POSTULATES CONCERNING POSSIBLE MECHANISMS OF ACTION OF PULSED ELECTROMAGNETIC FIELD THERAPY OF OSTEOARTHRITIS

POSTULATES CONCERNING POSSIBLE MECHANISMS OF ACTION OF PULSED ELECTROMAGNETIC FIELD THERAPY OF OSTEOARTHRITIS

Richard Markoll, MD, PhD.

Clinically the effects of PEMF in the treatment of osteoarthritis have been shown to include decreased pain and increased functional capacity, as well as decreased pain on passive motion and joint tenderness. There are many possible mechanisms which could be underlying these clinical effects, since PEMF have been shown to have several biological effects in laboratory experiments which could be relevant to the pathogenesis of osteoarthritis. Therefore, in this document, we will first summarize known relevant biological effects; second, we will mention known bioelectric phenomena which occur in dense connective tissues which are relevant to the normal physiology of joint tissues, and third, we will put these points in the perspective of possible reasons for the clinical benefits of PEMF observed in patients with osteoarthritis.

I. Relevant biological effects of electrical fields and PEMF.

Direct electrical stimulation has been shown to increase cartilage repair (induced epicondylar defects) in rabbits as well as increasing repair of experimental tendon defects (using chick tendon explants maintained in tissue culture media). The first studies of this physical modality demonstrated increased bone formation. PEMF have been used to induce electrical currents in tissues, producing similar results. This has been most extensively studied for bone; the FDA approved the device generating such pulses in 1979 as the “Bone Growth Stimulator.”
Among the tissues that are responsive to PEMF in the laboratory, the dense connective tissues have been studied most extensively. Fibroblasts from tendons of various species, fibroblasts from skin, chondrocytes from epiphyseal and articular cartilage of several species (especially chick, rabbit and bovine) and osteocytes have all been shown to increase collagen and/or glycosaminoglycan synthesis. Other tissues have been shown to increase protein synthesis, as well as mRNA synthesis (the precursor step which leads to protein synthesis). In each instance the nature of the proteins made by a given cell line was unchanged; whatever they were making before, they made more of it when stimulated by PEMF. This statement is most important regarding collagen; specifically, chondrocytes, which make type II collagen, made more type II, while skin fibroblasts, which make type I collagen made more of that type of collagen.

II. Bioelectric phenomena in joint tissues.

The cells in dense connective tissues in animals respond to mechanical stress by making more tissue components. These tissue components are primarily outside the cells, such as collagen and the proteoglycans (large protein-polysaccharide complexes). The mechanism by which these cells become aware of use (mechanical stress) is not fully understood, but in each tissue there is clear evidence for a mechanical-electrical transduction constituting the signaling mechanism. Bone has been the most extensively studied, and knowledge of

the response of bone to electric stimuli led to the development of the device that generates PEMF as an aid to bone healing (the bone growth stimulator). The
specific mechanism by which the mechanical stimuli are changed to electrical signals has been extensively studied and shown to be based on fluid movement in the bone, causing charged ions to flow past tissue components which are stationary and carry electric charges (fixed charge groups). This phenomenon, called streaming potentials, also occurs in cartilage where compression causes the very high water content of the extracellular matrix to flow, carrying the positively charged sodium ions with it, leaving un-neutralized negatively charged groups on the proteoglycans. Streaming potentials are important in signaling the chondrocytes, and also occur in other dense connective tissues such as tendon. This signaling mechanism can be imitated by the induced currents caused by PEMF in these tissues, as in bone.

III. Postulates:

A. Consideration of the causes of symptoms in osteoarthritis.

The causes of pain in patients with osteoarthritis are vague, controversial and undoubtedly multiple. The articular cartilage is the site of the most important, fundamental pathology, but not the symptoms since there are no nerve endings in articular cartilage. The bone, especially the periosteum covering the bone, is especially rich in pain receptors and much of the pain arises from that tissue. The capsule of the joint, which is dense collagenous tissue, is also rich in nerve endings and another site of pain detection. The lining of the joint, the synovium, is another site of some of the pain and a primary source of the production of prostaglandins, which sensitize nociceptive (pain-detecting) nerve endings.
Processes which put stress on the bone near the joint or the joint capsule, or cause microfractures of the bone plates under the joint surface (the trabeculae) or cause inflammation of the synovial membrane, all can contribute to the pain in these patients. In addition, outgrowths of bone and cartilage at the joint margins (especially where the capsule inserts into the junction of the articular cartilage and the bone) called osteophytes, are a site of pain during the period in which these outgrowths are forming. After the osteophytes are fully-grown and apparent on x-ray, pain from this source may stop.

Relief of pain could thus result from:
- suppression of sensitivity of pain receptors and/or production of prostaglandins (i.e. the effect of peripherally acting analgesics such as aspirin and other NSAIDS),

- suppression of transmission and sensitivity to pain centrally (e.g. occurs with narcotics such as morphine, codeine, etc.)

- change in the physical stresses of pain sensitive structures, such as the underlying bone or capsule; this could result from regeneration of articular cartilage, making it better able to absorb compressive stress, or strengthening of other joint tissue components by new collagen formation, making them better able to absorb stresses.

- other undefined mechanisms are definitely possible.

B. Possible mechanisms of action of PEMF in osteoarthritis.

1. Could PEMF aid the mechanism of repair of articular cartilage? In osteoarthritis degeneration and erosion of the articular cartilage is a basic aspect of the pathologic process, but there is abundant evidence for reversibility to this process. There is proliferation of chondrocytes at the site of the lesions, and the increased synthesis of proteoglycans and collagen occurring in the cartilage at the site at which there is accelerated loss of these matrix components. These phenomena can slow or even reverse the lesions, and there is evidence for such reversibility clinically under certain circumstances (a prime example is the appearance of new cartilage in the hip joint following a surgical procedure known as a Pauwels osteotomy, in which the site of weight bearing stress in the hip joint is shifted.) No present nonsurgical therapy has been shown to cause reversal of the lesions, but it is potentially possible. How such a process would affect the pain is not known; however, the ability of the cartilage to absorb compressive stress would be augmented, and therefore the physical stresses on the underlying bone and other joint tissues which have nerve endings, such as the capsule, would be diminished. During the course of the study of PEMF therapy of osteoarthritis it should become possible to investigate the possibility that this treatment slows progression or causes some reversal of the pathology of the disease. Such studies should give us a better idea of the mechanism of action of this form of therapy.

2. Could PEMF cause repair of microfractures in trabeculae underlying the joint, stopping production of pain from these structures? PEMF were first introduced into clinical medicine as treatment for unhealed fractures, and are also used to promote healing or ordinary fractures. They have also been shown to cause thickening of bone in circumstances in which bone loss (osteoporosis) has occurred. Treatment of patients with osteoarthritis might increase formation of bone at sites where it is needed, causing painful microfractures to heal and make the subarticular bone denser and better able to withstand physical stress without causing pain.

3. Could the PEMF affect the forces leading to osteophyte formation? When osteophytes (outgrowths of cartilage and bone at the joint margins seen in osteoarthritic joints) are forming, they are often the site of considerable pain and on physical examination of the joint, the site of swelling, warmth and tenderness. The mechanism responsible for osteophyte formation is not yet known, but given the knowledge of the role of electrical signals in causing bone formation, alterations in the patterns of such signals by the articular cartilage breakdown is a possible basis. Since PEMF alter the electrical signals in joints, they could affect the process of osteophyte formation. Turning off osteophyte formation could stop pain and account for the decreased tenderness seen in treated patients.

4. Could PEMF lead to collagen production in other joint structures, especially the capsule, strengthening it and making it better able to withstand abnormal physical stresses of an osteoarthritic joint during joint use without generating pain signals? These and other hypotheses have been suggested as possible mechanisms of action of PEMF. They can serve as the basis for design of further studies. Based on the convincing clinical evidence of efficacy we feel that such studies will be worthwhile and will eventually lead to knowledge of the mechanism of action and answer such vital questions as whether PEMF can alter the progression of the basic disease processes occurring in osteoarthritis.