



JOURNAL OF BIOELECTRICITY

Journal of Bioelectricity

Since World War II, the scope of electromagnetic radiation use in medicine, industry, science, and the home has grown to the point where almost everyone living in a developed country is directly or indirectly affected by it virtually every day of their lives.

While the direct effects—better communications, faster cooking, safer flying, to name a few—are clear, the indirect effects—to public health and safety—are far less well known. The study of the interactions between non-ionizing radiation and biological tissue and systems has become a burgeoning new field of scientific investigation that seeks to discover answers to such questions as: What are the relationships between RF radiation and cataracts and high blood pressure, between super high voltage power lines and ELF radio waves and nervous disorders? Can a computer's memory be constructed out of magnetically stimulated "bytes" of living bacteria? Does electric stimulation of damaged tissue spur new growth and regeneration where ordinarily none would be possible? What role does intrinsic electromagnetism play in the regulation of living systems?

As the official journal of the International Society for Bioelectricity, the **Journal of Bioelectricity** publishes original work on all aspects of electromagnetic radiation (from direct current through visible light) and life in order to promote understanding of all significant aspects of their relationship.

To accomplish this, the **Journal of Bioelectricity** brings together comprehensive reports of the latest research being carried out in a variety of fields by some of the most active and innovative scientists in their respective specialties into a single, handy compendium of important current information.

Biophysicists, public health specialists, government officials, orthopedic surgeons, oncologists, physiologists, neurophysiologists, biochemists, biologists, and public health specialists are only some of the professionals who will find the information contained in each issue of the **Journal of Bioelectricity** to be eminently useful as an adjunct to their work.

NEUROELECTRIC MEDICINE

William Bauer, M.D., M.S.
Medical Plaza - Suite 204
58 Hospital Road
Newman, GA 30263

HISTORY

The use of electrical currents in medicine is not new (1). Records indicate electrical stimulation was prescribed as early as 46 A.D. The Greek physician, Scribonious Largus, prescribed the "seashore treatment" for numerous patients suffering acute pain. During this treatment, the patient would place one foot on a species of fish which used mild electrical shocks as a defense mechanism, and the other foot on wet sand, thus completing an electrical circuit.

In modern times, the science of electricity began with William Gilbert, an English physician. In 1600 he published De Magnete in which he established the difference between electricity and magnetism. In 1791, Luigi Galvani discovered that if the exposed nerve of a frog's leg was stimulated with a metal probe near an electrical field, a contraction would occur. This led Galvani to explain muscular contraction in terms of an inherent, stored electrical nervous fluid or "animal electricity". Alessandro Volta, in 1800, contested Galvani's explanation in a bitter dispute, claiming electricity does not originate or reside in animal tissues, and all that was needed were two dissimilar metals separated by a poor conductor. This heated debate continued until 1830 when Carlo Matteucci, a professor of physics at Piza, was able to prove beyond a doubt that an electrical current was generated by injured tissue, and "animal electricity" did indeed exist (2).

Medical and related texts of the 19th century outlined the wide use of electrical medicine (3). Instrumentation employed the use of storage batteries and provided a continuous or pulsating DC current. Frequency, waveform, duration and current output were rather erratic at best. Good results were reported for the following disorders: dyspepsia, epilepsy, anemia, nervous debility, neuralgia, sciatica rheumatism, diabetes, and paralysis. By 1894, an estimated 10,000 physicians within the borders of the United States used electricity as a therapeutic agent daily in their practice. All of this persisted until after the turn of the century when the most obvious of the charlatans entered the scene. They, in concert with the almost total lack of standards in medical education and practice at that time, produced a deplorable situation.

This situation was recognized by the Carnegie Foundation, which established a commission headed by Abraham Flexner to investigate it. The commission's final report was published in 1910 and it produced an almost instantaneous revision of medical education. Electrotherapy became a scientifically unsupportable technique, and it disappeared from medical practice (2).

During recent years, however, knowledge of the action of electricity in the treatment of disease has developed considerably, and the contempt with which medical electricity was regarded has gradually changed.

INSTRUMENTATION

The development of our present day theory of neuroelectric activity has depended on improvement of electrical and electronic devices. Each development in recording technique has made its contribution to electrophysiology. The galvanometer enabled Matteucci to prove that injured tissue generated an electrical current. Related instruments, the ohmeter and the voltmeter, made possible the discovery of the electrocardiogram, electromyogram, and electroencephalogram. With the invention of non-polarized electrodes, the measurement of individual cellular action potentials and cell membrane potentials

became possible, leading to the establishment of classical electrophysiology (4).

Diagnostically, the utilization of extremely strong magnetic fields created by superconducting magnets, permits imaging of soft tissues without ionizing radiation in the newly-developing field of nuclear magnetic resonance (NMR) (5). Similarly, the invention of the SQUID (superconducting quantum interference device) permits detection of low intensity magnetic fields around the body (6,7). The magnetoencephalogram (MEG) is a new measurement which uses this technology and compliments the electroencephalogram (EEG) (8).

Thereapeutically, the most prominent application of electrical instruments has been to alleviate pain with transcutaneous electrical nerve stimulation (TENS) (9-11). Empirically, the characteristics that determine the adequacy of the electrical current to interact with biological systems are waveform, repetition rate, duration, and magnitude of change (12).

Experimentation in areas of both transcutaneous and percutaneous stimulation indicates a balanced waveform of the square or rectangular configuration as producing maximal effects. Such waveforms are preferred to the conventional sinusoidal wave. Since it is similar to naturally-occurring body signals, the pulsed waveform tends to be most effective in stimulating points of the anatomy. Significant importance is attached to the frequency when applied for therepeutic purposes, but there is no general agreement concerning optimal frequency levels.

Neuroelectric therapy (NET) is the latest development in electrical stimulation because the addition of a computer to the pulse generator has made possible the creation of precise and effective waveforms that use a minimum of voltage and current. This is accomplished by first sensing the existing electrical impedance of the tissues. This information is then fed through a computer which modifies the next waveform to be delivered. In this way, an alternating current with varying waveforms of the biphasic rectangular type may be specifically tailored for the area to be treated. The current is in the range of 25-500 microamperes (13), and the frequency is from 0.5-320 Hz, and it is delivered to the area of treatment via external electrodes.

NEUROPHYSIOLOGY

Ionic Basis of Excitation and Conduction

Membrane Potential: The best understood bioelectric phenomenon is the concept of the cell membrane potential (resting membrane potential) (14). This potential has its basis on an unequal distribution of ions across the cell membrane. In nerve, as in other tissues, Na^+ is actively transported out of the cell, and K^+ is actively transported in. K^+ diffuses back out of the cell down its concentration gradient, and Na^+ diffuses back in, but since the permeability of the membrane to K^+ is much greater than it is to Na^+ at rest, the passive K^+ efflux is much greater than the passive Na^+ influx. Since the membrane is permeable to most of the anions in the cell, K^+ efflux is not accompanied by an equal number of anions, and the membrane is maintained in a polarized state with the outside positive to the inside. The resting membrane potential is due to both active and passive processes, and is dependent on membrane permeability.

Action Potential: This potential has its origin in the movement of ions across the cell membrane. In nerve as in other tissues, a slight decrease in resting membrane potential leads to increased movement of K^+ out of and Cl^- into the cell, repolarizing and restoring the resting membrane potential. In the case of nerve and muscle, however, there is a unique change in the cell membrane when depolarization exceeds 70 mV. This change is a voltage-dependent increase in membrane permeability to Na^+ . Since the electrical and concentration gradients for Na^+ are both directed inward, the consequent Na^+ influx swamps the repolarizing processes and runaway depolarization results, producing the action potential.

Nerve Impulse: Axonal nerve tissue is a relatively poor passive conductor. Conduction is an active self-propagating process working through the mechanism of the action potential. Positive charges from the cell membrane ahead of and behind the action potential flow into the area of the negativity represented by the action potential ("current sink"). By drawing off positive charges, this flow decreases the polarity of the membrane ahead of the action

potential. This sequence of events moves regularly along an unmyelinated axon to its end. Thus, the self-propagating nature of the nerve impulse is due to circular current flow and successive depolarization of the firing level of the membrane ahead of the action potential. The nerve impulse varies in frequency, not amplitude, with the strength of the stimulus.

Semiconduction and Piezoelectricity

In the early years of the present century, the only known theoretical mechanisms of electrical conduction were metallic and ionic. Even then a class of minor substances were known to exist between the conductors and insulators called semiconductors. It was soon discovered that the crystalline lattice of the semiconductor permitted small numbers of electrons to move throughout the entire crystal with ease. In other words, electrical currents could flow through semiconductors.

In 1941, Szent-Gyorgyi postulated that the atomic structure of such biological molecules as proteins was sufficiently organized to function as a crystalline lattice (15). In the case of the fibrous proteins, he proposed that they could join together in extended systems with common energy levels permitting semiconduction current over long distances. An extension of this new thought was the idea by Yasuda in 1954 that bone might be piezoelectric. He was able to demonstrate the piezoelectricity in bone that year, and in the following year he stimulated bone growth in experimental animals by the application of electric currents (16). Piezoelectricity has been found in collagen fibres from many different tissues including tendon, dentin, aorta, trachea, and intestine. The concept of biological direct currents related to semiconduction was further researched by Marino and Becker (17,18).

Non-Ionic Basis of Biological Electrical Currents

Generator Impulse: Certain cells specialize in the reception of external stimuli. The hair cells in the ear respond to sound; thermal receptors in the skin respond to cold; and mechanoreceptors in muscles respond to mechanical stimuli. These cells convert the particular form of energy to which they are attuned into the electrical energy of the nerve impulse.

In all these receptors, mechanical energy produces a weak local current, the generator current. The generator current, unlike the nerve impulse which is all or none, increases in amplitude in direct relation with the increase in the energy of the stimulus, and regardless of its magnitude it is nonpropagating. The generator impulse produced by the nerve ending in the mechanoreceptor does not itself travel along the nerve fibre. It serves merely to trigger the nerve impulse which does propagate along the nerve circuit, often for considerable distances (19).

While the generator potential is often postulated to be produced by ionic movement through a semi-permeable membrane as in the action potential, this view is not supported by the same kind of data as for the action potential. There are, for example, several conditions that abolish the action potential and leave the generator potential undiminished (e.g., low concentration of tetrodotoxin and reduced sodium concentration in tissue fluids around the receptor). In addition, the electrical response is quite unusual. Not only is it graded and nonpropagating, but it is also biphasic, with a potential of one polarity and magnitude upon application of pressure, and a potential of equal magnitude but opposite polarity upon release of pressure. This is an action usually associated with a piezoelectric material (2).

Biological Direct Currents: Actual electrical currents separate from the nerve impulse outside of nerve cells were discovered by Gerard and Libet in frogs (20). In experiments using isolated but living frog brains, they found slowly oscillating potentials and "travelling waves" of potential change moving across the cortical layers of the brain at speeds approximately 6 cm/sec. If a cut was made on the cortical surface and the edges separated, the travelling wave could not cross the cut. However, if the edges were brought into physical contact, the waves crossed unimpeded. This ruled out the action potential and nerve impulse as the source of the potential, since disruption prevents a nerve from conducting an impulse even when approximated.

In a further series of studies on the intact brain, Libet and Gerard

described the existence of a steady direct-current (DC) potential present longitudinally from front to back in the brain, with the frontal lobes being normally negative by several millivolts to the occipital lobe (21).

Other investigators substantiated the existence of DC potentials (22,23, 24). Caspers in 1961 measured DC potentials in unanesthetized, unrestrained animals engaged in normal activity. He reported that increased activity, such as incoming sensory stimuli and motor activity, were associated with negative potentials, while decreased activity such as sleep was associated with positive DC shifts.

The glia, the "supporting" cells that constitute 90% of the total mass of the brain, were implicated with this DC electrical activity (25,26). Electron microscopy revealed close and involved associations between the glia and neurones as well as between the glia cells themselves (tight junctions, etc.) (27). The counterpart of the glia cell, the Schwann cell, was found to invest all peripheral cells outside the brain and spinal cord. They appeared to be syncytial in nature; that is, to be in continuous cytoplasmic contact along the entire length of each nerve. In 1964, Kuffler and Potter reported electrophysiological measurements on the glia cells of the leech (28). DC potentials in these cells spread through some low resistance coupling to other glia cells.

Neurohumoral Transmitters: Transmission of nerve impulses across cell synapses in mammals is predominantly chemically mediated. (Electrical transmission from one neurone to another across low resistance bridges, has been shown to occur in fish and birds.) Various substances have been suspected of being transmitters. Agents found in nerve endings in the CNS include: acetylcholine, norepinephrine, dopamine, serotonin, and prostaglandins. These mediators work by inhibiting or exciting cell membrane potentials and thereby regulating neuronal activity (14).

The recent demonstration of specific opiate binding sites in the brain and spinal cord, and the discovery of the endogenous transmitter substances,

enkephalins and endorphins, which have morphine-like activity (29), may support the view that there is a neural system in the brain to produce pain relief. Activation of this system may be brought about either pharmacologically, through direct receptor stimulation with morphine-like drugs, or electrically, by inducing release of the endogenous substance (30,31,32). This has been postulated because of the pain-reducing effect from either method of treatment (chemical or electrical) is reduced by the administration of the antagonist action of naloxone (33).

Neural Integration

Since the nature of the nerve impulse and its neurochemical propagation have been determined, it now becomes necessary to formulate theories explaining how these impulses interact to produce complex regulatory and behavioral patterns. Two mutually inclusive theories which help to elucidate this problem are the Gate Theory and the Electrical Modulation Theory. The Gate Theory gives an anatomical mechanism for the psychophysical phenomenon of pain through neuronal reflexes, and it has been the model for TENS. The Electrical Modulation Theory postulates that neuronal impulses may be regulated by a direct-current system only now being elucidated.

Gate Theory: It explained the mechanism of pain perception on an anatomical basis which could account for emotional and psychophysiological modifications of pain which previous theories could not do. In 1965, R. Melzack and P.D. Wall received the Nobel Prize for the Gate Theory (34).

In essence, the Gate Theory or Double-Gate Theory proposed that the non-pain-carrying, myelinated A-fibres block transmission of pain by the non-myelinated C-fibres. This is produced by synaptic inhibition in the substantia gelatinosa. A second "gate" is proposed to exist at a higher level in the brain stem and thalamus, which is inhibited by afferents through the sensory dorsolateral path which is faster than the pain carrying dorsal column-medial lemniscus.

Electrical Modulation Theory: That direct currents can influence the behavior of neurones themselves was shown by Terzuolo and Bullock (35), who

isolated neurones that spontaneously generated action potentials at a steady rhythmic rate. They demonstrated that very small currents and voltages could modulate the rate of firing without depolarization of the nerve cell membrane. They concluded that the great sensitivity of neurones to small voltage differences supports the view that electric field action can play a role in the determination of probability of firing units.

To some investigators, it seemed quite possible that Libet and Gerard had been right when, in the 1940's, they described electrical currents of nonionic nature flowing outside of the neurones of the brain. This appeared to be a mechanism of coding and data transmission that related to the problem of integrating the entire activity of the brain (36).

While these studies were going on in relation to the DC electrical activity of the brain and its integrative function, other investigators were working on the integration of the total organism, and were convinced that a similar DC electrical system was in operation. Lund at the University of Texas (37) and Burr at Yale (38) published many articles in the 1940's and 1950's reporting electrical measurements on the surface of a variety of intact living organisms which could be correlated with a number of physiological variables. Both investigators arrived at the concept of a "bioelectric" or "electrodynamic" field; a DC potential field that pervaded the entire organism, providing integration and direction for biological functions.

BIOLOGICAL EFFECTS OF ELECTROMAGNETIC FIELDS

That electromagnetic fields can have biological effects on humans is known, but not generally accepted as being significant. Neural, behavioral, chemical and histopathological evidence shows that these effects are real and indeed significant.

Histopathological Studies

Microscopic studies of brain tissue of animals exposed to electromagnetic fields have disclosed several kinds of histopathological effects. Kholodov (39) reported changes in brain tissue of rabbits and cats exposed to 200-300

gauss for up to 70 hours. In the sensorimotor cortex, he found hyperplasia, hypertrophy, atrophy, and dystrophic nerve lesions. Tokgskaya and colleagues have documented many studies of the histopathological effects of electromagnetic fields (40). In 1973 they described results of a time study of the effects of 3 GHz, 60-320 $\mu\text{W}/\text{cm}^2$ (1 hour per day for 22 weeks) on the morphology of the hypothalamus of the rat. After 2-3 weeks of exposure, there was an increase in neurosecretory material in cells in the anterior region and along fibres of the hypothamo-hypophysial tract. Six weeks following termination of exposure, the rats exhibited a normal histological appearance.

High-frequency electromagnetic fields seem to have a general stimulatory effect on the thyroid. At 70 MHz, 150 V/m, 3 months exposure resulted in an increase in the height of the follicular epithelium in rats (41). The adrenal-medulla cross-sectional area of rats exposed to 70 MHz, 150 V/m increased by 60% after 3 months exposure for 1 hour.

Endocrinological Studies

Fisher, et al. (42) found that 50 Hz, 530 V/m, resulted in a rise of norepinephrine in rat brain. Noval, et al. (43) found that the activity of choline acetyltransferase was significantly reduced in the brainstem portion of brains from rats exposed to 10-100 V/m, 45 Hz for 30-40 days. Three hour daily exposures at 90 gauss, 50 Hz, resulted in increased catecholamines in the adrenals after 6 months (44).

Increased levels of serum corticoids, pituitary ACTH, and ACTH-releasing factor were found in the hypothalamus by Novitskiy (45) in rats exposed to 10-1000 $\mu\text{W}/\text{cm}^2$ at 2.4 GHz. In a study involving the endocrine function of the pancreas, rats were exposed to 200 gauss, 50 Hz, continuously or intermittantly (6.5 hours per day for 7 days) (46). In both cases, an insulin insufficiency was produced.

In a study of skeletal-muscle metabolism, rats were exposed to 300-900 gauss, 7 kHz for up to 6 months (1.5 hours per day) (47). Creatine phosphate and ATP levels decreased, and ADP levels were increased following exposure. The changes were consistent with both an increased energy requirement, and an adverse effect on ATP formation.

Noval, et al. studied the effect on growth rate of rats of exposure to 0.5-100 V/m, 45 Hz, as compared to the growth rate of control rats maintained under Faraday-cage conditions. He found consistent depression of body weights of exposed animals, even for fields as low as 0.5 V/m. Low-frequency fields, electric and magnetic, also produced growth depression in 25-day-old chicks (43).

Hematological and Immunological Studies

Changes have been reported in the cellular composition of blood of rats, mice, dogs, guinea pigs, and rabbits following exposure to both high and low frequency. Graves exposed mice continuously to 25 and 50 kV/m for 6 weeks, and found that the white-blood-cell count was increased by 20%-60%. Intermittent exposure (30 minutes per day) to 100 kV/m, 50 Hz, for 8 weeks, produced elevated neutrophil levels and depressed lymphocyte levels (48).

The immune response has also been altered by electromagnetic fields. Szmigielski, et al. studied the action of an electromagnetic field on the granulopoietic reaction in rabbits that been exposed to an acute staphylococcal infection. Rabbits were exposed to $3000 \mu\text{W}/\text{cm}^2$, 3 GHz, 6 hours per day, for 6 or 12 weeks, and then were infected intravenously with S. aureus Wacherts. Four to six days after infection, the 6-weeks exposed animals displayed stronger granulocytosis than did the control animals. These changes were accomplished by a consistent reduction in the bone-marrow reserve pool, and a depressed lysozyme activity (49). Mice exposed intermittently to $500 \mu\text{W}/\text{cm}^2$, 2.95 GHz for 6 and 12 weeks showed a significantly different antibody-forming cell population compared to controls (50).

Neurological and Cardiological Studies

EEG changes have been found in the form of increased delta waves and desynchronization reactions (39) on rabbits exposed to 200-1000 gauss. In 1975, Frey reported an increase in the permeability of the blood-brain barrier of rats exposed to $2400 \mu\text{W}/\text{cm}^2$ (continuous) or $200 \mu\text{W}/\text{cm}^2$ pulsed at 1.2 GHz (51,52).

Changes in ECG have been recorded in animals exposed to electromagnetic fields. Mice exposed for 1000 hours to 100 kV/m, 50 Hz showed lengthening of the PR interval and QRS duration. Guinea pigs exposed to the same field exhibited sinus arrhythmias. Fischer, et al. exposed rats to 50 and 5300 V/m, 50 Hz and observed bradycardia (53).

Behavioral Studies

The ability to concentrate was altered in human subjects exposed to a 60 Hz, 1 gauss field (54), and reaction time to visual or auditory stimulus was altered in humans by low-frequency electromagnetic fields (55). Motor activity in rats was affected by various electromagnetic fields (56).

MODELS OF TISSUE INTERACTIONS WITH ELECTROMAGNETIC FIELDS

Theories for the physical interaction of electromagnetic fields with the molecular structure of cell membranes must be forthcoming to adequately explain the mechanism of Neuroelectric Therapy.

Basically, absorption of electromagnetic energy increases the kinetic energy of molecular constituents of the absorption medium. There is evidence that the molecular organization in biological systems needed to sense stimuli, whether thermal, chemical or electromagnetic, may reside in cooperative "interactions" of molecular assemblies or subsets of these assemblies (57). These assemblies can undergo sudden transitions to new and stable states. Several models have been developed which explain cellular sensitivity to electromagnetic energy.

Macromolecular Phase Transition Model

Grodsky (58) has hypothesized that excitable membranes are energetically equivalent to sheets of giant dipoles bathed in controlled external energy fields. His formulation envisages the outer layer of phospholipid polar heads as a two-dimensional crystal mosaic of multipolar charge sites (p-sites), sprinkled with islands of glycoproteins with cationic binding sites (c-sites). With the addition of an external low frequency electric field to the

system, Grodsky hypothesized that when the frequency of an allowed mode of oscillation reached zero, the system would become a macroscopic quantum amplification device and would exhibit long-range order phase changes that generated energy into the zero-frequency mode. The model has merit in seeking a basis in membrane ultrastructure, but necessarily rests on the severe constraint of a rigidly ordered, spatially symmetric lattice having certain minimal dimensions. A structural counterpart of such a highly ordered lattice remains to be detected in biological membranes (59).

Charge Population Transition Model

The biological membrane may also be considered as a chemically pumped, open, steady-state system with energy provided for the membrane system from a sequence of feedback loops linking the steady-state concentrations of oscillatory biochemical reactions (60). Frolich has hypothesized that extremely low frequency electric oscillations in the brain may be connected with such a system requiring relatively small activation energies, but protected from thermal fluctuations. He saw collective chemical oscillations in which globular proteins and the surrounding ions and structural water behave as an entity, and oscillate between a strongly electrically polar excited state and a weakly polar ground state. A slow chemical oscillation is thus connected with a corresponding electrical vibration (60).

Tunneling Model

The possibility of biological tunneling has been considered for excitatory processes and for the hemoglobin molecule in binding oxygen. It has been proposed that the "window" phenomena noted in several types of electromagnetic field interactions with tissues may arise in charge tunneling across an energy barrier (62).

Neuroelectric therapy uses weak electromagnetic fields in the range of the order of 10^{-7} V/cm, which corresponds to the strength of the extremely low frequency fields used in orientation, navigation and prey attack in marine vertebrates (63), in bird navigation, and in mammalian biorhythms (64).

Similar extremely low frequency (ELF) fields modify calcium binding in cat and chick cerebral tissue (65). By contrast, the gradient of membrane potentials in brain tissue is about 10^5 V/cm (66). The disparities emphasize the importance of understanding the concept of transductive coupling of weak extracellular fields.

In summary, the mechanism of tissue interactions with electromagnetic fields may be as follows: an electromagnetic field of the correct magnitude and frequency causes a "perturbation" or repositioning of the molecular plasma membrane of cells. This in turn may influence membrane enzyme systems by favorably altering stereoscopic configurations of molecules in much the same manner as a chemical catalyst holds molecules in the correct orientation for chemical reactions. The best known cell-membrane enzyme is adenylate cyclase which converts ATP (adenosine triphosphate) to cyclic-AMP (adenosine monophosphate) which then acts as a second messenger intra-cellularly. In other words, an electromagnetic field may act in the same way as a hormone upon the cell membrane.

CLINICAL USE OF NEUROELECTRIC THERAPY

Neuroelectric therapy has been used in several pilot studies at the Veterans Administration Medical Center in Cleveland (CVAMC). The device used to deliver the electrical stimulus was the Alpha Stim 2000 and Alpha Stim 350.

Pain

Head and Neck Cancer Pain: Severe pain associated with cancer of the head and neck in eight successive patients responded very well to electrical stimulation. All patients had recurrent tumor present in the orolaryngopharynx or neck, and were considered therapeutic failures (77). All had received either full-course radiation of 6000-7000 rads, surgery, or a combination of surgery and radiation. Pain had become the main immediate problem in these cases, and all were maintained on strong analgesic medication including codeine, meperidine hydrochloride, and morphine sulfate.

Electrical treatment consisted of stimulating directly over the painful area with 500 microamperes at 0.5 Hz for six to ten minutes. All patients

were asked to grade their pain before treatment on a scale of one to ten in severity. In all cases, the pain was reduced to no more than two. In most of the cases, the pain was completely alleviated. The effect lasted from a minimum of eight hours, to a maximum of three weeks. Those patients treated as in-patients could be kept off pain medication completely because they could be regularly stimulated. No side-effects such as respiratory depression occurred.

Low Back Pain: A 60 year old white male with unremitting low back pain was treated with electric stimulation after being referred from the pain clinic. He had failed all forms of therapy, including nine operations on the lower back (rhizotomy, cordotomy, and electrical implantation). He was not receiving satisfactory relief from codeine and other medication. He had already undergone a gastrectomy due to bleeding from excessive aspirin with codeine.

After stimulation for twenty minutes with 500 microamperes at 0.5 Hz over the involved areas, he had a reduction in pain on the scale from eight to a two. He immediately had increased mobility and flexibility. This initial effect lasted 16 hours and allowed a pain-free night. The second stimulation lasted 24 hours, and all subsequent stimulations lasted 36 hours.

A second patient was similarly referred from the pain clinic with mid-back and left rib-cage pain due to an injury. He was also a therapeutic failure. He responded to neuroelectric therapy, and is pain-free up to four weeks between stimulation.

Tennis Elbow Pain: A 31 year old white tennis professional suffered from right elbow pain for 3 years. Pain medication failed to ease the pain, and steroid injection in the elbow gave no relief. Stimulation with 500 microamperes at 0.5 Hz gave relief of pain immediately with the effect lasting ten hours, even while he continued to play tennis. A second treatment lasted three days while he did not play and gave the arm rest. The pain that recurred was much less than that with which he originally presented. Subsequent stimulations have reduced the pain to a very tolerable level of about

one or two even while playing. He has remained at this level without further stimulation for three weeks.

Sensorineural Hearing Loss and Tinnitus

A prospective study is presently underway at the CVAMC using NET for the treatment of sensorineural hearing loss and tinnitus. Since there is presently nothing that medicine or surgery offers in treating these disorders, any new therapy will be significant. Two patients have completed treatment.

Treatment consists of stimulating acupuncture points on the ear and its vicinity. At least twelve points per ear are used and stimulated for a period of 36 seconds to two minutes. Various frequencies from 0.5 Hz to 60 Hz are used at an intensity of 50 microamperes. Initial audiometry was performed including: pure tones, bone conduction, speech discrimination, and tinnitus matching.

The first patient had a mild bilateral sensorineural hearing loss with tinnitus. She noticed a marked decrease in tinnitus in both ears after the first treatment. She also claimed the fullness and uncomfortable feeling deep in her ears had disappeared, and her hearing felt much clearer. In other words, she had immediate subjective improvement in auditory function. Repeat audiometry demonstrated these changes objectively. She showed as much as a 15 db improvement in pure tone sensorineural level at 250 Hz. She improved from 5-10 db in several other frequencies. Her speech discrimination also improved from 82% to 96% and her tinnitus matching confirmed a decrease in pitch and intensity. Follow-up after treatment indicates stimulation should be repeated about once every two weeks to maintain these effects.

The second patient had a severe bilateral sensorineural hearing loss due to noise trauma in World War II. He also had bilateral tinnitus with decreased discrimination in both ears. He claimed the same subjective improvements as the first patient. He felt his hearing was clearer and that the tinnitus, at times, disappeared with each treatment. Objectively, it was possible to demonstrate a decrease in his tinnitus with audiometrics.

In both patients, the decrease in tinnitus lasted up to three days, but the comfortable aural feeling and the impression of clarity has been indefinite. There have been no side-effects.

Radiation Therapy Side-Effects

Patients receiving radiation therapy for carcinoma of the upper oroespiratory tract routinely suffer from varying degrees of mucosities. Their symptoms are burning, dry mouth and throat, and varying degrees of aching pain. Often these symptoms force interruption of treatment.

Three successive patients suffering from carcinoma of the nasopharynx, posterior tongue and larynx were treated with NET during the same period they were undergoing radiation therapy. In no case did the patients suffer the usual side-effects described, and there was no interruption of radiotherapy.

Since the NET uses energy well outside the range of the ionizing radiotherapy, there should be no expected interference in modalities, and to date there have been no side-effects from the NET.

Neurological Disease

Neurological disease offers one of the greatest areas for NET. It has been used to treat two patients with multiple sclerosis.

The first patient was a 38-year-old female physician who had multiple sclerosis for eight years. Her symptoms included a right hemiparesis, optic neuritis, and instability. She had undergone prednisone and ACTH therapy in the past which had induced a remission of her symptoms. When she presented, she was in an exacerbation of her symptoms, but was not anxious to undergo ACTH treatment again because of side effects, and opted to try neuroelectric therapy.

She was stimulated with 500 microamperes at 3.5 Hz on the scalp corresponding to the areas of neurological deficit. She was also stimulated on acupuncture points on the involved limbs. She noticed an immediate improvement in her optic neuritis, and her stability improved. Her overall strength improved and she was able to discontinue medication for depression because her

mood also improved. This was the same effect that ACTH treatment had on her. Presently, she requires treatment once a week at home for one hour to keep her at her present level of performance.

The second patient was a 60 year old white female who had multiple sclerosis of the brainstem variety since 1975. Her symptoms had been progressively downhill with no real evidence of remission. She had undergone prednisone therapy, ACTH, and plasma-phoresis with no lasting results.

Again predominantly cerebral stimulation was used as well as distant acupuncture points. She noticed an immediate improvement in stability, decrease in swelling in involved limbs, increased motor functions, and improvement in bladder function. To date, the effects have lasted two months, with stimulation necessary about twice a week.

The only side-effect noted was an increase in instability when treated across the skull from mastoid process to mastoid process. This was attempted in a search for easily-accessible electrode sites for home treatment. This eventually resolved with no subsequent side-effects.

CONCLUSION

NET is an extremely effective method of treatment for a wide variety of medical disorders. We have demonstrated a high rate of success in most cases of intractable pain which have failed all other modalities of treatment, including the newly-developed TENS. In addition, the effectiveness of this treatment in multiple sclerosis in two successive patients has been demonstrated. Other formerly untreatable diseases such as sensorineural hearing loss and tinnitus have also shown improvement with treatment.

The lack of side-effects makes this an especially encouraging area for clinical research. The wealth of physiological and biochemical research already in the literature lays a sound foundation for rational explanations of the biological effects of electromagnetic energy. Perhaps most important is the fact that a new conceptual model of the body is being formed. Essentially, a new system may be introduced which appears to have its own

physiology. It is hoped that this paper will provide background material for further research in this new field of Neuroelectric Medicine. Presently, clinical application needs much development. Methods of application such as electrode placement, dosage, frequency, and intensity must be explored and documented. Just as the Gate Theory of Melzak and Wall provided the foundation for the general acceptance of electrical stimulation (TENS) for pain; the theory of a biological "electromagnetic system" provides the logic for the electromagnetic treatment of a wide variety of formerly untreatable diseases.

REFERENCES

- (1) Kellaway, P.: The Part Played by Electric Fish in the Early History of Bioelectricity and Electrotherapy, *Bull. Hist. Med.* 20, 112, 1946.
- (2) Becker, R.A. and Marino, A.A.: *Electromagnetism and Life*, State University of New York Press, Albany, 1982.
- (3) Osler, W.: Practice of Medicine, Appleton & Co., New York, 3rd Edition, 1898.
- (4) Neuman, M.: Biopotential Electrodes, *Med. Instr. Application and Design*, 215-272, 1978.
- (5) James, A.E., Price, R.R., and Partain, C.L.: Nuclear Magnetic Resonance Imaging, *JAMA*, 248(8), 1982.
- (6) Cohen, D.: Magnetic Fields of the Human Body, *Physics Today* 28, 34, 1970.
- (7) Wikswo, J.P., Barach, J.P., and Freeman, J.A.: Magnetic Field of a Nerve Impulse: First Measurement, *Science* 208, 53, 1980.
- (8) Cohen, D.: Magnetoencephalography: Detection of the Brain's Electrical Activity with a Superconducting Magnetometer, *Science* 175, 664, 1972.
- (9) Shealy, C.N.: Transcutaneous Electrical Stimulation for Control of Pain, *Clin. Neurosurg.* 21, 269-277, 1974.
- (10) Ersek, R.A.: Transcutaneous Electrical Neurostimulation: A New Therapeutic Modality for Controlling Pain, *Clin. Ortho. Rel. Res.* 128, 314-324, 1977.
- (11) Hymes, A.C., Raab, D.E., Yonehiro, E.G., Nelson, G.D., Printy, A.L.: Acute Pain Control by Electrostimulation: A Preliminary Report, *Adv. Neurol.* 4, 761-767, 1974.
- (12) Newland, N.J.: Electro-Medical Therapeutics, Century Medical Distributors, Inc. 1977.
- (13) Charles, R.D., McDonald, D.M.: Electrical Neurological Stimulation Systems: A Review of Contemporary Methodology, *Surg. Neurol.* 4, 82, 1975.

- (14) Ganong, W.: Review of Medical Physiology, Lange Medical Publications, 1969.
- (15) Szent-Gyorgyi, A.: Towards a New Biochemistry?, *Science* 93, 609, 1941.
- (16) Yasuda, I.: On the Piezoelectric Activity of Bone, *J. Jap. Orthop. Surg. Soc.* 28, 267, 1954.
- (17) Marino, A.A. and Becker, R.O.: Piezoelectric Affect and Growth Control in Bone, *Nature* 228, 473, 1970.
- (18) Marino, A.A., Cullen, J.M., Reichmanis, M., Becker, R.O., and Hart, F.X.: Sensitivity to Change in Electrical Environment: A New Bioelectric Effect, *Am. J. Physiol.* 239R, 424, 1980.
- (19) Lowenstein, W.R.: Biological Transducers, Scientific American, August, 1960.
- (20) Libet, B. and Gerard, R.W.: Steady Potential Fields and Neurone Activity, *J. Neurophysiology* 4, 438, 1941.
- (21) Libet, B. and Gerard, R.W.: An Analysis of Some Correlates of Steady Potentials in Mammalian Cortex, *Electroenceph. Clin. Neurophysiol.* 14, 445, 1962.
- (22) Bishop, G.H.: The Relation of Bioelectric Potentials to Cell Functioning, *Ann Rev. Physiol* 3, 1, 1941.
- (23) Caspers, H.: The Cortical DC Potential and Its Relationship with the EEG, *Clin Neurophysiol.* 13, 651, 1961.
- (24) Becker, R.O.: Search for Evidence of Axial Current Flow in Peripheral Nerves of the Salamander, Science, 1962.
- (25) Galambos, R.: The Glia-Neuronal Interaction: Some Observations, *J. Psychiat. Res.* 8, 219, 1971.
- (26) Tasaki, L. and Chang, J.J.: Electrical Response of Glia Cells in Rat Brain, *Science* 128, 1209, 1958.
- (27) Walker, F.D. and Hild, W.J.: Neuroglia Electrically Coupled to Neurones, *Science* 170, 602, 1969.
- (28) Kuffler, S.E. and Potter, D.D.: Glia in the Leech, *J. Neurophysiol.* 27, 290, 1964.
- (29) Snyder, S.H., Pert, C.B., Pasternak, G.W.: The Opiate Receptor, *Ann. Int. Med.* 81, 534-540, 1974.
- (30) Hughes, J., Smith, T.W., Kosterlitz, H.W.: Identification of Two Related Pentapeptides from the Brain with Potent Opiate Agonist Activity, *Nature* 258, 577-579, 1975.
- (31) Goldstein, A.: Opioid Peptides in the Pituitary and Brain, *Science* 193, 1081-1086, 1976.
- (32) Sjolund, B.H. and Eriksson, M.B.E.: Electriacupuncture and Endogenous Morphines, *Lancet* 2, 1085, 1976.
- (33) Pmeranz, B. and Chiu, D.: Nalaxone Blockade of Acupuncture Analgesia: Endorphin Implicated, *Life Sci.* 19, 1757, 1976.

- (34) Melzak, R. and Wall, P.D.: Pain Mechanisms: A New Theory, Science 150(3699), 971,978, 1965.
- (35) Terzuolo, C.A. and Bullock, T.H.: The Measurement of Imposed Voltage Gradient to Modulate Neuronal Firing, Proc. Nat. Acad. Sci. (USA) 42, 687, 1956.
- (36) von Neuman, J.: The Computer and the Brain, Yale University Press, New Haven, 1958.
- (37) Lund, E.J.: Bioelectric Fields and Growth, University of Texas Press, Austin, 1947.
- (38) Burr, H.S.: The Meaning of Bioelectric Potentials, Yale J. Biol. Med. 16, 353, 1944.
- (39) Kholodov, Yu, A.: The Effect of Electromagnetic and Magnetic Fields on the Central Nervous System, N6731733, 1966.
- (40) Tolgskaya, M.S. and Gordon, Z.V.: Pathological Effects of Radio Waves, Consultants Bureau, New York, 1973.
- (41) Demokidova, N.K.: The Nature of Change in Some Metabolic Indices in Response to Nonthermal Intensity Radiowaves, JPRS, 70101, p.69, 1977.
- (42) Fischer, G., Udermann, H., and Knapp, E.: Ubt Das Netzfrequente Wechsefeld Zentrale Wirkungen Aus?, Zbl. Bakt. Hyg., I. Abt. Orig. B. 166, 381, 1978.
- (43) Noval, J.J., Sohler, A., Reisberg, R.B., Coyne, H., Straub, K.D., and McKinney, H.: Extremely Low Frequency Electric Field Induces Changes in Rate and of Growth and Brain and Liver Enzymes of Rats, Compilation of Navy-Sponsored ELF Biomedical and Ecological Research Reports, Vol. 3, AD AD 35959, 1976.
- (44) Chernysheva, O.N. and Kholodub, F.A.: Effect of a Variable Magnetic Field on Metabolic Processes in the Organs of Rats, JPRSL/5615, p. 33, 1975.
- (45) Novitskiy, A.A., Murashov, B.F.: Functional State of the Hypothalamus-Hyphisis-Adrenal Cortex System as a Criterion in Setting Standards for Superhigh Frequency Electromagnetic Radiation, Voenn. Zh. 10, 53, 1977.
- (46) Kolesova, N.I.: Pathogenesis of Insulin Deficiency on Exposure to Commercial-Frequency Alternating Magnetic Field, JPRS, 73777, p.8, 1978.
- (47) Kholodov, F.A., Yevtushenko, H.I.: The Effects of Low Frequency Electromagnetic Field Pulses on Skeletal Muscle Metabolism, JPRS, 62462, p.6, 1973.
- (48) Graves, H.B., Long, P.D.: Biological Effects of 60 Hz Alternating Current Fields: A Cheshire Cat Phenomenon?, in Biological Effects of Extremely Low Frequency Electromagnetic Fields, DOE-50, p.184, U.S. Dept. Energy, Washington, D.C., 1979.
- (49) Symigielski, S.: Acute Staphylococcal Infections in Rabbits Irradiated with 3 GHz Microwaves, Ann. N.Y. Acad. Sci. 247, 305, 1975.
- (50) Czernski, P.: Microwave Effects on the Blood-Forming System with Particular Reference to the Lymphocyte, Ann. N.Y. Acad. Sci. 247, 232, 1975.

- (51) Frey, A.H., Feld, S.R., and Frey, B.: Neural Functioning and Behavior: Defining the Relationship, *Ann. N.Y. Acad. Sci.* 247, 433, 1975.
- (52) Oskar, K.J. and Hawkins, T.D.: Microwave Alteration of the Blood-Brain Barrier System of Rats, *Brain Res.* 126, 281, 1977.
- (53) Prokhvatilo, Ye.V.: Reduction of Functional Capacities of the Heart Following Exposure to an Electromagnetic Field of Industrial Frequency, *JPRS*, 70101, p.76, 1977.
- (54) Gibson, R.S.: The Effects of Extremely Low Frequency Magnetic Fields on Human Performance, AD A005898, NAMRL-1195, Naval Aerospace Medical Research Library, 1974.
- (55) Konig, H.L.: Uber den Einfluss Besonders Niederfrequenter Electricischer Vorgange in der Atmosphere auf den Menschen, *Naturwissenschaften* 47, 486, 1970.
- (56) Korbel, E. and Thompson, W.D.: Behavioral Effects of Stimulation by VHF Radio Fields, *Psychol. Rept.* 17, 595, 1965.
- (57) Katchalsky, A., Scriven, L.E., and Bluementhal, R. (Editors): Dynamic Patterns of Brain Cell Assemblies, *Neurosci. Res. Program Bull.* 12, 1-195, 1974.
- (58) Grodsky, I.T.: Possible Physical Substrates for the Interaction of Electromagnetic Fields with Biological Membranes, *Ann. N.Y. Acad. Sci.* 247, 117-123, 1975.
- (59) Adey, W.R.: Tissue Interaction with Nonionizing Electromagnetic Fields, *Phys. Rev.* 61(2), 435-500, 1981.
- (60) Noyes, R.M. and Field, R.J.: Oscillatory Chemical Reactions, *Annu. Rev. Phys. Chem.* 25, 95-119, 1974.
- (61) Frohlich, H.: Long Range Coherence and the Action of Enzymes, *Nature (London)* 228, 1093, 1970.
- (62) Adey, W.R.: Experiment and Theory of Long-Range Interactions of Electromagnetic Fields at Brain Cell Surfaces, *Neurosci. Res. Program Bull.* 15, 1-141, 1977.
- (63) Bullock, T.H.: Electromagnetic Sensing in Fish, *Neurosci Res. Bull.* 15, 17-22, 1977.
- (64) Wever, R.: Human Circadian Rhythms Under the Influence of Weak Electric Fields and the Different Aspects of These Studies, *Int. J. Biometeorol.* 17, 227-232, 1973.
- (65) Bawin, S.M. and Adey, W.R.: Sensitivity of Calcium Binding in Cerebral Tissue to Weak Environment Electric Fields Oscillating at Low Frequency, *Proc. Nat. Acad. Sci. (USA)* 73, 1999-2003, 1976.
- (66) Elul, R.: Dipoles of Spontaneous Activity in the Cerebral Cortex, *Exp. Neurol.* 6, 285-299, 1965.
- (67) Bauer, W.: Electrical Treatment of Severe Head and Neck Cancer Pain, *Arch. of Otol.* 109, 382-383, 1983.