated partly as streaming potentials by the flow of blood through capillary loops. He goes on to say that these potentials control calcification by causing a return current through pathways in the soft tissues, with subsequent deposition of calcium salts at the positive end. He also gives evidence that the return pathways of the current are partly ionic and partly electronic, the latter comprising chains of molecules such as vitamin D or A with alternating single or double bonds. Others[40] with models have shown that dc of 2-3 microamperes caused in 2-3 weeks a marked enhancement of bone healing in experimental as compared with control rabbits.

Niemeyer[41] points out the importance of the colloid negative charge, which decreases at the time of injury and does not recover for 3 weeks after, during which time collagen does not appear in the wound until most of the negative charge has been restored. He also stresses another important function of mucopolysaccharides, namely the water binding property of hyaluronic acid in connective tissue.

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